The assessment and treatment of cognitive function with the use of food supplements in a healthy elderly population.

A THESIS SUBMITTED TO THE UNIVERSITY OF SURREY FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

Rachael Anne Dawe

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Abstract

In recent years it has become apparent that the proportion of elderly people in the Western World is rising. There are a number of variables that can adversely affect cognitive function such as illness, drug treatment and nutritional status. Based on this idea, it was hypothesised that improved nutritional status would result in improved cognitive function. In order to assess this hypothesis, it was important tests to assess cognitive function.

The first method for assessing cognitive function was with the use of a subjective rating scale to assess activities of daily living (ADL). It was reported that elderly subjects were unaware of any problems with cognitive function. The second method for the assessment of cognitive function was with the use of objective tests. A test battery was identified and examined for the effects of age and sex on performance. It was reported that a number of the tests were age sensitive. Having identified a test methodology, the effects of improved nutritional status were investigated.

239 healthy community dwelling elderly volunteers received multivitamins daily for 36 weeks. It was reported that supplementation with multivitamins had no effect on performance of the tasks. In terms of deficiency 30% of the sample were at a high risk of deficiency of vitamin B6 and 10% at a high risk of deficiency of vitamin B2. Risk of deficiency had no effect on psychometric task performance, however it was reported that risk of deficiency affected mood, subjects with a moderate risk of deficiency reported higher anxiety rates than subjects with either a low or high risk of deficiency.

16 healthy community dwelling elderly volunteers received Ginkgo Biloba (100mg) daily for eight weeks. It was reported that supplementation with Ginkgo Biloba had no effect on performance of the tasks.

24 healthy community dwelling elderly volunteers received an acute dose of
glucose (50g) and placebo (saccharin 23.7 mg). Cognitive performance was assessed at baseline, 30 and 50 minutes post dose. It was reported that supplementation with glucose had no effect on performance of the tasks. It was questioned whether glucose tolerance was associated with differences in mood and task performance. It was reported that subjects with falling blood glucose levels showed improved performance on the Sternberg memory task and reported feeling more vigorous and less fatigued than subjects with rising blood glucose levels.

The results of these experiments would seem to indicate that the test methods selected for assessment of cognitive function may not be suitable for the assessment of cognitive enhancement in a healthy elderly population. Based on the findings, implications for future gerontological intervention research were discussed.
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Chapter One: An Ageing Society

1.1 Chapter Outline

This chapter discusses society's trend towards increased longevity and implications of this. The chapter discusses the variables that affect cognitive function and highlights the need for alternative treatments for elderly ailments, especially memory problems. One major factor that affects cognition is nutritional status. The chapter addresses the incidence of nutritional deficiency in the elderly population and outlines methods for the assessment and treatment of cognition.

1.2 Introduction

In recent years, it has become apparent that the proportion of elderly people in the Western World is rising, this rise is possibly due to improved sanitation, nutrition, better living conditions, advances in medicine etc. At the turn of the century, life expectancy was 49 years, today life expectancy is exceeding 70 years (current population reports). The rise in numbers of elderly persons is even greater in the oldest age group. Green and Davis (1993) report that persons aged over 85 years, represent the fastest growing proportion of society. It is predicted that subjects over 80 will rise from 2.1% to 5% of the total population from the years 1980 to 2030 (OCED, 1987). In 1980, 12% of the population were aged over 65 years, by 2030 it is estimated that this figure will rise to 22%, an estimated 55 million people (OCED, 1987). This represents a continuing trend towards an increasingly aged population.

The implications of increased longevity are that greater numbers of subjects are at risk of the diseases associated with ageing such as dementia, diabetes, Parkinson's and Alzheimer's disease etc. illnesses that will exacerbate cognitive decline in subjects who due to their age, will already be experiencing a certain degree of cognitive decline.
Increases in life expectancy will inevitably mean that the elderly person will be exposed to more and more drug treatments for specific ailments. The elderly as a group are the most frequent users of psychoactive drugs (Whittington, Petersen, Dale and Dressel, 1981) and are the group most sensitive to the unwanted side effects. Psychotropic drug use has been associated with unwanted side effects such as performance impairment which can be detrimental to the elderly population increasing the potential for accidents both in and around the home.

In a sector of the population already prone to age related deficits in cognitive performance, society needs to take measures that will limit drug usage in this population, hence the search for alternatives to drug treatment would be specifically useful for this age group.

There are a number of variables that affect the elderly making them more susceptible to decrements in cognitive function, these variable include, drug usage, concurrent illness and nutritional status.

It is quite difficult to limit the cognitive deficits associated with age associated illnesses and drug therapies, however it is possible to improve nutritional status which may in turn help to limit some of the cognitive decline.

The elderly, for a variety of reasons are vulnerable group in society, prone to vitamin and mineral deficiencies. Ageing is accompanied by a variety of changes, e.g. social, economic, and psychological that can compromise nutritional status. A number of physical changes associated with ageing also affect the elderly persons needs for certain nutrients. For example, ageing decreases the skin's capacity to produce vitamin D, age related decline of vitamin B$_2$, B$_6$, B$_{12}$ and folic acid are common occurrences in the elderly, mainly due to reduced enzyme activity, impaired absorption of vitamins in the
gastric system and disease states common in the elderly such as respiratory conditions, diabetes, hypertension and Parkinson's disease.

Numerous physiological factors place the elderly at risk of nutritional decline, such as a decline in the sense of smell (Chauhan, Hawrysh, Gee, Donald and Basu, 1987), and taste (Murphy, Cain and Hegsted, 1989), dental problems which can limit the type of food eaten, e.g. the elderly often avoid fresh fruit and vegetables due to poor, ill-fitting dentures (Me Gandy, Russell, Hartz, Jacob, Tannenbaum, Peters, Sahyoun and Otradovec, 1986). The natural ageing process also places the elderly at risk of vitamin and mineral deficiency, changes in the gastric system often mean that foods are malabsorbed due to a decrease in gastric acid secretion, or as a result of interactions with medications Suter, Golner, Goldin, Morrow and Russell, (1991) suggest that as many as 30% of persons over the age of 65 are affected. Neurological impairments can decrease mobility and affect the purchase and preparation of food (Roe, 1988; Smiklas-Wright, 1990).

A number of life changes affecting the elderly such as retirement from paid employment, the loss of a spouse, and social isolation all affect the nutritional state of the elderly. For example people are more reluctant to prepare food for one, and hence often eat snack type foods or ready prepared meals rather than prepare fresh meals daily. A reduction in daily food intake and the tendency of the elderly to repeatedly eat the same foods place the elderly at risk of vitamin and mineral deficiency. Economic factors affect the nutritional state of the elderly they often cannot afford to purchase foods rich in essential nutrients (Stitt, O'Connell and Grant, 1995), or they cannot afford to travel to shopping centres to purchase fresh foods. The sedentary life style of an elderly person decreases the need for energy and hence results in reduced food intake, thereby increasing the risk of nutritional deficiency.
One important question for researchers is, "how common are vitamin deficiencies in the elderly?" A number of studies have highlighted the fact that the elderly are a sector of society particularly vulnerable to sub-clinical vitamin and mineral deficiencies.

Researchers identify vitamin deficiency with the use of three popular methods, dietary diaries, structured interviews with nutritionists or dieticians and assessment of actual blood vitamin level.

The use of dietary diaries, is a common method adopted by research teams to examine the vitamin content of subjects diets. Subjects have to weigh and record all food consumed over a three or five day period. This method has been used by a number of researchers (Mc Clean, Weston, Beaven and Riley, 1976; Ortega, Andres, Redondo, Zamora, Lopez-Sobaler, and Encinas-Sotillos, 1995; Ahrari and Kimiagar, 1997). Yearick, Wang and Pisis, (1980), combined analysis of dietary diaries with comprehensive interviews with a nutritionist. Both methods have identified multivitamin deficiencies in elderly populations (See Table 1).

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>n</th>
<th>A</th>
<th>B₁</th>
<th>B₂</th>
<th>B₆</th>
<th>C</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>McClean et al. 1976</td>
<td>72-96</td>
<td>35</td>
<td></td>
<td>34%</td>
<td></td>
<td></td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>Yearick et al. 1980</td>
<td>63-96</td>
<td>100</td>
<td>22%</td>
<td>16%</td>
<td></td>
<td>10%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ortega 1995</td>
<td>65-89</td>
<td>60</td>
<td>46%</td>
<td>15%</td>
<td>21%</td>
<td>58%</td>
<td>11%</td>
<td>83%</td>
</tr>
<tr>
<td>Ahrari 1997</td>
<td>70-87</td>
<td>100</td>
<td>85%</td>
<td></td>
<td>94%</td>
<td>2%</td>
<td>49%</td>
<td></td>
</tr>
</tbody>
</table>

Another method to determine vitamin deficiency, possibly a more accurate method than dietary diaries, is to assess actual blood vitamin level. In this method, blood samples are taken and assayed to determine blood vitamin concentration. These levels can be compared with tables of vitamin deficiency cut off's, hence a more accurate picture of blood vitamin status can be determined. This method was adopted by Goodwin, Goodwin and Garry, (1982); Vannucchi, da Cunha, Bernardes, and Unamuno, (1994); Tolonen,
Halme and Sarna, (1988); Monguet, Galan, Preziosi, Keller, Bourgeois, Arnaud, Favier and Hercberg, (1996). A number of multivitamin deficiencies in elderly populations have been identified through this method.(see Table 2).

Table 2: Showing the vitamin deficiencies determined via assessment of blood vitamin level.

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>n</th>
<th>A</th>
<th>B₁</th>
<th>B₂</th>
<th>B₆</th>
<th>C</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwin et al. (1982)</td>
<td>60-94</td>
<td>260</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23%</td>
<td>1%</td>
</tr>
<tr>
<td>Vannucci et al. (1994)</td>
<td>102</td>
<td>13%</td>
<td>34%</td>
<td></td>
<td></td>
<td></td>
<td>56%</td>
<td>25%</td>
</tr>
<tr>
<td>Tolonen et al. (1988)</td>
<td>64-96</td>
<td>243</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>25%</td>
<td></td>
</tr>
<tr>
<td>Monguet et al. (1996)</td>
<td>66-103</td>
<td>756</td>
<td>14%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>65%</td>
</tr>
</tbody>
</table>

All three methods have been used to identify vitamin deficiency amongst elderly populations world-wide. These studies provide clear scientific evidence that vitamin deficiencies are common occurrences among elderly populations.

These tables reveal that vitamin deficiencies are quite common even amongst free living healthy elderly subjects. In some cases these deficiencies affect more than 50% of the population sampled.

If as the previous research would indicate, the elderly are susceptible to nutritional deficiencies and this in turn effects everyday cognitive functioning, then this leads gerontologists and cognitive psychologists alike to ask a number of questions. In particular, what happens to cognitive functioning as a result of age, can we directly measure or observe these changes either with the use of psychometric assessments, or self rating questionnaires, and more importantly can we intervene with dietary supplements to try and slow down the rate of cognitive decline?

Chapter two will discuss and consider why a deficiency in certain multivitamins results in performance decrements. The multivitamin review reports that poor diet can adversely affect cognitive functioning especially in healthy elderly
subjects. With this information in mind, the following two chapters examine how researchers can assess changes in cognitive function.

Chapter three assesses perceived cognitive function with the use of a self rated activity of daily living (ADL) questionnaire that aims to identify problems with aspects of cognition encountered in the day to day living of a healthy elderly sample.

Chapter four examines the role of objective cognitive tasks as assessment tools for measuring changes in actual cognitive functioning. The tasks assessed include the Syndrom Kurtz Task (SKT), the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT) and the HPRU Sternberg Memory Task (SMT).

Having identified a battery of subjective and objective tasks for the assessment of cognition in healthy subjects, there will follow three experimental chapters examining the efficacy of compounds thought to have cognitive enhancing properties, in the hope that they would slow down the rate of cognitive decline. The compounds/supplements examined include multivitamins, ginkgo biloba and glucose.

Chapter five details the results of an a parallel placebo controlled double-blind study in which 250 subjects were randomly allocated to received either a multivitamin or placebo preparation for 36 weeks. Assessments were made at baseline, week 12, 24, and 36 weeks using the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT), HPRU Sternberg memory task (SMT), the Syndrom Kurtz Task (SKT), Ravens Standard Progressive Matrices (RSPM), Cognitive Failures Questionnaire (CFQ), the Hospital Anxiety and Depression Scale (HADS).

Chapter six details the results of a crossover placebo controlled double-blind study in which 16 subjects were randomly allocated to received both ginkgo
biloba (100 mg daily) and placebo for 8 weeks, with a 4 week washout period between treatments. Cognitive assessments were made at baseline, week 2, 4, 6, 7 and 8 using the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT), HPRU Sternberg Memory Task (SMT), the Syndrom Kurtz task (SKT), Milford Memory Task (MMT), and the Cognitive Failures Questionnaire (CFQ).

Chapter seven details the results of an a crossover placebo controlled double-blind study in which 24 subjects were randomly allocated to receive acute doses of glucose (50g) and placebo saccharin (23.7 mg). Cognitive assessments were made at baseline, and 30 minutes post dose using the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT), HPRU Sternberg Memory Task (SMT), the Syndrom Kurtz task (SKT), a word list task (WLT) and the profile of mood states (POMS).

Chapter eight is the discussion chapter that will attempt to pull together all the findings reported in this thesis, and more importantly will discuss the implications of this research for future gerontological intervention research.
2 Chapter Two: Vitamins and their Dietary Importance

2.1 Chapter Outline

Micronutrients

*Vitamin A* (retinol)
*Vitamin B₁* (thiamine)
*Vitamin B₂* (riboflavin)
*Vitamin B₃* (niacin)
*Vitamin B₅* (pantotenic acid)
*Vitamin B₆* (pyridoxine)
*Vitamin B₁₂* (cyanocobalamin)
*Vitamin C* (ascorbic acid)
*Vitamin E* (alpha tocopherol)
*Vitamin K*
*Folic Acid*

Minerals

*Iron* (Fe)
*Calcium* (Ca)
*Chlorine* (Cl)
*Magnesium* (Mg)
*Manganese* (Mn)
*Molybdenum* (Mo)
*Selenium* (Se)
*Bioflavinoids* (vitamin P)
*Zinc* (Zn)

The Role of Multivitamins in the Central Nervous System

*Neurotransmitter Synthesis*
*Antioxidant Protection*
The Release of Energy From Foods

The Effects of Vitamin Supplementation on Aspects of Cognition, Mood and Behaviour.

This chapter discusses the importance of nutritional status and its role in determining cognitive function. This is especially important for elderly subjects, who due to their age, may already be suffering from cognitive decrements that may be exaggerated by poor nutritional status.

2.2 Vitamins and their dietary importance

The importance of micronutrients in the diet was not realised until the early part of the 20th Century. Before this time, it was believed that the only components of a diet essential for adequate health and functioning were proteins, fats and carbohydrates. However, it soon became evident that a certain amount of trace elements were required for adequate health. These essential elements were termed vitamins from the Latin ‘vital’ ‘amines’ as it was incorrectly thought all were amines.

The importance of vitamins in the diet was a discovery made early this century. Hopkins (1912) demonstrated scientifically that animals required a diet of more than just fat, protein and carbohydrates for normal growth. Hopkins postulated that animals needed one or more “accessory factors” present in certain natural foods that were necessary for nutrition of animals.

In the same year Casimir Funk obtained a concentrate of an amine from rice husks and polishings that alleviated the symptoms of the disease beri beri. Funk coined the name vitamine, denoting an amine essential for life - however many of the substances classed as vitamins are not amines. It soon became clear that
there must be several vitamins vital for the normal growth and functioning of animals.

Vitamins are classified into two large groups these being water soluble and fat soluble. Water soluble vitamins include vitamin B\textsubscript{1} (thiamine), B\textsubscript{2} (riboflavin), B\textsubscript{3} (niacin), B\textsubscript{5} (pantotenic acid), B\textsubscript{6} (pyridoxine), vitamin B\textsubscript{12} (cobalamin), folic acid, biotin and vitamin C (ascorbic acid). The fat soluble vitamins include vitamins A (retinol), D, E (alpha tocopherol) and vitamin K. Most of the water soluble vitamins function as necessary building block components of a number of different co-enzymes important in central metabolic pathways. As well as vitamins there are also trace elements and minerals that play important roles in the body. These include iron, calcium, chlorine, magnesium, manganese, molybdenum, selenium, bioflavinoids and zinc.

Vitamins are defined as organic compounds present in foods in extremely small concentrations. Vitamins are essential for normal health and growth and when absent from the diet or not properly absorbed cause a specific disease deficiency. Vitamins cannot be synthesised by the person and hence have to be obtained exclusively from the diet. Each of the vitamins outlined above will be considered in greater detail in the following section.

2.3 Vitamins

2.3.1 Vitamin A (retinol)

Vitamin A is one of the fat soluble vitamins from a group of compounds including retinol, retinal, carotene and caroteniods. Retinol is the form of vitamin A found in animal products and the carotenes are found in fruit and vegetables. Retinol is the main active form of vitamin A, the chemical structure of which was determined by Paul Karrer in 1931. The carotenoids are precursors to vitamin A and when ingested they get converted in the liver to vitamin A. The active form of vitamin A is the aldehyde retinal which is vital for the proper
formation of rhodopsin - the light sensitive pigment in vertebrate rod cells in the eyes. Deficiency of vitamin A leads to a whole number of complications such as night blindness, defective development of the teeth, stunted growth, various skin eruptions, problems of the mucous membranes and reduced defence against infections. Vitamin A is often thought of as the anti infection vitamin as it plays an important role in maintaining the immune system. Vitamin A is stored in the liver and it has a half life of 200-300 days therefore, the vital balance is only disturbed if the intake of vitamin A is too low over a period of months.

2.3.2 Vitamin B₁ (thiamine)

Vitamin B₁ is one of the B complex water soluble vitamins. Vitamin B₁ cannot be stored in the body in large quantities as there is only a small reserve in the liver, heart and brain, any excess is therefore excreted in the urine. The chemical structure of vitamin B₁ was discovered in 1936 by Robert Williams. Deficiency of vitamin B₁ has been associated with a whole range of symptoms including anxiety, irritability, depression, loss of weight and appetite, sleep disturbances, inactivity, malaise, forgetfulness and poor co-ordination (Brin, 1962; Williams et al., 1942). Long term deficiency leads to a condition known as beri beri, a deficiency state where the patient suffers nerve inflammation, muscular weakness and eventually heart failure. It is thought that about half the population of western industrialised countries suffer from minor long term vitamin B₁ deficiency. Marginal deficiency in thiamine is quite a common occurrence in elderly populations, and is quite difficult to recognise clinically because the effects of deficiency are non specific. Vitamin B₁ is required for glycolysis in the conversion of Pyruvate to acetyl coenzyme (CoA) which then enters the citric acid cycle, where the acetate is further oxidised to carbon dioxide and water in reaction involving pantotenic acid, thiamine, riboflavin and nicotinamide. One of the first responses to a thiamine deficient diet is an inability to concentrate, confusion of thought, uncertainty of memory, anorexia, irritability and depression (Williams et al., 1942). When thiamine is
reintroduced into the diet, dramatic changes occur, appetite is restored and personality changes for the better (Brozek and Guetzkow, 1957).

### 2.3.3 Vitamin B$_2$ (riboflavin)

Vitamin B$_2$ is known as riboflavin, it is another water soluble B complex vitamin. Vitamin B$_2$ was first detected in 1879 by Blyth and it's chemical structure was isolated in 1935 by Paul Karrer and Richard Kuhn. Riboflavin is largely stored in red blood cells and reserves in the human body seem to be fairly stable, with any excess being eliminated in the urine. Vitamin B$_2$ deficiency can result in inflammation of the tongue and lips, scaly scalp, eczema, hair loss, dizziness, insomnia, hacks to the corner of the mouth and over sensitivity to light. It is estimated that vitamin B$_2$ deficiency is one of the commonest deficiencies, affecting some 20% of the population. Riboflavin has an important role in the energy release from carbohydrates and is also involved in the production of the brain neurotransmitters serotonin, noradrenaline and acetylcholine.

### 2.3.4 Vitamin B$_3$ (niacin)

Niacin is a water soluble vitamin that can be produced in the body from the essential amino acid tryptophan. It is found in two different forms, nicotinic acid and nicotinamide. The vitamin has a number of beneficial actions in the body, including the breakdown of glucose. In the Krebs cycle it is used biosynthetically to derive the co-enzyme nicotinamide adenine dinucleotide (NAD) which is essential to a number of oxidation reduction reactions that occur in the breakdown of glucose and fatty acids. Niacin is also used for the maintenance of the nervous system, normal functioning of the gastrointestinal tract, maintenance of healthy skin and the synthesis of sex hormones. Niacin expands arteries and hence aids efficient blood circulation and removal of low density lipoprotein cholesterol from the blood. Niacin is used for a number of complaints including the treatment of dizziness, burns, sleeping disorders, schizophrenia and migraine. Deficiency of niacin results in a disease state
known as pellagra which results in diarrhoea, dermatitis, confusion, delirium and dementia. Mild deficiency produces symptoms such as muscle weakness, fatigue, loss of appetite, nausea, skin eruptions, headache, depression and insomnia.

2.3.5 Vitamin B<sub>5</sub> (pantotenic acid)
Vitamin B<sub>5</sub> is a water soluble vitamin required for the efficient functioning of the body. The structure was first isolated by J. R. Williams in 1940. Vitamin B<sub>5</sub> is essential for the metabolism of sugars, fats and proteins, as it forms part of co-enzyme A, which plays an important role in the transfer of acetyl groups from various compounds in the Krebs cycle. Vitamin B<sub>5</sub> is important in the formation and growth of new hair and skin and in the production of essential fatty acids. It is critical for the production of antibodies. Deficiency of vitamin B<sub>5</sub> is extremely rare and is normally only observed in experimental conditions where subjects receive diets free of vitamin B<sub>5</sub>, under such conditions, symptoms include asthma, muscle cramps, insomnia, fatigue, reduced antibody production and increased susceptibility to allergy and infection.

2.3.6 Vitamin B<sub>6</sub> (pyridoxine)
Vitamin B<sub>6</sub> is another water soluble vitamin part of the B complex vitamins. The structure of vitamin B<sub>6</sub> was deduced by Richard Kuhn in 1939. The vitamin is essential for maintaining healthy skin and nerves and in the formation of red blood cells providing general resistance to disease and to stop premature ageing. The major function of vitamin B<sub>6</sub> includes enzyme reactions, the formation of brain hormones, the formation of haemoglobin and the maintenance of homeostatic balance of sodium and potassium in the body. Vitamin B<sub>6</sub> improves the activity of both B and T lymphocytes in our immune system and this in turn helps in the prevention of diseases such as cancer, asthma, arthritis, coronary heart disease, various allergies and circulatory disorders. Pyridoxine is essential for the formation of the haem rup in haemoglobin, it also has a hormonal function acting to stop the aggregation of blood platelets in blood vessels which
commonly cause blood clots. Deficiency of vitamin B\textsubscript{6} can result in loss of appetite, anaemia, emaciation, depression, fatigue, general apathy, nervousness, insomnia and poor memory. Vitamin B\textsubscript{6} is involved in a number of crucial steps in the synthesis of several neurotransmitters, in the decarboxylation of glutamic acid into gamma amino butyric acid (GABA). GABA is an inhibitory transmitter substance that helps to control the neuronal firing in the brain, hence controls seizures.

### 2.3.7 Vitamin B\textsubscript{12} (cyanocobalamin)

Vitamin B\textsubscript{12} is another one of the water soluble B complex vitamins. The vitamin was first isolated in 1948. Deficiency of vitamin B\textsubscript{12} affects nearly all tissues in the body. Symptoms of vitamin B\textsubscript{12} deficiency include fatigue, irritability, loss of appetite, diarrhoea, stomach complaints, problems with the circulation and heart, and yellowing of the skin. Long term deficiency leads to a condition known as pernicious anaemia which is associated with a number of mental problems including loss of concentration, depression, paranoia and irritation. Long term deficiency can lead to brain damage and degeneration in the nervous system such as loss of sensation and poor co-ordination. Vitamin B\textsubscript{12} deficiency leads to a whole range of symptoms such as depression, agitation, irritability, negativism, bipolar disorder, confusion, memory loss, disorientation, concentration and apathy. (Dommisse, 1991). Deficiency in vitamin B\textsubscript{12} is more common than generally thought, Dommisse (1991) reports that the deficiency may be responsible for a number of psychiatric disorders. The human body needs the B complex vitamins to be able to utilise the energy in the diet. The B complex vitamins are particularly useful for the brain and the nervous system, there is a possibility that the lack of B vitamins may also contribute to confusion in older people.

### 2.3.8 Vitamin C (ascorbic acid)

Vitamin C is a water soluble vitamin, which was first isolated in 1932 by Charles Glen King. Deficiency of vitamin C can lead to the disease state scurvy,
a condition where the gums get inflamed and bleed leading to loss of teeth. Over time the deficiency results in anaemia, mouth ulceration and induration of leg muscles. Vitamin C is essential for the formation of collagen and connective tissues it is also important for maintaining the strength of capillary walls and aiding the absorption of iron. Vitamin C is important as it improves the bodies ability to fight infection and helps fight diseases such as cancer, high blood pressure and arteriosclerosis, by improving the function of phagocytes and activating white blood cells and antibodies. Vitamin C has an important function in the brain as it protects against the effects of ischaemia or oxygen deficiency, mainly due to its antioxidant properties.

2.3.9 Vitamin E (alpha tocopherol)
Vitamin E is a fat soluble vitamin first discovered in 1923. Vitamin E is essential for muscle development and is important for the production of red blood cells. The most important action of vitamin E is as a lipid-soluble antioxidant protecting cell membranes from free radical damage. The vitamin also acts as an anticoagulant preventing the formation of blood clots and cataract formation. Vitamin E is useful in the treatment of cancer, coronary heart disease and has also been found to be useful in the treatment of Parkinson's disease. Alpha tocopherol interacts with cell membranes, traps free radicals and interrupts the chain reaction that damages cells. In animal models, alpha tocopherol reduced the degeneration of hippocampal cells after cerebral ischemia (Hara, Kato and Kogure, 1990). In hypoxic cultured neurons alpha tocopherol reduced cell death associated with beta amyloid protein.

2.3.10 Vitamin K
Vitamin K is a fat soluble vitamin that exists in three forms K₁ (a yellow substance produced naturally by plants), K₂ (a pale yellow substance synthesised by micro-organisms that live in the gastrointestinal tract in humans) and K₃ (of synthetic origin). Vitamin K is a member of the quinone group essential for human health. The vitamin was first discovered by Henrik Dam in
1935. It is very important in the synthesis of coagulation factors such as prothrombin. As well as being used in the blood clotting process, vitamin K is involved in two components of energy metabolism, the electron transport chain and oxidative phosphorylation.

2.3.11 Biotin
Biotin also known as vitamin H, is another of the water soluble B complex vitamins. Biotin was first identified by Albert Szent-Györgyi, Vincent Du Vigneaud and co-workers in 1940. Biotin is an active compound that participates in many enzymatic reactions. One of its main uses is in the production of energy from dietary glucose and the production of energy from non glucose source. It is a co-enzyme in the synthesis of fatty acids and purine in the body. Biotin is also used in the production of antibodies and increases the effectiveness of the immune system. Deficiency of biotin leads to loss of appetite, infections of the mucous membranes, depression, insomnia, muscle pain, rashes, discomfort and increased level of cholesterol in the blood.

2.3.12 Folic Acid
A deficiency of folic acid is thought to be associated with a whole range of problems including neurological problems (Reynolds, Rothfield and Pincus, 1973) and psychiatric disorders (Carney, Williams and Sheffield, 1979; Abou-Seleh and Coppen, 1986). Abou-Seleh and Coppen (1986) believe that folic acid deficiency might be responsible for some of the depressions noted in society. When the deficiency is advanced it can lead to megaloblastic anaemia. Deficiency of folic acid may also result in reversible dementia (Lishman, 1978). Botez, Botez and Maag (1984) described a group of patients with low serum folic acid levels whose intelligence scores increased by over 9 points following supplementation with folic acid. The role of folic acid in the biochemistry of cognitive function is unknown, but it is believed that folic acid is important for the synthesis of neurotransmitters serotonin, noradrenalin and dopamine all of these neurotransmitters are thought to be important modulators of attentional
and higher order memory functions (Wolkowitz, Tinklenberg and Weingartner, 1985).

2.4 Minerals

2.4.1 Iron (Fe)
Iron occurs in three forms, haem iron (derived from meat), non heam iron (derived from vegetables) and non haem iron that is added to food stuffs. Iron is needed by the body for the production of red blood cells and the transport of oxygen around the body. Iron is also used in the formation of many enzymes required for energy production in the cell, it is essential for the metabolism of B vitamins and the functioning of T-lymphocytes. Iron deficiency results in anaemia, the symptoms of which include fatigue, pale skin, breathlessness, loss of strength, feeling weak, susceptibility to illness and infection due to a weakening of the white cell defence system.

2.4.2 Calcium (Ca)
Calcium allows the uptake of vitamin $B_{12}$ from the intestines. In babies and small children, calcium is required for healthy teeth and bone growth. Calcium is required for the transmission of nerve impulses, maintaining the fluid balance and muscle contraction, coagulation of the blood and cardiac activity. Deficiencies of calcium are rare but can occur, when it does it results in the deficiency state rickets.

2.4.3 Chlorine (Cl)
Chlorine is essential for the formation of digestive stomach acids. It is also required for the correct functioning of the carbon dioxide transport system in the blood. Chlorine regulates the acid-base balance, the fluid balance and the osmotic pressure in the blood.
2.4.4 Magnesium (Mg)
Magnesium is found in the intracellular fluids of the body. It is required for the production and activation of many enzymes that regulate the metabolism of proteins, carbohydrates, lipids, nucleic acids and nucleotides. Magnesium is also required for the proper functioning of neurochemical transmission, is vital for normal muscle function, cell division, healthy bones and teeth, proper nerve function, plays a role in cell and antibody mediated immune response and prevents increases in blood pressure. Magnesium deficiency leads to muscle weakness, fatigue and in extreme cases cardiac arrhythmia. Symptoms of deficiency include anxiety, loss of appetite, hormonal disorders, insomnia, hypoglycaemia, muscle weakness, muscle cramps and pre-menstrual tension.

2.4.5 Manganese (Mn)
Manganese possess antioxidant properties, it is used for the formation of strong, healthy bones, healthy nerves and muscles and for the control of growth. Manganese is also important for the metabolism of carbohydrates and fats. Deficiency of manganese results in reduced hair growth, rashes and emaciation.

2.4.6 Molybdenum (Mo)
Molybdenum is a metallic element whose role in the human body is unknown. It is thought to be essential for the formation of at least 3 enzymes that act to neutralise toxic sulphur compounds. Molybdenum is also thought to be important for the production of haemoglobin and helps prevent dental caries.

2.4.7 Selenium (Se)
Selenium was first discovered in 1817 by Jöns J. Berzelius. Selenium has a number of different tasks in the human body. It acts as an antioxidant preventing peroxidation of lipids in the cell, it boosts the immune system by improving the operation of the T-lymphocytes and macrophages. Selenium also
helps to inhibit the toxic effects of heavy metals such as mercury, cadmium, lead and arsenic.

2.4.8 Bioflavinoids (vitamin P)
This is the name given to a group of naturally occurring pigments produced by plants. They are used by the body to strengthen the walls of blood capillaries to prevent bleeding into tissues. They are essential for the absorption of vitamin C, and are used to help healing of muscles, sprained joints and chafed skin.

2.4.9 Zinc (Zn)
Zinc is a metallic element that is very important for good health. Zinc forms part of the active site of around 200 enzymes used to form bone tissue, heal wounds and sores, produce protein and regulate carbohydrate metabolism, and required for the synthesis of ribosomes and ribonucleic acids. Zinc helps boost the immune system. Zinc also forms part of the enzyme that allows the release of insulin from the pancreas. Zinc deficiency results in the body being unable to utilise vitamin A, which causes problems with the skin, can reduce healing of wounds. Zinc deficiency can also result in decreased alertness, poor appetite, susceptibility to infection and injury, hormonal disturbances and fatigue.

2.5 The role of multivitamins in the Central Nervous System (CNS)
Numerous lines of research have shown that vitamins and their derivatives play important roles in the nervous system.

2.5.1 Neurotransmitter synthesis
Many trace elements such as vitamins B₁, B₂, B₆, B₁₂ and folate are involved in the metabolic pathways that lead to the synthesis of neurotransmitters such as dopamine, acetylcholine, noradrenaline, serotonin and GABA.
Ascorbic acid is necessary for the synthesis of noradrenaline, dopamine and acetylcholine.

Vitamin B₆ is a cofactor in the irreversible synthesis of several essential neurotransmitters including adrenaline, noradrenalin, serotonin and γ-aminobutyrate.

Folic acid and vitamin B₁₂ are important coenzymes for the breakdown of catecholamines.

2.5.2 Antioxidant protection
The beneficial effects on cognition may also be due to the fact that many micronutrients possess antioxidant functions. For instance, vitamins C, E and beta carotene help to protect the cerebral lipids and neurotransmitters from oxidation (Di Mascio, Murphy and Sies, 1991; Halliwell and Gutteridge, 1989; Stocker and Frei, 1991) whilst antioxidants also help to protect brain function by inhibiting arthrosclerosis (Gey, 1994).

2.5.3 The release of energy from foods
Vitamin B₁ is an active component necessary for the enzyme responsible for the metabolism of carbohydrates. Vitamin B₂ is a component of coenzymes necessary for oxidation-reduction of fatty acids pyruvate and amino acids, and are also needed in the process of electron transport. Vitamin B₁₂ is essential in the nutrition of higher animals and coenzyme B₁₂ is essential for the transfer of hydrogen atoms between adjacent carbon atoms. Biotin is the prosthetic group of certain carboxylases responsible for the carrying of carbon dioxide. Folic acid is a precursor for a coenzyme responsible for the enzymatic transfer of certain one carbon compounds.
Vitamins are also required for the metabolism of neurotransmitters e.g. vitamin \( B_1 \) is essential for the breakdown of glucose, nicotinamide and vitamin \( B_2 \) play important roles in energy production.

2.6 The effects of vitamin supplementation on aspects of cognition, mood and behaviour

Changes in cognitive function can have detrimental effects on everyday functioning, these changes can be a result of a whole range variables such as illness, drug treatments and nutritional status. Declines in cognitive function are especially a problem for older subjects, who simply because of their age are already exposed to disruptions in cognitive function.

A number of studies were conducted in the 1940's whereby the micronutrient content of diets were restricted by omitting certain important nutrients which resulted in dramatic changes both behaviourally and psychologically.

Berryman, Henderson, Wheeler, Cogswell, Spinella, Grundy, Johnson, Wood, and Denko (1947) reported that consuming diets deficient in certain B vitamins (vitamin \( B_1, B_2, B_6, \) nicotinic acid, folic acid, pantotenic acid and biotin) was associated with changes in personality (higher self reporting of hysteria, depression and hypochondriasis) and poor motor performance. When the subjects were supplemented moderate improvements in psychometric test scores were noted.

Williams, Mason, Smith and Wilder (1942) reported that consuming diets deficient in vitamin \( B_1 \) resulted in an inability to concentrate, confusion of thought, uncertainty of memory, anorexia, irritability and depression.

Farmer (1944) reported that a diet low in vitamin C is associated with poor reaction times, severe fatigue and changes in personality (Kinsman and Hood,
1971). Low levels of dietary vitamin B₂, folic acid and vitamin C have been linked to feelings of tiredness, fatigue, confusion and depression (Bell, Edman, Morrow, Marby, Mirages, Perrone, Kayne and Cole, 1991; Brozek and Guetzkow, 1957; Sterner and Price, 1973; Kinsman and Hood, 1971). Low levels of niacin, vitamin B₁, vitamin B₁₂ and folic acid have been associated with psychiatric syndromes including depression and dementia (Strachan and Henderson, 1967; Hunter, Jones, Jones, Matthews, 1967; Abou-Saleh and Coppen, 1986; Sommer and Wolkowitz, 1988; Deijen, van der Beek, Orlebeke and van der Berg, 1992). Low levels of vitamin B₆ have been associated with sleep disturbances, insomnia and irritability (Brin and Bauernfeind, 1978), premenstrual tension (Abraham and Hargrove, 1980). Low levels of vitamin B₁, vitamin C and folate are associated with poor mood (Heseker, Kubler, Westenhofer and Pudel, 1991). One of the most important things to note is that many of the above symptoms are evident long before clinical symptoms of deficiency are observed.

Vitamin B₁₂ deficiency presents a wide variety of symptoms including, paraesthesia, ataxia, mood disturbance, delusions and paranoia. Vitamin B₆ deficiency is reported to produce peripheral neuropathy and convulsions in humans.

Folate deficiency has been associated with irritability, forgetfulness and paranoia. A high incidence of folate deficiency has been observed in patients with psychiatric disorders including depression, dementia, schizophrenia and epilepsy.

It is important to note that many of these studies were conducted during the war, and as well as vitamin deficiency, these subjects were suffering from a whole range of social and emotional problems that may have contributed to such changes. Despite this minor criticism, these studies highlight the fact that diet,
more importantly an inadequate diet can have a profound effect on aspects of
cognitive and psychomotor performance.

Since vitamins play such a vital role in the nervous system, vitamin deficiency
is likely to affect human cognition and behaviour. We should not assume that
sub-clinical malnutrition is not present simply because of the absence of
physical signs and symptoms. Nutritionists have calculated a person's everyday
requirements for multivitamin nutrition, these requirements are termed
Recommended Daily Allowances (RDA's), however current definitions of
adequate nutrition (RDA's) are based on physical conditions rather than mental
function. Hence what is adequate to prevent physical signs and symptoms may
not be adequate to prevent impaired mental function.

Nutritionists maintain that micronutrient deficiencies rarely occur in Western
industrialised societies, they have been virtually eradicated due to better
standards of living and improved nutritional awareness.

Despite the fact that nutrition and health care have improved over the years, the
previous chapter reports that subclinical or 'marginal' nutritional deficiencies
do exist, however, the extent and impact of these subclinical deficiency states
are largely unknown. Evidence does seem to indicate that there are vulnerable
sectors in the population particularly young children, teenagers and the elderly.

If nutritional deficiency results in a disturbance of cognitive function, then
research teams must endeavour to adopt appropriate assessment methods
designed to detect declines in cognitive performance. Without such methods,
then it would not be possible to assess what aspects of cognitive function are
affected when a nutritional deficiency exists, and more importantly, it would not
be possible to detect improvements in performance as a result of improved
nutritional status.
There are two methods available for the assessment of cognitive function. Firstly, assessment with the use of subjective rating questionnaires and secondly assessment of actual cognitive function with the use of valid and reliable test measures. Two chapters will be dedicated to the assessment of cognitive function in healthy elderly volunteers. Chapter three will consider the role of an activity of daily living scale (ADL) for the subjective assessment of human cognitive function. Chapter four will examine cognitive function with the use of objective test measures.
3 Chapter Three: What problems do the elderly face in regard to the performance of everyday activities as assessed using An Activity of Daily Living Scale (ADL)?

3.1 Chapter Outline

The use of rating scales for the assessment of cognition and everyday activities in the elderly.

Analysis of self reported activity of daily living in the elderly

Identifying groupings within the ADL questionnaire – Principal Components Analysis

Two Factor Solution

Four Factor Solution

Three Factor Solution (Attention, Orientation/comprehension, Memory)

Analysis of the tasks that cause the elderly problems

Analysis of factor scores

The effects of age and gender on attention factor score

The effects of age and gender on orientation factor score

The effects of age and gender on memory factor score

Analysis of mean scores

The effects of age and gender on attention mean score

The effects of age and gender on orientation mean score

The effects of age and gender on memory mean score

Analysis of tasks that subjects no longer perform

The effects of age and gender on attention factor score

The effects of age and gender on orientation factor score

The effects of age and gender on memory factor score

Analysis of tasks that subjects have never performed

The effects of age and gender on attention factor score
This chapter considers the assessment of cognitive function with the use of a subjective rating scale-an Activity of Daily Living Scale (ADL) comprising 59 items. The chapter aims to identify cognitive decline in a sample of 160 healthy drug free elderly volunteers. Answers to the 59 questions were analysed using a principal components analysis in order to identify cognitive groupings within the scale, so as to determine the effects of age on the separate cognitive groupings.

3.2 Introduction : The use of rating scales for the assessment of cognition and everyday activities in the elderly

Chapter two would seem to indicate that cognitive function is adversely affected by a number of variables such as age, poor nutritional status and poor health etc. Decrements in cognitive function can have profound effects on performance in everyday life, increasing the risk of accidents in and around the home.

One important question arises, if the elderly suffer from decrements in cognitive function, then how can these changes be detected or measured, and more importantly do these changes in cognitive function adversely affect the performance of everyday activities.

Gerontologists and psychologists commonly use two methods for assessing cognitive function in the elderly. Researchers can use objective psychometric tests to assess actual cognitive function, or alternatively they can use subjective rating scales/questionnaires designed to evaluate what the person feels is happening to cognitive function.
The assessment of cognitive function with the use of performance tests is a well documented and respected method for the assessment of age related change, known to be valid, reliable and sensitive to both age and drug related change. Objective test measures are often the preferred choice for assessing functional and cognitive abilities in elderly subjects. However, several drawbacks have been associated with these measures namely, the relationship of such tasks to everyday life is questionable, they are time consuming and often expensive and they also require space, specially trained staff and technical equipment. Due to these constraints such measures are only suitable for the assessment of small numbers of subjects, therefore many elderly people who are experiencing problems with their functional ability may never get tested. Another drawback of psychometric tests are often compromised by ailments suffered by the elderly such as poor hearing, eyesight, problems with motor ability and many drugs used to treat disorders can preclude performance on some psychomotor tests e.g. benzodizepines, old generation antidepressants and antihistamines etc.

3.3 Subjective rating scales for the assessment of cognitive function

A less expensive method for assessing cognitive function is with the use of subjective rating scales. Generally two types of subjective ratings are available, self rating and informant rating scales (completed by the subjects close relatives or carer). The use of subjective rating scales is very popular in the assessment of elderly persons, as if you want to know what is happening to cognitive function as a result of age, then the most direct way, is to ask an elderly person what problems they are experiencing.

The use of rating scales in psychological research is becoming a popular method of assessment, as the scales are quick and easy to administer, relatively inexpensive compared with the cost of using psychometric assessments. Rating scales are not compromised by drug treatment and illness, they can be
administered to large numbers of the population, generate large amounts of data in a very short time duration, they can be completed in the comfort of the subjects home, and hence are less daunting than a laboratory situation. Self rating questionnaires are an innocuous way of obtaining large amounts of data from subjects and can be used to examine a wide spectrum of cognitive performance/behaviour in everyday life.

The use of rating scales in psychogeriatric research is not a new method for assessment. There are numerous scales available for the assessment of cognitive function. Assessment of self reports, and in particular problems with the performance of everyday living is a very important factor for determining quality of life. For example if the elderly person is unable to prepare meals, dress themselves, operate household appliances, or manage their finances, then there is a strong possibility that they will lose their independence and be taken into a residential home or nursing home for the elderly.

Self reports are very important for giving an overall picture of what is happening to the elderly person and can be especially useful when used to assess functional change in Alzheimer's Disease. As Kaplan (1979) points out "Almost never is a senile first identified as a result of poor performance in a psychological test. Sometimes the complaint presented when an older person or his family seeks professional advice is the loss of a long practised skill involving both short term and long term memory, such as the ability to dial a telephone number accurately or to tell the time correctly. Deterioration in self care is often associated with developing dementia. Such losses may indicate serious impairments since they relate to abilities that have been practised for many years" (pp 45-77).
3.4 The history of ADL self rating scales

There are numerous rating scales for the assessment of everyday activities in the elderly. However the development of these scales rests heavily on the earlier scales developed for the assessment of functional change in patient populations, hence their utility in the everyday world with apparently healthy subjects is limited.

Functional ability is essentially defined as the ability to perform basic activities of daily life without support, this being the key factor for determining overall independence and quality of life. Functional ability has long been the cornerstone of rehabilitation. There are many instruments for functional ability assessment namely the Barthel ADL index (Mahoney and Barthel 1965); the Disability Impairment Interview Schedule (DISS) (Bennett, Garrard and Halil, 1970); Disability Rating Scale (Akthar, Broe, Agnes, Crombie, Andrews and Caird, 1973); the GERRI- The Geriatric Evaluation by Relatives Rating Scale (Schwarz, 1983); the Ward Function Inventory (Norton, Romano, and Sandifer, 1977) to name but a few.

There are two main types of functional assessment instrument, the Activity of Daily Living scale (ADL self report questionnaire) and the Instrumental Activity of Daily Living scale (IADL self report questionnaire). The Activity of Daily Living scale (ADL), assesses capability to perform basic activities such as dressing, bathing, toileting, feeding etc. – basic skills essential for self maintenance. One of the most popularly used ADL scales is Katz, Ford, Moskowitz, Jackson and Jaffee (1963) Activities of Daily Living scale (ADL).

The second type of self report assessment is the Instrumental Activities of Daily Living scale (IADL). Instrumental activities of daily living focus on higher order activities which enable a person to adapt to the environment and to live independently in the community. These IADL scales assess tasks such as housekeeping, shopping, handling finances, managing medication, using the telephone and wider mobility such as using public transport etc. IADL's are
more sensitive than ADL scales in detecting modest functional loss. One of the most widely used IADL scales is the Lawton and Brody (1969) Instrumental Activities of Daily Living (IADL).

3.5 Criticisms of ADL self rating scales

World-wide there are more than 200 published scales for the assessment of ADL and IADL, however many of these scales have not been validated and are not suitable for the assessment of functional impairment in normal, healthy elderly populations. Each country tends to rely on their own culturally specific scales for the assessment of elderly persons, the advantages of this are that each country is able to detect their elderly persons specific needs, and therefore the people are not being questioned about activities that they do not perform. However the disadvantage of cultural specific scales is that research teams are unable to make cross cultural generalisations, therefore when such scales are included in clinical trials researchers are unable to compare results across cultures. This is major criticism of many of the scales used today. Another general criticism of many of the scales is they often yield a single global score, which makes it very difficult to identify specific aspects of cognitive decline. It is possible that a person is experiencing problems with memory function rather than any other aspect of cognitive ability, this information would be lost when assessing cognitive change in terms of a single global score.

There are a number of rating scales available to identify specific aspects of cognitive function e.g. memory. Memory questionnaires have proved very popular in psychology, as instead of trying to observe a person's success or failure at a memory task, the questionnaires describe a prototypical memory situation and ask respondents to rate their memory performance in terms of the situation.
Worries about decline in memory are particularly prevalent in aged subjects. Poon (1985) reports that "Middle-aged and elderly persons universally complain about the fact that their ability to remember and retrieve information is not as good as it used to be" (p 427-462). Guttman (1980) reported that after arthritis/rheumatism, memory loss was the second most frequent problem described by elderly Canadians.

One of the most fundamental issues in terms of the use of questionnaires for the assessment of cognitive function in aged subjects is, are the subjective complaints of change in cognitive efficiency with age accurate? Do these subjective impressions reflect real changes in their cognitive performance, or rather are they manifestations of other variables such as general state of health, depression, self esteem etc?

A number of researchers have tried to assess the validity of self reports in aged subjects, either by comparing answers to such questions with young subjects, assessing changes in memory with age, or by comparing subjective answers with objective task performance.

3.6 The use of subjective rating scales for the assessment of cognitive function in the elderly

Zarit (1982) assessed memory in a sample of 79 healthy elderly persons aged 50-82 years (mean age 66.5 years) with the use of a structured interview. The interview consisted of 11 questions assessing ability to remember information from a few minutes ago, days and years ago, remembering names, facts, words, directions, the locations of household items and daily tasks. Subjects were also asked to make a global rating of memory. It was reported that most subjects reported having some difficulty with memory. Twenty five percent of the sample reported that they had a lot of trouble remembering recent events and events that happened a long time ago; 61% percent of the sample reported
problems with remembering names. Subjects were also asked to rate their memory when they were young and at the present time using a 10 point scale. They rated memory when they were young to be 8.11 and this fell to 5.73 when they were old.

Jorm, Christensen, Hendersen, Korten, Mackinnon and Scott (1994) assessed cognitive complaints in elderly subjects aged greater than 70 years. Subjects were asked to answer 4 questions. "Overall do you feel you can remember things as well as you used to?", "Does this interfere in any way with your daily life?", "Do you feel you can think and reason as clearly as earlier in life?" and "Does this interfere in anyway with your day to day life?". It was reported that 60% of subjects sampled believed that their memory was worse than in earlier life, whereas only 6% felt that the decline in memory interfered with their daily life. 30% of the subjects felt that they could not think and reason as well as in earlier life, only 5% felt that this interfered with their life.

Hultsch, Hertzog and Dixon (1987) designed a metamemory in adulthood questionnaire to gain information on memory beliefs of older subjects. They reported that older adults gave lower estimates of their memory capacity, reported more decline in memory function with increased age, and were less inclined to believe that they had any control over their own memory capacity.

Johansson, Allen-Burge and Zarit (1997) assessed memory complaints in a sample of 267 elderly subjects (172 women, 95 men) aged 84-90 years (mean age 86.85 years). Subjects were asked to rate their memory, by answering 4 questions. "On the whole, do you think that your memory is good or poor?", "Do you think you have problems with your memory that make your life more difficult?", "Do you think that your memory has gotten worse during the last 2 years?" and "On the whole, do you think that you have problems remembering things that you want to do or say?".
Subjects also completed a depression scale (CES-D, The center for epidemiological studies depression scale). They reported that subjects who had reported that their memory had declined had significantly lower self evaluation scores.

Maylor (1990) compared average scores on Broadbent's Cognitive Failure's Questionnaire (CFQ) obtained from 3509 subjects aged 50-86 years with average scores obtained from 475 young subjects collected by Matthews (1990). They reported that older subjects reported fewer lapses than young subjects on all except four questions. Older subjects reported that they forgot people's names, forget whey they went from one part of the house to another, find they experience "tip of the tongue" and forget what they wanted to buy in shops more frequently than younger subjects. It was also reported that female subjects aged 50-86 years, reported more memory lapses than male subjects.

3.7 Drawbacks of subjective rating scales

Martin (1986) conducted a study to examine whether self ratings were different for different age groups. Two groups of subjects 30 young subjects (aged 18-30 years, mean age 22.9 years); and 30 elderly subjects (aged 60-78 years, mean age 66.3 years) completed an Everyday Memory Questionnaire (EMQ), an Everyday Attention Questionnaire (EAQ) and the Cognitive Failures Questionnaire (CFQ). It was reported than there were no significant differences between the mean scores on any of the questionnaires between the age groups. However, there were differences between the groups when separate questions in the questionnaires were examined. In the Everyday Memory Questionnaire (EMQ), older subjects reported more problems with names, faces and telephone numbers, however the older subjects were better than younger subjects at remembering appointments, colours, paying bills and taking medication. On the Cognitive Failures Questionnaire (CFQ) older subjects were more likely to report forgetting names than younger subjects, however were less likely to
report conversational failure, day dreaming, word misuse, laterality errors, reading distraction and colliding. This experiment highlights the fact that global scores may mask any problems, as analysis of global scores revealed that there were no significant differences between the groups, and the differences were not apparent until actual questions were analysed. The experiment also highlights the fact that it is often the case that younger subjects report more problems with memory and cognitive function with the use of a questionnaire than older subjects. A number of researchers have reported that younger subjects report having poorer memories than older subjects.

Tenney (1984) administered a lost and found questionnaire to 281 young subjects (aged 17-26 years) and 153 old subjects (50-92 years) to examine incidents in which objects were misplaced and recovered. There was no significant difference between the number of incidences reported by the young (31.3%) and old subjects (26.1%). More old than young subjects reported finding the object in plain sight, in its proper place, and in a place already searched, suggesting a tendency with age to overlook objects in obvious places. It was expected that the elderly subjects would report more incidences of misplacing objects, however it was reported that young subjects reported more instances. This in itself is not surprising, after all young subjects are usually leading busier lifestyles than the elderly therefore the scope for forgetting is much greater.

A similar finding was reported by Rabbitt and Abson (1991) they assessed cognitive failure in a sample of 322 subjects aged 50-96 years, using Broadbent's cognitive failures questionnaire (CFQ), they found that subjects aged 50 reported more lapses of memory than subjects aged 60-70 years.

Herrmann (1982) reviewed the properties of 14 questionnaires (including the Cognitive Failures Questionnaire, the Inventory of Learning Processes, and the Memory Change Questionnaire, Everyday Memory Questionnaire) developed
independently to assess people's beliefs about their memory performance in
natural circumstances. They were assessed in terms of their reliability in
reporting what is happening to memory, by comparing the results given on
them, with actual memory performance. It was reported that very few of the
questionnaires correlated with actual memory performance, and even when
there was a correlation, it was very small. Research has found that responses to
these questionnaires are reliable but that they correspond only moderately with
a person's memory performance. Apparently beliefs about their memory
performance are stable but not accurate. Research also has found that responses
to memory questionnaires vary with several variables: the kind of memory
failure, susceptibility to cognitive failures under stress, confidence in memory
performance, age of subjects and the medical and emotional status of the
subject. Thus, although memory questionnaires are only moderately successful
indicators of memory performance, they may nevertheless elucidate the
properties of beliefs that underlie performance. Perhaps the most interesting
finding is that out of all 14 questionnaires examined, only five of the
questionnaires were found to correlate with objective performance tasks, and
even when they were correlated, the correlations were very small indicating that
memory questionnaires cannot be used as a substitute measure of memory
performance.

Rabbitt and Abson (1990) assessed self ratings of memory in elderly subjects
and reported that they are useful sources of information, however they do not
portray a true reflection of the elderly persons cognitive functioning. The
authors propose a number of reasons to try and account for this. Firstly one of
the main drawbacks of self rated questionnaires is that it is not possible to
validate a persons response on a self rated questionnaire, as Hermann (1982)
reported, responses on subjective questionnaires do not correlate with objective
performance tasks. Many of the self rated questionnaires report a global score
(which is gained by summing results on all questions). This method tends to
obscure the results, as two people with different failures in cognitive function
may get the same global score, indicating that the subjects had similar problems with cognitive function. However, it is possible that one subject was suffering problems with memory, whereas the other person had problems with attention/concentration.

Another problem with self rating questionnaires are that they probe the number and variety of lapses, but not the reasons why people make them, which may prove to be misleading. For example, it has been reported young subjects often report more lapses with memory than older subjects (Martin, 1986; Rabbitt and Abson, 1991; Tenney 1984) which could be taken as evidence that younger subjects experience more decline than older subjects. However, when you examine the life styles of the subjects, it become apparent that younger subjects lead busier lives than older subjects and hence they experience more occasions in which to forget/lapse than older subjects.

Other problems with self rated questionnaires are that individuals with poor memories may 'forget that they forgot' and so under report their lapses, The reverse is also possible. Older subjects may exaggerate the rate of decline simply because they are complying to a self fulfilling prophesy, as they believe that as they get older they will experience more decline and hence they will mistakenly attribute occasional absentmindedness to age related decline (Kahn, Zarit, Hilbert and Niderehe, 1975).

Nisbett and Wilson (1977) report that people have limited conscious access to their own cognitive processes and hence have to rate their ability by comparing it with other people, or in terms of their success in coping with the particular demands that their lives place on them. This often means that the results obtained are unreliable. Older people suffering from a reduction in the speed of information processing may be unable to allocate sufficient resources to monitor performance adequately and hence may be unable to achieve awareness of their lapses/errors. Results on self rating questionnaires often reflect differences in
confidence, self regard and mental state (i.e. depression) rather than actual cognitive function.

3.8 Conclusions

Despite the caveats, cognitive gerontologists regard self assessment questionnaires as unique useful tools to discover what changes in cognitive efficiency people experience as they grow old, and how these changes affect their daily lives. It is important to recognise that self reports can be informative even if they are 'invalid' in the sense that they cannot be validated against objective test measures. Despite the caveats, self ratings are useful in the fact that they simultaneously tell us a variety of very different things, they are indicators of cognitive decline and offer clues about the person's abilities, strengths and weaknesses as well as information about self esteem, confidence, anxiety, depression, knowledge and intelligence etc.

3.9 Aims of the present chapter: Analysis of self reported activity of daily living in the elderly

In the previous chapter, it was noted that nutritional deficiency can predispose subjects to cognitive decline. However before we can examine the role of improved nutritional status on cognitive functioning we must first identify the types of behaviour that decline with age.

This chapter details the use of an activity of daily living scale (ADL) for the detection of cognitive decline in healthy elderly subjects. The scale was a draft version of the Bayer International ADL scale for the assessment of elderly subjects world wide regardless of their cognitive status.

The chapter aimed to firstly identify relationships between the different questions posed, in the hope that rather than gain a global score, it would be
possible to identify groupings contained within the questionnaire. Therefore enabling the effects of age on different aspects of cognitive decline i.e. memory and attention to be ascertained. Secondly, having identified separate groupings, the effects of age and gender will be examined on each of the groupings.

3.10 Methods

3.10.1 Subjects
160 elderly subjects (70 males, and 90 females) aged 61-84 years, mean age 70.25 years, (mean age for males was 75.86 years and mean age for females was 65.59 years). All subjects were community dwelling elderly volunteers in good health and were free from current drug usage.

3.10.2 Procedure
In order to assess problems that the elderly are experiencing with the performance of everyday activities, a sample of 160 healthy non-drug taking elderly subjects completed an activities of daily living questionnaire containing 59 questions. The questionnaire was sent to 250 elderly subjects, 64% of the questionnaires were returned.

Answers to the questionnaire were analysed using principal components analysis to determine relationships between questions, and more importantly to identify what aspects of cognition were causing the elderly the greatest problems.

The ADL includes codes which reflected increasing difficulty with task (0-3), but also used codes 4 and 5 for cases where the individual no longer performs the task (4), and never performed the task (5). The tasks that are posing problems (i.e. those rated 0-3) were analysed together, tasks no longer performed (rated 4) and tasks never performed (rated 5) were analysed independently.
3.10.3 Assessment

All subjects completed a draft version of the Bayer International Activities of Daily Living Scale (ADL). The original scale consisted of 63 questions, however for this analysis only 59 questions were analysed (4 of the questions were removed from the analysis as they were questions about current employment and were not responded to). The questions aimed to identify problems that elderly persons were experiencing with the performance of their everyday tasks, such as housework, operating household appliances, the use of the telephone, shopping, travelling and visiting friends, managing finances and medication etc.

The questionnaire aimed to address all behaviours thought to reflect aspects of cognitive performance such as memory, attention, concentration, orientation, comprehension etc.

Subjects were required to rate how often they have experienced a problem with the performance of each task during the last four weeks.
Subjects had to answer each question using the scale:-

0 = The task has never posed a problem
1 = The task sometimes posed a problem
2 = The task often posed a problem
3 = The task always posed a problem
4 = I no longer perform this activity
5 = I have never performed this activity

3.11 Results: Identifying groupings within the ADL questionnaire – principal components analysis

The 59 items were subject to a principal components analysis using Statistica. Factors with Eigenvalues equal to or greater than 1 were retained for an oblimin
rotation. When test items loaded on more than one factor, they were included in a factor according to their maximal weighting. Factor scores were calculated for each subject by summing the raw scores on each of the individual items in each factor. This produced 18 factors for the assessment of functional capacity with Eigenvalues greater than or equal to 1 (see Table 3 and Figure 1).

![Factor Scree Plot](image)

**Figure 1:** Showing the scree plot from the principal.

**Table 3:** Showing the results of the principal components extraction (Eigenvalue, the percentage of variance accounted for by each factor, and the cumulative percentage) for 18 factors.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>Cumulative %</th>
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<tr>
<td>15</td>
<td>1.1</td>
<td>1.9</td>
<td>61.0</td>
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</table>
Overall, 18 factors account for a total of 66.4% of the variance of the ADL scale. However, as there are only 59 questions in the scale, many of the factors, particularly the last few factors may only consist of one or two questions per factor. It is unlikely that one or two questions could be classified as a reliable index of everyday activity therefore a more economical solution was sought.

The 18 factor solution can be seen in appendix 2.

Examination of the scree plot would seem to indicate that the data could be reduced to either 2, 3 or a maximum of 4 factors.

3.11.1 Two Factor Solution

Principal components extraction was repeated to obtain 2 factors. When 2 factors were extracted the factors seemed to relate to familiar actions/behaviours and unfamiliar actions/behaviours. Factor one (familiar actions) factor accounted for 15.8% of the variance, and the second factor (unfamiliar actions) account for approximately 8% of the variance. Therefore accounting for a total of 23.8% of the variance (see Table 4).

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<thead>
<tr>
<th>Factor</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>Cumulative %</th>
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<td>2</td>
<td>4.7</td>
<td>8.0</td>
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</table>

The 2 factor solution can be seen in appendix 3.
3.11.2 Four factor solution

A four factor solution was also examined. Extraction of four factors revealed that the factors accounted for a total of 32.2% of the variance (see Table 5).

Table 5: Showing the results of the principal components extraction (Eigenvalue, the percentage of variance accounted for by each factor, and the cumulative percentage) for 4 factors.

<table>
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<th>Factor</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>Cumulative %</th>
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<td>4</td>
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</table>

When the data was extraction to 4 factors, interpretation of the factors appeared to be quite difficult, it was possible to identify 2 quite distinct factors (attention, orientation) the third and fourth factors were more difficult to interpret, and appeared to be similar to each other, both were comprised of memory type questions. Consequently a three factor solution was imposed on the data.

The four factor solution can be seen in appendix 4.

3.11.3 Three factor solution

A three factor solution was examined. Extraction of 3 factors accounts for 28.3% of the total variance. The first factor accounted for 9.3% of the variance, this factor was termed the attention/concentration factor. Factor 2 accounted for 4.7% of the variance and was termed the orientation/comprehension factor, and the third factor accounted for 2.6% of the variance and was termed the memory factor (see Table 6 and Table 7).

Table 6: Showing the Eigenvalue, percentage of variance and cumulative percentage of the three factor solution.

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<th>Cumulative %</th>
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Table 7: Showing the results of the principal components extraction (Eigenvalue, the percentage of variance accounted for by each factor, and the cumulative percentage) for 3 factors.

<table>
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<th>Factor Two (Orientation)</th>
<th>Factor Three (Memory)</th>
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<td>56</td>
<td>.49</td>
<td>.05</td>
<td>.05</td>
</tr>
<tr>
<td>57</td>
<td>.52</td>
<td>.12</td>
<td>.18</td>
</tr>
<tr>
<td>58</td>
<td>.52</td>
<td>.08</td>
<td>.11</td>
</tr>
<tr>
<td>59</td>
<td>.43</td>
<td>.13</td>
<td>.11</td>
</tr>
</tbody>
</table>

The 3 factor solution.

