## **Helping your Aging Memory**

An edited collection of articles and news reports from the Mempowered website

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# The role of mental stimulation in aiding memory

- Participation in mentally stimulating activities appears to reduce your risk of developing Alzheimer's and other dementias.
- It also seems to reduce general cognitive decline in older adults, with level of activity directly correlated to cognitive performance and health.
- Social engagement also appears to help cognitive performance, and health.
- Feelings of low self-worth, depression and anxiety, may be associated with a greater risk of developing Alzheimer's, and with deterioration of brain tissue.
- Changes in sensitivity to stress may be a factor in age-related cognitive decline.
- It seems likely that negative thoughts, sensitivity to stress, poor health, and lack of involvement in social and intellectual activities, all contribute to age-related cognitive decline, both directly and indirectly (through their influence on each other).
- We cannot say for sure that mental stimulation helps prevent cognitive decline. It may be that early precursors of cognitive decline affect a person's level of activity, or that there is another factor that makes you more likely to engage in mentally stimulating activities as well as less likely to suffer cognitive decline.
- A plausible common factor would be level of cognitive ability. There is evidence that those with greater education are at reduced risk of developing Alzheimer's, as are those with larger brains (where the important factor is not the size of brain you are born with, but the growth in brain tissue in the early years - something which reflects degree of stimulation).
- However, it is at least equally likely that stimulation is the critical factor underlying all this. Stimulation in the early years grows complex brains (builds more neurons and richer networks of connections between them). Education may be presumed to provide stimulation - thus, more years of

formal education would correlate with more years of stimulation, as well as providing training that encourages the individual to continue to find mental stimulation rewarding. Occupation similarly, can also readily be seen to be correlated with level of stimulation. In the older years, stimulation may keep connections active, and help the brain find new ways of doing things when old ways become more difficult.

#### Does mental stimulation protect you from Alzheimer's and other dementias?

A number of studies in the past few years have supported the theory that engaging in mentally stimulating activities can help keep your mind sharp. Most of these studies have, understandably, been concerned with the effect of stimulation on the aging mind, and in particular on the question of whether it helps protect against dementia:

- one study found that participation in leisure activities of all kinds was associated with a risk in dementia risk, although intellectual activities had the most beneficial effect. [1]
- a large-scale study of seniors aged 65 years and older found that participation in various cognitive activities (such as reading a newspaper) was positively associated with a decreased risk of developing Alzheimer's. This effect remained even after education and occupation (both associated with Alzheimer's risk) had been taken into account. Physical activity had no effect. [2]
- a large-scale study of seniors found that more frequent participation in cognitively stimulating activities (such as reading books, newspapers or magazines, engaging in crosswords, puzzles, board or card games, going to museums) was significantly associated with a reduced risk of Alzheimer's disease. [3]
- a study involving seniors aged 75 or older found those who participated at least twice weekly in reading, playing games (chess, checkers, backgammon

or cards), playing musical instruments, and dancing were significantly less likely to develop dementia. Although the evidence on crossword puzzles was not quite statistically significant, those who did crossword puzzles four days a week had a much lower risk of dementia than those who did one puzzle a week. Only one physical activity had any significant impact — ballroom dancing — possibly because of the mental demands of remembering dance steps, responding to music and coordinating with a partner. [4]

## Does mental stimulation protect you from general age-related cognitive decline?

General cognitive decline has been found to be less among those seniors who did more cognitively stimulating activities. In particular, working memory, perceptual speed, and episodic memory (all processes particularly affected by aging) were all helped. [2]

Another study followed a large group of seniors, aged 70-93 at the beginning of the study, over a seven-year period. Most participants, unsurprisingly, reduced their level of activity over the period. The rate at which individuals reduced their activity level was substantially correlated with changes in cognitive and health measures, although some decline in cognitive performance was evident even in those who maintained their activity levels. [5]

In a recent large-scale British study of civil servants aged between 35 and 55, participation in various leisure activities was associated with level of cognitive ability. Specifically, regular cultural visits to theatres, art galleries and stately homes, were associated with the highest level of cognitive ability, closely followed by reading and listening to music, then by involvement in clubs and voluntary organizations, and participation in courses and evening classes. [6]

Interestingly, this particular study found that the association between the selected 13 leisure activities and cognitive ability was slightly stronger for men than for

women. One reason for this may be that women are more likely to engage in activities other than those selected.

In particular, it has been speculated that women are more likely to engage in more social interaction, which may be beneficial. There is some evidence that social interactions benefit cognitive functioning.

#### Just talking may help prevent cognitive decline

"Social engagement" can be measured by how often people talk on the phone with friends, neighbors and relatives, how often they get together with them, how many people they can share their most private feelings and concerns with. A series of studies by Dr Oscar Ybarra [7] have found that, across all age groups, the more socially engaged people are, the lower their level of cognitive impairment and the better their working memory performance.

This does not necessarily mean that more social contact leads to a sharper mind. People in better shape mentally are probably more inclined to be social in the first place.

However, the studies do build on earlier research. One study found that seniors who reported more demands from social relationships had better cognitive functioning. This may reflect the benefit of complex social interaction (or of course, it may simply reflect the fact that those with better cognitive function are more likely to have demands made on them). [8]

Social engagement also appears to have an effect on health. A study growing out of the Seattle Longitudinal Study found low levels of social networks were associated with more hospital and doctor visits, and higher health costs. Those with greater health problems were more likely to be socially isolated, and also had lower levels of education and income. [9]

#### Personality variables also play a role

The association between all these factors is assuredly complex. One aspect to it may be that people with low self-worth may be less likely to engage in stimulating activities (social, intellectual, and physical). Recent research has found that age-related cognitive decline is more likely in those with low self-worth, and that the brains of those with less self-worth were significantly smaller than those of people who felt good about themselves. So perhaps those with low self-worth don't bother to do much, and their brains shrink, reflecting this lack of use, in the same way that our stomachs shrink when we feed them less. [10]

Self-worth is also associated with anxiety and depression, and these factors have been shown to be associated with an increased risk of developing Alzheimer's in several studies:

- a seven-year study found that those with the greatest number of depressive symptoms at the start of the study were more likely to develop Alzheimer's disease and also showed more rapid cognitive decline. [11]
- a longitudinal study found that those who most often experience negative emotions like depression and anxiety were twice as likely to develop Alzheimer's disease as those who were least prone to experience negative emotions. [12]
- a study of Alzheimer's patients found that their level of impairment in episodic memory on initial evaluation was related to their tendency to experience psychological distress (as assessed by a knowledgeable informant) prior to developing Alzheimer's. This was not, however, a factor in the rate at which cognitive function declined over the course of the disease. [13]

A person's tendency to experience psychological distress has been shown to be a stable personality trait throughout adulthood. In the second study, proneness to stress was specifically associated with a decline in episodic memory (measured by asking participants to recall a list of words or a story) — an area particularly problematic for those with Alzheimer's. Episodic memory ability declined 10 times faster in those high in proneness to distress than in those low in this response.

This result was not altered when participants' engagement in cognitively stimulating activities was taken into account, suggesting that this personality factor is independent of activity level.

The way in which we respond to stress may also change as we get older, and this may contribute to poorer memory performance in old age. A study involving 14 healthy seniors compared memory performance on two tasks, one of them assumed to be stressful (a public speaking task) and one not (an attentional task). It was found that declarative memory (conscious recollection of learned information) was impaired on the stressful task, but not on the nonstressful task. Nondeclarative memory (information retrieved without conscious or explicit effort) was not affected by stress. Measurement of cortisol levels suggested that it was the anticipation of stress rather than the stress itself that affected memory. It is speculated that an altered cortisol responsivity to acute and/or chronic stress may be partly responsible for age-related cognitive decline. [14]

But what do all these studies really mean? It must always be remembered that correlation doesn't mean causation. The fact that depressed people are more likely to develop Alzheimer's doesn't mean depression *causes* Alzheimer's. Physical changes in the brain that occur long before symptoms appear may also make it more likely that the individual will suffer depression, for example. The fact that people who lead busier, more active and involved lives, tend to perform better on memory and cognitive tasks, doesn't mean that it is their activities that keep their minds sharp. It may be that those whose minds are sharp are more likely to engage in such activities.

#### Is higher mental ability protective against cognitive impairment?

The main problem with determining the relationship between cognitive activities and cognitive performance is that we don't usually know the previous history of cognitive performance. Level of education, occupation, socio-economic class, these are all indicators, but to know whether a person engages in more cognitive activities because he is intellectually able, or whether he has retained more mental ability because he has kept himself mentally active, we really need to know his cognitive abilities at an earlier age.

A recent longitudinal study bears on this question (unfortunately, only preliminary results are as yet available). The Scottish Mental Survey assessed 87,498 eleven-year-olds in 1932, and another 70,805 in 1947. In a fascinating follow-up to this study, over 1000 of these students were contacted and re-assessed, on the exact same tests. It was found that, first of all, the seniors did rather better than they had at age 11, and more importantly, that differences in mental ability remained fairly stable with age — "with some interesting exceptions, the high scorers did well and the modest remained so." [15]

A study of 215 seniors aged 66-75 found that those with a larger head size had significantly higher scores on intelligence tests, and also showed less decline in memory performance over the 3 ½ year follow-up period. Those with the smallest heads had a fivefold increased risk of cognitive decline compared to those with the largest. However, there was no correlation with head size at birth, indicating that it is brain development in the early years that is important. During the first year of life, babies' brains double in size, and by the time they are six, their brain weight has tripled. These, it appears, are the crucial years for laying down brain cells and neural connections (pointing to the importance of providing both proper nourishment and intellectual stimulation in these early years). [16]

There is also evidence that the more formal education you have, and the greater your head size (reflecting brain size), the more you are protected from the effects of Alzheimer's. That is, these factors don't reduce your likelihood of developing Alzheimer's, but, by providing reserve brain capacity — a "cognitive reserve" — normal function can be retained for longer. [17]

Interestingly, a longitudinal study found that those who wrote more densely (packed more ideas into the sentences) of autobiographical essays written when they were young were less likely to get Alzheimer's disease six decades later. [18] However, it must also be remembered that the effects of education and occupation on Alzheimer's risk seem to be greatly reduced when you take into account mentally stimulating activities [2]. That is, those with higher levels of education and higher income are more likely to engage in mentally stimulating activities, and this accounts for much (though not all) of the effects of education and occupation.

Clearly all these factors impact on each other: physical health, cognitive function, social engagement, depression, self-worth, income, education. It does seem most plausible, however, that stimulation is a critical factor. Stimulation in the early years grows complex brains (builds more neurons and richer networks of connections between them). Education may be presumed to provide stimulation - thus, more years of formal education would correlate with more years of stimulation, as well as providing training that encourages the individual to continue to find mental stimulation rewarding. Occupation similarly, can also readily be seen to be correlated with level of stimulation.

#### Why should mental stimulation help prevent cognitive decline?

Stimulation clearly helps the growing brain. But why should stimulating activities help the aging brain? One reason may be that stimulation helps older brains retain sufficient flexibility to compensate for difficulties it experiences by finding different ways of doing things. Keeping the brain active with a variety of cognitive tasks may be one way to retain flexibility. Imaging studies have provided evidence that better-performing seniors show different patterns of brain activity compared to both younger adults and poorer performing seniors, implying that those who perform well in old age are those who have found new ways of processing information. [19]

Activities such as reading, doing crosswords, indeed anything that uses language and keeps you meeting new words, have also been suggested as helping reduce the occurrence of those occasions when you feel you know something, "on the tip of your tongue", but can't quite recall it. Participation in such activities is thought to help by keeping your memory links strong. [20]

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#### Conclusion

My own opinion is that mental stimulation is absolutely critical at all stages of one's life - in infancy and childhood, in early adulthood and middle life, and in old age. While the whole question of neurogenesis (the making of new nerve cells) in adult brains is still unclear, there is no question that connections between neurons continue to be made throughout one's life. We know that connections are stronger when they are used, and grow weak when they have not been used for a long while. We know that the more connections there are, the more possible paths to a memory there are. How could it not be, that the more you use existing connections, and the more connections you make, the easier it will be to remember and think?

#### **References**

### **Mental stimulation**

- Growing evidence points to greater education, and mentally stimulating occupations and activities providing a cognitive reserve that enables people with developing Alzheimer's to function normally for longer.
- There is also evidence that physical exercise and mental stimulation protect against the development of Alzheimer's, by preventing accumulation of beta-amyloid.
- Physical exercise and mental stimulation also seem to help protect against age-related decline in cognitive function, possibly for similar reasons -- by stimulating growth of new blood vessels and keeps existing vessels open and functional.
- Mental stimulation is not only gained by more obvious intellectual pursuits, but also by activities as simple as talking to people or going to the theater.
- Education also seems to help seniors retain their mental flexibility, enabling their brains to change strategies as age effects make different strategies more effective.

The evidence that diet, physical exercise, and mental stimulation all help prevent age-related cognitive decline and reduce the risk of mild cognitive impairment and Alzheimer's, is now very convincing.

Studies of mice and (rather intriguingly) beagles, have provided evidence that 'enriched' environments — ones that provide opportunities for regular exercise and mental stimulation — reduce or prevent age-related cognitive decline, and reduce the risk of Alzheimer's.

Studies of genetically engineered mice have also now shown how an enriched environment protects against Alzheimer's — by preventing accumulation of beta-amyloid, and helping these peptides to be cleared away.

It's been suggested that the benefits of physical and mental activity, which now seem undeniable, may simply be a matter of blood flow — that physical and mental activity stimulates growth of new blood vessels and keeps existing vessels open and functional.

These findings from animal studies have been supported by a number of human studies.

#### **Physical exercise**

A large, six-year study of adults aged 65 and older found that physical fitness and exercise were both associated with a significantly lower risk of dementia. Encouragingly, for those who are more frail, even modest amounts of exercise (such as walking 15 minutes a day) appear beneficial, and the more frail the person was, the more they benefited from regular exercise.

#### Education

Findings from two long-running studies of aging and cognition — the Nun Study and the Religious Orders Study — have revealed that formal education helps protect people from the effects of Alzheimer's disease.

Note that I said "from the effects". Education doesn't prevent or delay the disease from developing, but it does provide a "cognitive reserve", which allows the individual to function normally in the presence of brain abnormalities (the presence of an Alzheimer's pathology is thus only evident when the brain is autopsied postmortem).

As you would expect, the more years of education, the greater the cognitive reserve — the less effect the same number of plaques have on cognitive performance. It's worth noting that the populations in these studies are all relatively well-educated — even the least educated had some college attendance — suggesting that the effect of education would be even more marked in the general population.

However, there is some evidence that, once the disease progresses to the point that it has noticeable effects, those effects progress faster. This is thought to be simply because the damage is so much greater by the time it becomes observable in behavior.

A general population study still in train has provided preliminary findings indicating that prevalence of mild cognitive impairment also is less common among those with more education.

Higher education also seems to help protect older adults from cognitive decline in general. One reason is clearly the cognitive reserve aspect, but an imaging study has also revealed another reason. In young adults performing memory tasks, more education was associated with less use of the frontal lobes and more use of the temporal lobes. For older adults doing the same tasks, more education was associated with less use of the temporal lobes and more use of the frontal lobes. Previous research has indicated frontal activity is greater in old adults, compared to young; this study therefore implies that this effect is related to the educational level

in the older participants. The higher the education, the more likely the older adult is to recruit frontal regions, resulting in a better memory performance.

An earlier brain-scan study also provided support for the theory that the brain may change tactics as it ages, and that older people whose brain is more flexible can compensate for some aspects of memory decline.

Results from a large study of older adults from a biracial community in Chicago suggest that the benefits of education are not necessarily education *per se*. Although both education and occupation were associated with Alzheimer's risk in this study, their effects were substantially reduced when cognitive activity was taken into account.

In keeping with these findings, several smaller studies have also provided evidence that other aspects of mental activity are also associated with a reduced risk of cognitive decline and dementia.

#### Mental activity

People with Alzheimer's have been found to be more likely to have had less mentally stimulating careers, and those who are more active in high school and have higher IQ scores are apparently less likely to have mild memory and thinking problems and dementia as older adults.

A study of 469 people aged 75 and older found that those who participated at least twice weekly in reading, playing games (chess, checkers, backgammon or cards), playing musical instruments, and dancing were significantly less likely to develop dementia. Although the evidence on crossword puzzles was not quite statistically significant, those who did crossword puzzles four days a week had a much lower risk of dementia than those who did one puzzle a week.

Another study of 700 seniors found that more frequent participation in cognitively stimulating activities, such as reading books, newspapers or magazines, engaging

in crosswords or card games, was significantly associated with a reduced risk of Alzheimer's disease.

And more recently, a comprehensive review of the research into 'cognitive reserve', involving 29,000 individuals across 22 studies, concluded that complex mental activity across people's lives almost halves the risk of dementia. Encouragingly, all the studies also agreed that it was never too late to build cognitive reserve.

Looking at the question of cognitive decline in general, a large-scale British study of people aged 35—55 found that those who scored highest on tests of cognitive ability made regular cultural visits to theatres, art galleries and stately homes. Other activities were also associated with higher cognitive ability (in order of importance):

- reading, and listening to music
- involvement in clubs and voluntary organizations
- participation in courses and evening classes

Interestingly, the association was stronger among men.

Another study, of people aged 30—88, has found that those who were fluent in two languages rather than just one, were sharper mentally. This was true at all age groups, but bilinguals were also much less likely to suffer from the mental decline associated with old age. The participants were all middle class, and educated to degree level.

#### Social networks

There has been some evidence suggesting that simply talking helps keep your mind sharp at all ages, and that older people with more extensive social networks are less likely to suffer cognitive impairment.

More recently, a study has provided evidence that social networks also offer a 'cognitive reserve' that protects people from the ravages of Alzheimer's disease. To

determine social network, participants were asked about the number of children they have and see monthly; about the number of relatives, excluding spouse and children, and friends to whom they feel close and with whom they felt at ease and could talk to about private matters and could call upon for help, and how many of these people they see monthly. Their social network was the number of these individuals seen at least once per month.

Post-mortem analysis revealed that, as the size of the social network increased, the same amount of Alzheimer's pathology in the brain (i.e., extent of plaques and tangles) had less effect on cognitive test scores. In other words, for persons without much pathology, social network size had little effect on cognition. However, as the amount of pathology increased, the apparent protective effect on cognition also increased.

#### What you can do

The thought that your education, occupation, degree of physical fitness, and social involvedness, over the years, affects your risk of losing cognitive function, may relieve your anxieties or depress you. But if it depresses you, take heart from a recently-reported pilot study involving people aged 35–69. These people had some mild memory complaints but performed normally on tests. Nevertheless, in a mere two weeks, a program combining a brain healthy diet plan (5 small meals a day; diet rich in omega-3 fats, antioxidants and low-glycemic carbohydrates like whole grains), relaxation exercises, cardiovascular conditioning (daily walks), and mental exercise (such as crosswords and brain teasers) resulted in these participants' brain metabolism decreasing 5% in working memory regions, suggesting an increased efficiency. Compared to the control group, participants also performed better in verbal fluency, and felt as if they were performing better.

### **Preventing Dementia: Mental stimulation**

**Stimulating activities** 

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A 5-year study<sup>1</sup> involving 488 people age 75 to 85 found that, for the 101 people who developed dementia, the greater the number of stimulating activities (reading, writing, doing crossword puzzles, playing board or card games, having group discussions, and playing music) they engaged in, the longer rapid memory loss was delayed. Similarly, a study<sup>2</sup> involving 1321 randomly selected people aged 70 to 89, of whom 197 had mild cognitive impairment, has found that reading books, playing games, participating in computer activities or doing craft activities such as pottery or quilting was associated with a 30 to 50% decrease in the risk of developing memory loss compared to people who did not do those activities.

