CHAPTER 2

Cognitive, emotional and behavioral dysfunctions in aging and dementia

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Introduction

There has been extensive research into psychological dysfunctions in aging and senile dementia over the past 30 years. A number of papers have appeared on deficits in intellectual, memory, language, and several other cognitive functions. The research knowledge has been acquired generally in group comparison studies and — unfortunately — only very recently attempts have been made to use this knowledge for the assessment of individual patients. In addition, attempts to relate the psychological dysfunctions to the underlying cerebral substrate have been relatively scarce.

Assessment of the very early stages of senile dementia is important for several reasons. First of all, it is important to differentiate between 'normal' aging and various psychiatric and neurological diseases, in view of the possible intervention in the disease process by biological (drugs) and non-biological (training, psychotherapy) methods. Treatment in an earlier stage of the disease process can be expected to be more successful in view of the less pronounced structural changes. Secondly, when a person can be diagnosed as being in a (very) early stage of senile dementia, the 'profile' of behavioral, emotional, and cognitive deficits may give some clue as to a possible 'cause' of the disease(s) and its pathogenesis.

In this chapter the research on psychological dysfunctions in aging and dementia, focusing on cognitive and behavioral dysfunction is critically evaluated. Because of the fact that at present early assessment is difficult, this paper also tries to provide some information on the paradigms and methods that are used in the assessment of (senile) dementia and especially in (senile) dementia of the Alzheimer type. It also summarizes the present knowledge on the cerebral substrate involved in aging and dementia, as far as can be concluded from behavioral research in patients. The reader is referred to others for more extensive reviews on the psychological dysfunctions in aging (Botwinick, 1977, 1981; Jolles and Hjimjan, 1983), memory (Craik, 1977; Russell, 1981), dementia (Miller, 1981) and psychological assessment in senile dementia (Jolles, 1985; Miller, 1984; Brancornier and DeVitt, 1984).

Cognitive functions in aging and dementia

Perceptual functions

Aging. Several experimental paradigms have been used to study perception in the aged, and the results, generally, point in the same direction. The effect of sensory stimulation seems to persist longer in the central nervous system (CNS) of the aged subject, leading to a less efficient response to subsequent stimulation. This notion evolved from experiments, which started in the forties, with the
so-called ‘critical flicker fusion’ technique: a brief (e.g. 20 ms) light stimulus was presented, followed by others which were separated by a brief time interval of the same duration. When this time interval is progressively shortened, the sequence of light stimuli is ‘fused’ and the subject sees one steady light. Old people experience fusion at longer interstimulus intervals than young people. This indicates that stimuli are perceived for a longer period of time after discontinuation of the physical stimulus (e.g. Misiak, 1947). Similar findings were obtained with sounds and tactile stimuli (see Botwinick, 1981 for references).

Other studies supporting the stimulus persistence theory either used the technique of ‘backward masking’ or that of ‘stimulus enhancement’: two (different) stimuli are presented, separated by a short time period. When the second stimulus is a masking stimulus, old people are inferior in the recall of the first stimulus (e.g. Kline and Szafran, 1975). When the second stimulus is an ‘enhancing’ stimulus (that is, when it adds information which is missing in the first), old people performed better than younger persons (Kline and Orme-Rogers, 1978). All the studies mentioned are thus in line with the notion that elderly people perceive the first stimulus for a longer time. Similarly, visual after-effects seem to be present for a longer time period in the old (Kline and Nestor, 1977). Neuropsychologically, a lack of inhibition of irrelevant information may underly this stimulus persistence.

Elderly subjects required more time to process visual input (Eriksen et al., 1970) and they have been found to be inferior in tasks in which parts of a complex visual figure have to be integrated to a meaningful whole (Hooper, 1958). In addition, figure-background discrimination is harder for the elderly than for the young (Axelrod and Cohen, 1961).

In conclusion, elderly people are inferior in tasks of simple and complex perception. This may partly be because stimuli, once perceived, are present for a longer period of time, partly because an efficient perception takes more time.

**Dementia.** Some perceptual deficits have been demonstrated in demented patients (Willander and Klee, 1966). Visuospatial functions deteriorate as deduced from observations in visuoconstructive tasks in which the patient is required to copy drawings. These tasks are among the tests frequently used in the assessment of demented patients (Strub and Black, 1981). Patients with senile dementia have difficulty in solving paper and pencil mazes; they also have an impaired appreciation of reflected space (such as mirrorview) (Botwinick, 1981). Demented subjects may also experience a disintegration of the body scheme and they are impaired in tasks that require the subject to fit together pictures of different parts of the human body (Miller, 1981).

Data are scarce with respect to the question whether deficits in simple sensory functions exist in dementia. Some studies suggest that elementary perceptual functions might stay intact longer than more complex functions in Alzheimer-type dementia (see Sulkava and Amberla, 1982).

**Language functions**

**Aging.** A large body of evidence suggests that verbal abilities do not deteriorate with age. Indeed, many authors have demonstrated that some verbal abilities in normal elderly subjects are superior to those of young controls (e.g. Goldstein and Shelly, 1975; Goldstein, 1980). Waugh and Barr (1980) thus demonstrated that normal elderly subjects are slightly faster than young normals in a naming latency task which assessed the speed of retrieval of words from the internal lexicon. A similar conclusion has been reached by others (Drachman and Levitt, 1972; Eysenck, 1975) in experiments using ‘category instance fluency’ tests for free and cued production of exemplars of specific categories. Word finding difficulties are seldom observed in normal aging, in contrast to difficulties with respect to finding names or episodes (see below, ‘memory functions’). Several authors suggest that the fairly stable verbal IQ in ‘normal’ aging is a manifestation of the verbal functions which do not deteriorate.
ate with age (see below, 'intellectual functions' and Botwinick, 1981).

