A BIOLOGICAL-PSYCHOLOGICAL VIEW ON AGEING

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Abstract

In this paper two major views on ageing: the 'genetic' ('programmed') types of theories and the 'wear-and-tear' ('damage' or 'error') theories are presented. The genetic theories, saying that specific genes regulate ageing, explain the species differences better, while the wear-and-tear theories, implying that damages in the genome lead to ageing, explain the male-female differences better. The 'survival curve' (human's survival as a function of time), shows that the maximum age is fixed, but that the average age still increases. Good food, a safe hygienic environment and adequate medical care play a positive role in human longevity. Notwithstanding that it can be stated that ageing is associated with somatic and, in particular, with cognitive decline. Brain degeneration as expressed in the diseases of Alzheimer and Parkinson are rather typical ageing disorders. However, natural ageing is also accompanied by mental and physical decline, presumably due to brain cell loss and loss of contacts between nerve cells. Presently, it becomes more and more clear that the decline due to ageing can be delayed or slowed down to a certain degree. Keeping the body and the brain active might be associated by a reduction in the loss of synapses, or even in the formation of extra synapses. This forms a compensation buffer for the decrease of general bodily processes, including cognitive functions. Especially, elderly people complain about memory problems. The memory decline is particularly in episodic memory. However, the procedural memory (for the performance of complex activities and skills) does not decline and the semantic memory (the memory concerned with meanings and concepts) even sometimes profits of the rise in age. Though old people have episodic memory problems, they have compensating types of memory, which delivers them to have an adequate response to life situations. This can be regarded as an increase in wisdom.

Keywords: ageing, biological, psychological

Abstrak

Tulisan ini memaparkan dua cara pandang utama dalam menjelaskan proses penuaan, yaitu yang mengacu kepada the genetic atau programmed theories dan the wear-and-tear (damage or error) theories. Pendekatan genetic theories menyatakan bahwa penuaan terjadi karena gen-gen tertentu dalam tubuh manusia akan mengalami penuaan pada waktunya, sedangkan pendekatan wear-and-tear (damage or error) theories menekankan bahwa penyebab penuaan adalah terjadinya kerusakan pada kumpulan kromosom sehingga perbedaan penuaan pada wanita dan pria lebih mudah dijelaskan melalui pendekatan ini. Makanan dan lingkungan yang sehat serta pemeliharaan kesehatan yang baik berperan penting dalam pencapaian usia lanjut. Meskipun demikian, proses penuaan juga terkait dengan penurunan fisik dan fungsi kognitif. Degenerasi otak sebagaimana terjadi pada penyakit Alzheimer dan Parkinson adalah gangguan khas pada usia tua, namun proses penuaan yang wajar juga disertai penurunan fungsi mental dan fisik yang disebabkan hilangnya sel otak atau persambungan antara sel syaraf. Saat ini proses penuaan semakin memungkinkan untuk ditunda sampai taraf tertentu, antara lain dengan tetap mempertahankan aktivitas tubuh dan otak, karena dengan demikian hilangnya synapsisdapat dikurangi, atau justru dapat menumbuhkan synapsis baru,

dan hal ini akan membantu mengatasi penurunan fungsi fisik dan kognitif. Jika para lansia mengeluhkan masalah ingatan, maka yang sebenarnya terjadi adalah episodic memory. Pada procedural memory (yang terkait ketrampilan dan aktivitas kompleks) dan semantic memory (yang berhubungan dengan makna dan konsep) umumnya tidak terjadi penurunan, dan justru berperan mendukung proses lansia dalam menghadapi berbagai situasi dan bahkan meningkatkan kearifan mereka sebagai lansia.

Kata kunci : penuaan, biologis, psikologis

Theories of ageing

Ageing as a consequence of time and life is still a mysterious phenomenon. Some humans are active and vital at an age 90, while others are frail at an age of 60. Why is there so much variation in ageing among members of the same species? What in fact causes ageing? There are multiple theories about the causes of ageing, but one general all-explaining theory is yet not available. The ageing theories fall into two main categories: the theories that ageing is determined by genes (the 'genetic' or 'programmed' theories), and the theories stating that damages and errors in the genome are the cause of ageing (the 'wear-and-tear' theories, also indicated as the 'damage' or 'error' theories) (Lin, 2010).

Figure 1. Ageing as a consequence of time and life is still largely a mystery. Unsolved questions are why body cells and organs change with age, why they give it up after a certain time, why animal species have their own specific age, and why females grow older than males. (After Ricklefs & Finch, 1995).

The genetic theories assert that ageing is an essential and innate part of the biology of humans (Figure 2). Ageing is programmed into the body systems by the DNA in the genes. Genes regulate the biological clock indicating when proliferation starts, when it is time for maturity and for senescence, and also when it is time for the end of life. Humans are born with a unique genetic code, and the body is pre-programmed. Currently, a specific type of a genetic theory centres on telomeres, which are repeated DNA segments occurring at the ends of chromosomes. The number of repeats in a telomere determines the maximum life span of a cell, since each time a cell divides multiple repeats are lost. Once telomeres have been reduced to a certain size, the cell reaches a critical point and is prevented from dividing further. As a consequence, the cell dies. The number of times the cell can divide is called the Hayflick limit, after the American biologist Leonard Hayflick who proposed this as the first in 1965 (Hayflick, 1965; Shay & Wright, 2000).