Moreover, two activities during middle age (50-65) were also significantly associated with a reduced chance of later memory loss: participation in social activities and reading magazines. The value of social activities is consistent with another, small, study<sup>3</sup> that found that social networks, like education, offers a 'protective reserve' capacity that spares individuals the clinical manifestations of Alzheimer's disease. As the size of the social network increased, the same amount of Alzheimer's pathology in the brain had less effect on cognitive test scores. For those without much pathology (plaques and tangles), social network size had little effect on cognition.

This supports another study<sup>4</sup> involving 469 people aged 75 and older, that found that those who participated at least twice weekly in reading, playing games (chess, checkers, backgammon or cards), playing musical instruments, and dancing were significantly less likely to develop dementia. Although the evidence on crossword puzzles was not quite statistically significant, those who did crossword puzzles four days a week had a much lower risk of dementia than those who did one puzzle a week.

Similarly, a study<sup>5</sup> of 700 seniors found that more frequent participation in cognitively stimulating activities, such as reading books, newspapers or magazines, engaging in crosswords or card games, was significantly associated with a reduced risk of Alzheimer's disease. On average, compared with someone with the lowest

activity level, the risk of disease was 47% lower for those whose frequency of activity was highest.

In the first comprehensive review<sup>6</sup> of the research into 'cognitive reserve', which looks at the role of education, occupational complexity and mentally stimulating activities in preventing cognitive decline, researchers concluded that complex mental activity across people's lives almost halves the risk of dementia. All the studies also agreed that it was never too late to build cognitive reserve. The review covered 29,000 individuals across 22 studies.

A review<sup>7</sup> of research on the impact of cognitive training on the healthy elderly (not those with mild cognitive impairment or Alzheimer's disease), has found no evidence that structured cognitive intervention programs affects the progression of dementia in the healthy elderly population.

Post-mortem analysis of participants in a large, long-running study<sup>8</sup> has provided more support for the idea that mental stimulation protects against Alzheimer's. The study found a cognitively active person in old age was 2.6 times less likely to develop dementia and Alzheimer's disease than a cognitively inactive person in old age. This association remained after controlling for past cognitive activity, lifetime socioeconomic status, and current social and physical activity. Frequent cognitive activity during old age was also associated with reduced risk of mild cognitive impairment.

Research involving genetically engineered mice<sup>9</sup> has found that mice whose brains had lost a large number of neurons regained long-term memories and the ability to learn after their surroundings were enriched with toys and other sensory stimuli, pointing to the importance of maintaining cognitive stimulation as long as possible. Similarly, another mouse study<sup>10</sup> found that short but repeated learning sessions can slow the development of those hallmarks of Alzheimer's, beta amyloid plaques and tau tangles. And another<sup>11</sup> found that an enriched environment, with more opportunities to exercise, explore and interact with others, dramatically reduces levels of beta-amyloid peptides.

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#### **Education & iq**

A study<sup>12</sup> involving some 6,500 older Chicago residents being interviewed 3yearly for up to 14 years (average 6.5 years), has found that while at the beginning of the study, those with more education had better memory and thinking skills than those with less education, education was not related to how rapidly these skills declined during the course of the study. The result suggests that the benefit of more education in reducing dementia risk results simply from the difference in level of cognitive function.

Another study<sup>13</sup> has come out supporting the view that people with more education and more mentally demanding occupations may have protection against the memory loss that precedes Alzheimer's disease, providing more evidence for the idea of <u>cognitive reserve</u>. The 14-month study followed 242 people with Alzheimer's disease, 72 people with mild cognitive impairment, and 144 people with no memory problems.

Another study<sup>14</sup> has come out confirming that people with more years of education begin to lose their memory later than those with less education, but decline faster once it begins. Researchers note that since the participants were born between 1894 and 1908, their life experiences and education may not represent that of people entering the study age range today.

A study<sup>15</sup> of 312 New Yorkers aged 65 and older, who were diagnosed with Alzheimer's disease and monitored for over 5 years, found that overall mental agility declined faster for each additional year of education, particularly in the speed of thought processes and memory, and was independent of age, mental ability at diagnosis, or other factors likely to affect brain function, such as depression and vascular disease. It's suggested this may reflect the greater ability of brains with a higher cognitive reserve to tolerate damage, meaning the damage is greater by the time it becomes observable in behavior.

The Nun Study<sup>16</sup> found that nuns who completed 16 or more years of formal education or whose head circumference was in the upper two-thirds were four times less likely to be demented than those with both smaller head circumferences and lower education.

Post-mortem study<sup>17</sup> of the brains of 130 participants in the Religious Orders Study found that the relationship between cognitive performance and the number of amyloid plaques in the brain changed with level of formal education. The more years education you had, the less effect the same number of plaques had on actual cognitive performance. It's worth noting that this considerable difference was observed in a population where even the least educated had some college attendance; presumably the difference would be even more marked in the general population.

A long-running Finnish study<sup>18</sup> has found that compared with people with five or less years of education, those with six to eight years had a 40% lower risk of developing dementia and those with nine or more years had an 80% lower risk. Generally speaking, people with low education levels seemed to lead unhealthier lifestyles, but the association remained after lifestyle choices and characteristics such as income, occupation, physical activity and smoking had been taken into account.

An analysis of high school records and yearbooks from the mid-1940s<sup>19</sup>, and interviews with some 400 of these graduates, now in their 70s, and their family members, has found that those who were more active in high school and who had higher IQ scores, were less likely to have mild memory and thinking problems and dementia as older adults.

An analysis<sup>20</sup> of 184 people with dementia found that the mean age of onset of dementia symptoms in the 91 monolingual patients was 71.4 years, while for the 93 bilingual patients it was 75.5 years — a very significant difference.

A study<sup>21</sup> of 122 people with Alzheimer's and 235 people without the disease found that people with Alzheimer's are more likely to have had less mentally stimulating careers than their peers who do not have Alzheimer's.

A study<sup>22</sup> of 173 people from the <u>Scottish Mental Survey</u> of 1932 who have developed dementia has found that, compared to matched controls, those with <u>vascular dementia</u> were 40% more likely to have low IQ scores when they were children than the people who did not develop dementia. This difference was not true for those with Alzheimer's disease. The findings suggest that low childhood IQ may act as a risk factor for vascular dementia through vascular risks rather than the "cognitive reserve" theory.

#### **References**

# **Effects of mental exercise on cognitive function**

- Cognitive decline is less in those who engage more frequently in cognitively stimulating activities.
- Activities that keep you actively searching for words (such as scrabble and crosswords) may help reduce those tip-of-the-tongue experiences where particular words cannot quite be recalled.
- Cognitive training programs can reverse cognitive impairment in many seniors

### **News reports**

#### **Cognitive training**

#### Mental exercise helps maintain cognitive function during aging

A review of clinical trials which have examined the effect of cognitive exercise on longitudinal cognitive performance in healthy elderly individuals found 7 studies

that met the criteria, and concluded that cognitive exercise training in healthy older individuals produced strong and long-lasting protective effects on cognitive performance, although it has yet to be shown to prevent incident dementia. [1]

#### Brain exercises improve memory and processing speed

In the first study to link a commercially available software program to improvement on unaffiliated standard measures of memory and to better performance on everyday tasks, a study involving 487 healthy adults over the age of 65 has found that those who used the Brain Fitness Program for 40 hours over the course of eight weeks (an hour a day, five days a week) became twice as fast in processing, while those who spent the same amount of time watching videos on art, history and literature topics followed by quizzes showed no significant improvement. They also performed significantly better on memory and attention tests for which they did not train, and many also reported significant improvements in everyday cognitive activities such as remembering names or understanding conversations in noisy restaurants. The Brain Fitness Program consists of six auditory exercises designed to help the brain improve the speed and accuracy of processing. [2]

#### No support for 'brain exercise' software for healthy elderly

A review of research on the impact of cognitive training on the healthy elderly (not those with mild cognitive impairment or Alzheimer's disease), has found no evidence that structured cognitive intervention programs affects the progression of dementia in the healthy elderly population. This is not to say that it doesn't; the fault lies in the quality of the research. The researchers found only a very small number of studies that met their criteria. Those that did meet the criteria were mostly found to be limited in their methodologies or lacking in follow-up. They concluded that more random clinical trials in cognitive training need to be conducted with sufficient follow-up time that can actually measure changes in daily functioning. [3]

The Seattle Longitudinal Studies of adult intelligence suggested that the observed decline in many community-dwelling older people is probably a function of disuse and is often reversible. It was found that some 2/3 of participants in a cognitive training program showed significant improvement, and 40% of those who had declined significantly were indeed returned to their earlier (pre-decline) level of cognitive functioning. These training gains were retained over seven years. [4]

#### **Stimulating activities**

#### Some activities associated with less memory loss

A study involving 1321 randomly selected people aged 70 to 89, of whom 197 had mild cognitive impairment, has found that reading books, playing games, participating in computer activities or doing craft activities such as pottery or quilting was associated with a 30 to 50% decrease in the risk of developing memory loss compared to people who did not do those activities. Also, those who watched television for less than seven hours a day were 50% less likely to develop memory loss than people who watched for more than that. Other activities in later age were not significantly associated with a reduced chance of having MCI. Only two activities during middle age (50-65) were significantly associated with a reduced chance of later memory loss: participation in social activities and reading magazines. [5]

## More support for importance of stimulation to protect against cognitive decline

A British study questioned some 5,350 civil servants aged between 35 and 55 about their participation in 13 leisure activities, ranging from DIY and housework to cultural visits and evening classes. They were then given tests in verbal memory, mathematical reasoning, vocabulary and verbal fluency. Independent of socio-economic position, the highest level of cognitive ability was associated with regular cultural visits to theatres, art galleries and stately homes. This was closely followed by reading and listening to music, then by involvement in clubs and

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voluntary organisations, and participation in courses and evening classes. The association was stronger among men. While the researchers suggested that seeking mental stimulation may have a beneficial effect on cognition in middle age, and the research was popularly reported as indicating that "going to the pub is good for the brain" (going to the pub was indeed associated with a slightly higher cognitive ability, but less so that the afore-mentioned), it must be remembered that correlation does not imply causation. [6]

#### Regular participation in cognitive activities reduces Alzheimer's risk

6,158 persons aged 65 years and older from a biracial community in Chicago selfrated current frequency of participation in seven cognitive activities (e.g., reading a newspaper) and nine physical activities (e.g., walking for exercise). Four years later, 842 of those judged dementia-free were given a detailed clinical evaluation. 139 of these met criteria for Alzheimer's on clinical evaluation. When adjusted for age, education, sex, race, and possession of the gene allele associated with Alzheimer's, a one-point increase in cognitive activity score was associated with a 64% reduction in risk of Alzheimer's. Weekly hours of physical activity had no effect. Education and occupation were both associated with Alzheimer's risk, but these effects were substantially reduced when cognitive activity was taken into account. [7]

#### Mentally stimulating activities reduces cognitive decline

A study of 700 seniors over several years found that more frequent participation in cognitively stimulating activities, such as reading books, newspapers or magazines, engaging in crosswords or card games, was significantly associated with a reduced risk of Alzheimer's disease (AD). General cognitive decline was also less among people who did more cognitively stimulating activities, in particular, in working memory, perceptual speed, and episodic memory. It is not yet known whether engaging in such activities helps prevent cognitive decline, or whether those who develop cognitive impairment are less likely to engage in cognitively stimulating activities. [8]

#### Leisure activity decreases risk of Alzheimer's disease

1,772 people age 65 or older participated in a 7-year study that investigated the effect of leisure activities on risk of dementia. It was found that, even when controlling for factors like ethnic group, education and occupation, those with high leisure activity had 38% less risk of developing dementia. There also appeared to be a cumulative effect, with an additional 8% risk reduction associated with each leisure activity engaged. Activities of all kinds were shown to be beneficial, but intellectual activities were associated with the highest risk reduction. [9]

#### Being fluent in two languages may help keep the brain sharper for longer

A study of 104 people aged between 30 and 88 has found that those who were fluent in two languages rather than just one were sharper mentally. Those fluent in two languages responded faster on tasks assumed to place demands on working memory, compared to those who were fluent in just English, at all age groups. This is consistent with the theory that constant management of 2 competing languages enhances executive functions. Bilingual volunteers were also much less likely to suffer from the mental decline associated with old age. The finding is consistent with other research suggesting that mental activity helps in protecting older adults from mental decline. The participants were all middle class, and educated to degree level. Half of the volunteers came from Canada and spoke only English. The other half came from India and were fluent in both English and Tamil. [10]

#### Social stimulation

#### Active social life may delay memory loss among older adults

Data gathered from 1998 to 2004 from the very large U.S. Health and Retirement Study has supported previous research suggesting that social activity is associated with slower cognitive decline. Indeed, memory decline among those with the highest social integration was less than half the rate among the least integrated. Social integration was assessed by marital status, volunteer activity, and frequency of contact with children, parents, and neighbors. The findings were independent of sociodemographic factors (such as age, gender, and race) and health status in 1998. The researchers found that the protective effect of social integration was largest among individuals with fewer than 12 years of education. There was no evidence that a poor or declining memory caused social withdrawal. [11]

Incidentally, another study that appeared in the same issue found that larger social networks were associated with a lower risk of dementia in women aged 78 and older. The study examined 2249 members of a health maintenance organization who were free of dementia at the start of the study. 268 (12%) of these were identified as having dementia four years later. [12]

#### 10 minutes of talking has a mental payoff

A study of 3,610 people aged 24—96 examined mental functioning and social interaction, and found that, across all ages, cognitive functioning was better the The higher the level of participants' social interaction. Participants' level of social interactions was assessed by asking how often each week they talked on the phone with friends, neighbors and relatives, and how often they got together. Researchers controlled for age, education, race/ethnicity, gender, marital status and income, physical health and depression. In a second experiment involving college students, short-term social interaction lasting for just 10 minutes boosted participants' intellectual performance as much as engaging in so-called 'intellectual' activities for the same amount of time. [13]

#### Talking may help seniors guard against memory decline

Earlier research has indicated cognitively stimulating activities (such as doing crosswords, playing scrabble, bridge, etc.) may help protect against cognitive decline (and perhaps even Alzheimers). Now a new report (not yet published) from the Institute for Social Research at the University of Michigan supports and extends this research by suggesting that simply talking helps keep your mind sharp at all ages. The lead researcher also speculates that, by encouraging children to develop their social skills, parents and teachers could also be helping them to

improve their intellectual skills. And in the workplace, instead of encouraging employees to keep their noses to computer monitors and complete their tasks, effective supervisors might encourage them to take plenty of time out to socialize. [13]

#### Low self-esteem 'shrinks brain'

A 15-year study of 92 seniors found that those with a low sense of self worth were more likely to suffer from memory loss as they got older. Moreover, the brains of those with low self-worth were up to a fifth smaller than those who felt good about themselves. It is speculated that those who are anxious and think negatively may set themselves up for memory loss by not bothering to engage themselves in activities that would stimulate and enrich their brains. [14]

#### Education

#### Education may not affect how fast you will lose your memory

A study involving some 6,500 older Chicago residents being interviewed 3-yearly for up to 14 years (average 6.5 years), has found that while at the beginning of the study, those with more education had better memory and thinking skills than those with less education, education was not related to how rapidly these skills declined during the course of the study. The result suggests that the benefit of more education in reducing dementia risk results simply from the difference in level of cognitive function. [15]

#### Older adults with more schooling spend fewer years with cognitive loss

A seven-year study involving over 7,000 people 70 years and older has found that a 70-year old person with at least 12 years of education can expect to live 14.1 more years without cognitive impairment, which is two-and-a-half years more than 70-year olds with fewer than 12 years of education. They can then expect to spend 1 year with impairment, which is about 7 months less than a person with fewer years of education. The impairment is also likely to be more severe for the more educated, and associated with worse health. This is consistent with the idea of cognitive reserve — that education provides a "buffer" that enables people to continue functioning well despite physical damage in the brain. However, when the damage finally can no longer be compensated for, the effects will be greater. But it shouldn't be assumed that it is all downhill from there — even the severely impaired may recover, depending on the cause. Overall, about 11% of the mentally impaired recover, presumably because the decline is caused by a treatable condition. [16]

#### Risk of mild cognitive impairment increases with less education

A study of 3,957 people from the general population of Olmsted County, Minnesota is currently in train to find how many of those who did not have dementia might have mild cognitive impairment. A report on the findings so far suggests 9% of those aged 70 to 79 and nearly 18% of those 80 to 89 have MCI. Prevalence varied not only with age but also years of education: 25% in those with up to eight years of education, 14% in those with nine to 12 years, 9% in those with 13 to 16 years, and 8.5% in those with greater than 16 years. [17]

#### How higher education protects older adults from cognitive decline

Research has indicated that higher education helps protect older adults from cognitive decline. Now an imaging study helps us understand how. The study compared adults from two age groups: 18-30, and over 65. Years of education ranged from 11 to 20 years for the younger group, and 8 to 21 for the older. Participants carried out several memory tasks while their brain was scanned. In young adults performing the memory tasks, more education was associated with less use of the frontal lobes and more use of the temporal lobes. For the older adults doing the same tasks, more education was associated with less use of the frontal lobes and more use of the frontal lobes. Previous research has indicated frontal activity is greater in old adults, compared to young; the new study suggests that this effect is related to the educational level in the older participants. The

higher the education, the more likely the older adult is to recruit frontal regions, resulting in a better memory performance. [18]

#### Lifestyle

#### Age differences in cognitive benefits of exercise and mental stimulation

A mouse study has found that while physical exercise (a running wheel) and mental stimulation (toys), singly and together, improved memory in old mice, exercise alone or exercise and stimulation improved memory in middle-aged mice but not stimulation alone, and only exercise alone benefited young mice. The results suggest that as we get old and maybe less able to exercise, cognitive stimulation can help to compensate, but exercise is central to memory reinforcement at all ages. [19]

#### Simple Lifestyle Changes May Improve Cognitive Function

A study involving 17 people (35–69 years) with mild self-reported memory complaints but normal baseline memory performance scores, has found that 2 weeks on a program combining a brain healthy diet plan (5 small meals a day; diet rich in omega-3 fats, antioxidants and low-glycemic carbohydrates like whole grains), relaxation exercises, cardiovascular conditioning (daily walks), and mental exercise (such as crosswords and brain teasers) resulted in participants' brain metabolism decreasing 5% in working memory regions (left dorsolateral prefrontal cortex), suggesting an increased efficiency. Compared to the control group, participants also performed better in verbal fluency. [20]

#### Lifestyle changes improve seniors' memory surprisingly quickly

A small 14-day study found that those following a memory improvement plan that included memory training, a healthy diet, physical exercise, and stress reduction, showed a 5% decrease in brain metabolism in the dorsal lateral prefrontal region of the brain (involved in working memory) suggesting they were using their brain more efficiently. This change in activity was reflected in better performance on a

cognitive measure controlled by this brain region, and participants reported that they felt their memory had improved. The memory training involved doing brainteasers, crossword puzzles and memory exercises. Diet involved eating 5 small meals daily (to prevent fluctuations in blood glucose levels) that were rich in omega-3 fats, low-glycemic index carbohydrates (e.g., whole grains) and antioxidants. Physical exercise involved brisk walking and stretching, and stress reduction involved stretching and relaxation exercises. [20]

#### Diet, exercise, stimulating environment helps old dogs learn

A new study of beagles provides more evidence that diet and mental stimulation are important in reducing or preventing age-related cognitive decline. The study, involving 48 older beagles (aged 7 to 11), compared four combinations of behavioral enrichment (regular exercise and lots of mental stimulation) and supplementation of diet with antioxidants had on a beagle's ability to learn: regular diet and regular experience; regular diet and enriched experience; regular experience and an enriched diet; and enriched diet and an enriched experience. The study followed the beagles over two years. Those in the groups with either an enriched diet or enriched environment did better than those without either, but those who had both the enriched diet and an enriched environment did noticeably better than all the rest. [21]

#### **References**

### Memory training for seniors

A review of the research shows that memory training can significantly improve memory performance in older adults. What is intriguing is that it has much less effect on their beliefs about their memory abilities. This fits in, of course, with the general finding that people tend to be very poor in assessing their own memory abilities. Research indicates that training which includes instruction designed to modify people's expectancies and beliefs about memory, is more successful than training which deals solely with memory strategies. Providing more background information about the memory strategies - why it works, etc - also appears to lead to greater memory improvement. This is, of course, the basis for my own book on memory, and of this website.