The questions contained in each of the three factors (attention, orientation and memory).

3.11.4 Factor 1 - Attention/Concentration

52. Do you experience difficulty “doing two things at the same time?”
58. Is it difficult for you to keep your mind on a task when several other things are going on around you?
30. Do you have problems concentrating on conversation?
29. After reading a chapter or a few pages in a book or in an article, do you have difficulty describing what you have just read?
36. Do you experience problems concentrating on reading leisure material?
37. Do you have difficulty reading the newspaper thoroughly?
59. Do you put off things because you have difficulty getting them organised?
28. Do you need to read the same passage or part of a book (or other reading material) several times in order to remember it?

57. If you are interrupted whilst speaking, do you tend to forget what you were going to say?

34. Are you easily distracted whilst reading leisure reading material?

56. If you have to wait your turn to speak, do you have trouble keeping in mind what you were going to say whilst listening to someone else talk?

5. If you are interrupted during an activity of chore, do you have difficulty continuing where you left off?

32. Do you forget point in the middle of a conversation?

33. Do you have difficulty finding the correct word to use when speaking?

42. Do you forget names of people who have just been introduced to you?

49. Do you search for personal belongings?

6. Do you experience difficulty learning new directions regarding how to use simple household appliances (e.g. coffeemaker, iron, toaster)?

7. Do you experience difficulty learning new directions regarding how to use complex household appliances (e.g. microwave oven, vacuum cleaner, washing machine)?

9. When travelling to new places do you sometimes become overwhelmed with new information?

20. Do you find it difficult to complete forms?

40. Do you repetitively go from one room into another in order to do or get something but then forget what you wanted to do?

41. Do you have problems remembering important dates and events?

44. Do you have difficulty remembering telephone numbers which you frequently dial?

46. While counting something up, do you need to recount it several times?

47. When making telephone calls do you dial the wrong number?

48. Do you loose important things?

50. Do you forget anniversaries or birthdays you have always observed in the past?
53. When looking up an unfamiliar telephone number, do you have to refer back to it whilst dialling?
55. Do you forget to turn off the stove, turn out the lights, or lock the door when you should?

3.11.5 Factor 2 Orientation/Comprehension
17. Do you have difficulty touring an unfamiliar city or place on your own?
54. Do you have trouble following a map to a new place?
9. When travelling to new places do you sometimes become overwhelmed with new information?
16. Do you have difficulty reading a map of an unfamiliar city or place?
14. When driving a car, do you become unsure or uncertain about which exits to take to get to a familiar place?
11. When driving a car do you have problems recognising landmarks that would help you know where to turn?
12. When driving a car, do you have problems recalling landmark that would help you know where to turn?
10. Do you have difficulty driving from one familiar spot to another without preparation i.e. without carefully going over the route?

3.11.6 Factor 3 Memory
3. Do you forget about what you have just done (e.g. locking the door, pulling out a plug on an appliance)?
26. Do you go to social or cultural events on the wrong day or at the wrong time?
25. Do you invite friends or relative and forget that you have invited them?
43. Do you buy greetings cards, birthday or anniversary cards for close friends or relatives and forget to mail them?
19. If you use public transportation for a route you have never taken before, do you feel uneasy and uncertain about what you do?
4. Do you begin an activity or chore and then forget the steps or sequence of behaviours necessary for the completion of the activity?

27. Do you purchase tickets for an event only to find that you have booked tickets for a wrong date or time?

8. Do you become confused whilst performing several simple activities around the home at the same time?

24. Have you started to avoid discussions/conversations because of difficulty finding the correct word to use?

3.11.7 Validity of the factors

In order to determine the validity of the factors, split half reliability rates were calculated for each factor using Cronbach’s alpha.

Questions in each of the factors were divided into two groups (questions were allocated to two groups, alternate questions to group 1, answers to questions in group 1 were correlated with answers from group 2).

Table 8: Showing the split half reliability rate and standardised itemised alpha score for each of the three factors (attention, orientation and memory).

<table>
<thead>
<tr>
<th></th>
<th>Attention</th>
<th>Orientation</th>
<th>Memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Split half reliability</td>
<td>$r = 0.77$</td>
<td>$r = 0.80$</td>
<td>$r = 0.77$</td>
</tr>
<tr>
<td>Standardised itemised alpha</td>
<td>$r = 0.83$</td>
<td>$r = 0.82$</td>
<td>$r = 0.81$</td>
</tr>
</tbody>
</table>

All questions within each of the factors correlate very highly, therefore the factors have internal reliability.

Having identified three distinct factors (attention, orientation, memory) it is possible to determine the effects of age and gender on the factors, in the hope that it would be possible to identify age and gender differences within the factors.
3.12 What are the tasks that cause the elderly problems?

This set of analysis refers to the individuals who are still performing the tasks (items rated 0-3).

3.12.1 Analysis of factor scores

A factor score was calculated for each subject on each of the three factors (attention, orientation and memory). These scores were analysed to determine gender and age differences.

3.13 Effects of age and gender on new ADL factors

The interaction with age and gender was examined using a two way analysis of variance with two between subjects factors, (age band and gender) compared with each of the three factor scores (attention, orientation and memory).

3.13.1 Attention factor scores

There was no main effect of age ($F(4,153) = 1.25; p>0.05$) factor scores were comparable across the ages. There was a tendency for female subjects to report more problems with tasks assessing attention, more frequently than males, however this failed to reach statistical significance ($F(1,153) = 0.39; p>0.05$). There was no interaction between gender and age ($F(4,153) = 0.75; p>0.05$).

3.13.2 Orientation factor scores

There was no main effect of age ($F(4,153) = 0.27; p>0.05$) factor scores were comparable across the ages. There was no main effect of gender ($F(1,153) = 0.003; p>0.05$) factor scores were comparable for male and female subjects. There was no interaction between gender and age ($F(4,153) = 1.25; p>0.05$).
3.13.3 Memory factor scores
There was no main effect of age ($F(4, 153) = 0.66; p>0.05$) factor scores were comparable across the ages. There was no main effect of gender ($F(1, 153) = 2.28; p>0.05$) factor scores were comparable for male and female subjects. There was no interaction between gender and age ($F(4, 153) = 1.59 p>0.05$).

3.13.4 Conclusion
Based on the analysis of the factor scores (attention, orientation and memory). It appears that the ADL is insensitive to the effects of age and gender. Subjects of all ages reported similar rates in terms of the difficulty experienced with the performance of everyday tasks regardless of gender.

3.14 Analysis of subjects mean scores
A mean score was calculated for each subject by averaging the results of questions that subjects rated as causing them problems, i.e. any questions that subjects answered with either as causing a problem some of the time, often and always. Mean scores as well as factor scores were calculated because when mean scores are calculated, all the questions are weighted equally, however when factor scores are calculated, the fact that each item is not equally weighted is accounted for. The subjects mean score was analysed in relation to age, ageband and gender to determine whether subjects report more problems as age increases, or whether there are any differences between the types of problems reported by male and female subjects.

3.15 The effects of age and gender on new ADL factors analysis of subjects mean scores
The interaction with age and gender was examined using a two way analysis of variance with two between subjects factors, (age band and gender) and mean score for each of the factors as the dependant variable.
3.15.1 Attention factor
There was no main effect of age ($F(4, 150) = 0.96; p>0.05$) the ages are comparable in terms of reporting problems with tasks assessing attention. There was no main effect of gender ($F(1, 150) = 0.18; p>0.05$) factor scores were comparable for male and female subjects. There was no gender age interaction ($F(4, 150) = 0.80; p>0.05$).

3.15.2 Orientation factor
There was no main effect of age ($F(4, 151) = 0.94; p>0.05$) or gender ($F(1, 151) = 0.18; p>0.05$) and there was no age gender interaction ($F(4, 151) = 0.80; p>0.05$). The reporting of problems with orientation tasks was the same for all age and gender.

3.15.3 Memory factor
There was no main effect of age ($F(4, 153) = 0.51; p>0.05$) or gender ($F(1, 153) = 0.68; p>0.05$) and there was no gender age interaction ($F(4, 153) = 0.26; p>0.05$). The reporting of problems with memory tasks was the same for all age and gender.

3.16 Correlation between mean scores and factor scores
Mean scores and the factor scores for each of the subjects were correlated to determine whether there was a relationship between mean scores and the factor scores (see Table 9).
Table 9: Showing relationship between subjects mean scores and subjects factor scores (Pearson product moment).

<table>
<thead>
<tr>
<th></th>
<th>Attention factor</th>
<th>Orientation factor</th>
<th>Memory factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean attention score</td>
<td>0.54*</td>
<td>-0.64*</td>
<td>0.29*</td>
</tr>
<tr>
<td>Mean orientation score</td>
<td>0.27*</td>
<td>-0.23*</td>
<td>0.38*</td>
</tr>
<tr>
<td>Mean memory score</td>
<td>0.23*</td>
<td>-0.34*</td>
<td>0.65*</td>
</tr>
</tbody>
</table>

* level of significance p<0.05

As the attention and memory factors are positively correlated with the mean scores for both memory and attention, a higher factor score means the same as a higher mean score, i.e. the higher the factor score the more problems experienced. However as the orientation factor score is negatively correlated with the orientation mean score, a higher factor score is indicative of fewer problems with the task, and a lower factor scores is indicative of more problems.

3.17 Correlation between mean scores and the factor scores with actual age

The analyses reported above show that age groups differ little in terms of the difficulties they report. This issue was also addressed by examining the correlation between actual age and self reported difficulties. In order to do this mean scores and factor scores were correlated with actual age using Kendall’s tau (see Tables 10 and 11).

Table 10: Showing the correlation between factor scores and actual age.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>-.10</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Orientation</td>
<td>-.00</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Memory</td>
<td>.08</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>
Table 11: Showing the correlation between mean scores and actual age.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>-.06</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Orientation</td>
<td>-.008</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Memory</td>
<td>-.07</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

These correlational analyses confirm the results obtained from the earlier analyses. Using the three factor method of scoring the ADL, self reported difficulties in attention, orientation and memory do not alter with age.

3.17.1 Summary

The results so far, would seem to indicate that there is no evidence of differences between age groups, or of gender, on self reported difficulties in attention, orientation and memory, whether the data were analysed using subjects mean scores on the questions, or by the more precise measure of calculating factor scores for each of the three factors. As discussed above, these analyses reflect the difficulties with activities which individuals still perform, it may be however that gender and age differences do emerge in terms of the activities people no longer perform.

3.18 Analysis of the tasks that subjects no longer perform

As with the previous analysis of tasks that cause subjects difficulties, mean scores were calculated for tasks that subjects reported that they have given up (no longer perform), items rated 4.

3.19 Analysis of subjects mean scores for tasks that subjects no longer perform

The questionnaire also provided information to identify the tasks that subjects were no longer performing. Mean scores (i.e. numbers of activities referred to in
questions no longer performed) were analysed to assess any gender and age differences.

### 3.20 The effects of age and gender on new ADL factors

Data were analysed using a two way analysis of variance with age band and gender as between subjects factors, and mean score (attention, orientation and memory) as the dependant variable.

#### 3.20.1 Attention factor

There were no significant main effects of age ($F(4, 150) = 1.65; p>0.05$) mean scores were comparable across the ages. There was no main effect of gender ($F(1, 150) = 0.38; p > 0.05$). There was no interaction between gender and age ($F(4, 150) = 1.16; p>0.05$).

#### 3.20.2 Orientation factor

There was a significant main effect of age ($F(4, 152) = 6.45; p<0.0001$). There was a significant effect of gender ($F(1, 152) = 18.04; p<0.0001$). There was a significant interaction between gender and age band ($F(4, 152) = 2.34 p=0.05$). Post hoc testing revealed that the greatest divergence is in the highest age band i.e. very elderly women have given up more orientation tasks than very elderly men. (It may be that the difference in male and female longevity means that the weaker males die and hence the older males may be a more selected sample) (see Figure 2).

53
Incidence of giving up orientation tasks

Figure 2: Showing the incidence of orientation tasks that subjects no longer perform.

3.20.3 Memory factor
There was no significant main effect of age ($F(4, 153) = 0.41; p>0.05$) the mean scores were comparable across the ages. There was no main effect of gender ($F(1, 153) = 1.37; p>0.05$) i.e. males and females report similar rates of giving up memory type behaviours. There was no interaction between gender and age ($F(4, 153) = 0.45; p>0.05$).

3.21 Correlation between subjects mean scores and actual age
Analysis of the effects of age band on tasks that subjects no longer perform report no differences for attention and memory tasks, whereas older subjects frequently reported that they no longer performed orientation type tasks compared to their younger counterparts. This issue was addressed by examining the correlation between actual age and the reports of no longer performing tasks of everyday activities (see Table 12).
Table 12: Showing the correlation between mean scores and actual age.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>-0.07</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Orientation</td>
<td>0.10</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Memory</td>
<td>0.20</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

The correlational analysis with actual age and subjects mean scores for tasks that they no longer perform reported that there was no relationship between a subjects actual age and no longer performing attention, memory and orientation type tasks.

3.21.1 Summary

Unlike the self report data for tasks that subjects do perform, there were a few significant differences between the age groups and the genders in the data for tasks that subjects no longer perform.

In particular there were significant age and gender differences between subjects for reporting that they no longer perform orientation type tasks. Older subjects tended to report that they no longer performed orientation type tasks more frequently than younger subjects. Female subjects were also more likely to report that they no longer performed orientation tasks more frequently than male subjects. There was a significant interaction between gender and age, in that older female subjects reported that they no longer performed orientation type tasks significantly more frequently than older male subjects.

The data would seem to indicate that orientation type tasks pose more of a problem to the ageing population than tasks assessing attention and memory to the extent that older subjects no longer perform such activities.

It is possible that gender and age differences may also emerge when the activities that subjects have never performed are considered.
3.22 Analysis of the tasks that subjects have never performed

The activity of daily living self rating questionnaire also provided information relating to the types of tasks that subjects have never performed, items rated 5.

3.23 Analysis of subjects mean scores for tasks that subjects have never performed

As with activities no longer performed mean scores were calculated for the three types of behaviour and were analysed.

3.24 The effects of age and gender on new ADL factors

The data were analysed to assess differences between the age groups and gender in terms of tasks that they have never performed. The interaction with age and gender was also examined using a two way analysis of variance with two between subjects factors, (age band and sex) compared with each of the three mean scores (attention, orientation and memory).

3.24.1 Attention factor

There was no main effect of age ($F_{(4, 150)} = 1.39; p>0.05$) subjects of all ages reported similar rates for attention type tasks that they have never performed. There was no main effect of gender ($F_{(1, 150)} = 3.00; p>0.05$) males and females report similar rates for attention type tasks that they have never performed. There was no interaction between gender and age ($F_{(4, 150)} = 1.71; p>0.05$).

3.24.2 Orientation factor

There was a main effect of age ($F_{(4, 153)} = 4.50; p<0.001$) and a main effect of gender ($F_{(1, 153)} = 13.35; p<0.001$). There was a significant interaction between
gender and age ($F_{(4, 15)} = 2.35; p<0.05$), older female subject were more likely to report that they have never performed tasks assessing orientation (see figure 3).

![Incidence of orientation type tasks never performed](image)

Figure 3: Showing the incidence of orientation tasks that subjects have never performed.

### 3.24.3 Memory factor

There was a significant main effect of age ($F_{(4, 153)} = 3.16; p<0.01$), older subjects were significantly more likely to report that they have never performed memory type tasks, than younger subjects (see Figure 4). There was no main effect of gender ($F_{(1, 153)} = 0.001; p>0.05$), males and females had similar reports of memory tasks that they have never performed. There was no interaction between gender and age ($F_{(4, 153)} = 1.16; p>0.05$).
The main effect of age on memory tasks never performed

![Graph showing the incidence of memory tasks that subjects have never performed.](image)

Figure 4: Showing the incidence of memory tasks that subjects have never performed.

### 3.25 Correlation between subjects mean scores and actual age

Analysis of the effects of age on tasks that subjects have never performed report no differences for attention tasks, whereas older subjects frequently reported that they never performed orientation and memory tasks compared to their younger counterparts. This issue was addressed by examining the correlation between actual age and the reports of never performing tasks of everyday activities (see Table 13).

Table 13: Showing the correlation between mean scores and actual age.

<table>
<thead>
<tr>
<th>Factors</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>-.07</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Orientation</td>
<td>0.10</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Memory</td>
<td>0.20</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

The correlational analysis confirm the results obtained from the earlier analysis. Using subjects mean scores as a method for scoring the ADL, self reported ratings of no longer performing attention tasks do not alter with age. Whereas actual age was correlated with both memory and orientation type tasks.
3.25.1 Summary

There were main effects found of both age and gender on tasks that subjects have never performed. It was found that older subjects were more likely to report that they have never performed orientation and memory tasks than younger subjects. Female subjects were also more likely to report that they have never performed orientation type tasks than male subjects.

These differences between the ages and genders reflect past societal norms. Older subjects and female subjects had fewer opportunities to perform orientation type tasks e.g. driving. Fifty years ago, it was considered unnecessary for a woman to learn to drive, as driving was perceived as a predominantly male task.

3.26 Discussion

This chapter aimed to identify the types of behaviours that pose a problem in the everyday living of elderly persons with the use of a subjective rating scale, an activity of daily living scale (ADL). All subjects completed the questionnaire, rating the degree to which certain behaviours caused them problems on a day to day basis during the previous 4 weeks. The answers to the questionnaire were analysed using a principal component analysis to extract separate factors within the scale. It appeared that a 3 factor solution provided the optimal way of describing the questionnaire. The 3 factors related to tasks assessing attention, orientation and memory.

A mean score and a factor score were determined for each of the subjects. The mean scores and the factor scores were analysed in order to assess the influence of variables such as age, age band and gender on performance.

The reason for analysing with both mean and factor scores is that the two scores can give different results. When mean scores are calculated, all the questions are
weighted equally. However when factor scores are calculated, the fact that each item is not equally weighted is accounted for. Therefore some questions will hold more weight than others, and will account for more variability. As a result of this, it is possible that analysis with the factor score may be more representative than the mean scores.

Analysis of the data in terms of mean scores and the factor scores revealed that there were no significant gender or age differences between the reporting of what tasks cause the elderly problems on a day to day basis.

The questionnaire also provided information relating to what tasks the subjects were no longer performing i.e. the tasks that subjects had given up. Mean scores for tasks that are no longer performed were analysed in terms of age and gender. There were no significant differences between the rates of giving up for males and females of all ages for tasks assessing aspects of attention and memory. However, there were significant differences between the ages and gender in terms of giving up orientation type tasks. It was found that females were significantly more likely to report giving up tasks assessing orientation than male subjects, and older subjects were more likely to report that they had given up tasks assessing orientation when compared with younger subjects.

As well as being able to assess the types of tasks that subjects no longer perform, the questionnaire was also able to provide information relating to tasks that the subjects had never performed. Mean scores for tasks that have never been performed were analysed in terms of age and gender. The results of this mirror the results reported for tasks that subjects were no longer performing. It was found that there were no significant differences between the attention tasks that subjects have never performed. However there were significant age differences reported for tasks assessing memory, it was found that older subjects were more likely to report that they have never performed memory tasks more frequently than younger subjects. This could reflect the fact that the older
subjects are less likely to have performed memory tasks or simply it could reflect the fact that older subjects had forgotten what tasks they had performed.

There were also significant differences between the ages and gender in terms of orientation tasks that subjects have never performed. It was found that females were significantly more likely to report never having performed tasks assessing orientation than male subjects, and older subjects were more likely to report that they had never performed tasks assessing orientation than their younger subjects.

The results of the subjective rating scale for subjects who are currently conducting tasks involving attention, orientation and memory, would seem to indicate that age does not affect the rates at which subjects report problems with current performance of the tasks. However, there is a vast literature available to provide evidence that ageing results in a decline in aspects of cognitive function, especially aspects of attention, memory and the speed of information processing. Therefore the results of this experiment would seem to suggest that subjective ratings do not provide researchers with a true representation of what is happening with cognitive function as a result of age. Researchers have proposed a number of reasons why older subjects cannot accurately rate cognition.

Nisbett and Wilson (1977) noted that individuals cannot inspect their own cognitive processes, but can only make inferences about them from received social opinion, or by observing the overt effects of their behaviour on the external world. Hermann (1982) and Rabbitt and Abson (1990) have found that self rating questionnaires do not predict performance on everyday tasks and have suggested many logical and methodological reasons why we should not expect them to do so. Rabbit and Abson (1991) note that age differences in peoples answers to self rating questionnaires may strongly reflect changes in their general levels of confidence and their attitudes towards themselves rather
than actual changes in their objective abilities. Self reports are often very
difficult to interpret because people’s answers to such questionnaires often tell
us a variety of different things. For example, they offer an explanation of
peoples competencies and weaknesses, but they also give us information about
subjects self confidence, anxiety and depression, as well as the extent of their
knowledge and insight about subjects abilities, knowledge and beliefs about
how their memories work.

It is speculated that the elderly show a tendency to exaggerate or underestimate
the frequency of problems relating to aspects of cognition, as many elderly
persons believe that the results of such questionnaires may be used against them
e.g. if they express that they are experiencing problems with the performance of
their daily activities they are admitting that they can no longer fend for
themselves, and that they may be placed into sheltered accommodation or into a
home for the elderly. Therefore, many researchers believe that the results of self
reports should be treated with caution.

The absence of age differences in the current analysis of the self-reported
difficulties of the elderly may be due to such unreliable reporting, but may
equally reflect the absence of difficulties. Therefore one of the best ways in
which to assess cognitive function and more importantly decline with age, is to
assess actual decline with the use of reliable, validated objective test measures.
Chapter four will detail the results of psychometric test performance using a
battery of cognitive tasks designed to assess declines in cognitive function, in
the same sample of drug free healthy elderly volunteers, to determine actual age
related declines in cognitive function.
4 Chapter Four: What problems do the elderly experience with regard to actual performance and do these changes relate to subjective ratings?

4.1 Chapter Outline

The relationship between subjective and objective test measures

- Subjective ratings that correspond with objective measures.
- Subjective ratings that do not correlate with objective measures.

Analysis of objective task performance in a healthy elderly population.

- Tasks assessing aspects of attention.
- Tasks assessing aspects of orientation.
- Tasks assessing aspects of memory function.
- Tasks assessing the speed of information processing.

The effects of age and gender on the Syndrom Kurtz Task (SKT)
The effects of age and gender on the CFF, CRT and SMT task

Relationships between the cognitive function tasks:

- Principal components analysis
- Age and gender differences in performance of the SKT factor scores.
- Principal components analysis of the performance data.
- The effects of age and gender on the 5 performance factor scores
- Performance factor correlations with actual age
- ADL factor correlations with actual performance factors

The chapter details the assessments of cognitive function using a battery of tests designed to assess aspects of attention, memory, orientation and the speed of information processing.

The chapter considers the effects of age and gender on actual task performance, aims to identify relationships between the tasks in order to assess different
aspects of cognitive function, and finally considers the relationship between subjective and objective measures.

4.2 Introduction: Assessment of cognitive function in the elderly

In the previous chapter, 160 drug free healthy elderly subjects completed a subjective rating scale assessing cognitive problems encountered in everyday living. Analysis of the data would seem to indicate that the elderly were not aware of many of age related changes in day to day cognitive function.

Cognition comprises the mental processes through which knowledge in the world can be attained, retained and used, namely the so called higher order mental activities such as attention, memory, thinking, reasoning, problem solving, perception and language. The term cognition is derived from the Latin "cognoscere", meaning to know or have knowledge of. It is generally assumed that ageing is associated with a number of changes in cognitive function, on some but not all aspects of cognitive function. Generally, normal ageing is associated with a decline in certain aspects of memory, a general loss of processing resources and attention, decreases in problem solving ability, naming and fluency, whereas tasks involving language and other verbal skills remain relatively unaffected by age.

The effects of age on cognitive function have been described in terms of a computer analogy. "The cognitive system is much like a decaying computer which gradually looses memory and processing power and so progressively becomes unable to run more and more of a set of programmes, still perfectly preserved on floppy discs, which it could previously use with no trouble" (Rabbitt, 1993 p385-434).

The previous chapter raised a doubt on the credibility of self reports, there is some debate as to whether self rating questionnaires accurately depict problems
with cognitive function, especially memory. To examine this, research teams have asked subjects to rate their memory problems using a self rating questionnaire, and perform a battery of psychometric tests designed to objectively measure decrements in memory and cognitive function. Direct comparisons of the two methods should enable researchers to determine whether answers given on self reports accurately depict current cognitive status. If self reports are correlated with objective task performance, then answers on such rating scales could be regarded as reliable. However, if answers on rating scales do not correlate with actual task performance, then the accuracy of the self rating is somewhat doubtful, or rather the real world tests that feature in subjective ratings are different to those assessed in psychometric tests.

Numerous research teams have tested cognitive function in healthy elderly subjects with the use of both subjective rating scales and objective performance tasks.

4.3 Subjective ratings that correlate with objective measures

A number of researchers have reported correlation's between subjective ratings and objective test measures.

Johansson, Allen-Burge and Zarit (1997) assessed the relationship between self-evaluations, and cognition, in a sample of 267 subjects (mean age 86.85 years), taken from a longitudinal, population-based panel of the oldest old in Sweden. Subjects completed self-report measures on memory, and a comprehensive battery of structured behavioural, social, and biomedical assessments.

The self rating of memory consisted of 4 questions, subjects had to answer them using a Likert type response, the questions asked were "On the whole, do you think that your memory is good or poor?"; "Do you think that you have
problems with your memory that make your life more difficult?"; "Do you think that your memory has gotten worse during the past 2 years?" and "On the whole, do you think that you have problems remembering things that you want to do or say?". Cognitive performance was assessed using a battery of 5 tests, a memory in reality test (subjects had to place 10 objects in a model house, they then had to recall where all 10 items had been placed, and actually replace all the items in the house); prose recall task (subjects had to provide immediate recall of a story); clock test (subjects had to draw a clock and set the hands to a certain time, set the hands on a wooden clock with no numbers on the face, and had to state the times of the clocks); coin test (subjects were given 10 Swedish coins, they were asked to choose the least number of coins that added up to four pre selected totals); MMSE (Mini Mental State Examination).

Results indicated that overall cognitive ability, was associated among other things with self-reports of memory for the entire sample. The MMSE was significantly correlated to self evaluations, better performance on the MMSE was associated with fewer complaints. Self evaluations were also highly correlated with depression, less depressed subjects had a more positive evaluation of their memory. Self reported decline correlated with actual decline (as measured using the MMSE) and predicted decline correlated with 3 tests of memory, the coin task, prose recall and the memory in reality task although the magnitude of the relationship was small (.22, .34 and .32 respectively). The authors concluded that self reports of memory cannot substitute for objective assessment, however they may prove useful as detection tools for "at risk" subjects who would warrant for a complete objective assessment.

Zarit (1982) assessed memory complaints and actual memory in a sample of 79 elderly persons aged 50-82 years (mean age 66.56 years). Subjective ratings of memory were assessed in a structured interview, subjects were asked to give a global evaluation of memory, rate ability to remember information from a few minutes ago, days ago and years ago, ability to remember names, words, facts,
directions, daily tasks and the location of household items. Memory was assessed using a 15 item word list, recall of famous faces task, shopping list task, list of daily activities task, giving directions, a names and faces task and visual recall of a scene. The authors reported that subjective reports of difficulties with memory were associated with actual performance on the word list task, the shopping list task, daily tasks and tip of the tongue experiences on the famous faces task. It was reported that subjects with poor task performance reported more difficulty on the subjective memory interview.

Schofield, Marder, Dooneief, Jacobs, Sano and Stern (1997) investigated the relationship between memory complaints and cognitive performance among 364 healthy community-dwelling elderly subjects. Memory complaints were recorded as present or absent at the baseline evaluation. After 1 year, 169 of the subjects were re-evaluated. At baseline, 31% of the normal subjects and 47% of those with cognitive impairment had memory complaints. Subjects with memory complaints had higher Hamilton depression scale scores than subjects without memory complaints but equivalent scores on a measure of total recall. At follow-up, the subjects with baseline memory complaints had significantly greater decline in memory and cognition than subjects without memory complaints.

Jorm, Christensen, Henderson, Korten Mackinnon and Scott (1994) conducted a community survey in 877 elderly Australian subjects (aged 70+ years) to determine decline in memory and intelligence. 431 female and 446 male subjects and their informants (a close relative or friend) were asked to rate memory decline and intellectual decline, they were asked such question as "do you feel you can remember things as well as you used to?"; "Do you feel you can think and reason as clearly as earlier in life?"; "Does this interfere with your everyday life?" and "How long ago did this change start?". Everyday memory was also assessed, subjects were asked to answer questions such as "Do you have more trouble remembering things that have happened recently?"; "Are you
worse at remembering where your belongings are kept?"; "Do you have troubles recalling conversations a few days later?". Actual cognitive function was assessed using the Mini Mental State Examination (MMSE); the National Adult Reading Test (NART); symbol letter modalities test (test similar to the digit symbol substitution test and the symbol modalities test, where letters and geometric shapes are associated, subjects have to state which letter is associated with each shape) three-word recall and name and address recall, face recognition and figure reproduction. Scores on all 4 tests were summed to give an overall episodic memory score. Anxiety and personality were also assessed using an anxiety and depression questionnaire and the Eysenk Personality Questionnaire (EPQ). It was found that both informants and subjects commonly reported cognitive decline, intellectual decline was less frequently reported than memory decline, in most cases the decline was not seen as interfering with daily life. Answers relating to cognitive decline did correlate reliably with actual memory performance, however the correlation's were very small (MMSE – 0.13, Symbol-letter modalities –0.12 and episodic memory –0.12). When responses from subjects and informants were compared, agreement was found to be poor. For subjects, reports of cognitive decline were correlated with anxiety and depression symptoms and with trait neuroticism, self reports did not correlate with age. In contrast, informants' reports were correlated with the subjects cognitive test performance and age, but also with the informants own anxiety and depression symptoms, suggestion that informants ratings may be contaminated by the affective state of the informant. These findings cast doubt on the reliability of informants interpretations of cognitive decline in their partners or close friends.

4.4 Subjective ratings do not correlate with objective measures

While the above studies have reported that complaints of poor memory are typically considered to reflect actual functioning, several studies have found
discrepancies between subjective reports of poor memory and test scores. It is often the case that persons perform better on objective tests than their self ratings would seem to indicate (Perlmutter, 1978; Rabbitt and Abson, 1991; Jorm, Christensen, Korten, Henderson, Jacomb and Mackinnon, 1997).

Perlmutter (1978) assessed memory function with a questionnaire containing 60 questions and actual memory performance (incidental associative orienting task, recall and recognition of these words and recall and recognition of a word list task, and fact memory task). Sixty four subjects aged 20-25 years (mean age 23 years) and 60-65 years (mean age 62 years) completed the tasks. It was found that older subjects reported more memory problems than younger subjects, and they expected that their memory would get worse with age. However in terms of the actual performance tasks, older subjects performed better than younger subjects on the fact recall and recognition task. This study highlights the discrepancy between subjective and objective measures.

Rabbitt and Abson (1990) assessed subjective ratings and objective task performance in 422 subjects (330 women, 92 men) aged 50-80 years (mean age 63 years). Subjects completed the Cognitive Failure's Questionnaire (CFQ), the Memory Failure's Questionnaire (MFQ) and the Lost and Found Questionnaire (LF), and the Alice Heim AH4 intelligence task, the Mill Hill vocabulary task, 30 item word list and a cumulative learning task containing 15 items. They reported that there was no correlation between any of the subjective ratings and objective measures.

Rabbitt and Abson (1991) questioned whether elderly persons were able to gauge performance on memory tasks. In the experiment 322 subjects aged 50-96 years rated their memory performance using Broadbent's Cognitive Failures Questionnaire (CFQ), Memory Failures Questionnaire (MFQ) and they also completed the Beck Depression Inventory (BDI). Subjects ratings were compared with actual performance on a digit span task, recognition memory for
40 drawings, cumulative learning task containing 15 words, and a free recall task containing 30 words. No correlations were reported between subjective and objective measures hence Rabbitt and Abson concluded that subjects were unable to accurately rate memory performance.

Jorm, Christensen, Korten, Henderson, Jacomb and Mackinnon (1997) assessed whether cognitive complaints predict future or reflect past cognitive decline using data from a 2-wave longitudinal study of 70+ years old. Cognitive complaints were assessed on 2 occasions 3.6 years apart. The first assessment was made in 1990-1991 using 721 subjects and the second set of interviews were conducted in 1993-1994 in a total of 507 subjects. Results showed cognitive complaints did not predict future cognitive change on the Mini-Mental State Examination.

4.4.1 Conclusions
The discrepancy between subjective ratings and actual task performance would seem to indicate that, in order to gain an accurate representation of cognitive decline in aged samples, researchers should not rely on subjective ratings alone and should assess cognitive function using valid and reliable objective measures.

4.5 Aims of the chapter: Analysis of objective task performance in a healthy elderly population
This experiment aims to identify age related decrements in cognitive function using a battery of cognitive tasks. The tasks include the Syndrom Kurtz Task (SKT), Critical Flicker Fusion Task (CFF), Choice Reaction Time (CRT), and the HPRU Sternberg Memory Task (SMT).

As well as identifying age related decrements, this chapter questions whether there are any relationships between the cognitive and psychomotor tasks. The
relationships between tests will be identified with the use of a principal components analysis.

Finally having identified the relationships between the tests, the cognitive factors will be compared with the subjective (ADL) factors identified in the previous chapter. The analysis will aim to determine whether the performance factors relate in any way to the ADL factors.

4.6 Methods

4.6.1 Subjects
160 elderly subjects (70 males, and 90 females) aged 61-84 years (overall mean age 70.25 years, mean age for males was 75.86 years and mean age for females was 65.59 years) participated in the study as a whole. All subjects were in good physical and mental health and were free from current drug usage. Subjects were recruited from the general public via the HPRU data base or responses to adverts in the local press.

4.6.2 Procedure
All 160 drug free healthy elderly subjects completed a test battery assessing overall cognitive function consisting of the Syndrom Kurtz task (SKT), the Critical Flicker Fusion task (CFF), Choice Reaction Time task (CRT), and the HPRU Sternberg Memory task (SMT).
Performance on all measures were analysed with respect to gender, increasing age and interaction between gender and age.

4.6.3 Assessments
The tasks included in thesis can be considered in terms of the cognitive sub-groupings identified in the ADL chapter (attention, orientation, memory). In
addition to the three ADL groupings, an additional group entitled the speed of information processing was also identified.

In terms of the cognitive groupings the tasks assessing attention include Syndrom Kurtz subtests VI (counting symbols) and subtest VII (reverse naming task).

Tasks assessing orientation include SKT subtest IV (arranging blocks) and SKT subtest V (replacing blocks).

Tasks assessing memory included the HPRU Sternberg memory task (SMT), SKT subtest II (immediate recall), SKT subtest VIII (delayed recall), SKT IX (recognition memory).

Tasks assessing the speed of information processing include SKT subtests I (object naming), SKT subtest III (numerical naming), the Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT).

4.7 Tasks assessing aspects of attention

Attention is an important component of human performance, as the ability to remain alert and to select appropriate information from the environment is often a limiting factor especially in aged subjects.

Attention can be viewed as the capacity and limitations of an individual to select and process sensory information from the environment, as well as the ability to concentrate on information despite distracting stimuli or over long periods of time.

It is generally assumed that attention is not a single entity, rather it can be regarded as manifesting itself in a number of forms, these are usually defined as
sustained attention or vigilance, selective or focused attention, and divided attention. It is possible that certain aspects of attention are disrupted with age, whereas others are spared. Research would seem to indicate that ageing disrupts selective attention and divided attention, whereas sustained attention (vigilance) is relatively well preserved with age (Salthouse, 1982).

The test battery used throughout this thesis contains two selective attention tasks. The tasks are SKT subtests VI (counting symbols) and SKT VII (reverse naming task).

4.7.1 **SKT Subtest VI (a counting symbols task)**

*In the SKT subtest VI subjects are asked to count the number of symbols contained on a card. The card contained seven rows of different symbols e.g. flowers, circles, squares and triangles, the subject was asked to count aloud the number of circles seen on the card. The time taken to complete the task was recorded.*

This task, is essentially a selective attention task, whereby the subject has to attend to one symbol (e.g. the circles) whilst ignoring all other symbols, the task is very similar to a visual search task. There is also a speed element to the task, the slower the subject is at performing the task, the higher the penalties they incur. Hence a selective attention task with such a reliance on speed would be expected to show decrements with age.

Rabbitt (1965) assessed visual search in two groups of subjects, young subjects (mean age 19 years) and elderly subjects (mean age 67.4 years). Rabbitt reported that the elderly subjects were significantly slower at the visual search task, mean search time for the elderly groups was 27.8 seconds, compared to only 20.8 seconds for the younger subjects. Scialfa, Esau and Joffe (1998) used a visual search task to assess selective attention in which younger and older subjects had to find a single target in both feature and conjunction search
conditions. Display size varied between 2 and 8 items, and target distractor similarity ranged from low to high levels. It was reported that older adults had difficulty detecting the target in high similarly conjunction search displays containing a large number of distractors. Reaction times were also much longer for older subjects. The results were taken to indicate that there were age differences in selective attention, and older subjects suffer from an age-related slowing.

4.7.2 SKT VII (a reverse naming task)

Subtest VII is an interference test for the assessment of cognitive rigidity, it assesses the ability to adapt to change in well trained reactions. Subjects are presented with two rows of letters e.g. ABBAAB. The subject is required to mentally reverse the letters e.g. if they read the letter A they have to respond B, and if they read the letter B they have to respond A. Time taken to complete the task was recorded.

The reverse naming task is selective attention task, whereby subjects have to selectively attend to one aspect of the task whilst at the same time ignore certain aspects of the task (see the letter A, mentally reverse the letter and respond with the letter B).

This task has similar properties to the Stroop task, where subjects have to attend to all the information (coloured word written in another coloured ink) and selectively attend to only one aspect of the information (i.e. ink colour). Performance on the Stroop task has been shown to decline with age. Cohn, Dustman and Bradford (1984) administered the Stroop colour word test to 80 healthy males aged 21-90 years. They reported significant age effects on the task, performance in subject's aged 61-70 and 71-90 was significantly slower on the task than younger subjects. Similar results were reported by Comalli, Wapner and Werner (1962); Hartley (1993); Uttl and Graf (1997).
The reverse naming task (SKT VII) is also similar to the digit substitution task (DSST), whereby the subject is presented with a digit and an associated symbol/pattern. The subjects have the list of digits and symbols in front of them and are given a certain amount of time in which they have to complete the task. The subjects have to attend to the digit, whilst at the same time associate the digit with the designated symbol. Bryan and Luszcz, (1996) assessed selective attention using the digit symbol substitution task in two groups of subjects, 36 older adults (mean age 73 years) and 36 younger adults (mean age 21 years). Older subjects had poorer scores on the DSST than younger adults. Park, Smith, Lautenschlager, Earles, Frieske, Zwahr and Gaines (1996) assessed cognitive function using the digit symbol substitution task in a sample of 301 subjects aged 20-90 years. They reported significant declines in performance on this task with age. Similar results were reported by Gilmore, Royer and Gruhn (1983).

4.7.3 Summary
Research into the effects of age on selective attention using the Stroop task, visual search task and the digit symbol substitution task (DSST) would seem to indicate that ageing is associated with significant declines in performance (Rabbitt, 1965; Scialfa et al., 1998; Comalli et al., 1962; Cohen et al., 1984; Hartley, 1993; Uttl and Graf, 1997; Luszcz, 1996; Park et al., 1996; Gilmore, Royer and Gruhn, 1983).

Based on this evidence, age related declines in performance would be expected on both SKT VI (counting symbols) and SKT VII (reverse naming task).

4.8 Tasks assessing aspects of orientation

4.8.1 SKT IV (arranging blocks) and SKT V (replacing blocks)
There is some evidence to suggest that elderly subjects report problems with orientation type tasks, in particular they report problems with driving, giving
directions, following directions, map reading, orientation to time and location etc.

SKT subtests IV (arranging blocks test) and SKT V (replacing blocks) can loosely be regarded as orientation type tasks, as to perform the task, subjects have to be able to place 10 numbered blocks e.g. 23, 45, 96, 54 etc. into ascending order (SKT IV) and then replace the blocks in their original starting positions (SKT V). Subjects were not required to remember the spatial location of the blocks as it was clearly marked on the board, however if they were able to roughly remember the spatial location of the blocks then they would perform the task faster than subjects who were unable to remember the spatial locations. There is some evidence that memory for spatial information declines with increased age (Light and Zelinski, 1983).

Moore, Richards and Hood (1984) assessed spatial memory in a sample of subjects aged 19-76 years, subjects had to remember the spatial locations of wooden shapes, they reported that there were significant declines in the ability to recall spatial locations in aged subjects. Evans, Brennan, Skorpovich and Held (1984) conducted a study in which subjects had to recall the spatial location of buildings in their home town and place models of the buildings onto a map. It was reported that older subjects were poorer at the task than younger subjects, even though they had lived in the area longer than younger subjects. Both SKT IV and V rely heavily on speed as well as orientation/spatial information, the subjects have to place the blocks in the correct spatial locations as fast and accurately as possible, as the tasks rely heavily on speed, and age is known to result in slowing in performance, declines with increased age would be expected (Lindenberger et al., 1993).

4.8.2 Summary
Based on the above experimental evidence that elderly subjects have problems with orientation/spatial tasks (Light and Zelinski, 1983; Pezdek, 1983; Evans et
al., 1984; Moore et al., 1984), and that performance slows with advanced age (Lindenberger et al., 1993) significant age effects would be expected on SKT subtests IV (arranging blocks) and V (replacing blocks).

4.9 Tasks assessing aspects of memory function

A common finding in ageing research is that older subjects seem to have poorer memories than younger subjects (Dixon, Simon, Nowak and Hultsch, 1982). The elderly often report that problems with memory are one of the greatest problems they face with everyday living (Lowenthal, Berkman, Beuhler, Pierce, Robinson and Trier, 1967). Older people frequently express concern about failing memory. Lowenthal et al., (1967) reported that in community studies, more than half the persons aged 60+ reported serious memory problems.

Salthouse (1980) likened older memory to "the running of a voluminous library by an increasingly frail librarian" (47-65). This view helps summarise the effects of age on memory, however this opinion is not held by all researchers. Many believe that some elderly subjects do not experience such a dramatic decline in memory function, so it can be argued that Salthouse's opinion may paint a rather negative picture. The types of memory complaints commonly reported include problems with remembering names and faces, important events, appointments, telephone numbers and remembering where they have placed personal belongings such as their spectacles.

The tasks assessing memory that have been used in this thesis include the HPRU Sternberg memory task (SMT), SKT subtest II (immediate recall), SKT subtest VIII (delayed recall) and SKT subtest IX (recognition memory).

4.9.1 The HPRU Sternberg Memory Task (SMT)

The HPRU version of the SMT task is presented in computerised format using a personal computer and software from the HPRU test battery. Subjects responses
are made using a mouse, where one button is the “yes” response and the other button the “no” response. To complete the task subjects sit at a 75 cm desk with the computer screen 50 cm in front of them at eye level. All responses are recorded by the computer.

Subjects are required to memorise a series of target digits, ranging from single digits, sets of 3 digits and sets of 5 digits, these are termed the stimulus set (or target digits). These are presented at a rate of 800 ms per digit. One second after the presentation of the final digit an auditory warning signal (750 ms duration) sounds, followed by a series of 12 single probe digits. In the original Sternberg Memory Task, memory scanning ability was assessed by presenting a single digit probe (Sternberg, 1966, 1975). Subjects respond to the probes by pressing the “yes” button if the probe digit was contained in the stimulus set, or the “no” button if it is not. There are an equal number of positive and negative probe digits in each probe set. Subjects are presented with 6 stimulus sets, (two single digits, two 3 digit presentations and two 5 digit presentations). The computer records the subjects reaction times for all presentations. A total SMT score is derived by averaging responses to all stimuli.

Since memory is known to decline with advanced age, and speeded responses decline with age, then age related declines in performance would be expected on the HPRU version of the Sternberg memory task.

4.9.2 SKT subtest II (an immediate recall task)

In SKT II subjects were required to give an immediate recall of the 12 pictures in 60 seconds. Pictures had previously been seen and named in SKT subtest I. The number of forgotten items were recorded.

The immediate recall of objects task is a task thought to be affected by age. Marguerie De Rotrou, Le Poncin Lafitte and Lafitte (1986) assessed memory performance in 37 elderly subjects using a paired associate word list task, it was
reported that memory recall declined with age, subjects with the poorest performance had a mean age of 75.5 years and subjects with superior performance had a mean age of 65.7 years.

Ferris et al. (1980) assessed memory function in a sample of normal elderly subjects aged 60-88 years, and young subjects aged 17-39 years using a paragraph recall task, and a paired associate task, subjects were required to give immediate recall of the test material. It was reported that there were marked declines in immediate recall on the paragraph recall and the paired associate task with age, namely, older subjects recalled fewer items than younger subjects.

Delbecq-Derouesné and Beauvois (1989) conducted a word recall task in subjects aged 20-86 years. Immediate mean recall of 15 words was found to decline as age advanced so that mean recall for subjects aged 20-25 was 8.2 words, in subjects aged 56-65 mean recall was 6.2 and in subjects aged 65-86 years mean recall was 5.2 words.

4.9.3 SKT subtest VIII (a delayed recall task)

SKT subtest VIII is a delayed recall task (conducted approximately 10 minutes after the immediate recall task). Subjects were asked to provide delayed recall of as many of the 12 pictures originally seen in SKT subtest I.

Generally performance on a delayed recall task is poorer than performance on the immediate recall task, as the memories have faded during the passage of time. Delbecq-Derouesne and Beavois (1989) examined free recall in 75 subjects aged 20-86 years. Mean immediate recall for subjects aged 20-25 years was 3.97 and in subjects aged 65-86 years was 3.6. Delayed recall remained relatively stable in subjects aged 20-25, however fell to 1.53 in subjects aged 65-86 years. In particular in this task subjects were unable to rehearse the material as they had completed SKT subtests III to VII (which essentially act as
distractor tasks to block rehearsal) therefore delayed recall should be much poorer than immediate recall. Based on this information age related decrements in performance would be expected on the task.

4.9.4 SKT subtest IX (a recognition memory task)

In the recognition task (SKT subtest IX) subjects were shown a card containing 48 pictures of objects and are asked to indicate what objects they have seen before i.e. what objects they had previously seen in SKT I. The number of forgotten objects were recorded.

Recognition memory tasks are much easier to perform than recall tasks (Erber, 1974). Generally performance on recognition tasks are relatively unaffected by age, as the subjects has external cues to aid recognition (unless the distracting stimuli are too similar to the target stimuli, and hence disturb recognition). Hence age related decrements are not expected on recognition memory tasks.

4.9.5 Summary

Based on the experimental evidence on memory function in aged subjects, age related declines in performance are expected on immediate recall (SKT II), delayed recall (SKT VIII) and the HPRU Sternberg memory task. Whereas age effects would not be expected on the SKT recognition task (SKT subtest IX).

4.10 Tasks assessing the speed of information processing

The slowing of behaviour with increased age is generally accepted as a major consequence of age, and is widely documented (Salthouse, 1985; Welford, 1977). This slowing is expressed in terms of the processing time required to perform a particular task (Cerella et al., 1980). Salthouse (1985) suggests that a reduction in information processing speed is a marked concomitant of old age.
The tasks assessing the speed of information processing, include SKT subtest I (object naming), SKT subtest III (numerical naming) the Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT).

4.10.1 SKT subtest I (an object naming task)

In SKT subtest I, subjects are shown pictures of 12 familiar objects, subjects are asked to name the objects aloud, and more importantly try to remember them. The time taken to name the pictures is recorded.

4.10.2 SKT subtest III (numerical naming task)

In SKT subtest III subjects had to perform a numerical naming task. The task was carried out using a board with 10 magnetic disks on it. Each disk is numbered with two digits e.g. 23, 45, 96, 54 and 68 etc. Subjects are asked to read aloud the numbers as quickly as possible time taken to complete the task is recorded.

Both tasks (SKT I, III) rely heavily on speed, subjects have to name the objects/numbers as quickly and accurately as possible. Age effects on the object naming task would be expected, as not only does the task rely on speeded response but it is well documented that many elderly subjects suffer word finding difficulties (Burke, MacKay, Worthley and Wade, 1991) which would preclude performance on the task.

Numerical naming is essentially a procedural task, a task that is well learned, rehearsed and retained during the persons lifetime. Hence age effects would not be expected on such a task.

4.10.3 Summary

Age related declines in performance are expected on SKT I (object naming task) but are not expected on SKT III (numerical naming).
4.10.4 The Choice Reaction Time Task (CRT)

The Choice Reaction Time task (CRT) is used as an indicator of sensorimotor performance, assessing the efficiency of the attentional and response mechanisms in the information processing chain. The latency of a motor response to a stimulus is recorded, but since the stimulus is one of a number of alternatives, this enables the measurement of attention. The task allows for the measurement of three components, recognition reaction time (RRT) which can be regarded as the attentional aspect of the task, motor reaction time (MRT) which is used as a measure of the efficiency of the response output system, and total reaction time (TRT) which is the sum of RRT and MRT.

Reaction time tasks are often used to assess information processing, as response time to a stimulus is thought to have three components:-

1. Sensory input
2. Central processing
3. Behavioural output

Welford (1958) notes that as long as the stimulus is strong enough, decrement in performance is related to the central processing of the information.

For the task subjects sit at a table positioned to be 75 cm high, the CRT apparatus is laid flat on the table top 50 cm away from the subjects eye. The task consists of a flat box with a home key positioned in the centre and at the edge closest to the subject. Positioned equidistant in a semi circle around the home key are six red lights, positioned underneath these are light sensitive buttons. During the task the subjects are asked to place their index finger of the preferred hand on the home key and wait for one of the red lights to illuminate, as soon as this happens they have to remove their finger and place it onto the button which is positioned directly beneath the illuminated light, once they have done this they have to return to the home key and wait for the next light
stimulus. Subjects are presented with 20 such trials, mean reaction times are obtained from the average of 20 consecutive trials. The computer automatically records recognition reaction times (the time taken for the subject to remove their finger from the home key) and motor reaction times (the time taken for the subjects to reach the appropriate response button) and total reaction times (the sum of RRT and MRT).

Reaction time can be assessed using simple reaction time (SRT) i.e. response to one stimuli, or with choice reaction time tasks (CRT) i.e. response to more than one stimuli, or choice of responses. The definition of choice reaction time, i.e. the subjects has a number of choices, and the subject must select the appropriate response from a number of alternatives, highlights the fact that responses on such tasks is slower than responses on simple reaction time tasks.

Changes in the information processing rate can manifest themselves either as changes in response speed or of accuracy. Hence choice reaction time (CRT) is often used as a central indicator of information processing. It has been suggested that individual differences in choice reaction time may directly reflect differences in the efficiency of the central nervous system. The assessment of reaction time has real life impact, changes in reaction time of even a few milliseconds can have dramatic consequences in various situations (e.g. driving, crossing the road, removing your hand before you slice bread).

Reaction times have been found to decrease as age increases (Lindenberger, Mayr and Kliegl, 1993). The literature would seem to indicate that latencies in simple reaction time increase by 20% to 26% from age 20 to 60 years. It is accepted that responses by the elderly on choice reaction time tasks are disproportionately slower on choice reaction time tasks than simple reaction time tasks, generally the greater the number of choices, the more disadvantaged the elderly become. Choice reaction time tasks require more processing, as the
greater the range of choices means that more mental processing has to be done before a decision is reached and a response is reached.

Rabbitt and Phillips (unpublished data) assessed choice reaction time in 564 individuals aged 20 and 79 years. Performance was assessed on a serial, self-paced 10 choice reaction time (CRT) task. They reported that there were definite changes in CRT with age, between the age of 20 and 30 years the differences between CRT were small but significant and the rate of change progressively accelerates in all subsequent decades. Birren, Woods and Williams (1979) note that there is a 20% decrement in performance on the choice reaction time task between the ages of 20 and 60 years, and this decrements is even greater in older subjects. Gottsdanker (1982) assessed reaction time to a tone in subjects aged 18-93 years, it was reported that reaction times increased with age, by approximately 2 seconds per decade. Coleston and Hindmarch (1989) reported highly significant differences between reaction times in young and elderly subjects, elderly subjects had significantly slower reaction times.

Corpolongo and Salmon (1981) compared reaction times in 20 elderly subjects (aged 60-70 years) and 20 young subjects (aged 20-30 years), using 4 different reaction time tasks. Simple reaction time (subjects had to press a button when a light was illuminated), choice reaction time (subjects had to press the appropriate button when one of three lights illuminated), stimulus-response translation (in this task, one of three digits were randomly presented on the digital response unit, the subjects had three response buttons each corresponding to the digits so that subjects had to press the left button when the number 1 was presented, the centre button when number two was presented and the right button when the number three was presented) and stimulus-stimulus translation (up to three stimulus lights were presented simultaneously, the subjects were required to translate the number of lights into a response position code, so that subjects had to press the left button when one light was presented,
the centre button when two lights were presented and the right button when three lights were presented). Subjects had to complete 30 trials of each of the four tasks. The time difference between the two groups was equivalent for SRT, CRT and stimulus-response translation, however on the stimulus-stimulus translation (task 4), the elderly showed significantly poorer performance.

4.10.5 The Critical Flicker Fusion Task (CFF)

Critical flicker fusion task (CFF) is regarded as an index of overall CNS activity, the ability of the central nervous system to process discrete ‘bits’ of information Hindmarch (1980). Therefore an increase in CFF thresholds is associated with more efficient brain processing i.e. increased alertness and a greater capacity for information processing.

In the task subjects are asked to discriminate flicker from fusion, and fusion from flicker in a set of four red light emitting diodes (LED’s) set at the corners of a 1cm square. Subjects sit 1m from the lights to ensure that the diodes are viewed binocularly and in foveal fixation. The diodes flicker on and off at a 50/50 light-dark ratio according to a square waveform, and at a constantly increasing or decreasing rate of 1 Hz/s over a range of 12-50 Hz. Subjects responses are obtained via pressing a button that they hold in the preferred hand. Individual thresholds are determined via the psychophysical method of limits as an average of the responses on three ascending (flicker to fusion) and three descending (fusion to flicker) presentations, Woodworth and Schlosberg (1958).

The age related deficit with CFF was first noted in 1940’s when data were collected from subjects aged 18-80 years (Brozek and Keys 1945; Weekers and Roussel 1946; Misiak 1947). Colgan (1954) collected CFF data from 42 subjects aged 65 and 95 years, they reported a linear age related decline in CFFT. Coleston and Hindmarch (1989) notes that a decline in CFF threshold begins after 40 years. However Coppinger (1955) notes that the decline was only evident in subjects aged 70+ years.
4.10.6 Summary
Based on the experimental evidence of a slowing of information processing with age, age related declines are expected on the Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT).

4.11 The effects of age and gender on the Syndrom Kurtz Task (SKT)
The Syndrom Kurtz (SKT) is a short test designed to evaluate memory, attention and speed of information processing in elderly subjects. The task consists of 9 subtests assessing memory recall (SKT II, immediate recall, SKT VIII delayed recall) and recognition memory (SKT IX, recognition memory), verbal fluency (SKT I, object naming, SKT III, numerical naming) and attention/concentration tasks (SKT IV, arranging blocks, SKT V, replacing blocks, SKT VI, counting symbols, SKT VII, reverse naming). Each subtest takes a maximum of 60 seconds to complete.

A total of 154 (85 female and 69 male) elderly subjects completed the SKT task subjects were aged 60-85 years with a mean age of 70.8 years. Prior to analysis subjects were classified into one of 5 age groups (60-64, 65-69, 70-74, 75-79, 80+) Table 1 shows the demographics of the subjects.

Table 14: Showing the gender and ageband split of subjects who completed the Syndrom Kurtz Task (SKT).

<table>
<thead>
<tr>
<th>Age-band</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>15</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>65-69</td>
<td>19</td>
<td>21</td>
<td>40</td>
</tr>
<tr>
<td>70-74</td>
<td>20</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>75-79</td>
<td>8</td>
<td>16</td>
<td>24</td>
</tr>
<tr>
<td>80+</td>
<td>7</td>
<td>8</td>
<td>15</td>
</tr>
</tbody>
</table>
Performance on all SKT subtests were analysed to determine whether there were any differences between the subjects in terms of age and gender. The data were analysed using a two way analysis of variance with age band and gender as between subjects factors and the SKT subtests I, II, III, IV, V, VI, VII, VIII, and IX as the dependant variables.

4.11.1 SKT Subtest I (object naming).

*In SKT subtest I, subjects had to name and try to remember 12 objects. The time taken to name all 12 objects was recorded.*

On average subjects took 15.67 seconds to name all 12 objects (SD 5.56) (see Figure 5).

![Scatterplot of Age and SKT I (object naming)](scatterplot.png)

**Figure 5:** Shows the scatterplot of age on object naming (SKT I).

The main effect of age approached significance (F(4, 144) = 2.14; p = 0.06). There was a non-significant trend for age related changes in performance. In the present analysis, subjects aged 75-79 years were faster at the task. (see Table 15).
Table 15: Showing the mean scores and standard deviations in terms of age on performance of SKT I (object naming).

<table>
<thead>
<tr>
<th>Ageband</th>
<th>Mean Time taken to complete the task</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>16.47 seconds</td>
</tr>
<tr>
<td>65-69</td>
<td>15.06 seconds</td>
</tr>
<tr>
<td>70-74</td>
<td>16.80 seconds</td>
</tr>
<tr>
<td>75-79</td>
<td>13.00 seconds</td>
</tr>
<tr>
<td>80+</td>
<td>16.77 seconds</td>
</tr>
</tbody>
</table>

There was no main effect of gender ($F (1, 144) = 2.16; p >0.05$) indicating that object naming was comparable for both male and female subjects. There was no age and gender interaction ($F (4, 144) = 0.90; p >0.05$) on performance of SKT subtest I.

4.11.2 SKT subtest II (immediate recall)

In subtest II subjects had to provide an immediate recall of as many of the 12 items as possible, the number of omissions acted as the dependant variable.

On average subjects made 5.11 omissions from the list of 12 items (SD 1.57) (see Figure 6).
There was a main effect of age band ($F_{(4, 144)} = 2.56, p < 0.05$) indicating that the forgetting rate was significantly different across the age ranges. Post hoc testing revealed that subjects aged 75-79 years had significantly poorer immediate recall than subjects aged 60-64 and 70-74 years (see Figure 7).

There was no main effect of gender ($F_{(1, 144)} = 0.02, p > 0.05$), indicating that the amount forgotten for males and females was comparable. There was no age band gender interaction ($F_{(4, 144)} = 0.09; p > 0.05$).

**Figure 7:** Showing the main effect of age on immediate recall (SKT II).

### 4.11.3 SKT Subtest III (numerical naming)

*In subtest III subjects had to name 10 numbered blocks. The time taken to correctly name all 10 blocks was recorded.*
Scatterplot of Age on SKT III (numerical naming)

Figure 8: Showing the scatterplot of age on numerical naming (SKT III).

On average subjects took 7.88 seconds to name all 10 numbered blocks (SD 2.84) (see Figure 8).

There was no significant main effect of age ($F_{(4, 144)} = 0.21; p >0.05$) indicating that numerical naming was comparable across the age ranges (see Figure 8).

There was a main effect of gender ($F_{(1, 144)} = 4.18; p <0.05$). Female subjects were significantly slower at naming the numerals than male subjects (see Table 16). There was no significant interaction between gender and age ($F_{(4, 144)} = 0.73; p >0.05$).

Table 16: Showing the mean time for male and female subjects to name numerals.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>7.29 seconds</td>
</tr>
<tr>
<td>Female</td>
<td>8.32 seconds</td>
</tr>
</tbody>
</table>

4.11.4 SKT Subtest IV (arranging blocks)

In SKT subtest IV subjects had to arrange the 10 numbered blocks into ascending order. The time taken to complete the task was recorded.
On average subjects took 20.61 seconds to arrange 10 numbered blocks into ascending order (SD 6.66) (see Figure 9).

There was a significant main effect of age (F (4, 144) = 4.47; p= 0.001). Post hoc testing revealed that subjects aged 75-79 and 80+ were significantly slower at arranging the blocks than subjects aged 60-64, 65-69 years (p <0.05) (see Figure 10).

There was no main effect of gender (F (1, 144) = 1.41; p>0.05) and no age band gender interaction (F (4, 144) = 1.10; p>0.05).
4.11.5 SKT Subtest V (rearranging blocks)

In subtest V subjects had to replace the 10 numbered blocks into their original position which was clearly marked out on the board. The time taken to complete the task was recorded.

On average subjects took 14.67 seconds to replace the 10 numbered blocks (SD 3.35) (see Figure 11).

There was a significant main effect of age ($F(4, 144) = 3.67; p < 0.01$). Post hoc testing revealed that subjects aged 75-79 and 80+ were significantly slower at replacing the blocks than subjects aged 60-64, 65-69 and 70-74 years (see Figure 12).

There was a main effect of gender ($F(1, 144) = 4.90; p < 0.05$). Female subjects were significantly slower at replacing the blocks than male subjects (see Table 17). There was no age band gender interaction. ($F(4, 144) = 1.72; p > 0.05$).
Table 17: Showing the mean time for male and female subjects to replace blocks.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>14.37 seconds</td>
</tr>
<tr>
<td>Female</td>
<td>15.61 seconds</td>
</tr>
</tbody>
</table>

Main effect of age on SKT V (replacing blocks)

Figure 12: Showing the main effect of age on replacing blocks (SKT V).

4.11.6 SKT Subtest VI (counting symbols)

In subtest VI subjects had to count the number of symbols contained on a card. The card contained rows of symbols such as circles, triangles, squares and flowers, subjects had to count the number of circles on the card. The card consisted of approximately 119 symbols (43 of which were circles). The time taken to complete the task was recorded.
On average subjects took 19.41 seconds to count all 43 symbols (SD 4.30) (see Figure 13).

There was a main effect of age ($F(4, 144) = 3.08; p = 0.01$). Post hoc testing revealed that subjects aged 75-79 years were beginning to show an age decrement and performance in subjects aged 80+ was significantly slower than performance in subjects aged 60-64, 65-69 years and 70-74 years ($p < 0.05$). As age increased, time taken to complete the task increased, so that older subjects were slower at counting symbols than younger subjects (see Figure 14).