Dementia. Language deficits are a frequently observed symptom in Alzheimer's disease (AD) (Strub and Black, 1977, 1981). Word naming deficits appear already fairly early in the disease process (Benson, 1979) and the nature and extent of the language deficits change with progression of the disease. Ernst et al. (1970) showed that their demented subjects had a general poverty of vocabulary in narrative speech in common, but many dementing subjects showed impairments in object naming. In other studies, age-matched controls also showed a relative impairment in naming, although demented patients were clearly inferior in this respect (Barker and Lawson, 1968; Lawson and Barker, 1968). A demonstration of the way in which an object could be used (confrontation naming) improved naming in the demented patients but had no effect in the control subjects. This may mean that the demented patients do not recognize the object and are, therefore, not able to find the correct word. Patients who are aphasic due to a focal lesion in the posterior parts of the neocortex may also be deficient in object naming but the aphasic, in contrast to the demented patient, characteristically gives the strong impression that he knows what the object is without being able to find the right word to describe it (Rockford, 1971). In experiments designed to assess word production in demented patients, Miller and Hague (1975) used a fluency task in which the subjects were required to produce words beginning with a certain letter. It appeared that these patients produce fewer words in a 5-min period than controls, but demented patients did not rely on a small set of commonly used words, as might have been expected. In other words, the data are not consistent with the hypothesis that the pattern of word use is different in aged versus demented people.

When AD progresses to later stages, verbal output becomes 'empty' and circumlocutory. Demented patients increasingly show repetitive elements in their speech. This repetitiveness may in some instances be a type of perseveration resulting from linking a word inappropriately to an object when the same word has been linked appropriately just before (Botwinick, 1981). The lexicon becomes impoverished but there is evidence to suggest that syntactic processes are less affected (Irigaray, 1973). In addition to a deterioration of expressive language, receptive aspects of language are also impaired. At still later stages, the involuntary repetition of words spoken by others (echolalia) becomes more common. In the final stages of the disease global aphasia may be present, resulting in undirected babbling in which only syllables are uttered.

The clear-cut differences in language functions in aged versus demented subjects have led to proposals to use language tests in the clinical assessment of subjects suspected of incipient dementia. The use of 'category instance fluency' tests (Brannonnier and DeVitt, 1984) and the 'Nelson adult reading' test (Nelson and McKenna, 1975) are examples of such a strategy.

Memory functions

On memory and memory dysfunctions

Since memory complaints are among the most frequently reported signs of decreasing abilities in both normal aged and dementing subjects, an enormous amount of research has been directed at establishing the nature of memory disorders in aging and dementia. Generally, different kinds of memory and memory disorders have been characterized (see Russell, 1981). In the clinic the term 'remote memory' is used to describe retrieval of information which has been acquired many years ago. The term 'recent memory', on the other hand, is used to describe retrieval of information which has been acquired some months, weeks, or only days ago. Much research has been centered around the concepts of 'short-term memory' or 'long-term memory' in the sixties, whereas a more recent trend in memory research asks the question 'how information is processed and used'.

An information processing type of theory states
that information from the environment is sensed by the sensory registers (visual, auditory, tactile, etc.) and passed on to a central processing unit. There is temporary storage in short-term memory (primary memory), and the information is then transferred to long-term storage (secondary memory or long-term memory) by a process of ‘memory consolidation’. ‘Retrieval’ from storage in long-term memory makes the information available again. Recent trends in memory research discuss the importance of the strategies which subjects use to consolidate and retrieve information (encoding processes, rehearsal, use of mnemonic aids, active search, etc.).

A quantitative analysis of the temporal retention of verbal and non-verbal information has been used most extensively both in the laboratory and in the clinic to assess these different aspects of memory.

With respect to the methods of assessing retention, ‘recognition’ and ‘recall’ are direct and ‘relearning’ is indirect (Deese and Hulse, 1967). Tulving and Pearlstone (1966) have shown a distinction between what is in memory (‘availability’) and what can be retrieved from it (‘accessibility’). Recall performance has frequently been shown to be correlated with the degree of initial storage but to be an insensitive indicator of availability (Hulicka and Weiss, 1965; Sramecka, 1967). Recognition performance, on the other hand, is a more sensitive measure of availability than recall (accessibility).

Aging. Memory complaints are frequently encountered in elderly people and several memory deficits can indeed be assessed by psychometric tests. An impairment in the accessibility or availability of new (and old) information is thus a cognitive deficit associated with normal aging. This memory impairment is what Kral (1962) calls ‘benign senescent forgetfulness’ (BSF), the inability to recall unimportant or minor details of an episode while the episode itself can be recalled. This deficit is not permanent and the information might be recalled on a different occasion.

Research of memory deficits in aging has shown that elderly subjects have an impaired sensory memory. This first stage in information processing lasts several hundred ms in healthy young subjects (e.g. Sperling, 1960). When very short stimulus durations (50 ms) were used, only two out of ten elderly subjects showed normal sensory memory as compared to nine out of nine controls (Walsh, 1975). With stimulus presentations of longer duration (100 ms), sensory memory was present, but to a lesser extent than in young persons (Salthouse, 1976).

The second stage in information processing is also very temporary in nature. It lasts several seconds and is conceived by some as a kind of working memory: short-term memory is more a temporary ‘holding’ and organizational process than a structured memory store (Craik, 1977). According to Botwinick (1981) old and young subjects behave similarly in short-term memory tests as long as the number of items to be recalled does not exceed about four or five. However, in view of the fact that some authors define short-term memory as a type of memory that can retain seven items plus or minus two (Miller, 1956), older people may be somewhat impaired when compared to younger subjects.