It has also been suggested that a complex and intellectually stimulating environment helps prevent cognitive decline in later life. Certainly it seems that, for whatever reason, cognitive decline is less in those who engage more frequently in cognitively stimulating activities. It has also been suggested that word games (such as scrabble and crosswords) may help reduce those tip-of-the-tongue experiences where particular words cannot quite be recalled.

#### **Resources:**

I've had a look around the Web for sites that can offer opportunities to stimulate the brain or, even better, train it in particular memory skills. I've listed a few below. But my absolute favorite for training and practice in attention and memory skills is the Lumosity site, which is very nicely designed and based on the scientific research -- click here for a <u>Free Trial.</u>

Another general training site is the French-run Happy Neuron site.

Free resources are not of course nearly as sophisticated, but here's a few for you to play with:

There's some games <u>indexed here</u> that might help you increase your digit span (a measure of working memory capacity).

You can also work on improving your working memory capacity in the <u>Memory</u> <u>Gym</u> Brainfit also offers a few games for improving your attention and working memory capacity.

And <u>NASA has a few games</u> that I quite like this because it also offers information about how memory works in these particular situations.

#### Mental stimulation:

http://www.queendom.com/mindgames/

http://www.psychtests.com/mindgames/

#### word puzzles:

http://www.vocabulary.com/

http://www.rozies.com/Zzzz/Ringers/R-index.html

http://wordzap.com/enigma.asp

http://www.etymologic.com/

http://www.thepotters.com/puzzles.html

http://members.cox.net/jjschnebel/palin.html (thinking up palindromes)

for more, you can search <u>http://www.wolinskyweb.com/word.htm</u> where " most of the great sites on the web devoted to puns, slanguage, anagrams, puzzles, MadLibs, and lots more" have been catalogued.

#### Memory & cognitive tests:

test your memory for news events at: <u>http://memory.uva.nl/</u>

check your IQ at: http://www.iqtestexperts.com/

#### **Research report**

# Dunlosky, J. & Connor, L.T. (1997). Age differences in the allocation of study time account for age differences in memory performance. *Memory and Cognition*, *25*, 691-700.

- It is well-established that older adults commonly need to practice more than younger adults to achieve the same level of performance.
- It may be that such age deficits in remembering are at least partly due to poorer monitoring of their learning.

It has been well-established that, compared to younger adults, older adults require more practice to achieve the same level of performance<sub>1</sub>. Sometimes, indeed, they may need twice as  $much_2$ .

In the present study, two groups of adult subjects were given paired items to learn during multiple study-test trials. During each trial items were presented at the subject's pace. Afterwards the subjects were asked to judge how likely they were to be able to recall each item in a test.

It was found that people were very good at accurately judging the likelihood of their correct recall. Correlations between judgments and the amount of time the subjects studied the items suggested that people were monitoring their learning and using this to allocate study time.

However, older adults (with a mean age of 67) used monitoring to a lesser degree than the younger adults (with a mean age of 22), and the results suggested that part of the reason for the deficit in recall commonly found with older adults is due to this factor.

#### **References**

# **Effectiveness of training in cognitive strategies**

- Instruction in specific memory strategies has improved performance in older adults.
- The keyword mnemonic has been successfully used to teach Spanish words to elderly women.
- Computerized memory training has had some success in improving memory performance in seniors.

#### Gruneberg, M.M. & Pascoe, K. 1996. The Effectiveness of the Keyword Method for Receptive and Productive Foreign Vocabulary Learning in the Elderly. *Contemporary Educational Psychology*, 21, 102-9.

The mnemonic technique known as the keyword method is of demonstrated effectiveness in learning facts such as foreign language words. However, there has been little research looking at its effectiveness for elderly people specifically. In the experiment reported here, a group of elderly women were required to learn 20 Spanish vocabulary items using the keyword method of foreign language learning. This involves using a mediator to link an English word to its Spanish target. It was found that the keyword method was an effective means of learning new words, compared to being provided with no instruction for learning.

#### Rebok, G.W., Rasmusson, D.X., & Brandt J. 1996. Prospects for Computerized Memory Training in Normal Elderly: Effects of Practice on Explicit and Implicit Memory Tasks. *Applied Cognitive Psychology*, *10*, 211-223.

Twelve cognitively normal, elderly adults (mean age=76 years) were given training and practice on the Colorado Neuropsychology Tests, a computerized battery of explicit and implicit memory tasks. Half the participants practised on the explicit memory tasks for 1.5 hours a week for 9 weeks with the assistance of a psychologist, while the other half practiced on the implicit tasks for the equivalent amount of time.

Both training conditions produced significant improvement in their performance on the tests, with those in the implicit memory condition showing the most overall improvement.

In general, the participants responded positively toward the computer technology and demonstrated their capability in learning to operate the computer software. The results support the use computerized memory training with normal elderly adults.

#### **News reports**

#### Mental exercise helps maintain cognitive function during aging

A review of clinical trials which have examined the effect of cognitive exercise on longitudinal cognitive performance in healthy elderly individuals found 7 studies that met the criteria, and concluded that cognitive exercise training in healthy older individuals produced strong and long-lasting protective effects on cognitive performance, although it has yet to be shown to prevent incident dementia. [22]

#### Brain exercises improve memory and processing speed

In the first study to link a commercially available software program to improvement on unaffiliated standard measures of memory and to better performance on everyday tasks, a study involving 487 healthy adults over the age of 65 has found that those who used the Brain Fitness Program for 40 hours over the course of eight weeks (an hour a day, five days a week) became twice as fast in processing, while those who spent the same amount of time watching videos on art, history and literature topics followed by quizzes showed no significant improvement. They also performed significantly better on memory and attention tests for which they did not train, and many also reported significant improvements in everyday cognitive activities such as remembering names or understanding conversations in noisy restaurants. The Brain Fitness Program consists of six auditory exercises designed to help the brain improve the speed and accuracy of processing. [23]

#### No support for 'brain exercise' software for healthy elderly

A review of research on the impact of cognitive training on the healthy elderly (not those with mild cognitive impairment or Alzheimer's disease), has found no evidence that structured cognitive intervention programs affects the progression of dementia in the healthy elderly population. This is not to say that it doesn't; the fault lies in the quality of the research. The researchers found only a very small number of studies that met their criteria. Those that did meet the criteria were mostly found to be limited in their methodologies or lacking in follow-up. They concluded that more random clinical trials in cognitive training need to be conducted with sufficient follow-up time that can actually measure changes in daily functioning. [24]

#### Strategic video game improves critical cognitive skills in older adults

In the first study into the effects of playing video games for adults in their 60s and 70s, it's been found that playing a strategic video game that rewards nationbuilding and territorial expansion can have pronounced effects on cognitive skills not directly related to the skills learned in the video game. The finding is also exciting as a rare demonstration of a training program that improves more than simply the task being practiced. The game "Rise of Nations" was selected because of its emphasis on resource management and planning. The researchers hoped it would benefit executive function, which is one of the cognitive functions particularly impacted by age and includes things like scheduling, planning, working memory, multitasking and dealing with ambiguity. Half of the 40 older adults in the study received 23.5 hours of training in the game. As a group, the gamers became significantly better and faster at switching between tasks as compared to the comparison group. Their working memory and their reasoning ability was also significantly improved. To a lesser extent, their short-term memory of visual cues and their ability to identify rotated objects was also improved. Training had no effect on ability to recall a list of words in order, enumeration ability or ability to inhibit certain responses. The amount of improvement was linked to performance on the game. [25]

#### Searching the Internet increases brain function

A study involving 24 older adults (aged 55-76), of whom half had experience searching the Internet, and half no experience, has found that while all participants showed the same significant brain activity in language and visual regions while reading a book, when searching the internet the Web-savvy group also registered activity in regions controlling decision-making and complex reasoning (in the frontal, temporal and cingulate areas). Overall, volunteers with prior experience registered a twofold increase in brain activation when compared with those with little Internet experience. It's likely that inexperienced users failed to grasp the strategies needed to successfully engage in an Internet search. The findings add to the research pointing to the value of mentally stimulating activities for maintaining cognitive health in the older brain, and adds a new recommended activity to the list. The well-known researcher, Dr Gary Small, has also released a new book expanding on this research: "iBrain: Surviving the Technological Alteration of the Modern Mind." [26]

#### How to benefit from memory training

Brain and memory training programs are increasingly popular, but they don't work well for everyone. In particular, they tend to be much less effective for those who need them the most — those 80 and older, and those with lower initial ability. But a new study shows the problem is not intrinsic, but depends on the strategies people use. The study found that people in their 60s and 70s used a strategy of spending most of their time on studying the materials and very little on the test, and showed large improvements over the testing sessions. By contrast, most people in their 80s and older spent very little time studying and instead spent most of their time on the test. These people did not do well and showed very little improvement even after two weeks of training. [27]

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#### Aging adults have choices when confronting perceived mental declines

A researcher who has been studying changes we make – or fail to make – in the way we process and regulate our reading as we age has found that older adults who remember more of what they've read tend to have developed strategies to deal with the decline in some cognitive abilities that tends to occur as we get older. One thing they do is to spend more time building a "situation model" at the beginning of a story or book. They take time to get a feel for the setting, to get to know the characters, and to get grounded in important details of the story. This enables them to more easily integrate new information later on. They also pause longer and more often to integrate new concepts or to orient themselves to a change of setting in the text. [28]

#### Brain network associated with cognitive reserve identified

An imaging study involving young (18-30) and older (65-80) adults has identified a brain network within the frontal lobe that is associated with cognitive reserve, the process that allows individuals to resist cognitive decline due to aging or Alzheimer's disease. Those with higher levels of cognitive reserve were able to activate this network in the brain while working on more difficult tasks, while participants with lower levels of reserve were not able to tap into this particular network. The network was found more often in younger participants, suggesting the network may degrade during aging. [29]

#### Mental training helps maintain some seniors' cognitive skills

The Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) Study involved 2,832 adults aged 65 and older (average age 73.6 years). Participants were randomly assigned to four groups, three of which took part in training that targeted a specific cognitive ability (memory, reasoning or speed of processing). The fourth group was a control group and received no cognitive training. People in the three intervention groups attended up to 10 training sessions lasting 60 to 75 minutes each, over a five- to six-week time period. The memory

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group learned strategies for remembering word lists and sequences of items, text, and story ideas and details. The reasoning group learned strategies for finding the pattern in a letter or word series and identifying the next item in a series. The speed-of-processing group learned ways to identify an object on a computer screen at increasingly brief exposures, while quickly noting where another object was located on the screen. After the initial training, some also took part in 4 75-minute "booster" sessions at 11 and 35 months after training.

Immediately after the initial training, 87% of the speed-training group, 74% of the reasoning group and 26% of the memory group showed improvement in the skills taught. After five years, people in each group performed better on tests in their respective areas of training than did people in the control group. The reasoning-training and speed-training groups who received booster training had the greatest benefit. After five years, all three intervention groups still retained improvement in the cognitive abilities targeted by the intervention. They also reported less difficulty than the control group in tasks such as preparing meals, managing money and doing housework, but only the effect of reasoning training and follow-up booster training scored better on how quickly and accurately they could find items on a pantry shelf, make change, read medicine dosing instructions, place telephone calls and react to road traffic signs, but booster training for the other two groups did not have a significant effect on this ability. Booster training did however produce additional improvement in reasoning for the reasoning group. [30]

#### Actors' memory tricks help students and older adults

The ability of actors to remember large amounts of dialog verbatim is a marvel to most of us, and most of us assume they do by painful rote memorization. But two researchers have been studying the way actors learn for many years and have concluded that the secret of actors' memories is in the acting; an actor learning lines by focusing on the character's motives and feelings — they get inside the character. To do this, they break a script down into a series of logically connected "beats" or intentions. The researchers call this process active experiencing, which

uses "all physical, mental, and emotional channels to communicate the meaning of material to another person." This principle can be applied in other contexts. For example, students who imagined themselves explaining something to somebody else remembered more than those who tried to memorize the material by rote. Physical movement also helps — lines learned while doing something, such as walking across the stage, were remembered better than lines not accompanied with action. The principles have been found useful in improving memory in older adults: older adults who received a four-week course in acting showed significantly improved word-recall and problem-solving abilities compared to both a group that received a visual-arts course and a control group, and this improvement persisted four months afterward. [31]

#### 'Imagination' helps older people remember to comply with medical advice

A new study suggests a way to help older people remember to take medications and follow other medical advice. Researchers found older adults (aged 60 to 81) who spent a few minutes picturing how they would test their blood sugar were 50% more likely to actually do these tests on a regular basis than those who used other memory techniques. Participants were assigned to one of three groups. One group spent one 3-minute session visualizing exactly what they would be doing and where they would be the next day when they were scheduled to test their blood sugar levels. Another group repeatedly recited aloud the instructions for testing their blood. The last group were asked to write a list of pros and cons for testing blood sugar. All participants were asked not to use timers, alarms or other devices. Over 3 weeks, the "imagination" group remembered 76% of the time to test their blood sugar at the right times of the day compared to an average of 46% in the other two groups. They were also far less likely to go an entire day without testing than those in the other two groups. [32]

Older adults show two kinds of cognitive-processing deficits: under-recruitment, where appropriate areas of the brain are less likely to be utilised without specific instruction, and non-selective recruitment, where non-relevant regions of the brain are more likely to be used. A recent imaging study confirmed that older adults

were less likely than younger ones to use the critical frontal regions when performing a memory task, and more likely to use cortical regions that are not as useful. However, when subjects were given specific strategy instructions, the older adults showed increased activity in the frontal regions, and their remembering improved. Even with this support however, older adults still showed a greater tendency to use brain regions that were not useful. [33]

#### **References**

### **Mnemonics**

- Mnemonics can be effective strategies for older adults, but they require more training than younger adults
- Mnemonic strategies with less memory load, like the keyword and the facename association methods, are better strategies for older adults than strategies with a high memory load, such as the pegword and loci methods
- The durability and effectiveness of mental images are enhanced if you spend some time attending to the quality of the image (e.g., how pleasant it is)
- Because older adults have more trouble changing their habits, they are much less likely to continue to use a new method without explicit instructions to do so
- Mnemonics that involve words rather than images may be more useful for most older adults
- Mnemonics are not particularly useful for remembering information heard in the course of conversation, remembering an action performed, remembering to do something. Teaching yourself to repeat information is probably a more useful skill.

Aids to memory such as acronyms, rhymes, linking information by creating visual images or making up a story, are called mnemonics. Most popular memory courses teach mnemonic strategies. It is however only one type of memory strategy.

Mnemonics are however particularly appropriate for remembering names and dates. In a survey of over 100 elderly adults, learning and remembering people's names, and learning and remembering dates, were the two memory skills they most wanted to improve. [1]

However, although mnemonics can be very effective, they do require a great deal of effort to master. In this page I report on research into the usefulness of various mnemonic strategies for older adults.

#### **Pegword method**

The pegword mnemonic is a strategy for learning lists. You memorize a list that converts numbers into visual images (one is a bun, two is a shoe, etc), and then use those images as pegs for the items you wish to remember. Thus, to remember a shopping list you imagine each item in turn with these images: an apple in a bun; a shoe full of beans; etc.

While the pegword strategy is effective, it does require a lot of training to be used successfully, and doesn't appear to be a good strategy for older adults.

Four studies have found no lasting improvement in memory when middle-aged or elderly subjects have been instructed in the pegword technique. [2]

#### Method of loci

The method of loci (places) is the classic mnemonic, first invented by the ancient Greeks, and is considerably easier to learn than the pegword technique. Using a place you know very very well - perhaps a familiar route, your house, or a particular room in it - you mentally visualize the items you want to remember in particular places.

This technique has had somewhat more success in improving memory in older adults, although not to the extent seen in younger adults taught the strategy. This may be due to older adults' slower rate of processing information. Older adults who are already experienced in using imagery are likely to find the technique more useful.

One early study found elderly subjects successfully used the method, but only when explicitly instructed to do so. [3]

Later researchers found elderly subjects could be trained to use the method to remember shopping list items, but tended not to use it when asked to learn new lists several weeks later, and many reported not using the strategy when interviewed several years later. [4]

Other studies found the improved memory performance seen in elderly subjects was less than that found for similarly trained young adults. [5]

The reduced benefit of the method to older adults may be due to their slower rate of processing information. One study found that elderly adults who were experienced in using imagery (graphic designers) performed better than other elderly adults, although still not to the level of young adults. [6]

#### **Keyword method**

One of the most effective mnemonic strategies is the keyword method. This is particularly effective for learning new words. One study successfully taught a group of older women Spanish words using the keyword method of foreign language learning. [7]

#### **Face-name associations**

Perhaps the most widely used mnemonic is the face-name association method. This strategy involves choosing something distinctive about the face, finding a word or phrase (the "keyword") that is similar to the name, and creating a visual image that links the distinctive feature with the keyword.

One study found older adults significantly improved their memory of names using this method, although the improvement was limited (they still only remembered 24% of names - but this was double what they remembered prior to training). [8]

#### General remarks about mnemonic training

Long-lasting memory improvement is hampered by the difficulty older adults have in changing their habits - that is, they rarely use a new method without explicit instructions to do so.

The effectiveness of the method of loci and keyword method can apparently be increased by having the participants make affectiveness judgments (such as judging the degree of pleasantness) of each image they generate. This appears not only to increase the degree of improvement, but also the durability of the images (how long they are remembered for). [9]

While relaxation training may improve learning in elderly adults who are anxious, it appears to hinder learning if the participants have low anxiety levels! [10]

It does appear that age affects mnemonic training, in that it becomes less effective the older you are, especially with the more complex method of loci vs the simpler keyword methods. [11] This is not to say older adults cannot learn these techniques, merely that that older adults need extensive and intensive training to really benefit. [12]

Older adults can learn effectively by teaching themselves, but such instruction needs to be supplemented by periodic group discussions. [13]

Verbal mnemonics may be more useful for older adults who find imagery effortful. One study found that a take-home manual on the use of organization in aiding memory resulted in substantial improvement. [14] The story method has also been found to be of benefit [15], although its effectiveness depends on the person's ability to construct a narrative. [16] The most problematic memory tasks for older adults however are probably those which involve information experienced only once, incidentally – something heard in the course of conversation, remembering an action performed, remembering to do something. Training in the benefits of repetition is probably of more benefit than mnemonic training, for these instances.