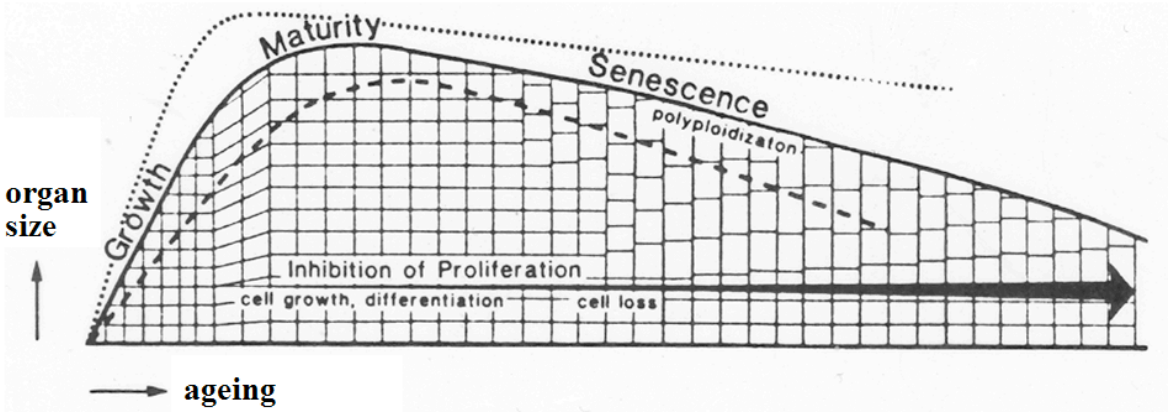

Figure 2. A graphic profile of the genetic theory of ageing. Genes determine the steps in human proliferation, growth, maturity and senescence. (After Tauchi and Sato, 1984).

The second set of theories are the wear-and-tear theories, stating that the effects of ageing are caused by errors, mainly occurring in the genome. Over time this is expressed in less functioning cells and body systems (Moody, 2010) (Figure 3). This theory was introduced by August Weismann in 1882, a German biologist, who believed that the body and its cells are damaged by use. Essentially, the bodily systems ‘wear out’. Once they have worn out completely, they can no longer function. A range of things can damage body systems. Errors can be induced in the genetic program by mutations, leading to changes in protein production and in a decreased functioning of cells and tissues. Exposure to radiation, toxins and ultraviolet light can impair the genes. But also the effects of the body's own functioning can cause damage. For example when the body metabolises oxygen, free radicals are produced that can cause impairments to the genome leading to malfunctioning of cells and tissues.

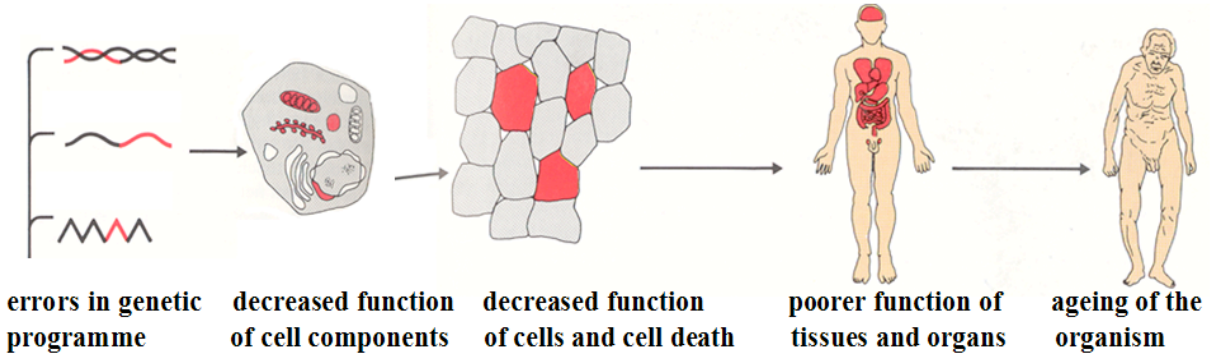

Figure 3. The 'wear-and-tear' ('damage') conception of ageing. Mutations in the genetic program, caused by destructive processes, change the protein structure leading to decreased functioning of cells, organs and tissues, and ultimately leading to death. (After Knook, 1982).

Currently the best theoretical concept of ageing is a mix of both types of theories. This two-process of ageing, best explains why species have their own specific age, but with a large variability. This large variability is due to errors and damages occurring in the course of life. A recent finding of the Dutch group of Riekelt Houtkooper (2013) fits in this two-process of ageing. This group was able to reduce in mice the mitochondrial activity of genes controlling age and noticed that the animals all reached a high age. Perhaps, by manipulating genes which determine ageing the maximal age can be manipulated.

Up to now the maximal age is fixed and determined by genetic programs, while the (lower) mean age can be attributed to the negative effects of mutations, damages and accidents. Longevity of humans with a maximal and mean age is expressed in a 'survival curve' (Cheung, et al., 2005; Strehler, 1975). The survival curve is a graph showing the proportion of a population living after a given age. In the ideal form the curve is rectangular. A rectangular shape is the ideal curve, because all people which are born reach than their maximal age. The ageing of the population is an issue in all countries worldwide because its expresses health and welfare of a population. Survival curves taken from demographic life tables may help shed light on the fact that humans are generally living longer and that human populations are growing older. The survival curves presented in Figure 4 show the trends in human longevity from ancient times to present. The curves illustrate the approach to the final rectangular shape. Main factors contributing to more rectangular survival curves are better life circumstances, improved medical care and reduced baby mortality.