The third stage in the processing of new information is the consolidation into long-term memory. An efficient consolidation requires some kind of organization of the information to be stored. The formation of new memories can be strengthened by rehearsal, mnemonic aids, imagery and other coding strategies, and it is especially the use of these strategies which seems to be impaired in the aged (Craik, 1977). Generally, elderly people are inferior in tasks involving acquisition and retrieval of new information. More specifically, some investigators found that aged subjects do not use memory search strategies spontaneously, even when the experimenter presents such a strategy (Arenberg and Robertson-Tchabo, 1977; Craik, 1977). It is only under some circumstances that the subjects can be encouraged to do so (Treat and Reese, 1976). These findings may indicate that
people are less able to (actively) manipulate and organize the content of short-term memory (Craik, 1977); there is an age-associated deficit in the use of cues which are important for encoding (consolidation) processes. A similar finding has been done with respect to retrieval processes. There is a preponderance of experimental evidence showing that an increase in age is associated with deterioration of recall performance while recognition is not affected (e.g. Schonfield and Stones, 1979; Erber, 1974). This observation has been interpreted in terms of a retrieval deficit which may be due to ineffective search (Braconnotier and DeVitt, 1984) and/or to ineffective use of strategies (Jolles and Hijman, 1983).

An important parameter with respect to the formation of stable memories is the speed with which the information is presented and/or reproduced. Old subjects performed less well than younger subjects, when the presentation rate in a word-learning test was high. This age-associated deficit was also present when the time to respond was short. When the time limits were not so strict, age-associated deficits were not found (Arenberg, 1965; Kinsbourne and Berryhill, 1972). Another parameter which has been studied in relation to aging is the susceptibility to interference: some studies claim that older people are more susceptible than younger subjects, but others conclude that such age differences do not exist (see Craik, 1977).

Dementia. Memory research in dementing subjects has, generally, been aimed at defining some stage in which these patients might be specifically impaired as compared to 'benign senescent forgetfulness' and depression (e.g. Braconnotier and DeVitt, 1984). Most of the research which has been carried out was concerned with the distinction between short-term and long-term memory.

There seems not to have been much research on sensory memory in demented patients, possibly because these experiments are difficult to conduct with these patients (Miller, 1981). One study used the 'backward masking paradigm' to measure iconic memory. Demented patients were inferior to non-demented controls in reporting the first stimulus, indicating that masking had occurred. According to Miller (1977), this could be due to a defect in attention or iconic memory, and/or an enhanced susceptibility to interference. According to the theory on stimulus persistence, there may have been a lack of inhibition of the first percept.

With respect to short-term memory, Inglis (1957, 1959) found that elderly psychiatric patients were slow to learn paired associates. Performance was inferior to that of controls in both recall and recognition. This is suggestive of a problem in acquisition rather than in retention (see Braconnotier and DeVitt, 1984). Later experiments favored the hypothesis that short-term memory did not function properly (Inglis, 1960, but see Miller, 1981). Experiments in which a word list had to be learned give some clue as to the differential involvement of short-term and long-term memory: characteristically, the first and the last words of such a list are learned better than words in the middle of the list. Better retention of the last words in the list is ascribed to the fact that these words are still in short-term memory, while the superior recollection of the first words is ascribed to the fact that these are already transferred to long-term memory. Characteristically, demented patients do not show a better retention of the first and last words of a list. This finding may be taken to indicate that demented patients experience both a short-term and a long-term memory deficit (Miller, 1981).

Of course, the long-term memory deficit could be secondary to the impairment in short-term memory. This hypothesis has been tested by Miller (1972). He presented the words in the list at a slower rate, and found that control subjects performed better in this condition, as indicated by the number of words recalled from the beginning of the list. The demented patients did not benefit from the slower presentation rate. These findings were interpreted to show that the patients did not use the opportunity to increase the consolidation of short-term into long-term memory, indicating that the memory impairment in dementia has at
least two components (involving STM and LTM). The notion that long-term memory is involved was supported by the finding that demented patients have appreciable difficulty in learning word lists which are longer than the memory span (i.e. the number of words that can be correctly recalled after a single presentation). Long-term memory is essential for this supra-span learning (Miller, 1972).

The performance deficits discussed above have been interpreted in different ways. Memory processes could be involved but the impairments could also be a secondary consequence of an attentional deficit or impaired sensory memory. Furthermore, a decreased ability in the use of coding strategies is also probable: this notion is supported by the fact that acoustically presented material was coded less efficiently by demented patients (Miller, 1972).

Word list learning experiments are also used to measure long-term memory. Experimentally, recall and/or recognition are tested after an interval in which distraction prevents the subject from rehearsing the words. It has been shown that demented patients perform badly in the delayed recall and delayed recognition condition (Miller, 1975). However, the patients are indistinguishable from controls in a 'partial information' condition in which the subjects were given the initial letters of the words as a cue. Similar findings have been observed in patients suffering from the amnesic syndrome (Warrington and Weiskrantz, 1970). The data indicate that some trace has been formed which is too weak to get expressed unless extra cues are given which enhance it. Such an interpretation suggests that retrieval is also inferior in demented patients in addition to an improper memory consolidation (resulting in weak traces). Again, this may be due to a decreased or inefficient use of coding strategies (see above). According to Miller (1981) there is not a clear difference between aged and demented subjects in this respect, but it is known that both groups of subjects perform worse than younger controls. An alternative explanation for the partial information effect was given by Warrington and Weiskrantz (1970): successful performance would depend not only on the ability to recall the correct words but also on the ability to inhibit the recall of incorrect words. However, Miller (1978) tested this 'disinhibition hypothesis' and did not find data to support it. It was observed, however, that demented patients became progressively less able to recognize a correct word from several alternatives as the number of alternatives increased. That the choice between alternatives is difficult for these patients was also found in an experiment in which a single choice (yes/no) was compared to a forced choice between yes and no (two alternatives). The forced choice appeared to lead to better performance (Whitehead, 1975), possibly because a response is elicited also when the patient is insecure. The personality characteristic 'overcaution' may prevent the elderly/dementing subject from responding in other choice situations. In other words, the elderly subject has a 'negative response bias'; he prefers to choose 'no' unless he is really sure that the answer has to be different.