#### **References**

### Effects of exercise on cognitive function

- A large-scale study of women aged 65 and older found that cognitive decline was least common in those who were most physically active.
- A large-scale study of men aged 71 and older found that those who walked less than a quarter of a mile a day were nearly twice as likely to develop dementia as those who walked more than two miles a day.
- Aerobic exercise appears to improve higher cognitive functions (planning, organization and working memory), in the elderly.
- One way physical training may help cognitive function in the elderly is by increasing their confidence in their abilities.

#### **News reports**

#### Resistance training improves attention in older women

A study involving 155 women aged 65-75 has found that those who participated in resistance training once or twice weekly for a year significantly improved their selective attention (maintaining mental focus) and conflict resolution (as well as muscular function of course!), compared to those who participated in twice-weekly balance and tone training. Performance on the <u>Stroop test</u> improved by 12.6% and 10.9% in the once-weekly and twice-weekly resistance training groups respectively, while it deteriorated by 0.5% in the balance and tone group. Improved attention and conflict resolution was also significantly associated with increased gait speed. [34]

#### **Exercise helps prevent, improve MCI**

A clinical trial involving 33 older adults (55-85) with mild cognitive impairment (MCI) has found that women who exercised at high intensity levels with an aerobics trainer for 45 to 60 minutes per day, four days per week, significantly improved performance on multiple tests of executive function, compared to those who engaged in low-intensity stretching exercises. The results for men were less significant: high-intensity aerobics was associated only with improved performance on one cognitive task, Trail-making test B, a test of visual attention and task-switching. [35]

In another report, a study involving 1,324 individuals without dementia found those who reported performing moderate exercise during midlife or late life were significantly less likely to have MCI. Midlife moderate exercise was associated with 39% reduction in the odds of developing MCI, and moderate exercise in late life was associated with a 32% reduction. Light exercise (such as bowling, slow dancing or golfing with a cart) or vigorous exercise (including jogging, skiing and racquetball) were not significantly associated with reduced risk for MCI. [36]

#### Physical activity reduces MCI

A German study involving nearly 4000 older adults (55+) has found that physical activity significantly reduced the risk of developing mild cognitive impairment over a two-year period. Nearly 14% of those with no physical activity at the start of the study developed cognitive impairment, compared to 6.7% of those with moderate activity, and 5.1% of those with high activity. Moderate activity was defined as less than 3 times a week. [37]

# Maintaining or Increasing Activity Levels May Slow Cognitive Decline in Elderly

A 7-year study of over 3000 seniors (70-79) using self-report physical activity (walking) found that 21% were consistently sedentary, 12% maintained their activity levels, 26% had declining levels, and 41% had increasing or fluctuating

levels. After adjustment for age, sex, race, education, study site, diabetes, hypertension, smoking, alcohol consumption and baseline cognitive score, they found that those who were sedentary throughout the study had the lowest levels of cognitive function at the beginning and experienced the fastest rate of cognitive decline; cognitive decline also was faster in those whose physical activity levels consistently declined during the study period. However, sedentary elders who increased their physical activity improved their cognitive function, especially the ability to process complex information quickly. [38]

# Whether lifelong physical activity helps or hurts the aging brain depends on extent

A study of 90 post-menopausal women found that long-term strenuous activity was consistently associated with poorer performance on all eight cognitive tests, in particular tests of semantic memory, <u>working memory</u>, delayed verbal recall, and sustained attention. However, moderate physical activity was consistently associated with better performance on all eight of the tests, especially cognitive flexibility, working memory, and sustained attention. [39]

#### Alzheimer's Gene May Reduce Benefits of Physical Activity for Cognitive Ability

A study of some 1800 seniors (60+) found that the association of physical activity with better cognitive function was significant only for those who didn't carry any copies of the "<u>Alzheimer's gene</u>" APOE-e4 (which is the majority of people), and was greater with age. [40]

#### Physical fitness improves memory in seniors

A study of 165 older adults (59-81) has found a significant association between physical fitness and performance on certain spatial memory tests. Fitness was also strongly correlated with <u>hippocampus</u> size. Although rodent studies have shown that exercise increases hippocampus size and spatial memory, this is the first study

to show that in humans. The findings provide more evidence for the benefits of physical exercise in preventing memory loss in older adults. [41]

#### Moderate exercise helps mild cognitive impairment

An Australian study involving 138 older adults (50 years and over) with mild cognitive impairment, has found that those who undertook to achieve 2 ½ hours of physical activity each week (three 50 minute sessions), ranging from walking, ballroom dancing to swimming, for a six month period, continually out-scored the control group on cognitive tests during the 18 month testing period — showing that memory improvement was still evident a year after the supervised exercise period. [42]

#### Age differences in cognitive benefits of exercise and mental stimulation

A mouse study has found that while physical exercise (a running wheel) and mental stimulation (toys), singly and together, improved memory in old mice, exercise alone or exercise and stimulation improved memory in middle-aged mice but not stimulation alone, and only exercise alone benefited young mice. The results suggest that as we get old and maybe less able to exercise, cognitive stimulation can help to compensate, but exercise is central to memory reinforcement at all ages. [43]

#### Fitness and childhood IQ indicators of cognitive ability in old age

Data from the Scottish Mental Survey of 1932 has revealed that physical fitness contributed more than 3% of the differences in cognitive ability in old age. The study involved 460 men and women, who were tested using the same cognitive test at age 79 that they had undergone at age 11. Physical fitness was defined by time to walk six meters, grip strength and lung function. Childhood IQ was also significantly related to lung function at age 79, perhaps because people with higher intelligence might respond more favorably to health messages about staying fit. But physical fitness was more important for cognitive ability in old age than

childhood IQ. People in more professional occupations and with more education also had better fitness and higher cognitive test scores at 79. [44]

#### Exercise helps sustain mental activity as we age

A review of the research on the effects of exercise on brain functioning supports the view that physical exercise helps people maintain cognitive abilities well into older age. There's also evidence that fitness training may improve some mental processes even more than moderate activity. The review examined three types of study: epidemiological studies, human intervention studies, and animal studies. All provide support for the benefits of physical activity for the aging brain. [45]

#### Simple Lifestyle Changes May Improve Cognitive Function

A study involving 17 people (35–69 years) with mild self-reported memory complaints but normal baseline memory performance scores, has found that 2 weeks on a program combining a brain healthy diet plan (5 small meals a day; diet rich in omega-3 fats, antioxidants and low-glycemic carbohydrates like whole grains), relaxation exercises, cardiovascular conditioning (daily walks), and mental exercise (such as crosswords and brain teasers) resulted in participants' brain metabolism decreasing 5% in working memory regions (left dorsolateral prefrontal cortex), suggesting an increased efficiency. Compared to the control group, participants also performed better in verbal fluency. [20]

### Review supports link between lifestyle factors and cognitive function in older adults

A review of 96 papers involving 36 very large, ongoing epidemiological studies in North America and Europe looking at factors involved in maintaining cognitive and emotional health in adults as they age has concluded that controlling cardiovascular risk factors, such as reducing blood pressure, reducing weight, reducing cholesterol, treating (or preferably avoiding) diabetes, and not smoking, is important for maintaining brain health as we age. The link between hypertension and cognitive decline was the most robust across studies. They also found a consistent close correlation between physical activity and brain health. However, they caution that more research is needed before specific recommendations can be made about which types of exercise and how much exercise are beneficial. They also found protective factors most consistently reported for cognitive health included higher education level, higher socio-economic status, emotional support, better initial performance on cognitive tests, better lung capacity, more physical exercise, moderate alcohol use, and use of vitamin supplements. Psychosocial factors, such as social disengagement and depressed mood, are associated with both poorer cognitive and emotional health in late life. Increased mental activity throughout life, such as learning new things, may also benefit brain health. [46]

#### Lifestyle changes improve seniors' memory surprisingly quickly

A small 14-day study found that those following a memory improvement plan that included memory training, a healthy diet, physical exercise, and stress reduction, showed a 5% decrease in brain metabolism in the dorsal lateral prefrontal region of the brain (involved in working memory) suggesting they were using their brain more efficiently. This change in activity was reflected in better performance on a cognitive measure controlled by this brain region, and participants reported that they felt their memory had improved. The memory training involved doing brainteasers, crossword puzzles and memory exercises. Diet involved eating 5 small meals daily (to prevent fluctuations in blood glucose levels) that were rich in omega-3 fats, low-glycemic index carbohydrates (e.g., whole grains) and antioxidants. Physical exercise involved brisk walking and stretching, and stress reduction involved stretching and relaxation exercises. [20]

#### Lifelong mild exercise decreases cellular aging in the brain

A rat study has provided evidence that regular, light exercise (say a daily 30minute walk or a light 1-mile run) decreases cellular aging in the brain. Those rats who had had access to an exercise wheel during their lives showed fewer byproducts of oxidative stress in their brains, and their DNA at two years resembled that of their 6 month old counterparts. [47]

#### Diet, exercise, stimulating environment helps old dogs learn

A new study of beagles provides more evidence that diet and mental stimulation are important in reducing or preventing age-related cognitive decline. The study, involving 48 older beagles (aged 7 to 11), compared four combinations of behavioral enrichment (regular exercise and lots of mental stimulation) and supplementation of diet with antioxidants had on a beagle's ability to learn: regular diet and regular experience; regular diet and enriched experience; regular experience and an enriched diet; and enriched diet and an enriched experience. The study followed the beagles over two years. Those in the groups with either an enriched diet or enriched environment did better than those without either, but those who had both the enriched diet and an enriched environment did noticeably better than all the rest. [48]

#### Maintaining physical activity linked to less cognitive decline in older men

Longer and more intense physical activity may help people maintain their cognitive skills as they age, according to a 10-year study of 295 men, born between 1900 and 1920, from the Finland, Italy and Netherlands Elderly (FINE) Study. The study showed that over 10 years the cognitive decline in men who had reduced their daily physical activity by an hour or more was 2.6 times greater than the decline in men who maintained their activity. Men who performed their daily physical activity with a lower intensity 10 years later had a 3.6 times stronger decline than men who maintained the intensity level. Men who engaged in activities of the lowest intensity had up to 3.5 times greater decline than men who participated in activities with a higher intensity. There was no decline among those who increased the duration or intensity of their activities. Activities of medium-to-low intensity, such as walking three miles per day, was associated with less cognitive decline than the lowest-intensity activity like walking less than three miles per day. [49]

#### Walking may protect elderly from dementia

A study of more than 2,200 Japanese-American men between the ages of 71 and 93 has found that elderly men who are sedentary or walk less than a quarter of a mile per day are nearly twice as likely to develop dementia and Alzheimer's disease compared to men who walk more than two miles per day. Those who walked less than a mile (and more than quarter of a mile) a day also showed a significantly greater risk of dementia than those walking more than two miles a day. [50]

#### Physical activity associated with better mental functioning in older women

Since 1986, 18,766 women, aged 70 to 81 years, have been questioned on their physical activity in biennial questionnaires. The women were divided into five groups depending on their average energy expenditures. Those in the highest activity grouping had a 20% lower risk of cognitive impairment than women in the lowest. Women who walked at an easy pace for at least 1.5 hours per week had higher cognitive scores than those who walked less than forty minutes per week. [51]

#### Exercise improves attention and decision-making among seniors

An imaging study involving adults ranging in age from 58 to 78 before and after a six-month program of aerobic exercise, found specific functional differences in the middle-frontal and superior parietal regions of the brain that changed with improved aerobic fitness. Consistent with the functions of these brain regions, those who participated in the aerobic-exercise intervention significantly improved their performance on a computer-based decision-making task. Those doing toning and stretching exercises did increase activation in some areas of the brain but not in those tied to better performance. Their performance on the task was not significantly different after the exercise program. The aerobic exercise used in the study involved gradually increasing periods of walking over three months. For the final three months of the intervention program, each subject walked briskly for 45 minutes in three sessions each week. [52]

#### High sugar blood levels linked to poor memory

A new study takes an important step in explaining cognitive impairment in diabetics, and suggests a possible cause for some age-related memory impairment. The study assessed non-diabetic middle-aged and elderly people. Those with impaired glucose tolerance (a pre-diabetic condition) had a smaller hippocampus and scored worse on tests for recent memory. These results were independent of age or overall cognitive performance. The brain uses glucose almost exclusively as a fuel source. The ability to get glucose from the blood is reduced in diabetes. The study raises the possibility that exercise and weight loss, which help control blood sugar levels, may be able to reverse some of the memory loss that accompanies aging. [53]

#### Imaging study confirms link between exercise and cognitive function

A number of studies have suggested a link between exercise and cognitive function in older adults, but now an imaging study shows that there are actual anatomical differences in the brains of physically fit versus less fit older adults (over 55). Specifically, they found very distinct differences in the gray and white matter in the frontal, temporal, and parietal cortexes. With aging, these tissues shrink, a reduction closely matched by declines in cognitive performance. Fitness, it appears, slows that decline. A related study, published in March, suggests that women may benefit more from exercise than men. [54]

#### Walking reduces cognitive decline in older women

A study that tested the cognitive abilities of 5,925 women who were 65 and older once and then again six to eight years later, found that the women who walked the least were most likely to develop cognitive decline -- 24 percent of them had significant declines in their test scores, compared to 17 percent of the most active group. The least active women walked an average of about a half mile per week, while the most active group walked an average of nearly 18 miles per week. While any exercise appeared to be helpful, the benefit increased with every extra mile walked per week. Examples of activities that would reduce the risk of cognitive decline were: playing tennis twice a week, walking a mile per day, playing golf once a week. [55]

#### Aerobic exercise improves some mental processes in older adults

The team of Duke University Medical Center researchers who demonstrated in late 1999 that aerobic exercise is just as effective as medication in treating major depression in the middle-aged and elderly has now reported that the same exercise program also appears to improve the cognitive abilities of these patients. The researchers found significant improvements in the higher mental processes of memory and the so-called executive functions, which include planning, organization and the ability to mentally juggle different intellectual tasks at the same time. Attention and concentration did not appear to be affected. Because it has been theorised that a reduction in blood flow to the brain might be one of the reasons why the elderly – especially those with coronary artery disease or hypertension – might suffer some degree of cognitive decline, it is speculated that exercise might improve cognitive functioning in such patients by improving the flow of oxygen-rich blood to specific regions of the brain. [56]

#### **References**

# Kramer, A.F., Hahn, S., Cohen, N.J., Banich, M.T., Mcauley, E., Harrison, C.R., Chason, J., Vakil, E., Bardell, L., Boileau, R.A. & Colcombe, A. 1999. Ageing, fitness and neurocognitive function. *Nature*, *400*, 418 - 419.

124 previously sedentary adults, 60 to 75 years old, were randomly assigned to either aerobic (walking) or anaerobic (stretching and toning) exercise over a period of 6 months. Those who received aerobic training showed substantial improvements in performance on tasks requiring executive control (such as planning, scheduling, inhibition and working memory) compared with anaerobically trained subjects. Executive control processes are particularly affected by aging. The walking condition involved walking rapidly for 45 minutes three days a week.

# Perrig-Chiello, P. 1998. The effects of resistance training on well-being and memory in elderly volunteers. *Age and Ageing*, 27

The benefits of physical exercise for cognitive and memory performance in the elderly have not been consistently demonstrated in research. This study, a longitudinal one (the Interdisciplinary Ageing (IDA) study), was designed to reduce perceived shortcomings of earlier research.

The 442 people (65 - 95 years old) involved in the study had had their medical data collected regularly since 1965. 46 volunteers from this group (18 women and 28 men; mean age 73.2 years) participated in an eight-week resistance training program. The program involved a warm-up lasting 10 min, followed by eight resistance exercises on machines.

Participants displayed a significant increase in muscular strength directly after the training, and this was still significant one year later. However, there was no improvement in any subjective health ratings or psychological well-being measures, with the exception of a decrease in self-attentiveness (fewer self-centred thoughts; less anxiety about themselves and the future).

There was however a positive effect on cognitive function. Memory recall and recognition were both improved, and was still significant a year later. It is unlikely that this long-term improvement can be directly due to such a short-term physical training program, but perhaps the experience of mastering a new situation and changing established habits increased participants' motivation to seek new challenges. This openness and self-confidence could be responsible for participants staying physically, socially and mentally active and being self-reliant, all of which are prerequisites for optimal cognitive functioning.

### Substances for an improved memory

Older people do seem to be much more vulnerable to deficits in thinking and remembering caused by poor diet.

Low levels of B-12 and folic acid in particular, appear to be involved in age-related cognitive decline.

Green leafy vegetables, citrus fruits and juices, whole wheat bread and dry beans are good sources of folate. Fruit and vegetables, whole grains, beans and other protein sources (nuts, meat, fish) are good sources of the B vitamins.

Experiments with rats suggest sunflower seeds (and other seeds high in linoleic acid) may help against cognitive decline caused by hypertension.

Fruits and vegetables high in antioxidants (for example, spinach, blueberries) may reduce and even reverse age-related impairment to neuron function.

Experiments in rats suggest that two chemicals normally found in the body's cells and available as dietary supplements may also improve memory function and increase energy in older people. One of these substances is found in meat and vegetables, the other in green leafy vegetables.

Carbohydrates, fat, and protein, all seem to have positive effects - different effects - on thinking and remembering. It has been shown that having breakfast has a positive effect on memory in older adults; perhaps low energy intake in general is partly responsible for cognitive decline in some older people.

### Effects of diet on cognitive function

This information should not be construed as medical advice. If you have a medical concern, consult your doctor.

- Older people are much more vulnerable to cognition deficits due to poor diet, medications or disease<sup>1</sup>.
- Breaking your fast with carbohydrates, fat, or protein, improves memory function. These different energy sources seem to improve different types of memory function.

- Coffee does appear to enhance memory function in the afternoon, in "morning people" at least (and most older adults may belong to this category).
- Cognitive decline in the elderly is associated with low levels of B-12 and folic acid.
- High cholesterol levels may increase the risk of cognitive impairment.
- Sunflower seeds (and other seeds high in linoleic acid) may help against cognitive decline caused by hypertension.
- Two chemicals normally found in the body's cells and available as dietary supplements may improve memory function and increase energy in older people.
- Fruits and vegetables high in antioxidants may reduce and even reverse agerelated impairment to neuron function.
- Light to moderate alcohol intake may reduce the risk of cognitive impairment in the elderly.