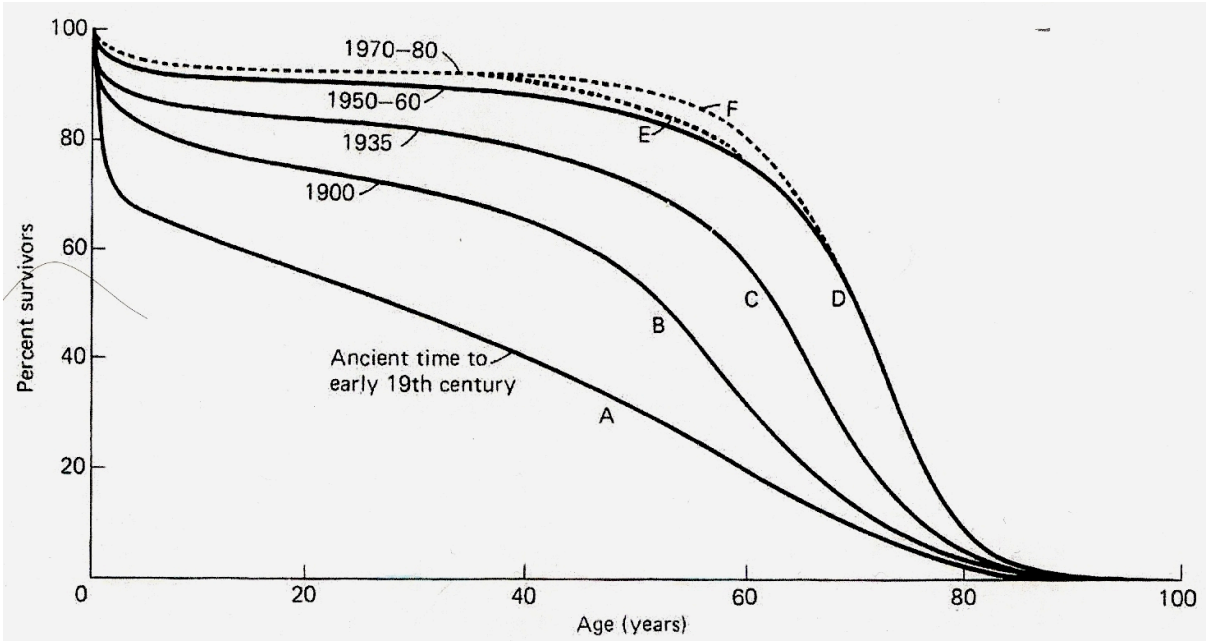

Figure 4. Trends in human longevity from ancient times to present. The factors leading to more rectangular survival curves in the course of years are shown. The shift from A to B is due to improved housing and sanitation, from B to C to better hygiene and to the introduction of immunisation, from C to D to the introduction of antibiotics and to improved nutrition, and from D to F to the influence of recent biomedical breakthroughs. E shows the recent male survival and F the female survival curve. (After Strehler, 1975).

The survival curves of Figure 4 show three important facts. The first is that all curves, whatever their shape is, converge to the same point on the horizontal age axis, roughly established at 90 years. This implies that the maximal age of the human species is fixed on approximately that age, with some biological variation, suggesting genetic determination. The maximal age of humans is thus not increasing, as is often stated. What is increasing, is the average, or mean, age of the population. That is the second important point. The more rectangular the curve is, the higher the mean age. The survival curve shows indirectly also the development of a country; the higher the development, with better housing and living situations and with higher quality of medical care, the more rectangular the curve. The curve under B in Figure 4 stands model for the survival curve for a less developed country, such as Indonesia, showing still a large difference with the curves under E and F, valid for a high developed country such as the Netherlands. Finally, the third point is the difference in longevity between men and women. In the Netherlands the average age of women is currently 84 years, while the mean age of men is 79 years; this is in Indonesia 74 years for women and 69 years for men. It is not clear why there is a difference between men and women (although there is a trend that he difference becomes smaller), but it points to the damage theory of ageing, since the maximal ages are identical. The most accepted view is that female hormones, such as oestrogens, protect the body for diseases by increasing the body resistance, while the male hormones, such as testosterone, leads to behaviours with a larger risk on damages.

Figure 5. Women grow older than men, but a main question is whether this brings more happiness and welfare to women. A caricature is 'Men die quicker, but women get sicker', given the heightened risk in women on ageing diseases and mental decline, and, in particular, on feelings of loneliness and desolation. Shown here is the drawing 'Ah! those happy days are fled forever' of the Mary Evans Picture Library.

Changes in body and brain

What happens in body and brain during ageing? Figure 6 gives several examples (Shock, 1963). The body condition drops down, by a decrease of heart and lung capacity. The athletic performance becomes less, due to the loss of power of the muscles by a reduction of contractile fibres. The body shape slowly changes as a result of the increase of body fat at the cost of body water. The loss of muscle strength and elasticity is expressed in hearing losses, especially for the higher tones, because the tiny muscles in the ear cannot follow the high frequency sound vibrations, and in the necessity of wearing reading glasses since the accommodation of the eyes is diminished.