There was no main effect of gender ($F(1, 144) = 0.97; p > 0.05$), indicating that performance of males and females was comparable. There was no interaction between ageband and gender ($F(4, 144) = 0.08; p > 0.05$).
4.11.7 SKT subtest VII (reverse naming)

In subtest VII subjects had to perform a reverse naming task, subjects were presented with two rows of letters e.g. ABBAABAB, subjects had to mentally reverse the letters so that when they saw the letter A they had to respond B and vice versa. The time taken to complete the task was recorded.

On average subjects took 23.01 seconds to perform the reverse naming task (SD 6.27) (see Figure 15).
There was a significant main effect of age (F(4, 144) = 9.79; p < 0.001). Post hoc testing revealed that performance in subjects aged 75-79 and subjects aged 80+ was significantly slower than performance in subjects aged 60-64, 65-69 years and 70-74 years (p < 0.05). Older subjects took longer to perform the reverse naming task. (see Figure 16)

There was no main effect of gender (F(1, 144) = 1.11; p > 0.05), indicating that performance of males and females was comparable. There was no age band gender interaction (F(4, 144) = 1.24; p > 0.05).

Figure 16: Showing the main effect of age on the reverse naming task (SKT VII).

4.11.8 SKT subtest VIII (delayed recall)

In subtest VIII subjects had to provide a delayed recall of the 12 objects that they had seen in subtest I. Delayed recall took place approximately 10 minutes after initial presentation. The number of omissions were recorded.
On average subjects omitted 4.55 of the 12 objects (SD 2.00) (see Figure 17). There was a main effect of age band ($F(4, 144) = 2.73; p < 0.05$). Delayed recall was significantly poorer in older subjects. Post hoc testing with Newman Keul's revealed that performance in subjects aged 75-79 was significantly poorer than subjects aged 60-64 years (see Figure 18).

There was no main effect of gender ($F(1, 144) = 0.00; p > 0.05$), forgetting rates of males and females were comparable. There was no age band gender interaction ($F(4, 144) = 0.31; p > 0.05$).
4.11.9 SKT subtest IX (recognition memory)

In subtest IX subjects had to perform recognition task, they had to identify the original 12 objects from a list of 48 objects. Recognition memory was tested after approximately 12 minutes had elapsed, during which time subjects had completed SKT subtests II to VIII. The number of omissions were recorded.

On average subjects failed to recognise 0.59 objects (SD 1.26) (see Figure 19). There was no main effect of age band ($F_{(4, 144)} = 0.22; p >0.05$) indicating that recognition memory was comparable across the age ranges.
There was no main effect of gender \( (F (1, 144) = 0.77; p >0.05) \), performance of males and females was comparable. There was no age band gender interaction \( (F (4, 144) = 1.11; p >0.05) \).

### 4.11.10 The effect of actual age on SKT task performance

The SKT data were analysed using the Kendall's tau to determine whether there was a relationship between task performance and actual age.

It was reported that there were significant correlations between actual age and performance on SKT II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming) and SKT VIII (delayed recall) (see Table 18).

#### Table 18: Showing the correlation between SKT task performance and actual age.

<table>
<thead>
<tr>
<th>SKT Task</th>
<th>Kendall's Tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKT I (object naming)</td>
<td>-0.04</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>SKT II (immediate recall)</td>
<td>0.04</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>SKT III (numerical naming)</td>
<td>-0.03</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>SKT IV (arranging blocks)</td>
<td>0.20</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>SKT V (replacing blocks)</td>
<td>0.13</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>SKT VI (counting symbols)</td>
<td>0.12</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>SKT VII (Reverse naming)</td>
<td>0.26</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>SKT VIII (delayed recall)</td>
<td>0.19</td>
<td>p&lt;0.0005</td>
</tr>
<tr>
<td>SKT IX (recognition memory)</td>
<td>0.06</td>
<td>p&gt;0.05</td>
</tr>
</tbody>
</table>

### 4.12 The effects of age and gender on the CFF, CRT and SMT tasks

#### 4.12.1 Critical Flicker Fusion (CFF)

In the CFF task, subjects were required to discriminate flicker from fusion and vice versa, the mean of 6 presentation (3 ascending and 3 descending) were recorded.
A total of 154 elderly subjects (84 female, 70 male) aged 60-85 years (mean age of 70.19 years) completed the CFF task (see Table 19).

Table 19: Showing the gender and age-band split of subjects who completed the critical flicker fusion task (CFF).

<table>
<thead>
<tr>
<th>Ageband</th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>15</td>
<td>20</td>
<td>35</td>
</tr>
<tr>
<td>65-69</td>
<td>20</td>
<td>21</td>
<td>41</td>
</tr>
<tr>
<td>70-74</td>
<td>20</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>75-79</td>
<td>8</td>
<td>15</td>
<td>23</td>
</tr>
<tr>
<td>80+</td>
<td>7</td>
<td>8</td>
<td>15</td>
</tr>
</tbody>
</table>

The average CFF threshold was 29.20 Hz (SD 3.05) (see Figure 20).

There was no significant main effect of age (F (4, 144) = 0.70; p >0.05) CFF thresholds were comparable across the ages.

There was a main effect of gender (F (1, 144) = 9.16; p < 0.05), indicating that female subjects had lower CFF threshold than male subjects, indicative of poorer information processing capacity (see Table 20). There was no age sex interaction (F (4, 144) = 0.27; p >0.05).
Table 20: Showing the mean CFFT for male and female subjects.

<table>
<thead>
<tr>
<th>Gender</th>
<th>CFF Threshold (Hz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>29.98 Hz</td>
</tr>
<tr>
<td>Female</td>
<td>28.38 Hz</td>
</tr>
</tbody>
</table>

4.12.2 Choice Reaction Time (CRT)

In the CRT task subjects had to place their index finger on a home key, as soon as a light illuminated (1 of 6), had to move their finger from the home key to press a button which extinguished the light. Subjects were requited to respond to 20 stimuli.

A total of 126 (70 female and 56 male) elderly volunteers aged 60-85 years with a mean age of 70.26 years completed the Choice Reaction Time Task (CRT) (see Table 21).

Table 21: Showing the gender and ageband of subjects who completed the choice reaction time task (CRT).

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>11</td>
<td>16</td>
<td>27</td>
</tr>
<tr>
<td>65-69</td>
<td>17</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>70-74</td>
<td>17</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>75-79</td>
<td>7</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>80+</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

4.12.3 Recognition Reaction Time

Recognition reaction time is the time take to realise that a stimulus has been presented, the time taken for the subject to remove their finger from the home key. It is generally regarded as the attentional aspect of the reaction time task.
Figure 21: Scatterplot of age on reaction time (RRT).

On average subjects mean RRT was 424.54 ms (SD 74.78 ms) (see Figure 21). There was no main effect of age ($F(4, 116) = 0.74; p >0.05$) indicating recognition reaction times were comparable for old and young subjects.

There was a main effect of gender ($F(1, 116) = 6.73; p <0.01$) male subjects had significantly faster recognition reaction times than female subjects (see Table 22). There was no age gender interaction ($F(4, 116) = 2.07; p >0.05$).

Table 22: Showing the mean RRT for male and female subjects.

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean RRT (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>409.10 (60.53)</td>
</tr>
<tr>
<td>Female</td>
<td>436.85 (82.82)</td>
</tr>
</tbody>
</table>

4.12.4 Motor Reaction Time

Motor reaction time is the time taken to respond to the stimulus (i.e. move the finger from the start point to the response button).
The mean motor response time was 330.22 ms (SD 79.65) (see Figure 22). There was no main effect of age ($F_{(4,116)} = 0.54; p >0.05$) indicating that motor reaction time was comparable for the ages.

There was no main effect of gender ($F_{(1,116)} = 0.006; p >0.05$), performance in males was comparable to females. There was no age gender interaction ($F_{(4,116)} = 1.29; p >0.05$).

### 4.12.5 Total Reaction Time

*Total reaction time is the sum of RRT and MRT. It is the time taken for the subject to move their finger from the home key, press the appropriate button and return back to the home key.*
The mean motor response time was 753.60 ms (SD 119.19 ms) (see Figure 23). There was no main effect of age ($F_{(4, 116)} = 0.66; p > 0.05$) total reaction time was comparable for the ages.

There was no significant main effect of gender ($F_{(1, 116)} = 3.25; p > 0.05$. There was no age gender interaction ($F_{(4, 116)} = 1.39; p > 0.05$).

### 4.12.6 The HPRU Sternberg memory task (SMT)

*In the HPRU Sternberg Memory Task (SMT) subjects are required to memorise a set of digits (the stimulus set) ranging from single digits to sets of three and five digits. Following this sequence, subjects are presented with 12 single digit probes, subjects are required to decide whether the probe digits were a part of the stimulus set or not.*

A total of 125 elderly volunteers (69 female and 56 male) elderly volunteers (aged 60-85 years with a mean age of 70.32 years) completed the HPRU Sternberg memory Task (SMT) (See Table 23).
Table 23: Showing the gender and ageband of subjects who completed the Sternberg Memory Task (SMT).

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>11</td>
<td>15</td>
<td>26</td>
</tr>
<tr>
<td>65-69</td>
<td>17</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>70-74</td>
<td>17</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>75-79</td>
<td>7</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>80+</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
</tbody>
</table>

Performance

Figure 24: Showing the scatterplot of age on Sternberg memory performance.

The mean response time was 1258.26 ms (SD 269.62 ms) (see Figure 24).

There was no main effect of age band ($F_{(4, 115)} = 2.07; p > 0.05$) indicating that there was no significant difference between Sternberg Memory performance across agebands. However, there was a trend for older subjects to have slower responses on the task (see Table 24).
Table 24: Showing the ageband mean responses.

<table>
<thead>
<tr>
<th>Ageband</th>
<th>Mean Responses</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>1181.87</td>
</tr>
<tr>
<td>65-69</td>
<td>1194.73</td>
</tr>
<tr>
<td>70-74</td>
<td>1282.35</td>
</tr>
<tr>
<td>75-79</td>
<td>1348.08</td>
</tr>
<tr>
<td>80+</td>
<td>1374.73</td>
</tr>
</tbody>
</table>

There was no main effect of gender ($F_{(1, 115)} = 0.51; p >0.05$), performance of males and females was comparable. There was no age band gender interaction ($F_{(4, 115)} = 0.42; p >0.05$).

4.12.7 The effect of actual age on CFF, CRT and SMT

The CFF, CRT and SMT data were analysed using the Kendall's tau to determine whether there was a relationship between actual age and task performance. It was reported that there was a significant correlation between actual age on recognition reaction time, and Sternberg Memory performance (see Table 25).

Table 25: Showing correlation between CFF, CRT and SMT task performance and actual age.

<table>
<thead>
<tr>
<th>Task</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFF</td>
<td>-0.05</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>RRT</td>
<td>0.15</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>MRT</td>
<td>0.48</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>TRT</td>
<td>0.14</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>SMT</td>
<td>2.19</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>

4.12.8 Summary

SKT subtests were analysed to determine age and gender effects. It was reported that there were main effects of age on immediate recall (SKT II), arranging blocks (SKT IV), replacing blocks (SKT V), counting symbols (VI) the reverse naming task (SKT VII), and delayed recall (SKT VIII) older subjects were significantly slower at performing the speeded tasks, and had poorer memory recall than younger subjects.
There were no age differences on the object naming (SKT I), numerical naming (SKT III), recognition memory (SKT IX) Critical Flicker Fusion task (CFF), Recognition Reaction Time (RRT), Motor Reaction Time (MRT), Total Reaction Time (TRT) or the HPRU Sternberg Memory Task (SMT).

There were no main effects of gender on any of the SKT tasks, Motor Reaction Time (MRT), Total Reaction time (TRT) or the HPRU Sternberg Memory Task (SMT) and no gender-ageband interactions.

Main effects of gender were reported on the CFF task, female subjects had lower CFF thresholds than male subjects, indicative of poorer information processing capacity. There was a main effect of gender on the recognition reaction time task, female subjects had significantly slower recognition reaction times than male subjects. Main differences between the sexes were also reported on SKT V (replacing blocks), and the numerical naming task, female subjects were significantly slower than male subjects on performance of the tasks.

4.13 Relationships between the cognitive function tasks

Having identified age related decrements on the performance tasks, a principal components analysis was performed on the SKT data to try and identify relationships between the SKT subtests. It was hoped that the principal components analysis would identify which aspects of human cognition the SKT subtests were assessing.

4.14 Principal components analysis

Principal components analysis with oblique rotation, and pairwise deletion of missing data were performed on the SKT subtests. Total SKT score was omitted from the analysis, as this score is compiled from the scores on each of the 9
subtests, hence including total score in the analysis would be regarded as double handling data.

Three factors were reported to have Eigenvalues greater than 1 (See Figure 25). Together these accounted for 61.0% of the total variance.

![Factor Scree Plot](image)

**Figure 25:** Showing the scree plot from the principal components analysis of the SKT task.

### 4.14.1 Three Factor Solution

A three factor solution was explored, the 3 factor solution accounted for 61% of the total variance (see Table 26 and Table 27).

<table>
<thead>
<tr>
<th>Factor</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>Cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.73</td>
<td>30.4%</td>
<td>30.4%</td>
</tr>
<tr>
<td>2</td>
<td>1.67</td>
<td>18.6%</td>
<td>49.0%</td>
</tr>
<tr>
<td>3</td>
<td>1.08</td>
<td>12.0%</td>
<td>61.0%</td>
</tr>
</tbody>
</table>
Table 27: Showing the factor loadings for the three factor solution.

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKT I</td>
<td>0.15</td>
<td>0.29</td>
<td>-0.74</td>
</tr>
<tr>
<td>SKT II</td>
<td>0.29</td>
<td>0.29</td>
<td>0.67</td>
</tr>
<tr>
<td>SKT III</td>
<td>0.46</td>
<td>-0.09</td>
<td>-0.57</td>
</tr>
<tr>
<td>SKT IV</td>
<td>0.73</td>
<td>0.15</td>
<td>0.05</td>
</tr>
<tr>
<td>SKT V</td>
<td>0.78</td>
<td>0.12</td>
<td>0.001</td>
</tr>
<tr>
<td>SKT VI</td>
<td>0.63</td>
<td>-0.07</td>
<td>-0.09</td>
</tr>
<tr>
<td>SKT VII</td>
<td>0.78</td>
<td>-0.008</td>
<td>0.06</td>
</tr>
<tr>
<td>SKT VIII</td>
<td>0.30</td>
<td>0.60</td>
<td>0.51</td>
</tr>
<tr>
<td>SKT IX</td>
<td>-0.04</td>
<td>0.84</td>
<td>-0.10</td>
</tr>
</tbody>
</table>

In factor one, SKT subtests IV (arranging blocks), SKT V (replacing blocks) and SKT VII (the reverse naming task) are heavily loaded. These tasks are attention type tasks hence the factor was termed the attention factor.

In factor two, SKT VIII (delayed recall) and SKT IX (recognition memory) were heavily loaded, SKT II (immediate recall) also loaded on the factor, hence this factor was termed the memory factor.

In the third factor a number of the subtests load quite highly, namely SKT I (object naming), SKT II (immediate recall), SKT III (numerical naming) and SKT VIII (delayed recall). Essentially these are speed of naming tasks (I and III) and memory tasks (SKT II, SKT VIII). Since recognition memory did not load very highly, and the memory subtests load with factor two, this factor was termed the speed of naming factor.

Lehfeld, Rudinger, Reitz, Heinrich, Wied, Fornazzari, Pittas, Hindmarch and Erzigkeit (1997) conducted a study in which SKT raw data from subjects in 5 countries were analysed to determine individual factors. Data from the SKT was collected in Germany, Chile, Greece, Russia and England.

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The English sample consisted of 193 healthy elderly community dwelling subjects (128 female, 64 male) aged 60-97 years (with a mean age of 72.17 years). The English subjects attended the HPRU in order to complete the SKT.

Lehfeld et al., (1997) performed a principal components analysis with varimax rotation on the English SKT raw data (SKT subtests I-IX). Instead of factor loadings, the authors chose to use a "perfect congruent weights" approach that uses maximum similarity of factor weights as a rotation criteria. This method was chosen as factor weights are not as dependant on sample characteristics as loadings, hence the authors believed that their method would yield more reliable results.

The authors reported that three factor solution best explained the data. Lehfeld et al. (1997) termed the three factors attention, speed of naming and memory.

The subtests that loaded with factor one were SKT subtests IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols) and SKT VII (reverse naming task). Factor one was termed the attention factor.

Factor two consisted of SKT subtests II (immediate recall), SKT VIII (delayed recall) and SKT IX (recognition memory) this factor was termed a memory factor. Finally The third factor was termed the speed of naming factor and consisted of SKT subtests I (object naming) and SKT III (numerical naming).

Table 28 shows the factor loadings in the German unimpaired subjects (very similar results were obtained in the English sample, however the authors do not report the English factor loadings.)
Table 28: Shows the factor loadings identified by Lehfeld et al., (1997) using the German unimpaired subsection.

<table>
<thead>
<tr>
<th>SKT</th>
<th>Attention Factor</th>
<th>Memory Factor</th>
<th>Speed of Naming Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>0.09</td>
<td>0.006</td>
<td>0.69</td>
</tr>
<tr>
<td>II</td>
<td>0.22</td>
<td>0.78</td>
<td>0.03</td>
</tr>
<tr>
<td>III</td>
<td>0.03</td>
<td>-0.02</td>
<td>0.77</td>
</tr>
<tr>
<td>IV</td>
<td>0.77</td>
<td>0.13</td>
<td>0.07</td>
</tr>
<tr>
<td>V</td>
<td>0.82</td>
<td>0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>VI</td>
<td>0.68</td>
<td>0.12</td>
<td>0.10</td>
</tr>
<tr>
<td>VII</td>
<td>0.73</td>
<td>0.13</td>
<td>-0.02</td>
</tr>
<tr>
<td>VIII</td>
<td>0.37</td>
<td>0.79</td>
<td>-0.01</td>
</tr>
<tr>
<td>IX</td>
<td>-0.04</td>
<td>0.65</td>
<td>0.01</td>
</tr>
</tbody>
</table>

4.14.2 Conclusion

The three factor solution of the SKT raw data (SKT I-IX) agrees with the results obtained by Lehfeldt et al., 1997. Factor one (attention factor) included SKT subtests IV, V, VI and VII. In the present analysis of factor two (memory), SKT VIII and IX load highly and produce results similar to Lehfeldt et al., 1997. However, in the present analysis SKT II did not load very highly with factor two. In the present analysis of factor three, SKT I, II and III load very highly which again agrees with 1997 analysis (with the exception of SKT II).

Overall there was high agreement rate between the two sets of analysis, which helps to substantiate that the factors are genuine and not just specific to a particular sample.

4.15 Age and gender differences in performance of the SKT Factor scores

Having identified SKT factor scores (attention, memory and the speed of naming) the effects of age and gender were examined on each of the factors. The data were analysed using a two way analysis of variance with age band and gender as between subjects factors and the SKT factor scores as the dependant factors.
4.15.1 SKT Factor 1 (attention)
SKT subtests included in the SKT attention factor included arranging blocks (SKT IV), replacing blocks (SKT V), counting symbols (SKT VI) and the reverse naming task (SKT VII).

There was no significant main effect of age (F (4, 144) = 1.45, p>0.05). There were no main effects of gender (F (1, 144) = 1.35, p>0.05) and there was no significant gender ageband interaction (F (4,144) = 1.32, p>0.05).

4.15.2 SKT Factor 2 (speed of naming)
SKT subtests included in the SKT speed of naming factor included SKT I (object naming) and SKT III (numerical naming).

There was no significant main effect of age (F (4, 144) = 1.15, p>0.05). The speed of naming scores were comparable across the ages.

There was no significant main effect of gender (F (1, 144) = 0.14; p>0.05). There was a significant gender ageband interaction (F (4, 144) = 2.85; p<0.05) (see Table 29).

Table 29: Showing the mean factor scores in terms of age and gender for the speed of naming factor

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>60-64</td>
<td>-0.25</td>
<td>0.17</td>
</tr>
<tr>
<td>65-70</td>
<td>0.09</td>
<td>-0.02</td>
</tr>
<tr>
<td>70-74</td>
<td>0.30</td>
<td>-0.67</td>
</tr>
<tr>
<td>75-79</td>
<td>0.08</td>
<td>0.17</td>
</tr>
<tr>
<td>80+</td>
<td>0.33</td>
<td>0.52</td>
</tr>
</tbody>
</table>

4.15.3 SKT Factor 3 (memory)
SKT subtests included in the SKT memory factor included SKT II (immediate recall), SKT VIII (delayed recall) and SKT IX (recognition memory).
There was no significant main effect of age \( (F_{(4, 144)} = 0.04; \ p > 0.05) \) there were no differences between the factor scores of subjects. There were no significant main effect of gender \( (F_{(1, 144)} = 1.06; \ p > 0.05) \) and no significant gender ageband interaction \( (F_{(4, 144)} = 0.35; \ p > 0.05) \).

4.15.4 Summary

There were no age effects for scores on attention or memory, however there was a significant gender ageband interaction on the memory factor, suggesting that there was a tendency for older female subjects to be slightly slower than male subjects on tasks assessing the speed of naming.

4.16 The effect of actual age on SKT factor scores

Analysis of the effects of age band on the factor scores would seem to reveal that there were no effects of ageband on any of the factors. However, it is possible that splitting the data in terms of age band may have affected the results, therefore actual age was correlated with the SKT factor scores using the Kendall’s tau (see Table 30).

<table>
<thead>
<tr>
<th>Task</th>
<th>Kendall's tau</th>
<th>p level</th>
</tr>
</thead>
<tbody>
<tr>
<td>attention factor</td>
<td>-0.04</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>memory factor</td>
<td>0.07</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>speed of naming factor</td>
<td>0.008</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

It was reported that there were no significant correlation's between actual age and the SKT factor scores.
4.17 Principal Components Analysis of the performance data

Principal components analysis was used in the same way as the SKT principal components analysis to determine relationships between all the psychometric tests.

The psychometric tests included in the analysis were SKT subtests 1 to 9, CFF, SMT RRT and MRT. (Total SKT and total reaction time (TRT) were omitted from the analysis as the total SKT scores can be regarded as the sum of the penalties occurred in SKT subtests 1-9, and TRT is the sum of both RRT and MRT, including them in the data could be regarded as double counting).

The data were subject to a principal components analysis with oblique rotation, pairwise deletion of missing data (see Figure 26).

![Plot of Eigenvalues](image)

Figure 26: Showing the Scree plot of the performance data.

Examination of the scree plot would seem to reveal factor solutions consisting of five factors. A five factor solution was explored.
4.17.1 A five factor solution

The five factor solution accounted for 64.7% of the total variance (see Table 31 and 32).

Table 31: Showing the Eigenvalues and percentage of variance.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>Cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1</td>
<td>3.1</td>
<td>23.8</td>
<td>23.8</td>
</tr>
<tr>
<td>Factor 2</td>
<td>1.8</td>
<td>13.8</td>
<td>37.7</td>
</tr>
<tr>
<td>Factor 3</td>
<td>1.3</td>
<td>10.1</td>
<td>47.8</td>
</tr>
<tr>
<td>Factor 4</td>
<td>1.1</td>
<td>8.6</td>
<td>56.5</td>
</tr>
<tr>
<td>Factor 5</td>
<td>1.0</td>
<td>8.1</td>
<td>64.7</td>
</tr>
</tbody>
</table>

Table 32: Showing the factor loadings for each of the psychometric tests on the five factors.

<table>
<thead>
<tr>
<th></th>
<th>Factor 1</th>
<th>Factor 2</th>
<th>Factor 3</th>
<th>Factor 4</th>
<th>Factor 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKT I</td>
<td>0.01</td>
<td>-0.10</td>
<td>0.84</td>
<td>0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>SKT II</td>
<td>0.10</td>
<td>0.82</td>
<td>-0.13</td>
<td>-0.13</td>
<td>-0.05</td>
</tr>
<tr>
<td>SKT III</td>
<td>0.38</td>
<td>-0.09</td>
<td>0.61</td>
<td>-0.09</td>
<td>-0.29</td>
</tr>
<tr>
<td>SKT IV</td>
<td>0.65</td>
<td>0.29</td>
<td>0.13</td>
<td>0.10</td>
<td>0.07</td>
</tr>
<tr>
<td>SKT V</td>
<td>0.67</td>
<td>0.26</td>
<td>0.20</td>
<td>0.19</td>
<td>0.09</td>
</tr>
<tr>
<td>SKT VI</td>
<td>0.71</td>
<td>-0.09</td>
<td>0.04</td>
<td>-0.009</td>
<td>0.08</td>
</tr>
<tr>
<td>SKT VII</td>
<td>0.76</td>
<td>0.19</td>
<td>0.05</td>
<td>0.003</td>
<td>-0.03</td>
</tr>
<tr>
<td>SKT VIII</td>
<td>0.11</td>
<td>0.86</td>
<td>-0.02</td>
<td>0.08</td>
<td>0.17</td>
</tr>
<tr>
<td>SKT IX</td>
<td>0.06</td>
<td>0.14</td>
<td>0.02</td>
<td>0.02</td>
<td>0.86</td>
</tr>
<tr>
<td>CFF</td>
<td>0.05</td>
<td>-0.01</td>
<td>-0.38</td>
<td>0.66</td>
<td>-0.08</td>
</tr>
<tr>
<td>RRT</td>
<td>0.24</td>
<td>-0.17</td>
<td>-0.16</td>
<td>0.67</td>
<td>0.08</td>
</tr>
<tr>
<td>MRT</td>
<td>0.11</td>
<td>0.23</td>
<td>0.04</td>
<td>0.56</td>
<td>-0.47</td>
</tr>
<tr>
<td>SMT</td>
<td>0.58</td>
<td>-0.08</td>
<td>-0.25</td>
<td>0.37</td>
<td>-0.20</td>
</tr>
</tbody>
</table>

Examination of the factor loadings revealed that each of the tasks could be assigned to a factor, and the factors seemed logical. They were termed attention, memory recall, speed of information processing, speed of naming and recognition memory (see Tables 33 and 34).
Table 33: Showing the factors and subtasks included in the 5 factor solution.

<table>
<thead>
<tr>
<th>Factor Names</th>
<th>Subtests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor 1 (attention)</td>
<td>SKT IV, V, VI, VII, SMT</td>
</tr>
<tr>
<td>Factor 2 (memory recall)</td>
<td>SKT II, VIII</td>
</tr>
<tr>
<td>Factor 3 (speed of naming)</td>
<td>SKT I, III</td>
</tr>
<tr>
<td>Factor 4 (speed of information processing)</td>
<td>CFF, RRT, MRT</td>
</tr>
<tr>
<td>Factor 5 (recognition memory)</td>
<td>SKT IX</td>
</tr>
</tbody>
</table>

Table 34: Showing the Eigenvalue, and percentage of variance accounted for by each of the 5 factors.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Tasks in each factor</th>
<th>Factor name</th>
<th>Eigenvalue</th>
<th>% variance</th>
<th>cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>SMT, SKT 4, 5, 6, 7</td>
<td>Attention</td>
<td>3.1</td>
<td>23.8</td>
<td>23.8</td>
</tr>
<tr>
<td>2</td>
<td>SKT 2, 8</td>
<td>Memory recall</td>
<td>1.8</td>
<td>13.8</td>
<td>37.7</td>
</tr>
<tr>
<td>3</td>
<td>CFF, RRT, MRT</td>
<td>Speed of information processing</td>
<td>1.3</td>
<td>10.1</td>
<td>47.8</td>
</tr>
<tr>
<td>4</td>
<td>SKT 1, 3</td>
<td>Speed of naming</td>
<td>1.1</td>
<td>8.6</td>
<td>56.5</td>
</tr>
<tr>
<td>5</td>
<td>SKT 9</td>
<td>Recognition memory</td>
<td>1.0</td>
<td>8.1</td>
<td>64.7</td>
</tr>
</tbody>
</table>

4.18 The effects of age and gender on the 5 performance factor scores

The interaction with age and gender was examined using a two way analysis of variance with two between subjects factors (age band and gender) and factor score for each of the performance factors as the dependant variable.

4.18.1 Factor 1- Attention Factor

Factor 1 consists of the HPRU Sternberg Memory Task (SMT), SKT subtest IV (arranging numbers), SKT Subtest V, (rearranging numbers) SKT Subtest VI, (counting symbols) and SKT Subtest VII, (reverse naming task).

There was no main effect of age $F(4, 114) = 0.33; p>0.05$. There was no difference between the attention factor scores in terms of age. There was no
significant main effect of gender ($F_{(1, 114)} = 0.72; p >0.05$), and there was no significant age and gender interaction ($F_{(4, 114)} = 1.67; p >0.05$).

### 4.18.2 Factor 2 - The Memory Recall Factor

Factor 2 consists of SKT subtest II (immediate memory recall) and SKT Subtest VIII (delayed memory recall).

There was no significant main effect of age ($F_{(4, 114)} = 0.73; p >0.05$) there was no difference between the memory recall factor scores in terms of age. There was no significant main effect of gender ($F_{(1, 114)} = 1.31; p >0.05$). There was no significant age and gender interaction ($F_{(4, 114)} = 1.09; p >0.05$).

### 4.18.3 Factor 3 - The Speed of Naming Task

Factor 3 consists of SKT subtest I (object naming) and SKT Subtest III (numerical naming).

There was no significant main effect of age ($F_{(4, 114)} = 0.53; p >0.05$). There was no difference between the speed of naming factor scores in terms of age. There was no significant main effect of gender ($F_{(1, 114)} = 0.88; p >0.05$). There was no significant age and gender interaction ($F_{(4, 114)} = 0.23; p >0.05$).

### 4.18.4 Factor 4 - The Speed of Information Processing Task

Factor 4 consists of the Critical Flicker Fusion task (CFF) Recognition Reaction Time (RRT) and Motor Reaction Time (MRT).

There was no significant main effect of age ($F_{(4, 114)} = 0.35; p >0.05$). There was no difference between the speed of information processing factor scores in terms of age. There was a significant main effect of gender ($F_{(1, 114)} = 0.47; p = 0.001$). Female subjects were poorer at information processing tasks than male
subjects. There was no significant age and gender interaction \( (F (4, 114) = 1.00; \ p >0.05) \).

### 4.18.5 Factor 5 - Recognition Memory

Factor 5 consists of SKT subtest IX (recognition memory).

There was no significant main effect of age \( (F (4, 114) = 1.82; \ p >0.05) \). There was no difference between the recognition memory factor scores in terms of age. There was no significant main effect of gender \( (F (1, 114) = 1.85; \ p >0.05) \). There was no significant age and gender interaction \( (F (4, 114) = 1.17; \ p >0.05) \).

### 4.19 Performance Factor correlation's with actual age

Analysis of the effects of ageband on the five performance factors would seem to reveal that there was no effect of age band on any of the five performance factors. However, it is possible that splitting the data in terms of age band may have affected the results, therefore actual age was correlated with task performance using Kendall's tau.

In terms of actual age, it would seem that using factor scores, it is possible to predict performance on the recognition task (SKT IX) simply in terms of a subjects age. Actual age was not correlated with task performance on any of the other performance factors (see Table 35).

Table 35: Showing the results of the Kendall's tau. The correlation between actual age and task performance.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Kendall's tau</th>
<th>p Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>124</td>
<td>-0.01</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Memory recall</td>
<td>124</td>
<td>0.06</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Speed of information processing</td>
<td>124</td>
<td>0.006</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Speed of naming</td>
<td>124</td>
<td>0.004</td>
<td>p&gt;0.05</td>
</tr>
<tr>
<td>Recognition memory</td>
<td>124</td>
<td>-0.15</td>
<td>p&lt;0.05</td>
</tr>
</tbody>
</table>
4.20  ADL Factor correlations with actual performance factors

Having identified performance factor scores, and previously identified ADL factor scores, it was questioned whether there is a relationship between ADL and performance factor scores.

An important issue for gerontologists is whether there is a relationship between what the elderly believe is happening to cognitive function (expressed as a subjective rating) and what is happening to them in terms of actual cognitive function (assessed with the use of psychometric tests). If subjective ratings were reliable, then subjects experiencing actual cognitive decline should "feel" that they were experiencing such decline. This is an important issue, as many researchers rely on subjective ratings as accurate reflections of cognitive decline.

A correlation was performed to examine the relationship between the ADL factor scores and the performance factor scores. There are no significant correlations between subjective factor scores (ADL) and the objective factor scores (performance factor scores). Therefore, subjects self reports of what they felt was happening to them was not confirmed when they performed objective tests, to determine what was actually happening to them as a result of age. The subjects did not feel that they were experiencing changes in cognition as a result of age (as expressed in their ADL factor and mean scores). However, it has been shown that age related decrements were noted in actual task performance.

Table 36: Showing the correlation matrix between performance factor scores and ADL factor scores. Performance factor scores 1-5.

<table>
<thead>
<tr>
<th>ADL Factors</th>
<th>Attention</th>
<th>Memory recall</th>
<th>Speed of naming</th>
<th>Speed of information processing</th>
<th>Recognition memory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attention</td>
<td>0.54</td>
<td>0.06</td>
<td>-0.02</td>
<td>0.08</td>
<td>-0.07</td>
</tr>
<tr>
<td>Orientation</td>
<td>-0.09</td>
<td>-0.09</td>
<td>-0.01</td>
<td>0.01</td>
<td>0.08</td>
</tr>
<tr>
<td>Memory</td>
<td>0.10</td>
<td>0.14</td>
<td>0.04</td>
<td>-0.05</td>
<td>-0.05</td>
</tr>
</tbody>
</table>
These results support previous research where actual task performance did not bear any relationship on subjective ratings (Rabbitt and Abson, 1991; Jorm et al., 1997).

Rabbitt and Abson (1990), questioned whether elderly persons were actually aware of their everyday performance capabilities. This research raises the question 'Should we rely on the self reports of elderly persons?'. It would appear that a clearer picture of age related change in performance are only obtained when actual performance is assessed, rather than simply relying on subjective self reports. Perhaps the ideal assessment tool would incorporate both subjective and objective measures.

4.21 Discussion

This chapter aimed to answer three fundamental questions, 'What are the effects of age on the cognitive and psychomotor tasks?', 'How do the tests used relate to each other?' and finally 'Is there a relationship between the subjective and objective assessments of human cognitive function?'

A review of the performance literature on ageing reported that age decrements in performance would be expected on tasks of attention, immediate recall and delayed recall and tasks relying on the speed of information processing.

In terms of the tests included in this thesis age related decrements were expected on SKT I (object naming), SKT II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming task), SKT VIII (delayed recall), the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT) and the HPRU Sternberg Memory Task (SMT).

Age related decrements were not expected on SKT IX (recognition memory) or SKT III (numerical naming).
The results indicated that as expected age related decrements were noted on SKT II (immediate recall), SKT subtests IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming task) and SKT VIII (delayed recall). Age related decrements are noted on tasks assessing selective attention (SKT VI and VII), attention-orientation type tasks requiring a speeded response (SKT IV and V), and immediate and delayed recall (SKT II, VIII).

However age related decrements were not evident on SKT subtest I (object naming), SKT III (numerical naming), SKT IX (recognition task), the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT) or the HPRU Sternberg Memory Task (SMT).

A number of reasons have been proposed to try an account for the lack of age related decrement.

Age related decrements were not observed on SKT I (object naming). Despite the fact that elderly subjects experience word finding difficulties, no age effects were reported on the object naming task. It is possible that the task was too simple for healthy subjects and did not place them under great cognitive demand, given that they only had to name 12 objects. It is possible that age related decrements would only be observed in subjects with cognitive decline, or would only become evident in healthy subjects when the number of stimuli were increased.

There was also no main effect of age on SKT IX (recognition memory). Generally age related decrements are not reported on recognition memory tasks, as the material presented acts as a cue to aid recall (unless the material is too similar to the stimuli and hence disrupts recognition). The lack of effect may also be attributed to a methodological flaw. In general recognition tasks are...
tested exclusively (i.e. without previously testing immediate and delayed recall). However in the SKT task subjects are asked to recognise the stimuli after they have performed both immediate and delayed recall tasks. Therefore, the task is not strictly assessing recognition memory per se.

The Critical Flicker Fusion task (CFF) is a measure of overall central nervous system efficiency, essentially it is a measure of how efficient subjects are at processing information. As information processing is known to decrease with increased age (Salthouse, 1985) age related decrements would be expected on the task. A number of previous researchers have reported age related declines in performance on the CFF (Brozek and Keys 1945; Weekers and Roussel 1946; Misiak 1947; Colgan, 1954). However in this experiment no age effects were reported. Age related decrements were expected on the CFF task, especially as age related slowing in performance had been observed on SKT subtests IV (arranging blocks), V (replacing blocks) and SKT VI (counting symbols), these three tests assess aspects of attention and speed. If no age related decrements were noted on speeded tasks, then the lack of effect on the CFF would have been expected. The lack of an age effect on the CFF maybe due to a failure on the subjects part to learn and fully understand the task. However, since all subjects had at least 6 practice sessions before taking part in the study, it is more likely that the task in it's present form is not age sensitive.

The Choice Reaction Time is a task that has previously been reported as sensitive to the effects of age (Birren, Woods and Williams, 1979; Lindenberger et al, 1993; Corpolongo and Salmon, 1981). However no age effects were reported on the task. It is possible that the methodology of the task was responsible for the lack of effect. This version of the choice reaction time is too simple, subjects only have to respond to one of 6 stimuli, age effects may have been noted if the number of stimuli had been increased.
The Sternberg Memory Task (SMT) employed is not the original Sternberg Memory Scanning task (1966, 1975). In Sternberg's original task, following presentation of the test material, a single digit probe is presented to test the ability to scan the memory set. In the present HPRU version of the task, 12 single digit probes are presented, so subjects have to scan the memory set 12 times, which is very different from the original Sternberg Memory Scanning task. This methodological difference between the tasks may be responsible for the lack of effect of age.

To conclude, the test battery used in this thesis, contained some tasks that were sensitive to the effects of age these included SKT subtests II (immediate recall), IV (arranging blocks), V (replacing blocks), VI (counting symbols), SKT VII (reverse naming) and SKT VIII (delayed recall). A number of tasks that were not found to be age sensitive these included SKT I (object naming), SKT III (numerical naming), SKT IX (recognition memory), the Critical Flicker Fusion task, Choice Reaction Time or the HPRU Sternberg Memory Task.

Having assessed the tasks for age and gender effects, it was then decided to try and identify relationships between the tasks using a principal components analysis. Clear relationships between the psychometric test were identified. Firstly, the SKT task was analysed using the principal components analysis to reveal that a three factor solution identified the most sensible relationships between the subtests. The three factors were termed attention (SKT IV, V, VI, VII), the speed of naming (SKT I and III) and memory (SKT II, VIII, IX). These results mirrored those reported by Lehfeld et al., (1997).

Having identified clear relationships between SKT subtests, a principal components analysis was performed on all the psychometric data (SKT subtests I, to IX, CFF, RRT, MRT and SMT). A five factor solution was accepted. The factors were termed attention (SMT, SKT IV, V, VI and VII), memory recall
(SKT II, VIII), speed of naming (SKT I, III), speed of information processing (CFF, RRT, MRT and TRT) and recognition memory (SKT IX).

Finally, having identified five performance factors and previously identifying three ADL factors a correlation was performed to determine whether there was any relationship between the performance factor scores (attention, memory recall, speed of naming, speed of information processing and recognition memory) and the ADL factor scores (attention, orientation and memory). It was reported that there were no significant correlations between subjective factor scores (ADL) and the objective factor scores (performance factor scores). Subjects self reports of changes in cognition as a result of age were not confirmed in objective tests.

The subjects did not feel that they were experiencing changes in cognition as a result of age (as expressed in their ADL scores) even though age related decrements were noted on some of the objective performance tasks.

These results support previous research where actual task performance did not bear any relationship on subjective ratings (Rabbitt and Abson, 1991; Jorm et al., 1997). Based on this, it was concluded that self report ADL scales may not provide scientists with an accurate picture of cognitive decline. The ideal assessment schedule should include both subjective and objective measures, rather than solely relying on subjective ratings.

Having identified, some tasks that are sensitive to the effects of age, and previously noting that nutritional deficiencies may predispose elderly subjects to cognitive decline. Three experimental chapters have been devoted to assessing the effects of nutritional/dietary supplements on aspects of cognitive and psychomotor performance in samples of healthy community dwelling elderly subjects.
The nutritional supplements examined were multivitamins, ginkgo biloba and glucose.
Chapter Five: The effects of long term multivitamin supplementation on aspects of cognition in an elderly population

5.1 Chapter Outline

The relationship between multivitamin status and cognitive function in patient populations

The effects of nutritional status on cognitive function in elderly populations

The effects of vitamin supplementation on attention in elderly populations

The effects of vitamin supplementation on memory in elderly populations

The effects of vitamin supplementation on the speed of information processing in elderly populations

The effects of vitamin supplementation on intelligence in elderly populations

The effects of vitamin supplementation on mood, well being and behaviour in elderly populations

The effects of long term multivitamin supplementation on aspects of cognitive function

The change in blood vitamin levels

Vitamin A
Vitamin B₁
Vitamin B₂
Vitamin B₆
Vitamin B₁₂
Vitamin E
Vitamin C
Biotin
Folic Acid
The effects of long term multivitamin supplementation on mood and cognitive function in the elderly

The effects of multivitamin supplementation on attention
The effects of multivitamin supplementation on tasks assessing memory recall
The effects of multivitamin supplementation on the speed of naming
The effects of multivitamin supplementation on the speed of information processing
The effects of multivitamin supplementation on recognition memory
The effects of multivitamin supplementation on intelligence
The effects of multivitamin supplementation on mood

This chapter details a study assessing the long term effects of multivitamin supplementation on cognitive function in a sample of 239 healthy community dwelling elderly subjects.

The effects of multivitamin supplementation were examined on objective tasks assessing memory, attention, the speed of information processing, intelligence, and subjective ratings of cognitive failure, anxiety and depression.

The chapter reviews the previous literature in terms of the effects of supplementation on aspects of memory, attention, the speed of information processing and subjective mood and general well being in healthy elderly samples.

5.2 The relationship between multivitamin status and cognitive function

A number of researchers have assessed nutritional deficiencies in samples of elderly subjects, it has been reported that in many cases, the deficiency rates exceed 50% of the population sampled. With such high incidences of
deficiency, researchers have questioned whether nutritional deficiency adversely affects cognitive function.

Researchers have questioned whether poor nutritional status is associated with impaired cognitive function and even psychiatric illness. If the two were linked, then it would be expected that subjects with nutritional deficiency would show impaired cognitive function or may be suffering psychiatric disorders. In chapter two, it was reported that vitamin deficiency was associated with a number of dramatic changes in mood, personality and cognitive function. Disorders such as depression were linked to deficiency in vitamins B₁, B₃, B₆, B₁₂ and biotin; dementia associated with deficiency in vitamins B₁, B₃, B₆, B₁₂ and folic acid, problems with concentration and thought associated with deficiency in vitamins B₁, B₃, B₁₂; and insomnia associated with B₃, B₆ and biotin.

5.3 Nutritional status in patient populations

To test this hypothesis, researchers have assessed blood vitamin concentration in samples of subjects with psychiatric syndromes.

Carney, Ravindran, Rinsler and Williams (1982) examined blood levels of vitamin B₁, B₂ and B₆ in 172 unselected patients admitted to a psychiatric hospital. It was reported that a total of 53% of those admitted were deficient in at least one of the vitamins (41% in one vitamin and 12% in more than one vitamin), more importantly 30% of the sample were deficient in vitamin B₁ and 29% of the sample were deficient in vitamin B₂ even though none of the patients showed any physical signs of deficiency.

Hancock, Hullin, Aylard, King, and Morgen (1985) examined the nutritional status of 216 elderly women admitted to a psychiatric hospital. It was reported that compared to healthy elderly women, the psychiatric patients had lower
blood levels of vitamins C, B₂ and B₆. Interestingly the patients with dementia had worse protein and vitamin status than patients with depression.

Hunter, Jones, Jones and Matthews (1967) assessed blood levels of vitamins B₁₂ and folate in a sample of 150 psychiatric patients aged 17-86 years. It was found that only 3% of the patients had low levels of vitamin B₁₂, whereas 50% of the patients were found to have low levels of folate.

Spindler and Renvall (1989) tested the hypothesis that poor nutritional status is associated with poor cognitive functioning. Blood vitamin status and cognitive function were assessed in 73 subjects aged 77-83 years. The authors reported that if a decline in cognitive function is associated with poor nutritional status, then subjects with cognitive impairment should have lower nutritional status than subjects with optimal cognitive function. All subjects kept three day dietary diaries so that nutritional status could be estimated. Cognitive function was assessed using the Mini Mental Status Examination (MMSE). Subjects were assigned to one of two groups on the basis of their MMSE scores. Group one consisted of subjects with MMSE scores between 21 and 25, they were classed as having mild impairment. The other group consisted of subjects with MMSE scores less than or equal to 20, these were classed as having moderate impairment. Results of the dietary diaries were compared in both groups and with a sample of healthy elderly subjects. A number of marked differences emerged between the three groups. It was reported that subjects with low levels of vitamin B₁, B₂, B₁₂ and folate, had poorer cognitive functioning than those with higher levels of nutritional status. Interestingly serum B₁₂ levels decreased with increasing impairment. This study provides tentative evidence that nutritional status can adversely affect cognitive function.

Sommer and Wolkowitz (1988) conducted a study that assessed the relationship between folic acid levels and cognitive function in a sample of 13 patients aged 51-93 years, who had been admitted into hospital as a result of memory
complaints. Ten of the 13 patients had been diagnosed with probable Alzheimer’s disease. Cognitive function was assessed using the MMSE, the Mattis Dementia Rating Scale, California verbal learning task, Benton naming task and the Benton visual retention task. Mean scores on the MMSE were 18.5 (± 6.3) and it was found that scores on the MMSE were highly correlated with folic acid level. Patients with low folic acid levels had poorer MMSE scores than subjects with higher folic acid levels, indicative of poorer cognitive functioning. It is interesting to note that in this sample folic acid levels were found to affect cognitive function, and all patients had folic acid levels in the normal range. Despite the small sample size included in the study, the results are interesting and warrant further investigations.

Levitt and Karlinsky (1992) examined the relationship between folate, vitamin B₁₂ and severity of cognitive impairment in patients with Alzheimer’s disease. Ninety seven patients were assessed (40 patients had probable AD, 31 had other dementia’s and 26 had mild cognitive impairment). Blood samples were taken to determine blood vitamin levels and patients completed the Mini Mental State Examination. In the Alzheimer’s group vitamin B₁₂ level was significantly correlated with MMSE scores, so that subjects with low blood vitamin B₁₂ levels had poorer MMSE scores than subjects with higher blood vitamin B₁₂ levels. There were no correlations between folate or vitamin B₁₂ level and MMSE in any of the other subjects. These findings suggest a specific relationship between vitamin B₁₂ levels and the severity of cognitive impairment in patients with Alzheimer’s disease.

However it is important to note that the causal relationship in the reported studies is very difficult to decipher, the vitamin deficiency may lead to mental impairments, or the fact that the patient is mentally impaired may lead to poor nutritional status simply because the patient forgets to eat or consume a diet lacking in the essential vitamins. Reynolds et al. (1979) believe that the two could be linked in a vicious circle.
A finding common to all the above studies is vitamin deficiency and disturbances in either cognitive function, mood or personality. Hence these studies would seem to prove tentative evidence that nutritional deficiencies may be associated with psychiatric disorders.
Table 37: Showing the relationship between nutritional status and cognitive functioning in patient populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carney (1982)</td>
<td>Psychiatric inpatients</td>
<td>172</td>
<td>aged 18+</td>
<td>Assessed blood levels of vitamins B, B₂ and B₆</td>
<td>30% deficient in B₁, 29% deficient B₂, 53% deficient in at least 1 vitamin</td>
</tr>
<tr>
<td>Hancock et al. (1985)</td>
<td>Psychiatric inpatients</td>
<td>216</td>
<td>aged 18+</td>
<td>Assessed nutritional status</td>
<td>Patients had lower blood levels of vitamins B₂, B₆, C than controls</td>
</tr>
<tr>
<td>Hunter et al. (1967)</td>
<td>Patients</td>
<td>150</td>
<td>17-86 years</td>
<td>Assessed folate and vitamin B₁₂ status</td>
<td>50% of patients had low folate levels and 3% low vitamin B₁₂</td>
</tr>
<tr>
<td>Spindler and Renvall (1989)</td>
<td>Patients</td>
<td>36</td>
<td>77-83 years</td>
<td>Assessed nutritional status and MMSE</td>
<td>Poor MMSE scores associated with low blood levels of vitamins B₁, B₂, B₁₂ and folate</td>
</tr>
<tr>
<td>Sommer and Wolkowitz (1988)</td>
<td>Patients with memory complaints</td>
<td>13</td>
<td>51-93 years</td>
<td>Assessed folic acid levels, MMSE, Mattis dementia rating scale, California verbal learning task, Benton naming and visual retention tasks</td>
<td>Patients with low folic acid levels had poor MMSE scores</td>
</tr>
<tr>
<td>Levitt and Karlinsky (1992)</td>
<td>Alzheimer's patients</td>
<td>97</td>
<td></td>
<td>Assessed blood vitamin level and cognitive function using the MMSE</td>
<td>Poor MMSE score was correlated with poor vitamin B₁₂ status</td>
</tr>
</tbody>
</table>
5.4 The effects of nutritional status on cognitive function in elderly populations

Based on the above findings where psychiatric disorders have coincided with poor nutritional status, a number of researchers have examined the effect of nutritional status on cognitive function by measuring blood vitamin levels and cognitive function in elderly populations and comparing the two, or by examining the impact of vitamin supplementation on cognitive function in both healthy elderly subjects and patient populations. Researchers have examined the effects of nutritional status on aspects of attention, memory, intelligence and the speed of information processing.

5.5 The effects of vitamin supplementation on attention in elderly populations

Attention is thought to be one aspect of cognitive function which is particularly susceptible to decrements with age (Plude and Hoyer, 1986). Researchers have examined the association between nutritional status or the effects of single and multivitamin supplementation on aspects of attention in elderly subjects.

Bohnen, Jolles and Degenaar (1992) assessed the relationship between nutritional status and cognitive function in a sample of 80 healthy subjects aged 17-85 years. Blood samples were taken to determine vitamin B12 status of the subjects. Cognitive function was assessed using the Stroop task. Subjects were required to complete 4 components of a Stroop task. In the first version subjects had to name 100 colour words (red, yellow, green and blue). In the second version subjects had to name 100 colour spots (red, yellow, green and blue), whilst in the third version, subjects had to complete the classic Stroop task, where 100 colour words were written in coloured ink, the subjects were required to name the colour of the ink. In the fourth version of the task, 20 items from subtest III were randomly selected, small rectangles were drawn around the words, subjects were required to read the word within the rectangle. This
final version of the task induced greater interference than the classic Stroop task. It was reported that subjects with lower blood vitamin levels exhibited poorer Stroop task performance than those with higher blood vitamin levels, especially on version IV the modified Stroop task with increased complexity.

Deijen, van der Beek, Orlebeke and van der Beek (1992) examined the effect of vitamin supplementation on attention in 76 healthy men aged 70-79 years. Subjects were supplemented with vitamin B₆ or placebo for a period of 3 months. Attention was assessed using a cognitrone (a task in which 5 display fields appear on the screen, 4 at the top, 1 at the bottom. The subjects had to compare the figure at the bottom of the screen with the four figures at the top. If the figures at the bottom matched one of the figures at the top of the screen, then the subjects had to press the "yes" response key, and the "no" response key if the figure did not match). The number of correct responses and reaction times were recorded. The task measured aspects of selective attention, form perception and memory. Performance was assessed at baseline and after three months of treatment. It was reported that supplementation had no effect on task performance.

Botez, Botez and Maag (1984) conducted a study in which 49 folate deficient patients aged 22-76 years (mean age 42.2 years) were supplemented with folate 10 mg daily for 7-11 months. Cognitive function was assessed using a digit symbol substitution task, a similarities task and a block design task. It was reported that supplementation with folate resulted in improved performance on all three tasks.

5.5.1 Summary

The Bohnen et al. (1992) study, implicated that selective attention was affected by nutritional status. Two studies have examined the effects of vitamin supplementation on attention in elderly subjects. Deijen et al. (1992) reported that short term supplementation with vitamin B₆ had no effect on performance
of the cognitrone - a task assessing selective attention, form perception and memory. Botez et al. (1984) reported that folate supplementation in depressed folate deficient patients resulted in significant improvements on the DSST, block design and similarities tasks.

Bohnen et al. (1992) observed that Stroop task performance was poorer in subjects with lower blood vitamin B₁₂ levels, the Stroop task is an attention demanding task, requiring the subjects to selectively attend to some aspects of the task (i.e. ink colour) whilst ignoring other aspects of the task (i.e. the written word) therefore, it is possible that nutritional status may affect performance on the task. However to date, no studies have supplemented subjects with multivitamins and examined the effects. In the Deijen et al. (1992) study, performance was assessed using a cognitrone, this task requires elements of attention, speed, form perception and memory, the multi-nature of the task, may result in negative effects simply, because the task requires more than just attention in order to complete it.
Table 38: Summarising the effects of vitamin supplementation on aspects of attention in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Supplement</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bohm et al. (1992)</td>
<td>Healthy subjects</td>
<td>80</td>
<td>17-85 years</td>
<td>No supplement</td>
<td>The relationship between blood vitamin B&lt;sub&gt;6&lt;/sub&gt; level and Stroop task performance</td>
<td>Subjects with poor vitamin B&lt;sub&gt;6&lt;/sub&gt; status had poorer Stroop task performance</td>
</tr>
<tr>
<td>Dejean et al. (1992)</td>
<td>Healthy male subjects</td>
<td>76</td>
<td>70-79 years</td>
<td>Vitamin B&lt;sub&gt;6&lt;/sub&gt; for 3 months</td>
<td>Cognitine</td>
<td>Supplementation had no effect on the task</td>
</tr>
<tr>
<td>Botez et al. (1984)</td>
<td>Folate deficient depressed patients</td>
<td>49</td>
<td></td>
<td>Folate 10 mg for 7-11 months</td>
<td>Block design</td>
<td>Performance on all tasks was improved</td>
</tr>
</tbody>
</table>
5.6 The effects of vitamin supplementation on memory in elderly populations

Problems with memory are common complaints among the elderly (Dixon, Simon, Nowak and Hultsch, 1982, Lowenthal, Berkman, Pierce, Robinson and Trier, 1967).

A number of studies have demonstrated that a deficiency in certain blood vitamin concentrations have resulted in decrements in memory performance.

Goodwin, Goodwin, and Garry (1983) assessed the effect of nutritional status on cognitive functioning in 250 elderly subjects aged 60-94 years. Blood vitamin levels were assessed and correlated with performance on a memory task. Memory was assessed using the paragraph recall task, taken from the Wechsler Memory Scale (subjects had to listen to a paragraph read to them by the investigator, and were required to give immediate recall of the paragraph and delayed recall some 30 minutes later). It was reported that blood vitamin concentration was an important determinant of memory function, in particular low concentrations of vitamin B$_1$, B$_{12}$, vitamin C and folic acid were associated with poor memory recall.

La Rue, Koehler, Wayne, Chiulli, Haaland, and Garry (1997) conducted a follow up to the Goodwin et al. (1983) study in which associations between nutritional status and cognitive performance were examined in 137 elderly subjects (aged 60-90 years). Cognitive performance was assessed using three memory tasks, the WAIS paragraph recall task, WAIS visual reproduction and the Rey Osterreith complex figures test. In the paragraph recall task subjects had to listen to 2 short stories and were required to give immediate recall and delayed recall (30 minutes later). Visual reproduction (subtest from the Wechsler Memory Scale) subjects had to study 4 geometric shapes and attempt to draw them from memory, immediately and after 30 minutes delay. Subjects also had to complete the Rey Osterreith complex figures test which is much the same as
the visual reproduction task but with greater degree of difficulty, both immediate and delayed (30 minutes delay) reproduction of the figures were required. In this study the researchers examined current nutrition-cognition correlations and past nutrition-cognition correlations.

There were several correlations between both current and past vitamin status and task performance. Current use of vitamin C and niacin was positively correlated with Rey Osterreith task performance and approached significance on the visual reproduction test. There were no associations between current vitamin use and paragraph recall. Overall, it was reported that subjects with superior cognitive performance had higher nutrition concentrations.

The study also looked at performance in subjects currently taking supplements and compared to test scores with subjects who were not taking any supplements. There was no difference in performance on the logical memory task or visual reproduction between supplement users and non users.

Past vitamin use was correlated with current psychometric task performance. Past vitamin B users had significantly higher mean scores on the Rey Osterreith immediate and delayed recall. Past vitamin C users had higher visual reproduction and Rey copying scores. Past vitamin E use was correlated with higher scores on Rey copying (immediate) Rey recall (delayed), and visual reproduction scores. Current vitamin E takers also had higher Rey recall (delayed). Generally higher past intakes of vitamins A, E, B6 and B12 were associated with better visuospatial recall. The results of past vitamin intake and current psychometric task performance are interesting, however it must be remembered that past nutritional/supplement use is only one variable that may have affected cognitive function, there are a number of variables that may have effects such as age, current health state, drug use and the time of delay with taking versus not taking vitamins etc. and therefore these results are merely speculative. Nonetheless the findings of this study suggest some associations.
between cognitive performance and dietary intake and/or plasma concentrations of specific nutrients among normally ageing older adults.

Riggs, Spiro, Tucker and Rush (1996) assessed the relationship between blood level of vitamin B$_6$ and B$_{12}$ on cognitive functioning in 70 male subjects aged 54-81 years. Memory was assessed using a word list task, backward digit span, pattern memory and memory for ordered actions. The word list task taken from the CERAD test battery, 10 words were presented at a rate of one every 2 seconds, immediate recall was required. Three consecutive word lists were presented, the total number of words recalled were recorded (maximum 30 words). Performance on the WAIS-R backward digit span, and memory for actions was also assessed. To test memory for ordered actions, subjects were given a sheet listing all the tasks they had completed, they were required to number the tasks in the order they believed they had completed them. To test Pattern memory, a target pattern was presented to the subject, after a brief interval 3 patterns are shown to the subjects, the task is to identify the target pattern, the number of correct responses were recorded.

The authors reported that higher blood levels of vitamin B$_6$ were associated with improved performance on the backward digit span task and the memory for actions task.

The authors also reported a negative finding, there was a trend for subjects with higher plasma concentrations of vitamin B$_{12}$ to show poorer recall on the word list task. Despite this negative finding, the study provided tentative evidence that higher levels of vitamin B$_6$ facilitated performance on complex sequential information processing tasks, i.e. backward digit span (working memory) and memory for actions (episodic memory), where as higher levels of vitamin B$_{12}$ resulted in poorer short term memory.
Tucker, Penland, Sandstead, Milne, Heck, and Klevay (1990) examined the relationship between nutritional status and cognitive function in a sample of 28 healthy elderly subjects aged 60-87 years. Blood vitamin status was assayed to determine blood vitamin status. Cognitive function was assessed using a digit span task (both forward and backward) and tonal memory (subjects heard two sequences of tones, the subjects were required to decide whether the tones were the same or different, the length of the tones increased with successive trials, subjects were required to decide whether the tones were the same both forwards and backwards). Blood vitamin level was correlated with actual task performance. It was reported that carotene level was positively correlated with backward digit span, higher blood levels of carotene were associated with improved digit span performance. Higher blood levels of vitamin B$_2$ were associated with poorer backward digit span. Higher blood levels of carotene were associated with poorer tonal memory, whereas higher blood levels of iron were associated with better tonal memory performance.

Lauque, Wegner, Ousset, Ghisolfi-Marque, Faisant, Baudoin, Petithory, Antoine, Allard, Vellas, and Albaréde (1995) conducted a study that suggested that poor nutritional status may affect cognitive functioning. Lauque et al. (1995) assessed cognitive function using the WAIS picture reproduction task in 91 elderly subjects (mean age 71 years). Based on the results of the WAIS test, subjects were divided into 2 groups, high score and low score. In the high score group, the mean score for women was 55.9 and 55.3 for men. In the low score group, the mean score for women was 28.4 and 23.8 for men. Nutritional intakes were assessed in all subjects, by assessing the content of 3 day dietary diaries. It was reported that subjects in the high score group, had higher intakes of vitamins B$_1$, B$_6$, C and zinc than subjects in the low score group. The study was taken as tentative evidence that insufficient intake of micronutrients might result in cognitive alterations.
5.6.1 Summary
The studies assessing nutritional status and memory function in healthy elderly subjects resulted in a number of correlations between blood vitamin status and cognitive function. In particular it would seem that deficiencies in certain blood vitamin levels have resulted in decrements in memory task performance, decrements have been observed on the paragraph recall task (Goodwin et al., 1983; La Rue et al., 1997), memory for geometric shapes -visual memory and the Rey Osterreith complex figures test (La Rue et al., 1997), backward digit span (Riggs et al., 1996), and memory for actions task (Riggs et al., 1996).

Tucker et al. (1990) reported that lower blood vitamin levels of iron and carotene were associated with poorer digit span performance and improved tonal memory. Lower levels of vitamin B_2 were associated with better backward digit span.