Taken together, the memory studies indicate that demented patients are inferior to age-matched controls in several aspects of memory, especially those relating to the acquisition of new information (sensory memory, short-term memory and long-term memory; recent memory). With respect to remote memory, the issue is less clear. The commonly held belief that old people have a good preservation of remote memory may not be right. Clinical observations suggest that some 'childhood memories' can become dominant at the cost of other memories, indicated by many gaps in remote memory (Jolles and Hijnman, 1983).

Intelligence

Aging. The question whether intelligence decreases with age has been extensively studied during the last decades. However, despite many studies, in which a gradual decrease in intelligence test scores was found with age, the matter is still controversial (Botwinnick, 1977, 1981). Tradition-
aily, research into intelligence of aged (or de-
mented) subjects has been performed according to
the psychometric tradition, which uses standard-
ized test batteries. An important parameter which
has often been studied with the Wechsler Adult
Intelligence Scale (WAIS), is the differential re-
sponse on 'verbal' versus 'performal' subtests of
this test battery. It has been demonstrated many
times that the verbal IQ (VIQ) does not decline
significantly until fairly old age in normal subjects
whereas the performal IQ (PIQ) decreases more
rapidly with age. Several interpretations have been
offered to explain this differential response. A
suggestion which has often been made takes speed
factors into account. The inferior performance on
performal subtests of the WAIS might be due to a
general slowness in the subjects studied, as these
tests tend to be timed, whereas the verbal subtests
are not (Botwinick, 1977; Miller, 1981). However,
slowing becomes a less attractive explanation as
scores on other intelligence tests (such as the Mill
Hill Vocabulary Scale and Progressive Matrices)
are also decreased though these tests are not timed
(Miller, 1981). According to another explanation,
the VIQ/PIQ discrepancy reflects the fact that the
performance on visuo-constructive tasks deter-
mines the PIQ, indicating that a selective loss of
visuo-constructive (or visuo-integrative) ability
might underlie the intellectual deterioration. The
most probable interpretation, however, refers to
the fact that the verbal subtests measure well-
practised and overlearned activities whereas the
performal subtests measure the ability to deal with
new tasks and the acquisition of new information
(Botwinick, 1977, 1981; Miller, 1981). The selec-
tive deficit of aging subjects on performal subtests
of the WAIS may thus have to do with impaired
memory or learning ability more than with any-
thing else (Miller, 1981). In addition to speed,
memory, verbal and perceptual factors, a factor
called 'general ability' is an important determinant
for the performance on intelligence tests. This
indicates that educational level is important for the
IQ score found, and explains the finding that the
correlation between chronological age and intelli-
gence is rarely as high as .50 (Botwinick, 1981).
Taken together, studies with intelligence tests have
not provided unequivocal results with respect to
the nature of the deficits in aging. The same applies
for dementia.

Dementia. As the term 'dementia' implies a
disturbance in cognitive functioning, many studies
have addressed themselves to the determination of
intellectual deficits in dementing subjects. As was
evident from the foregoing discussion, intellectual
changes become evident in the course of the illness.
These clinical observations have been substanti-
ated in experimental studies in which demented
patients showed a lowered mean IQ (Miller, 1977)
compared to age-matched controls. Unfortunately,
research into the differential performance on
'verbal' versus 'performal' subtests of the WAIS
has not yielded clear insights into the cognitive
functions underlying the intellectual deterioration
of dementing patients. The interpretational prob-
lems are similar to those encountered in the study
of intellectual functioning in normal aged subjects.
Thus, the performal IQ of demented patients is
much more decreased than the verbal IQ, but it is
not easy to characterize the underlying deficit as
being due to general slowness, failing memory or
problem solving ability, or other factors (Miller,
1981). Those authors who conceive of dementia as
disease process in which 'crystallized intelligence'
(abilities which are well practised and
overlearned) is relatively more preserved than
'fluid intelligence' (new activities which do not
relly upon familiar or routine strategies), simply
rephrase the findings in other terms and thus add
little to our knowledge of what is happening in
dementia (Miller, 1981). The findings, until now,
do not indicate that there is more than a
quantitative difference between normal aging and
dementia of the Alzheimer type.

Recently, some attention has been given to the
notion that the profile of scores on the WAIS
subtests might be characteristic of a particular type
of dementia (for review see Fuld, 1984). It has been
suggested that such a profile might be of relevance
for the clinical differentiation of AD from other dementing processes. Unfortunately, the results add little to our insight into the nature of the cognitive deficits in dementia.

**Behavioral organization**

Elderly people perform badly on those tasks which require the initiation, planning and evaluation of complex behavioral acts. This has been interpreted by some as a deficit in 'problem solving' (by Arenberg, 1965), by others as an impaired 'planning' or 'behavioral organization' (e.g. Luria, 1966, 1973). In addition, several studies have attributed the difficulties to 'inflexibility', defined in terms of 'giving up a selection procedure that once was effective but no longer is' (Heglin, 1956), or the 'inability to shift concepts' (Wetherick, 1965). Others have shown that elderly people generally are less able to discern relevant from irrelevant information: a redundancy of irrelevant information was found to be disruptive to problem solving behavior (Arenberg, 1965). In addition, there was less efficient use of environmental cues for an optimal plan of action. For instance, when asking for extra information regarding the problem to be solved, old subjects performed in a more haphazard fashion. Likewise, there was a lack of order in their information seeking (see Botwinick, 1981 for references). Characteristically, they did not have explicit knowledge of their goal until very late (Jerome, 1962). Interestingly, certain personality characteristics which are often found in, and attributed to aged people, can be interpreted in terms of inflexibility, decreased concept shift and impaired ability to use (new) environmental information. This applies especially to trends towards introversion, conservatism and cautiousness, and to the reluctance in making decisions, especially when the outcome is uncertain (Botwinick, 1981).