Often associated with ageing are somatic diseases, such as various types of cancer, diabetes 2 with a shortage of insulin in the blood, and benign prostate hypertrophy in men. A typical phenomenon of ageing is the slow rise of blood pressure (Feskens, et al., 1993) (Figure 7). Both the systolic and the diastolic blood pressure climbs up as a consequence of atherosclerotic processes. This forms a main risk factor for cardiovascular diseases, such as heart attacks and brain strokes, since the formation of thrombi in atherosclerotic vessels becomes more probably. Transient ischemic attacks (TIA's) are warning signals and after having experienced a TIA, the daily use of the aspirin Ascal, to keep the blood thin and fluid enough, may prevent more serious attacks ((Fields, et al., 1977).

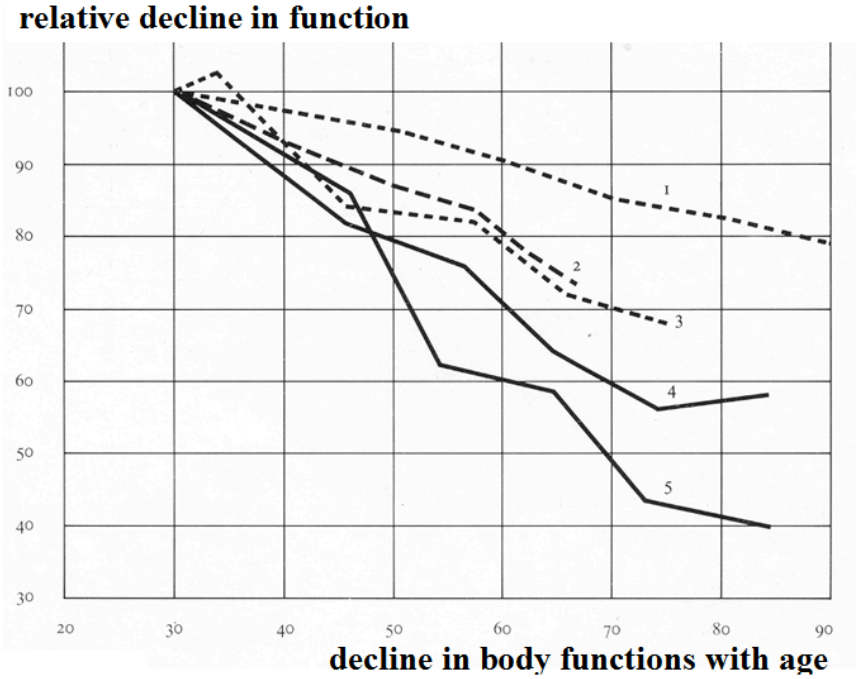

Figure 6. Decline in body functions with age, indicated on the X-axis). 1. decrease in metabolic activity. 2. speed of propagation of the nerve impulse over the axon slows down, 3. the diminishment of body water, accompanied by an increase of body fat (ratio water versus fat decreases), 4. heart minute volume is going down, 5. capacity of lungs declines. (After Shock, 1963).

There is substantial evidence that there is not only deterioration of the body but also of the brain with ageing (Deary, et al., 2009). Typical diseases associated with ageing are degenerations of the brain as expressed in Alzheimer's disease, whereby cortical regions are specially affected, and Parkinson's disease, with a degeneration of thalamus and basal ganglia. The disease of Alzheimer leads inevitable to severe cognitive decline, while the disease of Parkinson is more expressed on a behavioural level with milder cognitive deterioration. But it is also generally accepted that a certain decline in cognitive performance is an unavoidable concomitant of normal ageing. Figure 8 gives a rough idea of the impairments of cognitive functions across the life span (Hertzog, et al., 2009). At an age of 90 cognitive performances generally sink below the functional threshold, but it has to be noticed that the variance is extraordinary large. Aged people have in particular problems with the learning in memory of words and events (Le Moal, et al., 1997). This type of memory is called the episodic memory. Figure 9 shows the decline in episodic memory in the form of a free recall test.

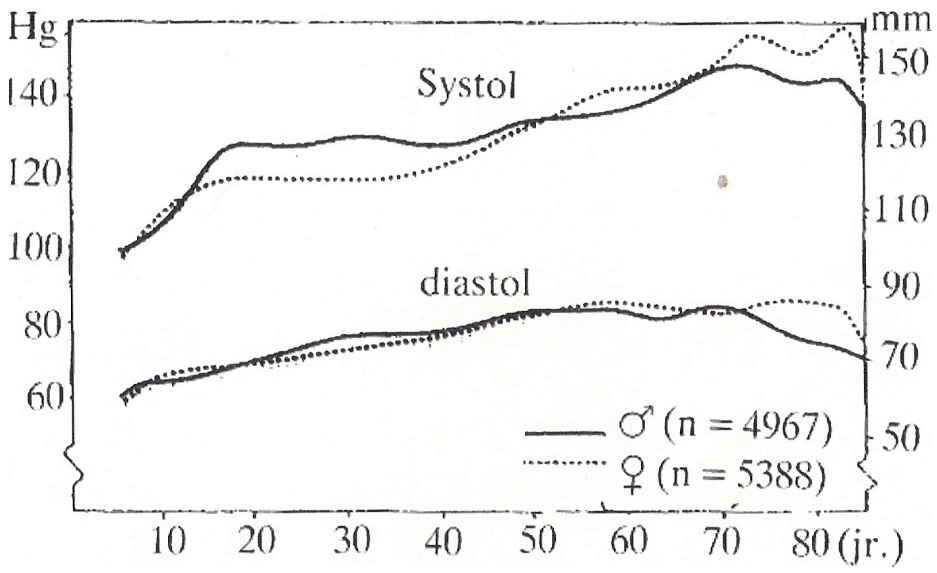

Figure 7. This graph shows the increase of the systolic as well as the diastolic blood pressure with ageing in men and women. Age is on the X-axis and blood pressure in mm Hg on the Y-axis. (After Feskens, et al., 1993).