Lauque et al. (1995) reported that subjects with poorer picture reproduction scores had lower intakes of vitamins B_1, B_6, C and zinc.
Table 39: Showing the relationship between blood vitamin status and memory performance in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwin et al.</td>
<td>Healthy elderly</td>
<td>250</td>
<td>60-94</td>
<td>The relationship between blood vitamin status and paragraph recall</td>
<td>Low levels of vitamins B&lt;sub&gt;1&lt;/sub&gt;, B&lt;sub&gt;12&lt;/sub&gt; and C were associated with poor recall</td>
</tr>
<tr>
<td>(1983)</td>
<td>subjects</td>
<td></td>
<td>years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>La Rue et al.</td>
<td>Healthy subjects</td>
<td>137</td>
<td>60-90</td>
<td>The relationship between blood vitamin status and paragraph recall, visual reproduction and Rey Osterreic complex figures</td>
<td>Higher levels of vitamin C and B&lt;sub&gt;3&lt;/sub&gt; resulted in better performance on the Rey Osterreic complex figures. Higher past intakes of vitamins E, A, B&lt;sub&gt;6&lt;/sub&gt;, B&lt;sub&gt;12&lt;/sub&gt; result in better visuospatial recall</td>
</tr>
<tr>
<td>(1997)</td>
<td></td>
<td></td>
<td>years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Riggs et al.</td>
<td>Healthy male</td>
<td>70</td>
<td>54-81</td>
<td>The relationship between vitamin B&lt;sub&gt;6&lt;/sub&gt; and B&lt;sub&gt;12&lt;/sub&gt; on word list task, backward digit span, pattern memory and memory for actions</td>
<td>Higher levels of vitamin B&lt;sub&gt;6&lt;/sub&gt; were associated with better backward digit span, and memory for actions. Higher levels of vitamin B&lt;sub&gt;12&lt;/sub&gt; associated with poorer word list recall</td>
</tr>
<tr>
<td>(1996)</td>
<td>subjects</td>
<td></td>
<td>years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tucker et al.</td>
<td>Healthy subjects</td>
<td>28</td>
<td>60-87</td>
<td>The relationship between vitamin status and digit span and tonal memory</td>
<td>Higher levels of carotene were associated with better digit span and poorer tonal memory. Higher iron levels associated with better tonal memory and higher vitamin B&lt;sub&gt;2&lt;/sub&gt; with poorer backward digit span</td>
</tr>
<tr>
<td>(1990)</td>
<td></td>
<td></td>
<td>years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lauque et al.</td>
<td>Healthy elderly</td>
<td>91</td>
<td>Mean</td>
<td>The relationship between nutritional status and picture reproduction scores</td>
<td>Subjects with better picture reproduction scores had higher intakes of vitamins B&lt;sub&gt;1&lt;/sub&gt;, B&lt;sub&gt;6&lt;/sub&gt;, C and zinc</td>
</tr>
<tr>
<td>(1995)</td>
<td></td>
<td></td>
<td>age 71</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.7 The effects of multivitamin supplementation on memory in elderly populations

Based on the above findings, where poor nutritional status was associated with decrements in cognitive function, a number of researchers have attempted to improve nutritional status in healthy elderly and patient populations by supplementation with either single or multivitamins, and have observed the effects of improved nutritional status on aspects of memory performance.

Deijen, van der Beek, Orlebeke, and van den Berg (1992) conducted a 12 week study to examine the effects of vitamin B₆ supplementation on cognitive functioning in 38 elderly men aged 70-79 years. Memory was assessed at baseline and after 12 weeks using the Sperling whole report task, a paired associate word list task, and a short term memory task.

The Sperling whole report task, an iconic/sensory memory task in which 30 slides of 12 letters were flashed onto the screen for duration's of 250, 150 and 50 ms. Immediately after each flash, subjects had to recall as many letters as possible in 6 seconds. In the paired associate word list task, 9 pairs of words were presented onto a computer screen at a rate of one set every 3 seconds. After all 9 pairs had been presented with one of the pairs of words and were required to provide its paired word, by pressing the key that corresponded with the word, e.g. the words John and grocer were presented, so when presented with the name John subjects have to press the grocer key. Recall of the paired word was required immediately and after a delay of one hour. Subjects also had to complete a short term memory task, much like the Sternberg memory task, but with letters rather than numbers. A memory set of four letters is flashed on a screen for five seconds, following the memory set a number of 41 trials is presented containing two or four letters, placed on the corners of an imaginary square. If a letter from the memory set is flashed onto the screen then subjects have to press "yes", and "no" if the letter was not from the memory set. Deijen et al. (1992) found that supplementation with vitamin B₆ had no effect on short
term memory, immediate recall of the paired associate task, the short term memory task, or the Sperling whole report task. However supplementation with vitamin B₆ facilitated delayed recall of the paired associate word list task.

Tolonen, Halme, and Sarna (1988) assessed the effect of supplementing 44 elderly subjects with vitamin B₆ or placebo for 12 months. Memory was assessed using the digit span task (forward and backward); paragraph recall (immediate and delayed recall) and the clock test ( a visual recognition and motor production task). After 12 months of supplementation, the vitamin B₆ treated group showed performance improvements on the immediate story recall, and the clock task, compared to the placebo treated group. Performance in the placebo group deteriorated on immediate story recall, and the clock recognition task.

Burr, Hurley, and Sweetnam, (1975) assessed blood level of vitamin C in 828 community dwelling elderly subjects aged 59-97 years. Two hundred and ninety seven of the subjects with low vitamin C level were admitted to a two year controlled trial, in which subjects received either placebo or vitamin C for two years (150 mg/day for 12 weeks and 50 g/day maintenance dose for the rest of the two years). The authors were interested to see whether supplementation with vitamin C would affect mental functioning on the Inglis test of short term memory- a paired associate word list task (in which a higher score is indicative of poorer memory). It was reported that long term supplementation with vitamin C had no effect on performance of the task.

A number of researchers have assessed the effects of vitamin supplementation on memory function in patient populations.

Botez, Botez and Maag (1984) conducted a study in which 49 folate deficient patients aged 22-76 years (mean age 42.2 years) were supplemented with 10 mg
folate daily for 7-11 months. Memory was assessed using the digit span task. It was reported that performance on the task was significantly improved.

Šrám, Binková, Topinka, Kotešovec, Hanel, Fojtíková, Klaschka, Prošek and Gebhart (1990) assessed the effect of supplementation with vitamin C and E on memory performance in a sample of 160 subjects from two homes for the elderly. Subjects were aged 60-90 years. Subjects were supplemented with antioxidant vitamins C and E for a period of 2 years. A sample of 80 subjects completed psychometric tasks to assess the effects of antioxidant supplementation on cognitive performance. Cognitive performance was assessed using the digit span task (forward and backward), and paragraph recall. Performance was assessed at baseline and after 3, 6, 12, 18 and 24 months. It was found that supplementation with vitamin C and E had no effect on the digit span or paragraph recall tasks.

5.7.1 Summary
Memory is an aspect of cognitive function that has shown to be sensitive to the effects of nutritional status. Examination of the deficiency studies, report that poor nutritional status is associated with decrements in memory performance especially on the backward digit span task, paragraph recall task and visual memory tasks.

In chapter two, some consideration was given to the role of vitamins within the body and central nervous system. Analysis of this data would seem to suggest that a deficiency in B complex vitamins would result in memory problems, this is true for vitamins B1, B2, B3, B6, B12 and folic acid as all these vitamins are essential for the synthesis of neurotransmitters.

Based on such evidence, a number of research teams have assessed the effects of multivitamin supplementation on memory function. The results would seem to indicate that supplementation with the B complex vitamins was associated
with a number of performance improvements, these were evident on delayed recall of the paired associate word list task (Deijen et al., 1992), immediate recall of the paragraph recall task and the clock task (Tolonen et al., 1988), and supplementation with folate was associated with improved digit span (Botez et al., 1984).

Two researchers have previously examined the effects of vitamin C and E on memory performance, it would appear that supplementation with vitamin C and E had no reported effect on memory function. However, as this conclusion has been reached using only two studies, further research is warranted in order to resolve the issue.
Table 40: Summarising the effects of vitamin supplementation on aspects of memory in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Supplement</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deijen et al.</td>
<td>Healthy elderly men</td>
<td>38</td>
<td>70-79 years</td>
<td>Vitamin B₆ for 3 months</td>
<td>Sperling whole report, paired associate</td>
<td>Vitamin B₆ facilitated long term recall of the paired associate word list, short term memory task</td>
</tr>
<tr>
<td>(1992)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>word list, short term memory task</td>
<td></td>
</tr>
<tr>
<td>Tolonen et al.</td>
<td>Elderly subjects</td>
<td>44</td>
<td>66-96 years</td>
<td>Vitamin B₆ for 1 year</td>
<td>Digit span, logical memory, clock test</td>
<td>Supplementation improved immediate recall of the logical memory task and the clock test</td>
</tr>
<tr>
<td>(1988)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burr et al. (1975)</td>
<td>Healthy elderly subjects</td>
<td>297</td>
<td>Mean age 78 years</td>
<td>Vitamin C for 2 years</td>
<td>Inglis short term memory task</td>
<td>No effect</td>
</tr>
<tr>
<td>Botez et al. (1984)</td>
<td>Folate deficient depressed patients</td>
<td>49</td>
<td>22-76 years</td>
<td>Folate 10 mg daily for 7-11 months</td>
<td>Digit span task</td>
<td>Folate supplementation significantly improved performance on the task</td>
</tr>
<tr>
<td>Šrám et al. (1990)</td>
<td>Elderly subjects in a residential home</td>
<td>80</td>
<td>60-90 years</td>
<td>Vitamin C and E for 2 years</td>
<td>Paragraph recall, Digit span</td>
<td>No effect</td>
</tr>
</tbody>
</table>
5.8 The effects of vitamin supplementation on the speed of information processing in elderly populations

The speed of information processing is an aspect of cognitive function that is susceptible to decrements with age (Salthouse, 1985; Welford, 1977; Lindenberger et al., 1993). A number of studies have been conducted to assess the effects of nutritional status or multivitamin supplementation on the speed of information processing.

Riggs, Spiro, Tucker and Rush (1996) assessed the relationship between blood level of vitamin B₆ and B₁₂ on cognitive function using a pattern comparison task and a continuous performance task in 70 male subjects aged 54-81 years. In the pattern comparison task subjects had to choose the odd pattern from 3 similar patterns, the time taken to respond was recorded. In the continuous performance task, a string of letters were presented on a computer screen, subjects had to press a button every time they saw a capital letter S, response times were recorded. It was reported that there was no relationship between nutritional status and performance on either task.

Deijen, van der Beek, Orlebeke, and van den Berg (1992) supplemented 38 healthy men aged 70-79 years, with vitamin B₆ for 3 months. Performance was assessed using the Vienna task, and a speed of processing task, essentially a multistimuli reaction time unit, optical stimuli in a number of colours (white, yellow, red, green and blue) are represented in 10 different positions. Subjects have to respond by pressing one of 5 reaction keys assigned to each of the colours. Two additional white lamps set apart from the coloured lamps, are also illuminated, these lamps were extinguished by stepping on left or right foot pedals. Two acoustic stimuli (high/low tone) are assigned to 2 rectangular "tone" keys, and had to be pressed when the tone was heard. The number of correct, incorrect, delayed and missed responses were recorded.
In the speed of processing task - a cross was randomly presented in one of the 4 corners of a screen for 100 ms, subjects had a response key pad with buttons at the 4 corners, when an cross appeared in a corner the subjects had to press the button diagonally opposite to where the cross appeared. Subjects had to complete a total of 51 trials, reaction time and number of correct responses were recorded.

Deijen et al. (1992) reported that supplementation with vitamin B₆ had no effect on performance of either the perceptual motor skill or the speed of processing task.

Burr, Hurley and Sweetnam (1975) assessed cognitive performance using a reaction time task. In the task, subjects had to respond by pressing a button when a light illuminated. Performance was assessed in a sample of 297 elderly subjects aged 59-97 years with low blood vitamin levels of vitamin C. Subjects were supplemented with oral vitamin C 150 mg for 12 weeks to initially raise the blood vitamin levels and then 50 mg daily dose until two years had elapsed. After the two year period, performance was reassessed, no performance improvements were associated with a rise in blood vitamin C levels.

5.8.1 Summary
In the reported studies, Riggs et al. (1996) reported that there was no relationship between nutritional status and tasks assessing the speed of information processing. Deijen et al. (1992) and Burr et al. (1975) reported that supplementation with vitamin B₆ or vitamin C had no effect on tasks assessing the speed of information processing.
Table 41: Summarising the effects of nutritional status on the speed of information processing in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Supplement</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deijen <em>et al.</em> 1992</td>
<td>Healthy elderly men</td>
<td>38</td>
<td>70-79 years</td>
<td>Vitamin B₆ for 3 months</td>
<td>Vienna test battery, speed of processing task</td>
<td>B₆ had no effects on the tasks</td>
</tr>
<tr>
<td>Burr <em>et al.</em> 1975</td>
<td>Healthy elderly subjects</td>
<td>297</td>
<td>59-97 years</td>
<td>Vitamin C for 2 years</td>
<td>Reaction time</td>
<td>Vitamin C had no effect on the task</td>
</tr>
<tr>
<td>Riggs <em>et al.</em> 1996</td>
<td>Healthy subjects</td>
<td>70</td>
<td>54-81 years</td>
<td>No supplement</td>
<td>Relationship between nutritional status and performance on a continuous performance task and pattern comparison</td>
<td>No relationship between nutritional status and performance on the tasks</td>
</tr>
</tbody>
</table>
5.9 The effects of vitamin supplementation on intelligence in elderly populations

Previous research has revealed that supplementation has beneficial effects on intelligence scores of school children and teenagers (Benton and Roberts, 1988; Benton and Butts, 1990; Benton and Cook, 1991).

Since the speed of processing is thought to reflect intelligence and age results in decrements in the speed of information processing (Salthouse, 1985; Welford, 1977; Rabbitt 1965) age related decrements would be expected on tasks assessing intelligence. In line with this the effects of supplementation on intelligence in elderly subjects would be expected to be similar to the results of supplementation on the speed of information processing.

La Rue, Koehler, Wayne, Chiulli, Haaland, and Garry (1997) assessed cognitive performance in 137 elderly subjects (aged 60-90 years). Cognitive performance was assessed using the abstraction scale from the Shipley-Hartford intelligence scale (subjects had to specify missing items in serial logically determined series (e.g. AB BC CD D) ). This study was a follow up to the Goodwin et al. (1983) study, and hence the researchers were able to compare both current use and past use of vitamins on cognitive performance. It was found that subjects previously taking vitamins A, B6, B12 and E had better abstract task performance. Higher vitamin B1, B2 and folate levels were positively correlated with abstraction test performance, so subjects with higher vitamin B1, B2 and folate levels had better abstract performance. Current vitamin E use was associated with higher mean abstraction scores than non users.

Smith, Clark, Nutt, Hayward and Perry (in press) assessed the effects of anti-oxidant supplementation on intelligence in healthy elderly volunteers. Two hundred and five healthy elderly volunteers aged 60-80 years were supplemented with either an anti-oxidant preparation (consisting of beta carotene 12 mg, vitamin E 400 mg and vitamin C 500 mg) or placebo for 12
months. Intelligence was assessed using the New Adult Reading Task (NART). Blood samples were taken and performance assessed at baseline and after 4, 8 and 12 months. It was reported that subjects who showed a large increase in vitamin C level following supplementation made significantly fewer errors on the NART.

Researchers have assessed the effects of multivitamin supplementation on intelligence patient populations using the Mini Mental State Examination (MMSE).

Abalan, Mancier, Dartigues, Décamps, Zapata, Saumtally and Galley, (1992) conducted a pilot study to assess the impact of nutritional supplementation on cognitive function in 29 patients with Senile Dementia of the Alzheimer Type (SDAT). All patients were aged over 66 years, had a score between 2 and 23 on Folstein's Mini Mental State Examination (MMSE), and had fulfilled the NINCDS-ADRDA criteria of SDAT. Patients were randomised to receive either a multivitamin supplement (n = 15) or placebo (n = 14) for a period of 105 days. (The multivitamin supplement consisted of vitamins A, C, E, B₁, B₂, B₆, B₁₂, biotin, folic acid, calcium, magnesium, phosphorus, L-tryptophan, iron, zinc and a number of trace elements). Cognitive function was assessed using the MMSE at baseline, and after 35, 70 and 105 days.

At baseline there was no significant difference between the MMSE scores of the 2 groups. However, after treatment for 105 days, the supplemented group showed a significant improvement in MMSE scores compared to baseline and the placebo group. This pilot study provided tentative evidence for a role of nutrition in the pathogenesis of SDAT.

Blass, Gleason, Brush, DiPonte, and Thaler (1988) noted that a number of studies have implicated that the activities of thiamine-dependant enzymes appear to be reduced in the brains of patients with Alzheimer's disease. Based
on this hypothesis, Blass et al. (1988) supplemented 11 elderly patients (aged 59-83 years) with vitamin B₁ or placebo for a period of 3 months. All patients had a diagnosis of probable senile dementia of the Alzheimer’s type (SDAT). The patients received vitamin B₁ and placebo for a period of 3 months in a crossover design. Performance was assessed using the (MMSE). It was reported that supplementation with vitamin B₁ scores on the (MMSE) were significantly improved.

Cunha, Rocha, Peixoto, Motta, and Barbosa (1995) assessed the effect of vitamin B₁₂ supplementation on performance in 19 demented patients with a mean age of 77.5 years who were deficient in vitamin B₁₂. It was reported that 16 of the 19 patients continued to show progressive decline during follow up visits (3 to 24 months). The only patients who showed some improvement on the MMSE had mild dementia with a history of less than 2 years. The authors concluded that screening for vitamin B₁₂ deficiency should be considered in patients with early of dementia symptoms.

Sano, Ernesto, Thomas, Klauber, Schaf, Grundman, Woodbury, Growdon, Cotman, Pfeiffer, Schneider and Thals (1997) supplemented 341 dementia patients with selegiline, vitamin E or placebo for a period of 2 years. Patients were randomised to receive selegiline 10 mg daily (n = 87); vitamin E 200 iu a day (n = 85); selegiline and vitamin E (n = 85) or placebo (n = 84). Assessments were made using the MMSE. After 2 years it was found that the placebo group had the highest score on the MMSE and the vitamin E treated group had the lowest.

Two studies have reported no effect and even a continued decline in cognitive function following treatment with multivitamins or vitamin B₁.

Burns, Marsh and Bender (1989) supplemented 19 geriatric patients (age 76-86 years) with multivitamins and placebo for 6 weeks in a crossover design. All
patients were previously diagnosed as having multi-infarct dementia (MID), patients were assessed using the MMSE. It was reported that supplementation resulted in no changes on MMSE scores.

Nolan, Black, Sheu, Langberg, and Blass (1991) 15 outpatients aged 59-87 years were enrolled in a study which assessed the effects of vitamin B₁ on dementia progression in a year long study. Fifteen subjects aged 59-87 years were randomly allocated to receive either placebo or vitamin B₁ (3g/d) for 12 months. Cognitive function was assessed using the Mini Mental State Examination (MMSE). Cognitive function was assessed at baseline and at 3 monthly intervals. Ten patients completed the trial (5 from the placebo group and 5 from the vitamin B₁ group). Cognitive function was found to decline in both groups for example MMSE scores fell from 16.6 to 10.4 in the vitamin B₁ group, and in the placebo group they fell from 16.3 to 12.5 during the 12 month trial. This double blind placebo controlled parallel group study did not support the hypothesis that vitamin B₁ either improves cognition or slows the progression of cognitive decline in patients with SDAT. The two studies that have failed to show any protective effects on cognition following treatment with either mono vitamin or multivitamin supplementation only contain very small sample sizes, and it is possible that more positive effects may have been evident had the sample sizes been increased. Therefore, the studies do not satisfactorily refute the hypothesis that nutritional supplementation affects cognitive function.

5.9.1 Summary
Since choice or complex reaction time is thought to reflect intelligence, it was assumed that the effects of supplementation on intelligence would echo the results of supplementation on information processing. However it was reported that the effects of supplementation on intelligence in elderly subjects were much the same as those reported in children and teenagers.
It was reported that higher blood levels of vitamins B₁, B₂, folate and vitamin E had higher abstraction scores than subjects with poorer blood vitamin status (La Rue et al., 1997). In SDAT and MID patients, MMSE scores were found to be improved following supplementation with certain vitamins, vitamin B₁ (Blass et al., 1988); multivitamins (Abalan, et al., 1992); Vitamin B₁₂ (Cunha et al., 1995) and Vitamin E (Sano et al., 1997).

Two patients studies reported that supplementation with multivitamins or vitamin B₁ had no effect on MMSE scores of SDAT or MID patients (Burns et al., 1989; Nolan et al., 1991). In the Burns et al. (1989) study 19 patients were supplemented with multivitamins for a period of 6 weeks, and in the Nolan et al. (1991) study only 15 patients were supplemented with vitamin B₁ for 12 months. It is possible that multivitamins need to be given for longer than 6 weeks, as it usually takes about 12 weeks to observe increases in blood vitamins. Hence if patients had been treated for longer periods, beneficial effects may have been reported. In the Nolan et al. (1991) study, there were only 10 evaluable patients at the end of the treatment period, hence it is possible that the small sample size may be responsible for the lack of effect.

The results of the supplementation studies in patients report many inconsistencies, however this may be due to the fact that the rate of cognitive decline in patients with probable SDAT varies immensely. In the Nolan et al. (1991) study some patients showed no change on the MMSE, however others declined by 12 points. Therefore any results are merely speculative, but the mixed results certainly highlight the fact that certain sectors of society would benefit from supplementation.

Many of the above studies have demonstrated the benefits of obtaining a nutritionally balanced diet, providing all the required vitamins and minerals necessary for optimal functioning. This chapter has also outlined the fact that there are sectors in society particularly elderly persons who do not gain enough
nutrients from their daily diet, therefore supplementation may be a way to help correct nutritional deficiencies.
Table 42: Showing the effects of nutritional status on intelligence in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Supplement</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>La Rue et al. (1997)</td>
<td>Healthy subjects</td>
<td>137</td>
<td>60-90 years</td>
<td>No supplement</td>
<td>Relationship between nutritional status and Abstraction task</td>
<td>Higher levels of Vitamin B₁, B₂, folate and niacin associated with better performance. Past use of vitamin A and E and current use of vitamin E supplement was associated with improved performance</td>
</tr>
<tr>
<td>Smith et al. (1999)</td>
<td>Healthy elderly</td>
<td>205</td>
<td>60-80 years</td>
<td>Anti-oxidant (beta carotene, C and E) or placebo for 1 year</td>
<td>New Adult Reading Task (NART)</td>
<td>Subjects who showed a large increase in vitamin C level following supplementation made significantly fewer errors on the NART.</td>
</tr>
<tr>
<td>Abalan et al. (1992)</td>
<td>SDAT patients</td>
<td>29</td>
<td>78-92 years</td>
<td>Multivitamin for 105 days</td>
<td>MMSE</td>
<td>MMSE improved</td>
</tr>
<tr>
<td>Blass et al. (1988)</td>
<td>Alzheimer's patients</td>
<td>11</td>
<td>59-83 years</td>
<td>Vitamin B₁ for 12 weeks</td>
<td>MMSE</td>
<td>MMSE improved</td>
</tr>
<tr>
<td>Cunha et al. (1995)</td>
<td>Demented patients</td>
<td>19</td>
<td>Mean age 77.5 years</td>
<td>Vitamin B₁₂</td>
<td>MMSE</td>
<td>MMSE returned to normal in 3 patients, got worse in 16 patients</td>
</tr>
<tr>
<td>Sano et al. (1997)</td>
<td>Alzheimer patients</td>
<td>341</td>
<td>65-81 years</td>
<td>Selegiline, Vitamin E or placebo for 2 years</td>
<td>MMSE</td>
<td>Supplementation with vitamin E was associated with improved MMSE</td>
</tr>
<tr>
<td>Burns et al. (1989)</td>
<td>SDAT patients</td>
<td>19</td>
<td>76-86 years</td>
<td>Multivitamins for 6 weeks</td>
<td>MMSE</td>
<td>No change in MMSE</td>
</tr>
<tr>
<td>Nolan et al. (1991)</td>
<td>Alzheimer patients</td>
<td>15</td>
<td>59-87 years</td>
<td>Vitamin B₁ for 12 months</td>
<td>MMSE</td>
<td>MMSE scores got worse</td>
</tr>
</tbody>
</table>
5.10 The effects of vitamin supplementation on mood, well being and behaviour in elderly populations

Vitamins are important for the synthesis and production of neurotransmitters especially serotonin, dopamine, noradrenaline and GABA, hence a deficiency in certain multivitamins may result in observed changes in mood and personality. A number of researchers have assessed the effects of altered blood vitamin level and supplementation with single and multivitamins on aspects of subjective mood, general well being and behaviour in elderly subjects.

Chomé, Paul, Pudel, Bleyl, Heseker Huppe, and Kubler (1986) assessed mood and personality in elderly subjects aged 59-91 years. Subjects were divided into 2 groups on the basis of nutritional status, a deficient group (which consisted of subjects with a deficiency in at least one vitamin) and a control group (non deficient subjects). Mood and personality were assessed using the Freiburg Personality Inventory (FPI- which assess 12 personality traits) it was reported that vitamin deficient subjects had higher depression, fatigue and emotional instability scores than control subjects.

Smith, Clark, Nutt, Hayward and Perry (in press) assessed the effects of anti-oxidant supplementation on mood and cognitive failure in healthy elderly volunteers. Two hundred and five healthy elderly volunteers aged 60-80 years were supplemented with either an anti-oxidant preparation (consisting of beta carotene 12 mg, vitamin E 400 mg and vitamin C 500 mg) or placebo for 12 months. Mood was assessed using the Profile of Mood States (POMS) and cognitive failure assessed using Broadbent et al. (1982) Cognitive Failure's Questionnaire (CFQ). Blood samples were taken and assessments were made at baseline and after 4, 8 and 12 months. It was reported that subjects who showed a large increase in vitamin C level following supplementation felt significantly more composed, elated and confident than subjects who showed small declines in their vitamin C level, similarly these subjects reported fewer errors of memory, attention and action during their everyday activities.
Bouchet, Guillemin and Briançon (1996) assessed the quality of life (QOL) in 1896 volunteers aged 35-60 years. Subjects were randomly allocated to one of four groups: group 1 (n = 180) who were supplemented with a multivitamin complex (consisting of vitamins A, C, E, zinc and selenium) for 2 months, group 2 (n = 180) received placebo for 2 months and groups 3 (n = 768) and 4 (n = 768) received no treatments. All subjects were sent a QOL questionnaire (The Short Form Health Survey Questionnaire) in December 1993 and again in 2 months later. It was reported that supplementation with multivitamins had no effect on any of the measures of quality of life which included physical and social function, physical role, emotional role, mental health, energy-fatigue, pain and general health perceptions.

Šrám, Binková, Topinka, Kotešovec, Hanel, Fojtíková, Klaschka, Prošek and Gebhart (1990) assessed the effect of supplementation with vitamin C and E on memory performance in a sample of 160 subjects from two homes for the elderly. Subjects were aged 60-90 years. Subjects were supplemented with antioxidant vitamins C and E for a period of 2 years. A sample of 80 subjects completed psychometric tasks to assess the effects of antioxidant supplementation on subjective ratings. Various aspects of mood were assessed including pain, fear, eating difficulties, sleep disorders, anger, fatigue, memory disturbances and motoric difficulties. Subjective ratings were completed at baseline and after 3, 6, 12, 18 and 24 months. It was reported that supplementation with vitamin C and E significantly improved ratings on the scale, especially motoric ability and mood.

Smidt, Cremin, Grivetti, and Clifford (1991) assessed the effects of vitamin B₁ supplementation on the general health and well being of 80 elderly women aged 65-92 years with marginal vitamin deficiency. Subjects were treated with either vitamin B₁ or placebo for a period of 6 weeks. Well being was examined by getting the subject to rate a number of mood states using a 10 point scale (where
0 = never have the condition and 10 = always have the condition), the conditions examined were concentration, tenseness, appetite, soreness/burning hands and feet, sleep, general well being (how they felt) and ability to perform activities required. It was found that the B₁ supplemented group showed improved feelings of general well-being, 88% of the vitamin B₁ treated subjects reported feeling "brighter" and "cheerier" than before supplementation. They also felt less fatigued, had improved appetite, showed an increase in activity, a reduction in daytime sleep and had improved sleep patterns compared to subjects treated with placebo.

Schorah, Newill, Scott and Morgan (1979) assessed the effects of supplementation with vitamin C on functional ability using an Activity of Daily Living Scale (ADL) in 118 subjects aged 59-97 years. Subjects were supplemented with vitamin C for 1 month. They found that supplemented subjects showed marginal improvements in their ADL scores, whereas the ADL scores of placebo treated subjects declined.

Blass, Gleason, Brush, DiPonte and Thaler (1988) supplemented 11 elderly patients (aged 59-83 years) with vitamin B₁ or placebo for a period of 3 months. All patients had a diagnosis of probable senile dementia of the Alzheimer's type (SDAT). The patients received vitamin B₁ and placebo for a period of 3 months in a crossover design. Behavioural change was assessed using the Blessed Dementia Rating Scale and the Haycox Behavioural Rating Scale. It was reported that supplementation had no effect on either scale.

Clausen, Nielsen, and Kristensen (1989) supplemented 97 elderly patients (aged 50-94 years) with multivitamins or placebo for a period of 12 months. Cognitive ability was assessed using the Gottfries, Brane and Steen rating scale for dementia. It was reported that after 12 months treatment, the multivitamin supplemented group showed an improvement (that just failed to reach statistical
significance) on the dementia scale, whereas the placebo group declined during the first 6 months, and only showed a very slight improvement after 12 months.

Sano, Ernesto, Thomas, Klauber, Schafer, Grundman, Woodbury, Growdon, Cotman, Pfeiffer, Schnieder and Thal (1997) supplemented 341 dementia patients with selegiline, vitamin E or placebo for a period of 2 years. Patients were randomised to receive selegiline 10 mg daily (n = 87); vitamin E 200 iu a day (n = 85); selegiline and vitamin E (n = 85) or placebo (n = 84). Assessments included the Alzheimer's Disease Assessment Scale (ADAS) and other real life measures such as time taken to die, the time taken to be institutionalised, time taken to reach a diagnosis of severe dementia (classed as a scores of 3 on the clinical dementia rating scale) and the time taken until the patient could no longer perform 2 out of 3 basic activities of daily living (Blessed dementia scale). After 2 years it was found that vitamin E treated group showed a longer delay in the need for hospitalisation than any of the other groups. Both selegiline and vitamin E delayed the progression of the disease and lengthened the time taken for institutionalisation, and hence for this reason, the authors believe that both selegiline and vitamin E should be considered for use in patients with moderate dementia. This study demonstrates the real world approach of clinical trials, as the prolongation of life and the delay in the need for institutionalisation is more meaningful to family members and clinicians rather than a slight improvement in the scores on a rating scale or psychometric test.

Burns, Marsh and Bender (1989) supplemented 19 geriatric patients (age 76-86 years) with multivitamins and placebo for 6 weeks in a crossover design. All patients were previously diagnosed as having multi-infarct dementia (MID), patients were assessed using the CAPE behaviour rating scale and the Hachinski dementia rating scale. It was found that supplementation had no effect on either scale.
5.10.1 Summary

The effects of multivitamin supplementation on mood and general well-being in elderly subjects, is somewhat contradictory. It would appear that supplementation with certain vitamins has beneficial effects on some aspects of well-being.

The Chomé et al. (1986) study would seem to provide evidence that vitamin deficiency may result in changes in mood and personality, resulting in higher scores of depression, fatigue and emotional instability.

Schorah et al. (1979) reported that supplementation with vitamin C resulted in improvements in activity of daily living (ADL) scores. Smidt et al. (1991) supplemented healthy elderly females with vitamin B₁, supplementation resulted in subjects feeling cheerier and brighter, less fatigued, increased activity, a reduction in daytime sleep, improved sleep patterns and improved appetite. Smith et al. (in press) reported that subjects who showed large increases in vitamin C reported feeling more confident, elated, composed and reported fewer errors on the cognitive failures scale.

Šrám, et al. (1990) reported that treatment with vitamin C and E for 2 years resulted in improvements on a subjective rating scale.

Bouchet et al. (1996) supplemented subjects with multivitamins for a period of 2 months, they reported that supplementation had no effect on subjects quality of life. It is possible that the lack of effect reported by Bouchet et al. (1996) may be due to a design fault, as supplementation for only 8 weeks is unlikely to result in any dramatic changes in blood vitamin status, hence would be unlikely to result in changes in subjective ratings.

Despite the inconsistencies, it would appear that supplementation with either single or multivitamins is likely to result in changes in subjective ratings.
Table 43: Showing the effects of vitamin supplementation on mood, well being and dementia progression in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Supplement</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chomé et al. (1986)</td>
<td>Elderly subjects</td>
<td>60</td>
<td>65-91 years</td>
<td>No supplement</td>
<td>Freiberger personality inventory</td>
<td>Deficient subjects had higher depression, fatigue and emotional instability scores</td>
</tr>
<tr>
<td>Smith et al. (in press)</td>
<td>Healthy elderly subject</td>
<td>205</td>
<td>60-80 years</td>
<td>Anti-oxidant (beta carotene, E and C) or placebo for 1 year</td>
<td>Profile of Mood States Cognitive Failures Task</td>
<td>Subjects who showed a large increase in vitamin C level following supplementation felt significantly more composed, elated and confident and reported fewer errors of memory, attention and action during their everyday activities.</td>
</tr>
<tr>
<td>Bouchet et al. (1996)</td>
<td>Healthy adult subject</td>
<td>1896</td>
<td>35-60 years</td>
<td>Multivitamin or placebo for 2 months</td>
<td>Quality of Life Scale (QOL)</td>
<td>Multivitamin supplementation had no effect</td>
</tr>
<tr>
<td>Schmidt et al. (1991)</td>
<td>Elderly women</td>
<td>80</td>
<td>65-92 years</td>
<td>Vitamin B₁ for 6 weeks</td>
<td>Well being scale</td>
<td>Vitamin B₁ treated subjects reported improved feeling of wellbeing</td>
</tr>
<tr>
<td>Šrárn et al. (1990)</td>
<td>Elderly people</td>
<td>160</td>
<td>60-90 years</td>
<td>Vitamin C and E for 2 years</td>
<td>Subjective Rating Scale</td>
<td>Improvements on the scale, especially motoric ability and mood</td>
</tr>
<tr>
<td>Schorah et al. (1979)</td>
<td>Geriatric patients</td>
<td>118</td>
<td>59-97 years</td>
<td>Vitamin C for 1 month</td>
<td>Activity of Daily Living Scale (ADL)</td>
<td>Supplementation resulted in improved ADL scores</td>
</tr>
<tr>
<td>Blass et al. (1988)</td>
<td>Probable Alzheimer patients</td>
<td>11</td>
<td>59-83 years</td>
<td>Vitamin B₁ for 3 months</td>
<td>Blessed dementia Rating Scale, Haycox Behaviour Rating Scale</td>
<td>No change in ratings</td>
</tr>
<tr>
<td>Author</td>
<td>Sample</td>
<td>n</td>
<td>Age</td>
<td>Supplement</td>
<td>Assessment</td>
<td>Outcome</td>
</tr>
<tr>
<td>-----------------</td>
<td>-------------------------------------</td>
<td>-----</td>
<td>-------------------</td>
<td>-----------------------------------------</td>
<td>------------------------------------------------</td>
<td>--------------------------------------------------</td>
</tr>
<tr>
<td>Sano et al.</td>
<td>Alzheimer patients</td>
<td>341</td>
<td>65-81 years</td>
<td>Selegiline, Vitamin E or placebo for 2 years</td>
<td>ADAS</td>
<td>Vitamin E treated patients showed a longer delay to institutionalisation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Blessed dementia Scale</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time taken to be institutionalised</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Time taken to reach a diagnosis of severe Dementia</td>
<td></td>
</tr>
<tr>
<td>Clausen et al.</td>
<td>Elderly subjects in residential homes</td>
<td>97</td>
<td>50-94 years</td>
<td>Multivitamin or placebo for 1 year</td>
<td>Mattis Dementia Rating Scale</td>
<td>Multivitamin treated group showed a non significant trend towards improvement</td>
</tr>
<tr>
<td>(1989)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Burns et al.</td>
<td>SDAT patients</td>
<td>19</td>
<td>76-86 years</td>
<td>Multivitamin for 6 weeks</td>
<td>CAPE Behaviour Rating Scale, Hachinski Dementia Rating Scale</td>
<td>No effect</td>
</tr>
<tr>
<td>(1989)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
5.11 Conclusions

From the above evidence it would be expected that long term multivitamin supplementation could have profound effects on cognitive function in elderly subjects, both healthy and patient populations.

5.12 Aims of the present study: The effects of long term multivitamin supplementation on aspects of mood and cognitive function in a healthy elderly population

The present study aims to assess the effects of long term multivitamin supplementation on aspects of cognitive function and mood in elderly subjects. The psychometric tasks completed by the volunteers assessed attention, memory, intelligence, the speed of naming, the speed of information processing, and subjective ratings of cognitive failure, anxiety, and depression, as used in the previous analysis.

Based on the previous literature, poor vitamin B\textsubscript{12} status was associated with poor Stroop task performance (Bohnen et al., 1988), and supplementation with folate resulted in improvements on the digit symbol substitution task. In terms of the tasks assessing aspects of attention in the present experiment, multivitamin supplementation would be expected to improve performance on the reverse naming task (SKT VII) and the counting symbols task (SKT VI) as these tasks are similar to the Stroop task and visual search tasks.

The effects of multivitamin supplementation on the arranging blocks and replacing block tasks (SK IV, V) would only be expected to show improvements. If multivitamin supplementation had any effects on tasks assessing the speed of information processing, as the tasks not only incorporate aspects of attention, but also require a speeded element.
In terms of multivitamin supplementation on the speed of information processing, only a small number of researchers have assessed the relationship between nutritional status and the speed of information processing. Based on the fact that Riggs et al. (1996) reported no correlation between nutritional status and the speed of information processing, and together with the fact that Deijen et al. (1992) and Burns et al. (1989) found no beneficial effects of supplementation on tasks of attention, supplementation with multivitamins would not be expected to report any performance improvements on the Critical Flicker Fusion task (CFF), the Choice Reaction Time task (CRT), object naming task (SKT I) or the numerical naming task (SKT III).

The beneficial effects of supplementation are particularly evident on memory tasks. Vitamin deficiency was associated with decrements in paragraph recall, backward digit span, visual memory, word list recall and Rey complex figures task. Supplementation with both single and multivitamins have been associated with improvements on the delayed recall of the paired associate word list task (Deijen et al., 1992), immediate paragraph recall (Tolonen et al., 1988), and digit span (Botez et al., 1984).

In terms of the memory tasks included in the present experiment, multivitamin supplementation would be expected to improve delayed object recall (SKT VIII). Less dramatic effects would be expected on the immediate recall of objects (SKT II), as the previous literature would seem to indicate that short term memory is relatively unaffected by supplementation with either single or multivitamins. Supplementation with multivitamins was not expected to produce any dramatic effects on the recognition memory task (SKT IX). Therefore, the effects of supplementation would be expected on the immediate recall task (SKT II), delayed recall task (SKT VIII), and no effects on the recognition task (SKT IX).
There is quite large amounts of literature reporting that intelligence scores of children and teenagers are improved following supplementation with multivitamins (Benton and Roberts, 1988; Benton and Butts, 1990; Benton and Cook 1991; Schoenthaler et al., 1991). There have been few studies assessing the effects of multivitamin supplementation on intelligence scores of healthy elderly subjects. However there have been a number of studies assessing the effects of supplementation on Mini Mental State Examination (MMSE) scores of patient populations. Based on these results, and on the fact that the present population believed that they were experiencing a certain degree of cognitive decline, it was thought that supplementation with multivitamins for a period of 36 weeks would result in improvements on the Ravens Standard Progressive Matrices (RSPM).

In terms of subjective ratings, Chomé et al. (1986) reported that vitamin deficient subjects had higher depression, fatigue and emotional instability scores than non deficient patients. Based on these results, it was speculated that supplementation with multivitamins would result in lower reports of anxiety and depression rated using the Hospital Anxiety and Depression Scale. There has been one study that has examined the effect of anti-oxidant supplementation on cognitive failures (Smith et al., in press), it was reported that subjects with higher vitamin C levels reported fewer errors on the CFQ. Therefore, it was speculated that improved vitamin status would result in fewer subjective reports of cognitive failure.

5.13 Method

5.13.1 Subjects

239 healthy community dwelling elderly subjects (112 males and 127 females) aged between 60 and 82 years, (mean age 69.5 years) were enrolled in the study. All subjects were in good physical and mental health. They had no significant history of hepatic, renal, respiratory, endocrine, gastrointestinal,
haematological, central nervous or cardiovascular disorders (determined by medical examination). Subjects were recruited from the general public via the HPRU database, newspaper and poster advertisements. For the demographics see Table 44.

<table>
<thead>
<tr>
<th></th>
<th>Multivitamin group</th>
<th>Placebo group</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>Males</td>
</tr>
<tr>
<td>age 60-64</td>
<td>15</td>
<td>23</td>
<td>14</td>
</tr>
<tr>
<td>age 65-69</td>
<td>16</td>
<td>16</td>
<td>21</td>
</tr>
<tr>
<td>age 70-74</td>
<td>11</td>
<td>19</td>
<td>14</td>
</tr>
<tr>
<td>age 75-79</td>
<td>10</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>age 80+</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>63</td>
<td>56</td>
</tr>
</tbody>
</table>

5.13.2 Treatments

Subjects were randomly allocated, under a double-blind procedure to treatment with either the multivitamin supplement or placebo. Treatments were administered orally as two soft gelatine capsules each day. The capsules were identically packaged. The placebo capsule contained rape seed oil. The vitamin preparation contained: vitamin A, B\textsubscript{1}, B\textsubscript{2}, B\textsubscript{6}, B\textsubscript{12}, vitamin C, vitamin E, folic acid, biotin and nicotinamide. The dosing was calculated to provide the equivalent of 1 Recommended Daily Allowance of vitamin A, and 10 US RDA's for the remaining vitamins (RDA Recommended Daily Allowances, 9th edition, 1980 USRDA). All capsules were provided by Roche Pharmaceuticals.

Table 45: Showing the composition of the multivitamin preparation.

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Amount</th>
<th>USA Recommended Daily Allowance's</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>3334 IU</td>
<td>1 US Recommended Daily Allowance</td>
</tr>
<tr>
<td>Vitamin B\textsubscript{1}</td>
<td>14 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Vitamin B\textsubscript{2}</td>
<td>16 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Vitamin B\textsubscript{6}</td>
<td>22 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Vitamin B\textsubscript{12}</td>
<td>0.03 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>600 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>100 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
</tbody>
</table>
### Vitamin Amount USA Recommended Daily Allowance's

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Amount</th>
<th>USA Recommended Daily Allowance's</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biotin</td>
<td>2 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>4 mg</td>
<td>10 US Recommended Daily Allowance's</td>
</tr>
</tbody>
</table>

#### 5.13.3 Procedure

Prior to participation on the study, subjects were familiarised and trained on all psychometric tests. Four test sessions took place (baseline, week 12, week 24 and week 36).

Subjects entered the unit fasted, underwent a brief medical assessment and a 20 ml blood sample which was taken by the study nurse. Following a light breakfast subjects underwent testing on the psychometric test battery.

#### 5.13.4 Psychometric Assessments

Psychometric assessments included the Critical Flicker Fusion Task (CFF); Choice Reaction Time (CRT); HPRU Sternberg Memory Task (SMT); the Syndrom Kurtz Task (SKT); Ravens Standard Progressive Matrices (RSPM). Subjective assessments included the Cognitive Failures Questionnaire (CFQ) and Hospital Anxiety and Depression Scale (HADS) Table 46 summarises the test schedule.

<table>
<thead>
<tr>
<th>Table 46: Summarising the assessment test schedule at each visit.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Flicker Fusion</td>
</tr>
<tr>
<td>----------------------------</td>
</tr>
<tr>
<td>Choice Reaction Time</td>
</tr>
<tr>
<td>HPRU Sternberg Memory Task</td>
</tr>
<tr>
<td>Cognitive Failures Questionnaire</td>
</tr>
<tr>
<td>Ravens Matrices</td>
</tr>
<tr>
<td>Hospital Anxiety Depression Scale</td>
</tr>
<tr>
<td>Syndrom Kurtz Task</td>
</tr>
<tr>
<td>Blood Vitamin Assessment</td>
</tr>
</tbody>
</table>

#### 5.13.5 Critical Flicker Fusion Task (CFF)

The Critical Flicker Fusion task (CFF) is regarded as an index of overall CNS activity, the ability of the central nervous system to process discrete 'bits' of
information Hindmarch (1980). Therefore an increase in CFF threshold is associated with increased alertness and a greater capacity for information processing.

5.13.6 Choice Reaction Time Task (CRT)
The Choice Reaction Time task (CRT) is used as an indicator of sensorimotor performance, assessing the efficiency of the attentional and response mechanisms in the information processing chain. The task is comprised of three components recognition reaction time (RRT), motor reaction time (MRT) and total reaction time (TRT).

5.13.7 HPRU Sternberg Memory Task (SMT)
The HPRU Sternberg memory task is a technique based upon a reaction time method where subjects are required to memorise a set of target digits. In the HPRU Sternberg memory task, the ability to scan the memory set was assessed by getting subjects to attend to a series of digits, then presenting 12 single digits and asking the subjects whether that digit was in the original memory set.

5.13.8 Syndrom Kurtz Task (SKT)
The SKT task is comprised of 9 subtasks assessing aspects of attention (arranging blocks (SKT IV), replacing blocks (SKT V), counting symbols (SKT VI), reverse naming (SKT VII)), memory (immediate recall, (SKT II), delayed recall (VIII) and recognition memory (SKT IX)) and the speed of naming (object naming (SKT I) and numerical naming (SKT III)) Erzigkeit (1989).

5.13.9 Ravens Standard Progressive Matrices (RSPM)
The Ravens progressive matrices is a test of non verbal intelligence (Raven, Court and Raven, 1992). The tasks tests a persons capacity to find relationships between "meaningless figures" and in doing so develop a systematic method of reasoning. The matrices consist of 60 problems divided into five sets of 12
problems (A, B, C, D and E). Subjects are presented with a diagram of a puzzle, each puzzle has a part missing, the subjects has to choose (from a set of 4 or 6) the missing part of the puzzle. Each of the 5 sets start with a puzzle which is, as far as possible, self-evident, and develops a theme in the course of which the problems build on the argument of what has gone before and thus becomes progressively more difficult.

5.13.10 Cognitive Failures Questionnaire (CFQ)
The Cognitive Failures Questionnaire (CFQ) was developed by Broadbent, Cooper, Fitzgerald and Parkes (1982). It is a measure of self-reported failures in perception, memory and motor function. Subjects are required to answer 25 questions, rating the frequency of problems over the past four months, using a scale where 0 = never and 5 = very often.

5.13.11 Hospital Anxiety and Depression Scale (HADS)
The Hospital Anxiety and Depression Scale (HADS) was designed by Zigmond and Snaith (1983) as a self rating scale for the assessment of anxiety and depression. The scale consists of 14 items, 7 of which measure anxiety and 7 measure depression.

5.13.12 Blood Vitamin Levels
To determine the blood/serum vitamin levels, various assays were carried out. To identify levels of B1, B2 and B6, whole blood was tested. The plasma levels of vitamin A, C, C, B12, Biotin and folic acid were determined.

All biochemical assays were carried out in the laboratories of F. Hoffman-La Roche. Twenty ml of blood was drawn from fasted subjects and divided into two heparinized tubes. A sample of 3-4 ml of whole blood was placed into an ampoule containing acid-citrate-dextrose. This was express posted to the laboratory where the status of vitamins B1, B2 and B6 were assessed using apoenzyme tests (Vuilleumier et al, 1983; 1990). The remaining blood was
centrifuged and the plasma stored at -20 degrees centrigrade. For vitamin C analysis, 0.5 ml of plasma was added to 4.5 ml of 5% metaphosphoric solution prior to freezing, with plasma concentration being determined using a fluorometric method (Brubacher and Vuilleumier, 1974). The analysis of vitamin B₁₂ and folic acid was carried out using the solid phase no boil vitamin B₁₂ and folic acid radioassay kits (Diagnostic products Corporation). Biotin plasma levels were assayed using a microbiological method (Frigg and Brubacher, 1976). Vitamins A, E and beta-carotenes were assayed by a high-performance liquid chromatography (Vuilleumier et al, 1983; Hess et al, 1991).

5.14 Results

The blood vitamin data were analysed using a 2 way analysis of variance with treatment (multivitamin or placebo) and visit (baseline, week 12, 24 and 36) as between subjects factors. Any complex significant differences were analysed using the Newman Keul's post hoc test.

5.15 The change in blood vitamin levels

The aim of this analysis was to examine whether supplementation with multivitamins would affect blood vitamin concentration levels.

5.15.1 Vitamin A

There was no main significant effect of treatment (F (1, 222) = 0.67; p> 0.05), there was no significant difference in the blood levels of vitamin A for either the multivitamin supplemented or the placebo group. There was no significant time effect (F (3, 666) = 0.90; p > 0.05) showing that blood vitamin levels did not change significantly over time. This was due to the fact that the supplement contained vitamin A level equivalent to 1 USA RDA's, as any higher could result in toxicity. There was no significant treatment and time interaction, however it approached statistical significance (F (3, 666) = 2.44; p = 0.06).
5.15.2 Vitamin B₁
There was significant main effect of treatment ($F_{1, 22} = 24.72; p < 0.001$), with means showing that the treatment group had higher levels of B₁ than the placebo group. There was a significant time effect ($F_{3, 66} = 88.47; p < 0.001$) with means showing that the multivitamin treated group had blood levels that changed significantly over time. There was a significant treatment and time interaction ($F_{3, 66} = 72.24; p < 0.0001$) multivitamin treated group showed a significant increase in blood levels of vitamin B₁ at week 12. Blood vitamin B₁ levels remained significantly higher than the placebo condition at weeks 24 and 36, blood vitamin B₁ levels in the placebo group remained stable over time. (see Figure 27).

Main effect of treatment was analysed using post hoc testing, which revealed that at baseline there was no difference between the blood vitamin B₁ levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of vitamin B₁ ($p<0.0001$).

![The change in blood level of vitamin B1](image)

Figure 27: Showing the change in blood level of vitamin B₁ ($* p<0.0001$).
5.15.3 Vitamin B₂

There was significant main effect of treatment ($F_{(1, 222)} = 52.69; p < 0.001$), with means showing that the multivitamin treated group had higher blood levels of vitamin B₂ than the placebo treated group. There was a significant time effect ($F_{(3, 666)} = 55.36; p < 0.01$) with mean showing that the multivitamin treated group had blood levels that changed significantly over time. There was a significant treatment and time interaction ($F_{(3, 666)} = 90.39; p < 0.0001$) with means showing that the multivitamin treated group showed an increase in blood levels of vitamin B₂ at week 12. Blood vitamin B₂ levels remained significantly higher than the placebo condition at weeks 24 and 36. Blood vitamin B₂ levels in the placebo group remained stable over time. (see Figure 28).

The main effect of treatment was analysed using post hoc testing to revealed that at baseline there was no difference between the blood vitamin B₂ levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of vitamin B₂ than the placebo group ($p<0.0001$).

![The change in blood level of vitamin B₂](image)

Figure 28: Showing the change in blood level of vitamin B₂ (* $p<0.0001$).
5.15.4 Vitamin B₆

There was significant main effect of treatment ($F_{(1, 222)} = 868.59; p < 0.001$), with means showing that the multivitamin treated group had higher blood levels of vitamin B₆ than the placebo group. There was a significant time effect ($F_{(3, 666)} = 955.96; p < 0.001$) with mean showing that the multivitamin treated group had blood levels that changed significantly over time. There was a significant treatment and time interaction ($F_{(3, 666)} = 862.31; p < 0.0001$) the multivitamin treated group showed an increase in blood levels of vitamin B₆ at week 12. Blood vitamin B₆ level remained significantly higher than the placebo condition at weeks 24 and 36. Blood levels in the placebo group remained stable over time (see Figure 29).

The main effect of treatment was analysed using post hoc testing to reveal that at baseline there was no difference between the blood vitamin B₆ level of the subjects, however at weeks 12, 24 and 36 the multivitamin treated group had significantly higher blood level of vitamin B₆ than the placebo treated group ($p<0.0001$).

![The change in blood level of vitamin B6](image)

Figure 29: Showing the change in blood level of vitamin B6 (* $p<0.01$).
5.15.5 Vitamin B₁₂
There was significant main effect of treatment ($F_{(1, 222)} = 21.83; p < 0.001$), with means showing that the multivitamin treated group had higher levels of vitamin B₁₂ than the placebo treated group. There was a significant time effect ($F_{(3, 666)} = 19.80; p < 0.001$) with means showing that the multivitamin treated group had blood levels that changed significantly over time. There was also a significant treatment and time interaction ($F_{(3, 666)} = 38.39; p < 0.0001$) the multivitamin treated group showed a significant increase in blood levels of vitamin B₁₂ over time (see Figure 30).

Post hoc testing of the main effect of treatment revealed that at baseline there was no difference between the blood vitamin B₁₂ levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of vitamin B₁₂ than the placebo group ($p<0.0001$).

![The change in blood level of vitamin B12](image)

Figure 30: Showing the change in blood vitamin level of vitamin B12 (ng/L) ($p<0.0001$).

5.15.6 Vitamin E
There was significant main effect of treatment ($F_{(1, 222)} = 68.61; p < 0.001$), with means showing that the multivitamin treated group had higher levels of vitamin E than the placebo group. There was a significant time effect ($F_{(3, 666)} =
33.47; p < 0.001) with mean showing that the multivitamin treated group had blood levels that changed significantly over time. There was also a significant treatment and time interaction ($F (3, 666) = 50.99; p < 0.0001$) with the multivitamin treated group showing a significant increase in blood levels of vitamin E at week 12. Blood levels of vitamin E remained significantly higher than the placebo condition at week 24 and 36 (see Figure 31). Blood levels of vitamin E in the placebo group remained stable over time.

Post hoc testing of the main effect of treatment revealed that at baseline there was no difference between the blood vitamin E levels of the subjects. However, at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of vitamin E than the placebo treated group ($p<0.0001$).

![The change in blood level of vitamin E](image)

**Figure 31:** Showing the change in blood level of vitamin E (mg/L) ($p<0.0001$).

### 5.15.7 Vitamin C

There was significant main effect of treatment ($F (1, 222) = 69.52; p < 0.001$), there was a significant difference in blood levels of vitamin C between the treatment groups, with means showing that the multivitamin treated group had higher vitamin C levels than the placebo treated group. There was a significant time effect ($F (3, 666) = 14.01; p < 0.001$) with means showing that the multivitamin treated group had blood levels that changed significantly over
There was also a significant treatment and time interaction ($F(3, 66) = 17.80; p < 0.0001$) the multivitamin treated group showed an increase in blood levels of vitamin C over time (see Figure 32).

Post hoc testing of the main effect of treatment revealed that at baseline there was no difference between the blood vitamin C levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of vitamin C than the placebo treated group ($p<0.0001$).

![The change in blood level of vitamin C](image)

Figure 32: Showing the change in blood level of vitamin C (mg/L) ($p<0.0001$).

### 5.15.8 Biotin

There was significant main effect of treatment ($F(1, 222) = 133.03; p < 0.001$), there was a significant difference in blood levels of biotin between the treatment groups, with mean showing that the multivitamin treated group had higher blood biotin levels than the placebo group. There was a significant time effect ($F(3, 666) = 32.43; p < 0.001$) with means showing that the multivitamin treated group had biotin blood levels that changed significantly over time. There was also a significant treatment and time interaction ($F(3, 666) = 32.67; p < 0.0001$) the multivitamin treated group showed an increase in blood levels of biotin over time (see Figure 33).
The main effect of treatment was analysed using Post hoc testing it was revealed that at baseline there was no difference between the blood biotin levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of biotin than the placebo group (p<0.0001).

Figure 33: Showing the change in blood biotin level (nmol/L) (P<0.0001).

5.15.9 Folic Acid
There was significant main effect of treatment ($F_{(1, 222)} = 896.67; p < 0.001$), there was a significant difference in blood levels of folic acid between the treatment groups, with means showing that the multivitamin treated group had higher levels of folic acid than the placebo group. There was a significant time effect ($F_{(3, 666)} = 215.92; p < 0.001$) the multivitamin treated group had blood levels of folic acid that changed significantly over time. There was also a significant treatment and time interaction ($F_{(3, 666)} = 192.34; p < 0.0001$) the multivitamin treated group showed an increase in blood levels of folic acid at week 12 which remained significantly higher than the placebo condition at week 24 and 36. Blood levels of folic acid in the placebo group remained stable over time (see Figure 34).
Post hoc testing revealed that at baseline there was no difference between the blood folic acid levels of the subjects, however at weeks 12, 24 and 36 the multivitamin supplemented group had significantly higher blood level of folic acid than the placebo group (p<0.0001).

![The change in blood level of Folic Acid](image)

Figure 34: Showing the change in blood level of Folic Acid (nmol/L) (* p<0.0001).

5.15.10 Blood vitamin summary

The effect of supplementing diet with a multivitamin preparation resulted in a significant increase in blood vitamin level in most cases after only 12 weeks of treatment (with the exception of vitamin A, this was due to the fact that the multivitamin supplementation consisted of a lower dose of vitamin A equivalent of 1 US RDA was given so to reduce the risk of vitamin A toxicity). What is of importance here, is whether a significant increase in blood vitamin level has an effect on psychometric performance. The hypothesis was that higher blood vitamin levels would result in superior psychometric task performance, and lower self reports of cognitive failure, anxiety and depression.
5.16  The effects of long term multivitamin supplementation on cognitive function in an elderly sample

The data were analysed using a 3 way analysis of variance with treatment and age as between subject factors and visit as the within subject factor. The performance data were analysed in terms of the cognitive groupings that were identified in chapter 4. The groupings included:-

1. Attention (HPRU Sternberg memory Task, SKT subtests IV, V, VI, and VII).
2. Memory recall (SKT subtest II and VIII).
3. Speed of naming (SKT subtest I and III)
4. Speed of information processing (CFF, TRT, RRT and MRT).
5. Recognition memory (SKT subtest IX).

The study also examined the effect of multivitamin supplementation on intelligence (Ravens Standard Progressive Matrices) and subjective ratings of mood and cognitive failure (Hospital Anxiety and Depression Scale (HADS), Cognitive Failures Questionnaire, (CFQ).

5.17  The effects of multivitamin supplementation on attention in an elderly population

In chapter 4 the effects of ageing on tasks that assessed attention were examined, it was concluded that there was a main effect of age on SKT IV, V, VI and VII, as age increases performance on selective attention tasks declined. The purpose of this experiment was to assess the effects of supplementation on attention tasks. In chapter 4 as a result of a principal components analysis a number of tasks were classed as assessing attention they included SKT subtests IV, V, VI, VII and the HPRU Sternberg Memory Task.
5.17.1 SKT subtest IV (arranging blocks)

In this task subjects is presented with a 10 numbered blocks arranged in 2 rows (e.g. 23 45 53 65). Subjects were required to arrange the blocks into ascending order. The time taken for the subjects to complete the task was recorded.

There was a main effect of age ($F(4, 213) = 8.69 \ p<0.001$). There was no main significant effect of treatment ($F(1, 213) = 0.56; \ p > 0.05$), there was no significant difference in performance for either supplemented or the placebo group (see table 47).

Table 47: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>20.41</td>
<td>20.42</td>
</tr>
<tr>
<td>Placebo</td>
<td>20.29</td>
<td>20.18</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F(1, 213) = 0.33; \ p > 0.05$) there was no significant change in performance over time. There were no significant interactions between age treatment and visit ($F(4, 213) = 0.43; \ p>0.05$).

Post hoc testing of the main effect of age using the Newman Keul's test, revealed that subjects aged 60-64 years were significantly faster at arranging the blocks than subjects aged 70-74, 75-79 and 80+. (See Figure 35).
5.17.2 SKT subtest V (replacing blocks)

In subtest V subjects then had to replace the 10 numbered blocks into their original starting positions which were clearly marked on the board. Time taken to replace the blocks was recorded.

There was a main effect of age (F (4, 213) = 8.69 p<0.001). There was no main effect of treatment (F (1, 213) = 0.16; p > 0.05), there was no significant difference in performance for either supplemented or the placebo group (see Table 48).

Table 48: Showing the treatment means at each visit (seconds)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>15.35</td>
<td>15.04</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.86</td>
<td>14.65</td>
</tr>
</tbody>
</table>

There was no significant time effect (F (1, 213) = 2.65; p > 0.05) there was no significant change in performance over time. There were no significant interactions between age treatment and visit (F (4, 213) = 0.64; p>0.05).

The main effect of age was analysed using the Newman Keul's task, it was found that subjects aged 60-64 years were significantly faster at replacing the
blocks subjects aged 70-74, 75-79 and 80+ (p<0.001), performance on the task was shown to slow with increasing age. (See Figure 36).

![The main effect of age on replacing blocks (SKT V)](image)

Figure 36: The main effect of age on performance on replacing blocks (SKT subtest V).

### 5.17.3 SKT subtest VI (counting symbols)

In this task, subjects were required to count symbols. The symbols are printed onto a card, which contained 7 rows of 3 different symbols (e.g. circle, star, flower). Subjects were required to count the number of circles on the card. The time taken to complete the task was recorded.

There was no main effect of age ($F(4, 213) = 1.26 \ p > 0.05$) time taken to count symbols was comparable between the age bands. There was no main effect of treatment ($F(1, 221) = 1.95; \ p > 0.05$), there was no significant difference in performance for either supplemented or the placebo group (see Table 49).

| Table 49: Showing the treatment means at each visit (seconds) |
|-----------------|-----------------|-----------------|
|                 | Baseline        | Week 36         |
| Multivitamin    | 20.18           | 20.63           |
| Placebo         | 19.42           | 19.90           |
There was no significant time effect \((F_{(1, 221)} = 1.84; \ p > 0.05)\) there was no significant change in performance over time. There were no significant age treatment or time interactions \((F_{(4, 213)} = 1.06; \ p > 0.05)\).

5.17.4 SKT subtest VII (reverse naming task)

In subtest VII subjects had to complete a reverse naming task, subjects were required to name a row of letters e.g. AABABBA when subjects read the letter 'A' they were required to say 'B' and vice versa. The task consisted of 34 letters, the time taken to complete the task was recorded.

There was a main effect of age \((F = (4, 213) = 10.85 \ p < 0.001)\). There was no main effect of treatment \((F = (1, 213) = 0.46; \ p > 0.05)\), there was no significant difference in performance for either supplemented or the placebo group (see Table 50).

Table 50: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>24.30</td>
<td>22.86</td>
</tr>
<tr>
<td>Placebo</td>
<td>23.46</td>
<td>22.82</td>
</tr>
</tbody>
</table>

There was no main effect of time \((F = (1, 213) = 2.57; \ p > 0.05)\) there was no significant change in performance over time. There was a significant age and visit interaction \((F_{(4, 213)} = 2.59; \ p < 0.05)\).

Post hoc testing of the main effect of age revealed that on performance on the task declines with age (see Figure 37).
The main effect of age on the reverse naming task (SKT VII)

![Figure 37: Showing the main effect of age on the reverse naming task (SKT VII).](image)

Post hoc testing of the age visit interaction revealed that there were no significant changes in performance between the baseline and week 36 tests point for subjects aged 60-64, 65-69, 70-74 and 80+. Subjects aged 75-79 were significantly faster at the reverse naming task at week 36 compared to their baseline score (see Figure 38).