It will be clear that an inferior performance of elderly people on complex tests of memory, perception and other cognitive functions can be attributed to difficulties in behavioral organization/ problem solving ability, unless care is taken that instructions and procedure are really understood by the subject. Neuropsychologically, the deficits described (inflexibility, difficulty with concept shifts, deficient use of environmental information to guide one's own behavior) may be indicative of a primary deficit in the planning, control and evaluation of the behavior, and thus of frontal cortex involvement (Luria, 1966, 1973; Fuster, 1980; Jolles, 1985). For the frontal neocortex monitors and programs activity of the whole cortex and creates the necessary conditions for the integration of environmental information with memories, to make an optimal action plan and to monitor its outcome.

The nature of the deficits in planning and behavioral organization in (Alzheimer type) dementia, seem similar to those in 'normal' aging but are much more readily apparent. Unfortunately, only a few studies have been performed with AD patients (but see Lawson et al., 1967; Hibbard et al., 1975).

**Motor functions**

There has been a substantial amount of research on motor dysfunctions in aging. Welford (1977) in his comprehensive review of the literature, and his own research over the past 30 years, used an information processing model to describe the different aspects of motor functioning. In his view, the flow of information may be envisaged to pass through several discrete stages, such as (1) sensation (level of the senses), (2) perception (within CNS), (3) translation from perception to action (CNS), (4) effector control (CNS), and (5) motor output (level of peripheral nerves and muscles). Stages 3 and 4 refer to the integration of information from the senses, the generation of plans to use this information for an act, and the compuation of the motor performance. This planning is a prerequisite in order to perform the planned action in a sequential order (Luria, 1973, 1966).

According to Welford (1977) the main limita-
tions in motor performance which elderly people experience seem due to a combination of a reduced speed, and less efficient information processing in stages 3 and 4. He concluded that aged subjects are considerably slower in performing relatively large movements at maximum speed. This seems primarily due to peripheral (e.g., muscular) limitations. Most other movements are not limited by muscular factors but by the speed of the decisions that have to be made to guide movements. When decisions can be made beforehand, such as in simple reaction time tasks, and in simple repetitive movements, the change with age is relatively small. The performance on a new or complex task, however, is much slower; the extra time is needed for the planning of (the stages of) the motor act. In addition, elderly people pay more attention (and thus more time) to the signals presented before they act. This is especially the case when the relation between signal and response is not straightforward. The performance of elderly people becomes slower and less accurate when the subject has to choose between alternatives or when an extra judgement of spatial relations has to be made (see Welford, 1977). Clearly, such a complex motor task has the characteristics of a problem solving task as discussed above.

Thus, the performance on simple tasks which do not require a complex ‘computation’ of the motor act is relatively normal in aged people. The performance in complex motor tasks and in tasks requiring complex sensorimotor integration is inferior in old, compared to young people because of the extra time needed for decision making and planning of the movement to be performed. This is, once again, an indication for a planning deficit more than a deficit in motor performance per se.

Discussion

The performance in virtually all the cognitive functions which can be tested decreases with age. Elderly subjects are characterized by a deterioration in intellectual functioning, memory, language functions, problem solving and perception. It seems that specific parameters are more involved than others. For instance, elderly people are not inferior in tasks in which they can rely on well-established skills and knowledge, whereas they perform poorly in tasks involving new information, especially in situations in which the planning of new activities or the active use of coding strategies in recent memory is important. In addition, trends towards inflexibility, cautiousness and conservatism are found, which are paralleled by ‘stimulus persistence’. Finally, the speed of information processing seems to decrease with age.

With respect to AD, evidence has not been found to show that the pattern of cognitive deficits would be different from that seen in ‘normal’ aging (Jolles and Hijman, 1983), especially with respect to the earlier stages in the development of the dementia. Dementing subjects perform significantly inferiorly to age-matched controls on all functions tested, but there is not a different pattern in their deficits. Thus, more or less profound deterioration is found with respect to perception, memory, language, higher cognitive functions, planning, rate of information processing and other cognitive functions (Jolles and Hijman, 1983; Miller, 1981). In addition to the deficits seen in normal subjects, AD patients also deteriorate with respect to recognition memory and verbal IQ measures which stay at a fairly constant level in normal aging.

It is important to acknowledge that the major part of the studies described above reflects group comparison data. Unfortunately, this reduces the direct application of the results in clinical assessment of (individual) patients. Several investigators have proposed particular methods of investigation which are based upon the knowledge which has been described (see, for instance Braconnier and DeVitt, 1984). There are several additional methodological problems. There are important differences between the studies with respect to the characteristics of the patient population described. Some studies do not clearly discern primary degenerative dementia from dementias of other origin. Furthermore, the progress of the disease
(the stage) is not described, which makes the comparison of different studies difficult, if at all possible. This indicates that future research in this field may benefit from a careful clinical diagnosis of the patients involved, and from the use of standardized classification systems such as DSM-III (Clayton and Martin, 1981). In addition, control groups of age-matched or other control subjects should also be assessed carefully, especially in view of differences in personality characteristics, which tend to confuse age-associated cognitive changes: for instance, some people over 65 years of age do not retire and remain active until high age. Other elderly people retire and become inactive (see Botwinnick, 1981; Miller, 1981); either because they want to, or because society isolates them. These social and personality factors will have a profound influence on psychological (coping) mechanisms and the social relations of these subjects, and thus on their cognitive functioning. In addition to the factors mentioned, the studies reviewed differ with respect to the age of the subjects but the brain of a subject aged 85 with incipient dementia can be expected to differ from that of a similar patient, aged 65! Future research must take these methodological points into consideration.