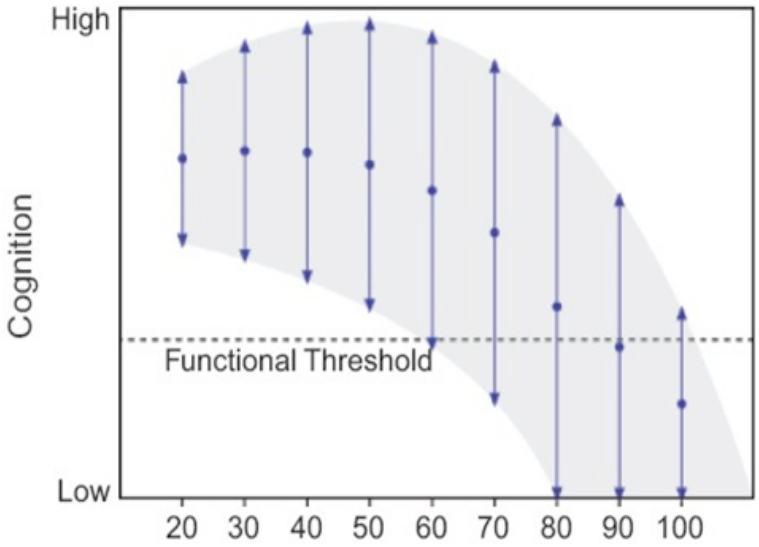

Figure 8. A rough scheme of the decline of cognitive performances, such as memory, learning, and attention, across the life span of (healthy) people. (After Hertzog, et al., 2009).

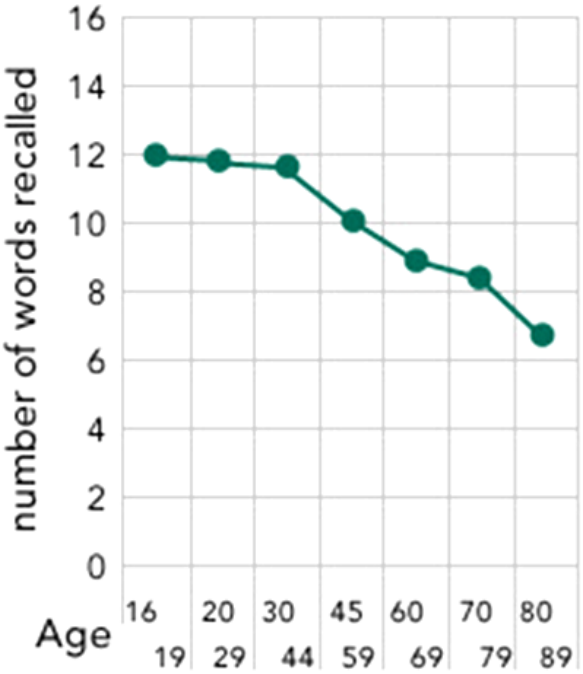

Figure 9. The recall of words of the 15-words test, recalled one day after learning. For young people the common score is 12, but at an age of 80 years this is reduced till approximately 6 words. This is a reduction of 50%!

A common aspect of ageing is the drop in activity over the day, which seems a natural characteristic of ageing. Figure 10 shows the age-related activity decrease in leisure and social activities (Marcum, 2011). Elderly people take life more easy and it seems more difficult to find the motivation for performing enduring activities. The result is that approximately 70% of the entire population is insufficiently active. Evidence accumulates that a firmly reduced activity is negative for maintaining optimal health. Physical activity may reduce the risk of poor cognition and early cognitive decline. Also the sleep in the night changes with age (Figure 11). Generally sleep is experienced as less satisfactory due to more fragmentation, compared to the sleep of youngsters (Carskadon, et al., 1982; Feinberg, 1974). It last longer before elderly people fall into sleep, and when they finally sleep, they wake up many times a night. This leads to a reduction in both deep sleep and REM sleep. So considering the diminished activity during the day, even often strengthened with some daily naps, and the nightly sleep with more waking, it can be stated that the 'circadian amplitude' is reduced (Carrier, et al., 1996). This amplitude is considerably larger in young people, with a large distance between the high daily vigilance and the low vigilance during the deep nightly sleep. In the electroencephalogram of old people signs of sleep can seen in the recordings made during wakefulness, while more waking activity is present during sleep recordings (Figure 12).