The interaction between age and visit on the reverse naming task (SKT VII)

![Figure 38: The interaction between age and visit on the reverse naming task (SKT subtest VII).](image)
5.17.5 HPRU Sternberg Memory Task (SMT)

Subjects were required to memorise a set of digits (the stimulus set), ranging from single digits, sets of three and sets of five digits. Following the series, subjects were presented with 12 single probe digits, the subjects were required to decide whether the probe digits were a part of the stimulus set or not.

There was a main effect of age ($F(4, 203) = 4.38; p < 0.01$). There was no main effect of treatment $F(1, 203) = 0.27; p > 0.05$), there was no significant difference in performance for either supplemented or the placebo group (see Table 51).

However examination of the treatment means would seem to indicate that baseline performance on the task was poorer in the multivitamin group than the placebo group.

| Table 51: Showing the treatment means at each visit (milliseconds) |
|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
|                          | Baseline                 | Week 12                  | Week 24                  | Week 36                  |
| Multivitamin             | 1412.50                  | 1361.52                  | 1281.48                  | 1201.93                  |
| Placebo                  | 1137.11                  | 1271.00                  | 1245.82                  | 1196.79                  |

There was a significant time effect ($F(3, 609) = 19.88; p < 0.001$). There was a significant age and time interaction $F(12, 609) = 3.32; p <0.001$).

The main effect of age was analysed using post hoc Newman Keul's it was found that performance on the task declines as age increases, older subjects took longer to respond to the stimuli. (See Figure 39).
The main effect of age on the Sternberg Memory Task (SMT)

Figure 39: Showing the main effect of age on the HPRU Sternberg Memory Task (SMT)

The significant time effect was analysed using Newman Keul's, it was reported that performance on the task got significantly faster over time, possibly reflecting a practice/familiarity effect. (See Figure 40)

The main effect of time on The Sternberg Memory Task (SMT)

Figure 40: Showing the main effect of time on the HPRU Sternberg Memory Task (SMT)

Post hoc analysis of the interaction between age and time revealed that performance in subjects aged 60-64, 65-69 and 70-74 showed a significant improvement in response times over the test period. In subjects aged 75-79 and
80+ there was no improvement in performance until week 36, subjects 80+ showed poorer response times at week 12 and 24 (see Figure 41).

![The interaction between age and visit on the Sternberg Memory Task (SMT)](image)

Figure 41: The interaction between age and visit on the HPRU Sternberg Memory Task (SMT).

5.17.6 Summary
There were no main effects of treatment on any of the tasks thought to assess attention, multivitamin supplementation had no effect on attention, other than an interesting interaction between age and visit on the HPRU Sternberg Memory Task, where subjects aged 60-74 showed a significant improvement in performance over time, whereas there was no improvement over time for subjects aged greater than 75 years.

In line with chapter 4, main effects of age were reported on both the arranging and replacing blocks task (SKT IV, V); the reverse naming task (SKT VII). In the present analysis age effects were also reported on the HPRU Sternberg Memory Task (SMT). In general older subjects were slower at performing the tasks, and long term supplementation with multivitamins did not help to reduce the age related deficit.
The effects of multivitamin supplementation on memory recall

In chapter 4 the effects of ageing on tasks that assess memory recall SKT II (immediate recall) and SKT VIII (delayed recall) were assessed. It was concluded that there were significant main effect of age of performance of memory recall tasks. The purpose of this experiment was to assess the effects of supplementation on memory recall, in the hope that long term multivitamin supplementation would reduce the age related deficit.

SKT subtest II (immediate recall)

In subtest II subjects were required to provide immediate recall of the 12 items (that they had previously seen in subtest I). Subjects only had 60 seconds in which to recall the 12 items, the number of omissions were recorded.

There was a significant main effect of age ($F(4, 213) = 3.67; p<0.01$). There was no main significant effect of treatment ($F(1, 213) = 1.26; p > 0.05$), there was no significant difference in performance between the multivitamin supplemented or the placebo group (see Table 52).

| Table 52: Showing the treatment means at each visit (number of omissions). |
|-----------------|-----------------|
| Baseline        | Week 36         |
| Multivitamin    | 4.39            | 4.99            |
| Placebo         | 4.45            | 5.15            |

There was a significant time effect ($F(1, 213) = 15.42; p < 0.001$) there was a significant change in performance on the task over time, subjects forgot more items after 36 weeks of treatment.

There was no significant age, treatment and time interaction ($F(4, 213) = 1.64; p>0.05$).
The main effect of age was analysed using the Newman Keul's post hoc test, it was revealed that immediate memory recall declines as age increases, memory recall was poorest in subjects aged 75-79 years (see Figure 42).

![The main effect of age on immediate recall (SKT II)](image)

Figure 42: The main effect of age on immediate recall (SKT subtest II).

**5.18.2 SKT subtest VIII (delayed recall)**

*In subtest VIII subjects were required to provide delayed recall of the 12 items, that they had seen some 10 minutes ago. Subjects only had 60 seconds in which to recall the 12 items, the number of omissions were recorded.*

There was a main effect of age ($F_{(4, 213)} = 5.39; p < 0.001$). There was no main significant effect of treatment ($F_{(1, 213)} = 0.05; p > 0.05$), there was no significant difference in performance for either supplemented or the placebo group (see Table 53).

**Table 53:** Showing the treatment means at each visit (number of omissions).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>4.09</td>
<td>4.65</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.88</td>
<td>4.60</td>
</tr>
</tbody>
</table>
There was a significant time effect ($F_{(1, 213)} = 9.65; p < 0.01$) subjects forgot more items over time. There was no significant age treatment and time interaction ($F_{(4, 213)} = 0.58; p>0.05$).

The main effect of age was analysed using post hoc testing which revealed that subjects aged 60-64 years forgot significantly fewer items than older subjects (see Figure 43).

![The main effect of age on delayed recall (SKT VIII)](image)

**Figure 43:** The main effect of age on delayed recall (SKT subtest VIII).

### 5.18.3 Summary

In line with chapter 4 main effects of age were reported on both the immediate recall task (SKT II) and the delayed recall task (SKT VIII), older subjects tended to forget more items that younger subjects.

There was no main effect of treatment on tasks assessing memory recall, both the placebo and the multivitamin group had similar forgetting rates on both the immediate (SKT II) and delayed recall tasks (SKT VIII). Supplementation with multivitamins did not reduce the age deficit in memory recall.
5.19 The effects of multivitamin supplementation on the speed of naming

In chapter 4 the effects of ageing on tasks that assess the speed of naming were assessed. The tasks considered to assess the speed of naming included SKT I (object naming) and SKT III (numerical naming) it was concluded that there were main effects of age on the object naming task, so that older subjects were slower at naming the 12 objects, however there were no main effects of age on the numerical naming task. This experiment assessed whether the age related decrement in object naming could be alleviated with long term supplementation of multivitamins.

5.19.1 SKT subtest I (object naming)

The subjects is shown a card containing 12 pictures of objects. They were required to name the objects as quickly as possible, remembering to try and commit the objects to memory as they would have to recall and recognise the objects. The number of omissions were recorded.

There was no main effect of age ($F_{(4, 213)} = 1.32; p > 0.05$) time taken to name objects was comparable for all ages. There was no main significant effect of treatment ($F_{(1, 213)} = 2.63; p > 0.05$), there was no significant difference in the time taken to name objects for the supplemented or the placebo group (see Table 54)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>13.61</td>
<td>14.37</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.77</td>
<td>15.29</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F_{(1, 213)} = 0.01; p > 0.05$) there was no significant change in performance over time. There was no significant age treatment and time interaction ($F_{(4, 213)} = 1.36; p >0.05$).
5.19.2 SKT subtest III (naming numerals)

The subjects had to name a set of 10 randomly chosen numbered blocks e.g. 24, 36, 53, 65 etc. The time taken to name all numbers was recorded.

There was no main effect of age ($F_{(4, 213)} = 0.56; p > 0.05$) time taken to name numerals was comparable for all ages. There was no main significant effect of treatment ($F_{(1, 213)} = 2.64; p > 0.05$), there was no significant difference in the time taken to name numerals for the supplemented or the placebo group (see Table 55).

Table 55: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>7.57</td>
<td>7.64</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.74</td>
<td>8.38</td>
</tr>
</tbody>
</table>

There was a significant time effect ($F_{(1, 213)} = 5.80; p < 0.01$), subjects got slower at naming numerals over time.

There was a significant interaction between treatment and visit ($F_{(1, 213)} = 5.07; p < 0.01$), subjects in the placebo group showed a decline in performance over time, i.e. responses got slower whereas performance in subjects treated with multivitamin supplementation remained stable, this could be taken as evidence of an effect of supplementation even though performance in the supplemented group did not improve, the supplementation had the effect of retarding the decline that was observed in the placebo condition, acting with a protective effect (see Figure 44).
5.19.3 Summary

In chapter 4 a main effect of age was reported on the objects naming task (SKT subtest I), however in this sample there were no main effect of age, subjects of all ages were comparable in the time taken to name 12 objects. In line with chapter 4 there was no main effect of age on numerical naming.

There were no main effect of treatment on tasks assessing the speed of naming (SKT I or III), supplementation did not improve performance on SKT task I (object naming), however in SKT III (numerical naming task) supplementation seemed to protect against the decrement in performance that was noted in the placebo condition over time, whereas in the multivitamin group performance remained stable over time.

5.20 The effect of multivitamin supplementation on the speed of information processing

In chapter 4 the effects of ageing on tasks that assessing the speed of information processing were examined, it was concluded that there was no main
effect of age on the speed of information processing assessed using the Critical Flicker Fusion task (CFF), or the Choice Reaction Time tasks (CRT).

5.20.1 Critical Flicker Fusion (CFF)

Subjects completed 6 trials, 3 ascending and 3 descending trials, the average of which was taken as the subjects critical flicker fusion threshold.

There was no main effect of age \( (F(4, 209) = 1.09; p > 0.05) \) critical flicker fusion thresholds were comparable for the ages. There was no main significant effect of treatment \( (F(1, 209) = 0.69; p > 0.05) \), there was no significant difference in critical flicker fusion thresholds for either supplemented or the placebo group (see Table 56).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>28.96</td>
<td>28.68</td>
<td>28.96</td>
<td>28.84</td>
</tr>
<tr>
<td>Placebo</td>
<td>29.41</td>
<td>29.48</td>
<td>28.89</td>
<td>29.88</td>
</tr>
</tbody>
</table>

There was no significant time effect \( (F(3, 627) = 0.23; p > 0.05) \) there was no significant change in critical flicker fusion thresholds over time. There was no significant age treatment and time interaction \( (F(12, 629) = 0.88; p>0.05) \).

5.20.2 Total Reaction Time (TRT)

Total reaction time was measured using a choice reaction time task, containing 6 lights, subjects had to respond by extinguishing the lights as fast as possible. Total reaction times were obtained from the average of 20 stimuli. Total reaction time was defined as the time taken for subjects to remove their finger from the home, reach the appropriate response key and return back to the home key.
There was a main effect of age ($F_{(4, 209)} = 6.50; p<0.001$). There was no main significant effect of treatment ($F =_{(1, 209)} = 0.007; p >0.05$), there was no significant difference in total reaction times between the multivitamin and the placebo groups (see Table 57).

Table 57: Showing the treatment means at each visit (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>803.42</td>
<td>813.77</td>
<td>767.44</td>
<td>752.47</td>
</tr>
<tr>
<td>Placebo</td>
<td>783.50</td>
<td>791.60</td>
<td>780.29</td>
<td>742.91</td>
</tr>
</tbody>
</table>

There was a significant time effect ($F_{(3, 627)} = 13.37; p < 0.001$) total reaction times decreased over time. There was a significant age and visit interaction ($F_{(12, 627)} = 1.96; p <0.05$) (see Figure 45).

Post hoc testing of the main effect of age revealed that performance on the task declined with increased age, and younger subjects had significantly faster response times than older subjects (see Figure 45).

The main effect of age on Total Reaction Time (TRT)

![Figure 45: Showing the main effect of age on total reaction time (TRT).](image)

Post hoc testing of the main effect of time revealed that subjects got faster at the task over time, possibly indicating a practice/familiarity effect (see Figure 46)
The main effect of time on Total Reaction Time (TRT)

![Graph showing TRT over time](image)

**Figure 46:** Showing the main effect of time on total reaction time (TRT).

The significant age and visit interaction was analysed using separate one way analyses of variance, it was revealed that at every visit, there were significant differences. All age groups showed significant improvements in reaction times over the testing period. However in subjects aged 80+ there was quite a dramatic improvement in reaction time by week 36 (see Figure 47).

![Graph showing age and visit interaction](image)

**Figure 47:** The interaction between age and visit on total reaction time (TRT).
5.20.3 Recognition Reaction Time (RRT)

Recognition reaction time was measured using a choice reaction time task, containing 6 stimuli, subjects had to respond by extinguishing the lights as fast as possible. Recognition reaction time is the time taken for the subject to lift their finger from the home key.

There was no main effect of age ($F(4, 197) = 0.15; p>0.05$) there was no significant difference between recognition reaction time for the ages. There was no main significant effect of treatment ($F(1, 197) = 0.25; p > 0.61$), there was no significant difference in recognition reaction time between the multivitamin and placebo group (see Table 58).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>445.07</td>
<td>459.61</td>
<td>442.37</td>
<td>470.02</td>
</tr>
<tr>
<td>Placebo</td>
<td>455.67</td>
<td>466.99</td>
<td>460.05</td>
<td>454.45</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F(3, 591) = 2.16; p>0.05$) recognition reaction time remained stable over time. There was a significant treatment and visit interaction ($F(3, 591) = 2.97; p <0.05$) (see Figure 48).

Post hoc testing of the treatment/visit interaction revealed that there was a significant difference between the baseline RRT scores for the 2 groups. There were significant differences between the multivitamin RRT scores, the baseline score was significantly different from week 12 and week 36. There were no significant differences between the RRT scores in the placebo group.
Figure 48: The interaction between treatment and visit on recognition reaction times (RRT).

5.20.4 Motor Reaction Time (MRT)

Motor reaction time was measured using a choice reaction time task, containing 6 stimuli, subjects had to respond by extinguishing the lights as fast as possible. Motor reaction time was defined as the time taken for the subject to reach the appropriate response button.

There was no main effect of age ($F(4, 197) = 1.29; p > 0.05$), there were no significant differences between motor reaction times for the ages. There was no main significant effect of treatment ($F(1, 197) = 0.30; p > 0.05$), there was no significant difference in motor reaction time between the multivitamin and placebo group (see Table 59).

Table 59: Showing the treatment means at each visit (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 12</th>
<th>Week 24</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>354.13</td>
<td>355.43</td>
<td>329.52</td>
<td>294.44</td>
</tr>
<tr>
<td>Placebo</td>
<td>343.60</td>
<td>349.90</td>
<td>315.96</td>
<td>286.86</td>
</tr>
</tbody>
</table>

There was a significant main effect of time ($F(3, 591) = 21.56; p < 0.001$) post hoc testing revealed that reaction times got faster over time, motor reaction times at week 36 were significantly faster than reaction times at baseline, week
12 and week 24 this possibly reflects a learning/familiarity effect (see figure 49). There were no significant age treatment and visit interactions ($F_{(12, 591)} = 1.19; p>0.05$).

![The main effect of visit on MRT](image)

Figure 49: The main effect of time on motor reaction time (MRT).

5.20.5 Summary
In line with chapter 4 there were no main effects of age on tasks assessing the speed of information processing (CFF, RRT, MRT,) despite previous literature (Coleston, 1989). In chapter four there were no main effects of age on TRT, however in the present analysis, effects of age on TRT were observed.

There were no main effects of treatment, supplementation with multivitamin had no effect on either Critical Flicker Fusion thresholds or the Choice Reaction Time task.

5.21 The effects of multivitamin supplementation on recognition memory
In chapter 4 the effects of ageing on tasks that assess recognition memory were assessed, it was concluded that there was no main effect of age on recognition
memory. In chapter 4 the SKT subtest IX was classed as assessing recognition memory. The purpose of this experiment was to assess the effects of supplementation on recognition memory.

5.21.1 SKT subtest IX (recognition memory)

In this task subjects were required to recognise the original 12 objects (seen in subtest I) from a set of 48 pictures of objects. The number of omissions were recorded.

There was a main effect of age ($F(4, 213) = 7.07; p<0.001$). There was a main significant effect of treatment ($F(1, 213) =5.61; p < 0.01$). There was no significant time effect ($F(1, 213) = 1.07; p > 0.05$) there was no significant change in recognition memory over time. There was a significant interaction between age, treatment and test ($F(4, 213) = 3.77; p < 0.005$).

The main effect of age was analysed using post hoc testing with the Newman Keul's test, it was revealed that there was a significant increase in forgetting rates as age increased, subjects aged 80+ had the poorest recognition memory (see Figure 50)

![The main effect of age on SKT IX](image)

**Figure 50:** Showing the main effect of age on recognition memory (SKT IX).
Post hoc testing of the main effect of treatment revealed that forgetting rates were higher in the placebo treated group (placebo = 0.84, multivitamin = 0.51).

Post hoc testing of the age treatment and time interaction revealed a number of significant differences. In the placebo group there was no significant difference between the baseline and week 36 test point for subjects aged 60-64, 65-69 and 70-74. Subjects aged 75-79 years showed a significant increase in forgetting rates at week 36 compared to baseline, and subjects aged 80+ showed a significant improvement in forgetting rate at week 36 compared to the baseline visit.

In the multivitamin treated group, there was no significant difference between the baseline and week 36 test point for subjects aged 60-64, 65-69, 70-74 and 75-79 years. Subjects aged 80+ showed a significant increase in forgetting rates at week 36 compared to baseline (see Figure 51).

![Figure 51](image)

**Figure 51:** The significant interaction between age treatment and test on recognition memory (SKT IX).

### 5.21.2 Summary

In this sample there was a main effect of age reported on recognition memory, in particular the oldest subjects, those aged 80+ had the poorest recognition memory. In chapter 4 there were no main effects of age on recognition memory.
scores. There was an interaction between age treatment and visit, it was revealed that in the older subjects (i.e. those aged 75-79 and 80+) there were a number of differences between the treatment groups. In the placebo group subjects aged 75-79 showed an increase in their forgetting rates over the test period, whereas subjects aged 80+ showed an improvement over time. In the multivitamin group, subjects aged 80+ showed an increase in their forgetting rate over time.

5.22 The effects of multivitamin supplementation on intelligence

Much of the research conducted in this area particularly with teenagers and young children would seem to imply that intelligence, particularly non verbal intelligence is strongly affected by improved nutritional status. The effects of multivitamin supplementation on non verbal intelligence in an elderly sample.

5.22.1 Ravens Standard Progressive Matrices (RSPM)

Subjects completed the Ravens Standard Progressive Matrices, consisting of 60 problems.

There was a main effect of age ($F(4, 211) = 5.70; p<0.001$). There was no main significant effect of treatment ($F(1, 211) = 1.13; p > 0.05$), there was no significant difference in Ravens scores between the supplemented or the placebo group (see Table 60).

<table>
<thead>
<tr>
<th>Table 60: Showing the treatment means at each visit.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Baseline</strong></td>
</tr>
<tr>
<td>Multivitamin</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
</tbody>
</table>

There was a significant time effect ($F(1, 211) = 5.60; p < 0.01$) post hoc testing revealed that both the placebo and multivitamin supplemented groups showed
an improvement in Ravens scores over the testing period. There were no significant age treatment and time interactions ($F(4,211) = 1.25; p>0.01$).

Post hoc testing revealed that Raven’s mean scores declined as age increased, older subjects had lower scores than younger subjects (see Figure 52).

![The main effect of Age on the Ravens Task](chart)

**Figure 52:** The main effect of age on Ravens Standard Progressive Matrices.

### 5.22.2 Summary

There was a main effect of age on the Ravens standard progressive matrices, so that older subjects had poorer intelligence scores than younger subjects.

Despite previous findings, there was no main effect of treatment on non verbal intelligence. Perhaps this effect is specific to children or subjects with poor diet, or rather the effect is specific to the test.

### 5.23 The effects of multivitamin supplementation on mood

Subjective mood is another aspect of human functioning that is thought particularly susceptible to nutritional deficiencies, in particular deficiencies in the B complex vitamins have been associated with mood disturbances, and extreme changes in mood such as depression. In this experiment the impact of
multivitamin supplementation on subjective ratings of anxiety, depression were examined using the Hospital Anxiety and Depression Scale (HADS) and cognitive failures, such as slips of the tongue, disturbances in attention and memory etc were examined using the Cognitive Failures Questionnaire (CFQ).

5.23.1 The Hospital Anxiety and Depression Scale (HADS): Anxiety

Subjects completed Zigmond and Snaith's (1983) Hospital Anxiety and Depression Scale (HADS), 7 of the 14 items assess anxiety.

There was no main effect of age ($F(4, 211) = 0.63; p > 0.05$) there was no significant difference between anxiety scores and the ages. There was no significant main effect of treatment ($F(1, 211) = 1.11; p > 0.05$) there was no significant difference in anxiety scores between the supplemented or placebo group (see Table 61).

Table 61: Show ing the anxiety treatment means at each visit.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>6.58</td>
<td>6.61</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.76</td>
<td>6.05</td>
</tr>
</tbody>
</table>

There was no significant main effect of time ($F(1, 211) = 0.00; p > 0.05$) there was no significant change in anxiety scores over time. There was a significant age, treatment and time interaction ($F(4, 211) = 3.12; p < 0.01$).

Post hoc testing of the age treatment and time interaction revealed that in the placebo group subjects aged 60-64 and 80+ showed a slight fall in anxiety scores over time, subjects 65-69, 70-74 showed a slight increase in anxiety scores over time. Subjects aged 75-79 years showed a significant increase in anxiety scores over time.
In the multivitamin treated group, subjects aged 60-64 and 65-69 reported no differences in their anxiety scores over time. Subjects aged 70-74 showed a significant increase in anxiety scores over time. Subjects aged 75-79 showed a slight decrease in anxiety scores over time and subjects aged 80+ reported no difference in their anxiety scores over time. (see Figure 53)

![Anxiety treatment age and time interaction](image)

Figure 53: The interaction between age treatment and visit in anxiety scores.

5.23.2 The Hospital Anxiety and Depression Scale (HADS): Depression

Subjects completed Zigmond and Snaith's (1983) Hospital Anxiety and Depression Scale (HADS). 7 of the 14 items assess depression.

There was no main effect of age \((F (4, 211) = 2.22; p > 0.05)\) there was no significant difference between depression scores and the ages. There was no main significant effect of treatment \((F (1, 211) = 2.22; p > 0.05)\), there was no significant difference in depression scores for either the supplemented or the placebo groups (see Table 62).

<table>
<thead>
<tr>
<th>Table 62: Showing the depression treatment means at each visit.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>------------</td>
</tr>
<tr>
<td>Multivitamin</td>
</tr>
<tr>
<td>Placebo</td>
</tr>
</tbody>
</table>
There was no significant time effect ($F(1, 211) = 0.08; p > 0.05$) there was no significant change in depression scores over time. There was no significant age, treatment and time interaction ($F(4, 211) = 0.98; p > 0.05$).

5.23.3 The Cognitive Failures Questionnaire (CFQ)

Subjects completed a self rating questionnaire consisting of 25 questions subjects had to rate how frequently they had experienced cognitive failures e.g. absentmindedness, forgetting appointments, directions, errands (since their last visit).

There was no main effect of age ($F(4, 206) = 0.85; p > 0.05$) there was no significant difference between cognitive failure scores and the ages. There was no main significant effect of treatment ($F(1, 206) = 2.87; p > 0.05$), there was no significant difference in the cognitive failure scores for either the supplemented or the placebo group (see Table 63).

**Table 63:** Showing the treatment means at each visit.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multivitamin</td>
<td>39.80</td>
<td>38.90</td>
</tr>
<tr>
<td>Placebo</td>
<td>36.96</td>
<td>37.31</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F(3, 618) = 0.44; p > 0.05$) there was no significant change in the cognitive failure rate over time. There was no significant age, treatment and time interactions ($F(12, 618) = 0.81; p > 0.05$).

5.23.4 Summary

There was no main effect of age or treatment on either anxiety or depression scores. Subjects self ratings of depression and anxiety were comparable in both the multivitamin and placebo groups.
There was no main effect of age or treatment on the self reporting of failures in everyday life such as forgetting appointments, conversations, errands, directions, absentmindedness, tip of the tongue experiences and the ability to learn. Supplementation had no effect on subjective ratings of failure.

5.23.5 Blood vitamin summary

The effect of supplementing diet with a multivitamin preparation resulted in a significant increase in blood vitamin level in most cases after only 12 weeks of treatment (with the exception of vitamin A, this was due to the fact that the multivitamin supplementation consisted of a lower dose of vitamin A equivalent of 1 US RDA was given so to reduce the risk of vitamin A toxicity). What is of importance here, is whether a significant increase in blood vitamin level has an effect on psychometric performance. The hypothesis was that higher blood vitamin levels would result in superior psychometric task performance, and lower self reports of cognitive failure, anxiety and depression.

5.24 Deficiency in the population sampled

Having analysed the data it became apparent that cognitive decrements should only be observed in subjects with a defined vitamin deficiency. In terms of the baseline data there were a number of subjects who were experiencing vitamin deficiency. Roche Pharmaceuticals provided vitamin deficiency cut off rates, in terms of low, moderate and high risk of deficiency. Table 64 shows the risk of deficiency for subjects in the present study.

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin A</td>
<td>237</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin B₁</td>
<td>223</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Vitamin B₂</td>
<td>149</td>
<td>57</td>
<td>24</td>
</tr>
<tr>
<td>Vitamin B₆</td>
<td>120</td>
<td>38</td>
<td>72</td>
</tr>
<tr>
<td>Vitamin B₁₂</td>
<td>222</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>234</td>
<td>0</td>
<td>3</td>
</tr>
</tbody>
</table>
Having identified that the present population did contain a number of subjects who were at either moderate or high risk of vitamin deficiency. It was then possible to examine the effect of the change in vitamin status in subjects with a different risk of deficiency. It was possible to compare the effect of vitamin supplementation in subjects with good nutritional status compared with subjects with poorer nutritional status.

In order to do this, subjects were classified into one of three groups, low risk subjects (n = 97), moderate risk subjects (n = 70) and subjects at high risk (n = 56). High risk subjects were subjects with at least one moderate and one high risk of deficiency.

<table>
<thead>
<tr>
<th>Vitamin</th>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E</td>
<td>237</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Biotin</td>
<td>194</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>178</td>
<td>60</td>
<td>0</td>
</tr>
</tbody>
</table>

It was hypothesised that subjects with a greater risk of deficiency would "respond" to a greater extent than subjects with a low risk of vitamin deficiency, i.e. high risk subjects would show a greater degree of improvement of cognitive function than subjects with a low risk of vitamin deficiency.
The data were analysed using a three analysis of variance (ANOVA) with tests as the within subjects factor and risk of deficiency (low, moderate and high) and treatment (multivitamin, placebo) as between subjects factors. The data were analysed to determine whether the risk of deficiency interacted with a change in performance.

It was revealed that none of the performance analyses on any of the cognitive tasks (CFF, CRT, SMT, SKT, Ravens or the cognitive failures questionnaire) showed any reliable involvement of severity in performance changes.

There was an interaction between risk of deficiency and change in mood, as measures using the Hospital Anxiety and Depression Scale. It was reported that subjects in the moderate group had higher anxiety levels following supplementation that subjects in either the high or low risk groups \((F(3, 225) = 4.88; p<0.05)\). There was a three way interaction between treatment severity and tests in terms of the depression scale on the HADS. It was reported that placebo treated subjects with a high risk of deficiency became more depressed over time compared to subjects with low of deficiency who became less depressed over time \((F(12, 225) = 4.44; p<0.05)\).

5.25 Discussion

Despite the fact that supplementation with a multivitamin supplement for 36 weeks lead to a significant increase in blood vitamin levels over time, this increase in blood vitamin levels had no beneficial effects in terms of cognitive and psychomotor performance. It was hypothesised that subjects with higher blood vitamin levels would show superior cognitive functioning to subjects with low blood vitamin levels.

This experiment failed to demonstrate any beneficial effects of supplementation on tasks assessing attention, memory recall, speed of naming, speed of
information processing, recognition memory, intelligence or any effects on subjective mood ratings or perceived cognitive failures. There was one finding that although was not an improvement could be taken as evidence of a protection on decline, subjects treated with multivitamins had stable performance on the recognition memory task, whereas subjects treated with placebo showed a decrement in performance over time.

In terms of deficiency the sample was very well nourished, only 30% of the sample were at a high risk of deficiency of vitamin B₆ and only 10% of the sample were at a high risk of deficiency of vitamin B₂. Data was analysed to determine whether subjects with a high risk of deficiency showed differences in performance from subjects with a low risk of deficiency. It was reported that there were no performance differences between subjects in terms of the risk of deficiency. There was a significant difference between the subjects in terms of mood ratings. It was reported that subjects with a moderate risk of vitamin deficiency reported higher anxiety levels following supplementation that subjects with either a high or low risk of deficiency. In terms of supplementation it was reported that placebo treated subjects with a high risk of deficiency reported feeling more depressed over time, whereas those with a low risk of deficiency reported feeling less depressed over time. There were no other differences reported in terms of the risk of deficiency.

In previous studies, there were no effects of supplementation reported on tasks assessing attention. In the present study, there were five tasks assessing attention SKT IV (arranging blocks); SKT V (replacing blocks); SKT VI (counting symbols); SKT VII (reverse naming); and the HPRU Sternberg Memory Task (SMT). SKT subtests IV and V represent spatial tasks, simply requiring the subjects to arrange numbers into an order, hence do not place the subjects under a great deal of cognitive demand, therefore improvements on these tasks, following a nutritional supplement would not be expected. SKT VI (counting symbols) is a vigilance/selective attention task, requiring the subjects
to concentrate on counting a number of symbols, contained in a list of a number of symbols. SKT VII (reverse naming) is a fairly complex selective attention task similar to the Stroop task, where subjects have to process information and respond in another way, e.g. see a letter A and say B. There have been no studies examining the effects of supplementation on the Stroop task, however Bohnen et al. (1992) reported that subjects deficient in vitamin B₁₂ had poorer Stroop task performance than subjects with high blood vitamin B₁₂ levels. Therefore it was thought that supplementation with multivitamins would enhance performance on the task.

In the HPRU Sternberg Memory Task, subjects were required to memorise a small series of numbers, the task being very similar in nature to the digit span forward task. In terms of the effects of supplementation on the forward digit span task, previous studies have reported mixed findings. Botez et al. (1984) reported that treatment with folate for 7-11 months resulted in improved digit span performance, whereas Tolonen et al. (1992) reported that vitamin B₆ had no effect on the task. Based on the results from this present study, performance improvements following supplementation were expected on the task.

These results as a whole would seem to mirror previous studies, where no beneficial effects of supplementation were reported on tasks assessing attention.

Memory is an aspect of cognitive function that is thought to be sensitive to nutritional status. In particular, it has been reported that deficiency in certain vitamins has resulted in decrements on a number of tasks e.g. paragraph recall, backward digit span and visual memory tasks. In terms of supplementation, the results of experimental work seem somewhat contradictory, Deijen et al. (1992) reported that the effects of supplementation with vitamin B₆ seemed to have dramatic effects on long term memory. However Tolonen et al. (1988) reported that supplementation with vitamin B₆ for one year resulted in improved immediate paragraph recall and performance on the clock test. Botez et al.
(1984) reported that supplementation with folate for 7-11 months resulted in significant improvements on performance of the digit span task.

In terms of the immediate and delayed recall memory tasks used in this experiment, SKT subtest II (immediate recall) and SKT VIII (delayed recall) are age sensitive tasks, that showed a decline with advanced age. It was hoped that supplementation with multivitamins would help to eliminate the age related decrement. However it would appear that the tasks were not responsive to multivitamin supplementation. The recognition memory task (SKT IX) was not sensitive to the effects of age, and hence performance could not be expected to show any improvements following multivitamin supplementation.

There have been two studies examining the effect of vitamin supplementation on the speed of information processing in healthy elderly subjects (Deijen et al., 1992; Burr et al., 1975). Neither study reported any beneficial effect of supplementation on the speed of information processing. In line with this, the present study reported that multivitamin supplementation had no effect on tasks assessing the speed of information processing (CFF, TRT, RRT, MRT).

There have been no studies that have examined the effect of supplementation on the speed of naming. However, as these tasks are similar to tasks assessing the speed of information processing for which no effect of supplementation was reported. Therefore, no effects of supplementation were expected on SKT I (object naming) and SKT III (numerical naming), and this was found to be the case.

Intelligence, particularly non verbal intelligence has been shown to improve following supplementation in children (Harrell, 1946; Boggs et al., 1965; Schoentahler et al., 1991; Benton and Roberts, 1988; Benton and Butts, 1990; Benton and Cook, 1991). There have been few studies examining the effects of supplementation on intelligence in healthy and elderly patient populations, the
few studies that have assessed aspects of intelligence have reported that supplementation had the effect of improving scores. Therefore it is possible that the beneficial effects are not just limited to child samples. The present study assessed the effect of multivitamin supplementation on performance of the Ravens task, a non verbal test of intelligence. However unlike previous studies, it was reported that multivitamin supplementation had no effect on Raven's scores. The beneficial effects reported in the previous studies have been on the abstraction task, a subtask of the WAIS used for the assessment of intelligence, and the Mini Mental State Examination (MMSE). It is possible that these tasks measure other aspects of cognitive function, rather than intelligence per se.

Mood was assessed using the Hospital Anxiety and Depression scale, no effects of supplementation were observed. In a previous study Chomé et al. (1986) reported that multivitamin deficient subjects had higher depression scores than non deficient subjects. Smidt et al. (1991) reported that supplementation with vitamin B₁ for 6 weeks resulted in improved feelings of well being.

A number of differences between the present study and earlier research may help to explain why this long term intervention study failed to demonstrate any beneficial effects on cognitive functioning in the elderly.

The present study did not include any of the tasks used by previous research teams. It is possible that the tasks selected for use in this experiment were not sensitive to detect slight performance improvements, even though many of them were sensitive to the effects of age (SKT II, IV, V, VII, VIII, IX, HPRU Sternberg memory task, Total Reaction Time and Ravens Standard Progressive Matrices).

It is quite possible that these tasks were not sensitive to the effects of improved nutrition, treatment with an over the counter supplement at best could only be expected to produce modest improvements, it is possible that these modest
improvements were to subtle to be detected by the cognitive and psychomotor tasks included in this study.

The age differences between the previous studies and this present study may also have contributed to the lack of effect, although this study included subjects aged 60-85 years, the vast majority of the sample were aged 60-70 years, (the mean age of the subjects was only 69.5 years ) which in terms of experimental studies can be classed as young elderly subjects. The mean age of subjects in the previous studies was slightly higher than the mean in this study (see Table 30 with the exception of Riggs et al., 1997 and Smith et al., in press), and it is possible that the older subjects in the previous studies were experiencing more decline in cognitive and psychomotor function than the subjects included in this experiment.

Another major difference between the present study and previous studies, concerns the sample population size. The present study contained 239 healthy elderly subjects, whereas previous studies have sampled much smaller populations (with the exception of Goodwin et al., 1983; Burr et al., 1975; Smith et al., in press)

Table 66: Showing the age ranges, and mean ages of subjects included in previous studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Age Range</th>
<th>Mean Age</th>
<th>Sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burr et al. (1975)</td>
<td>above 70 years</td>
<td>78 years</td>
<td>297</td>
</tr>
<tr>
<td>Goodwin et al. (1983)</td>
<td>60-94 years</td>
<td>71 years</td>
<td>250</td>
</tr>
<tr>
<td>Chomé et al. (1986)</td>
<td>65-91 years</td>
<td>not quoted</td>
<td>60</td>
</tr>
<tr>
<td>Šrám et al. (1990)</td>
<td>60-90 years</td>
<td>not quoted</td>
<td>80</td>
</tr>
<tr>
<td>Tucker et al. (1990)</td>
<td>60-87 years</td>
<td>not quoted</td>
<td>28</td>
</tr>
<tr>
<td>Lauque et al. (1995)</td>
<td>above 60 years</td>
<td>73 years</td>
<td>91</td>
</tr>
<tr>
<td>Riggs et al. (1996)</td>
<td>54-81 years</td>
<td>66.1 years</td>
<td>70</td>
</tr>
<tr>
<td>La Rue et al. (1997)</td>
<td>66-90 years</td>
<td>76.9 years</td>
<td>137</td>
</tr>
<tr>
<td>Smith et al. (in press)</td>
<td>60-80 years</td>
<td>66 years</td>
<td>205</td>
</tr>
</tbody>
</table>
Finally the recruitment procedure may have hindered the experiment, all the subjects volunteered to take part in the study and were obtained via advertisements in Doctors surgeries and local newspapers, or from the HPRU data base. When experiments are conducted using volunteer samples, a biased sample is generally obtained, consisting of subjects who are very fit, health conscious, eager and highly motivated therefore it can be argued that the sample included in this study were probably not suffering from any degree of cognitive decline.

In terms of future research, it might be more suitable to include tasks that have previously proved sensitive to the effect of multivitamin supplementation in order to try an clarify whether the effects observed were universal, or use tests that assess similar aspects of cognitive function to those found to be sensitive to the effects of supplementation. It would also be more representative of the population if a wider selection of elderly subjects were included as subjects, rather than just relying on volunteers, given that it may be the case that performance improvements can only be expected in subjects who are already experiencing a certain degree of cognitive decline.
Chapter Six: The effects of repeated dosing with Ginkgo Biloba on aspects of cognitive function in a healthy elderly population.

6.1 Chapter outline

What is Ginkgo Biloba

The mechanism of action of Ginkgo Biloba

Cognitive enhancing and mood enhancing properties

The effects of GBE supplementation on attention in adult populations
The effects of GBE supplementation on memory in adult populations
The effects of GBE supplementation on the speed of information processing in adult populations
The effects of GBE supplementation on mood and well being in adult populations

The effects of long term supplementation with GBE on cognitive function in a healthy elderly population.

The effects of Ginkgo Biloba on attention
The effects of Ginkgo Biloba on memory recall
The effects of Ginkgo Biloba on the speed of naming
The effects of Ginkgo Biloba on the speed of information processing
The effects of Ginkgo Biloba on recognition memory
The effects of Ginkgo Biloba on subjective ratings of ADL

This chapter reviews the literature in which elderly subjects were treated with ginkgo biloba and reports an original study which investigated the effects of repeated dosing of ginkgo biloba 100 mg daily on aspects of cognition (attention, memory recall, speed of information processing, speed of naming, and recognition memory) in a sample of 16 healthy elderly volunteers.
6.2 **Introduction: Ginkgo Biloba**

There are a number of compounds that have been implicated as possible enhancers of human cognition, the actions of which either aim to improve cerebral blood flow or increase oxygen and glucose availability for the brain.

The Chinese herbal remedy Ginkgo Biloba Extract (GBE) is a potential cognitive enhancing drug, improving aspects of memory and cognition, particularly in elderly samples (Israel, Dell’Accio, Martin and Hugonot (1987); Dieli, La Mantia, Saetta and Constanzo, (1981); Taillandier, Ammar, Rabourdin, Ribeyre, Pichon, Niddam, and Pierart, (1986); Weibrecht and Jansen, (1986); Wesnes, Simmons, Rook, and Simpson, (1987); Franco, Cuny and Nancy (1991); Rai, Shovlin, and Wesnes, (1991); Le Bars, Katz, Berman, Itil, Freedman and Schatzberg (1997) and Maurer, Ihl, Dierks and Frölich (1997).

Ginkgo biloba is one of the most widely used natural products of plant origin (Beyreuther, 1991). The tree is regarded as a living fossil, it has been on earth for approximately 200,000,000 years, has probably existed longer than any other tree (Nakanishi, 1988). Treatment with GBE can be traced back to the origins of Chinese herbal medicine approximately 5000 years ago, in the past GBE was used to treat bronchitis and asthma. Treatment with the leaves and the fruit of the tree are still recommended for diseases of the heart and lungs (Chang and But, 1987).

Extracts of GBE were introduced into medical practice some 30 years ago, where it was used to treat disturbances in cerebral and peripheral blood flow (Ambrosi and Bourde, 1975; Courbier, Jauissseran and Reggi, 1977; Bauer, 1984, Berndt and Kramer, 1987; Deihm, Heinrich and Mörl, 1990). The first GBE was registered by German physician-pharmacist Dr Willmar Schwabe in 1965. GBE has been prescribed as a drug in France for over 20 years. GBE is also accepted as a drug in a number of countries e.g. Germany, Spain,
Switzerland, Luxembourg, Greece, Italy and Ireland. In the UK GBE is considered as a food supplement and hence is readily available over the counter in pharmacists, health food stores and supermarkets.

6.3 What is Ginkgo Biloba

GBE contains many different substances including flavonoids, proanthocyanidines, ginkgolides and biobalide. The protective effects of GBE are probably due to the main constituents the flavonoids (e.g. ginkgo flavone glycosides) and the terpenoids (ginkgolides). Ginkgolide B is one of the ginkgolides present in the extract (others are ginkgolide A, B, C and J). Metabolites of the ginkgo biloba extract have been found to cross the blood brain barrier, when radio-labelled GBE was given to rats traces of the compound were found in a number of organs including the brain. Seventy two hours post dose the highest concentration of GBE was found in the hypothalamus, striatum and hippocampus (Moreau, Eck, McCabe and Skinner, 1988).

6.4 The possible mechanisms of action

The pharmacological action of GBE is often described as ‘polyvalent’, the major mechanisms include ‘vaso’ and ‘tissue protective’ and ‘cognitive enhancing’ including mood elevating action which makes it beneficial in the treatment of elderly patients suffering from senile dementia. It was first thought that the mechanism of action of GBE was via vasoregulation, however, as research continued other possible mechanisms of action have been proposed, such as antioxidant properties trapping free radicals therefore protecting cells from damage, more recently GBE has been shown to act upon cerebral plasticity (Lacour, Ez-Zaher and Raymond, 1991).

GBE has been shown to protect cells by acting as a scavenger of free radicals (Pincemail and Deby, 1986) that prevents peroxidation of membrane lipids by
oxygen free radicals (Dorman, Côté and Buck, 1992), ginkgolide B has been shown to have a protective effect against brain ischemia, this effect might be due to an effect on cerebral blood flow and/or brain glucose utilisation. The neuroprotective effect of ginkgolide B due to the specific platelet-activating factor receptor antagonist activity. Krieglstein, Beck and Seibert (1986) found that the drug increases cerebral blood flow without reducing metabolic demand, this was ascertained by giving intravenous injections of GBE (130 mg/kg) to rats 20 minutes before deoxyglucose administration, this had the effect of increasing cerebral blood flow by 50-100 % but had no effect on brain glucose utilisation. A drug/compound with such a profile would be useful in the treatment of brain ischemia.

Originally it was thought that the mechanism of action was that, GBE was a triple vasoregulator, modulating capacity in arteries, veins and capillaries, enabling them to dilate or constrict depending on the disease state.

Several mechanisms contribute to the drugs vaso and tissue protective action, GBE can act on arterial, venous and capillary components of the vascular system, as well as on formed elements of the blood. GBE also has anti-thrombotic, anti-ischaemic and anti-edema properties, the combined action of all mechanisms appear to be responsible for the vasoregulatory action of GBE. It is postulated that the flavonoids are responsible for GBE ability to relax contracted blood vessels.

6.5 Cognitive enhancing and mood enhancing properties

The cognition enhancing properties of GBE appear to be related to a number of actions e.g. the anti-ischaemic and anti-edema properties, free radical scavenging and enzyme inhibitor activities of its flavonoid constituents might be involved. The cognitive enhancing properties may be due to GBE involvement in inhibition of biogenic amine uptake (Auguet, De Feudis and
Clostre, 1982). GBE has also been shown to have a tyramin-like effect, releasing noradrenaline. It is possible that certain phenolic compounds (either present in GBE or formed after its administration in the intact animal) enhance the release of catecholamines and other important neurotransmitters such as acetylcholine from nerve terminals in the brain and it is this mechanism that is responsible for the mood enhancing properties of GBE.

Another mechanism that could be responsible for the cognitive enhancing action of GBE would be the inhibition of enzymes in particular catechol-0-methyl transferase and monoamine oxidase (MAO) by its flavonoid constituents, inhibition of the enzymes leads to increases in catecholamines in synaptic clefts. The mood elevating effects could be due to protease-inhibitors that GBE contain, e.g. Captopril a protease-inhibitor has been shown to improve mood in depressed patients (Zubenko and Nixon, 1984). The protease-inhibitor in GBE would probably be due to its flavonoid constituents.

Ginkgo Biloba also appears to affect the cholinergic system, by enhancing the density of cholinergic muscarinic receptors (Taylor, 1985). GBE has been shown to increase glucose consumption in ischaemic areas in both human and animal brains (Rapin and Le Poncin Laffitte, 1979); and increase muscarinic receptor population in the hippocampus of the aged rat (Taylor, 1986).

Ginkgo biloba is also thought to possess anti-edema and anti-ischaemic properties, these are probably due to the actions of the flavonol glycosides and bilobalide.

Studies have assessed the pharmacokinetics of ginkgo biloba, to determine the peak plasma levels and elimination half life of the compound from the body. Wójcicki, Gawro ska-Szklarz, Bieganowski, Patalan, Smulski, Samachowiec and Zakrzewski (1995) assessed the pharmacokinetics and bioavailability of 3 different formulations of ginkgo biloba (capsule, drops and tablet formats).
Eighteen healthy subjects aged 18-45 years (mean age 30 years) received the three formulations, and blood samples were taken at baseline and after 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 6.0, 8.0, 12.0 and 24 hours post dose. It was reported that peak plasma levels for all formulations appeared approximately 3 hours post dose, the drug was rapidly eliminated, and was totally eliminated after 24 hours. The drug has a short elimination half life of 2.84 hours and total body clearance was achieved after 44.72 hours.

A number of researchers have examined the effects of ginkgo biloba on aspects of cognitive function in healthy adult, elderly and patient populations to assess the effects of supplementation on aspects of attention, memory, the speed of information processing and mood.

6.6 The effects of GBE supplementation on attention in adult populations

There have been no clinical studies examining the effect of ginkgo biloba on aspects of attention in healthy elderly subjects. However there have been studies in which the effects of ginkgo have been observed on tasks assessing attention in patient populations.

Weibrecht and Jansen (1986) assessed the effect of ginkgo biloba (120 mg) compared with placebo on the digit symbol substitution task (DSST) in 40 patients with mild to moderate primary degenerative dementia aged 60-80 years taken for 3 months. Performance was assessed at baseline, and after 4, 8 and 12 weeks. It was reported that scores on the DSST in the ginkgo biloba treated group increased significantly.

Wesnes, Simmons, Rook and Simpson (1987) assessed the effects of ginkgo biloba on cognitive performance in 44 elderly patients aged 62-85 years. Patients were showing mild signs of cognitive impairment as assessed using the Crichton Geriatric behavioural rating scale. Patients were treated with ginkgo
biloba (120 mg) or placebo for 12 weeks. Performance was assessed using the DSST and a number matching task at baseline and after 4, 8 and 12 weeks. It was reported that there was a non significant trend towards improvement on the DSST in the GBE condition during week 12. Following treatment with GBE subjects made significantly more correct responses on the number matching task after 8 and 12 weeks.

Maurer, Ihl, Dierks and Frölich (1997) assessed the effects of GBE on performance of the Syndrom Kurtz Task (SKT) and a trail making task in 20 patients with Alzheimer's disease. Patients were treated with GBE 240 mg or placebo for a period of 3 months. It was reported that following treatment the GBE treated group showed a significant improvement on total SKT scores (scores fell from 19.67 to 16.78 after 12 weeks) and a non significant trend towards improvement on the trail making task.

Kanowski, Herrmann, Stephan, Wierich and Hörr (1995) assessed performance using the SKT task in a sample of 216 elderly patients with a mean age of 69.5 years. All patients had a diagnosis of presenile or senile dementia of the Alzheimer type. Patients were treated with GBE 240 mg or placebo for 2 years. Cognitive function was assessed using the SKT task, it was reported that following treatment 38% of the GBE group and 18% of the placebo treated group showed overall improvements (of greater than 4 points) on the task.

The results of both Maurer et al. (1997) and Kanowski et al. (1995) are interesting, however as the SKT task incorporates tasks of attention and memory, it is not possible to determine whether the beneficial effects were observed on tasks of attention or whether the improvements were primarily on the memory tasks alone, without separate analyses of the subtests, then it is not possible to determine the specific effects.
6.6.1 Summary

To date there have been no reported studies examining the effect of ginkgo biloba on attention in healthy adult subjects. However there have been a number of studies examining the role of ginkgo biloba on aspects of attention in elderly patient populations.

A number of researchers have examined the effects of GBE on aspects of attention in patient populations. The results of which appear somewhat inconclusive. Treatment with GBE has resulted in a number of non significant trends towards improvement (Wesnes et al., 1987; Maurer et al., 1997 and Weibrecaht and Jansen, 1986) and significant effects on the SKT task (Maurer et al., 1997; Kanowski et al., 1997), the number matching task (Wesnes et al., 1987) and the trail making task (Maurer et al., 1997).

In general beneficial effects have only been observed when patients have been supplemented with large daily doses of GBE 240 mg (Maurer et al., 1997; Kanowski et al., 1997).

Based on these rather limited effects, and the fact that in the present study healthy subjects will only receive 100 mg daily for 8 weeks, supplementation with ginkgo biloba would probably have no effect on the performance of tasks assessing attention.

A 100 mg daily dose was selected as the study was designed to assess the cognitive enhancing effect of ginkgo biloba in the "real world", hence the recommended daily dose was selected.
Table 67: Summarising the effects of supplementation with ginkgo biloba on aspects of attention in adult and patient populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>Age</th>
<th>n</th>
<th>GBE Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weibrecht and Jansen (1986)</td>
<td>Patients with mild to moderate dementia</td>
<td>60-80 years</td>
<td>60</td>
<td>120 mg for 3 months</td>
<td>DSST</td>
<td>DSST showed a non significant trend towards improvement</td>
</tr>
<tr>
<td>Wesnes et al. (1987)</td>
<td>Patients with cognitive impairment</td>
<td>62-85 years</td>
<td>44</td>
<td>120 mg for 12 weeks</td>
<td>DSST</td>
<td>Non significant improvement in DSST and improved performance on the matching task at 8 and 12 weeks.</td>
</tr>
<tr>
<td>Maurer et al. (1997)</td>
<td>Patients with mild to moderate dementia</td>
<td>Aged 50-80 years</td>
<td>20</td>
<td>240 mg for 3 months</td>
<td>Trail making task</td>
<td>There was a non significant trend towards significance on the trail making task</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Mean age 69.5 years</td>
<td>216</td>
<td>240 mg for 2 years</td>
<td>SKT</td>
<td>Significant improvement on the SKT</td>
</tr>
<tr>
<td>Kanowski et al. (1997)</td>
<td>Patients with dementia</td>
<td></td>
<td></td>
<td></td>
<td>SKT</td>
<td>38% showed significant improvements on SKT task</td>
</tr>
</tbody>
</table>
6.7 The effects of GBE supplementation on memory in adult populations

There have been no studies examining the effects of ginkgo biloba on memory in healthy elderly subjects, although there have been a number of studies examining the effect of ginkgo biloba treatment on memory in healthy adult populations in patients with senile dementia of the Alzheimer type (SDAT).

Subhan and Hindmarch (1984) assessed the impact of acute dosing of ginkgo biloba (120, 240 and 600 mg) on cognitive performance in a sample of 8 healthy female volunteers aged 25-40 years (mean age 32 years). Performance was assessed using the HPRU version of the Sternberg memory task (subjects were required to remember digit strings containing 4, 5 and 6 digits, the number of correct and incorrect responses were recorded as was reaction time to the stimuli) performance was assessed 1 hour post dose. It was found that reaction time on the Sternberg memory task was significantly reduced following a single 600 mg dose of ginkgo biloba. There were no effects reported on the Sternberg memory task with either the 120 mg or 240 mg dose.

Parkin, Dawe and Hindmarch (1995) produced a drug-induced cognitive deficit in healthy volunteers. Prior to dosing with either GBE or placebo subjects were given a single 1 mg dose of flunitrazepam to induce a short term memory deficit. The aim of the study was to determine whether a single 600 mg acute dose of GBE would prevent a benzodiazepine induced memory impairment.

10 healthy female volunteers aged between 25 and 40 years (mean age 36.2 years), received an acute 600 mg dose of GBE and completed the HPRU version of the Sternberg memory task (subjects had to memorise memory sets, containing 1, 2 and 3 digits) and a word recognition task (much the same as the Sternberg memory task, a recognition and response time task for words, subjects were required to memorise a list of 14 words, and had to recognise the 14 words). Assessments were made at baseline, 1, 2, 4, and 6 hours post dose.
There were no significant differences reported between GBE and placebo on the tasks. It was possible that the deficit induced was too great therefore the experiment was repeated using a lower dose of flunitrazepam (0.5 mg). Psychometric assessments were made at baseline, 1.5, 3, 4 and 6 hours. There were no significant differences between the treatments (GBE/flunitrazepam, and placebo/flunitrazepam) on performance of the Sternberg memory task or the word recognition task.

Dawe, Kerr, Yoon and Hindmarch (1995) conducted a pilot study examining the effect of GBE on cognitive and psychomotor function in a sample of young healthy volunteers. Eleven young volunteers (mean age 28.6 years) received 200 mg GBE and placebo daily for a period of 14 days, in a randomised cross over fashion. Psychometric tests were completed at baseline, day 7 and 14, performance was assessed using the HPRU Sternberg memory task (subjects had to memorise memory sets, containing 1, 3 and 5 digits), and a picture memory task (subjects were shown 12 pictures of objects for a 30 second period, they were required to give immediate recall of the pictures, delayed recall 10 minutes later and recognition some 20 minutes later). In the HPRU Sternberg memory task an interaction of drug and visit that approached significance was observed (p = 0.051) the interaction resulted in improvements over the visits with GBE compared to placebo. There were no effects of GBE on the picture memory task.

Warot, Lacomblez, Danjou, Weiller, Payan and Puech (1991) investigated the effects of GBE on memory function in a sample of 12 healthy female volunteers (aged 19-30 mean age 22.3 years). Subjects were randomly allocated to a single dose of GBE 600 mg or placebo. Memory tests including recognition of numbers task (a Sternberg memory task subject had to remember 40 sequences of number sets containing 4, 5 or 6 stimuli), free recall and recognition of images (subjects were shown 40 items, 20 of which they had previously seen), subjects had to provide immediate recall and recognition after 30 minutes).
There were no significant differences observed between the treatments with regard the Sternberg Memory Task or the picture recognition task. It was reported that treatment with GBE resulted in a stabilising of free recall of images, whereas performance in the placebo condition declined.

Allain, Raoul, Lieury, LeCoz, Gandon and d'Arbigny (1993) assessed the effects of 2 doses of GBE (320 mg and 600 mg) compared to placebo in a sample of 18 healthy elderly subjects aged 60-80 years (69.3 years). Performance was assessed using a dual coding task in which subjects had to process and recall pictures of drawings and words, which were presented at a rate of 1920 ms through to 120 ms. It was reported that following treatment with both doses of GBE, there was a significant improvement in performance.

Israel, Dell'accio, Martin and Hugonot (1987) assessed the effects of GBE on memory performance in a sample of 80 geriatric patients (aged 56-83 years, mean age 68.4 years). Subjects were randomly allocated to one of four conditions (placebo, placebo plus memory training, GBE 160 mg, or GBE 160 mg plus memory training exercises). Patients were treated for 3 months. Memory was assessed using measures of short term memory and general memory recall. Significant improvements in short term memory were observed. There was also a non significant improvement in general recall. The greatest improvements were noted in the GBE plus mental exercise condition.

Rai, Shovlin and Wesnes (1991) conducted a double-blind placebo controlled study in 31 patients aged 54-89 years presenting mild to moderate memory impairment as defined by the NINCDS-ADRDA standard classification. Patients received a 120 mg daily does of GBE for 6 months. Performance was assessed using a digit recall task. Assessments were made at baseline, week 12 and week 24. It was reported that GBE treatment had no effect on the task.
Wesnes, Simmons, Rook and Simpson (1987) assessed the effect of GBE on memory performance in 44 elderly patients aged 62-85 years experiencing mild cognitive impairment. Cognitive performance was assessed using the digit span task, immediate word recall and recognition of 10 words. Patients were treated with GBE 120 mg or placebo for 12 weeks. Assessments were made at baseline, week 4, 8 and 12. It was reported that following treatment with GBE, responses on the word recognition task were significantly improved. There was a non significant trend towards improvement on the backward digit span during week eight.

Weibrecht and Jansen (1985) assessed the effects of GBE 120 mg daily for 12 weeks in elderly patients with primary degenerative Dementia. Memory was assessed using the digit span task. Performance was assessed at baseline and after 4, 8 and 12 weeks. It was reported that digit span was significantly improved after 12 weeks of treatment.

Augustin (1979) assessed the effects of treatment with GBE on memory function in a sample of 189 elderly patients. Patients were randomly allocated to treatment with GBE 120 mg or placebo for 6 months. Memory was assessed using the digit span task, Rey learning task and the Benton Visual retention task. It was reported that following treatment with GBE, 61.6% of patients showed significant improvements on the tasks compared to 28% of the placebo group.

Maurer, Ihl, Dierks and Frlich (1997) assessed the effects of GBE on performance of the SKT task in 20 patients with Alzheimer's disease. Patients were treated with GBE 240 mg or placebo for a period of 3 months. It was reported that following treatment the GBE treated group showed a significant improvement on total SKT scores (scores fell from 19.67 to 16.78 after 12 weeks).
Similar results were observed by Kanowski et al. (1996) in the study of 216 elderly patients with a mean age of 69.5 years. All patients had a diagnosis of presenile or senile dementia of the Alzheimer type. Patients were treated with GBE 240 mg or placebo for 2 years. Cognitive function was assessed using the SKT task, it was reported that following treatment 38% of the GBE group and 18% of the placebo treated group showed overall improvements (of greater than 4 points) on the task. These results of these two experiments are interesting, however as the SKT task incorporates subtests assessing aspects of attention as well as memory, it is not possible to determine whether the beneficial effects of GBE were limited to tasks of memory, attention or whether they are a combination of improvements on both types of task.

6.7.1 Summary
A number of studies have examined the effects of GBE on memory performance in healthy adult populations. The results of which have proved fairly inconclusive. In young healthy adults Subhan and Hindmarch (1984) reported that an acute 600 mg dose of GBE significantly improved reaction time on the Sternberg Memory Task (SMT). This effect was reported as an effect on memory, however it is probably an effect on the speed of information processing rather than an effect on memory.

Other researchers examining the effects of GBE supplementation on memory performance in healthy adult populations have noted a trend towards improvement on the SMT (Parkin and Dawe, 1995; Dawe et al., 1995), and on free recall of images (Warot et al., 1991).

It was reported that GBE had no effects on a word recognition task (Parkin and Dawe, 1995), a number recognition task (Warot et al., 1991), immediate recall, delayed recall and recognition of pictures (Dawe et al., 1995). Based on these findings, it seems conclusive that GBE has very little effect on memory function in healthy adult populations.
In terms of patient populations, there have been a number of researchers who have examined the effects of ginkgo biloba on memory function. The results of which seem to indicate that in some patient populations treatment with GBE has resulted in a number of memory improvements. Significant improvements have been noted on a recall of words and pictures task following doses of 320 mg and 600 mg (Allain et al., 1993), general memory recall following 120 mg dose for 3 weeks (Wesnes et al., 1987) and the digit span following 120 mg daily dose for 12 weeks (Weibrecht and Jansen, 1985).

Based on the above findings, it is possible that treatment with GBE 100 mg in healthy subjects would result in some performance improvements.
Table 68: Summarising the effects of ginkgo biloba treatment on aspects of memory in healthy adult and patient populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subhan and Hindmarch (1984)</td>
<td>Healthy female subjects</td>
<td>8</td>
<td>25-40 years</td>
<td>120 mg, 240 mg 600 mg</td>
<td>Sternberg Memory Task</td>
<td>Reaction time on the SMT significantly improved following 600 mg</td>
</tr>
<tr>
<td>Parkin and Dawe (1995)</td>
<td>Healthy female subjects</td>
<td>10</td>
<td>25-40 years</td>
<td>600 mg</td>
<td>Sternberg Memory Task Word recognition task</td>
<td>Less impairment on the Sternberg Memory Task</td>
</tr>
<tr>
<td>Dawe et al. (1995)</td>
<td>Healthy subjects</td>
<td>11</td>
<td>22-45 years</td>
<td>200 mg for 2 weeks</td>
<td>HPRU SMT Memory for pictures</td>
<td>No effects on memory for pictures task. non significant improvement drug visit interaction</td>
</tr>
<tr>
<td>Warot et al. (1991)</td>
<td>Female subjects</td>
<td>12</td>
<td>19-30 years</td>
<td>600 mg</td>
<td>SMT Number Recognition task Image recall and recognition</td>
<td>No effect on SMT free recall of images remained stable in GBE condition fell following placebo</td>
</tr>
<tr>
<td>Allain et al. (1993)</td>
<td>Elderly subjects</td>
<td>18</td>
<td>Mean age 69.3 years</td>
<td>320 mg, 600 mg placebo</td>
<td>Recall of words and pictures</td>
<td>Significant improvement following both doses</td>
</tr>
<tr>
<td>Author</td>
<td>Sample</td>
<td>Dose</td>
<td>Assessment</td>
<td>Outcome</td>
<td></td>
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</tr>
<tr>
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<td></td>
<td></td>
</tr>
<tr>
<td>Israel et al. (1987)</td>
<td>Geriatric patients</td>
<td>80 aged 56-84 years, 160 mg placebo for 3 months</td>
<td>Short term memory and general memory recall</td>
<td>Significant improvement in general memory recall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel et al. (1991)</td>
<td>Mild to moderate dementia</td>
<td>31 60-80 years, 120 mg placebo for 6 months</td>
<td>Digit recall</td>
<td>No effect</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Augustin (1979)</td>
<td>Elderly patients</td>
<td>189 Aged 60+ 120 mg or placebo for 6 months</td>
<td>Digit span</td>
<td>Responses on the word recall were significantly improved. There was a non significant trend towards improvements on the digit span task</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wesnes et al. (1987)</td>
<td>Elderly subjects with mild cognitive decline</td>
<td>44 62-85 120 mg for 12 weeks</td>
<td>Digit span</td>
<td>Immediate word recall and recognition task</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wesnes et al. (1987)</td>
<td>Mild to moderate dementia</td>
<td>60 60-80 years, 120 mg for 3 months</td>
<td>Digit span</td>
<td>Digit span</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wehbricht and Jansen (1986)</td>
<td>Elderly subjects with mild cognitive decline</td>
<td>60 60-80 years, 120 mg for 3 months</td>
<td>Digit span</td>
<td>Digit span</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
6.8 The effects of GBE supplementation on information processing in adult populations

There have been no studies examining the effects of ginkgo biloba on the speed of information processing in healthy elderly subjects, however there have been a number of studies examining the effect of ginkgo biloba treatment on the speed of information processing in healthy adult populations and in patients populations.