**Differential diagnosis and stages in Alzheimer’s disease**

**Differential diagnosis**

Traditionally, (neuro)psychologists working in a psychiatric setting are frequently asked to assess whether a particular patient is dementing or not. It appears very difficult to differentiate early stages of senile dementia from depression. In the first place, early stages in dementia are very frequently accompanied by a depressed mood (Jolles and Hijman, 1983; Strub and Black, 1981). This depression is most probably a secondary consequence of the subjective feeling that there is cognitive deterioration (see for instance Strub and Black, 1981). There is evidence to suggest that the major catecholaminergic pathways that are involved in depression (Van Praag, 1982) are also involved in the pathogenesis of AD (Rossor, 1982). There may thus be a common cerebral substrate in both depression and dementia. Secondly, profoundly depressed patients frequently display overt signs of dementia such as slowness, general inertia, disorientation and memory disturbances. The differentiation of depression and dementia based on clinical observation alone thus appears very difficult. A thorough neuropsychological investigation may be of importance in this respect. Preliminary results presented in Jolles (1985) suggest that neuropsychological methods and theory may contribute to the differentiation of depression and dementia.

With respect to the differentiation of ‘normal’ aging from senile dementia, it is very difficult to discriminate between BSF and incipient dementia. Very recently, some authors have proposed the use of some newer methods to accomplish this discrimination. Much emphasis is given to the differentiation between active recall and passive recognition in learning tasks, and to the use of verbal tasks such as the ‘Nelson adult reading task’ (Nelson and McKenna, 1975), ‘category instance fluency’ tests (Brancumier and DeVitt, 1984) and computer-aided tests based upon an information processing paradigm (see below and Poon, 1983; Jolles, 1985).

Clear differences seem to exist in the pattern of cognitive deficits seen in other types of dementia. For instance, the (pre)senile dementia of Pick’s type shows pronounced behavioral disturbances such as inappropriate social behavior and bizarre behavior, and deficits in the planning and organization of behavior. These deficits are not accompanied by intellectual deterioration or amnesia and are characteristic for dysfunctions of the frontal lobe. This neuropsychological interpretation is in line with current knowledge on the cerebral substrate of Pick’s disease which appears to be a fairly specific degeneration of frontal lobe areas (see Strub and Black, 1981).

A differentiation between primary degenerative
dementia (e.g. AD) and dementias of vascular origin can usually be made after careful examination of the pattern of cognitive deficits. Those dementias which depend primarily on vascular disorders ('multiinfarct dementia') seem to be characterized more often by focal deficits. For instance, a patient who has difficulty in object naming (anomia) without a concomitant impairment in object recognition or apraxia may be suffering from localized cerebral dysfunctions, as a result of cerebral vascular insufficiency in the left temporoparietal region. Likewise, a patient with modality-specific deficits for complex visual material and disorientation in space without a memory deficit for verbal material, almost certainly does not suffer from a primary degenerative dementia but may have had infarct(s) confined to right hemisphere structures. The interpretation proposed here may be problematic because of the fact that in primary degenerative dementia multiple small infarctions may accompany the degeneration of cortical tissue, such that the cognitive dysfunctions which are evident in a particular patient may result from both the infarctions and neuronal degeneration (Strub and Black, 1981; Jolles, 1985).

The progression of clinical signs of dementia

The signs and symptoms of AD have been described by many investigators and researchers. However, there are few detailed accounts of the symptomatic progression of the disease. Sjögren and coworkers (1952) have defined three clinically distinct stages. Stage I is characterized by — among others — incipient dementia, memory disturbances (including anomia) and spatial disorientation. In stage II, the dementia becomes more pronounced with marked disturbances in memory and disorientation with apraxia, agnosia, aphasia, etc. In the terminal stage (III) there is no cognitive activity left and only vegetative functions remain. Reisberg (1983) and Reisberg et al. (1982) describe the progression of symptoms in seven stages which range from 'normal' via 'early', 'middle' and 'late confusion' to 'early', 'middle' and 'late dementia'.

The classification proposed by Reisberg is appealing in its systematic description of cognitive and observational items that help in the characterization of the stage of the disease. It will be evident that a more systematic classification will be of much value both for clinical and scientific purposes.

The following account of the progression of the symptomatology of AD is based upon the work of Strub and Black (1981). They described a clear evolution of the successive stages in the temporal sequence of the disease:

Stage 1. Changes in social behavior and expressed emotions are among the very early signs of primary degenerative dementia. There is a lack of normal initiative and interest in family, work and other activities. Increased fatigue and restlessness are frequently noted in this stage, as well as depression and anxiety. Some patients are overly concerned with somatic complaints whereas others deny any problem. There is often an accentuation of previous personality traits super-imposed upon a background of euphoria or apathy. In other patients, personality changes are noted which are quite uncharacteristic of the premorbid personality (e.g. inappropriate or bizarre behavior). This applies especially to patients with extensive frontal lobe lesions such as those suffering from Pick's disease, Huntington's chorea or general paresis.

Cognitive changes such as memory deficits are the most frequently noted early signs of the disease process. The patient forgets names and recent events, and experiences increasing trouble in finding things around the house. Recent memory seems to be affected more than remote memory. In addition to memory, general problem solving ability deteriorates; this is most evident in new tasks in which the patient cannot rely upon well-established skills and routines. Furthermore, comprehension and the expression of complex ideas, abstract thinking and critical judgement deteriorate. More basic cognitive deficits also become evident, such as an impaired visuo-motor integrative ability. A routine neurological examination is usually normal in this stage.
Stage 2. The signs noted in stage 1 accentuate. The patient is less able to manage his personal and business affairs, because of failing memory and lack of initiative. Several language problems also become evident although they do not yet reach the level of clear-cut aphasia: speech remains fluent at first, but circumlocutions and paraphasias appear, and the patient experiences difficulties in word finding. The ability to express abstract thoughts decreases and there is an overall decrease in intellectual functioning. The restlessness already noted in stage 1 increases; patients become upset at night, and they tend to wander around. They may constantly be manipulating things in their hands. Emotionally, patients in this stage often retain sufficient insight into their condition to develop secondary anxiety and depression; the dementia may thus appear more severe than it is.