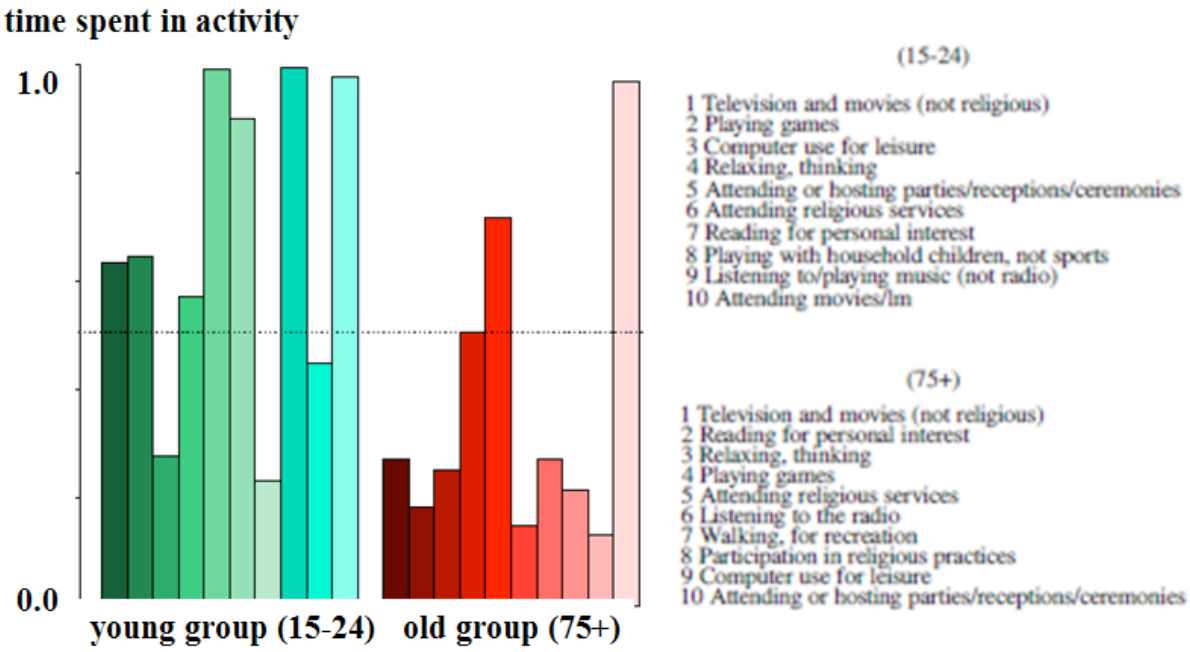

Figure 10. Reduction of time spent in several leisure and social activities by 75+ people compared to youngsters of 15-24 years. Each bar of the two sets represent an activity shown at right. The total amount of time (in person-hours) spent in doing each type of activity is indicated along the Y-axis. (After Marcum, 2011)

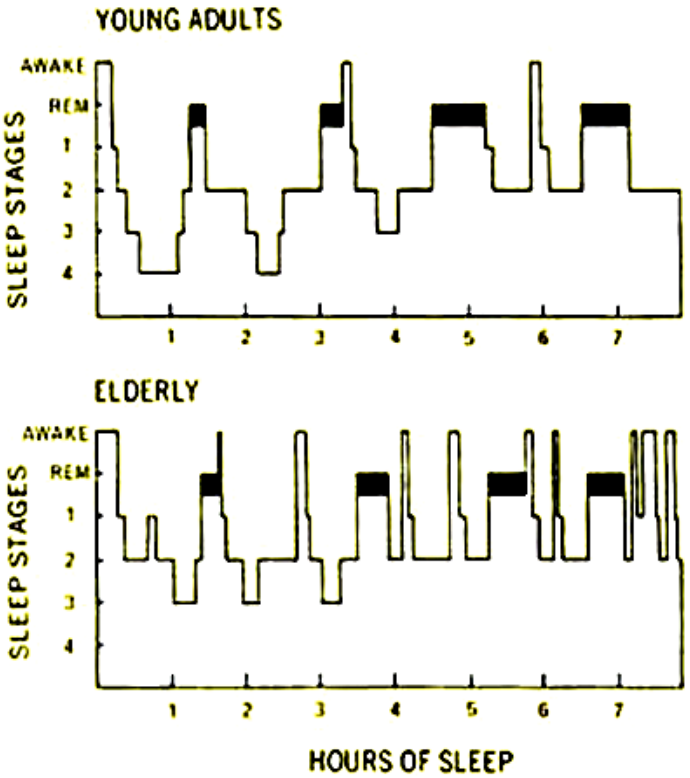

Figure 11. Changes in the sleep pattern in the elderly. Older people show a decrease in deep sleep as well as in REM sleep and a highly fragmented sleep, with many arousals and awakenings. Despite the lighter and fragmented sleep, elderly people tend to lie longer in the bed (not shown). (After Ehlers & Kupfer, 1983).