Subhan and Hindmarch (1984) assessed the impact of acute dosing of ginkgo biloba (120, 240 and 600 mg) on cognitive performance in a sample of eight healthy female volunteers aged 25-40 years (mean age 32 years). Performance was assessed using the Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT) performance was assessed after one hour post dose. Ginkgo biloba had no effect on performance of the tasks.

Parkin and Dawe (1995) produced a drug-induced cognitive deficit in healthy volunteers. Prior to dosing with either GBE or placebo subjects were given a single 1 mg dose of flunitrazepam to produce a benzodiazepine-induced short term memory deficit. The aim of the study was to determine whether a single 600 mg acute dose of GBE would prevent a benzodiazepine induced memory impairment, that in turn would affect other aspects of cognitive functioning, i.e. the speed of information processing. Ten healthy female volunteers aged between 25 and 40 years (mean age 36.2 years) were treated with a single 600 mg dose of GBE or placebo followed 5 minutes later by a single 1 mg dose of flunitrazepam. Cognitive performance was assessed using the Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT). Assessments were made at baseline, 1, 2, 4, and 6 hours post dose. There were no significant differences reported between GBE and placebo on the CFF or CRT tasks. The results of this experiments showed that a deficit was induced by the flunitrazepam, however the impairment produced was too great to be alleviated by a single 600 mg dose of GBE. Therefore a second study was performed.
using a lower dose of flunitrazepam to induce impairment. In the second experiment the same methods and techniques from experiment 1 were used in experiment 2, except the dose of flunitrazepam was reduced to 0.5 mg, and psychometric assessments were made at baseline, 1.5, 3, 4 and 6 hours. There were no significant differences between the treatments (GBE/flunitrazepam, and placebo/flunitrazepam).

Dawe, Kerr, Yoon and Hindmarch (1995) conducted a pilot study examining the effect of GBE on cognitive and psychomotor function in a sample of young healthy volunteers. Eleven young volunteers (mean age 28.6 years) received 200 mg GBE and placebo daily for a period of 14 days, in a randomised cross over fashion. Psychometric tests were completed at baseline, day 7 and 14. The psychometric assessment included Critical Flicker Fusion task (CFF) and the Choice Reaction Time task (CRT). It was reported that GBE had no effect on CFF thresholds, but recognition reaction time was improved following treatment with GBE.

Warot, Lacomblez, Danjou, Weiller, Payan and Puech (1991) investigated the effects of GBE on memory function in a sample of 12 healthy female subjects (aged 19-30 mean age 22.3 years). Subjects received 600 mg acute dose and performance was assessed one hour post dose. Performance was assessed using Critical Flicker Fusion (CFF), Choice Reaction Time (CRT). It was reported that GBE had no effect on performance of the CFF or CRT.

Weibrecht and Jansen (1986) assessed the effects of GBE 120 mg compared to placebo on the speed of information processing in patients with mild to moderate dementia. Patients aged 60-80 years, (mean age 71.7 years) received GBE 120 mg or placebo for 3 months. Performance was assessed using the Critical Flicker Fusion task and the Choice Reaction Time task, at baseline, week 4, 8 and 12. It was reported that following treatment with ginkgo biloba, CFF thresholds increased significantly, and Choice Reaction Times decreased
significantly, both effects were indicative of an improvement in the speed of information processing.

Wesnes et al. (1987) assessed the effect of 120 mg of GBE on performance on a choice reaction time task in 44 elderly patients exhibiting signs of cognitive decline. Patients were treated with GBE (120 mg) or placebo for 12 weeks. Performance was assessed using a Choice Reaction Time task at baseline and weeks 4, 8 and 12. It was reported that after 12 weeks of treatment the GBE group had significantly faster reaction times compared to placebo.

6.8.1 Summary
The results of these experiments would seem to indicate that ginkgo biloba has no effect on tasks assessing the speed of information processing in healthy adult populations, assessed using the Critical Flicker Fusion and Choice Reaction Time tasks (Subhan and Hindmarch, 1984; Parkin and Dawe, 1995; Warot et al., 1991).

In the Dawe et al. (1995) study, following a daily dose of ginkgo biloba (200 mg) for 14 days, improvements in recognition reaction time were observed. These effects are possibly not an effect on the speed of information processing but rather an effect on attention or memory, as recognition reaction time represents the attentional aspect of the choice reaction time task, and also represents the "what do I do" part of the task which relies on memory.

In patient populations it appears that ginkgo biloba does have beneficial effects on the speed of information processing, Weibrecht and Jansen (1986) reported that following 120 mg daily dose for 3 months Critical Flicker Fusion thresholds in patients with mild to moderate dementia improved and reaction times were decreased. Wesnes et al. (1987) also reported that following 120 mg daily dose for 3 months, reaction times were significantly decreased in patients with mild cognitive impairment.
Based on these findings, it is possible that slight improvements in the speed of information processing would be noted in healthy elderly.
### Table 69: Summarising the effects of treatment with GBE on the speed of information processing in healthy adult and patient populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subhan and Hindmarch (1984)</td>
<td>Healthy female subjects</td>
<td>8</td>
<td>25-40 years</td>
<td>Acute 600 mg</td>
<td>CFF CRT</td>
<td>No effect on CFF or CRT</td>
</tr>
<tr>
<td>Parkin and Dawe (1995)</td>
<td>Healthy Female subjects</td>
<td>10</td>
<td>25-40 years</td>
<td>Acute 600 mg</td>
<td>CFF CRT</td>
<td>No effect on CFF or CRT</td>
</tr>
<tr>
<td>Warot <em>et al.</em> (1991)</td>
<td>Healthy female subjects</td>
<td>12</td>
<td>19-30 years</td>
<td>Acute 600 mg</td>
<td>CFF CRT</td>
<td>No effect on CFF or CRT</td>
</tr>
<tr>
<td>Dawe <em>et al.</em> (1995)</td>
<td>Healthy subjects</td>
<td>11</td>
<td>22-45 years</td>
<td>200 mg for 14 days</td>
<td>CFF CRT</td>
<td>No effect on CFF Recognition Reaction Time significantly improved</td>
</tr>
<tr>
<td>Weibrecht and Jansen (1986)</td>
<td>Mild to moderate dementia</td>
<td>60</td>
<td>60-80 years</td>
<td>120 mg for 3 months</td>
<td>CFF CRT</td>
<td>CFF thresholds increased and CRT decreased</td>
</tr>
<tr>
<td>Wesnes <em>et al.</em> (1987)</td>
<td>mild cognitive impairment</td>
<td>44</td>
<td>62-85 years</td>
<td>120 mg for 3 months</td>
<td>CRT</td>
<td>CRT decreased</td>
</tr>
</tbody>
</table>
6.9 The effects of GBE supplementation on mood and well being in adult populations

There have been no studies examining the effects of ginkgo biloba on mood and general well being in healthy elderly subjects, however there have been a number of studies examining the effect of ginkgo biloba treatment on mood and general wellbeing in healthy young and elderly patient populations.

Subhan and Hindmarch (1984) assessed the impact of acute dosing of ginkgo biloba (120, 240 and 600 mg) on cognitive performance in a sample of 8 healthy female volunteers aged 25-40 years (mean age 32 years). Subjective mood was assessed using line analogue rating scale (LARS) 1 hour post dose. It was reported that GBE had no effect on the mood variables.

Parkin and Dawe (1995) induced a benzodiazepine cognitive deficit in healthy volunteers with a 1 mg dose of flunitrazepam. Five minutes following the dose, subjects received a 600 mg dose of GBE or placebo. The aim of the study was to determine whether a single 600 mg acute dose of GBE would prevent a benzodiazepine induced impairment, and whether this would in turn produce changes in mood. Mood was assessed in 10 healthy female volunteers aged between 25 and 40 years (mean age 36.2 years) using line analogue rating scale (LARS). The LARS assess tiredness, drowsiness and alertness. Assessments were made at baseline, 1, 2, 4, and 6 hours post dose. There were no significant differences reported between GBE and placebo on any of the subjective measures. The deficit induced by the 1 mg dose of flunitrazepam was too great therefore a second experiment was conducted using a lower dose. The second experiment used the same methods and techniques from experiment 1, except the dose of flunitrazepam was reduced to 0.5 mg, and psychometric assessments were made at baseline, 1.5, 3, 4 and 6 hours. It was reported that there were no significant
differences between the treatments (GBE/flunitrazepam, and placebo/flunitrazepam).

Warot et al. (1991) investigated the effects of two types of GBE on mood in a sample of healthy female volunteers (aged 19-30 mean age 22.3 years). Mood was assessed using a visual analogue rating scale (VARS). It was reported that ginkgo biloba had no effect on variables of mood.

Franco, Cuny and Nancy (1991) conducted a long term study examining the effects of GBE on subjective ratings, in 78 elderly persons aged 60-85 years. Subjects received 120 mg GBE daily for 12 months. All subjects were experiencing difficulties with the performance of everyday life, subjective ratings were completed using the McNair self assessment scale of cognitive deficits (CDS). The scale assessed cognitive disorders in terms of quality of life assessing components of attention, concentration, psychomotor co-ordination, orientation, short term and long term memory. It was reported that subjects who received GBE showed significant improvements of more than 11.6 points on the scale.

Taillandier, Ammar, Rabourdin, Ribeyre, Pichon, Niddam and Pierart (1989) conducted a study in 166 patients with cerebral insufficiency. Patients were randomly allocated to treatment with placebo or GBE 160 mg for a period of 12 months. Patients were assessed using the Geriatric Clinical Evaluation Scale (GCES) which is designed to assess intellectual function, memory, alertness, attention, mood, social insertion and neurosensorial disturbances. Assessments were made at baseline and after 3, 6, 9 and 12 months. It was reported that GBE treated patients, showed a significant improvement in GCES as early as 3 months, and the improvement continued throughout the duration of the trial.
Weibrecht and Jansen (1986) assessed the effect GBE on the Crichton Geriatric Rating Scale. Forty patients aged 60-80 years were randomly allocated to treatment with GBE 120 mg or placebo for 3 months. Assessments were made using the Crichton Rating Scale (which included 11 items assessing mobility, orientation, communication, co-operation, restlessness, dressing, feeding, continence, sleep and mood). Performance was also assessed using the Sandoz Clinical Assessment Scale (assessing confusion, mental alertness, impairment of recent memory, disorientation, mood, depression, emotional liability, self care, anxiety, motivation, irritability, hostility, bothersome, indifference to surroundings, unsociability, uncoopertiveness, fatigue, appetite, dizziness and overall impression of the patient). Assessments were made at baseline and after 4, 8 and 12 weeks. It was reported that following treatment with GBE after just 8 weeks, patients reported improvements in sleep, health score and general well being. Scores on the Sandoz Clinical Assessment Scale significantly decreased by week 8.

Wesnes et al. (1987) assessed a double blind study to investigate the effects of GBE 120 mg on the quality of life of 44 elderly patients aged 62-85 years. All patients showed signs of cognitive impairment in their everyday function as assessed with the Crichton Geriatric rating Scale. Quality of life was measured using a behaviour rating scale. The scale was completed at baseline and after 12 weeks. It was reported that following 12 weeks of treatment the GBE group showed increased interest taken in everyday activities.

Kanowski et al. (1996) assessed the effects of GBE on ADL and Clinical Global Impression (CGI) in 216 elderly patients with SDAT (aged greater than 55 years). Patients were treated with GBE 240 mg for 2 years. Assessments were made using the Clinical Global Impression (CGI) and the Nürnberger Alters-Beobachtungsskala behavioural assessment of activities of daily living (ADL). It was reported that the CGI scores were significantly higher following treatment with GBE and
there was a non significant trend towards improvement on the ADL following GBE.

Maurer et al. (1997) assessed the effect of treatment with GBE on Alzheimer's disease progression. Twenty patients aged 50-80 years were treated with GBE 240 mg or placebo for 3 months. Alzheimer's disease progression was assessed using the Alzheimer's Disease Assessment Scale (ADAS) and the Clinical Global Impression (CGI) at baseline and at monthly intervals. It was reported that treatment with GBE resulted in improvements in CGI scores. There was trend towards improvement on the ADAS in the GBE treated group, however this trend failed to reach statistical significance.

Vorberg (1985) assessed the effects of GBE treatment in patients with cerebral insufficiency. One hundred and twelve patients aged 55-94 years (mean age 70.5 years) were treated with GBE 120 mg for 12 months. Subjects were required to self rate changes in mood and vigilance using a specially designed questionnaire. The questionnaire consisted of a four point scale for assessing memory (memory for order, occasional memory gaps concerning unimportant recent events, moderate memory gaps concerning unimportant recent events and occasional forgetfulness of important events or severe memory gaps concerning trivial and important events). Patients were also required to assess vigilance using a four point scale (normal alertness and vigilance, minor loss of imagination, concentration and speech, moderate loss of imagination, concentration and response, or definite loss of imagination and concentration). It was reported that following treatment with GBE disturbances in short term memory and vigilance underwent a significant improvement over the treatment period.

Le Bars, Katz, Berman, Itil, Freedman, and Schatzberg (1997) assessed the efficacy of GBE on subjective ratings in a sample of 309 patients with Alzheimer's Disease
or multi-infarct dementia. Patients were randomly assigned to treatment with GBE (120 mg daily) or placebo for a period of 12 months. Assessments were made at baseline and after 12, 26 and 52 weeks. Subjective ratings were made using the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog), the Geriatric Evaluation by Relatives Rating Instrument (GERRI) and the Clinical Global Impression of Change (CGI). It was reported that the Ginkgo treated group had a 1.4 point higher score on the ADAS-Cog and a 1.4 higher score on the GERRI than the placebo treated group. In real terms, this equated to 27% of the GBE treated group showing a 4 point improvement on the ADAS-Cog, compared to 14% in the placebo condition. 37% of the GBE treated group showed improvements on the GERRI compared to 23% of those treated with placebo. There were no differences between the 2 groups in terms of scores on the CGI.

6.9.1 Summary
The results of these experiments would seem to indicate that ginkgo biloba has no effect on mood as assessed using line analogue rating scales, in healthy adult populations (Subhan and Hindmarch, 1984; Parkin and Dawe, 1995, Warot et al., 1991).

In patient populations, there were beneficial effects on subjective ratings following treatment with GBE. Treatment with GBE 120 mg for 3 months resulted in improvements in sleep and general well being (Weibrecht and Jansen, 1986), increased interest in everyday activities expressed on the Crichton Geriatric Rating Scale (Wesnes et al., 1987), improvements on the Clinical Global Impressions (Maurer et al., 1997), McNair Self Assessment Scale (Franco et al., 1991), Geriatric Clinical Evaluation Scale (Tailandier et al., 1989), Sandoz Clinical Assessment Scale (Weibrecht and Jansen, 1986), Alzheimer's Disease Assessment Scale-Cognitive Subscale and the Geriatric Evaluation Rating Scale (LeBars et al.,
1997) and improvements on the Activity of Daily Living Scale (Kanowski et al., 1997).
<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>Dosage</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subhan and Hindmarsh (1994)</td>
<td>Healthy female subjects</td>
<td>120 mg</td>
<td>LARS</td>
<td>No effect</td>
</tr>
<tr>
<td>Parkin and Dawe (1995)</td>
<td>Healthy female subjects</td>
<td>600 mg</td>
<td>LARS</td>
<td>No effect</td>
</tr>
<tr>
<td>Warot et al. (1991)</td>
<td>Healthy female subjects</td>
<td>12</td>
<td>VARS</td>
<td>No effect</td>
</tr>
<tr>
<td>Franco et al. (1991)</td>
<td>Elderly persons</td>
<td>120 mg for 12 months</td>
<td>MCSNar CDS</td>
<td>Improved by 11.6 points</td>
</tr>
<tr>
<td>Tsai and CDS (1986)</td>
<td>Patients with cerebral</td>
<td>160 mg for 12 months</td>
<td>CGES</td>
<td>Improvement in sleep, health score and general well being. Significant decrease in SCAG</td>
</tr>
<tr>
<td>Weisbrod and Jansen (1986)</td>
<td>Mild to moderate dementia</td>
<td>120 mg or placebo for 3 months</td>
<td>Crichton Rating Scale</td>
<td>Increased interest in everyday activities</td>
</tr>
<tr>
<td>Wesnes et al. (1987)</td>
<td>Mild cognitive impairment</td>
<td>120 mg for 12 weeks</td>
<td>Crichton Rating Scale</td>
<td>Crichton Rating Scale</td>
</tr>
</tbody>
</table>

Table 70: Summarising the effects of treatment with ginkgo biloba on aspects of subjective mood and general well being.
<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kanowski et al. (1996)</td>
<td>SDAT</td>
<td>216</td>
<td>greater than 55 years</td>
<td>240 mg for 2 years</td>
<td>CGI ADL</td>
<td>Improved CGI scores Non significant trend towards improvements on the ADL scale.</td>
</tr>
<tr>
<td>Maurer et al. (1997)</td>
<td>Mild to moderate dementia</td>
<td>20</td>
<td>50-80 years</td>
<td>240 mg for 3 months</td>
<td>ADAS CGI</td>
<td>Improved CGI scores Trend towards improvement on the ADAS</td>
</tr>
<tr>
<td>Vorberg (1985)</td>
<td>Cerebral insufficiency</td>
<td>112</td>
<td>55-94 years</td>
<td>120 mg for 12 months</td>
<td>Subjective rating of memory and vigilance</td>
<td>Both ratings improved following treatment</td>
</tr>
<tr>
<td>Le Bars et al. (1997)</td>
<td>SDAT</td>
<td>309</td>
<td>&gt; 45 years</td>
<td>120 mg for 12 months</td>
<td>GERRI CGI ADAS-Cog</td>
<td>27% of GBE treated patients showed 4 point improvement on ADAS, 37% on GERRI and no effect on CGI</td>
</tr>
</tbody>
</table>
6.10 Conclusions

To date relatively few studies have been published on the effects of ginkgo biloba extract on cognitive function in healthy elderly subjects. Of the studies that have been conducted, very few psychological tests have been utilised. In terms of the research to date, it would seem that GBE has little effect on cognitive function in healthy adult populations. The effects of GBE on cognitive function in healthy elderly subjects who believe they are experiencing a certain degree of cognitive decline is yet to be revealed. Health food stores in the UK, promote the use of ginkgo biloba stating that when used as a supplement ginkgo improves memory performance, however it would seem that there is little evidence to support such a claim.

6.11 Aims of the present study: Analysis of the effects of long term supplementation with Ginkgo Biloba on cognitive function in healthy elderly subjects

This experiment aimed to assess the impact of the recommended daily dose of ginkgo biloba (100 mg) in healthy subjects experiencing a mild degree of forgetfulness. This study aimed to examine the actions of GBE on cognitive function, the effects of ginkgo biloba were examined on tasks assessing attention, memory recall, the speed of information processing, speed of naming, memory recall, and cognitive failures in everyday living.

In chapter 4 the effects of age on the tasks was determined on cognitive function in healthy drug free elderly subjects. It was reported that main effects of age were reported on the speed of naming objects (SKT I), immediate recall of objects (SKT II), arranging blocks (SKT IV), replacing blocks (SKT V), counting symbols (SKT VI), reverse naming (SKT VII) and delayed recall of objects (SKT VIII).
The primary aim of this experiment was to assess whether ginkgo biloba would help alleviate the age related decline reported on the tasks, as well as assess the effects on other memory tasks such as memory for faces, digit span forwards and backwards, shopping list task and the object task.

Based on previous research, it was postulated that treatment with GBE in healthy elderly subjects would result in improvements in some aspects of attention, SKT VII (reverse naming task), memory, (the HPRU Sternberg memory task and the digit span task). Since Maurer et al. (1997) and Kanowski et al. (1996) reported that treatment with GBE resulted in improvements on the SKT task in patient populations, it was questioned whether such improvements would be noted in healthy elderly subjects who believed they were experiencing mild cognitive decline.

6.12 Methods

6.12.1 Subjects

16 healthy community dwelling elderly subjects (7 males and 9 females) aged between 61 and 84 years (mean age 70.18 years) were enrolled in the study. All were in physical and mental good health, and were not taking any concomitant treatments that would interfere with the test measures. Subjects were recruited from the general public via the HPRU database and poster advertisements, all believed that they were experiencing problems with their memory functioning.

6.12.2 Treatments

The treatments comprised ginkgo biloba 100 mg and placebo, each were taken for a period of 8 weeks with a 4 week washout period between treatments. Double-blind crossover design was employed therefore subject received both treatments.
Treatments were administered orally as 1 tablet taken once a day (with breakfast), the tablets were identically packaged in blister packs.

6.12.3 Procedure
Prior to participation in the study, subjects were familiarised and trained on all psychometric tests, 12 test sessions took place (at baseline, week 2, 4, 6, 7 and 8 for each treatment).

Subjects attended the unit at the same time of day for each of the test sessions. They performed all assessments. Testing took approximately 45 minutes. Tablets were dispensed to patients at the baseline visit, and they returned any unused tablets after the 8 week period, and were used as a measure of compliance.

6.12.4 Assessments
Assessments were made on a regular basis, subjects were assessed on days 1 (baseline), 14 (week 2), 28 (week 4), 42 (week 6), 49 (week 7) and 56 (week 8). Assessments included CFF, CRT, HPRU Sternberg Memory Task (which were completed at each visit) SKT and MMT (were completed on alternate visits) and an activity of daily living scale (ADL) which was completed at the beginning and end of each treatment.

The psychometric tasks completed by the subjects assessed attention (SKT IV, V, VI, VII and SMT); memory (SKT II, VIII, shopping list task, shopping list recognition task, object memory task, object recognition task, memory for faces task, digit span task); speed of information processing (CFF, CRT); and speed of naming (SKT I, III). The study also assessed self reporting of cognitive failure, with an activity of daily living scale (ADL). Table five summarises the testing schedule.
### Table 71: Summarising the assessment test schedule at each visit.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical Flicker Fusion</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Choice Reaction Time</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>HPRU Sternberg Memory Task</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Syndrom Kurtz Task</td>
<td>*</td>
<td></td>
<td>*</td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Shopping List Task</td>
<td></td>
<td>*</td>
<td>*</td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Object Memory</td>
<td></td>
<td></td>
<td></td>
<td>*</td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Facial Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Digit Span</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
<tr>
<td>Activity of Daily Living</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>*</td>
</tr>
</tbody>
</table>

#### 6.12.5 Critical Flicker Fusion Task (CFF)

The critical flicker fusion task (CFF) is regarded as an index of overall CNS activity, the ability of the central nervous system to process discrete 'bits' of information. Therefore an increase in CFF thresholds is associated with increased alertness and a greater capacity for information processing.

#### 6.12.6 Choice Reaction Time (CRT)

The choice reaction time task (CRT) is used as an indicator of sensorimotor performance, assessing the efficiency of the attentional and response mechanisms in the information processing chain. The task is comprised of three components: recognition reaction time (RRT), motor reaction time (MRT) and total reaction time (TRT).

#### 6.12.7 HPRU Sternberg Memory Task (SMT)

The HPRU Sternberg memory task is a technique based upon a reaction time method where subjects are required to memorise a set of target digits. In the original Sternberg memory task, the ability to scan the memory set was assessed by getting subjects to attend to a series of digits, then presenting one digit and asking the subjects whether that digit was in the original memory set. In the HPRU version
of the task, memory scanning ability is assessed with the presentation of 12 single probe digits.

6.12.8 The Syndrom Kurtz Task (SKT)
The SKT task is comprised of 9 subtasks assessing aspects of attention (SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), VII (reverse naming)), memory (SKT II (immediate recall) SKT VIII delayed recall) and SKT IX (recognition memory)) and the speed of naming (SKT I (object naming), SKT III (numerical naming)).

6.12.9 Milford Object memory task
In the task, subjects are required to memorise 12 photographs of objects e.g. a car, tree, iron and mug etc. (items are presented one item per page). After the subjects have seen and named all 12 items they are asked to recall as many of the 12 items as possible.

6.12.10 Milford Object recognition task
In the recognition task, subjects are then required to complete a forced choice task, in which they have to recognise the original photograph of the object from a set of 24 photographs. The items are presented 2 per page. For example using the above example, the subjects would be presented with a photograph of a car and a train, the subject is required to say that the car was in the booklet and the train was not.

6.12.11 Milford Shopping list task
In the shopping list task, subjects are shown a shopping list containing 12 shopping items, e.g. sausages, cabbage, toothpaste, lemons, gravy etc. (items are presented one item per page). After the subjects have seen and named all 12 items are asked to recall as many of the 12 items as possible.
6.12.12 Milford Shopping list recognition task
The subjects are then required to complete a forced choice task. In this task subjects are presented with 24 shopping items, the 12 original shopping items plus 12 distractor items. The items are presented 2 per page (an original picture and a distractor), the subject is required to identify which of the 2 shopping items were on their original shopping list. For example using the above shopping list as an example, the subjects would be presented with the words sausages or beefburgers, the subject is required to say that sausages were on their list and not beefburgers.

6.12.13 Milford Memory For Faces Task
In this task, subjects are presented with named photographs of faces, the subjects are required to memorise the name and face, Subjects are required to memorise sets of one, three, five and seven faces.

6.12.14 Milford Digit Span task
Subjects are aurally presented with a series of numbers (increasing in length form 3 digits through to 9 digits). Subjects are required to repeat the digit sequence. Subjects were only given one chance to correctly repeat the sequence, if they failed to repeat the correct sequence, the task was abandoned. Subjects had to repeat the sequence of digits in the order in which they heard them, starting with 3 digits, increasing by 1 digit at a time until the subject failed to repeat the correct sequence, or to the end of the task when the subjects had recalled all 9 digits.

In the second part of the task, subjects had to repeat a sequence of digits in reverse order. Again subjects were first presented with 3 digits to recall in reverse order increasing by 1 digit at a time until the subject failed to repeat the correct sequence, or to the end of the task when the subjects had recalled all 9 digits.
This version of the digit span was a little different from the standard method employed in the Wechsler scale where subjects have 2 attempts in which to correctly recall the digit strings.

6.13 Results

The data were analysed using a 2 way analysis of variance with treatment and visit as within subject factors. The performance data were analysed in terms of the cognitive groupings that were identified in chapter 4. The groupings included:

1. Attention (HPRU Sternberg memory Task, SKT subtests IV, V, VI, and VII).
2. Memory recall (SKT subtest II, VIII, shopping list task, object recall, memory for faces task, digit span forward, digit span backward).
3. Speed of naming (SKT subtest I and III)
4. Speed of information processing (CFF, TRT, RRT and MRT).
5. Recognition memory (SKT subtest IX, shopping list forced choice task, objects forced choice task).

The study also examined the effect of ginkgo biloba supplementation on an Activities of Daily Living (ADL).

6.14 The effect of Ginkgo Biloba on aspects of attention

In chapter 4 the effects of ageing on tasks that assessed attention were examined, it was concluded that there was a main effect of age, as age increases performance on orientation tasks declined. The purpose of this experiment was to assess the effects of GBE supplementation on attention tasks. In chapter 4 a number of tasks were classed as assessing attention they included SKT subtests IV, V, VI, VII and the HPRU Sternberg Memory Task.
6.14.1 SKT subtest IV (arranging blocks)

In this task, subjects were presented with 10 numbered blocks, they were required to place the blocks in ascending order as quickly as possible, the time taken to complete the task was recorded.

There was no main effect of treatment (F (1, 29) = 1.99; p>0.05), the time taken to arrange blocks was comparable for both treatments (see Table 72).

Table 72: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>19.18</td>
<td>16.93</td>
<td>16.87</td>
</tr>
<tr>
<td>Placebo</td>
<td>21.60</td>
<td>18.20</td>
<td>17.26</td>
</tr>
</tbody>
</table>

There was a main effect of visit (F (2, 58) = 7.56; p<0.001) subjects got faster at arranging blocks over time. There was no interaction between treatment and visit (F (2, 58) = 0.60; p>0.05).

The main effect of time was analysed using the Newman Keul’s task. It was revealed that performance at weeks 4 and 7 were significantly faster than at baseline, perhaps reflecting a practice effect (see Figure 54).
6.14.2 SKT subtest V (replacing blocks)

In this task, subjects had to replace the 10 numbered blocks to their original starting position (this was marked on the magnetic board).

There was no main effect of treatment ($F_{(1,29)} = 0.20; p>0.05$), the time taken to replace blocks was comparable for both treatments (see Table 73).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>15.12</td>
<td>13.43</td>
<td>13.18</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.66</td>
<td>13.26</td>
<td>12.66</td>
</tr>
</tbody>
</table>

There was a main effect of visit ($F_{(2,58)} = 6.78; p<0.001$) subjects got faster at replacing blocks over time. There was no interaction between treatment and visit ($F_{(2,58)} = 0.05; p>0.05$).
Post hoc testing on the main effect of time with Newman Keul's revealed that performance of the task at weeks 4 and 7 was significantly faster than performance at baseline, perhaps reflecting a practice effect (see Figure 55).

![The main effect of time on replacing blocks (SKT V)](image)

Figure 55: The main effect of time on performance of SKT subtest V (replacing blocks).

### 6.14.3 SKT subtest VI (counting symbols)

Subjects had to count the number of symbols contained on a sheet, e.g. squares. The sheet contained a number of symbols including flowers, circles, and squares. Time taken to complete the task was recorded.

There was no main effect of treatment ($F_{(1, 29)} = 0.08; p>0.05$), the time taken to count symbols was comparable for both treatments (see Table 74).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>22.00</td>
<td>19.62</td>
<td>18.68</td>
</tr>
<tr>
<td>Placebo</td>
<td>21.46</td>
<td>18.06</td>
<td>19.40</td>
</tr>
</tbody>
</table>
There was a main effect of visit ($F(2, 58) = 5.99; p<0.005$) subjects got faster at counting symbols over time. There was no interaction between treatment and visit ($F(2, 58) = 0.74; p>0.05$).

Post hoc testing of the main effect of time with Newman Keul's revealed that performance of the task at weeks 4 and 7 was significantly faster than performance at baseline, perhaps reflecting a practice effect (see Figure 56).

![The main effect of time on counting symbols (SKT VI)](image)

**Figure 56:** The main effect of time on performance of SKT subtest VI (counting symbols).

### 6.14.4 SKT subtest VII (reverse naming task)

*In this task, subjects had to perform a reverse naming task, subjects were presented with 2 rows of letters (e.g. ABBABAB), everytime the subjects read the letter A they had to say B had when the read B they had to say A. The time taken to complete the task was recorded.*
There was no main effect of treatment \((F (1, 29) = 0.005; p>0.05)\), the time taken to complete the reverse naming task was comparable for both treatments (see Table 75).

Table 75: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>22.06</td>
<td>20.31</td>
<td>18.81</td>
</tr>
<tr>
<td>Placebo</td>
<td>22.33</td>
<td>18.93</td>
<td>20.33</td>
</tr>
</tbody>
</table>

There was a main effect of visit \((F (2, 58) = 8.04; p<0.001)\) subjects got faster at performing the reverse naming task over time. There was no interaction between treatment and visit \((F (2, 58) = 1.88; p>0.05)\).

Post hoc testing of the main effect of time revealed that performance of the task at weeks 4 and 7 was significantly faster than performance at baseline, perhaps reflecting a practice effect (see Figure 57).

![The main effect of time on the reverse naming task (SKT VII)](image)

Figure 57: The main effect of time on performance of SKT subtest VII (reverse naming task).
6.14.5 HPRU Sternberg Memory Task (SMT)

In this task, subjects had to memorise a memory set (varying in size from 1, 3 to 5 digits). Immediately following the memory set, a random series of 12 digits were presented, subjects were required to state whether the digit present, was contained in the memory set, by pressing the "yes" response button and "no" if it wasn't. Time taken to respond was recorded.

There was no main effect of treatment (F (1, 24) = 0.60; p>0.05), performance was the comparable for both treatments (see Table 76).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBE</td>
<td>798.86</td>
<td>817.81</td>
<td>794.81</td>
<td>782.97</td>
<td>751.73</td>
<td>738.54</td>
</tr>
<tr>
<td>Placebo</td>
<td>894.38</td>
<td>850.69</td>
<td>912.80</td>
<td>844.05</td>
<td>772.39</td>
<td>724.00</td>
</tr>
</tbody>
</table>

There was no main effect of visit (F (5, 120) = 1.62; p>0.05) there was no change in performance across visits. There was no interaction between treatment and visit (F (5, 120) = 0.40; p>0.05).

6.14.6 Summary

There were no main effects of treatment on tasks assessing attention in a healthy elderly population. In most cases there are main effects of time, possibly indicating practice effects (even though the subjects were trained on the tasks before participation in the study). It is possible that the practice effects hide smaller treatment effects.
6.15 The effect of Ginkgo Biloba on memory recall

In chapter 4 the effects of ageing on tasks that assess memory recall were analysed, it was concluded that there was no main effect of age of performance of memory recall tasks. The purpose of this experiment was to assess the effects of GBE supplementation on memory recall. In chapter 4 a number of tasks were classed as assessing memory recall they included SKT subtests II, and SKT subtest VIII. The effects of GBE on memory for a shopping list, object memory, face memory and digit span were also examined.

6.15.1 SKT subtest II (immediate recall)

The subjects were required to provide immediate recall of 12 previously named objects. The number of omissions and time taken to complete the task were recorded. Subjects were allocated 60 seconds in which to respond.

There was no main effect of treatment \( (F_{(1,29)} = 0.02; \ p>0.05) \), the number of omissions was comparable for both treatments (see Table 77).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>5.00</td>
<td>5.00</td>
<td>4.75</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.66</td>
<td>5.06</td>
<td>4.80</td>
</tr>
</tbody>
</table>

There was no main effect of visit \( (F_{(2,58)} = 0.44; \ p>0.05) \) there was no change in the number of omissions across visits. There was no interaction between treatment and visit \( (F_{(2,58)} = 0.30; \ p>0.05) \).
6.15.2  SKT subtest VIII (delayed recall)

Subjects were required to provide delayed recall of 12 previously named objects, recall was required 10 minutes after initial presentation. The number of omissions and time taken to complete the task was recorded.

There was no main effect of treatment ($F_{(1, 29)} = 0.21; p>0.05$), delayed recall was the comparable for both treatments (see Table 78).

| Table 78: Showing the treatment means at each visit (number of omissions). |
|--------------------|----------------|----------------|----------------|
|                    | Baseline      | Week 4        | Week 7        |
| Ginkgo Biloba      | 5.00          | 5.06          | 4.62          |
| Placebo            | 5.20          | 4.53          | 4.13          |

There was no main effect of visit ($F_{(2, 58)} = 2.03; p>0.05$) there was no change in delayed recall across visits. There was no interaction between treatment and visit ($F_{(2, 58)} = 0.65; p>0.05$).

6.15.3  Milford shopping list task

Subjects were required to read and try and remember a list of 12 shopping items e.g. sausages, lemons, toothpaste, gravy etc. Immediately following presentation, subjects had to recall as many of the 12 items as possible. The number of correct items recalled were recorded.

There was no main effect of treatment ($F_{(1, 26)} = 1.60; p>0.05$), recall of the shopping list task was the comparable for both treatments (see Table 79).

| Table 79: Showing the treatment means at each visit (number of correct responses). |
|--------------------|----------------|----------------|----------------|
|                    | Baseline      | Week 4        | Week 7        |
| Ginkgo Biloba      | 8.50          | 7.58          | 7.58          |
There was no main effect of visit ($F_{(2, 52)} = 2.01; p>0.05$) there was no change in shopping list recall across visits. There was no interaction between treatment and visit ($F_{(2, 52)} = 0.41; p>0.05$).

### 6.15.4 Milford object memory task

*Subjects were required to observe and try and remember 12 pictures of objects e.g. a tree, car, iron, mug etc. Immediately following presentation, subjects were required to recall as many of the 12 items as possible. The number of correct items recalled were recorded.*

There was no main effect of treatment ($F_{(1, 26)} = 0.18; p>0.05$), recall of objects was the comparable for both treatments (see Table 80).

**Table 80:** Showing the treatment means at each visit (number of correct responses).

<table>
<thead>
<tr>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>7.33</td>
<td>7.66</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.25</td>
<td>7.75</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(2, 52)} = 0.58; p>0.05$) there was no change in object recall across visits. There was no interaction between treatment and visit ($F_{(2, 52)} = 0.47; p>0.05$).

### 6.15.5 Milford memory for faces task

*Subjects were presented with named photographs of faces, subjects were required to memorise the name and face of each photograph. Photographs were presented in series of 1, 3, 5 and 7 faces. After subjects had seen all the names and faces in each series, they were then presented with just the photographs of the faces, subjects had*
to name the photograph. The number of correct faces identified in each series were recorded.

6.15.6 Recall of 1 and 3 faces
There was no main effect of treatment, time or interaction, as all subjects were able to recall one and three faces.

6.15.7 Recall of 5 faces
There was no main effect of treatment \( F(1, 26) = 0.00; p>0.05 \), on recall of 5 faces (see Table 81).

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>2.58</td>
<td>2.58</td>
<td>2.58</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.75</td>
<td>2.87</td>
<td>2.18</td>
</tr>
</tbody>
</table>

There was no main effect of visit \( F(2, 52) = 2.38; p>0.05 \) there was no change in face recall across visits. There was no interaction between treatment and visit \( F(2, 52) = 0.08; p>0.05 \).

6.15.8 Recall of 7 faces
There was no main effect of treatment \( F(1, 26) = 0.08; p>0.05 \), on recall of 7 faces (see Table 82).

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>3.08</td>
<td>2.50</td>
<td>2.83</td>
</tr>
<tr>
<td>Placebo</td>
<td>2.75</td>
<td>2.93</td>
<td>2.18</td>
</tr>
</tbody>
</table>
There was no main effect of visit ($F(2, 52) = 0.67; p>0.05$) there was no change in face recall across visits. There was no interaction between treatment and visit ($F(2, 52) = 1.27; p>0.05$).

6.15.9 Digit Span Forward Task

This task was adapted from the Wechsler adult intelligence task. Subjects were aurally presented with a series of numbers (increasing in length from 3 through to 9 digits) required to recall the strings of numbers in the order in which they were presented. Subjects were required to recall as many of the strings as possible, subjects were only given one chance in which to correctly repeat the string, when an error was made, the task was abandoned. The subjects longest span was recorded.

There was no main effect of treatment ($F(1, 26) = 0.22; p>0.05$), on forward digit span recall (see Table 83).

Table 83: Showing the treatment means at each visit (longest span).

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>5.83</td>
<td>6.50</td>
<td>6.08</td>
</tr>
<tr>
<td>Placebo</td>
<td>6.31</td>
<td>6.56</td>
<td>6.12</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F(2, 52) = 2.39; p>0.05$) there was no change in digit recall across visits. There was no interaction between treatment and visit ($F(2, 52) = 0.55; p>0.05$).

6.15.10 Digit Span Backward Task

This task was adapted from the Wechsler adult intelligence task. Subjects were aurally presented with a series of numbers (increasing in length from 3 through to 9 digits) required to recall the strings of numbers in the reverse order in which they
were presented. Subjects were required to recall as many of the strings as possible, subjects were only given one chance in which to correctly repeat the string, when an error was made, the task was abandoned. The subject's longest span was recorded.

There was no main effect of treatment ($F_{(1, 26)} = 0.46; p>0.05$), on backward digit span recall (see Table 84).

Table 84: Showing the treatment means at each visit (longest span).

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>4.83</td>
<td>5.16</td>
<td>4.66</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.31</td>
<td>4.81</td>
<td>4.56</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(2, 52)} = 0.81; p>0.05$) there was no change in digit recall across visits. There was no interaction between treatment and visit ($F_{(2, 52)} = 0.16; p>0.05$).

6.15.11 Summary
There were no main effects of treatment on tasks assessing memory recall in a healthy elderly population.

6.16 The effect of Ginkgo Biloba on the speed of naming
In chapter 4 the effects of ageing on tasks assessing the speed of naming were examined, it was concluded that there was no main effect of age on tasks assessing the speed of naming. The purpose of this experiment was to assess the effects of GBE supplementation the speed of naming. In chapter 4 a number of tasks were classed as assessing speed of naming they included SKT subtests I, and SKT subtest III.
6.16.1 SKT subtest I (object naming)

Subjects were shown a card containing 12 pictures of objects, subjects were required to name the objects and try to commit them to memory, as they would be asked about them at a later date.

There was no main effect of treatment ($F_{(1, 29)} = 0.02; p>0.05$), time taken to complete the object naming task was the comparable for both treatments (see Table 85).

Table 85: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>18.25</td>
<td>19.12</td>
<td>20.50</td>
</tr>
<tr>
<td>Placebo</td>
<td>21.33</td>
<td>17.00</td>
<td>20.73</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(2, 58)} = 1.51; p>0.05$) there was no change in time taken to complete the task across visits. There was no interaction between treatment and visit ($F_{(2, 58)} = 1.51; p>0.05$).

6.16.2 SKT subtest III (naming numerals)

Subjects were required to name 10 numbered blocks, the time taken to name the blocks was recorded.

There was no main effect of treatment ($F_{(1, 29)} = 0.41; p>0.05$), the time taken to name numerals was comparable for both treatments (see Table 86).

Table 86: Showing the treatment means at each visit (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>8.00</td>
<td>7.56</td>
<td>7.93</td>
</tr>
</tbody>
</table>
There was no main effect of visit \( (F(2, 58) = 1.33; p>0.05) \) there was no change in the time taken to complete the task across visits. There was no interaction between treatment and visit \( (F(2, 58) = 1.08; p>0.05) \).

### 6.16.3 Summary

There were no main effects of treatment on tasks assessing the speed of naming in a healthy elderly population.

### 6.17 The effect of Ginkgo Biloba on the speed of information processing

In chapter 4 the effects of ageing on tasks that assessed information processing were examined, it was concluded that there was no main effect of age of performance of information processing tasks. The purpose of this experiment was to assess the effects of GBE supplementation on information processing. In chapter 4 a number of tasks were classed as assessing speed of information processing they included the Critical Flicker Fusion Task (CFF), Total Reaction Time (TRT), Recognition Reaction Time (RRT) and Motor Reaction Time (MRT).

#### 6.17.1 Critical Flicker Fusion (CFF)

_Critical flicker fusion threshold was determined by getting subjects to complete 3 ascending and 3 descending trials, the mean of all 6 trials was recorded._

There was no main effect of treatment \( (F(1, 24) = 1.75; p>0.05) \), critical flicker fusion thresholds were the comparable for both treatments (see Table 87).
Table 87: Showing the treatment means at each visit (Hz).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBE</td>
<td>29.75</td>
<td>29.85</td>
<td>29.54</td>
<td>30.70</td>
<td>29.66</td>
<td>30.78</td>
</tr>
<tr>
<td>Placebo</td>
<td>30.76</td>
<td>30.90</td>
<td>30.67</td>
<td>31.27</td>
<td>31.28</td>
<td>31.55</td>
</tr>
</tbody>
</table>

There was a main effect of time \( (F_{(5, 120)} = 3.23; p<0.05) \) performance on the task improved over time, perhaps reflecting a practice effect (see Figure 58). Post hoc testing with Newman Keul's revealed that CFF thresholds were significantly higher at week 8 than all other assessments. There was no interaction between treatment and visit \( (F_{(5, 120)} = 0.58; p>0.05) \).

![The main effect of time on critical flicker fusion task (CFF)](image)

Figure 58: The main effect of time on performance of the critical flicker fusion (CFF).

6.17.2 Total Reaction Time (TRT)

In this task, subjects had to place their index finger on a home key and respond to stimuli, when a light illuminated, subjects had to remove their finger from the home key and extinguish the illuminated light. Total Reaction time was determined by taking the mean response time from 20 stimuli.
There was no main effect of treatment ($F_{(1, 24)} = 0.04; p>0.05$), total reaction time was the comparable for both treatments (see Table 88).

### Table 88: Showing the treatment means at each visit (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBE</td>
<td>630.09</td>
<td>598.20</td>
<td>613.83</td>
<td>594.87</td>
<td>617.83</td>
<td>609.56</td>
</tr>
<tr>
<td>Placebo</td>
<td>621.32</td>
<td>620.04</td>
<td>615.11</td>
<td>604.08</td>
<td>620.15</td>
<td>623.04</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(5, 120)} = 1.04; p>0.05$) there was no change in total reaction times across visits. There was no interaction between treatment and visit ($F_{(5, 120)} = 0.36; p>0.05$).

#### 6.17.3 Recognition Reaction Time (RRT)

In this task, subjects had to place their index finger on a home key and respond to stimuli, when a light illuminated, subjects had to remove their finger from the home key and extinguish the illuminated light. Recognition reaction time was defined as the time taken for the subject to remove their finger from the home key.

There was no main effect of treatment ($F_{(1, 24)} = 0.02; p>0.05$), recognition reaction time was the comparable for both treatments (see Table 89).

### Table 89: Showing the treatment means at each visit (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBE</td>
<td>409.80</td>
<td>386.91</td>
<td>409.87</td>
<td>388.17</td>
<td>409.22</td>
<td>396.41</td>
</tr>
<tr>
<td>Placebo</td>
<td>403.04</td>
<td>395.27</td>
<td>407.59</td>
<td>402.52</td>
<td>406.58</td>
<td>408.47</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(5, 120)} = 1.12; p>0.05$) there was no change in recognition reaction times across visits. There was no interaction between treatment and visit ($F_{(5, 120)} = 0.41; p>0.05$).
6.17.4 Motor Reaction Time (MRT)

In this task, subjects had to place their index finger on a home key and respond to stimuli, when a light illuminated, subjects had to remove their finger from the home key and extinguish the illuminated light. Motor reaction time was defined as the time taken for the subjects to move from the home key to the illuminated light.

There was no main effect of treatment ($F_{(1, 24)} = 0.29; p>0.05$), motor reaction time was the comparable for both treatments (see Table 90).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 2</th>
<th>Week 4</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBE</td>
<td>220.28</td>
<td>211.27</td>
<td>203.93</td>
<td>206.70</td>
<td>208.60</td>
<td>300.97</td>
</tr>
<tr>
<td>Placebo</td>
<td>215.39</td>
<td>224.76</td>
<td>207.55</td>
<td>201.56</td>
<td>211.27</td>
<td>214.55</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(5, 120)} = 1.56; p>0.05$) there was no change in motor reaction times across visits. There was no interaction between treatment and visit ($F_{(5, 120)} = 1.33; p>0.05$).

6.17.5 Summary

There were no main effects of treatment on tasks assessing the speed of information processing in a healthy elderly population.

6.18 The effect of Ginkgo Biloba on recognition memory

In chapter 4 the effects of ageing on tasks that assess recognition memory were assessed, it was concluded that there was no main effect of age on recognition memory. The purpose of this experiment was to assess the effects of GBE supplementation on recognition memory. In chapter 4 the SKT subtest IX was
classed as assessing recognition memory. The effects of GBE were also examined on the shopping list forced choice and object forced choice tasks.

6.18.1 SKT subtest IX (recognition memory)

In the recognition memory task, subjects had to recognise the 12 original pictures of objects (originally seen in subtest I) from a series of 48 pictures. The number of omissions were recorded.

There was no main effect of treatment \( (F(1,29) = 0.04; p>0.05) \), recognition memory was the comparable for both treatments (see Table 91).

| Table 91: Showing the treatment means at each visit (number of omissions). |
|-----------------|----------|----------|----------|
|                 | Baseline | Week 4   | Week 7   |
| Ginkgo Biloba   | 0.81     | 0.56     | 0.87     |
| Placebo         | 1.26     | 0.73     | 0.46     |

There was no main effect of visit \( (F(2,58) = 2.05; p>0.05) \) there was no change in recognition memory performance across visits. There was no interaction between treatment and visit \( (F(2,58) = 2.05; p>0.05) \).

6.18.2 The Milford forced choice shopping list recognition task

In this task, subjects were presented with the word pairs containing the shopping list item plus a distractor item, the subjects had to decide which was the original shopping list item. The number of correctly recognised words were recorded.

There was no main effect of treatment \( (F(1,26) = 0.28; p>0.05) \), on shopping list recognition (see Table 92).
Table 92: Showing the treatment means at each visit (correct responses).

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>11.25</td>
<td>11.41</td>
<td>11.75</td>
</tr>
<tr>
<td>Placebo</td>
<td>11.56</td>
<td>11.37</td>
<td>11.62</td>
</tr>
</tbody>
</table>

There was no main effect of visit \(F(2, 52) = 0.27; p > 0.05\) there was no change in performance across visits. There was no interaction between treatment and visit \(F(2, 52) = 2.18; p > 0.05\).

6.18.3 The Milford forced choice object recognition task

In this task, subjects were presented with the picture pairs containing the original picture plus a distractor picture, the subjects had to decide which was the original picture. The number of correctly recognised pictures were recorded.

There was no main effect of treatment \(F(1, 26) = 0.85; p > 0.05\), on object recognition (see Table 93).

Table 93: Showing the treatment means at each visit (correct responses).

<table>
<thead>
<tr>
<th></th>
<th>Week 2</th>
<th>Week 6</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>11.66</td>
<td>11.75</td>
<td>11.58</td>
</tr>
<tr>
<td>Placebo</td>
<td>11.56</td>
<td>11.37</td>
<td>11.62</td>
</tr>
</tbody>
</table>

There was no main effect of visit \(F(2, 52) = 0.03; p > 0.05\) there was no change in performance across visits. There was no interaction between treatment and visit \(F(2, 52) = 0.57; p > 0.05\).

6.18.4 Summary

There were no main effects of treatment on tasks assessing recognition memory in a healthy elderly population.
6.19 The effect of Ginkgo Biloba on Subjective Ratings of ADL

Subjects completed a shortened version of the Bayer Activity of Daily Living scale, consisting of 14 self rating questions, assessing everyday problems with memory, perception and failures in attention. (The shortened questionnaire can be seen in appendix 5).

There was no main effect of treatment ($F_{(1, 30)} = 0.08; p>0.05$), total ADL score was the comparable for both treatments (see Table 94).

Table 94: Showing the treatment means at each visit.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Week 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginkgo Biloba</td>
<td>14.24</td>
<td>12.07</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.34</td>
<td>13.46</td>
</tr>
</tbody>
</table>

There was no main effect of visit ($F_{(1, 30)} = 2.45; p>0.05$) there was no change in total ADL score across visits. There was no interaction between treatment and visit ($F_{(1, 30)} = 0.31; p>0.05$).

6.19.1 Summary

There were no main effects of treatment on subjective ADL ratings in a healthy elderly population.

6.20 Discussion

The hypothesis tested was that treatment with ginkgo biloba would help alleviate the age related decline reported on the psychometric tasks (see chapter 4). However there were no main effects of treatment on any of the aspects of cognitive
functioning (attention, memory recall, recognition memory, speed of information processing or the speed of naming) or on subjective ratings of daily activities.

Main effects of time, i.e. changes in performance over the testing sessions, were observed on some of the tasks (SKT IV, V, VI, VII and the Critical Flicker Fusion task). These changes were possibly attributed to practice/learning effects, or simply the subjects were beginning to feel more comfortable with the testing situation. It is very difficult to eliminate learning effects in an elderly population, even when the subjects have been sufficiently trained, as this particular age group, are not familiar with computers and the laboratory environment. Prior to participation, all subjects were trained on the tasks, completing the tasks at least 6 times (as it was thought that subjects reach performance plateau after 6 tests, Parkin et al., 1996). However it would appear that subjects were not sufficiently trained.

There have been no studies examining the effect of long term supplementation with ginkgo biloba on tasks assessing attention in health adult populations, and any studies that have been conducted in patient populations have revealed improvements on the digit symbol substitution task (Weibrecht and Jansen, 1986) and the digit copying test (Rai et al., 1991). No improvements were noted on the trail making task a test of attentional/executive control (Maurer et al., 1997). The tasks assessing attention in the present study included SKT IV (arranging blocks); SKT V (replacing blocks); SKT VI (counting symbols); SKT VII (reverse naming task) and the HPRU Sternberg memory task (SMT). SKT IV and V are spatial tasks, requiring subjects to arrange and replace numerical blocks into ascending order, SKT VI is a simple counting task that places emphasis on attention and vigilance, and SKT VII is a complex reverse naming task, in which subjects are required to perform a mental reversal of letters, so that when they read the letter A they had to say B, and vice versa. This task can be likened to the digit symbol substitution task (even though in the DSST task subjects provide a written response...
and the subjects can choose their own pace), and based on the similarity might have been expected to report drug effects, however no effects were observed.

The beneficial effects of ginkgo biloba treatment on memory function seem to be limited to patient populations, as results in healthy adult populations seem somewhat inconclusive, any effects in healthy adults have been observed when large doses of GBE have been administered, Subhan and Hindmarch, (1984) administered a single acute 600 mg dose and reported an improvement on the Sternberg memory task, however no improvement was noted at lower doses (120 and 240 mg). Following 200 mg daily dose for 14 days, a trend towards memory improvement on the Sternberg memory task was noted (Dawe et al., 1995). However it is possible that these effects are "noise" effects and not true drug effects. Since a relatively low dose (the manufacturers recommended daily dose 100 mg was used in the present study) then no effects on memory could have been expected in a healthy population.

As with the effects of GBE on memory function, the beneficial effects of GBE on the speed of information processing, seem to be limited to patient populations. Results in healthy adult populations revealed that GBE had no effect on such tasks, only one pilot study reported improvements on the recognition component of the choice reaction time task, and in this study subjects had received a 200 mg daily dose for 14 days (Dawe et al., 1995). Hence based on these findings, treatment with a 100 mg daily dose of GBE would not have been expected to result in significant improvements.

There have been no studies examining the effect of ginkgo biloba on the speed of naming, however since these tasks rely heavily on timing, any effects would be expected to mirror results obtained on tasks assessing the speed of information processing, therefore since GBE had no effect on tasks assessing the speed of
information processing (CFF, CRT, SKT total score) then effects on the speed of naming (SKT I, III) would not be expected.

The results of this experiment would seem to indicate that 100 mg ginkgo biloba is not beneficial for treating cognition especially in healthy elderly subjects who believed they were experiencing problems with their memory. It is possible that more dramatic effects may have been demonstrated if the dose of GBE had been increased to at least 120-200 mg daily or, if the subjects included in the trial had been experiencing definite memory decline. The subjects included in the experiment complained of memory problems, however they were very fit and healthy, and were probably not experiencing any great degree of cognitive decline. Based on this evidence it was concluded that a 100 mg daily dose of ginkgo biloba had no beneficial effects on cognition in a sample of healthy elderly subjects.
Chapter Seven: The effects of an acute dose of glucose on cognitive and psychomotor functioning in an elderly population

7.1 Chapter Outline

The important role of glucose to the brain
What happens once glucose has entered the body
The uptake of glucose to the brain- the glucose transport mechanism
The possible mechanisms for glucose's role in the enhancement of cognition
The effect of glucose on neurotransmitter synthesis and function
The effects of ageing on glucose regulation
The effect of glucose administration on performance in elderly subjects
The effect of glucose on attention in healthy elderly subjects
The effect of glucose on memory function in healthy elderly subjects
The effect of glucose on the speed of information processing in healthy elderly subjects
The effect of glucose on mood in healthy elderly subjects

Assessing the effects of glucose administration on cognitive function and mood in a healthy elderly population.

Blood glucose level
The effect of glucose on attention
The effect of glucose on memory recall
The effect of glucose on the speed of naming
The effect of glucose on the speed of information processing
The effect of glucose on recognition memory
The effect of glucose on subjective mood ratings – The Profile of Mood States

The effect of hypoglycaemia on psychometric test performance

The literature suggests that glucose enhances some aspects of cognitive performance especially in aged samples. This study aims to assess the impact of a 50g glucose drink on cognitive and psychomotor performance in a sample of 24 healthy elderly volunteers. The effects of glucose administration were examined on tasks assessing memory, attention, the speed of information processing and subjective ratings of mood.

The chapter reviews the previous literature in terms of the effects of glucose administration on aspects of cognitive function and mood in both healthy elderly and patient populations.

7.2 The important role of glucose

There a numerous lines of evidence to suggest that blood glucose levels play an important role in cognitive function. Glucose administration has improved various aspects of cognition including memory, attention, reaction time and aspects of mood. The beneficial effects have been demonstrated in young healthy populations (Lapp, 1981; Benton and Owens, 1993; Benton, Owens and Parker, 1994; Craft, Murphy and Wemstrom, 1994; Foster, Lidder, and Sünram, 1997) elderly populations (Gonder-Frederick, Hall, Vogt, Cox, Green and Gold, 1987; Hall, Gonder-Frederick, Chewning, Silveira and Gold, 1989; Manning, Hall and Gold, 1990; Manning, Parsons and Gold, 1992; Parsons and Gold, 1992) and in patients with Alzheimer's Disease (Craft, Murphy and Wemstrom, 1994; Manning, Ragozzino and Gold, 1993; Craft, Newcomer, Kanne, Dagogo-Jack, Cryer, Sheline, Luby, Dagogo-Jack and Alderson, 1996).
The belief that glucose may be responsible for some of the cognitive enhancing effects was noted by Wenk (1989) he reported that many of the nootropic drugs i.e. those that improve memory and attention, produce their effect by increasing the availability and uptake of glucose. He noted that many of the cognitive enhancing drugs do not cross the blood brain barrier, many are effective when injected peripherally but not when injected directly into the brain, and a number of cognitive enhancing drugs are not effective following adrenalectomy. Based on this evidence, it was believed that glucose was directly involved in determining cognitive function.

Based upon this evidence, a number of research teams have supplemented subjects with glucose in the belief that it could be used as an alternative method for improving/enhancing memory and cognition. It is thought that the available glucose would enter the blood stream and be carried to the brain to act as a fuel source for brain cells.

The brain is the most metabolically active organ in the human body, it accounts for only 2-2.7% of total body weight, but it consumes approximately 20% of the bodies oxygen supply, 25% of the bodies glucose supply and 19% of the bodies blood supply (Holiday, 1979; Garrow and Blaza, 1982).

The human brain utilises glucose as its primary source of energy, it uses approximately 70 mg of glucose every minute, it has been calculated that without replacement the brains supply would be completely used up in 10-15 minutes (Marks and Rose, 1981). It is estimated that the brain consumes approximately 17 calories per 100g of brain tissue (Siebert, Gessner and Klasser, 1986). Glucose is the brain's primary source of fuel, however it can in very extreme conditions such as extreme starvation, utilise other fuels mainly ketone bodies (Gottstein, Held,
Muller and Berghoff, 1970). The brain is also able to utilise glycogen as a fuel, however the brain has a limited store of glycogen (2-4 mmol/g) and it is estimated that glycogen would only manage to provide energy for the brain for approximately 3 minutes (Siesjo, 1978). Alternative fuels do not readily cross the blood brain barrier and hence are only used under extreme conditions, and under normal conditions the brain is dependant upon a continuous blood supply of glucose (Krassner, 1986).

7.3 What happens to glucose once it has entered the body

Before the cognitive effects of glucose are explored, the fate of glucose in the body will be examined. Following a meal or glucose drink, blood glucose levels rise for approximately 30 minutes after which they fall and return to baseline levels within about 2 hours. When there is an excess supply of glucose in the blood, the liver converts the excess glucose into glycogen for storage in the liver cells, and when the level of blood glucose falls, the hormone glucagon converts the glycogen into glucose and it is released into the blood stream.

Insulin acts in three ways:

1. It increases glucose utilisation by body cells
2. It suppresses hepatic glucose production
3. It promotes glycogen formation in order to maintain glucose levels within narrow limits.

This biological mechanism ensures a continual optimal supply of glucose for the brain (See figure 59).
Figure 59: Showing the conversion of glucose into glycogen and vice versa with the role of the glucoregulatory hormones glucagon and insulin.

7.4 Uptake of glucose to the brain - the glucose transport mechanism

At present 5 proteins have been identified as responsible for the transport of glucose across the cell membranes into the brain. With the exception of the lumen in the small intestine and the proximal tube of the kidney, the transport of glucose across the cell membranes occurs by a process of facilitated (carrier mediated) diffusion (Pessin and Bell, 1992). The 5 proteins are termed:-

1. GLUT1 (found in the erythrocytes)
2. GLUT2 (found in the liver)
3. GLUT3 (found in the brain)
4. GLUT4 (found in the muscle/fat)
5. GLUT5 (found in the small intestine)

Proteins GLUT1 and GLUT3 are present in the brain and work together to ensure a continual supply of glucose to the brain cells. GLUT1 is found in endothelial cells and appears to be responsible for the transport of glucose across the blood brain...
barrier and delivery of glucose to underlying tissues. GLUT3 mediates glucose transport across neuronal cell membranes. At present the role of the other glucose proteins is unclear. Once the glucose has crossed the blood brain barrier, it then diffuses through the extracellular space and across the neuronal membranes. Once glucose enters the cell, it is broken down by a process of glycolysis (see figure 2)
Figure 60: The breakdown of glucose by glycolysis.
7.5 The possible mechanisms for glucose’s role in the enhancement of cognition

Two possible routes have been identified to account for glucose’s beneficial effects. A number of lines of evidence have been provided to substantiate the 2 possible routes. Enhancement of glucose can be via a central route (directly in the brain) or via a peripheral route.

Researchers who favour the peripheral route, have assessed the effects of fructose on memory performance. Fructose (unlike glucose) does not cross the blood-brain barrier, therefore if any memory improvements were evident following ingestion of fructose, then it must be via a peripheral route. It was found that 2g/kg fructose enhanced memory in much the same way as 2g/kg of glucose. However, 100g/kg fructose had no effect on memory, whereas 100g/kg glucose acted to enhance memory. This lead researchers to believe that 100 mg/kg glucose exerted its positive effects via a central route.

The central route is believed to be attained by glucose acting directly on a substrate in the brain, possibly the cells of the hippocampus, to produce the enhancement of memory. Messier, Durkin, Mrabet and Destrade (1989) postulated that the mechanism could involve an interaction with acetylcholine.