#### **Reference**

#### **News reports**

#### A diet that may reduce age-related cognitive decline

The Dietary Approaches to Stop Hypertension (DASH) diet lowers blood pressure and is often recommended by physicians to people with high blood pressure or prehypertension. An 11-year study of over 3800 seniors found that those with higher DASH diet adherence scores had higher cognitive scores at the beginning of the study and increasingly so over time. Four of the nine food-group/nutrient components were independently associated with cognitive scores -- vegetables, whole grains, low-fat dairy, nut/legumes. When a score based on just these four components was used, the difference between those in the highest quintile and those in the lowest was even greater, particularly by the end of the study. [57]

#### Simple Lifestyle Changes May Improve Cognitive Function

Helping your aging memory by Dr Fiona McPherson

A study involving 17 people (35–69 years) with mild self-reported memory complaints but normal baseline memory performance scores, has found that 2 weeks on a program combining a brain healthy diet plan (5 small meals a day; diet rich in omega-3 fats, antioxidants and low-glycemic carbohydrates like whole grains), relaxation exercises, cardiovascular conditioning (daily walks), and mental exercise (such as crosswords and brain teasers) resulted in participants' brain metabolism decreasing 5% in working memory regions (left dorsolateral prefrontal cortex), suggesting an increased efficiency. Compared to the control group, participants also performed better in verbal fluency. [20]

#### Lifestyle changes improve seniors' memory surprisingly quickly

A small 14-day study found that those following a memory improvement plan that included memory training, a healthy diet, physical exercise, and stress reduction, showed a 5% decrease in brain metabolism in the dorsal lateral prefrontal region of the brain (involved in working memory) suggesting they were using their brain more efficiently. This change in activity was reflected in better performance on a cognitive measure controlled by this brain region, and participants reported that they felt their memory had improved. The memory training involved doing brainteasers, crossword puzzles and memory exercises. Diet involved eating 5 small meals daily (to prevent fluctuations in blood glucose levels) that were rich in omega-3 fats, low-glycemic index carbohydrates (e.g., whole grains) and antioxidants. Physical exercise involved brisk walking and stretching, and stress reduction involved stretching and relaxation exercises. [20]

#### Diet, exercise, stimulating environment helps old dogs learn

A new study of beagles provides more evidence that diet and mental stimulation are important in reducing or preventing age-related cognitive decline. The study, involving 48 older beagles (aged 7 to 11), compared four combinations of behavioral enrichment (regular exercise and lots of mental stimulation) and supplementation of diet with antioxidants had on a beagle's ability to learn: regular diet and regular experience; regular diet and enriched experience; regular experience and an enriched diet; and enriched diet and an enriched experience. The study followed the beagles over two years. Those in the groups with either an enriched diet or enriched environment did better than those without either, but those who had both the enriched diet and an enriched environment did noticeably better than all the rest. [48]

#### Fruit & vegetables

#### Drinking Concord grape juice may improve memory in older adults

A small pilot study, involving only 12 older adults with early memory decline, has found that those who drank Concord grape juice daily for a 12-week period showed significant improvement in list learning compared to those taking a placebo, and trends suggested improved short-term retention and spatial memory. [58]

#### How blueberries help the aging brain

An animal study has found that supplementing the regular diet of older animal with blueberries over a 12-week period, produced improvements in spatial working memory tasks emerged within three weeks. This improvement was associated with the activation of the protein <u>CREB</u> and increases in the level of <u>BDNF</u> in the <u>hippocampus</u>. Blueberries are a major source of flavonoids, in particular <u>anthocyanins</u> and flavanols. [59]

#### Vegetables, not fruit, help fight memory problems in old age

A study of 3,718 Chicago residents aged 65 and older found that people who ate at least 2.8 servings of vegetables a day had a 40% slower rate of cognitive decline compared to people who consumed less than one serving of vegetables a day — equivalent to about five years of younger age. Green leafy vegetables had the strongest association to slowing the rate of cognitive decline. The benefit was greater the older the person. However, unexpectedly, fruit consumption was not associated with cognitive change. [60]

#### Apple consumption protects against age-related cognitive decline

Previous research has found apple juice concentrate alleviated cognitive decline in genetically engineered mice compromised by a deficient diet. A study in normal, aging mice has now found that regular consumption of apple juice (in the context of a balanced diet) protected against the oxidative damage to brain cells that occurs in normal aging. Further, stronger mental acuity resulted when the mice consumed the human equivalent of 2-3 cups of apple juice or 2-4 apples a day. Apples are high in antioxidants. [61]

#### Grape juice may help memory in older adults

A study of older rats has found that Concord grape juice significantly improved their short-term memory in a water maze test as well as their neuro-motor skills in some coordination, balance and strength tests. The results are similar to those found with blueberries. Concord grape juice has the highest total antioxidants of any fruits, vegetables or juices tested (I assume the point of using "Concord" grape juice is the concentration of grape juice, not that this effect is specific to Concord grapes – although the fact that it is a "purple" grape juice is probably significant). [62]

### More support for value of antioxidants in protecting against age-related cognitive decline

Several studies have come out supporting the value of a diet rich in antioxidants to help stave off cognitive impairment in old age. A recent study has found that old dogs on an antioxidant-rich diet performed as well as young animals on a variety of cognitive tests. Young dogs did not benefit from the diet. Two years ago, researchers reported that a blueberry-enriched antioxidant diet may prevent agerelated deterioration of object recognition memory in aged rats. A new report, from a study of the same rats, reveals that the diet also prevented an age-related increase in a protein (NF-kappaB) that responds to oxidative stress, a probable cause of brain aging. This adds to growing evidence that a buildup of oxidative damage is an important factor in brain aging. Another rat study has found that blueberries can help lessen some of the damage caused by a brain injury. [63]

#### Antioxidant-rich diets improve age-related cognitive decline in rats

Two new animal studies add to the growing body of evidence that certain fruits and vegetables may slow down or reverse age-related cognitive decline. In the first study, older rats fed a diet rich in spinach for six weeks learned a simple association faster than those fed regular rat food. The second study compared three different foods - one group of older rats ate a diet supplemented by spirulina (high in antioxidants), another was fed a daily ration of apple (moderate in antioxidant activity), and the third was given a cucumber-enriched diet (low in antioxidants). Those fed either spirulina-or apple-enriched diets for two weeks demonstrated improved neuron function, and a suppression of inflammatory substances in the brain. Indeed, spirulina reversed the impairment in adrenergic neural function normally associated with aging. There was no improvement in rats fed a diet supplemented with cucumber. The best fruits and vegetables for antioxidant activity are generally the most colorful. [64]

#### Energy consumption, fats & sugars

#### Blood sugar linked to normal cognitive aging

Following research showing that decreasing brain function in the area of the hippocampus called the dentate gyrus is a main contributor of normal age-related cognitive decline, an imaging study has been investigating the cause of this decreasing function by looking at measures that typically change during aging, like rising blood sugar, body mass index, cholesterol and insulin levels. The study of 240 community-based nondemented elders (average age 80 years), of whom 60 had type 2 diabetes, found that decreasing activity in the dentate gyrus only correlated with levels of blood glucose. The same association was also found in aging rhesus monkeys and in mice. The finding suggests that maintaining blood sugar levels, even in the absence of diabetes, could help maintain aspects of

cognitive health. It also suggests that one reason why physical exercise benefits memory may be its effect on lowering glucose levels. [65]

#### High-fat diets impair memory

Several rodent studies have found evidence that a diet high in fat and empty calories may impair memory.

In one study, young adult male mice were divided into four groups by diet: normal (control) diet, high-saturated-fat diet, high-sugar diet, and diet high in saturated fats and sugar. They were kept on the diet for four months, during which mice on the high-fat and high-fat-&-sugar diets gained significantly more weight than those on the control and high sugar diets. At the end of that time, the mice were tested on a maze task. Mice on the high-fat and high-fat-&-sugar diets performed worse than the other mice. The mice were then exposed to a neurotoxin called kainic acid, which is known to damage nerve cells in the hippocampus. Mice on the high-fat and high-fat-&-sugar diets were significantly more impaired by the neurotoxin. In another mouse study, obese mice were fed a diet containing about 10% fat for seven months, while control mice were fed standard lab chow containing only 5% fat. On testing, it was found that the obese mice took significantly more trials than the normal-weight mice to both acquire and retain a memory of a foot shock. They also required significantly more trials than control mice to learn to press a lever for milk reinforcement.

A rat study explored whether a diet high in cholesterol and hydrogenated fats affected working memory in middle-aged rats (corresponding to 60 and older for humans). The high-fat, high-cholesterol diet produced significantly higher plasma triglycerides, total cholesterol, high density lipoprotein cholesterol, and low density lipoprotein cholesterol compared with controls. Weight increase and food consumption were similar between the groups. Animals on the high-fat regimen made more errors than animals fed the control diet, especially during the trial that placed the highest demand on their working memory.

Another rat study found that a diet high in fats and carbohydrates worsened cognitive deficits in rats exposed to repeated brief periods of low oxygen during sleep (as experienced by people with sleep apnea). [66]

#### High sugar blood levels linked to poor memory

A new study takes an important step in explaining cognitive impairment in diabetics, and suggests a possible cause for some age-related memory impairment. The study assessed non-diabetic middle-aged and elderly people. Those with impaired glucose tolerance (a pre-diabetic condition) had a smaller hippocampus and scored worse on tests for recent memory. These results were independent of age or overall cognitive performance. The brain uses glucose almost exclusively as a fuel source. The ability to get glucose from the blood is reduced in diabetes. The study raises the possibility that exercise and weight loss, which help control blood sugar levels, may be able to reverse some of the memory loss that accompanies aging. [53]

#### Energy consumption improves memory performance in the elderly

On four occasions, a small group of older people (61–79 years) were given, after the night's fast, either a drink containing protein (whey), carbohydrate (glucose), fat (safflower oil), or a nonenergy placebo. Cognitive tests were given 15 and 60 minutes later. Only the carbohydrate drink increased blood glucose levels, but all 3 of the energy drinks improved memory for paragraphs. Other memory improvements were specific to the type of drink. For example, fat was the only one that enhanced attention. In general, improvement was greater 60 minutes after drinking than 15 minutes after. [67]

#### A good breakfast improves memory function in older adults

A study of 41 healthy seniors aged 60 to 84 found that memory function was improved after a breakfast of wholegrain unsweetened cereal, milk, and juice (compared to no breakfast). This improvement was greatest for those with memory problems and those with early signs of adult-onset diabetes. [67]

#### **Calorie restriction**

#### Cognitive benefit of reduced calories for older adults

Helping your aging memory by Dr Fiona McPherson

Recent rat studies have indicated that significant calorie restriction lengthens lives, but the evidence for humans is rather more mixed. Now a German study of 50 healthy but overweight older adults (average age 60) has found that those who were on a balanced but severely restricted diet (reduced by 30%) for 3 months significantly improved their performance on a verbal memory test. Those who didn't reduce their calorie intake but increased their consumption of unsaturated fatty acids (linked to improved cognition), and those who didn't change their diets, showed little or no improvement. It's important to note that the participants were overweight to start with; further research will be needed to see whether the same effect occurs with normal-weight older adults. [68]

#### Calorie restriction leads to some brain benefits but not others in mice

A mouse study has found that although severe calorie restriction prevents certain aging-related changes in the brain, such as the accumulation of free radicals, and impairments in coordination and strength, the reduced diet did not seem to prevent age-related cognitive impairment. [69]

#### Calorie restriction reduces age-related brain cell death

A recent rat study has shown that certain proteins that increase with age and are linked to cell death were significantly reduced in the brains of rats whose calories were limited (but nutritionally dense, to guard against malnutrition). Moreover, the levels of a beneficial protein known to protect against neuron death were twice as high in older rats whose calories were restricted by 40%. This is consistent with a number of studies of other species that have found calorie restriction not only boosts life span and general health but also increases mental capacity. [70]

#### Fish

#### Eating fish may prevent memory loss and stroke in old age

A large study involving 3,660 people age 65 and older over five years, has found that those who ate broiled or baked tuna and other fish high in omega-3 fatty acids

three times or more per week had a nearly 26% lower risk of having silent brain infarcts that can cause dementia and stroke, compared to people who did not eat fish regularly. One serving a week reduced risk by 13%. Regular fish consumption was also associated with fewer changes in white matter. Types of fish that contain high levels of DHA and EPA nutrients include salmon, mackerel, herring, sardines, and anchovies. Eating fried fish was not protective. Silent brain infarcts are only detected by brain scans, and are found in about 20% of otherwise healthy elderly people. [71]

However, in the same journal, another study reports findings that in a double-blind, placebo-controlled, study of 302 healthy older adults, 26 weeks of EPA-DHA supplements had no effect on cognitive performance. Of course, if the effect of fish oil is primarily on preserving brain health, it may well be (indeed is likely) that the study was too short to impact cognitive performance. It is also possible that supplements are not as effective as whole foods — many studies have found that it is much more effective to receive needed vitamins and minerals through nutrition rather than supplementation. [72]

#### Eating fish associated with slower cognitive decline

Analysis of data from an ongoing longitudinal study of older adults has found that the rate of cognitive decline over a six-year period was reduced by 10-13% in those who ate fish at least once a week. [73]

#### Other

#### Low vitamin D levels associated with poorer cognition in older men

A study of over 3,100 older men (49-71) from across Europe has found that men with higher levels of vitamin D performed consistently better in an attention and speed of processing task. There was no difference on visual memory tasks. Although previous studies have suggested low vitamin D levels may be associated with poorer cognitive performance, findings have been inconsistent. Vitamin D is primarily synthesised from sun exposure but is also found in certain foods such as oily fish. [74]

#### Copper increases cognitive decline in older adults on high-fat diet

A six-year study involving 3,718 Chicago residents age 65 years and older has found that among the 16% who had high levels of saturated and trans fats in their diets, cognitive function deteriorated more rapidly the more copper they had in their diets. Copper intake wasn't a factor for the rest of the group. Previous studies have found higher levels of copper in the blood of patients with Alzheimer's disease. The finding will need to be confirmed by further research. The dietary recommended allowance of copper for adults is .9 milligrams per day. Organ meats, such as liver, and shellfish are the foods with the highest copper levels, followed by nuts, seeds, legumes, whole grains, potatoes, chocolate and some fruits. [75]

#### Curry helps older brains

Turmeric, an ingredient of curry, contains curcumin, which is a powerful antioxidant and anti-inflammatory that may inhibit the build-up of amyloid plaques in people with Alzheimer's. Now an investigation of 1010 older Asians (between 60 and 93 years) has found that those who ate curry "occasionally" (once or more in 6 months but less than once a month) and "often" (more than once a month) performed better on a standard test of cognitive function than those who only ate curry "never or rarely". [76]

# Sunflower seeds helpful in reducing hypertension and associated cognitive impairment

Research in rats has found that linoleic acid improved not only blood pressure, but also hypertension-induced memory decline, suggesting that the early incorporation of linoleic acid in the diet, may not only help in controlling hypertension, but may also improve hypertension-induced cognitive impairment. Linoleic acid is found in vegetable seed oils, such as safflower, sunflower, and hemp seed. [77]

#### Coffee, tea, chocolate

#### Caffeine reverses memory impairment in Alzheimer's mice

Consistent with earlier indications that moderate caffeine consumption may protect against memory decline, a study of <u>genetically engineered mice</u> has found that when the old mice began to show memory impairment, those given caffeine for 2 months performed as well as normal aged mice on cognitive tests, while those given plain drinking water continued to do poorly. The Alzheimer's mice received the equivalent of five 8-oz. cups of regular coffee a day (or two cups of Starbucks coffee, or 14 cups of tea). Moreover, the brains of the caffeinated mice showed nearly a 50% reduction in levels of <u>beta amyloid</u>. The effect appears to be through suppression of both <u>β-secretase</u> and <u>presenilin 1</u>/<u>g-secretase</u> expression. Caffeine had this effect only on those with Alzheimer's; normal mice given caffeine through adulthood showed no cognitive benefit. [78]

#### Midlife coffee drinking reduces risk of dementia

A large, long-running Finnish study has found that those who were coffee drinkers at midlife had lower risk for dementia and Alzheimer's later in life compared to those drinking no or only little coffee midlife. The lowest risk was found among moderate coffee drinkers (drinking 3-5 cups of coffee/day). Tea drinking was relatively uncommon and was not associated with dementia. [79]

#### Chocolate, wine and tea improve brain performance

A study of over 2000 older Norwegians (aged 70-74) has found that those who consumed chocolate, wine, or tea had significantly better cognitive performance and lower risk of poor cognitive performance than those who did not. Those who consumed all 3 studied items had the best performance and the lowest risks for poor test performance. The associations between intake of these foodstuffs and cognition were dose dependent, with maximum effect at intakes of around 10 grams a day for chocolate and around 75–100 ml a day for wine, but approximately linear for tea. The effect was most pronounced for wine and modestly weaker for

chocolate intake. The finding is consistent with research indicating that those who consume lots of flavonoids have a lower incidence of dementia. [80]

#### Coffee helps you retain mental sharpness later in the day

A recent study of 40 older adults (over 65) confirmed the popular belief in the value of caffeine in helping overcome a decline in mental sharpness later in the afternoon. All the participants (like three-quarters of all people in that age group, studies suggest) described themselves as "morning people". Testing confirmed that they were less alert later in the day. Given coffee, but not told whether it was "real" coffee or decaffeinated, those who drank the regular coffee did not experience mental declines in the afternoon tests. Note that participants were already regular coffee drinkers (and were asked to abstain before arriving for the test). [81]

#### Cholesterol

#### Low levels of good cholesterol linked to memory loss, dementia risk

Previous research has focused on total or LDL cholesterol levels because they are proven risk factors for cardiovascular disease, but data from the Whitehall II study has found that low levels of high-density lipoproteins (HDL) — the "good" cholesterol — in middle age were associated with a significantly greater risk of memory loss by age 60. Total cholesterol and triglycerides did not show a link with memory decline. To raise HDL and lower LDL cholesterol, the American Heart Association recommends exercising regularly; eliminating trans fats from the diet; reducing the intake of all fats, especially saturated fats; and consuming monounsaturated fats, such as olive, canola and peanut oils. (for more advice on cholesterol see <u>www.americanheart.org/cholesterol</u>) [82]

#### Not enough 'good' cholesterol makes it harder to recover from stroke

A large study involving men and women over age 35 in the United States, Canada, and Scotland who had suffered a mild to moderate stroke within the past three months, found several factors predicted memory and disability problems after

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stroke: increased age, non-Caucasian race, recurrent stroke, diabetes, stroke in the left hemisphere of the brain, higher levels of homocysteine and lower levels of high-density lipoproteins (HDL), otherwise known as "good" cholesterol. "People with low levels of HDL, high levels of homocysteine, and diabetes are twice as likely as those without such problems to have poorer cognitive function and greater disability after stroke ... (and) stroke recovery was the most difficult for people over the age of 57 with high levels of homocysteine". [83]

#### Low cholesterol also associated with impaired cognition

Data from 789 men and 1,105 women from the Framingham Heart Study has found that those who had the lowest total cholesterol performed significantly more poorly on tests of similarities, word fluency, and attention/concentration than patients with higher cholesterol levels. Those in the lowest total cholesterol group (a level of under 200) were 49% more likely to perform poorly and 80% more likely to perform very poorly than were participants in the highest total cholesterol group (240 to 380). The finding should not be taken as a warning against those with high cholesterol taking medication to lower it; the study applies to those with naturally low cholesterol levels, and previous studies have shown that both high and low cholesterol have led to poor cognitive performance. [84]

#### More support that high cholesterol is a risk factor for cognitive impairment

A new study has found that patients with a history of high cholesterol had a lower risk of cognitive impairment three to six months after stroke. The finding likely relates to high cholesterol treatment, rather than any positive effect of cholesterol. About 45% of the patients were being treated with cholesterol-lowering drugs known as statins before their stroke. Previous observational studies have indicated that statin therapy is associated with a reduced risk of Alzheimer's disease and vascular dementia.