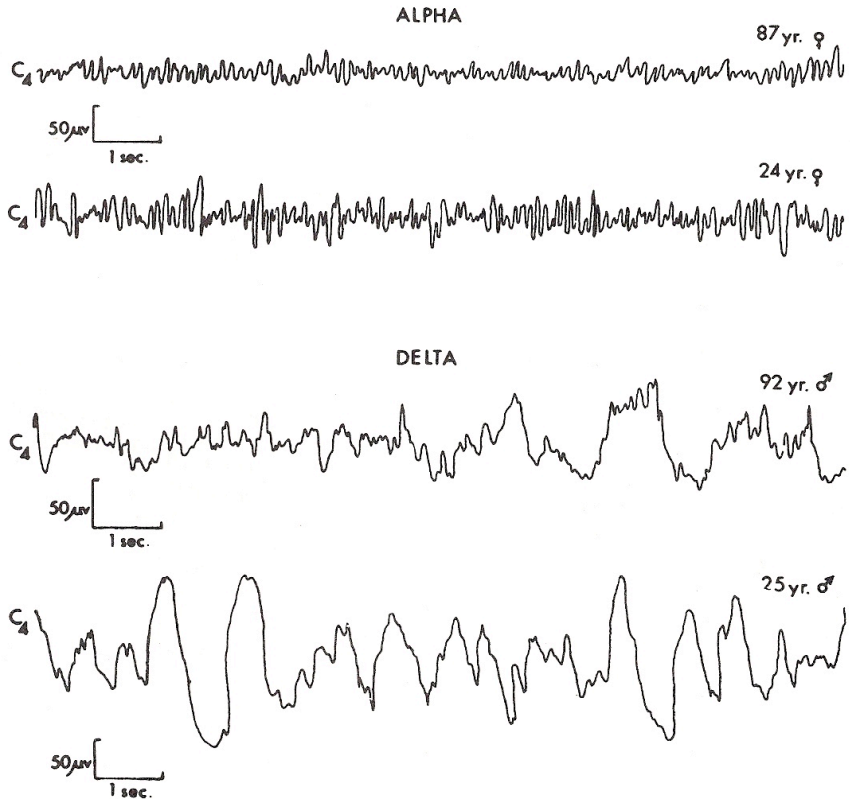

Figure 12. Electroencephalographic traces of the alpha rhythm of an 87-years old woman (top trace) and a 24-years young woman (second trace). The two lower traces show delta waves of a 92-years old man (third trace) and a 25-years young man (fourth trace). The alpha and delta traces of the old people show more similar features, than the alpha and delta activities of the youngsters. (After Prinz, 1976).

There seem to be two factors responsible for the decline in brain capacities. First there is a loss of brain cells (programmed cell death or apoptosis), and secondly, and presumably even more important, there is a reduction of contacts of brain cells with other cells and with muscles. There appears to be even a considerable loss of synaptic contacts (Figure 13). This happens abundantly in Alzheimer's disease, but is also a feature of normal ageing, though it happens than on an older age and less intensely (DeKosky & Scheff, 1990).

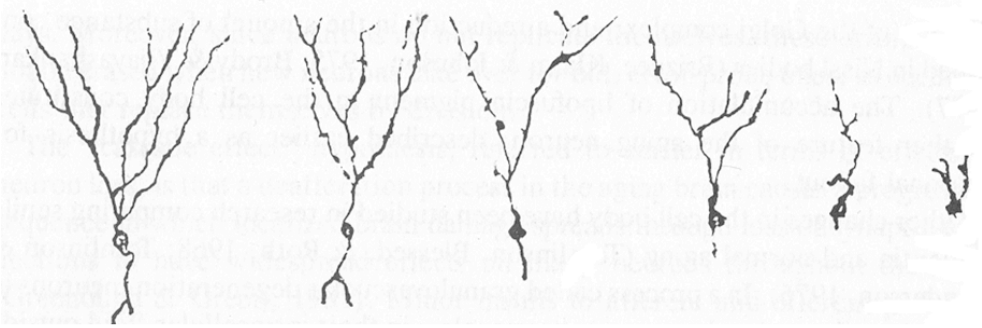

Figure 13. Nerve cells drawn from Golgi-stained sections showing the morphological changes with ageing. The neurons shrink and become stripped and bold, with less and shorter dendrites and much less synaptic contacts. (After Scheibel, et al., 1975).

Ageing affects cognition, but it is well established that ageing affects cognition differentially. Stimulating surroundings and experiences in an 'enriched environment' may have modulating effects and might slow down the decline in cognition capabilities across the life span. It has been proved that this can be attributed to the formation of extra synapses. This is shown in rats (Rosenzweig & Bennett, 1996) (Figure 14), as well as in fish (Coss, et al., 1980) (Figure 15).

