Age-related cognitive decline and the borderland between normal aging and dementia

J. JOLLES

Key words: Age, cognition, dementia
Acta Neuropsychiatrica 1997; 9: 94-96

INTRODUCTION

It is now generally agreed that healthy individuals are characterized by cognitive decline during the later decades of adult life. The acquisition of new information becomes less efficient, which, coupled with a diminished retention of this information for later use, results in substantially poorer memory performance. The ability to plan new activities, solve problems and make complex decisions, as well as cognitive flexibility is noticeably diminished. In addition, attentional processes appear to be invariably poorer in old subjects than in young subjects (for review[1,2]). While it is quite clearly established that elderly subjects (i.e. after 65 years of age) show a deterioration of cognitive functioning, there is also evidence that this deterioration may start in middle age (40 years). There is large individual variance in age groups; for instance, some old individuals perform on many neurocognitive tests as well as young individuals do. Rowe and Kahn[3] proposed in their influential article to discern between successful aging and usual aging. Successful aging would be due to the effect of chronological age, whereas additional factors would be responsible for usual aging. An important point is the nature of the borderland between usual cognitive aging and pathological conditions such as dementia. Various health-related factors are thought to be important in this respect. They may be a determinant for the transition between successful aging to normal aging and into the borderland with dementia. The Brain & Behavior Research Institute in Maastricht investigates the determinants of successful and pathological aging in a number of related and multidisciplinary projects. This paper describes some major findings of this research programme and gives a theory on the interaction of vulnerability factors and protective factors in their effect on cognitive aging.

BIOLOGICAL LIFE EVENTS (BLE)

The Maastricht Memory Study (MMS) investigated neurocognitive performance in relation to health in 260 subjects aged 20-80. These subjects were regarded as normal and healthy persons according to regular gerontological criteria. We discerned two groups. Group one consisted of subjects who were really healthy and had never experienced any relevant health problem. The second group was composed of healthy subjects who did experience a health problem, health problems being:

- Mild brain trauma;
- Surgery under general anaesthesia;
- Diabetes;
- Prolonged treatment with sleep medication;
- Migraine;
- Other conditions probable but disputed relation with brain function.

It turned out that the really healthy subjects did not show any appreciable deficit in memory acquisition over the six decades covered. On the other hand, the second group showed a clearcut deterioration in memory performance with age. Similar findings were done with respect to performance on information processing speed and other cognitive variables. Thus, relatively mild health-related factors do appear to have an effect on cognitive performance. Group one can be considered to age successfully. Group two is 'usual' or 'normal' aging. The health-related factors have been defined as so-called Biological Life Events (BLE), meaning events which have happened at some moment in the past with possible influence on the brain. We hypothesized that cognitive aging is determined by age and vulnerability factors; BLE are such vulnerability factors.

Acknowledgement

The author wishes to thank his coworkers Dr. F. Verhey, Dr. P. Houw, Drs. M. van Boxtel, Drs. R. Ponds, Dr. W. Riedel and Dr. K. Commissaris for their invaluable contributions to cognitive aging research in the Maastricht Brain & Behavior Institute.
It goes without saying that it would be of considerable importance when it could be shown that the borderland between usual aging and frank dementia is filled with non-sick subjects who are compromised in their cognitive performance by health-related factors. It is for that reason that we started the Maastricht Aging Study as a large cross-sectional and longitudinal study into cognitive aging.

MAASTRICHT AGING STUDY (MAAS)

The Maastricht Aging Study investigates healthy subjects aged 25, 30, 35 etcetera till 80 years of age. Education and sex are balanced. There are 1,900 subjects who are given an extensive neurocognitive investigation and medical screening for health and BLE. There is a 3-, 6-, 9- and 12-year longitudinal follow-up. Dependent variables are neurocognitive measures and neuropsychology and psychopathology. The first cross-sectional phase on 1,900 subjects has been finished. Among the relevant findings is a sub-study into particular BLE in their influence on cognition.

In the first place, mild neurotrauma was investigated in a case-control set up. Healthy subjects who had undergone mild traumatic brain injury (TBI) on the average 15 years ago were compared with matched healthy controls without any BLE. There appeared to be a major effect of head trauma. Healthy subjects with this BLE performed worse than matched controls. It is relevant that the trauma was not acute: it was suffered many years ago and the subjects considered themselves as healthy.

In the second place, there was an interaction with age. It is of quite some relevance that the effect of age is much more pronounced in the trauma group than in the controls. This is a strong indication that trauma may be a vulnerability factor for the effect of age.