Numerous investigations were taken to identify possible mechanisms for the peripheral enhancement of memory following glucose ingestion. It was first thought that insulin release following glucose ingestion was responsible for the memory enhancement. However no memory enhancement was observed when animals were injected with insulin. The insulin probably promoted the absorption of glucose by insulin sensitive tissues, thus reducing glucose availability.
The second approach was to investigate the role of the adrenal medulla. There is a wealth of evidence that adrenalin has a memory enhancing effect (Gold, and van Buskirk, 1975; Gold and Zometzer, 1983). Increases in blood glucose cause the adrenal medulla to release adrenalin, therefore if this mechanism were responsible for the memory enhancement, then no memory enhancement would be observed in animals who have had their adrenal medullas removed. However it was reported that the response in these animals was exactly the same response as “normal” animals. Therefore the memory enhancing effect of glucose could not be mediated by adrenalin release from the adrenal medulla.

The peripheral route may be mediated via the organ responsible for glucose metabolism, the liver. In order to investigate this, the celiac ganglion was destroyed. The celiac ganglion is the route through which the autonomic nerves from the liver pass to the CNS. Celiac ganglion lesions eliminated the memory enhancing effects of glucose. This finding suggests that the memory enhancing effects of glucose may be mediated through the liver. A possible mechanism would be, a rise in blood glucose is detected by the liver and transduced into neural signals which are transmitted to the brain via the autonomic nervous system. However this is purely speculative as no information is presently available as to how the proposed neural signal from the liver might influence memory when it reaches the brain.

7.6 The effect of glucose on neurotransmitters synthesis and function

The beneficial effects of glucose may also be attributed to the interaction of glucose with neurotransmitter synthesis/function particularly acetylcholine, dopamine and the opiates.
Several lines of evidence have been proposed to suggest that glucose may interact with central cholinergic mechanisms. Glucose has been shown to alleviate scopolamine-induced amnesia (Meisser, Durkin, Mrabet and Destrade, 1990), alleviate the depletion of acetylcholine following treatment with quinuclidinyl benzilate (QNB) (Ricny, Tucek, and Novakova, 1992) glucose also helped to reduce the loss of atropine-induced acetylcholine in the caudate nucleus, whereas glucose had no effect on acetylcholine content in animals who had not received atropine (Dolezal and Tucek, 1982). Glucose also increases extracellular acetylcholine following scopolamine injections (Durkin, Messier, de Boer and Westerink 1992). The above evidence would seem to indicate that glucose is taken into cholinergic presynaptic terminals and transformed into acetylcoenzyme A which is then used to synthesize acetylcholine.

Glucose also interacts with a number of other neurotransmitters. It is possible that the memory improving action of peripherally-injected dopamine drugs may be mediated by glucose. Animal experiments whereby the rats were pre-trained on two radial maze tasks and injected with the D2 receptor agonist quinpirole and D1 agonist SKF 38393. It was found that performance on the maze tasks were improved following treatment with quinpirole and not SKF 38393, interestingly the injection of quinpirole was found to increase blood glucose whilst SKF 38393 did not (Clayson, 1971). Peripheral injections of glucose can suppress the firing of nigrostriatal dopamine-containing neurons and lower dopamine metabolite content (Chance, Cao and Fisher, 1989). Manipulation of blood glucose levels alters the response to drugs such as haloperidol and amphetamine.

Glucose has also been shown experimentally to interact with the opiates. Glucose has also been shown to reverse the amnesia produced by morphine (Stone, Walker, Gold and Gold, 1991). Morphine injections are believed to reduce the hippocampal
acetylcholine output, and when glucose is administered it attenuates the reduction of acetylcholine.

7.7 The effects of ageing on glucose regulation

Ageing is a natural state associated with a number of changes in cognition such as decline in attention and memory performance and a slowing of information processing. It is not known precisely what biological mechanisms are responsible for cognitive decline, however it has been postulated that abnormalities in glucose metabolism may play a role in this cognitive decline.

Human ageing is associated with a number of disruptions in glucose regulation and utilisation such as elevated blood glucose levels following the ingestion of a glucose drink (O'Sullivan, 1974); decreased peripheral glucose metabolism (Fink, Koltermann, Griffen and Olefsky, 1983) and decreased central glucose metabolism (Kuhl et al, 1984; Riege et al, 1985).

There are many lines of evidence that would seem to indicate that the aged human brain suffers from reduced cerebral glucose utilisation. Hoyer (1988) notes that 2 enzymes essential for the breakdown of glucose (glycolysis) Hexokinase and phosphofructokinase are reduced in aged human brains.

A number of studies have provided evidence to support the claim that a reduction in cerebral metabolism (a condition commonly noted in an elderly population) results in a decline in cognitive function. Riege, Metter, Kuhl and Phelps (1985) reported that elderly subjects (aged greater than 48 years) differed from younger subjects (aged less than 42 years) on a number of occasions. 23 healthy adults aged 27-78 years performed a total of 18 different memory tests. It was reported that elderly subjects with high superior frontal and lower caudate thalmic metabolic
rates performed better on tests of memory for stories, sentences, complex designs and patterns. Beradi, Haxby, Grady and Rapoport, (1991) found that elderly subjects with higher verbal memory scores also had a high rate of glucose utilisation in the right hemisphere. However Duara, Grady, Haxby, Sundaram, Cutler, Heston, Moore, Schlageter and Larson (1984) Duara, Grady, Haxby, Ingvar, Sokoloff, Margolin, Manning, Cutler and Rapoport (1986) failed to report any relationship between cognitive function and resting metabolic rate.

Despite the minor inconsistencies there seems to be evidence to indicate that in elderly subjects there is a relationship between the ability to metabolise glucose and cognitive performance, higher glucose metabolism being associated with superior cognitive performance.

Poor glucose regulation and metabolism has been put forward as a risk factor for Alzheimer's disease. Landin, Blennow, Wallin and Gottfries (1993) defined Alzheimer's disease as a "hypometabolic brain disease" disrupted glucose regulation and utilisation often seen in Alzheimer's disease may be responsible for the memory disturbances observed in this disorder. Duara et al (1986) notes that Alzheimer's patients show more extreme abnormalities of the glucose system than age matched healthy subjects. Hoyer (1992) notes that patients with Alzheimer's disease showed a 44% reduction in glucose utilisation. Foster, Chase, Manis, Brooks, Fedio, Patronas and Di Chiro (1984) reported that overall glucose utilisation was 10 - 49% lower in a sample of Alzheimer patients than a control group. The areas of the brain most affected were the parietal lobes (32% reduction) and the temporal lobes (34% reduction), whereas the frontal cortex was relatively unaffected (19%).
7.8 The effects of glucose administration on performance in elderly subjects

There have been a number of experiments assessing the effects of glucose on cognitive function in samples of elderly subjects, a sector of the population known to exhibit a decline in cognition.

It would seem that as a result of the ageing process, the elderly are more susceptible to fluctuations in blood glucose (Kent, 1976). The elderly have been shown to suffer a decline in cerebral glucose utilisation, and it is possible that this is responsible for the cognitive deficits present in the population. Based on this hypothesis it was questioned whether supplementation with glucose would enhance aspects of cognitive functioning.

A review of the literature assessing the role of glucose in psychometric task performance in both diabetic and healthy subjects has lead researchers to believe that psychometric test performance deteriorates when blood glucose levels are low (< 2.2 mmol/L) and tends to improve when blood glucose levels are raised to within normal limits (4.0 - 7.0 mmol/L). (Holmes, Hayford, Gonzales and Weydert, 1983; Cox, Gonder-Frederick, Schroeder, Cryer, and Clarke, 1983; Kerr, MacDonald and Tattersall, 1989; Kerr, MacDonald and Tattersall, 1991; Perlmutter, Malekeh, Hodgson-Harrington, Ginsberg, Katz, Singer and Nathan, 1984; Perlmutter, Tun, Sizer, McGlinchey and Nathan, 1987; Maassen, Lingenfelser, Glück, Renn, Eggstein, and Jakober, 1990)

7.9 The effect of glucose on attention in healthy elderly subjects

Attention is an aspect of cognitive functioning thought to be susceptible to fluctuations in blood glucose levels and which has been shown to improve
following treatment with glucose in young samples (Benton, Owens and Parker, 1994).

Research in diabetic subjects would seem to indicate that attention is an aspect of cognition that is susceptible to fluctuations in blood glucose level, in particular it would seem that low blood glucose levels (or poor glycaemic control) are associated with poorer attentional task performance (Maassen, Lingenfelser, Glück, Renn, Eggstein, and Jakober, 1990; Perlmutter, Malekeh, Hodgson-Harrington, Ginsberg, Katz, Singer and Nathan, 1984).

There have been five studies to date, that have assessed the effect of glucose on attention in healthy elderly subjects.

Manning, Hall and Gold (1990) examined the effects of glucose on attention in 17 healthy elderly volunteers aged 62-84 years, (mean age 73 years). Subjects were treated with glucose 50 g or saccharin 23.7 mg and performance was assessed using the letter cancellation task. It was reported that supplementation with glucose had no effect on performance of the task.

Craft, Murphy and Wemstrom (1994) conducted a study which assessed the effects of glucose on attention in a sample of 32 elderly subjects aged 58-77 years (mean age of 68.5 years). Subjects were treated with glucose (50 g) and saccharin (23.7 mg). Performance was assessed using the paced auditory serial addition test (PASAT) and the Stroop task. In the paced auditory serial addition task subjects had to add 60 pairs of randomised digits presented in a continuous string. In the Stroop task subjects had to complete three conditions, in the first condition subjects had to read 100 coloured words, in the second condition the subjects had to name the colours of 100 blocks, and finally the subjects were presented with coloured words written in discordant colours, subjects were required to ignore the written
word and name the colour of the ink. It was reported that glucose administration had no effect on performance of the either the PASAT or the Stroop task.

Craft, Newcomer, Kanne, Dagogo-Jack, Cryer, Sheline, Luby, Dagogo-Jack and Alderson (1996) questioned whether the improvements in cognitive performance were attributable to the glucose or simply due to raised plasma insulin levels as a result of the excess glucose intake. To examine this the researchers assessed cognitive function in 13 healthy adults (mean age 71 years), under three conditions. In condition one, plasma insulin levels were maintained at 6 U/ml and dextrose was infused to keep plasma glucose levels of 90 mg/dl. In the second condition insulin levels were allowed to vary naturally and dextrose was infused to maintain plasma glucose levels at 225 mg/dl. Finally in the third condition both glucose and insulin were maintained at baseline levels (insulin 7 U/ml and glucose 90 mg/dl). Cognitive performance was assessed 30 minutes after the blood glucose and insulin levels had been adjusted and stabilised for 30 minutes. Cognitive performance was assessed using the Stroop task. It was reported that when plasma insulin levels were raised and glucose levels remained at baseline there was no effect on performance of the Stroop task. Therefore the effect was not just due to the raised insulin levels.

Allen, Gross, Aloia and Billingsley (1996) assessed the effects of glucose on attention in 28 healthy elderly subjects aged 61-87 years (mean age 73 years). Subjects were treated with glucose (50 g). Performance was assessed using the trail making A and B tests and a dichotic listening task (subjects had to attend to 2 auditory signals, one to each ear, two triads of one syllable words were presented simultaneously to the right and left ears. Subjects completed 11 trials, and after they had heard all the words they had to recall as many of the words as possible). It was reported that subjects with poor glucose control (which was defined as a change in blood glucose level greater than 100 mg dl\(^{-1}\) ) had poorer performance on
the dichotic listening task. Glucose administration had no effect on performance of the trail making tasks.

Craft, Zallen and Baker (1992) assessed the effects of glucose on performance on a single and two feature detection task in 14 healthy elderly subjects (mean age 71.4 years). Subjects were treated with glucose 50 g or saccharin 23.7 mg, following treatment subjects completed a single feature detection task (subjects watched a computer screen, two rows of geometric shapes (circles and triangles) appeared on the screen, subjects were required to respond by pressing the "yes" button if a triangle appeared, and "no" if it was a circle, subjects had to complete 60 trials. In the two feature detection task, the 2 rows of geometric shapes consisted of large and small circles/triangles were presented, subjects were required to respond to the large triangles. It was reported that glucose treatment had no effect on performance of the tasks.

A number of research teams have examined the effects of supplementation with glucose on aspects of attention in patient populations.

Craft, Zallen and Baker (1992) assessed the effects of glucose on performance of a single and two feature detection and localisation task in 21 elderly patients (mean age 73.5 years) with very mild, mild and probable Senile Dementia of the Alzheimer Type (SDAT). Subjects were treated with glucose 50 g or saccharin 23.7 mg, following treatment subjects completed a single feature detection task (subjects watched a computer screen, two rows of geometric shapes (circles and triangles) appeared on the screen, subjects were required to respond y pressing the "yes" button if a triangle appeared, and "no" if it was a circle, subject shad to complete 60 trials. In the two feature detection task, the 2 rows of geometric shapes consisted of large and small circles/triangles, subjects were required to respond to the large triangles. It was reported that treatment with glucose facilitated performance on the
single feature detection task, glucose had no effect on the two feature detection task, this was possibly due to the fact that the two feature detection task was too difficult for the SDAT patients.

Craft, Newcomer, Kanne, Dagogo-Jack, Cryer, Sheline, Luby, Dagogo-Jack and Alderson (1996) questioned whether the improvements in cognitive performance were attributable to the glucose or simply due to raised plasma insulin levels as a result of the excess glucose intake. To examine this, the researchers assessed cognitive function in 21 patients with SDAT (mean age 71 years), under three conditions. In condition one, plasma insulin levels were maintained at 60U/ml and dextrose was infused to keep plasma glucose levels of 90 mg/dl. In the second condition insulin levels were allowed to vary naturally and dextrose was infused to maintain plasma glucose levels at 225 mg/dl. Finally in the third condition both glucose and insulin were maintained at baseline levels (insulin 7 U/ml and glucose 90 mg/dl). Cognitive performance was assessed 30 minutes after the blood glucose and insulin levels had been adjusted and stabilised for 30 minutes. Cognitive performance was assessed using the Stroop task. It was reported that when plasma insulin levels were raised and glucose levels remained at baseline there was no effect on performance of the Stroop task observed under any of the 3 conditions.

7.9.1 Summary

The results of these experiments would seem to indicate that glucose had no effect on attention in healthy elderly subjects whether assessed using the letter cancellation task (Manning et al., 1990), paced auditory serial addition task (Craft et al., 1994), Stroop task (Craft et al., 1994; Craft et al., 1996), trail making tasks (Allen et al., 1996) or feature detection task (Craft et al., 1992).
Allen et al. (1996) reported that subjects with poor glucose regulation had poorer dichotic listening performance. Suggesting that glucose may affect selective attention.

The results of the effects of glucose in patient populations diagnosed with Senile Dementia of the Alzheimer Type (SDAT) would seem to indicate that glucose had no effect on the Stroop task (Craft et al., 1996) or two feature detection task (Craft et al., 1992). However treatment with glucose facilitated performance on the single feature detection task (Craft et al., 1992) (See table 95).
Table 95: Summarising the effects of glucose on aspects of attention in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manning et al.</td>
<td>Healthy elderly</td>
<td>17</td>
<td>62-84 years</td>
<td>50 g glucose 23.7 mg saccharin</td>
<td>Letter cancellation</td>
<td>No effect on the task</td>
</tr>
<tr>
<td>Craft et al.</td>
<td>Healthy elderly</td>
<td>32</td>
<td>58-77 years</td>
<td>50 g</td>
<td>Paced serial addition task and Stroop task</td>
<td>No effect on either task</td>
</tr>
<tr>
<td>Craft et al.</td>
<td>Healthy adults</td>
<td>13</td>
<td>Mean age 71 years</td>
<td>Insulin levels manipulated</td>
<td>Stroop task</td>
<td>No effect on the task</td>
</tr>
<tr>
<td>Allen et al.</td>
<td>Healthy elderly</td>
<td>28</td>
<td>61-87 years</td>
<td>50 g glucose or 23.7 mg saccharin</td>
<td>Trail making A and B tasks</td>
<td>No effect on the trail making tasks. Subjects with poor glucose control had poorer dichotic listening performance</td>
</tr>
<tr>
<td>Craft et al.</td>
<td>Healthy elderly</td>
<td>14</td>
<td>Mean age 71.4 years</td>
<td>50 g glucose or 23.7 mg saccharin</td>
<td>Single and two feature detection task</td>
<td>No effects on the tasks</td>
</tr>
<tr>
<td>Craft et al.</td>
<td>SDAT patients</td>
<td>21</td>
<td>Mean age 73.5 years</td>
<td>50 g glucose or 23.7 mg saccharin</td>
<td>Single and two feature detection task</td>
<td>Performance on the single feature task was facilitated, no effect on the two feature task</td>
</tr>
<tr>
<td>Craft et al.</td>
<td>SDAT patients</td>
<td>21</td>
<td>Mean age 71 years</td>
<td>Insulin levels manipulated</td>
<td>Stroop task</td>
<td>No effect on the task</td>
</tr>
</tbody>
</table>
7.10 The effect of glucose on memory function in healthy elderly subjects

Memory is an aspect of cognition thought to be susceptible to fluctuations in blood glucose level. A number of researchers have reported that supplementation with glucose significantly improved memory performance in healthy young subjects (Benton and Owens, 1993; Craft, Murphy and Wemstrom, 1994; Benton, Owens and Parker, 1994; Foster, Lidder and Sünram, 1997).

Research in diabetic patients would also seem to implicate the role of glucose in memory function. Diabetes is a disease state in which the pancreas lacks the ability to produce insulin, or only produces small amounts of insulin, rendering the patient unable to convert excess glucose into glycogen for storage. Diabetic patients suffer from wide fluctuations in blood glucose levels, experiencing both hypoglycaemia (low blood glucose level) and hyperglycaemia (high blood glucose level) both hypo and hyper glycaemia affect the brain.

During hypoglycaemia (when blood glucose levels fall to levels less than 2.2 mmol/L) the brain suffers from a decrease in glucose supply which results in a state of confusion, inability to concentrate and memory disturbances (Hepburn, 1992). A number of studies have examined the effects of hypoglycaemia on memory function in both diabetic and non diabetic subjects. All studies reported that during hypoglycaemia memory function is disturbed (Perlmutter, Malekeh, Hodgson-Harrington, Ginsberg, Katz, Singer, and Nathan, 1984; Perlmutter, Tun, Sizer, McGlinchey, Nathan, 1987; Kalmijn, Feskens, Launer, Stijnen and Kromhout, 1995; Hvidberg, Fanelli, Hershey, Terkamp, Craft and Cryer, 1996)

A number of studies have assessed the role of glucose on memory performance in healthy elderly subjects.
Gonder-Frederick, Hall, Vogt, Cox, Green and Gold (1987) assessed the impact of glucose on memory performance in a sample of 11 healthy elderly persons aged 58-76 years. Memory was assessed using 4 scales of the Wechsler memory task: a paired associative word list (10 pairs of words, 6 easy and 4 difficult recall was required 24 hours after presentation), paragraph recall (subjects listened to a story and were required to recall the story 15 minutes after presentation), digit span (immediate recall of digits both forward and backward) and visual memory (geometric shapes were presented and subjects were required to give immediate recall of the shapes). A total memory score was calculated for all subjects by summing the scores on the 4 subtests. Subjects were supplemented with either glucose (50 g) or saccharin (23.7 mg). It was found that performance on the paragraph recall and total Wechsler memory scores were significantly improved in the glucose condition. Mean scores for the paired associate word list and the visual memory were higher in the glucose condition, however these failed to reach statistical significance.

Hall, Gonder-Frederick, Chewning, Silveira and Gold (1989) assessed the effects of glucose on tests of memory in 11 subjects aged 58-77 years (mean age 67.4 years). Subjects were treated with glucose (50 g) or saccharin (23.7 mg). Memory function was assessed using the same tests as Gonder-Frederick et al. (1987) a paired associate word list task, paragraph recall, digit span and immediate recall of a visual memory task. In line with Gonder-Frederick et al. (1987) it was reported that glucose significantly enhanced performance on the paragraph recall and total Wechsler memory scores. However Hall et al. (1989) reported that glucose significantly enhanced performance on the paired associate word list task and the visual memory task. Gonder-Frederick et al. (1989) reported a non significant trend towards improvement on these tasks, this lack of significance in the Gonder-Frederick et al. (1987) study, probably suggests that the improvement of
performance in the Hall et al. (1989) was a weak effect, that failed to reach statistical significance using the same method in the Gonder-Frederick et al. (1987) study.

Manning, Hall and Gold (1990) examined the effects of glucose on memory function in 17 healthy elderly subjects aged 62-84 years, (mean age 73 years). Subjects were supplemented with glucose (50 g). Performance was assessed using a selective reminding task (a list of 12 words were read out to subjects, they were asked to repeat as many as possible, the subjects then had to re-read all the words that they had failed to recall, they had to keep reading and recalling, until all 12 words had been recalled, or 12 trials had been completed), paragraph recall (subjects were required to recall the paragraph immediately after hearing it and after 40 minutes) digit span, (immediate recall of both forward digit and backward digit spans) and Rey-Osterrieth complex figures task, (subjects were required to give immediate recall of complex figures). It was reported that glucose significantly improved performance on the paragraph recall task and the selective reminding task but had no effect on the digit span, or Rey Osterreith complex figures test.

Manning, Parsons and Gold (1992) assessed the effect of administering glucose before and after the presentation of test material. Twenty two subjects aged 60-81 years were given either a drink containing glucose (50 g) or saccharin (23.7 mg) before or after hearing the Wechsler paragraph recall task. Recall of the passage was required after 24 hours. Enhanced memory performance was expected when subjects had received 50g glucose before hearing the passage, however the authors were interested to investigate whether giving glucose after the presentation of test material would result in enhanced memory performance. It was found that glucose administration both before and after the presentation of test material significantly improved the recall of the passage even after 24 hours had elapsed between test points.
Parsons and Gold (1992) assessed the effects of three doses of glucose (10 g, 25 g and 50 g) on memory performance in a sample of 10 healthy elderly subjects aged 60-82 years. Memory was assessed using the paragraph recall task (subject had to give immediate recall and recall 40 minutes after presentation). Parsons and Gold noted that glucose enhanced performance on the paragraph recall task in inverted U dose response manner. Memory performance was better when subjects had received 25 g glucose, compared to placebo, 10 g and 50 g glucose.

Craft, Murphy and Wenstrom (1994) conducted a study which assessed the effects of glucose on memory performance in a sample of 32 elderly subjects aged 58-77 years (with a mean age of 68.5 years). The subjects were treated with glucose (50 g) and saccharin (23.7 mg). Memory performance assessed using the paragraph recall task, (subjects were required to recall the story immediately after hearing it and after a delay of 10 minutes), procedural memory (subjects had to complete a serial reaction time task, in which they had to keep their middle and index fingers on 4 keys, that corresponded to the 4 corners of the computer screen, subjects had to press the corresponding key when an asterix appeared), pattern recall and recognition (subjects were presented with 3 patterns for 10 seconds, subjects had to reproduce the pictures immediately and after 10 minutes. Subjects were also required to perform a recognition task, they had to select the 3 pictures from a series of 12 pictures). It was found that glucose enhanced memory performance on the paragraph recall task in male subjects, especially those with good glucose tolerance. Glucose was found to have no effect on any other memory measures.

Allen, Gross, Aloia and Billingsley (1996) assessed the effects of glucose (50g) on memory function in 28 healthy elderly subjects aged 61-87 years (mean age 73 years). Performance was assessed using the Rey/Taylor complex figures test (subjects had to copy complex figures from memory and recall the figures after a
20 minute delay). It was reported that glucose administration resulted in significant improvements on the Rey/Taylor complex figures test.

Craft, Newcomer, Kanne, Dagogo-Jack, Cryer, Sheline, Luby, Dagogo-Jack and Alderson (1996) questioned whether the improvements in cognitive performance was attributable to the glucose or simply due to raised plasma insulin levels as a result of the excess glucose intake. To examine this the researchers assessed cognitive function in 13 healthy adults (mean age 71 years), under three conditions. In condition one, plasma insulin levels were maintained at 6 U/ml and dextrose was infused to keep plasma glucose levels of 90 mg/dl. In the second condition insulin levels were allowed to vary naturally and dextrose was infused to maintain plasma glucose levels at 225 mg/dl. Finally in the third condition both glucose and insulin were maintained at baseline levels (insulin 7 U/ml and glucose 90 mg/dl). Cognitive performance was assessed 30 minutes after the blood glucose and insulin levels had been adjusted and stabilised for 30 minutes. Cognitive performance was assessed using paragraph recall task (recall was required immediately and after a 10 minute delay). It was reported that manipulating plasma insulin levels had no effect on memory in healthy subjects.

A number of research teams have examined the effects of glucose supplementation on aspects of memory in patients with Senile Dementia of the Alzheimer's Type (SDAT).

Craft, Zallen and Baker (1992) examined the effect of glucose administration on memory performance in a sample of 21 patients with very mild, mild and probable senile dementia of the Alzheimer's type (SDAT). Patients were supplemented with glucose (50 g) or saccharin (23.7 mg), following supplementation cognitive function was assessed using a paired associate word list task (10 pairs of words were presented subjects were required to provide immediate recall and after a 20
minute filled gap); paragraph recall (immediate recall and recall after 15 minutes) and pattern recall and recognition (subjects were presented with 3 patterns for 15 minutes, subjects had to reproduce the patterns immediately after seeing them and after 20 filled minutes, subjects were also required to perform a recognition task, they had to recognise the 3 pictures from a series of 12). It was reported that subjects with poor glucose regulation (i.e. those whose blood glucose levels initially rose quite rapidly and remained elevated for some time ) showed a significant improvement on all tasks.

Craft, Dagogo-Jack, Wiethop, Murphy, Nevins, Fleishman, Rice, Newcomer and Cryer (1993) tested memory performance in 22 SDAT patients under 3 glycaemic conditions (fasted, raised to 175 mg/ml and 225 mg/ml). Memory was assessed using the paragraph recall task (immediate recall and after a 20 minute delay); paired associate learning task (8 pairs of words were presented to subjects, subjects had to recall the words immediately and after 20 minutes). It was reported that patients with mild SDAT showed better memory performance on the immediate paragraph recall task when blood glucose levels were raised to 225 mg/ml.

Manning, Ragozzino and Gold (1993) assessed the effects of glucose administration on memory in a sample of 23 SDAT subjects aged 68-94 years (mean age 82 years). Patients received treatment with glucose (75 g) or saccharin (34.8 mg). Memory function was assessed using paragraph recall (immediate recall); word list (containing 8 words, subjects were required to give immediate recall); face recognition task (subjects were presented with a series of faces, and were required to rate the faces as either pleasant or unpleasant, following this, subjects were shown a number of faces and they had to decide whether they had seen the faces before), and a word recognition task (subjects were presented with a list of words, they had to rate whether they liked the words or not, then they were presented with a list of words, subjects had to decide whether they had previously
seen the words). It was reported that glucose treatment facilitated performance on the paragraph recall task, facial recognition task and the word list task.

Craft, Newcomer, Kanne, Dagogo-Jack, Cryer, Sheline, Luby, Dagogo-Jack and Alderson (1996) questioned whether the improvements in cognitive performance observed in subjects was attributable to the glucose or simply due to raised plasma insulin levels as a result of the excess glucose intake. To examine this the researchers examined cognitive function in 21 SDAT patients (mean age 71 years), under three conditions. In condition one, plasma insulin levels were maintained at 6 U/ml and dextrose was infused to keep plasma glucose levels of 90 mg/dl. In the second condition insulin levels were allowed to vary naturally and dextrose was infused to maintain plasma glucose levels at 225 mg/dl. Finally in the third condition both glucose and insulin were maintained at baseline levels (insulin 7 U/ml and glucose 90 mg/dl). Cognitive performance was assessed 30 minutes after the blood glucose and insulin levels had been adjusted and stabilised for 30 minutes. Cognitive performance was assessed using paragraph recall task (recall was required immediately and after a 10 minute delay). It was reported that when plasma insulin levels were raised and glucose levels remained at baseline there was a significant improvement in performance on the task.

7.10.1 Summary
The benefits of glucose supplementation on memory performance in healthy elderly subjects seem somewhat inconclusive. It would seem that glucose enhances performance on some memory tasks but not others.

In particular it would seem that glucose enhances performance on the paragraph recall task, this was true for immediate recall and recall after 10, 20 or 40 minutes (Gonder Frederick et al., 1987; Hall et al., 1989; Parsons and Gold, 1992; Craft et al., 1994; Manning et al., 1990).
There is conflicting evidence from tasks of immediate memory where forming associations between items is crucial for task performance. For instance, Hall et al., (1989) noted that performance on a paired associate word list task and an immediate recall visual memory task showed an improvement following a glucose treatment, whereas Gonder Frederick et al., (1987) only noted non significant improvements on these tasks.

Glucose was also found to significantly improve performance on a selective reminding task, much like the previous tasks requires aspects of attention, learning and manipulation of information, not just memory (Manning et al., 1990). To conclude, glucose would seem to have beneficial effects on memory tasks that require the subjects to actively work on the information, either by making associations or learning and constantly monitoring the information.

Glucose supplementation was found to have no effect on the digit span task (Gonder-Frederick et al., 1987; Hall et al., 1989; Manning et al., 1990), in the digit span task, subjects simply have to remember digit strings in increasing length, performance on this task is fairly well maintained with age. Glucose also had no effect on the Rey Osterreith complex figures task (Manning et al., 1990), this is essentially a copying task, subjects are asked to look at a figure and reproduce it, even though some of the figures are quite complex, all the subjects have to do, is to form an image of the figure and hold it in memory long enough to be able to reproduce the pattern, contrary findings were reported by Allen et al., (1996).

Glucose had no effect on the procedural memory task (Craft et al., 1994) essentially a sequence learning task with no verbal component, a task that is not expected to show the same decrement or improvement as a verbal task. Allen et al. (1996) reported that glucose had no effect on a verbal fluency task. Glucose also
had no effect on performance of a pattern recall and recognition task, this is a highly procedural tasks that incorporates some reliance on spatial memory, and performance enhancement would not be expected on procedural tasks (Craft et al., 1994).

To conclude, it would seem that glucose improves performance in healthy subjects on tasks which involve substantial verbal re-coding of material, or perhaps comprehension of textual material, whereas other types of memory are not affected by glucose treatment.

In patient populations glucose has been shown to improve performance on the paragraph recall task (Craft et al., 1993; Manning et al., 1993) Craft et al., (1996) reported that when insulin levels were raised and glucose levels were maintained at baseline levels, performance on the paragraph recall task was facilitated. Poor glucose regulation was also associated with better paragraph recall (Craft et al., 1992).

Glucose supplementation has also had beneficial effect on a word list task and facial recognition task (Manning et al., 1993).
Table 96: Summarising the effects of glucose on aspects of memory function in elderly populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
</table>
| Gonder-Frederick et al. (1987) | Healthy elderly | 11 | 58-76 years | 50 g | Paragraph recall  
Paired associate word list task  
Digit span  
Visual memory | Glucose facilitated paragraph recall and total memory score (sum of all 4 tasks). No effect on digit span. Non significant trend towards improvement on visual memory and paired associate tasks. |
| Hall et al. (1989)      | Healthy elderly | 11 | 58-77 years | 50 g | Paragraph recall  
Paired associate word list task  
Digit span  
Visual memory | Glucose facilitated performance on the paragraph recall paired associate and visual memory and total memory score. No effect on digit span |
| Manning et al. (1990)   | Healthy elderly | 17 | 62-84 years | 50 g | Selective reminding task  
Paragraph recall  
Digit span  
Rey Osterreith complex figures | Glucose facilitated performance on the paragraph recall and selective reminding task. No effect on the digit span or Rey Osterreith complex figures |
| Manning et al. (1992)   | Healthy elderly | 22 | 60-81 years | 50 g | Paragraph recall | Glucose facilitated performance on the task |
| Parsons and Gold (1992) | Healthy elderly | 10 | 60-82 years | 10 g  
25 g  
50 g | Paragraph recall | Glucose facilitated performance on the task |
| Craft et al. (1994)     | Healthy elderly | 32 | 58-77 years | 50 g | Paragraph recall  
Procedural Memory  
Pattern recall and recognition | Glucose facilitated performance on the paragraph recall task. No effect on procedural or pattern memory |
<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen <em>et al.</em> (1996)</td>
<td>Healthy elderly</td>
<td>28</td>
<td>61-87 years</td>
<td>50 g</td>
<td>Rey/Taylor complex figures task</td>
<td>Glucose facilitated performance on the task</td>
</tr>
<tr>
<td>Craft <em>et al.</em> (1996)</td>
<td>Healthy elderly</td>
<td>13</td>
<td>Mean age 71 years</td>
<td>Altered insulin levels</td>
<td>Paragraph recall</td>
<td>Glucose had no effect on the task</td>
</tr>
<tr>
<td>Craft <em>et al.</em> (1992)</td>
<td>SDAT</td>
<td>21</td>
<td>Mean age 73.5 years</td>
<td>50 g</td>
<td>Word list task Paragraph recall Pattern recall and recognition task</td>
<td>Subjects with poor glucose regulation had better performance on the paragraph recall task</td>
</tr>
<tr>
<td>Craft <em>et al.</em> (1993)</td>
<td>SDAT</td>
<td>22</td>
<td>Mean age 67.8 years</td>
<td>Fasted 175 mg/ml 225 mg/ml</td>
<td>Paragraph recall Paired associate word list task</td>
<td>When blood glucose levels were 225 mg/ml performance on the paragraph recall task was facilitated</td>
</tr>
<tr>
<td>Manning <em>et al.</em> (1993)</td>
<td>SDAT</td>
<td>23</td>
<td>68-94 years</td>
<td>75 g</td>
<td>Word list task Paragraph recall Facial recognition task Word recognition task</td>
<td>Glucose facilitated performance on the word list task, paragraph recall and facial recognition tasks</td>
</tr>
<tr>
<td>Craft <em>et al.</em> (1996)</td>
<td>SDAT</td>
<td>21</td>
<td>Mean age 71 years</td>
<td>Altered insulin levels</td>
<td>Paragraph recall</td>
<td>When plasma insulin levels were raised, glucose facilitated performance on the task</td>
</tr>
</tbody>
</table>
7.11 The effect of glucose on the speed of information processing in healthy elderly subjects

There have been no studies where the effects of glucose supplementation have been examined on tasks assessing the speed of information processing in healthy elderly subjects. However, it would be expected that results of such experiments would mirror results of glucose supplementation on aspects of attention. As tasks that assess the speed of information processing, often involve aspects of attention.

Reaction time has been used as a measure of the speed of information processing in healthy young subjects, generally it has been reported that performance on a choice reaction time task is improved following glucose treatment (Benton and Owens, 1993).

Reaction time has been assessed in elderly diabetic subjects, the consensus of opinion is that low blood glucose concentration impairs aspects of reaction time, particularly choice reaction time (Kerr, MacDonald and Tattersall 1991; Maasen, Lingenfelser, Glück, Renn, Eggstein, and Jakober, 1990).

Benton, Owens and Parker (1994) assessed the effect of glucose on performance of a rapid information processing task (RIPT) in seventy female subjects with a mean age of 21.4 years. Subjects were treated with either two 50g glucose or placebo drinks subjects completed the RIPT for 20 minutes. The rapid information processing task required the subjects to monitor a computer screen, in which numbers were randomly flashed, subjects had to press the space bar when 3 odd or 3 even numbers appeared consecutively, response times and the number of correct and incorrect responses were recorded. It was found that reaction times on the RIPT were faster in subjects who had received the glucose drink or had higher blood glucose levels.
Moser, Plum and Buckman (1983) assessed the effects of glucose supplementation (25 g and 50 g) on reaction time in a sample of 21 subjects aged 19-31 years. Subjects completed the reaction time task for 45 minutes, it was reported that glucose enhanced reaction times.

Owens and Benton (1993) assessed the effects of glucose on reaction time in 96 young adults (mean age 21.2 years). Subjects were treated with glucose (50 g) or placebo. Performance was assessed using a choice reaction time task. It was reported that glucose facilitated performance on the task, in particular it was reported that subjects with increasing blood glucose levels had faster decision times than subjects with falling blood glucose levels.

### 7.11.1 Summary

There have been no studies examining the effect of glucose supplementation on tasks assessing the speed of information processing in healthy elderly subjects. However there have been studies examining the effects of glucose on reaction time in healthy young populations. These have reported that reaction times have improved following treatment with glucose.
Table 97: Summarising the effects of glucose on the speed of information processing.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerr et al. (1991)</td>
<td>Diabetic patients</td>
<td>9</td>
<td>21-50 years</td>
<td>Blood glucose lowered</td>
<td>Choice Reaction Time</td>
<td>CRT was impaired when blood glucose was lowered to 2.0 mmol/L</td>
</tr>
<tr>
<td>Maassen et al. (1990)</td>
<td>Diabetic patients</td>
<td>8</td>
<td>18-27 years</td>
<td>Blood glucose lowered</td>
<td>Simple Reaction Time</td>
<td>Reaction times slower when blood glucose was 2.2 mmol/L</td>
</tr>
<tr>
<td>Benton et al. (1994)</td>
<td>Healthy subjects</td>
<td>70</td>
<td>Mean age 21.4 years</td>
<td>50 g</td>
<td>Rapid Information Processing Task (RRIPT)</td>
<td>Glucose significantly improved performance on the task</td>
</tr>
<tr>
<td>Moser et al. (1983)</td>
<td>Healthy subjects</td>
<td>21</td>
<td>Age 19-31 years</td>
<td>25 g, 50 g</td>
<td>Choice Reaction Time</td>
<td>Glucose improved performance on the task</td>
</tr>
<tr>
<td>Owens and Benton (1993)</td>
<td>Healthy subjects</td>
<td>96</td>
<td>Mean age 21.2 years</td>
<td>50 g</td>
<td>Choice Reaction Time</td>
<td>Subjects with rising blood glucose levels had faster decision times</td>
</tr>
</tbody>
</table>
7.12 The effect of glucose on mood in elderly subjects

There is some evidence to suggest that glucose can affect subjective mood ratings, this is primarily based on the fact that glucose interacts with the synthesis and functions of a number of neurotransmitters namely acetylcholine, dopamine and the opiates. It is generally assumed that low blood glucose levels are associated with increased ratings of tiredness, tension and irritability (Gold, MacLeod, Frier and Dreary, 1995).

There have been no studies conducted, examining the effects of glucose on mood in healthy elderly subjects. However three studies have examined the effects in healthy young subjects. Benton and Sargent (1982) assessed blood glucose and mood in a sample of young healthy males with no previous history of aggressive behaviour. It was found that the subjects reported higher self ratings of aggression when blood glucose levels were less than 2.2 mmol/L.

Owens, Parker and Benton (1997) assessed the effect of glucose on mood in 96 young healthy subjects aged 17-27 years. It was reported that subjects with falling blood glucose levels had lower energy scores than subjects with rising blood glucose levels. Benton and Owens (1993) assessed the effect of glucose on mood in 354 subjects with a mean age of 21.7 years. Mood was assessed using the Activation-Deactivation check list (AD-ACL). It was reported that subjects with rising blood glucose levels reported higher energy scores and lower tension scores than subjects with falling blood glucose levels.

7.12.1 Summary

In healthy adult populations it has been reported that low blood glucose is associated with higher ratings of aggression (Benton and Sargent, 1982) lower
energy scores (Owens, Parker and Benton, 1997) and higher tension scores (Benton and Owens, 1993).
Table 98: Summarising the effects of glucose on aspects of mood in adult populations.

<table>
<thead>
<tr>
<th>Author</th>
<th>Sample</th>
<th>n</th>
<th>Age</th>
<th>Dose</th>
<th>Assessment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benton and Sargent (1982)</td>
<td>Healthy young</td>
<td>33</td>
<td>19-28 years</td>
<td>None</td>
<td>The effect of breakfast versus no breakfast</td>
<td>When blood glucose levels were less than 2.2 mmol/L subjects had higher ratings of aggression</td>
</tr>
<tr>
<td>Owens et al. (1997)</td>
<td>Healthy Young</td>
<td>96</td>
<td>17-27 years</td>
<td>50g</td>
<td>Activation-Deactivation check list (AD-ACL).</td>
<td>Falling blood glucose levels were associated with lower energy scores</td>
</tr>
<tr>
<td>Benton and Owens (1993)</td>
<td>Young healthy subjects</td>
<td>354</td>
<td>Mean age 21.7 years</td>
<td>50 g</td>
<td>AD-ACL</td>
<td>Rising blood glucose levels associated with higher energy and lower tension scores</td>
</tr>
</tbody>
</table>
7.13 Conclusions

To summarise it would seem that aspects of cognition and mood can be enhanced following the intake of a glucose drink. In elderly subjects glucose appears to facilitate aspects of memory function to a greater extent than non-memory tasks.

7.14 Aims of the present study: Assessing the effects of glucose administration on cognitive function and mood in a healthy elderly population

The aim of this study was to examine the effect of a single 50 g dose of glucose on cognitive and psychomotor performance in a sample of 24 healthy elderly subjects aged 64-84 years. Cognitive function was assessed prior to and following the administration of glucose and saccharin drinks. Tasks assessing attention included (HPRU SMT, SKT IV, V, VI, VII), memory recall (word list SKT II, VIII,), recognition memory (SKT IX), speed of information processing (CFF, RRT, MRT, and TRT), speed of naming (SKT I, III), and mood (Profile of Mood States).

On the basis of previous findings we would expect glucose to improve performance on verbal memory tasks requiring subjects to actively work on the information i.e. perform substantial verbal re-coding, or comprehension of textual materials. In terms of the tasks included in the present study glucose was expected to enhance performance on the word list task, SKT II (immediate recall), SKT VIII (delayed recall) and SKT IX (recognition memory). In terms of mood, it was expected that when supplemented with glucose, subjects would feel more energetic and less tense than when supplemented with saccharin.

Based on previous literature, significant improvements would not expected on SKT V (arranging blocks), SKT V (replacing blocks) SKT VI (counting symbols), SKT VII (reverse naming task), SKT I (object naming) and SKT III
(numerical naming) or the HPRU Sternberg Memory Task (SMT). Glucose was expected to induce improvements on the Critical Flicker Fusion task (CFF), Choice Reaction Time (CRT).

7.15 Method

7.15.1 Subjects
24 healthy volunteers (12 male and 12 female) aged 64-84 (mean age 69.66 years) participated in the study. Subjects were in good mental and physical health, and were not taking any concomitant medication that would affect performance on the test measures. Subjects were recruited from the general public via the HPRU subject database and poster advertisements.

7.15.2 Treatments
The treatments were in the form a 16 fl oz caffeine-free fruit flavoured drink sweetened with either glucose (50 g) or saccharin (23.7 mg). A double-blind crossover design was adopted, therefore subjects received both treatments. Both drinks were identical in colour, taste and mouth feel. Treatments were separated by at least 48 hours.

7.15.3 Procedure
Subjects attended the unit for a period of 3 visits, a training/familiarisation visit and 2 experimental visits (glucose and saccharin). Subjects entered the unit fasted (for a minimum of 3 hours) underwent a baseline test assessment comprising the Critical Flicker Fusion Task (CFF), Choice Reaction time (CRT), HPRU Sternberg Memory Task (SMT), The Syndrom Kurtz Task (SKT), 15 item word list (WLT) and Profile of Mood States (POMS).

Following the baseline testing, subjects received a fruit flavoured drink sweetened with either 50 g glucose or saccharin 23.7 mg, following a break of 30 minutes in which time the subject sat quiet waiting for the glucose to enter
the bloodstream, subjects then underwent another test battery (consisting of the same tasks used in the baseline tests battery, using different forms of the SKT and a different word list, the order was counterbalanced).

Three blood glucose measures were taken, at baseline, 30 minutes post dose, and at the end of the experimental psychometric assessment (50 minutes post dose).

The same procedure was conducted for both glucose and placebo treatments.

7.15.4 Assessments

7.15.5 Critical Flicker Fusion Task (CFF)
The critical flicker fusion task (CFF) is regarded as an index of overall CNS activity, the ability of the central nervous system to process discrete 'bits' of information Hindmarch (1980). Therefore an increase in CFF threshold is associated with increased alertness and a greater capacity for information processing.

7.15.6 Choice Reaction Time Task (CRT)
The choice reaction time task (CRT) is used as an indicator of sensorimotor performance, assessing the efficiency of the attentional and response mechanisms in the information processing chain. The task is comprised of three components recognition reaction time (RRT), motor reaction time (MRT) and total reaction time (TRT).

7.15.7 HPRU Sternberg Memory Task (SMT)
The HPRU Sternberg memory task is a technique based upon a reaction time method where subjects are required to memorise a set of target digits. In the HPRU version of the task subjects had to attend to the stimulus set (consisting
of sets of 1, 3 and 5 digit strings) memory scanning ability is assessed with the presentation of 12 single probe digits.

7.15.8 Syndrom Kurtz Task (SKT)
The SKT task is comprised of 9 subtasks assessing aspects of attention, memory and the speed of information processing. Attention is assessed using SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols) and SKT VII (reverse naming). Memory is assessed using SKT II (immediate recall), SKT VIII (delayed recall), SKT IX (recognition memory). The speed of naming assessed using SKT I (object naming) and SKT III (numerical naming).

7.15.9 Word List Task (WLT)
In the word list task, subjects were required to memorise a list of 15 words each having 6 letters and 2 syllables. Words were presented aurally (via headphones) at the rate of 1 per second. Immediately after hearing the list, subjects were required to write down the names of as many famous people as possible (e.g. film stars, authors, politicians, heads of state etc) in a 30 second period. Immediately after this, subjects were required to recall as many words as possible.

7.15.10 Profile of Mood States (POMS)
The Profile of Mood States was designed by McNair, Lorr and Droppleman, (1992) as a subjective assessment of mood. The scale assesses six affective states, tension-anxiety, depression-dejection, anger-hostility, vigour-activity, fatigue-inertia, confusion-bewilderment. Subjects are presented with a list of 65 mood adjectives, subjects are required to rate each item, as to how they have felt over the past week, using a 5 point scale.
7.15.11 Blood Glucose Assessment

Blood glucose was measured using an Accutrend blood glucose meter. The meter uses an enzymatic sensor to assess the level of glucose in the blood. A single pin prick of blood is used to obtain a measurement of peripheral blood glucose level which is believed to reflect the glucose concentration in the brain (Lund-Anderson, 1979). Blood glucose was assessed at the beginning of the experiment, 30 and 50 minutes after the glucose drink.

7.16 Results

The data were analysed using a two way analysis of variance (ANOVA) with treatment and visit as a within subject factors.

7.16.1 Blood glucose level

Blood glucose concentration was assessed at baseline, 30 minutes and 50 minutes post dose. The blood data were analysed to determine the main effects of treatment and time.

There was a main effect of treatment \( (F(1, 23) = 23.38; p<0.0001) \) blood glucose levels in the glucose treated group were significantly higher than blood glucose measurements in the placebo group. There was a main effect of time \( (F(1, 23) = 4.03; p <0.05) \) blood glucose measurements changed significantly over the three test points (baseline, post 30 minutes and post 50 minutes). There was a significant treatment and time interaction \( (F(2, 46) = 5.79; p <0.005) \).

Post hoc testing of the drug time interaction using the Newman Keul's task revealed that there were no significant differences between the blood glucose measurements at baseline, however at post treatment 30 and 50 minutes, the glucose treated group had significantly higher blood glucose levels \( (p<0.05) \). (See Figure 61)
The effect of treating subjects with a glucose drink resulted in a significant increase in blood glucose level. What is of importance is, whether an increase in blood glucose level has an effect on psychometric performance. It was postulated that higher blood glucose levels would result in superior psychometric performance compared to lower blood glucose levels, hence performance following the glucose treatment was expected to be superior than performance following the placebo treatment.

The data were analysed using a 2 way analysis of variance with treatment and visit as within subjects factors.

The performance data were analysed in terms of the cognitive groupings identified in chapter 4. The groupings included:-
1. Attention (HPRU Sternberg memory task (SMT), SKT subtests IV, V, VI and VII)
2. Memory Recall (SKT subtests II and VIII)
3. Speed of naming (SKT subtests I, III)
4. Speed of information processing (CFF, TRT, RRT, and MRT)
5. Recognition memory (SKT subtest IX)

The study also examined the effect of glucose on mood assessed using the Profile of mood states (POMS). Six mood states were assessed; these included (tension, depression, anger, vigour, fatigue and confusion).

7.18 The effect of glucose on attention

In chapter 4 the effects of ageing were examined on tasks that assessed attention, it was concluded that as age increases performance on the tasks declined. In chapter 4 tasks classed as assessing attention included SKT subtests IV, V, VI, VII and the HPRU Sternberg Memory Task (SMT).

7.18.1 SKT subtest IV (arranging blocks)

In this task subjects had to arrange 10 random numbered blocks into ascending order, the time taken to complete the task was recorded.

There was no main significant effect of treatment ($F_{(1, 23)} = 0.83; p > 0.05$), time taken to arrange blocks was comparable for both the glucose and placebo treatments (see Table 99).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>19.28</td>
<td>19.08</td>
</tr>
<tr>
<td>Placebo</td>
<td>18.70</td>
<td>18.70</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F_{(1, 23)} = 0.04; p > 0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.03; p > 0.05$).
7.18.2 SKT subtest V (replacing blocks)

In this task, subjects had to replace the 10 blocks to their original starting position, (which was marked on the magnetic board).

There was no main significant effect of treatment ($F_{(1, 23)} = 4.22; p = 0.05$) time taken to replace the blocks was comparable for both the glucose and placebo treatments (see Table 100).

Table 100: Showing treatment means (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>14.91</td>
<td>14.33</td>
</tr>
<tr>
<td>Placebo</td>
<td>13.58</td>
<td>14.08</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F_{(1, 23)} = 0.01; p > 0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 1.42; p > 0.05$).

7.18.3 SKT subtest VI (counting symbols)

In this task, subjects had to count the number of circles on a sheet which consisted of a number of symbols (e.g. circles, flowers etc.) time taken to complete this task was recorded.

There was no main significant effect of treatment ($F_{(1, 23)} = 3.37; p = 0.07$), time taken to count symbols was comparable for both the glucose and placebo treatments (see Table 101).

Table 101: Showing treatment means (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>19.25</td>
<td>19.00</td>
</tr>
<tr>
<td>Placebo</td>
<td>19.79</td>
<td>20.16</td>
</tr>
</tbody>
</table>
There was no significant time effect ($F_{(1, 23)} = 0.03; p > 0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 1.09; p > 0.05$).

7.18.4 SKT subtest VII (reverse naming task)

*In this task, subjects had to perform a reverse naming task, in which they were presented with 2 rows of letters (e.g. abbaabaab) every time the subjects read the letter A they had to say B and when they read B they had to say A. Time taken to complete the task was recorded.*

There was no main significant effect of treatment ($F_{(1, 23)} = 0.03; p > 0.05$), time taken to perform a reverse naming task was comparable for both the glucose and placebo treatments (see Table 102).

Table 102: Showing treatment means (seconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>21.45</td>
<td>21.50</td>
</tr>
<tr>
<td>Placebo</td>
<td>21.45</td>
<td>21.75</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F_{(1, 23)} = 0.13; p > 0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.06; p > 0.05$).

7.18.5 HPRU Sternberg Memory Task (SMT)

*In this task subjects had to memorise a memory set (varying in size from 1 digit, 3 digits and 5 digits). Following the memory set, a random series of 12 digits were presented, subjects were required to state whether the digit presented was a part of the memory set, by pressing the "yes" response button and "no" if it wasn't. The time taken to respond was recorded.*
There was no main effect of treatment \((F(1, 23) = 0.59; p > 0.05)\) performance on the Sternberg memory task was comparable in both the glucose and placebo treatments (see Table 103).

Table 103: Showing treatment means (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>1036.37</td>
<td>1006.58</td>
</tr>
<tr>
<td>Placebo</td>
<td>1062.58</td>
<td>1005.20</td>
</tr>
</tbody>
</table>

There was a main effect of time \((F(1, 23) = 15.08; p < 0.001)\) performance of the task significantly improved over time, possibly reflecting a learning/familiarity effect. (See Figure 62) There was no interaction between treatment and time \((F(1, 23) = 1.03; p > 0.05)\).

Figure 62: The main effect of time on performance of the Sternberg Memory Task (SMT).

7.18.6 Summary
In line with the previous research examining the effect of glucose on attention in healthy elderly subjects, there were no beneficial effects reported on tasks assessing attention, following glucose administration.
7.19 The effect of glucose on memory recall

In chapter 4 the effects of ageing on tasks that assess memory recall were assessed, it was concluded that there was no main effect of age of performance of memory recall. In chapter 4 tasks classed as assessing memory recall included SKT subtests II (immediate recall), and SKT subtest VIII (delayed recall) and recall of a 15 item word list was also examined.

7.19.1 SKT subtest II (immediate recall)

Subjects were required to provide immediate recall of 12 previously named objects, the number of forgotten items and time taken to complete the task were recorded (maximum time allocated was 1 minute).

There was no main significant effect of treatment \( (F (1, 23) = 0.15; p > 0.05) \), there was no significant difference in immediate memory for glucose or placebo treatments (see Table 104).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>4.66</td>
<td>5.83</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.79</td>
<td>5.50</td>
</tr>
</tbody>
</table>

There was a significant time effect \( (F (1, 23) = 11.37; p < 0.005) \) there was a significant change in performance over time, so that subjects forgot more items in the post dose assessment this was possibly attributable to interference from the baseline assessment (see Figure 63). There was no interaction between treatment and time \( (F (1, 23) = 0.71; p > 0.05) \).
The effect of time on immediate recall

Figure 63: The main effect of time on immediate recall of 12 objects.

7.19.2 SKT subtest VIII (delayed recall)

Subjects were required to provide delayed recall of 12 previously named objects, some 10 minutes after initial presentation. The number of forgotten items and time taken to complete the task were recorded.

There was a significant main effect of treatment ($F_{(1, 23)} = 5.92; p < 0.05$), there was a significant difference in delayed memory performance between the glucose and placebo treatments. Subjects in the glucose group forgot more items/objects than subjects in the placebo condition. There was a significant time effect ($F_{(1, 23)} = 20.31; p < 0.0001$) there was a significant change in performance over time, subjects forgot more objects in the post treatment assessment, this was possibly attributable to interference from the baseline assessment, as a different set of pictures had been presented at the baseline test point. With baseline mean equal to 4.60 items forgotten, and post dose mean equal to 6.04 items forgotten. There was no interaction between treatment and time ($F_{(1, 23)} = 2.98; p > 0.05$).
7.19.3 Word list recall

Subjects were presented aurally with 15 six lettered words, the words were presented 1 per second. Following presentation, to prevent rehearsal, subjects had 1 minute in which to write down the names of famous people (e.g. politicians, actors, authors etc.). Following this the subjects had to write down as many of the 15 words as possible, recall time was not restricted. The number of words recalled were recorded.

There was no main effect of treatment ($F (1, 23) = 1.17; p >0.05$), word list recall was comparable in both the glucose and placebo treatments (see Table 105).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>3.91</td>
<td>3.33</td>
</tr>
<tr>
<td>Placebo</td>
<td>3.37</td>
<td>3.08</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F (1, 23) = 2.00; p>0.05$) there was no change in performance over time. There was no interaction between treatment and time ($F (1, 23) = 2.53; p>0.05$).
7.19.4 Summary
There were no effects of glucose administration on performance of the word list task, or on immediate recall of the 12 pictures. In terms of delayed recall (SKT subtest VIII), glucose had a negative impact, subjects forgot more pictures when they were treated with glucose, these negative effects are possibly due to interference from previously presented pictures, this is backed up by the fact that subjects forgot more items over time.

7.20 The effect of glucose on the speed of naming
In chapter 4 the effects of ageing on tasks that assess the speed of naming were assessed, it was concluded that there was no main effect of age on tasks assessing the speed of naming. In chapter 4 tasks classed as assessing speed of naming included SKT subtests I (object naming), and SKT subtest III (numerical naming).

7.20.1 SKT subtest I (object naming)
Subjects were presented with 12 pictures of objects, they had to name the objects and try to commit them to memory, as they were to be recalled at a later date.

There was no main significant effect of treatment \( (F(1, 23) = 1.07; p > 0.05) \), time taken to complete the object naming task was comparable for both the glucose and placebo treatments (see Table 106).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>14.00</td>
<td>14.87</td>
</tr>
<tr>
<td>Placebo</td>
<td>14.58</td>
<td>15.54</td>
</tr>
</tbody>
</table>
There was no significant time effect ($F_{(1, 23)} = 2.78; p > 0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.0007; p > 0.05$).

### 7.20.2 SKT subtest III (naming numerals)

*Subjects were required to name 10 numbered blocks, the time taken to name the blocks were recorded.*

There was no main significant effect of treatment ($F_{(1, 23)} = 0.15; p > 0.05$), time taken to name numerals was comparable for both the glucose and placebo treatments (see Table 107).

**Table 107:**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>7.20</td>
<td>6.70</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.37</td>
<td>7.25</td>
</tr>
</tbody>
</table>

There was no significant time effect ($F_{(1, 23)} = 1.66; p < 0.05$) there no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.71; p > 0.05$).

### 7.20.3 Summary

There were no effects of glucose on the speed of naming, assessed using the SKT subtests I (object naming) and III (numerical naming).

### 7.21 The effect of glucose on the speed of information processing

In chapter 4 the effects of ageing on tasks that assessed information processing were assessed, it was concluded that there was no main effect of age of performance of information processing tasks. In chapter 4 tasks classed as assessing speed of information processing included the Critical Flicker Fusion
Task (CFF), Total Reaction Time (TRT), Recognition Reaction Time (RRT) and Motor Reaction Time (MRT).

7.21.1 Critical Flicker Fusion (CFF)

*Critical flicker fusion threshold was determined by subjects completing 3 ascending and 3 descending trials, the mean of all 6 presentations were recorded.*

There was no main effect of treatment ($F_{(1, 22)} = 0.00; p>0.05$) performance of the critical flicker fusion task was comparable in both the glucose and placebo treatments (see Table 108).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>29.71</td>
<td>28.93</td>
</tr>
<tr>
<td>Placebo</td>
<td>29.60</td>
<td>29.22</td>
</tr>
</tbody>
</table>

There was a main effect of time ($F_{(1, 23)} = 11.56; p<0.01$) there was a significant change in performance over time performance on the task decreased in the post treatment assessment, possibly reflecting a fatigue/boredom effect (see figure 65). There was no interaction between treatment and time ($F_{(1, 23)} = 2.78; p>0.05$).
The main effect of time on the Critical Flicker Fusion Task (CFF)

<table>
<thead>
<tr>
<th>Hz</th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>28.6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 65: The main effect of time on the critical flicker fusion task (CFF).

7.21.2 Total Reaction Time (TRT)

Subjects completed the choice reaction time task, subjects placed their index finger on a home key, and the task was to extinguish illuminated lights, by moving their finger from the home key to press a button placed directly under the illuminated light, subjects were required to respond to 20 stimuli illuminating 1 of 6 possible lights. Total reaction time was defined as the sum of both recognition and motor reaction time.

There was no main effect of treatment ($F_{(1, 20)} = 1.37; p>0.05$) total reaction time was comparable in both the glucose and placebo treatments (see Table 109).

Table 109: Showing treatment means (milliseconds).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>682.35</td>
<td>674.25</td>
</tr>
<tr>
<td>Placebo</td>
<td>704.97</td>
<td>721.10</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F_{(1, 20)} = 0.21; p>0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 20)} = 0.27; p>0.05$).
7.21.3 Recognition Reaction Time (RRT)

Recognition reaction time was defined as the time taken for the subjects to realise that a light was illuminated, and lift their finger from the home key.

There was no main effect of treatment \( (F(1,20) = 0.14; p>0.05) \) recognition reaction time was comparable in both the glucose and placebo treatments (see Table 110).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>460.31</td>
<td>439.48</td>
</tr>
<tr>
<td>Placebo</td>
<td>449.69</td>
<td>471.37</td>
</tr>
</tbody>
</table>

There was no main effect of time \( (F(1,20) = 0.07; p>0.05) \) there was no significant change in performance over time. There was no interaction between treatment and time \( (F(1,20) = 1.09; p>0.05) \).

7.21.4 Motor Reaction Time (MRT)

Motor reaction time was defined as the time taken for the subjects to move their finger from the home key, to touch the button placed directly under the illuminated light.

There was no main effect of treatment \( (F(1,20) = 2.38; p>0.05) \) motor reaction time was comparable in both the glucose and placebo treatments (see Table 111).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>233.66</td>
<td>234.77</td>
</tr>
<tr>
<td>Placebo</td>
<td>271.81</td>
<td>249.73</td>
</tr>
</tbody>
</table>
There was no main effect of time ($F_{(1, 20)} = 0.46; p>0.05$) there was no significant change in performance over time. There was no interaction between treatment and time ($F_{(1, 20)} = 0.04; p>0.05$).

### 7.21.5 Summary
Glucose administration was found to have no effect on tasks assessing the speed of information processing (CFF, TRT, RRT or MRT).

### 7.22 The effect of glucose on recognition memory
In chapter 4 the effects of ageing on tasks that assess recognition memory were assessed, it was concluded that there was no main effect of age on recognition memory. In chapter 4 the SKT subtest IX was classed as assessing recognition memory.

#### 7.22.1 SKT subtest IX (recognition memory)
In the recognition memory test, subjects had to recognise the 12 original pictures (presented in subtest I) from a series of 48 pictures. The number of omissions were recorded.

There was no main effect of treatment ($F_{(1, 23)} = 0.07; p>0.05$) recognition memory was comparable in both the glucose and placebo treatments (see Table 112).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>1.00</td>
<td>1.08</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.87</td>
<td>1.33</td>
</tr>
</tbody>
</table>
There was no main effect of time \((F_{(1, 23)} = 1.68; p>0.05)\) there was no significant change in performance over time. There was no interaction between treatment and time \((F_{(1, 23)} = 0.92; p>0.05)\).

7.22.2 Summary
Glucose had no effect on recognition memory.

7.23 The effect of glucose on subjective mood ratings - The Profile of Mood States (POMS)

Subjective mood is an aspect of human functioning that is thought particularly susceptible to fluctuations in blood glucose concentration. Diabetic subjects often experience feelings of tension, confusion and fatigue, when blood glucose concentrations fall to less than 2.2 mmol/L. This experiment assessed the impact of glucose on subjective ratings of tension, depression, anger, vigour, fatigue, confusion.

7.23.1 Tension
There was no main effect of treatment, however it approached significance \((F_{(1, 23)} = 3.84; p = 0.06)\) tension scores were comparable between glucose and placebo treatments (see Table 113).

Table 113: Showing tension treatment means.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>7.33</td>
<td>5.50</td>
</tr>
<tr>
<td>Placebo</td>
<td>5.54</td>
<td>4.75</td>
</tr>
</tbody>
</table>

There was a main effect of time \((F_{(1, 23)} = 0.92; p <0.05)\) there was a significant change in tension scores over time, tension scores were lower in the post treatment assessment, possibly due to the fact that the subjects had adapted to the testing situation at the post treatment assessment. (See figure 66). There was no interaction between treatment and time \((F_{(1, 23)} = 0.92; p>0.05)\).
7.23.2 Depression
There was no main effect of treatment ($F_{(1, 23)} = 2.62; p > 0.05$) depression scores were comparable between glucose and placebo treatments (see Table 114).