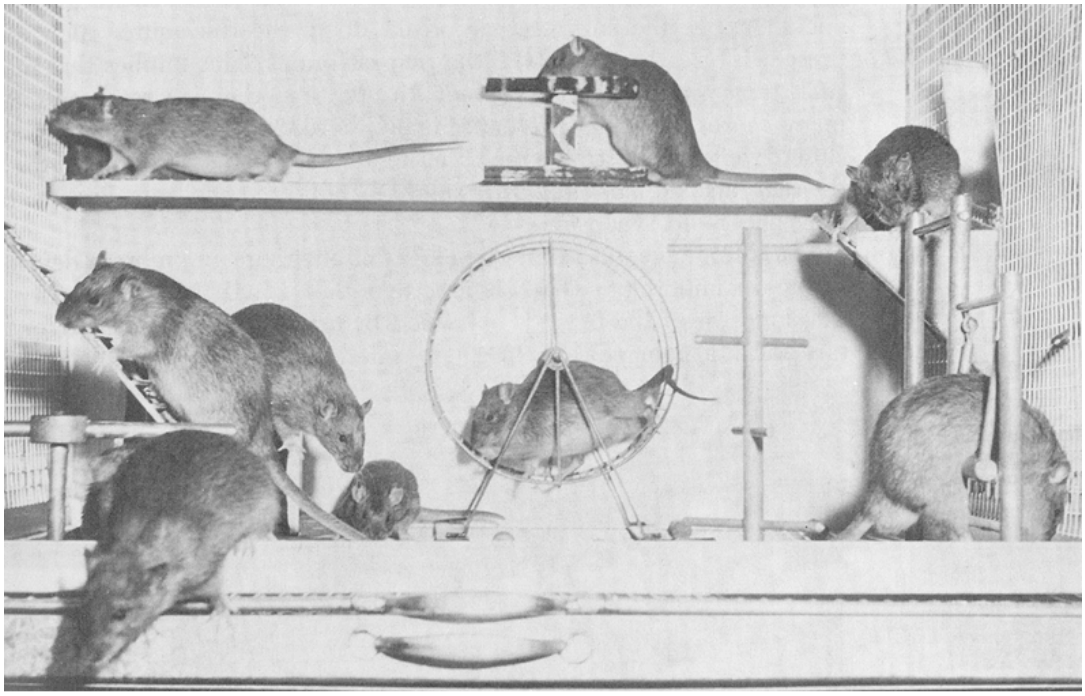

Figure 14. Photograph of a 'rich' environment. Rats reared in such environment develop more synapses than rats growing up alone in a small box without social contacts and toys ('impoverished environment'). The number of nerve cells, however, remains constant. (After Rosenzweig and Bennett, 1996).

From the experiments with rats and fish in the enriched environments, it is supposed that the neuronal changes, with more cellular branching and synaptic contacts, depend on new and interesting experiences, whereby also the increase of activity in this challenging environment plays a role. Maintaining an adequate physical activity keeps the physical machinery of the brain in a good shape. Exercise increases heart rate which pumps more blood with oxygen to the brain. It also leads to a release of several hormones, all of which are participating in providing a nourishing environment for the growth of nerve cells (Fabel & Kempermann, 2008). Hence, mental and physical exercise is a golden duo: both the increase in mental and in physical activity gives rise to the extra development of branching. The plasticity of he brain is maintained till a high age. Recent evidence proves that highly educated people are less sensitive for getting Alzheimer's disease (Sharp & Gatz, 2011). This is thought to be related to this plasticity with extra synaptic branching. This seems to form a compensating buffer. The use of cognitive capacities and physical skills enables the individual to establish a cognitive

compensation reserve (Figure 17). And it is this reserve which provides the basis for a successful compensation for the decline of cognition and health with ageing. This reserve, in the form of the extra produced synapses, keeps individuals in good health and forms a protection against diseases whereby synapses are ruined. There is already ample evidence for the view that educated people reach a higher age in good health than uneducated people (Sundquist & Johansson, 1997).

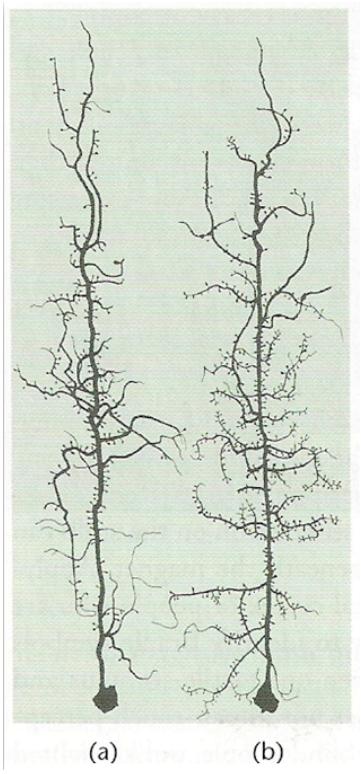

Figure 15. Effect of a stimulating environment on the formation of branches. Fish reared with other fishes develop more synaptic contacts (b), than fish reared in isolation (a). (After Coss et al., 1980).

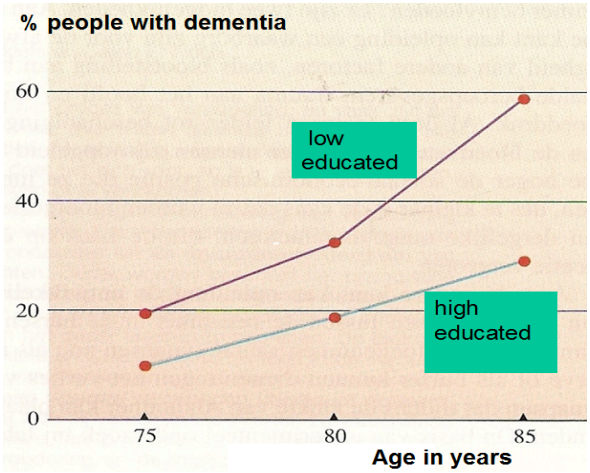

Figure 16. High educated people have a smaller chance to develop Alzheimer's disease than lower educated people. (After Ricklefs & Finch, 1995).

Figure 17. Maintaining mental, cognitive activity along with sufficient physical activity keeps older persons in good well-being and health. Engaging in stimulating activities protects neural networks and cognitive functions from declining with age.

Individuals with successful coping with normal age-associated cognitive decline are assumed to have a higher cognitive compensatory reserve. A higher level of intelligence and education (and thus cognitive capacities), explains why some individuals demonstrate more efficient coping in older age than others, because they have optimized their cognitive performance by more efficient use of the brain. Moreover, a final positive point in ageing is that old people do not loose all cognitive functions: their general knowledge of the world and the strategic insights do not decline The implicit, or procedural memory shows no decline with age (Fleischman, et al., 2004), while the semantic knowledge actually improves with age (Verhaeghen, 2003; Barrett & Wright, 1981). The vocabulary of older people even gathers strength, while complex activities and skills are still performed in an adequate way. Also the reactions to life situations are often quite competent. This compensates and masks in a way the decrease in other mental capabilities. Old people get wiser!

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