Longitudinal data have been obtained for the Maastricht Memory Study. It appeared that BLE five years ago predicted slowness as measured on the Stroop Colour Word Interference test. There is a clear interaction with age and the effect is visible in the senium. This is another finding in line with our hypothesis that health-related factors are a vulnerability factor which together with age affects cognitive performance in the elderly (Houx et al., in preparation).

As far as other potential BLE are concerned, relevant findings were done with respect to the BLE ‘surgery under general anaesthesia’. There was no indication whatsoever that this is a vulnerability factor. For instance, in the cross-sectional part of MAAS no effect on cognition was found in any subgroup by age or health. We did find effects however in a case control study with “regular use of sleep medication” as BLE. Subjects in this category had inferior cognitive functioning. Various other factors, varying from medical conditions to psychosocial factors such as socio economic status and loneliness are presently investigated.

LONGITUDINAL FOLLOW-UP IN THE MAASTRICHT MEMORY CLINIC

Apart from systematic research in healthy elderly subjects, it is of importance to investigate non-demented subjects with memory complaints. These subjects may be in a borderline state and possibly suffer from a prodrome of dementia. The Maastricht Memory Clinic is a health care facility which focusses on non-demented elderly complaining of cognitive dysfunction. Two years after the first diagnostic sessions at the memory clinic, a longitudinal follow-up was performed in 85 patients. We were interested in the question whether patients who are demented at the follow-up would be characterized by a particular profile of cognitive dysfunction. The total group consisted of 85 non-demented patients. Ten were demented at follow-up. A major determinant of deterioration was the factor age: older subjects have higher risks of deterioration. In the second place, also memory performance at baseline was a determinant of deterioration (Verhey and Visser, in preparation).

In conclusion, cognitive measures appear to predict dementia several years later. A large scale follow-up study in several hundred patients with Memory Complaints is presently in progress.

VULNERABILITY FACTORS AND AGE INTERACT IN THEIR EFFECT ON NEUROCOGNITIVE FUNCTION

The findings found in MAAS and related studies suggest that health-related factors or BLE merit consideration in research into cognitive aging and dementia. It is not only age which is relevant for cognitive aging in non-demented subjects. Factors other than age may determine whether or not the performance of an elderly subject falls beneath some functional limit. Thus, BLE might be a vulnerability factor and vulnerability factors may enlarge the impact of the factor chronological age. In other words, our data support the notion that BLE shift the onset of cognitive dysfunction to lower age.

Figure 1 shows the hypothesis in graphical form. The left upper panel shows cognitive performance in healthy, successfully aging subjects. It may be after a very long life that there is a real deterioration of cognitive function. By far the majority of people do not reach this age due to death from unrelated causes. This would be the so-called ‘terminal drop’. The right upper panel gives cognitive performance in healthy subjects who have suffered one or more BLE once in their life. The terminal drop is
shifted to lower age thereby making cognitive complaints and dysfunction manifest at an age where the subject has not yet died from other causes. The lower left panel gives a similar situation. There is circumstantial evidence that age as a vulnerability factor gives rise to an immediate deterioration of function in elderly subjects. For instance, it takes longer for the rest effects of mild brain trauma to disappear in elderly. Finally, the lower right panel gives a pathological condition such as Alzheimer’s disease, where brain degeneration and cognitive dysfunction are the result of other still unknown causes. The hypothesis is that the BLE/vulnerability factor may equally be relevant for AD, as also its onset and course can be shifted to lower age by BLE.

CONCLUDING REMARKS: ON BRAIN RESERVE CAPACITY AND PROTECTING FACTORS

It is of importance to relate the BLE-vulnerability hypothesis to the concept of brain reserve capacity. According to Satz there is a hypothetical level beyond which brain lesions become manifest as functional problems. The essence of Satz’ model for the effect of structural brain lesions is that the brain has reserve capacity. This reserve capacity prevents a lesion to lead to functional impairment.

This model can also be applied to cognitive aging and dementia. Age reduces the reserve capacity. On the other hand, there are protecting factors such as high education, good life-style and good socioeconomic conditions which prevent reduction of reserve capacity. But a BLE or combination of BLE and age may reduce reserve capacity which decreases performance below a functional limit, necessitating clinical intervention. These models should be used in further studies into the borderline between usual aging and dementia.

In addition and as a logical further step I propose that more attention should be given to possible protecting factors. Protecting factors may increase functional reserve capacity. Psychosocial factors, socio-economic factors and particularly education are relevant in this respect. Likewise, limitation of possible hazards to the brain by life-style may be much more important than has been thought up till now. After all, quite some variance in many studies is due to the fact that these variables have not been controlled. It is a fascinating possibility that medical, biological, psychosocial factors and their interrelations are investigated in one study and this is what we are presently investigating in MAAS and in related projects in the Maastricht Memory Clinic.

LITERATURE