Table 114: Showing depression treatment means.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>6.87</td>
<td>5.25</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.20</td>
<td>3.87</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F_{(1, 23)} = 3.69; p = 0.06$) there was no significant change in depression scores over time. There was no interaction between treatment and time ($F_{(1, 23)} = 1.65; p>0.05$).

7.23.3 Anger
There was no main effect of treatment ($F_{(1, 23)} = 0.36; p > 0.05$) anger scores were comparable between glucose and placebo treatments (see Table 115).
Table 115: Showing anger treatment means.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>2.00</td>
<td>1.54</td>
</tr>
<tr>
<td>Placebo</td>
<td>1.62</td>
<td>1.33</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F_{(1, 23)} = 0.85; p > 0.05$) there was no significant change in anger scores over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.04; p > 0.05$).

7.23.4 Vigour
There was a main effect of treatment ($F_{(1, 23)} = 6.37; p < 0.01$) there was a significant difference in vigour scores between glucose and placebo treatments. Vigour scores were higher following the placebo treatment (see Figure 67).
There was no main effect of time ($F_{(1, 23)} = 0.30; p > 0.05$) there was no significant change in vigour scores over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.00; p > 0.05$).

![The main effect of treatment on ratings of vigour](image)

Figure 67: The main effect of treatment on vigour scores.

7.23.5 Fatigue
There was no main effect of treatment ($F_{(1, 23)} = 3.22; p > 0.05$) fatigue scores were comparable between glucose and placebo treatments (see Table 116).
Table 116: Showing fatigue treatment means.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>5.70</td>
<td>6.37</td>
</tr>
<tr>
<td>Placebo</td>
<td>4.70</td>
<td>4.87</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F_{(1, 23)} = 0.47; p > 0.05$) there was no significant change in fatigue scores over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.11; p > 0.05$).

7.23.6 Confusion

There was no main effect of treatment ($F_{(1, 23)} = 1.05; p > 0.05$) confusion scores were comparable between glucose and placebo treatments (see Table 117).

Table 117: Showing confusion treatment means.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>7.66</td>
<td>8.08</td>
</tr>
<tr>
<td>Placebo</td>
<td>7.41</td>
<td>6.83</td>
</tr>
</tbody>
</table>

There was no main effect of time ($F_{(1, 23)} = 0.02; p > 0.05$) there was no significant change in confusion scores over time. There was no interaction between treatment and time ($F_{(1, 23)} = 0.95; p > 0.05$).

7.23.7 Summary

Overall higher blood glucose levels did not result in performance improvements. Glucose administration had no effect on attention, memory, speed of naming, information processing or subjective ratings of mood, contrary to previous research.
7.24 The effect of blood glucose level on psychometric performance

There is some evidence to suggest that the beneficial effects of treatment with glucose is often dependant on the person's ability to tolerate glucose. For example Allen et al (1996) reported that elderly subjects with poor glucose control (which was defined as a change in blood glucose following a glucose drink of greater than 100 mg dl\textsuperscript{-1}) had poorer performance on a dichotic listening task. Benton and Owens (1993) it was reported that subjects with rising blood glucose levels remembered more words on a word list than subjects with falling blood glucose levels.

Based on these results, it was questioned whether there would be differences between performance in subjects whose blood glucose rose or fell between the second and third blood glucose assessments (30 and 50 minutes post dose). All subjects in the glucose condition were classified as either risers (n = 15) or fallers (n = 9). Data was analysed using a two way ANOVA with change in blood glucose level (rising or falling) and task performance as variables.

It was reported that there was a significant difference between the Sternberg memory task performance in terms of the change in blood glucose levels. It was reported that performance in subjects with falling blood glucose levels had superior performance to subjects with rising blood glucose level (F (1,23) = 6.47; p<0.05). (See table 118)

<table>
<thead>
<tr>
<th>Blood Glucose Rising</th>
<th>Blood Glucose Falling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternberg Memory Task</td>
<td>1034.35</td>
</tr>
<tr>
<td></td>
<td>967.7</td>
</tr>
</tbody>
</table>

There were no significant differences between risers and fallers on any of the other psychometric tasks.
In terms of mood, there was a significant difference between the subjective ratings of vigour and fatigue. It was reported that subjects with falling blood glucose levels felt more vigorous ($F (1, 23) = 5.46; p<0.05$) and less fatigued ($F (1, 23) = 6.49; p<0.05$) than subjects with rising blood glucose levels (see table 119).

Table 119: Showing the mean fatigue and vigour ratings for subjects with rising or falling blood glucose levels.

<table>
<thead>
<tr>
<th></th>
<th>Blood Glucose Rising</th>
<th>Blood Glucose Falling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>24.0</td>
<td>4.0</td>
</tr>
<tr>
<td>Vigour</td>
<td>15.70</td>
<td>16.00</td>
</tr>
</tbody>
</table>

7.25 The effect of hypoglycaemia on psychometric performance

Previous researchers, examined the level of blood glucose and its effect on performance. It is generally assumed that low blood glucose levels have a detrimental effect on cognitive functioning. To explore this claim, psychometric test performance and mood measures were compared in subjects with blood glucose levels less than 2.2 mmol/L with psychometric test measures and mood scores from subjects with blood glucose levels greater than 2.2 mmol/L.

The baseline data were analysed using a 2 way analysis of variance with blood level (blood levels less than 2.2 mmol/L compared with blood levels greater than 2.2 mmol/L) and test performance as variables (CFF, CRT, SMT, and word list).

It was found that hypoglycaemic subjects were significantly slower at the Sternberg memory task than subjects with normal blood glucose concentrations ($F (1, 19) = 8.21; p<0.05$). Performance on the immediate recall task (SKT subtest II) was poorer in subjects with hypoglycaemic blood glucose levels. Performance on all other memory tasks was also worse for subjects with hypoglycaemic blood glucose levels, however these failed to reach statistical
significance. There were no significant differences between the two groups of subjects on any of the other psychometric tests (See Tables 120-123).

7.25.1 The effect of blood glucose level on attention

Table 120: Showing the effect of blood glucose level on attention.

<table>
<thead>
<tr>
<th>Psychometric test score</th>
<th>Hypoglycaemic</th>
<th>Normal blood glucose level</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMT</td>
<td>1145.22 ms</td>
<td>1018.83 ms</td>
<td>F(1, 19) = 8.21 p&lt;0.05</td>
</tr>
<tr>
<td>SKT IV</td>
<td>19.33 seconds</td>
<td>18.33 seconds</td>
<td>F(1, 22) = 0.41 p&gt;0.05</td>
</tr>
<tr>
<td>SKT V</td>
<td>14.55 seconds</td>
<td>13.00 seconds</td>
<td>F(1, 22) = 2.62 p&gt;0.05</td>
</tr>
<tr>
<td>SKT VI</td>
<td>19.77 seconds</td>
<td>19.80 seconds</td>
<td>F(1, 22) = 0.00 p&gt;0.05</td>
</tr>
<tr>
<td>SKT VII</td>
<td>21.22 seconds</td>
<td>21.60 seconds</td>
<td>F(1, 22) = 0.03 p&gt;0.05</td>
</tr>
</tbody>
</table>

7.25.2 Summary

Low blood glucose levels was associated with significantly slower reaction times on the Sternberg Memory Task, low blood glucose levels had no effect on any other measures of attention (SKT, IV, V, VI, VII).

7.25.3 The effect of blood glucose level on memory

Table 121: Showing the effect of blood glucose level on memory recall and recognition.

<table>
<thead>
<tr>
<th>Psychometric test score</th>
<th>Hypoglycaemic</th>
<th>Normal blood glucose level</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Word List (delayed)</td>
<td>2.55 words</td>
<td>3.75 words</td>
<td>F(1, 19) = 0.25; p&gt;0.05</td>
</tr>
<tr>
<td>SKT II</td>
<td>6.00 omissions</td>
<td>4.06 omissions</td>
<td>F(1, 22) = 10.29 p&lt;0.05</td>
</tr>
<tr>
<td>SKT VIII</td>
<td>4.88 omissions</td>
<td>3.53 omissions</td>
<td>F(1, 22) = 3.21 p&gt;0.05</td>
</tr>
<tr>
<td>SKT IX</td>
<td>1.22 omissions</td>
<td>0.66 omissions</td>
<td>F(1, 22) = 1.42 p&gt;0.05</td>
</tr>
</tbody>
</table>

7.25.4 Summary

Low blood glucose levels were associated with significantly poorer performance on immediate recall of 12 pictures, low blood glucose levels were associated with poorer memory performance on all other measures word list,
delayed recall or recognition memory, however the differences failed to reach statistical significance.

7.25.5 The effects of blood glucose on the speed of information processing

Table 122: The effect of blood glucose level on the speed of information processing.

<table>
<thead>
<tr>
<th>Psychometric test score</th>
<th>Hypoglycaemic</th>
<th>Normal blood glucose level</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CFF</td>
<td>29.47 Hz</td>
<td>29.70 Hz</td>
<td>$F_{(1,19)} = 0.03; p&gt;0.05$</td>
</tr>
<tr>
<td>RRT</td>
<td>416.20 ms</td>
<td>478.71 ms</td>
<td>$F_{(1,19)} = 1.76; p&gt;0.05$</td>
</tr>
<tr>
<td>MRT</td>
<td>267.85 ms</td>
<td>273.59 ms</td>
<td>$F_{(1,19)} = 0.01; p&gt;0.05$</td>
</tr>
<tr>
<td>TRT</td>
<td>684.06 ms</td>
<td>721.98 ms</td>
<td>$F_{(1,19)} = 0.63; p&gt;0.05$</td>
</tr>
<tr>
<td>SKT Total</td>
<td>0.88 total score</td>
<td>0.60 total score</td>
<td>$F_{(1,22)} = 0.71 p&gt;0.05$</td>
</tr>
</tbody>
</table>

7.25.6 Summary
There were no significant differences between performance of tasks assessing the speed of information processing for subjects with low or high blood glucose level.

7.25.7 The effect of blood glucose on the speed of naming

Table 123: Showing the effect of blood glucose level on the speed of naming

<table>
<thead>
<tr>
<th>Psychometric test score</th>
<th>Hypoglycaemic</th>
<th>Normal blood glucose level</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>SKT I</td>
<td>13.55 seconds</td>
<td>15.20 seconds</td>
<td>$F_{(1,22)} = 1.29 p&gt;0.05$</td>
</tr>
<tr>
<td>SKT III</td>
<td>7.22 seconds</td>
<td>7.46 seconds</td>
<td>$F_{(1,22)} = 0.06 p&gt;0.05$</td>
</tr>
</tbody>
</table>

7.25.8 Summary
Blood glucose levels did not affect performance on tasks assessing the speed of naming.
7.26 The effects of blood glucose level on mood

Mood data were also analysed using a two way analysis of variance with blood level (baseline blood glucose levels less than 2.2 mmol/L compared with blood glucose levels greater than 2.2 mmol/L) and self ratings of mood (tension, depression, anger, vigour, fatigue, confusion and overall mood score).

There were no significant differences between the 2 groups of subjects (low blood glucose versus high blood glucose level) on any of the subjective self ratings (See table 124).

Table 124: Showing the effect of hypoglycaemia on mood.

<table>
<thead>
<tr>
<th>Subjective Mood Rating</th>
<th>Blood Glucose &lt; 2.2 mmol/L</th>
<th>Blood Glucose &gt; 2.2 mmol/L</th>
<th>Level of Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tension</td>
<td>6.77</td>
<td>5.58</td>
<td>F (1, 19) = 0.25; p&gt;0.05</td>
</tr>
<tr>
<td>Depression</td>
<td>6.11</td>
<td>3.58</td>
<td>F (1, 19) = 1.05; p&gt;0.05</td>
</tr>
<tr>
<td>Anger</td>
<td>1.44</td>
<td>2.16</td>
<td>F (1, 19) = 0.17; p&gt;0.05</td>
</tr>
<tr>
<td>Vigour</td>
<td>17.22</td>
<td>18.75</td>
<td>F (1, 19) = 0.23; p&gt;0.05</td>
</tr>
<tr>
<td>Fatigue</td>
<td>7.11</td>
<td>4.00</td>
<td>F (1, 19) = 1.48; p&gt;0.05</td>
</tr>
<tr>
<td>Confused</td>
<td>8.00</td>
<td>7.58</td>
<td>F (1, 19) = 0.07; p&gt;0.05</td>
</tr>
<tr>
<td>Overall Mood</td>
<td>46.66</td>
<td>41.66</td>
<td>F (1, 19) = 0.56; p&gt;0.05</td>
</tr>
</tbody>
</table>

7.26.1 Summary

Blood glucose level did not affect subjective ratings of mood.

7.27 Conclusion

Subjects with hypoglycaemic blood glucose concentrations showed significantly poorer performance on the HPRU Sternberg Memory Task and made significantly more omissions on the immediate recall task than subjects with normal blood glucose concentrations. However task performance on all other measures were comparable to subjects with blood glucose concentrations.
greater than 2.2 mmol/L. Self ratings of mood were also similar for all subjects regardless of blood glucose level.

### 7.28 Discussion

This study demonstrated that treatment with glucose resulted in significantly higher blood glucose assessments than when treated with placebo/saccharin. However this raise in blood glucose level had no effect on any aspects of performance, namely attention, memory recall, recognition memory, the speed of information processing, the speed of naming or subjective ratings of mood.

Attention was assessed using SKT subtests IV, V, VI, VII and the HPRU Sternberg Memory Task. SKT IV(arranging blocks), SKT V (replacing blocks), are spatial tasks, requiring the subjects to place blocks into ascending order, and then replace the blocks to their initial start place, that is clearly marked on the board. SKT subtest VI is a attention/vigilance task and as previously found glucose had no effect on tasks assessing attention, hence improvements following treatment with glucose would not be expected on the task. SKT subtest VII is a reverse naming task, requiring the subjects to read a letter and respond verbally with another letter e.g. read A and say B, this task is similar in some respects to the Stroop and Digit symbol substitution tasks relying heavily on attentional processes to perform the task. As the previous studies have demonstrated, glucose had no effect on tasks assessing attention. Glucose also had no effect on the HPRU Sternberg memory task, this task does not assess verbal memory, and is much like the digit span task, where subjects are required to hold small amounts of information in memory for a short time, and then perform a scanning procedure, hence with such similarity to the digit span task, improvements following glucose would not be expected. These findings replicate previous studies, where glucose had no effect on tasks assessing attention.
The memory tasks included in this study did not require the subjects to perform associations, substantial verbal re-coding, or comprehension of textual materials, hence and best glucose would only have been expected to induce mild non significant trends towards improvement on SKT subtest II (immediate recall of 12 objects), SKT VIII (delayed recall of 12 objects), SKT IX (recognition memory of 12 objects), and the word list containing 15 words. The word list task only included single verbal items, in the previous literature with research in elderly subjects, it would seem that beneficial effects of glucose treatment would only be expected when subjects were required to perform complex verbal memory tasks such as in the paired associative word list, and the selective reminding task. As expected glucose had no effect on any measures of memory.

There were no studies conducted that assessed the role of glucose on tasks assessing the speed of information processing in healthy elderly subjects. In young healthy subjects improvements were noted on reaction time tasks following glucose treatment (Benton and Owens, 1993). However this study would seem to suggest that like attention, and aspects of memory, glucose has no effect on tasks assessing the speed of information processing in healthy elderly subjects (CFF, RRT, MRT, TRT).

There have been no studies that assessed the role of glucose on tasks the speed of naming, however in line with the findings on the speed of information processing, performance improvements following glucose treatment would not be expected.

Results supported this, glucose had no effect on SKT subtest I (naming objects) or SKT subtest III (numerical naming).

To conclude, it would seem that in healthy elderly subjects the benefits of glucose supplementation would seem to be specialised to verbal memory tasks,
or memory tasks requiring subjects to perform associations, substantial verbal re-coding, or comprehension of textual materials. In the present study, glucose has no effect on attention, non verbal memory tasks, the speed of information processing, or the speed of naming.

There have been no studies that have examined the role of glucose on aspects of mood in healthy elderly subjects. Research in young subjects would seem to indicate that higher blood glucose levels are associated with improved feelings of vigour, and lower ratings of tension and anxiety (Benton and Owens, 1993; Reid and Hammersly, 1995). The present study failed to replicate any findings, the only effects reported, seemed to indicate that subjects felt more vigorous following the placebo treatment, the opposite of what was expected. From this study it was concluded that glucose had no effect on mood in healthy elderly subjects.

In terms of the effect of the change in blood glucose level, it was questioned whether there would be a difference in performance in subjects whose blood glucose levels rose between the second and third assessments compared with subjects whose blood glucose levels fell between the second and third assessments. It was reported that subjects with falling blood glucose levels showed superior performance on the Sternberg memory task than subjects with rising blood glucose levels. Subjects with falling blood glucose levels also reported feeling more vigorous and less fatigued than subjects with rising blood glucose levels.

The main differences between the present study, and previous studies, are the tasks used, (however as shown above, some similarities can be drawn between tasks), and the numbers of subjects included in the studies. In the Gonder-Frederick et al., (1987) study, it was stated that only small numbers of elderly subjects were needed to demonstrate the beneficial effects of glucose on cognitive function, however in the present study, the numbers included
exceeded those used in previous studies, (with the exception of Craft et al., 1994 and Allen et al., 1996) and reported null results. It is possible that the small numbers of subjects included in the previous studies were not truly representative of the population as a whole, and if the numbers were increased, then the weak results would be diluted. (see Table 125)

Table 125: Showing Age and number of subjects included in the previous studies.

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of subjects</th>
<th>Age of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gonder-Frederick et al, (1987)</td>
<td>11</td>
<td>58-76 years</td>
</tr>
<tr>
<td>Hall et al, (1989)</td>
<td>11</td>
<td>58-76 years</td>
</tr>
<tr>
<td>Manning et al, (1990)</td>
<td>17</td>
<td>62-84 years</td>
</tr>
<tr>
<td>Manning et al, (1992)</td>
<td>22</td>
<td>60-81</td>
</tr>
<tr>
<td>Craft et al, (1996)</td>
<td>13</td>
<td>mean age 71 years</td>
</tr>
<tr>
<td>Parsons and Gold (1992)</td>
<td>10</td>
<td>60-82 years</td>
</tr>
<tr>
<td>Allen et al, (1996)</td>
<td>28</td>
<td>61-87 years</td>
</tr>
<tr>
<td>Craft et al, (1994)</td>
<td>32</td>
<td>58-77 years</td>
</tr>
</tbody>
</table>

A number of studies have examined the effect of glucose on attention in young healthy subjects. Benton et al. (1994) assessed performance using the Stroop task in young healthy subjects and unlike Craft et al. (1994; 1996) reported that glucose enhanced performance of the Stroop task. This contradicts findings in healthy elderly subjects, where no beneficial effects were reported. The differences between the two studies could reflect true age effects, or could be a result of different sample sizes. It could be argued that the effects on attention may be age specific, enhancing performance in young subjects, and not affecting elderly subjects. Another difference between these studies, relates to sample sizes, in the Craft et al. (1994) study, 32 subjects were supplemented, and in the Benton et al. (1994) study 50 young subjects were supplemented. Perhaps, larger elderly sample sizes may result in observed improvements.

Previous literature with young healthy subjects would seem to indicate that glucose does have a beneficial effect on recall performance of the word list task, contrary to the findings of this study. Benton, Owens and Parker, (1993)
reported that glucose facilitated memory recall of 30 nouns. In Benton and Owens (1993) subjects were presented with 15 item word list, following presentation, subjects had 30 seconds in which to write down as many US capitals as possible, following this, subjects were given 1 minute to recall the 15 words. It was reported that subjects with rising blood glucose levels remembered more words than subjects with falling blood glucose levels. The present study was conducted in much the same way as the Benton and Owens (1993) study, however instead of writing down US capitals, subjects had 30 seconds in which to write down the names of famous people. The different results between the age groups could represent true age differences, healthy elderly subjects may have been impaired by performing the distractor task (writing down the names of famous people) to a greater degree than young healthy subjects. It is possible that the differences could be a result of differences in task procedure, the differences in the distractor task, may help to produce differences in the results.

The tests themselves may be a factor that may have lead to a failure to produce any effects, it is possible that the tests used may not have placed the subjects under enough cognitive demand. In previous studies, tasks that have been enhanced by an increased availability of blood glucose either required a rapid response or had time constraints. For example glucose was found to improve performance on a choice reaction time task (reaction to a number of stimuli) and not a simple reaction time task (reaction to one stimuli) (Owens and Benton, 1994). Also increased glucose availability was shown to affect Stroop performance on the incongruent condition (difficult task whereby subjects are presented with colour names written in conflicting coloured ink for example the word red written in blue ink, the subjects has to tell the experimenter the colour of the ink ) and not the congruent condition (a colour word written in the same coloured ink e.g. the word red written in red ink, subjects have to give the colour of the ink). Beneficial effects of glucose have often only been observed after long periods of time during prolonged testing periods. For example Keul
(1982) found that glucose improved performance on a driving simulator task only after the subjects had travelled a long distance (70-110 Km), and performance on the rapid information processing task was found to be improved following glucose administration towards the end of the test session- after great cognitive demand had been placed on the subject.
Chapter Eight: The Discussion

The trend for an ever ageing population is associated with increased incidence of illness and the demand for treatment. The elderly as a group represent the highest users of medication in the population (Whittington and Petersen, 1979) and with an increase in population size coupled with an improved standard of living, the demand for treatment is expected to escalate in future years.

One of the greatest problems experienced by elderly populations is a decline in cognitive function. This decline is a consequence of ageing even before the elderly begin to encounter degenerative diseases and polypharmacy. An ageing society is at an increased risk of polypharmacy, multiple medication use is not only inconvenient for the patient, but can have hazardous effects, increasing the potential for adverse side effects, such as accidents both in and around the home.

The elderly suffer cognitive decline as a consequence of increased age, therefore if society can take steps to limit the decline in cognitive function experienced by elderly persons, then this could lead to improvements in an elderly persons quality of life. One method for doing this, is to try and limit the use of drugs for the treatment of disorders and identify alternative compounds which may help to alleviate cognitive decline.

The search for alternative therapies for the treatment of aged diseases is not new, at present Pharmaceutical companies are developing and testing hundreds of potential nootropic products, however to date, the only available treatments are very expensive and are associated with a number of side effects, which substantially limit their utility. With problems in the search for drugs which posses nootropic properties, a number of research teams have assessed the
effects of a number of readily available over the counter preparations in terms of their ability to enhance cognitive function.

Researchers who have taken steps to identify potential nootropic compounds have noted that there are a number of variables that affect human cognitive function, these include current state of health, medication use and nutritional status etc. There is some debate concerning whether poor nutritional status could adversely affect cognitive function. If this is true, then improved nutritional status should result in improved cognitive function. In chapter two the importance of vitamins in the diet was discussed, it would seem that vitamins are required by the body for the production of neurotransmitters, for the release of energy from foods and for their antioxidant properties. Since vitamins play such an important role in the body, then it is likely that a vitamin deficiency would result in noticeable changes in behaviour.

The search for potential nootropic compounds, and the measurement of the effects of vitamin deficiency on cognitive function is meaningless without firstly understanding the types of changes the elderly experience as a result of age, and secondly identifying valid and reliable test methods for assessment of human cognitive function. It is vitally important that researchers develop norms in terms of the types of age related changes one would expect on psychometric tasks, before they go on to assess the effect of a potential nootropic on human cognitive functioning.

There are two main methods available for the assessment of cognitive change in elderly subjects, it can be done via subjective rating scales or with the use of psychometric/performance type tasks. In terms of ease of applicability, subjective ratings are easier to conduct, cheaper as they do not require specialised facilities and trained staff to operate them, and can generate vast amounts of data in a short amount of time. However the main drawbacks with
subjective rating scales are that subjects may misinterpret what is being asked of them and hence the data collected may not be credible.

In this thesis, to test whether subjects were able to reliably report changes in cognitive function, 160 healthy elderly subjects aged 60-85 years completed an Activity of Daily Living Scale (ADL). The scale consisted of 159 questions assessing aspects of attention, memory, orientation and the speed of processing. Subjects were required to rate performance of daily activities in terms of the number of problems they had experienced over the previous month. Analysis of the data reported that the elderly were not aware of any problems with the performance of daily activities. The ADL scale did not identify any aspects of cognitive function that were proving difficult for an aged population. These results at first may seem surprising, however Rabbitt and Abson (1991) noted that self rating is very difficult for an aged population as reflections of self rating usually strongly reflect changes in general confidence and attitudes towards themselves rather than information on cognitive ability. Nisbett and Wilson (1977) report that individuals have difficulty inspecting their cognitive processes and can only make inferences about them from received social opinion, or by observing the overt effects of their behaviour on the external world. Hence it comes as little surprise that the elderly are not accurate at self rating changes in cognitive function. Based on these findings, it was concluded that the more preferred way to accurately measure cognitive decline in healthy elderly subjects was with the use of performance tasks.

In chapter four the effects and age and gender were determined on a battery of cognitive tasks that measures aspects of attention, memory and the speed of information processing. The test battery consisted of the Critical Flicker Fusion task (CFF), the Choice Reaction Time Task (CRT), HPRU Sternberg Memory Task (SMT) and the Syndrom Kurtz Task (SKT).
It was concluded that age related decrements in performance were expected on SKT II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming), SKT VIII (delayed recall), HPRU Sternberg Memory Task (SMT), Critical Flicker Fusion Task (CFF) and the Choice Reaction Time Task (CRT).

In terms of analysis it was reported that age effects were reported on SKT II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming), and SKT VIII (delayed recall). However no age related decrements were noted on the Critical Flicker Fusion Task (CFF), Choice Reaction Time (CRT) or the HPRU Sternberg Memory Task (SMT). However it must be stated that even when there were age effects, they were quite idiosyncratic i.e. performance didn't simply decline steadily with age. The lack of effect may be a result specific to the sample tested, it is possible that they were not experiencing an age related decrement on the tasks, however it is more likely that the actual tasks are not in fact age sensitive. In terms of age related declines on CFF, the majority of studies reported an age related decrement were published in the 1940's and 1950's and it is possible that age related declines are no longer evident on the task, whether this is due to changes in technology or methodology remains unknown. The lack of effect on the Choice Reaction Time task (CRT) may be due to a methodological flaw in the design, in the present task, subjects were only required to respond to one of six lights, it is possible that the task was too simple, and age related decrements may have been noted if the number of stimuli had been increased. The lack of effect on the HPRU Sternberg Memory Task (SMT) is also quite likely to be due to a flaw in the methodology. In the original Sternberg Memory Task subjects memory scanning ability was assessed with a single digit probe, and age related decrements were noted on this version of the task (Sternberg, 1966). However in the HPRU version of the task, memory scanning ability was assessed by presenting the subjects with 12 single digit probes, the subjects task was to determine whether the probe, a
single item presented after the main list, had been presented as part of a list. Hence this version of the task was assessing a different aspect of memory to the original Sternberg Memory Task. It would appear that the present HPRU version of the task is not sensitive to the effects of age.

Having identified the effects of age on the test battery, it was speculated that treatment with potential nootropic compounds may help to alleviate the age related decrement in performance. To test this hypothesis elderly subjects were treated with multivitamins, ginkgo biloba and glucose and performance was assessed on the test battery.

In chapter five, 239 healthy elderly volunteers aged 60-80 years were treated with either placebo or multivitamins for a period of 36 weeks. Cognitive function and blood samples were assessed at baseline, and after 12, 24 and 36 weeks. Based on previous research it was hypothesised that treatment with multivitamins would result in improved performance on SKT subtests II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VIII (delayed recall), the Ravens Standard Progressive Matrices (RSPM) and the Cognitive Failures Questionnaire (CFQ). It was also hypothesised that multivitamin supplementation would lower anxiety and depression scores on the Hospital Anxiety and Depression Scale (HADS). It was reported that long term multivitamin supplementation had no effect on the tasks. The lack of effect in the present study was possibly a result of the sample selection process, as subjects were volunteers, the large majority of subjects were well educated, wealthy health conscious individuals. The majority of whom were unlikely to be suffering from nutritional deficiency or any degree of cognitive decline. Indeed only 30% of the sample were at a high risk of deficiency of vitamin B6 and only 10% at a high risk of deficiency of vitamin B2. The data was also analysed taking into account the subjects risk of deficiency, it was reported that risk of deficiency had no effect on performance of the tasks. Risk of deficiency did however affect mood ratings, it was reported that subjects with a moderate risk
of deficiency had higher anxiety levels following supplementation. In terms of supplementation subjects supplemented with placebo with a high risk of deficiency reported greater depression rates over time compared to those with a low risk of deficiency who reported that they felt less depressed over time. Therefore the effects of vitamin deficiency may have more effects subjectively rather than objectively.

In chapter six, 16 healthy elderly volunteers aged 60-85 years were treated with ginkgo biloba 100 mg and placebo daily for 8 weeks in a randomised cross over design, with a 4 week washout period. Cognitive function was assessed at baseline and at weeks 2, 4, 6, 7 and 8. It was hoped that treatment with GBE would improve performance on the HPRU Digit Span Task, HPRU Sternberg Memory Task and aspects of the SKT especially SKT II (immediate recall), SKT VII (reverse naming) SKT VIII (delayed recall) and SKT IX (recognition memory). However it was reported that treatment with ginkgo biloba had no effect on performance of any tasks. The lack of effect of ginkgo biloba on cognitive function in the present study was possibly due to dosing of GBE. A 100 mg daily dose was selected as this was the recommended daily dose, and it was felt that it would be interesting to see if a recommended daily dose would induce positive beneficial effects on cognitive function. It is quite possible that if the daily dose was increased, more beneficial effects would have been observed.

In chapter seven, 24 healthy volunteers were treated with acute doses of glucose (50 g) and placebo (saccharin 23.7 mg) in a randomised cross over design. Blood glucose measurements were assessed at baseline, 30 and 50 minutes post dose. Cognitive function was assessed at baseline and 30 minutes post drink. Based on previous research it was hypothesised that treatment with glucose would improve performance on the word list task, SKT II (immediate recall), SKT VIII (delayed recall) SKT IX (recognition memory) would increase energy ratings and decrease tension ratings. It was reported that following the glucose
treatment blood glucose levels were significantly increased compared to placebo, however this increase in blood glucose had no effect on cognitive task performance. There are numerous studies that have reported benefits effects of glucose on cognitive function in elderly populations, however in the present study even though glucose levels were significantly higher following the glucose drink, the elevation in blood glucose had no observable effect on task performance. There is some evidence that a persons ability to tolerate glucose may have an effect on task performance, poor glucose tolerance is usually associated with poor task performance (Allen et al., 1996). In this sample it was reported that subjects with falling blood glucose (between the second and third samples) reported improved performance on the Sternberg memory task and felt more vigorous and less fatigued than subjects with rising blood glucose levels, possibly suggesting that the subjects were utilising the excess glucose and hence were reporting beneficial effects. There were no other reported differences. The main differences between the present study, and previous research lies in the number of subjects sampled. In previous studies, sample sizes ranged between 10 and 17 subjects (with the exception of Allen et al., 1996 and Craft et al., 1994). it is possible that the small sample sizes were not truly representative of the population as a whole and if numbers were increased the results may have been diluted. The test battery used in the present study was unique, none of the tasks had been used for the assessment of cognitive function following a glucose drink. It is possible that the tasks did not measure the correct aspects of cognitive function. In terms of future research it would be interesting to assess the effect of glucose on cognitive function in larger samples of healthy elderly subjects and incorporate some of the previously reported sensitive tasks into the test battery.

In terms of the experimental supplement chapters, it would appear that treatment with multivitamins, ginkgo biloba and glucose had no effect on any aspect of cognitive function in healthy elderly volunteers. However examination of the previous research would seem to indicate that performance improvements
have been noted in healthy adult, elderly and patient populations. In many cases the effects of supplementation are more dramatic in patient populations, but are still evident in healthy samples. These results would seem to be at odds with previous literature, however there are a number of reasons to account for the lack of treatment effect.

Firstly, it is possible that the samples included in the present studies, were not experiencing any form of cognitive decline (despite the fact they believed that they were experiencing difficulties with memory attention and slowness of thought). In terms of their baseline cognitive performance measures, their performance was almost comparable to healthy young subjects in many cases. Examination of the baseline scores reveal that the elderly subjects reported scores that corresponded with scores obtained by young samples. It is possible that the effects of supplementation with multivitamins, ginkgo biloba and glucose may be more dramatic in elderly subjects with definite cognitive decline. In terms of future experiments, it may be useful to pre-screen subjects in terms of cognitive decline, and only enrol subjects with definite degrees of cognitive decline, as the present analyses would seem to indicate that supplementation has no effect on cognitive performance in healthy elderly volunteers.

Analysis of the subjects age, may also help to account for the lack of effect, in many of the previous studies, the mean age of subjects were in the 70's. However in the present studies, despite the large age range 60-85 years, the mean age of subjects was approximately 65 years, which in aged research is considered as "young". The sample only contained small numbers of subjects who were aged over 70 years. In terms of future studies, it may be beneficial to include a larger sample of older subjects (aged 75+).

The recruitment procedure may also have contributed to the lack of effect. This was particularly true in the multivitamin study as volunteers responded to
advertisements in local papers and doctor's surgeries or were obtained from the HPRU database. People who volunteer for clinical trials via advertisements tend to be highly motivated and health conscious, therefore the selection process meant that only highly motivated healthy volunteers were available. The result is that the samples were probably not representative of the elderly population as a whole. In terms of future studies, it may be better to obtain volunteers from more varied sources, i.e. referrals from GP practices, health visitors and social workers as well as via advertisements.

The lack of effect may also be a result of inappropriate test measures. In chapter four the assessment methods were assessed in terms of their ability to detect age related changes. Despite the fact that a number of the tasks were age sensitive (SKT II (immediate recall), SKT IV (arranging blocks), SKT V (replacing blocks), SKT VI (counting symbols), SKT VII (reverse naming), and SKT VIII (delayed recall)). Supplementation with either multivitamins, ginkgo biloba or glucose did not remove this age related decrement. It is possible that the effects of supplementation were limited to aspects of cognitive function that were not addressed in the present analyses.

The SKT task is a short symptom task for use in elderly subjects experiencing cognitive decline, it is possible that the task is not suitable for use in healthy elderly subjects, and would appear that the task is not pharmaco-sensitive in healthy elderly subjects. However more research is warranted before such a conclusion is reached.

Analysis of age related effects on the Critical Flicker Fusion, Choice Reaction Time and the HPRU Sternberg Memory Task would seem to indicate that these tasks are not age sensitive and further analysis of the effects of supplementation on performance of the tasks would seem to indicate that the tasks are not pharmaco-sensitive in healthy elderly subjects. Perhaps the effects of treatment
on such tasks is limited to drugs that impair rather than improve performance, or rather the effects are specific to patient populations.

The results of this thesis raise a number of questions, they raise doubts on the credibility of the tasks used in this thesis, they raise doubts on the methodology of the tasks used in the thesis and they raise a number of questions of the laboratory versus real life tests. Chapter Four outlined the tasks used in the thesis and aimed to identify similarities between the present tests and other tasks used for the assessment of cognitive function, in order to understand and classify what aspects of cognitive function the tasks assess. It would appear that in many instances, it was quite difficult to identify similarities between the present tasks and currently valid and reliable methods. Examination of the methodology of the present tasks revealed that many of the tests were unique. In the HPRU version of the Sternberg Memory Task, memory scanning ability was assessed by presenting 12 single digit probes. The methodology employed by the HPRU does not parallel the method in the original Sternberg Memory Task, therefore it was not possible to make a direct comparison between the 2 tasks, and it was not possible to easily identify what aspect of cognitive function the task measured. Similar criticisms can be made of a number of subtests of the Syndrom Kurtz Task (SKT) and the Milford Memory Task. In the SKT both delayed and recognition memory were assessed. These aspects of memory are commonly assessed in psychopharmacological studies, as it is interesting to determine whether a particular drug adversely affects memory. The methodology of the SKT delayed and recognition tasks were quite unique. In the delayed recall task, subjects had 2 attempts to remember the information (information was first looked at before the immediate recall and straight after immediate recall subjects were given 5 seconds to refresh their memory of the information), normally delayed recall is assessed by allowing only one attempt at remembering. In this task, it is not possible to tell whether the subjects were recalling items that they recalled before, which you might hypothesise were easier items, or recalling from the original list. A similar argument can be used
for the recognition memory task, generally recognition tasks are tested exclusively (i.e. without previously testing immediate and delayed recall).

The methodology in the Milford Memory Task was also quite unique. The Milford digit span task was dramatically different from the original digit span task. In the Milford version, subjects were only given one chance to correctly recall the digit span, whereas in the original task, subjects were given two chances to recall the digit spans. Such dramatic differences between the present tasks and other tasks mean that cross comparisons are almost impossible and the task of identifying what aspects of cognitive function the task is assessing is also very difficult.

There are a number of variables that can affect performance on tasks, in the laboratory there are a number of steps scientists can take to limit the variance induced by the variables such as testing in the same environment with the same equipment, same experimenter and at the same time of the day. Practice effects are one of the greatest problems posed in psychopharmacology, if a subject is not fully trained on the task their performance will improve over time and can be misinterpreted as drug improvements. Parkin et al., (1996) assessed training needs for subjects, in particular how many times a subjects would need to complete the CFF and CRT tasks in order to reach performance plateau. 14 young healthy naive subjects completed the CFF and CRT tasks it was concluded that after just 6 sessions all subjects had reached performance plateau. This experiment was repeated in 26 elderly subjects aged 61-84 years (unpublished data) and much the same as the young subjects, the elderly had reached performance plateau after just 6 test sessions. Based on this evidence, prior to participation in clinical trials, all HPRU subjects are trained on the tasks (complete 6 sessions). Therefore in terms of HPRU criteria all elderly subjects were fully trained and had reached performance plateau. However analysis of the data within this thesis would seem to indicate that practice effects were evident despite the fact subjects were considered fully trained. Practice effects
were observed on the Critical Flicker Fusion, Choice Reaction Time and Sternberg Memory Tasks. These practice effects pose a number of questions on how should subjects be trained on tasks, should they have a practice before each visit, or even a number of practices before each visit.

Practice effects were noted on the Critical Flicker Fusion task in two of the experiments (glucose and ginkgo biloba experiments). The Critical Flicker Fusion task is a physiological measure of brain efficiency and as such, is a task that should have no learning curve and hence no practice effects. However practice effects were noted on the task, this indicates that the task in its present format probably does not measure what it is intended to measure.

These methodological differences may reflect the fact that many of the tasks used were designed in the 1970's when knowledge of the cognitive system was less advanced than what we know today. Therefore for these reasons, it can be argued that the tasks have limited utility as science and technology advances towards the millennium.

Finally the lack of effect with the three compounds (multivitamins, ginkgo Biloba and glucose) may be due to the low dosage given. This is unlikely to be true in the vitamin study as the dose given was equal to ten times the US recommended daily allowance. However the low dose may be responsible for the lack of effect in the Ginkgo Biloba and glucose studies. In the Ginkgo Biloba study a daily dose of 100 mg was given to subjects for 8 weeks. 100 mg is the recommended daily dose specified by the manufacturers (Pharma Nord), and as this thesis aimed to assess cognitive function and change in the "real life" setting, this dose was selected. From examination of the present Ginkgo Biloba study and the previous literature it would appear that a higher dose of Ginkgo Biloba would probably result in more favourable effects.
In the glucose study a 50 g dose of glucose was given to all subjects. A number of studies have previously reported an effect on cognitive function in the elderly with this dose. To help resolve this issue, it may have been better to design the studies using a dose range including both lower and higher doses of glucose e.g. 25 g, 50 g and 75 g. In the Ginkgo Biloba study perhaps it would have been better to assess the cognitive effects using GBE 100 mg and a 200 mg dose. Perhaps dose ranging studies would have found more effects.

In summary, the effects of improved nutritional status with multivitamins, Ginkgo Biloba or glucose failed to induce any beneficial reported effect on cognitive function in a healthy elderly population. Further research is needed to ascertain whether the null results are specific to the population sampled or are a true reflection of a lack of effect following dosing with over the counter nutritional supplements. In order to do this, larger sample sizes need to be included in such studies. For example, rather than rely on volunteers for such studies, perhaps local GP's and health visitors could help with the recruitment process. This would help eliminate the problem of only including fit, healthy, eager elderly subjects, making the sample more varied and representative of the population as a whole.

It would also be beneficial to conduct dose ranging studies, as it is possible that the dose selected in the present studies were either not potent enough or were too potent. It is quite possible that cognitive function is enhanced in an inverted U manner, so the dose of ginkgo biloba and glucose may have been to low and the dose of multivitamin too high. Dose ranging studies would help to provide answers to such questions.

The fact that the results of these studies do not reflect previously reported findings would seem to indicate that future research needs to be conducted in order to help determine whether nutritional supplements can have beneficial effects on human cognitive functioning.
References


Rabbitt and Phillips (Unpublished data)


Appendix

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# Appendix One: Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>ADAS</td>
<td>Alzheimer Disease Assessment Scale</td>
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<tr>
<td>ADAS-Cog</td>
<td>Alzheimer's Disease Assessment Scale Cognitive Subscale</td>
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<tr>
<td>AD-ACL</td>
<td>Activation Deactivation Check List</td>
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<tr>
<td>ADL</td>
<td>Activity of Daily Living Scale</td>
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<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
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<tr>
<td>BDI</td>
<td>Beck Depression Inventory</td>
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<tr>
<td>CDS</td>
<td>Cognitive Difficulties Scale</td>
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<td>CERAD</td>
<td>Consortium to Establish a Registry for Alzheimer’s Disease</td>
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<tr>
<td>CES-D</td>
<td>The Center for Epidemiological Studies Depression Scale</td>
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<tr>
<td>CFF</td>
<td>Critical Flicker Fusion Task</td>
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<tr>
<td>CFQ</td>
<td>Cognitive Failures Questionnaire</td>
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<tr>
<td>CGI</td>
<td>Clinical Global Impression</td>
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<td>CNS</td>
<td>Central Nervous System</td>
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<td>CoA</td>
<td>Coenzyme A</td>
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<td>CRT</td>
<td>Choice Reaction Time</td>
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<tr>
<td>DISS</td>
<td>Disability Impairment Interview Schedule</td>
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<td>DSST</td>
<td>Digit Symbol Substitution Task</td>
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<tr>
<td>EAQ</td>
<td>Everyday Attention Questionnaire</td>
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<tr>
<td>EMQ</td>
<td>Everyday Memory Questionnaire</td>
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<tr>
<td>EPQ</td>
<td>Eysenk Personality Questionnaire</td>
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<tr>
<td>FPI</td>
<td>Freiberger Personality Inventory</td>
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<tr>
<td>GERRI</td>
<td>Geriatric Evaluation by Relatives Rating Scale</td>
</tr>
<tr>
<td>GCES</td>
<td>Geriatric Clinical Evaluation Scale</td>
</tr>
<tr>
<td>GBE</td>
<td>Ginkgo Biloba Extract</td>
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<tr>
<td>HADS</td>
<td>Hospital Anxiety and Depression Scale</td>
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<tr>
<td>HPRU</td>
<td>Human Psychopharmacology Research Unit</td>
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<tr>
<td>IADL</td>
<td>Instrumental Activities of Daily Living</td>
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<tr>
<td>LARS</td>
<td>Line Analogue Rating Scale</td>
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<tr>
<td>LF</td>
<td>Lost and Found Questionnaire</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>MAO</td>
<td>Monoamine Oxidise</td>
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<tr>
<td>MFQ</td>
<td>Memory Failures Questionnaire</td>
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<tr>
<td>MID</td>
<td>Multi-infarct Dementia</td>
</tr>
<tr>
<td>MMSE</td>
<td>Mini Mental State Examination</td>
</tr>
<tr>
<td>NAD</td>
<td>Nicotinamide adenine dinucleotide</td>
</tr>
<tr>
<td>NART</td>
<td>National Adult Reading Test</td>
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<tr>
<td>NINCDS-ADRDA</td>
<td>Working group for the auspices of Department of Health and Human Services Task Force on Alzheimer’s Disease</td>
</tr>
<tr>
<td>POMS</td>
<td>Profile of Mood States</td>
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<tr>
<td>QOL</td>
<td>Quality of Life</td>
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<tr>
<td>RDA</td>
<td>Recommended Daily Allowance</td>
</tr>
<tr>
<td>RIPT</td>
<td>Rapid Information Processing Task</td>
</tr>
<tr>
<td>RSPM</td>
<td>Ravens Standard Progressive Matrices</td>
</tr>
<tr>
<td>SDAT</td>
<td>Senile Dementia of the Alzheimer Type</td>
</tr>
<tr>
<td>SKT</td>
<td>Syndrom Kurtz Task</td>
</tr>
<tr>
<td>SMT</td>
<td>HPRU Sternberg Memory Task</td>
</tr>
<tr>
<td>VARS</td>
<td>Visual Analogue Rating Scale</td>
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<tr>
<td>WAIS</td>
<td>Wechsler Adult Intelligence Scale</td>
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<tr>
<td>WLT</td>
<td>Word List Task</td>
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<tr>
<td>WMS</td>
<td>Wechsler Memory Scale</td>
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</table>
Appendix Two: Principal components analysis - 18 factor solution

The 59 items from the Activities of Daily Living Scale (ADL) was subject to a principal components analysis using Statistica. Factors with Eigenvalues equal to or greater than one, were retained for an oblimin rotation. When test items loaded on more than one factor, they were included in a factor according to their maximal weighting. There was pairwise deletion to missing data.

Factor 1
1. When driving an auto, do you have problems recognising landmarks that would help you know where to turn?
2. When driving an auto, do you have problems recalling landmarks that would help you know where to turn?
3. When travelling to new places do you sometimes become overwhelmed with new information?
4. When driving an auto, do you become unsure about which exit(s) to take to get to a familiar place?
5. Do you have difficulty reading the newspaper thoroughly?
6. When going on a vacation or to visit friends, do you have difficulty organising the trip yourself?
7. Do you have difficulty touring an unfamiliar city or place on your own?

Factor 2
1. Although you know your personal identification number- or you have it on a piece of paper- do you find you have difficulty operating an automatic teller machine for a simple transaction (e.g. withdrawal)?
2. Do you have difficulty making a transaction (i.e. take out money) at an automated bank machine?

Factor 3
1. While counting something up do you need to recount it several times?
3. Do you forget to turn of the stove, turn out the lights, or lock the door when you should?

Factor 4
1. When you look up an unfamiliar telephone number, do you have to refer back to it when dialling?
2. Do you forget names of people who have just been introduced to you?
3. Do you have difficulty remembering telephone numbers which you frequently dial?

**Factor 5**
1. Do you forget anniversaries or birthdays you have always observed in the past?
2. Do you have problems remembering important dates and events?
3. Do you buy greetings cards, birthday or anniversary cards for close relatives/friends and then forget to mail them?

**Factor 6**
1. If you are interrupted while speaking, do you tend to forget what you were going to say?
2. If you have to wait your turn to speak, do you have trouble keeping in mind what you want to say while listening to someone else to talk?
3. Do you experience difficulty “doing two things at the same time”?
4. If you have a new and or important idea do you have difficulty remembering it 5 minutes later if you don’t write it down immediately?

**Factor 7**
1. Do you experience problems concentrating on reading leisure material?
2. Are you easily distracted when reading leisure material?
3. After reading a chapter or a few pages in a book or in an article do you have difficulty describing what you read?
4. Do you need to read the same passage or part of a book (or other reading material) several times in order to remember it?

**Factor 8**
1. Do you experience problems playing card games (e.g. gin rummy, canasta etc.)?
2. Do you lose important things?
3. If you are interrupted doing an activity or shore do you have difficulty continuing where you left-off?
4. Is it difficult for you to keep your mind on a task when several other things are going on around you?
5. Do you repeatedly go from one room into another in order to do or get something but then forget what you wanted to do?

**Factor 9**

1. Do you have little to say in a conversation because of lack of thoughts or ideas?
2. Have you started to avoid discussions/conversations because of difficulty finding the correct words to use?
3. Do you have difficulty participating in hobbies?
4. Do you become confused while performing several simple activities around the home, at the same time?

**Factor 10**

1. Do you have difficulty driving from one familiar spot to another without preparation i.e. without carefully going over the route?
2. Do you experience difficulty understanding your bank statement?
3. When walking or hiking do you find that you have to concentrate more on landmarks and signposts in order to find the way back?

**Factor 11**

1. Do you forget about what you have just done (e.g. locking the door, pulling out a plug on an appliance)?
2. Have you had difficulty remembering where you've parked your car?

**Factor 12**

1. Do you forget a point in the middle of a conversation?
2. Have you become less certain about how to correctly spell words that you know?
3. Do you purchase tickets for an event only to find that you have bought tickets for a wrong date or time?

**Factor 13**

1. Do you experience difficulty learning new directions regarding how to use simple household appliances (e.g. coffee maker, iron, toaster)?
2. Do you experience difficulty learning new directions regarding how to use complex household appliances (e.g. microwave oven, vacuum cleaner, washing machine)?
Factor 14
1. Do you begin an activity or chore and then forget the steps or the sequences of behaviours necessary for the completion of the activity?
2. If you use public transport for a route you’ve never taken before, do you feel uneasy and uncertain about what to do?
3. Do you have trouble following a map to a new place?
4. Do you have difficulty reading a map of an unfamiliar city or place?

Factor 15
1. Are you uninterested in daily political events?
2. Do you find it difficult to complete forms?
3. Do you put off doing things because you have difficulty getting them organised?

Factor 16
1. Do you go to social/cultural events on the wrong day or at the wrong time?
2. Do you invite friends or relatives for a visit and then you find that you forgot that you invited them?

Factor 17
1. Do you have difficulty giving directions to a place that you used to go to frequently?
2. If asked for directions, do you have difficulty giving detailed information?

Factor 18
1. Do you have difficulty finding the correct word to use when speaking?
2. Do you search for personal belongings (e.g. spectacles)?
3. Do you have problems concentrating on conversations?
Appendix Three: Principal components analysis two factor solution

The 59 items from the Activities of Daily Living Scale (ADL) was subject to a principal components analysis using Statistica. Factors with Eigenvalues equal to or greater than one, were retained for an oblimin rotation. When test items loaded on more than one factor, they were included in a factor according to their maximal weighting. There was pairwise deletion to missing data.

Factor 1
Do you experience difficulty “doing two things at the same time”?
Do you have problems remembering important dates and events?
Do you put off doing things because you have difficulty getting them organised?
Do you have problems concentrating on conversation?
Do you need to read the same passage or part of a book (or other reading material) several times in order to remember it?
If you have to wait your turn to speak, do you have trouble keeping in mind what you want to say while listening to someone else talk?
If you are interrupted whilst speaking, do you tend to forget what you were going to say?
After reading a chapter or a few pages in a book or in an article do you have difficulty describing what you just read?
Do you lose important things?
Is it difficult for you to keep your mind on a task when several other things are going on around you?
Do you have difficulty finding the correct words to use when speaking?
If you have a new and/or important idea do you have difficulty remembering it 5 minutes later if you don’t write it down immediately?
Do you search for personal belongings?
Have you started to avoid discussions/conversations because of difficulty finding the correct word to use?
Are you easily distracted when reading leisure material?
Do you experience problems concentrating on reading leisure material?
Do you forget a point in the middle of a conversation?
Do you become confuse while performing several simple activities around the home at the same time?
Do you forget anniversaries or birthdays you have always observed in the past?
Do you buy greetings cards, birthday or anniversary cards for close relatives/friends and then forget to mail them?
If asked for directions do you have difficulty giving detailed information?
Do you have difficulty reading the newspaper thoroughly?
Do you experience problems playing card games (e.g. gin rummy, canasta etc.)?
Do you repeatedly go from one room to another, in order to do, or get something, but then forget what you wanted to do?
Do you go from social/cultural events on the wrong day or at the wrong time?
Do you forget to turn off the stove, turn out the lights, or lock the door when you should?
Do you forget about what you have just done (e.g. locking the door, or pulling out a plug on an appliance?)
Do you invite friends or relatives for a visit and then find that you forgot that you invited them?
Do you have difficulty giving detailed directions to a place that you used to frequently go?
Do you forget names of people who have just been introduced to you?
When making telephone calls do you dial the wrong number?
Do you have little to say in a conversation because of lack of thoughts or ideas?
Do you begin an activity/chore and then forget the steps or sequences of behaviours necessary for the completion of the activity?
Do you have difficulty remembering telephone numbers which you frequently dial?
Have you had difficulty remembering where you have parked your car?
While counting something up do you need to recount it several times?
When you look up an unfamiliar telephone number, do you have to refer back to it while dialling?

Factor 2
Do you have difficulty touring an unfamiliar city or place on your own?
Do you have trouble following a map to a new place?
When travelling to new places do you sometimes become overwhelmed with new information?
When driving an auto, do you become unsure or uncertain about which exits to take to get to a familiar place?

When walking or hiking do you find that you have to concentrate more on landmarks and signposts in order to find the way back?

Do you have difficulty reading a map of an unfamiliar city or place?

When driving an auto, do you have problems recognising landmarks that would help you know where to turn?

When driving an auto, do you have problems recalling landmarks that would help you know where to turn?

Do you experience difficulty learning new directions regarding how to use simple household appliances (e.g. coffeemaker, iron, toaster)?

Have you become less certain about how to correctly spell words that you know?

If you are interrupted during an activity or chore do you have difficulty continuing where you left off?

Do you experience difficulty learning new directions regarding how to use complex household appliances (e.g. microwave oven, vacuum cleaner, washing machine)?

Do you have difficulty driving from one familiar spot to another without preparation- i.e. without carefully going over the route?

When going on a vacation or to visit friends, do you have difficulty organising the trip yourself?

If you use public transportation for a route you’ve never taken before, do you feel uneasy and uncertain about what to do?

Do you find it difficult to complete forms?

Do you have difficulty making a transaction (i.e. take money out) at an automated bank machine?

Although you know your personal identification number- or you have it on a paper- do you have difficulty operating an automatic teller machine for a simple transaction (e.g. withdrawal)?

Do you experience difficulty understanding your bank statement?

Do you purchase tickets for an event only to find that you bought tickets for a wrong date or time?

Do you have difficulty participating in hobbies?

Are you uninterested in daily political events?

When making telephone calls do you dial the wrong number?
Appendix Four: Principal components analysis four factor solution

The 59 items from the Activities of Daily Living Scale (ADL) was subject to a principal components analysis using Statistica. Factors with Eigenvalues equal to or greater than one, were retained for an oblimin rotation. When test items loaded on more than one factor, they were included in a factor according to their maximal weighting. There was pairwise deletion to missing data.

Factor 1
Do you have problems concentrating on conversation?
Do you have little to say in a conversation because of lack of thoughts or ideas?
Do you become confused while performing several simple activities around the home at the same time?
Do you experience difficulty “doing two things at the same time”?
When going on vacation or to visit friends, do you have difficulty organising the trip yourself?
Is it difficult for you to keep your mind on a task when several other things are going on around you?
If you have to wait your turn to speak, do you have trouble keeping in mind what you want to say while listening to someone else talk?
If you are interrupted while speaking, do you tend to forget what you were going to say?
After reading a chapter or a few pages in a book or in an article, do you have difficulty describing what you just read?
Do you experience problems concentrating on reading leisure material?
have you started to avoid discussions/conversations because of difficulty finding the correct word to use?
Are you easily distracted when reading leisure material?
Do you have difficulty reading the newspaper thoroughly?
Do you put off doing things because you have difficulty getting them organised?

Factor 2
Do you need to read the same passage or part of a book (or other reading material) several times in order to remember it?
Do you have difficulty participating in hobbies?
Do you forget point in the middle of a conversation?
Do you have difficulty finding the correct words to use when speaking?
Are you uninterested in daily political events?
Do you have difficulty touring an unfamiliar city or place on your own?
When travelling to new places do you sometimes become overwhelmed with new information?
Do you experience difficulty learning new directions regarding how to use complex household appliances (e.g. microwave oven, vacuum cleaner, washing machine)?
When driving an auto, do you become unsure or uncertain about which exits to take to get to a familiar place?
Do you experience difficulty learning new directions regarding how to use simple household appliances (e.g. coffeemaker, iron, toaster)?
When driving an auto, do you have problems recognising landmarks that would help you know where to turn?
When driving an auto, do you have problems recalling landmarks that would help you know where to turn?
Although you know your personal identification number- or you have it on a piece of paper- do you have difficulty operating an automatic teller machine for a simple transaction (e.g. withdrawal)?
Do you have difficulty reading a map of an unfamiliar city or place?
Do you have difficulty making a transaction (i.e. take money out) at an automated bank machine?
When walking or hiking to you find that you have to concentrate more on landmarks and sign posts in order to find the way back?
If you are interrupted during an activity or chore do you have difficulty continuing where you left off?

Factor 3
Do you have difficulty following a map to a new place?
Do you forget to turn off the stove, turn out the lights, or lock the door when you should?
Do you invite friends or relatives for a visit and then find that you forgot that you invited them?
Have you had difficulty remembering where you have parked your car?
Do you go to social/cultural events on the wrong day or at the wrong time?
Do you buy greetings cards, birthday or anniversary cards for close friends or relatives and then find that you forgot to mail them?

If asked for directions, do you have difficulty giving detailed information?

If you have a new and/or important idea, do you have difficulty remembering it 5 minutes later if you don’t write it down immediately?

Do you forget about what you have just done (e.g. locking the door, pulling out a plug on an appliance)?

Have you become less certain about how to spell words that you know?

Do you find it difficult to complete forms?

If you use public transportation for a route you’ve never taken before, do you feel uneasy and uncertain about what you do?

Do you have difficulty giving directions to a place that you used to frequently go?

Do you have difficulty driving from one familiar spot to another without preparation i.e. without carefully going over the route?

Do you experience difficulty understanding your bank statement?

When making telephone calls do you dial the wrong number?

Do you forget anniversaries or birthdays you have always observed in the past?

Do you begin an activity/chore and then forget the steps or sequences of behaviours necessary for the completion of the activity?

**Factor 4**

Do you have difficulty remembering telephone numbers which you frequently dial?

Do you have problems remembering important dates and events?

Do you search for personal belongings?

When you look up an unfamiliar telephone number, do you have to refer back to it while dialling?

Do you repetitively go from one room into another in order to do or get something but then forget what you wanted to do?

Do you forget names of people who have just been introduced to you?

Do you lose important things?

Do you experience problems playing card games (e.g. gin rummy, canasta etc.)?

While counting something up do you need to recount it several times?

Do you purchase tickets for an event only to find that you bought tickets for a wrong date or time?
Appendix Five: Shortened ADL Scale
(14 Items)
Please complete the following questionnaire

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Please indicate your age and sex)</td>
<td></td>
</tr>
</tbody>
</table>

0 = never (no problems)  
1 = occasionally  
2 = some of the time  
3 = most of the time  
4 = always (on every occasion)

<table>
<thead>
<tr>
<th>Question / Item</th>
<th>Your Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>If you have an important idea and don’t write it down immediately</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>do you have difficulty remembering it 5 minutes later?</td>
<td></td>
</tr>
<tr>
<td>Do you have problems learning new information?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you find you forget what you have just done (e.g. locking the door, turning</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>the fire off etc.)?</td>
<td></td>
</tr>
<tr>
<td>Do you have difficulty travelling from one familiar spot to another</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>without preparation (i.e. without carefully planning your route)?</td>
<td></td>
</tr>
<tr>
<td>Do you forget the names of people who have just been introduced to you?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you have problems remembering important dates/events?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you need help completing household tasks, even though</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>physically capable of doing them?</td>
<td></td>
</tr>
<tr>
<td>Do you have difficulty finding the correct word to use when speaking?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you have problems concentrating on conversations?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you go from one room to another in order to get something (e.g. your</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>spectacles) and then forget what you wanted?</td>
<td></td>
</tr>
<tr>
<td>Do you become confused whilst performing more than one household activity at</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>the same time?</td>
<td></td>
</tr>
<tr>
<td>If you are interrupted whilst performing an activity, do you have difficulty</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>continuing where you left off?</td>
<td></td>
</tr>
<tr>
<td>Do you have difficulty following a map to a given destination?</td>
<td>0 1 2 3 4</td>
</tr>
<tr>
<td>Do you have difficulty remembering what you have just read?</td>
<td>0 1 2 3 4</td>
</tr>
</tbody>
</table>
Appendix Six: SKT Scoring Worksheet
A short cognitive performance test for assessing memory and attention

<table>
<thead>
<tr>
<th>Name</th>
<th>Age</th>
<th>Date of birth</th>
<th>Occupation</th>
<th>IQ group</th>
<th>Diagnosis</th>
<th>Remarks</th>
<th>Date</th>
<th>Time</th>
<th>RAW SCORES</th>
<th>NORM VALUES</th>
</tr>
</thead>
</table>

| Tester | | | | | | | | | | |

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
<th>RAW NORM</th>
<th>NORM SCORES</th>
<th>NORM VALUES</th>
</tr>
</thead>
</table>

### Naming objects

**Immediate recall**

<table>
<thead>
<tr>
<th>Apple</th>
<th>Feather</th>
<th>House</th>
<th>Leaf</th>
<th>Confabulations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cock</td>
<td>Car</td>
<td>Dice</td>
<td>Peg</td>
<td></td>
</tr>
<tr>
<td>Pot</td>
<td>Mouse</td>
<td>Spoon</td>
<td>Clock</td>
<td></td>
</tr>
</tbody>
</table>

**Tick objects named**

<table>
<thead>
<tr>
<th>Confabulations:</th>
</tr>
</thead>
</table>

**SHOW TABLEAU AGAIN FOR 5 SECONDS ONLY**

<table>
<thead>
<tr>
<th>Naming numerals</th>
<th>Seconds</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Arranging blocks</th>
<th>Seconds</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Replacing blocks</th>
<th>Seconds</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Counting symbols</th>
<th>Seconds</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Reversal naming</th>
<th>Correct sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>Feather</td>
</tr>
<tr>
<td>Cock</td>
<td>Car</td>
</tr>
<tr>
<td>Pot</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confabulations:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Delayed recall</th>
<th>Seconds</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Recognition memory</th>
<th>Confabulations:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>Feather</td>
</tr>
<tr>
<td>Cock</td>
<td>Car</td>
</tr>
<tr>
<td>Pot</td>
<td>Mouse</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Confabulations:</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Overall assessment of clinical degree of severity</th>
</tr>
</thead>
</table>