A study of 103 consecutive ischemic stroke patients — 41 diagnosed with VCIND (vascular cognitive impairment-no dementia) and 62 who had no evidence of cognitive impairment after their strokes — identified three statistically significant

predictors of cognitive impairment: the patient's level of education, the presence of heart disease, and a history of high cholesterol (hypercholesterolemia). When the researchers controlled for education level (education being an established protective factor for cognitive impairment), only hypercholesterolemia remained as a statistically significant predictor of the risk for cognitive impairment. [85]

#### Cholesterol bad for brain too

An analysis of data on 1037 older women who had participated in a clinical trial of hormone replacement therapy found that high cholesterol levels increase the risk of cognitive impairment. It is speculated that, in addition to clogging arteries, and possibly leading to vascular changes in the brain, cholesterol may promote the clumping of a protein called beta-amyloid, which is believed to damage the brain in Alzheimer's disease patients. [86]

#### Folate, B-12

#### Vitamin B12 may protect the brain in old age

A five-year study of 107 older adults (61—87) has found that those who had higher vitamin B12 levels were six times less likely to experience brain shrinkage compared with those who had lower levels of the vitamin in their blood, even though none of them had vitamin B12 deficiency. Vitamin B12 is found in meat, fish and milk, and is often deficient in older people. [87]

#### B-vitamin deficiency may cause vascular cognitive impairment

A new mouse study helps clarify the association between <u>homocysteine</u>, folate & B12, and cognitive impairment. The study found that mice fed a diet deficient in folate and vitamins B12 and B6 demonstrated significant deficits in spatial learning and memory compared with normal mice, developed plasma homocysteine concentrations that were seven-fold higher, and showed smaller capillary length and density in blood vessels in the <u>hippocampus</u>. Homocysteine is produced by the breakdown of a dietary protein called <u>methionine</u>; B-vitamins are required to

convert homocysteine back to methionine. A third group of mice were fed a diet enriched with methionine. These mice showed similar, but less pronounced effects. The findings indicate that increased levels of homocysteine, produced by low intake of folate and B vitamins, impairs cognition through microvascular changes. [88]

#### Vitamin B12, folate, and cognitive function

Confirming earlier studies, a large epidemiological study has found that older people with normal vitamin B12 status and high levels of folate had higher scores on a test of cognitive function. The study clarifies some inconsistencies in earlier research by disentangling the interaction between these factors. It appears seniors with normal levels of vitamin B12 perform better if folate level is high, but when vitamin B12 is low, high levels of folate are associated with poor cognitive performance, as well as a greater probability of anemia. There are also indications that the combination might be a factor in some other diseases. [89]

#### Folic acid supplementation may improve cognitive performance

A study involving 818 older adults with raised homocysteine levels and normal vitamin B12 levels found that those given daily folic acid supplements (800 micrograms) for 3 years had lower homocysteine levels and improved cognitive performance compared to those given a placebo. [90]

#### More evidence for value of folate for aging brains

Confirming a growing body of evidence, a study of 50-85 year old Boston-area men (members of the ongoing Normative Aging Study) found that men who obtained more folate in their diets showed significantly less of a decline in verbal fluency skills over the course of three years than did men with lower dietary folate intake. High folate levels also appeared protective against declines in spatial copying. The effects of folate were independent of its impact on homocysteine, which turned out to be more strongly associated with tests of memory. Folate is a B vitamin found particularly in leafy green vegetables and citrus fruit. [91]

# Preventing high levels of homocysteine may protect against age-related cognitive impairment

Previous studies have found a link between high levels of homocysteine and poor cognitive performance, but it has been difficult to work out just what the association is, in view of confounding factors such as cardiovascular risk factors and levels of folate, B12, and B6, all of which play a role in high levels of homocysteine. A new analysis has disentangled these factors, and has found that, in people over 60 (but not those under 60), higher levels of homocysteine are independently associated with lower levels of cognitive performance. Similarly, higher levels of vitamin B12 are associated with higher levels of cognitive performance. The researchers suggest vitamins B12, B6, and folate taken before 60 could help protect against later cognitive impairment. [92]

#### Folic acid and vitamin B-12 deficiencies linked to cognitive decline

Current estimates suggest that more than one million elderly in Europe and about 750,000 elderly in North America become cognitively impaired each year. Recent research suggests that deficiencies of folate or vitamin B-12 and elevations of plasma homocysteine (tHcy) may be partly responsible. A British study of 331 participants in a longitudinal survey found significant negative effects on cognition in the elderly subjects who had deficiencies of folic acid or vitamin B-12 and elevated tHcy. In the older group (aged 76-78), increased levels of tHcy correlated both with lower serum folate and vitamin B-12 concentrations and with lower cognitive test scores. In the younger group (aged 61-63),higher folate concentrations correlated with higher scores on one of the assessment tests, but otherwise no effects of B vitamins or tHcy were apparent. Green leafy vegetables, citrus fruits and juices, whole wheat bread and dry beans are good sources of folate. [93]

#### Gingko

#### Support for gingko biloba

A study of seniors with age-associated memory impairment found significant improvement in verbal recall among those who took gingko biloba for six months. PET scans revealed a correlation with better brain function in key brain memory centers, although there was no detectable changes in brain metabolism. Studies of gingko biloba have had conflicting results, and it is suggested that both length of time (most studies have looked at the effect over 3 months or less) and quality of supplement, may be important. [94]

#### No support for ginkgo as a memory enhancer

In a double-blind study of 230 healthy seniors, half of whom were given gingko biloba and half a placebo, ginkgo biloba was found to have no beneficial effect on memory and related mental functions after six weeks (the manufacturer claims beneficial effects can be noticed after four weeks). [95]

#### Ginseng

#### Pilot study finds ginseng may improve memory in stroke dementia patients

Following mouse studies showing that ginseng increased the activities of the brain chemicals acetylcholine and choline acetyltransferase, a pilot study of 40 patients (average age 67) with mild to moderate vascular dementia was undertaken by Chinese researchers. 25 patients were randomly selected to receive ginseng extract, while 15 received the drug Duxil® (used to improve memory in elderly dementia patients). Overall, researchers found that patients who took the ginseng compound significantly improved their average memory function after 12 weeks. More research (larger samples, placebo-controls) is needed before this finding can be confirmed. [96]

#### **Dietary supplements**

#### Evidence mounts against DHEA use in treating cognitive decline

DHEA is a naturally-occurring hormone in the human body that declines with age. Previous research looking at the effect of DHEA supplementation on cognitive function and quality-of-life has produced inconsistent results. In the first long-term study (12 months) of healthy older adults, 110 men and 115 women aged 55-85 received either daily 50 mg doses of DHEA or a similar looking placebo pill for 1 year. It was found that, although youthful levels of DHEA were restored in the treatment group, the supplements had no benefits for cognitive function or qualityof-life in this representative sample. [97]

#### French maritime pine bark improves memory in elderly

A double-blind, placebo controlled, matched pairs study examined the effects of Pycnogenol (an antioxidant plant extract from the bark of the French maritime pine tree) on a range of cognitive and biochemical measures in 101 senior individuals aged 60-85 years old. Participants had a daily dose of 150mg for three months. Pycnogenol improved both numerical working memory as well as spatial working memory. Blood samples revealed that F2-isoprostanes significantly decreased with Pycnogenol, a sign of reduced oxidation of nerve membranes, suggesting that the antioxidant activity of Pycnogenol plays a major role for the clinical effects. Several recent research studies have found Pycnogenol reduced ADHD symptoms such as hyperactivity and improved attention, concentration and motor-visual coordination in children with ADHD. Pycnogenol extract has been studied for 35 years and is available in more than 600 dietary supplements. [98]

#### Long-term beta carotene supplementation may help prevent cognitive decline

A large, long-running study has found that men who took beta carotene supplements for 15 years or longer had significantly higher scores on several cognitive tests compared with men who took placebo. There was no such effect in those men who took the supplements for a year. The researchers suggest that although the benefits were modest in themselves, they may predict substantial differences in eventual risk of dementia. However, it should be noted that beta carotene is not without risks—for example, it may increase the risk of lung cancer in smokers — and that it would be premature to advise use of such supplements. [99]

#### Dietary supplements improve old rats' memory and energy levels

After only a month, older rats fed two chemicals normally found in the body's cells and available as dietary supplements — acetyl-L-carnitine and an antioxidant, alpha-lipoic acid — performed better on memory tests, and had noticeably more energy (on a par with a "middle-aged" rat). It is thought that these chemicals act on the mitochondria, the "power-houses" of the cells. Mitochondria are increasingly being implicated as especially vulnerable to the aging process. Carnitine is a natural compound produced in the cell and obtained in the diet through meats and vegetables. It has been shown to improve balance and short-term memory in human. Lipoic acid is found in green, leafy vegetables.

The University of California has patented use of the combination of the two supplements to rejuvenate cells. Human clinical trials are currently underway. [100]

#### Alcohol

#### Regular moderate alcohol intake has cognitive benefits in older adults

A six-year study involving over 3,000 seniors (75+) has found that for those who had no cognitive impairment at the start of the study, moderate drinking (1-2 drinks a day) was associated with a 37% reduction in risk of developing dementia compared to individuals who did not drink at all. The type of alcohol didn't matter. However, for those who started the study with mild cognitive impairment, any consumption of alcohol was associated with faster rates of cognitive decline. Moreover, heavy drinkers were almost twice as likely to develop dementia during the study. The results are consistent with previous studies of middle-aged adults that suggest mild to moderate alcohol intake may reduce the risk of dementia, except in the case of individuals who already have mild to moderate cognitive impairment. [101]

# Moderate drinking can reduce risks of Alzheimer's dementia and cognitive decline

A review of 44 studies has concluded that moderate drinkers often have lower risks of Alzheimer's disease and other cognitive loss. Moderate alcohol consumption generally is defined as 1 drink or less per day for women and 1-2 drinks or less per day for men. [102]

### Moderate alcohol intake associated with better mental function in older women

A study of over 7,000 older women (65-80) found that those who drink a moderate amount of alcohol have slightly higher levels of mental function than non-drinkers, particularly in verbal abilities. The researcher warned that "Until we better understand the reasons why alcohol consumption is associated with better cognitive functioning, these results on their own are not a reason for people who don't drink to start or for those who drink to increase their intake." [103]

#### More support for benefits of some alcohol

A longitudinal study of an elderly community sample found that, over an average of 7 years, mild-to-moderate drinking was associated with less average decline in cognitive function compared to not drinking. [104]

#### Moderate alcohol intake may reduce cognitive decline in older women

Two recent large-scale epidemiological studies have come out recently with similar findings. Data from the Women's Health Initiative Memory Study (involving 4,461 women aged 65 to 79 years) has revealed that women who reported having one or more alcohol drinks daily had a 40% lower risk of significant declines in cognitive function over time, compared to women who reported no alcohol intake. It is possible that moderate alcohol intake may reduce the risk for narrowed vessels in the brain. In addition, alcohol may decrease the formation of plaque that is associated with Alzheimer's disease. [105]

Data from the Nurses' Health Study, begun in 1976 and involving 12,480 women, now aged between 70 and 81 years old, has found that women who had the equivalent of one drink a day had a 23% lower risk of becoming mentally impaired during a two-year period, compared with non-drinkers. It made no significant difference whether they drank beer or wine. [106]

# Drinking too much alcohol, and not enough, increases risk of cognitive impairment

In Finland, researchers re-examined 1018 participants from a study of 1464 men and women aged 65-79 studied in 1972 or 1977. They found that participants who drank no alcohol in midlife as well as those who drank alcohol frequently were twice as likely to have mild cognitive impairment in old age compared to those who drank alcohol infrequently. The effect of alcohol was however modified by the presence of the apolipoprotein e4 allele (implicated in dementia risk). People who were carriers of the apolipoprotein e4 allele had an increased risk of dementia with increasing alcohol consumption, with carriers of the gene significantly reducing their risk by never drinking. [107]

#### Moderate alcohol consumption may help prevent dementia

Recent research has suggested that moderate alcohol consumption may have positive health benefits for cardiovascular and cerebrovascular functioning. Given the connection between dementia in old age and cerebrovascular disease, a recent Italian study analyzed data from 15,807 patients (65 years of age or older) to assess whether there is any link between alcohol consumption and cognitive function. Signs of cognitive derangement were found in 19% of the participants who reported regular alcohol consumption, and in 29% of those who abstained from alcohol. The quantity of daily alcohol consumption was an important factor. The risk of cognitive impairment was reduced among women whose daily alcohol consumption was less than 40 grams and among men who drank less than 80 grams. Higher levels of alcohol consumption showed an increased risk of cognitive impairment when compared with both abstainers and moderate drinkers. [108] A Dutch study suggests that light-to-moderate alcohol consumption could reduce the risk of dementia among older people. Light-to-moderate alcohol consumption (1 to 3 drinks per day) was associated with a 42% risk reduction of all dementia, and around a 70% reduction in risk of vascular dementia. [109]

#### **References**

## **Preventing dementia: Diet & exercise**

It's increasingly clear that eating a healthy diet can have a big impact on whether or not you develop dementia.

A study<sup>1</sup> of nearly 2000 older adults has found that eating a Mediterranean diet was associated with less risk of developing mild cognitive impairment or of transitioning from MCI to Alzheimer's disease. The third with the highest scores for Mediterranean diet adherence had a 28% lower risk of developing MCI compared to the third with the lowest scores, and of those who already had MCI, those with the highest scores for Mediterranean diet adherence adherence had a 48% less chance of developing Alzheimer's.

Another, similar-sized study<sup>2</sup>, has found that those who adhered more strongly to a Mediterranean-type diet had a 40% risk reduction, and those who were very physically active had a 33% risk reduction of Alzheimer's -- doing both gave people a 60% reduction.

A Mediterranean-type diet is typically characterized by high intake of fish, vegetables, legumes, fruits, cereals and monounsaturated fatty acids; relatively low intake of dairy products, meats and saturated fats; and moderate alcohol consumption. Most of these components have been independently associated with reduced dementia risk. Let's look at them one by one.

#### Fruit & vegetables

A very large study<sup>3</sup> of older adults found that those who ate fruits and vegetables daily reduced their risk of dementia by 30% compared to those who didn't regularly eat fruits and vegetables. Another large, long-running epidemiological study<sup>4</sup> found that those who drank three or more servings of fruit and vegetable juices per week had a 76% lower risk of developing Alzheimer's disease than those who drank juice less than once a week. The benefit seemed greatest for those who carried the so-called "Alzheimer's gene".

This may not have anything to do with vitamin C. A five-year study<sup>5</sup> involving nearly 3000 people has found that use of Vitamin C or E or both was not associated with a reduced risk of developing dementia or Alzheimer's. However a study<sup>6</sup> involving 4,740 elderly found the greatest reduction in both prevalence and incidence of Alzheimer's in those who used individual vitamin E and C supplements in combination. There was no significant benefit in these vitamins alone.

Of course, it is now well understood that taking vitamins as supplements is not the same as receiving them in food.

Two studies have come out in favor of a diet rich in foods containing vitamin E to help protect against Alzheimer's disease. One study<sup>7</sup> involved 815 Chicago residents age 65 and older with no initial symptoms of mental decline, who were questioned about their eating habits and followed for an average of about four years. When factors like age and education were taken into account, those eating the most vitamin E-rich foods had a lower risk of developing Alzheimer's, provided they did not have the ApoE e4 allele. This was not true when vitamin E was taken as a supplement. The effect of vitamin C was not statistically significant.

The other study<sup>8</sup> involved 5,395 people in the Netherlands age 55 and older who were followed for an average of six years. Those with high intakes of vitamins E and C were less likely to become afflicted with Alzheimer's, regardless of whether they had the gene variation. This association was most pronounced for current smokers.

So beneficial effects of these vitamins may depend on genetics, smoking history, and possibly other lifestyle factors. But there are other valuable compounds common in fruits & vegetables. Another class of antioxidant chemicals, polyphenols, are now suspected. Polyphenols generally exist primarily in the skins of fruits and vegetables and are particularly abundant in teas, juices and wines.

A cell study<sup>9</sup> also found that quercetin (a flavonoid with greater antioxidant and anticancer properties than vitamin C) protects against cellular damage. Quercetin is particularly abundant in apples (mainly in the skin, and especially the red ones). Other good sources are onions, blueberries and cranberries.

Another cell study<sup>10</sup> found that compounds in blackcurrants (anthocyanins as well as polyphenols) strongly protect neuronal cells against the effects of amyloid-beta. Boysenberries contain the same compounds, and those that are darker are likely to be more potent.

The inconsistent findings regarding vitamins C and E may also have to do with the presence of folates. Data from the Baltimore Longitudinal Study of Aging<sup>11</sup> revealed that although those with higher intake of <u>folates</u>, vitamin E and vitamin B6 had a lower risk of developing Alzheimer's, statistical analysis showed it was only folate consumption that was significant. Those who had at least 400mcg of folates a day (the recommended daily allowance) had a 55% reduction in risk of developing Alzheimer's. Unfortunately, most people who reached that level did so by taking supplements, suggesting the difficulty of doing so through diet alone.

Folates are abundant in foods such as liver, kidneys, yeast, fruits (like bananas and oranges), leafy vegetables, whole-wheat bread, lima beans, eggs and milk; however, they are often destroyed by cooking or processing.

The benefits of folates probably has to do with its effect on homocysteine. A mouse study<sup>12</sup> indicates that increased levels of homocysteine are produced by low intake of folate and B vitamins, and impair cognition through microvascular changes.

High levels of homocysteine are associated not only with deficiencies in vitamin B12 and folate, but also with smoking.

High levels of homocysteine were associated in one study<sup>13</sup> with a more than fivefold increase in the risk for stroke, a nearly five-fold risk for vascular dementia, and almost triple the risk for Alzheimer's disease. Findings from the long-running Framingham study<sup>14</sup> found people with elevated levels of homocysteine in the blood had nearly double the risk of later developing Alzheimer's disease.

Moreover, evidence from a study<sup>15</sup> using genetically engineered mice suggests that increased levels of homocysteine in the brain cause damage to nerve cells in the hippocampus -- which can be repaired when there is an adequate amount of folate, but not when there is a deficiency.

#### Omega-3 oils & fish

One of the clearest findings in this area has been the benefits of regularly consuming omega-3 oils, fish oil, and fish. Several epidemiological studies have indicated that regularly eating fish (at least once a week) reduces risk of dementia. More recently, two very large studies have come out in support. One very large study<sup>3</sup> of older adults found that those who regularly consumed omega-3 rich oils, such as canola oil, flaxseed oil and walnut oil, reduced their risk of dementia by 60% compared to people who did not regularly consume such oils. Additionally, those who ate fish at least once a week had a 40% lower risk of dementia -- but only if they did not carry ApoE4 gene.

Moreover, for those who didn't have the gene, regular use of omega-6 rich oils, but not omega-3 rich oils or fish, were twice as likely to develop dementia compared to those who didn't eat omega-6 rich oils (e.g., sunflower or grape seed oil).

The second study<sup>16</sup> comes from the famous long-running Framingham Heart Study, which found that those with the highest levels of DHA (an omega-3 polyunsaturated fatty acid found in relatively high concentrations in cold-water fish) had a 47% lower risk of developing dementia. Those with these levels tended to eat an average three fish servings a week, as well as an average of .18 grams of DHA a day. Those at lower levels ate markedly less fish.

There is also some suggestion that omega-3 oils might help slow the progression of dementia. A Swedish study<sup>17</sup> found that, although fatty acids DHA and EPA didn't slow cognitive decline in those with mild-to-moderate Alzheimer's, they did slow decline in those with very mild cognitive impairment (a frequent precursor of dementia). It's been suggested that anti-inflammatory effects are an important reason for the benefit, why might explain why benefits only occur in the very early stages, when levels of inflammation seem to be higher.

Similar results were more recently reported<sup>18</sup> from a large 18-month trial. This one, however, suggested that genetic status might be a factor -- that those without the "<u>Alzheimer's gene</u>" ApoE4 might benefit even if impairment had progressed to mild-to-moderate Alzheimer's.