Stage 3. With further progression, the patients develop a clear aphasia, apraxia and agnosia. Spontaneous speech decreases further; there is a tendency to echo what is said (echolalia); there is greatly reduced comprehension and an inability to name objects. This anomia appears to be more than a simple problem in finding the correct word: the patient characteristically acts as if not recognizing the object and the failure therefore is a visual agnosia. An ideomotor apraxia develops, i.e. a difficulty with the execution of previously learned skilled movements, such as combing the hair. In addition, a so-called ideational apraxia develops, which is a total disruption in the ability to carry out a complex action composed of several relatively independent acts (such as taking a match from a box and lighting a cigarette). Inattention and distractibility become very common in this stage, as well as involuntary emotional outbursts. A number of primitive/infantile reflexes reappear and are now evident from neurological investigation. In addition, involuntary movements are noted, and urinary and fecal incontinence begins. In short, the patient experiences increasing difficulty in inhibiting natural reflexes. In some patients features of organic psychosis are prominent.

Stage 4. (terminal stage). The patient becomes uncommunicative, uttering only short phrases of undirected babbling. Emotions are involuntary, delusions appear and the patient finally gets completely apathetic and withdrawn. More neurological signs become apparent, including generalized seizures (in 22% of the patients during the last year of life) (Sjögren et al., 1952). Death usually results from pneumonia, aspiration or urinary infection (see Strub and Black, 1981 for more detailed account).

Stages in dementia: methodological issues

Alzheimer’s disease can occur at any age, and the course of the illness is variable; some patients live only a few months after initial assessment, but 25–30% of the patients live over 10 years, and some live over 20 years (Corsellis, 1976). The average life span from diagnosis to death is slightly over seven years (Sjögren et al., 1952). It is important to determine whether the dementing process is similar in these individuals of different ages. Although the succession of stages seems to be identical in presenile versus senile forms of AD (e.g. Sulkava and Amberla, 1982), there is an increasing amount of research papers describing differences in either neurobiological variables (e.g. Rossor, 1982) or neuropsychological variables (Friedland et al., 1985).

Although similarities exist between different forms of primary progressive dementia (e.g. Alzheimer’s disease versus Pick’s disease), several differences are also evident.

The sequence emerging in senile dementia of Alzheimer’s type is different from that noted in Pick’s disease although the terminal stages may be similar (Strub and Black, 1981). Careful examination of the mental status of the patient is therefore very important for an early diagnosis of any dementia, as neurological signs develop only in the terminal stages. An extensive neuropsychological evaluation may therefore be the only means for an early diagnosis (Jolles, 1985).

In view of the temporal sequence in the
development of symptoms, there is quite some variation within the demented groups: of course patients in the first stages differ in quantitative and qualitative ways from those in the later stages.

Besides, there is a quite considerable variation due to personality characteristics, as premorbid personality tends to be exaggerated in the first stages. This may explain an important part of the individual differences within a group of patients that may be pathogenetically homogenous. Whereas Reisberg (1983) differentiates seven stages in the disease process and Strub and Black (1981) discern four stages: others differentiate only between ‘mild’, ‘moderate’ and ‘severe’ dementia, but the criteria used for the inclusion of a patient in the different groups are usually vague. This may be an important reason for the difficulty in comparing different studies on dementing patients. Of course, the differentiation between different types of dementia is of utmost importance for treatment and management of the patient at home or in a nursing home, but also for the assessment whether the memory complaints may be indicative of a relatively ‘normal’ senescent forgetfulness or the early sign of beginning dementia.

Stages in Alzheimer’s disease: neuropsychological issues

It has been suggested that the stages in AD may be a behavioral parallel of similar stages in neuroanatomical degeneration (Jolles and Hijman, 1983). Interestingly, there is some experimental evidence in favor of such a notion.

Sulkava and Amberla (1982) in a study with the Luria-Christensen neuropsychological test battery found that different stages in the development of the disorder could be discriminated even at the later stages of dementia. Both presenile and senile AD patients deteriorate particularly in memory, higher cognitive, higher visual and motor functions and in orientation. Impressive and expressive speech were relatively spared. All functions deteriorated gradually during the disease process so that the differences between the various abilities and the slope of the performance profile were preserved. All neuropsychological abilities tested had disappeared in the final phase (Sulkava and Amberla, 1982). According to these authors, the clearly definable course of progression of both the presenile and the senile form of AD affects different functions of the brain in a certain order: symptoms such as general lowering of activity, deterioration of short-term memory and deterioration of awareness appear at an early stage of the disease. Consequent behavioral dysfunctions are disorientation and paranoid delusions. Theoretically, this may indicate that ascending fibers from brain stem to cortex are affected (see below and Luria 1966, 1973). Apraxia, agnosia and aphasia which appear in the next phase are taken to be indicative of cortical dysfunctions. The same applies to the deterioration of logical reasoning and loss of control over behavior. In the advanced stages of the disease only some basic automatic functions may still be preserved, correlating to extensive neocortical degeneration (Sulkava and Amberla, 1982; Jolles and Hijman, 1983).

Methods for early assessment of age-associated cognitive decline

Psychometrics

Generally, standardized tests have increased our knowledge of the development of deficits in normal aging and dementia. Unfortunately, this knowledge has been obtained from groups of elderly subjects and patients as a whole but psychometric tests appear not sensitive and reliable enough to be used in early assessment of individual subjects (e.g. Russell, 1981). Psychometric tests have a number of advantages: they are standardized and published norms are generally available. In addition, they are easy to administer and there is usually a good reliability. A drawback of the psychometric approach is that the use of test scores as such does not allow the identification of cognitive deficits that underly the performance changes. The traditionally used tests allow only a fairly crude
estimation of the cognitive functions and, in addition, do not properly differentiate between different aspects of these functions. This is a consequence of the empirical, non-theoretical nature of these tests, which have been developed for other purposes than to be used with brain-damaged subjects. For example, the ‘digit symbol’ subtest of the ‘Wechsler adult intelligence scale’ (WAIS) is the most sensitive among the 11 subtests, showing the greatest difference between the performance of young and old adults (Botwinnick, 1981). However, it is not clear whether psychomotor slowing, poor learning or retrieval of the digit-symbol codes, poor visual motor coordination or all of the above are responsible for the poor performance of the aged subject (Poon, 1983). The psychometric test measures thus give a quantitative index of 'performance below the norm' without any clue as to the nature of the cognitive deficit and the underlying cerebral substrate.