There are a number of reasons why DHA might help brains.

A study involving genetically engineered mice<sup>19</sup> has found that a diet high in DHA dramatically slowed the progression of Alzheimer's by cutting the harmful brain plaques that mark the disease. An earlier study<sup>20</sup> showed that DHA protected against damage to the synaptic areas where brain cells communicate and enabled mice to perform better on memory tests. More recent research<sup>21</sup> has revealed that DHA increases the production of LR11, a protein that is found at reduced levels in Alzheimer's patients and which is known to destroy the protein that forms the plaques associated with the disease.

Food sources of omega-3 fatty acids include fish such as salmon, halibut, mackerel and sardines, as well as almonds, walnuts, soy, flaxseed, and DHA-enriched eggs. These fish have high levels of DHA because they consume DHA-rich algae. Because these fishes' oiliness makes them absorb more mercury, dioxin, PCP and other metals, a less risky yet more costly strategy is to consume fish oil or purified DHA supplements made from algae.

#### Possible benefits of wine, tea, and coffee

There have been a number of reports that moderate alcohol consumption (generally defined as 1 drink or less per day for women and 1-2 drinks or less per day for men) may help reduce your risk of developing dementia, and a 2008 review of 44 studies<sup>22</sup> supported this conclusion.

However, given that alcohol has known negative effects on the brain, no one is recommending that non-drinkers take up the habit! All one can say is that there's no reason to alter your habits if you are a moderate drinker. On the other hand, if you drink more than this, you are probably best to knock it back to this level.

However, the evidence suggests that it is wine rather than alcohol in general that is beneficial for the brain. A large Danish study<sup>23</sup> found that those who drank wine occasionally in the 1970s had a lower risk of developing dementia in the 1990s (when participants were 65 or older). However, occasional beer drinking was associated with an increased risk of developing dementia. But we cannot draw too hard & fast a conclusion from this, as eating habits were not investigated, and research suggests that wine drinkers may have better dietary habits than beer and liquor drinkers. Moreover, a very large study of older adults<sup>3</sup>, that found a significant effect of some dietary factors, found no effect of wine.

There are, however, some good reasons for believing regular drinking of red wine may help the aging brain. Red grapes contain several <u>polyphenols</u> that have been shown to significantly reduce cognitive deterioration in genetically engineered mice, by preventing the formation of <u>amyloid beta</u>. One of these is resveratrol; the others are catechin and epicatechin. Resveratrol was much vaunted when its effects were first discovered, but unfortunately it requires extremely high doses. The more recent discovery<sup>24</sup> of the catechins is much more exciting, as they appear to be effective at much lower doses. The catechins are also abundant in tea and cocoa.

Tea, most particularly green tea, has also been found<sup>25</sup> to inhibit the activity of enzymes associated with the development of Alzheimer's Disease. Green tea also obstructed the activity of beta-secretase.

These inhibitory properties were not found in coffee. However, a large, longrunning Finnish study<sup>26</sup> has found that those who were coffee drinkers at midlife had lower risk for dementia and Alzheimer's later in life compared to those drinking no or only little coffee midlife. The lowest risk was found among moderate coffee drinkers (drinking 3-5 cups of coffee/day).

#### **Restricting your calories**

There has been some talk that calorie-restricted diets might help prevent Alzheimer's. So far, the only indications have come from experiments with genetically engineered mice. While there have been a number of studies providing evidence that high cholesterol, obesity, and other cardiovascular risk factors increase the likelihood of Alzheimer's, it is decidedly premature to say whether calorie-restricted diets would benefit humans. Particularly since one of the early signs of Alzheimer's is weight loss. So it is certainly not recommended that people severely restrict their diets. More useful is removing certain food types (e.g., the "bad" oils; sugar -- there is some evidence that Alzheimer's may be a type of diabetes), and increasing consumption of others (fish, "good" oils, fruit & vegetables).

There may also be a genetic link. A four-year study<sup>27</sup> of nearly 1000 older adults found that among those who carried the ApoE e4 gene, those who consumed the most calories had a 2.3 times greater chance of developing Alzheimer's compared to those who ate the fewest calories. But calories weren't a factor for those without the gene.

#### Cholesterol

A study<sup>28</sup> involving nearly 10,000 people who underwent health evaluations between 1964 and 1973 when they were between the ages of 40 and 45, has found

that those with total cholesterol levels between 249 and 500 milligrams were oneand-a-half times more likely to develop Alzheimer's disease than those people with cholesterol levels of less than 198 milligrams. People with total cholesterol levels of 221 to 248 milligrams were more than one-and-a-quarter times more likely to develop Alzheimer's disease. High cholesterol increased risk regardless of midlife diabetes, high blood pressure, obesity, smoking and late-life stroke.

A review<sup>29</sup> of autopsy cases of patients over 40 years old found that high blood cholesterol levels were correlated with the presence of amyloid deposits in the brain in the youngest subjects (aged 40-55).

An analysis<sup>30</sup> of data on 1037 older women who had participated in a clinical trial of hormone replacement therapy found that high cholesterol levels increase the risk of cognitive impairment.

A large-scale Finnish study<sup>31</sup> following 1449 men and women over 21 years found that raised systolic blood pressure and high serum cholesterol concentration, particularly in combination, in midlife, increase the risk of Alzheimer's disease in later life. Raised diastolic blood pressure had no significant effect.

However, the long-running, large-scale Framingham Heart study<sup>32</sup> found that, after adjustment for age, sex, APOE genotype, smoking, body mass index, coronary heart disease, and diabetes, there was no significant association between AD risk and cholesterol level.

Previous studies suggesting that fat may be involved in the development of dementia and Alzheimer's disease have been contradicted by a new study<sup>33</sup> involving over 5,000 elderly people over a period of six years. The study found no correlation between fat and cholesterol intake and risk of dementia, and no evidence for a reduction in risk for those taking cholesterol lowering medication.

A cell study<sup>34</sup> provides more understanding of why there might be a link between cholesterol and Alzheimer's disease. The study found that proteins which help control cholesterol levels in arterial walls were also present in neurons, and when

the genes for these proteins were over-expressed, production of amyloid beta protein fell. The finding suggests a new approach to slowing Alzheimer's. The study also showed that the apoE protein is extremely good at regulating cholesterol removal from neurons — the gene for this protein is a well-known genetic risk factor for Alzheimer's.

#### Diabetes

A large Swedish study<sup>35</sup> involving over 2000 men has found that those with low insulin secretion capacity at age 50 were nearly one-and-a-half times more likely to develop Alzheimer's disease than people without insulin problems. The risk was strongest in people who did not have the APOE4 gene.

A study<sup>36</sup> involving 918 individuals older than 65 years (average age 75.9) who did not have mild cognitive disorder or dementia when they enrolled has found that, over some 6 years, diabetes was related to a significantly higher risk of developing amnestic mild cognitive impairment, after controlling for other risk factors. The results support other findings that type 2 diabetes mellitus increases the risk of Alzheimer's.

The first study<sup>37</sup> to investigate the association over time between blood sugar and the risk of cognitive difficulties involved 1,983 post-menopausal women (mean age 67 years) and found that each 1% increase in their glycosylated hemoglobin level at the start of the four-year study period was associated with a 40% increased risk of developing MCI or dementia four years later. The glycosylated hemoglobin test gives a more stable measure of blood sugar level than the standard test, which measures blood sugar it the time of testing. A result of 7% or less indicates good long-term blood sugar control. Those with a level of 7% or more were four times more likely to develop MCI or dementia than women who tested at less than 7%.

Findings<sup>38</sup> from the Religious Orders Study add to research suggesting a link between diabetes mellitus and an increased risk of developing Alzheimer's disease.

A mouse study<sup>39</sup> has shed light on the connection between diabetes and Alzheimer's. It appears that the elevated blood glucose levels characteristic of diabetes interacts with beta amyloid in a way damaging to blood vessels in the brain.

A mouse study<sup>40</sup> suggests that low levels of insulysin, an enzyme that degrades insulin, could increase the risk for Alzheimer's, and points to a new mechanism linking diseases like diabetes and Alzheimer's — the competition of multiple substrates, such as insulin and amyloid-beta, for a limiting amount of the insulysin enzyme. The insulysin enzyme, it seems, also degrades amyloid-beta peptides, and even a partial decrease in insulysin activity was found to raise amyloid-beta peptide levels in the brain.

Indeed, in recent years, researchers have gone as far as to suggest that Alzheimer's is actually a third form of diabetes. One study<sup>41</sup> found that insulin and its related proteins are produced in the brain as well as the pancreas, and that reduced levels of these contribute to the degeneration of brain cells, an early symptom of Alzheimer's disease. Another<sup>42</sup> found that stimulation of a receptor in the brain that controls insulin responses prevents several components of neurodegeneration and preserves learning and memory in rats with induced Alzheimer's disease, raising the possibility that patients in the very early stages of Alzheimer's might be treatable. Another<sup>43</sup>, by depleting insulin and its related proteins in the brain, replicated the progression of Alzheimer's disease – including plaque deposits, neurofibrillary tangles, impaired cognitive functioning, cell loss and overall brain deterioration – in an experimental animal model. Brain deterioration was not related to the pancreas, providing more support for Alzheimer's as a neuroendocrine disorder, or a Type 3 diabetes.

More recently, a study<sup>44</sup> has found that the toxic protein <u>ADDL</u>, found in the brains of individuals with Alzheimer's, removes insulin receptors from nerve cells, rendering those neurons insulin resistant.

#### Obesity

A number of studies have found a connection between obesity and dementia.

A review<sup>45</sup> of 10 international studies published since 1995, covering just over 37,000 people, has found that obesity increased the relative risk of dementia by an average of 42% compared with normal weight. Being underweight increased the risk by 36%. For Alzheimer's Disease and vascular dementia, specifically, obesity was an even more significant risk: 80% and 73%, respectively. With regards to Alzheimer's, obesity was more likely to be a risk factor for women, but men were more affected when it came to vascular dementia.

A study<sup>46</sup> involving 6,583 people measured abdominal fat at age 40 to 45, and dementia occurrence some 36 years later. Those with the highest amount of abdominal fat were found to be nearly three times more likely to develop dementia than those with the lowest amount of abdominal fat. Having a large abdomen increased the risk of dementia regardless of overall weight and existing health conditions, although being obese as well did increase the risk. Those more likely to have abdominal obesity, were women, non-whites, smokers, people with high blood pressure, high cholesterol or diabetes, and those with less than a high school level of education.

A large Scandinavian study<sup>47</sup> has succeeded in calculating middle-aged people's chances of developing dementia later in life with 70% accuracy. The study confirms the importance of lifestyle factors. The study assessed factors such as blood pressure, body fat and cholesterol levels in 1,400 middle-aged Finns in the 1970s and 1980s, and found that those who at 40 were obese, or had high blood pressure, or high cholesterol levels, were twice as more likely to develop dementia by the age of 60. Having all three of these risk factors increased their chances six-fold.

It's interesting to note in this context, that genetically engineered mice fed a diet rich in fat, sugar and cholesterol for nine months developed a preliminary stage of the morbid irregularities that form in the brains of Alzheimer's patients<sup>48</sup>. The

findings suggest that a 'fast food' diet could be a contributory factor in those with the Alzheimer's gene.

#### Physical exercise & fitness

There has been quite a lot of research in recent years supporting the benefits of physical exercise for older adults, for cognitive fitness. There have also been a number of studies who have looked at the possible benefits of physical exercise for preventing, or delaying, dementia.

A study<sup>49</sup> of 121 people age 60 and older, of whom 57 were in the early stages of Alzheimer's disease, found that those with early Alzheimer's disease who were less physically fit had four times more brain shrinkage when compared to normal older adults than those who were more physically fit. The findings suggest the value of physical fitness in slowing down the progression of Alzheimer's disease.

A four-year study<sup>50</sup> involving 749 older adults found that the top one-third of participants who exerted the most energy in moderate activities such as walking were significantly less likely to develop vascular dementia than those people in the bottom one-third of the group. Contrary to some reports, no such association was found with Alzheimer's disease.

A study<sup>51</sup> following 2,288 older adults for six years found that those whose physical function was higher at the start of the study were three times less likely to develop dementia than were those whose physical function was lower.

A study<sup>52</sup> following 1,740 seniors (aged 65 and older) over a six-year period, found that those who exercised three or more times a week had a 30 - 40% lower risk for developing dementia compared with those who exercised fewer than three times per week. Even modest amounts, such as walking 15 minutes a day, appear beneficial, and the more frail the person was, the more they benefited from regular exercise.

#### **References**

## **Effects of estrogen on cognitive function**

## This information should not be construed as medical advice. If you have a medical concern, consult your doctor.

- Estrogen may be very specific in its effect on memory. Postmenopausal women may be experiencing a change in thinking rather than a decline.
- In older men a higher level of testosterone is associated with better cognitive performance. The level of estrogen had no apparent effect.
- Estrogen-only Hormone replacement therapy appears to have a positive effect on mental functioning for women 65 years and older, and especially for women over 85.
- Combined Hormone Therapy (estrogen and progestin) doubles the risk of dementia (including Alzheimer's).
- Older women taking estrogen only (but not estrogen and progesterone) performed better and more consistently on memory tests.
- The estrogen drug raloxifene may help prevent decline among women older than 70 and women whose cognitive performance is declining regardless of age.

### **News reports**

#### Combined hormone therapy doesn't boost memory

A study of 180 recently menopausal women found no effect of hormone therapy (a combination of estrogen and progesterone) on cognitive function. Previous research has indicated a positive benefit of estrogen on cognition, so it is speculated that progestin may counteract these positive effects. [110]

#### Removing ovaries before menopause increases risk of cognitive impairment

A very long-running study of some 1,500 women who underwent the removal of one or both ovaries for non-cancer-related reasons, has found that women who had

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one or both ovaries removed before menopause were nearly two times more likely to develop cognitive problems or dementia compared to women who did not have the surgery. In addition, those women who were younger when their ovaries were removed were more likely to develop dementia than women who were older when their ovaries were removed. This finding adds to other research suggesting that there may be a critical age window for the protective effect of estrogen on the brain in women. [111]

#### Fitness counteracts cognitive decline from hormone-replacement therapy

A study of 54 postmenopausal women (aged 58 to 80) suggests that being physically fit offsets cognitive declines attributed to long-term hormonereplacement therapy. It was found that gray matter in four regions (left and right prefrontal cortex, left parahippocampal gyrus and left subgenual cortex) was progressively reduced with longer hormone treatment, with the decline beginning after more than 10 years of treatment. Therapy shorter than 10 years was associated with increased tissue volume. Higher fitness scores were also associated with greater tissue volume. Those undergoing long-term hormone therapy had more modest declines in tissue loss if their fitness level was high. Higher fitness levels were also associated with greater prefrontal white matter regions and in the genu of the corpus callosum. The findings need to be replicated with a larger sample, but are in line with animal studies finding that estrogen and exercise have similar effects: both stimulate brain-derived neurotrophic factor. [112]

#### Cognitive benefit of estrogen minimal for the highly educated?

A mouse study sheds light on the mixed results coming from investigations into the cognitive effects of hormone replacement therapy. The study found no beneficial effect of estrogen in female mice who were raised in a stimulating environment. On the other hand, mice raised in standard conditions showed significant spatial and object memory improvement when treated with a high dose of estrogen (following removal of their ovaries). Among mice not treated with estrogen, an enriched environment alone significantly improved spatial memory. These results

might help to explain why studies of hormone replacement therapy do not show beneficial effects for all women. Most studies of HRT use very well-educated women. [113]

#### New insights into hormone therapy highlight when estrogen best aids brain

Several studies have been exploring some of the many variables that may be important in determining the effect of hormone replacement therapy. A mouse study compared the effects of receiving daily estrogen injections ("continuous treatment") with the effects of receiving it every four days ("cyclical treatment"). The treatment lasted three months. Ovariectomized mice receiving the continuous treatment performed better on memory tasks than those receiving cyclical treatment.

Another mouse study compared the brains of ovariectomized mice treated with continuous estrogen for 47 days with those not so treated, and found that, after five days on estrogen, estrogen-treated mice produced more of the proteins important for neuron repair and neuronal function. However, with prolonged, continuous estrogen treatment, this effect diminished, and by day 47 the estrogen-treated mice were similar to the non-estrogen-treated mice in levels of the repair proteins. Mice that did not receive estrogen showed an elevation of a brain protein associated with the negative aspects of brain aging, while estrogen-treated mice did not.

A rat study examined the effects of progesterone (a component of many hormone therapies), and found that ovariectomized rats receiving progesterone exhibited deficiencies in learning and memory, supporting the hypothesis that progesterone negatively affects memory during aging. It's suggested that the negative outcome of several studies evaluating combined estrogen/progesterone HT may be due, in part, to unfavorable effects of progesterone.

Other rat studies have found that two established protective actions of estrogen with relevance to Alzheimer's are negatively affected by the presence of progesterone.

Another study using neurons in culture demonstrated the importance of timing. Neurons exposed to estrogen prior to exposure to beta-amyloid (the protein implicated in Alzheimers) had a significantly greater rate of survival than those exposed to estrogen after being exposed to beta-amyloid. The results are consistent with clinical studies in which women who received estrogen hormone therapy at the time of menopause, before cognitive degeneration becomes apparent, have a lower risk of developing Alzheimer's disease than women who never receive any sort of HT, while for women in their 60s and 70s, hormone therapy may make things worse. [114]

#### Testosterone deprivation makes men forget

A study of men undergoing testosterone deprivation therapy for prostate cancer has found that verbal memory is significantly affected. While initial learning of words is unaffected, such testosterone-deprived men show marked forgetting after two minutes. This rapid drop in memory suggests the lack of testosterone affects the function of the hippocampus. Healthy older men, on average, have about a 40% loss in their normal levels of testosterone as they age, from the ages of 20 or 30, to 70. [115]

#### For women over 65, Combined Hormone Therapy increases risk of dementia

Much to the researchers' surprise and disappointment, a four-year experiment involving 4,532 women at 39 medical centers, has found that combined hormone therapy (involving both estrogen and progestin) doubles the risk of Alzheimer's disease and other types of dementia in women who began the treatment at age 65 or older, although the risk is still small : for every 10,000 women 65 and older who take hormones, 23 of the predicted 45 cases of dementia a year, will be attributable to the hormones. The study also found that the combined hormone therapy produced no improvement in general cognitive function, and in fact had adverse effects on cognition among some women. [116]

#### Why estrogen helps memory

Estrogen has been implicated as having a role in memory in a number of studies, although findings have been mixed as to the value of HRT for improving memory in post-menopausal women. A new study helps us understand why estrogen might

be helpful. The study details how nerve cells in the hippocampus "grow in complexity" when exposed to estrogen, increasing connections among the nerve cells. It may be that, without estrogen, the connections that are there might not work as efficiently in storing and recalling certain types of memories. Previous studies have shown that the ability of women to remember word lists varies during their normal monthly cycle. [117]

#### Estrogen may dictate the problem-solving strategy chosen

Several studies have suggested estrogen may be beneficial for cognitive functioning in women. New research using rats suggests estrogen may be very specific in what types of learning it helps - and what types it may impair. In rats, it appeared to enhance place-learning, at the expense of response learning. It is suggested that postmenopausal women may experience a shift into a problemsolving mode more common to men. "Women may actually get better at performing a task from a different approach, but they are not used to doing it that way, so they view the change as an impairment." [118]

#### Older men with higher testosterone levels performed better on cognitive tests

A study of the levels of estrogen and testosterone in 300 older men enrolled in a larger study of risk factors for osteoporosis in men found that a higher level of testosterone was associated with better performance on various cognitive tests. The level of estrogen had no apparent effect. The study looked only at natural levels of hormones, and it is too soon to say whether testosterone supplements would help prevent cognitive decline. Although some previous studies have suggested that testosterone might benefit the brain, most of these studies have been of younger men. [119]

#### Hormone replacement therapy may have cognitive benefits for older women

A study of more than 2,000 women 65 or older, found that those who underwent hormone replacement therapy after menopause appeared to enjoy better mental functioning. Women 85 and older did especially well. The improvements were seen only in women free from dementia. However, the sample does not reflect the general population - most of the participants were Mormon, and the prohibition of alcohol and tobacco might be a significant factor. [120]

#### The positive effects of estrogen on memory

Postmenopausal women who take estrogen and young college-aged women performed more consistently on memory tests compared with postmenopausal women not taking the hormone. Consistency differs from overall memory ability and is a relatively new area in research about the neuropsychology of aging. Consistency measures memory capability on multiple administrations of the same test or on several related tests in a short period of time. The study involved 48 postmenopausal women (aged 60 - 80), and 16 younger women (18 - 30). The older women were divided into three groups: 16 non-hormone users, 16 estrogenusers and 16 estrogen and progesterone-users. Younger women and older women taking estrogen performed more consistently than the older women not taking the hormone, as well as having higher overall memory scores. Women taking a combination of estrogen and progesterone did not perform as consistently as the estrogen-only users. This finding suggests progesterone may block some of the beneficial effects of taking estrogen alone. [121]

# The estrogen drug raloxifene may help prevent cognitive decline in women over 70

The designer estrogen drug raloxifene has been prescribed to millions of postmenopausal women for osteoporosis, but its effects on the aging brain are unclear. A new study shows that although raloxifene does not affect the cognitive performance of most women, it may help prevent decline among women older than 70 and women whose cognitive performance is declining regardless of age. [122]

#### **References**

## Glossary

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**amyloid ß-derived diffusible ligands** (ADDLs): tiny toxic <u>proteins</u> only discovered a few years ago, they attack specific synapses rather than the neurons themselves. The synapses attacked are those where there is a gene linked to memory that is normally expressed, thus disrupting the normal expression of the gene. ADDLs are a form of <u>amyloid beta</u>, but differ from <u>plaques</u> in that they are very much smaller, are soluble and diffuse between brain cells until they find vulnerable synapses. They are found in much higher quantities in the brains of those with Alzheimer's, and it is theorized that they accumulate at the beginning of Alzheimer's disease and block memory function. The process is predicted to be reversible, because the ADDLs disrupt communication between cells rather than destroying the cells.

**amyloid beta peptides** : <u>peptides</u> derived from <u>amyloid precursor protein</u>, these fragments of amyloid beta are the main protein component of plaques, and probably a major cause for the their toxicity. They are thought to bind to a receptor in the brain, blocking the signals needed for learning and memory. The peptides come in two forms: A-beta 42 and A-beta 40. Amyloid beta peptides routinely circulate in the human bloodstream, where they are harmless. Early beta amyloid accumulation within neurons is the trigger for the onset of memory decline in Alzheimer's.

**amyloid precursor protein** (APP): is found in many tissues besides brain, but its functions are largely unknown. It is anchored across the cell membrane, so part of it is inside and part of it is outside the cell. <u>Enzymes</u> snip it apart into three <u>protein</u> fragments, two of which are released outside the cell and one inside. One of those which is found outside the cell is made of <u>amyloid beta peptides</u>. It's speculated that the creation of amyloid plaque is a byproduct of a misregulation in normal APP processing. Mutation in the APP is thought to be involved in early-onset Alzheimer's; the APP gene is located on chromosome 21, at 21q21.

**anthocyanins**: perhaps the most important of the visible plant pigments, responsible for the reds, purples, and blues you see in plants, they have strong

antioxidant properties; found in fruit such as blackberries, raspberries, blueberries, etc, and vegetables such as red cabbage.

**apolipoprotein E (APoE)**: is a <u>protein</u> whose main responsibility is transporting cholesterol out of the cell. Too much of this protein results in an increase in the level of free cholesterol in the cells. An allele of the gene responsible for this protein has been identified as a major genetic risk factor for Alzheimer's (see <u>APOE gene</u>).

**apolipoprotein-E gene** (APOE): the e4 allele of the <u>apolipoprotein E</u> gene has been identified as a major genetic risk factor for Alzheimer's. There are three versions (alleles) of the APOE gene; the most common is e3, present in over half the population. Those who inherit one copy of the e4 allele are at higher risk of developing type 2 Alzheimer's, a late-onset form; those who inherit two copies are at greater risk. Most people with familial hypercholesterolemia have 2 copies of the e4 allele. One study suggests having the e4 allele is particularly risky in combination with a small head size. Similarly, calorie and fat intake appear to increase the risk of developing Alzheimer's in those with the allele. An Australian study has more recently identified the -491A allele as another risk factor. The same study found that people with these alleles were more likely to complain of memory difficulties. APOE is located on chromosome 19. A gene on chromosome 10 has also recently been identified as significantly increasing the risk of Alzheimer's when found in combination with APOE e4.

**beta-amyloid plaques:** are considered one of the hallmarks of Alzheimer's disease. The plaques are hard, insoluble aggregations of various peptides and proteins, chiefly and most important amyloid-beta peptides. Recent research suggests plaques attach primarily to blood vessels, damaging them.

**beta-secretase**: one of three forms of <u>secretase</u>, it and <u>gamma-secretase</u> are implicated in the formation of <u>plaques</u>.

**brain-derived neurotrophic factor**: a neuro<u>peptide</u> important for neuronal growth, survival, differentiation, connectivity and <u>synaptic plasticity</u>. The gene controlling BDNF expression comes in two variants, one of which is linked to poorer memory.

**cerebrum:** the largest structure of the brain; containing the cerebral cortex (the outer layer), which is made of <u>gray matter</u>, and an inner core composed of white matter (myelinated nerve fibers and gray basal ganglia); divided into a number of regions known as <u>lobes</u>.

**cingulate gyrus:** (fold) in the <u>limbic lobe</u>; implicated in self-reflective thought (thinking about yourself and your attributes).

**cognitive reserve**: the idea that education and mental stimulation during a lifetime can give older adults a cognitive reserve or neuroplasticity that can reduce the effect of brain abnormalities on cognitive function, allowing them to function normally for longer in the presence of such brain abnormalities.

**corpus callosum** : the main "bridge" between the left and right cerebral hemispheres; a broad bundle of myelinated fibers (white matter) carrying information from regions in one lobe to similarly placed regions in the opposing lobe.

**CREB**: <u>cAMP</u> response element–binding protein, an adenosine 3',5'monophosphate response element–binding protein; implicated in keeping memories stable, and more recently seen to be involved in determining which neurons store memories.

**cyclic adenosine monophosphate** (cAMP): a messenger chemical formed from ATP, that affects the ability of an action potential to continue.

**dentate gyrus**: a substructure of the <u>hippocampus</u>, highly active during encoding (learning) of face-name pairs.

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**early-onset Alzheimer's**: is characterized by symptoms appearing before age 65; it is thankfully rare (some 6-8% of Alzheimer's cases are early-onset). Early-onset Alzheimer's has a much stronger genetic basis that late-onset Alzheimer's, and is therefore also known as familial Alzheimer's. Three genes have been implicated, on chromosomes 1, 14 and 21 (see presenilins). Any one of these will almost certainly lead to early-onset Alzheimer's. Early-onset Alzheimer's can begin as early as the 30s or 40s but that is exceedingly rare; more usually it begins in the 50s.

**enzymes** : are a type of protein; they are responsible for catalyzing the chemical reactions in a living cell -- that is, they accelerate the rates of reactions.

**folate**: is a water-soluble B vitamin occurring naturally in food, especially green leafy vegetables, citrus fruits and juices, whole wheat bread and dry beans. Folic acid is a synthetic form of folate. Low levels of folate are associated with high levels of <u>homocysteine</u>.

**frontal lobe** : the frontal lobes (left and right) are situated at the "front" of the cortex, i.e. behind the forehead. They are the largest of the lobes in the cerebrum, and may be thought of as the "highest" part of our brain. The frontal lobes are critical for those faculties that humans regard as special to our species - reasoning, planning, attention, some aspects of language. Women have up to 15% more brain cell density in the frontal lobe, but with age, appear to shed cells more rapidly from this area than men. By old age, the density is similar for both sexes. The effect of this on performance is unknown.

**gamma-secretase**: is one of the two <u>secretases</u> implicated in <u>plaque</u> formation. Gamma-secretase makes the final cut in the <u>APP</u>, and it does so within the cell membrane, using the thickness of the membrane as a guide for where to cut. Membranes expand or contract depending on the lipid content of the cell, and so, therefore, does the length of the cut product. When the cleavage goes wrong, plaques result. Gamma-secretase is divided into several subunits, which have recently been discovered to act separately on different tissues. **genetically engineered mice**: mice that are genetically engineered to develop an Alzheimer's-like disease by the introduction of <u>transgenes</u>. Mice ordinarily do not develop symptoms of the disease. see

<u>http://www.mni.mcgill.ca/nm/1999f/en/transgenes.html</u> for a description of how this achieved.

**gray matter** : brain tissue is divided into two types: gray matter and white matter. Gray matter is made up of the cell bodies of nerve cells. The volume of gray matter tissue is a measure of the density of brain cells in a particular region.

**hippocampus** : means "sea horse", and is named for its shape. It is one of the oldest parts of the brain, and is buried deep inside, within the limbic lobe. The hippocampus is important for the forming, and perhaps long-term storage, of associative and episodic memories. Specifically, the hippocampus has been implicated in (among other things) the encoding of face-name associations, the retrieval of face-name associations, the encoding of events, the recall of personal memories in response to smells. It may also be involved in the processes by which memories are consolidated during sleep.

**homocysteine**: is a homologue of the naturally-occurring amino acid cysteine, produced from <u>methionine</u>. Elevated levels of homocysteine are associated with a greatly increased risk for coronary heart disease, stroke, vascular dementia, and Alzheimer's disease. Levels of homocysteine in the blood are strongly influenced by diet -- high levels are particularly associated with deficiencies in vitamin B12 and <u>folate</u> -- lifestyle factors such as smoking, and genetic factors.

**limbic lobe:** a <u>lobe</u> that lies deep within the <u>cerebrum</u> - a broad collar of cortex fringing the <u>corpus callosum</u> (limbic means "border"). The limbic lobe includes the <u>hippocampus</u>, cingulate gyrus, dentate gyrus, and the parahippocampal gyrus.

**lobes** : the <u>cerebrum</u> is highly convoluted - it is this deep and numerous folding that vastly increases the cortical area of the human brain. The deepest fissures provide somewhat arbitrary boundaries for the mapping of the brain. Following

these guidelines, the cerebrum is divided into five lobes: the <u>frontal</u>, <u>temporal</u>, <u>parietal</u>, <u>occipital</u> and <u>limbic</u> lobes.

**MCI-A**: mild cognitive impairment, amnesic subtype; patients with this disorder show memory impairments but not other cognitive impairments (e.g., in reasoning).

**MCI-MCD**: mild cognitive impairment, multiple cognitive domain subtype; patients with this disorder show mild impairments in cognitive tasks such as judgment or language, and mild or no memory loss.

**methionine**: is an amino acid found in beta-amyloid; suggested as being the source of the toxic free radicals produced by <u>amyloid-beta peptides</u>. Methionine is one of the essential amino acids that we require from food. Broken down, it produces <u>homocysteine</u>; B-vitamins are required to convert homocysteine back to methionine. High levels of methionine can be found in sesame seeds, Brazil nuts, fish, meats, and dairy products. Most fruits and vegetables contain very little -spinach, potatoes, and boiled corn are some of the exceptions.

**neurofibrillary tangles** : are tangled bundles of fibers inside neurons. Like <u>plaques</u>, they are considered one of the hallmarks of Alzheimer's disease, although they also occur in other neurological disorders. Tangles mainly consist of <u>tau</u> <u>protein</u>. By disrupting the structure of the neuron and disabling the transport of nutrients, tangles cause neurons to die. Plaques can induce tangles, but that is only one way in which tangles can form. Nicotine is, apparently, another.

**neurotransmitter** : a messenger chemical in the brain; it is through neurotransmitters that neurons communicate with each other. Examples are GABA, glutamate, acetylcholine, dopamine, serotonin, norepinephrine.

**occipital lobe** : one of the <u>lobes</u> of the <u>cerebrum</u>, situated at the back of the skull, and above the hindbrain. It borders with the <u>parietal lobe</u> (from which it is not clearly demarcated) and the <u>temporal lobe</u>. The occipital lobe contains the primary visual cortex, where visual information is processed.

**parietal lobe** : one of the <u>lobes</u> of the <u>cerebrum</u>, situated at the top, behind the <u>frontal lobe</u>. The primary sensory area is located in the parietal lobe - this is where nerve impulses carrying sensations of pain, temperature, touch, and pressure come. Areas in the parietal lobe are also involved in spatial orientation, speech and language development, and attention.

**peptide** : a compound of two or more amino acids linked by a peptide bond. Peptides differ from <u>proteins</u> by their size; peptides are shorter. Proteins can be broken down into peptides (this occurs during digestion).

**proteins** : are essential to living organisms; they are long chains of amino acids linked together by <u>peptide</u> bonds. <u>Enzymes</u>, hormones, and antibodies are all types of protein.

**polyphenols**: antioxidant chemicals that may help reduce the risk of Alzheimer's. Most exist primarily in the skins of fruits and vegetables and are particularly abundant in teas, juices and wines.

**presenilins**: are related genes implicated in <u>early-onset Alzheimer's</u>. Presenilin 1 (PS1) is found on chromosome 14, and PS2 on chromosome 1. Presenilins are involved in the production of <u>amyloid peptides</u>, but exactly how mutations in the genes cause Alzheimer's is not yet understood. Mouse studies have found that deletion of these genes causes memory loss and gradual death of nerve cells in the mouse brain, demonstrating that the protein products of these genes are essential for normal learning, memory and nerve cell survival.

**secretase**: is a <u>protease</u>. There are three known forms: alpha, <u>beta</u>, and <u>gamma</u>. They process <u>APP</u>.

**Scottish Mental Survey:** assessed 87,498 eleven-year-olds in 1932, and another 70,805 in 1947. More recently, over 1000 of these students were contacted and reassessed, on the exact same tests.

**Stroop effect**: concerns color-name interference: when you see the name of a color written in the same color, that's easier to process than when the color doesn't match the name (for example, 'red' written in blue ink). Comparison of the different reaction times (how long it takes you to process **RED** compared to **RED**) has been used to test attention, executive function, and processing speed, and less directly the presence of various disorders.

synapse : the site where one neuron makes contact with another

**synaptic plasticity**: the ability of <u>synapses</u> to be altered resulting in a modification of <u>synaptic transmission</u>; considered to be the foundation of learning and memory

synaptic transmission: the process of transfering information at a synapse

**tau proteins** : are <u>proteins</u> that form part of a structure called a microtubule, which helps transport nutrients and other important substances from one part of the nerve cell to another. In Alzheimer's disease, however, the tau protein is abnormal and the microtubule structures collapse, causing neuron death.

**temporal lobe** : one of the <u>lobes</u> of the <u>cerebrum</u>, situated below the <u>frontal</u> and <u>parietal</u> lobes, and above the hindbrain. The temporal lobe is primarily concerned with sensory experience - specifically, with hearing, and with the integration of information from multiple senses. Part of the temporal lobe also plays a role in memory processing. Patients with damaged temporal lobes appear to have impaired lexical retrieval of names of living things.

**transgenes**: genes from one organism that have been incorporated into another organism.

**vascular dementia**: dementia caused by poor blood flow, produced by a single, localized stroke, or series of strokes. It's the second most common type of dementia, after Alzheimer's, accounting for up to a third of diagnosed dementia cases.

**working memory**: includes the part of memory of which you are conscious; the "active state" of memory. Information being "put into" memory is held in working memory; memories being remembered are held in working memory. The capacity of working memory — how much information it can hold at one time — is severely limited. Working memory governs your ability to comprehend what you are reading or hearing, your ability to learn new words, your ability to plan and organize yourself, and much more.

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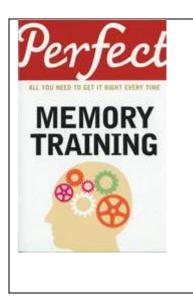
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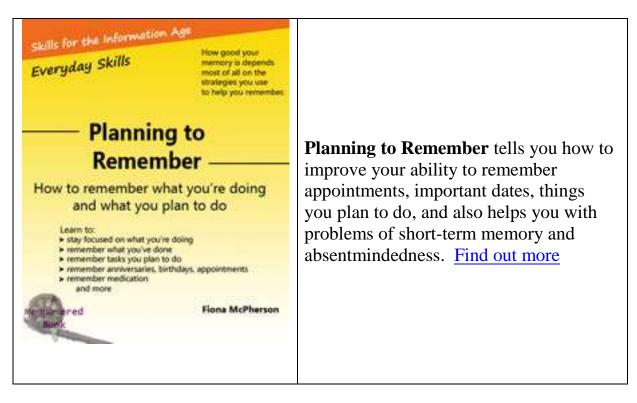
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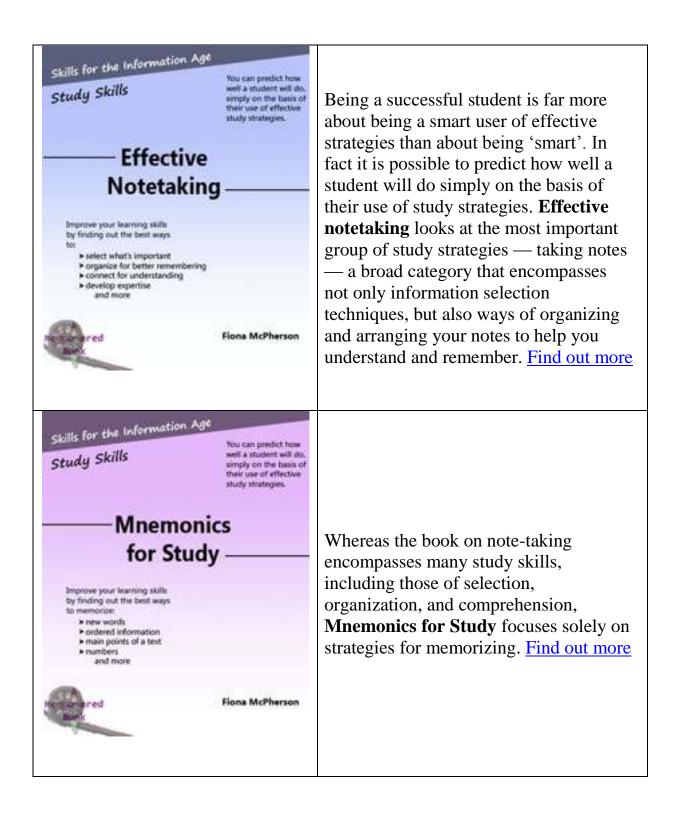
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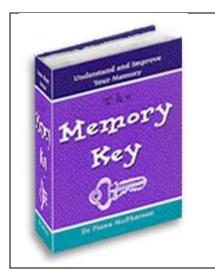
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