A second drawback of the traditional psychometric tests is the relatively long time needed for the test administration, when compared to the amount of data the test battery yields. For instance, the administration of the WAIS takes several hours, and yields only 11 (subtest) scores when the tests are used in the classical way. These scores are usually converted into two scores for verbal IQ and performance IQ, and are often combined into the total IQ. Another test battery such as the ‘Halstead Reitan neuropsychological test battery’ (HRNTB; administration in 5–6 h), has the disadvantage that standard norms are available until 55 years of age but not for older subjects.

Apart from the use of standardized test batteries (HRNTB, WAIS, the Nebraska battery), several more specific psychometric tests are used for the determination of deficits in aging and dementia. This applies especially to the determination of aspects of memory processes (see Jolles and Hijman, 1983). Characteristically, the resulting quantitative data are used for the analysis of group differences (e.g. ‘young’ versus ‘old’ adults). Generally, the nature of the quantitative results does not enable their use in individual diagnosis, especially in differentiating early dementia from other syndromes. More recently, there has been some development in the use of psychometric tests and test batteries in a less rigid and more qualitative way (e.g. Lezak, 1983; Goodglass and Kaplan, 1979). Proponents of such an approach make use of a combination of the quantitative results and more qualitative signs. Published data are not yet available on the use of this new approach in early diagnosis of senile dementia.

**Information processing**

Investigations of cognitive processes in the psychological laboratory have generally made use of an information processing paradigm. The strength of this approach is the theoretical framework. It is aimed at examining cognitive processes by analyzing behavior in quantifiable components and qualitative patterns. The information processing tasks characteristically are composed of subtasks, and reaction time measurements are used to probe into the different stages of information processing (e.g. Brand and Jolles, 1986; Poon, 1983).

The use of information processing tasks which are developed in the psychological laboratory and later adapted for use in clinical testing is still in its infancy. The ‘Sternberg memory comparison task’ (Sternberg, 1966, 1975) which has been used extensively in the laboratory, has been used in measuring the efficacy of drugs in clinical trials and in group comparison studies but not in individual psychodiagnosis. However, a recently developed ‘paper-and-pencil’ version appears to be a reliable and sensitive task which can be used in combination with clinical neuropsychological tests (Jolles and Gaillard, 1984). Data obtained with this test suggest that the intercept of the ‘reaction time – setsize function’ increases with age. This suggests that there is a decreased rate of memory search. However, there is an increased slope in those dementing subjects who are characterized by some aspects of frontal lobe dysfunctioning. This is suggestive of a fairly specific effect on search processes (Jolles, unpublished).
Other information processing paradigms have been recommended for use in geriatric psychopharmacology (Poon, 1983). These methods could also be important in the clinical assessment of subjects suspected of a developing dementia. According to Poon, these paradigms measure common behavioral complaints in community dwelling elderly as well as in elderly patient populations. A large amount of data has been obtained on speed, accuracy and the pattern of responses, especially with respect to the following functions: ability to attend and concentrate; ability to make decisions quickly; ability to acquire and retrieve new information; ability to retrieve familiar information (naming); ability to manipulate spatial information. It is important to note — again — that inferences are made with respect to aspects of cognitive functioning by the use of reaction time measurements. Poon (1983) recommends and describes the following procedures for use in geriatric assessment: (1) measurement of the alerting function to assess attention/arousal; (2) measurement of choice reaction time to assess decision making processes; (3) measurement of continuous recognition memory to assess retrieval from primary and secondary memory; (4) measurement of naming latency to assess retrieval from tertiary memory; and (5) measurement of mental rotation to assess spatial processing (a detailed description and rationale can be found in Poon, 1983).

It is of interest to note that several psychometric tests which have been in clinical use for several decades can be used as an information processing task: one example is the ‘Stroop test’ (see Lezak, 1983) which consists of three subtasks which measure: (1) the speed at which color names are read; (2) the speed at which colors are named; (3) the speed at which the color of printing ink is named when there is interference from the printed color name. An interference score can be calculated by subtracting the time scores on tasks 3 and 2. This is a relatively pure index which is not contaminated by a perceptual or motor component. A similar procedure can be performed with the ‘trail making test’ (see Lezak, 1983). The subtraction of time scores gives a timed measure for the ease at which a concept shift is made (here shifting between letters and digits, Vink and Jolles, 1985).

**Behavioral neurology**

A different approach to assess cognitive functioning in geriatry has been presented by the neuropsychologist Luria (1966, 1973). He presented a model of brain–behavior relationships which served as a basis for an extensive neuropsychological investigation. His approach consists of a set of procedures which systematically assess different aspects of cognitive functioning (see Table I). Luria's

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<td>Luria's neuropsychological investigation according to Christensen (1975)</td>
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- **Motor functions**
  - of the hands, oral praxis, speech regulation of the motor act

- **Acoustico-motor organization**
  - perception and reproduction of pitch and of rhythmic structures

- **Higher cutaneous and kinesthetic functions**
  - cutaneous and muscle and joint sensation, stereognosis

- **Higher visual functions**
  - visual perception, spatial orientation, intellectual operations in space

- **Impressive speech**
  - phonemic hearing, word comprehension, simple and complex grammar

- **Expressive speech**
  - articulation, reflected speech, nominative speech, narrative speech

- **Writing and reading**
  - word analysis and synthesis, writing, reading

- **Arithmetical skill**
  - comprehension of number structure, arithmetical operations

- **Mnestic processes**
  - learning processes, retention and retrieval, logical memorizing

- **Intellectual processes**
  - thematic pictures and texts, concept formation, discursive intellectual activity
method which has become well known in the adapted version of Christensen (1975), is qualitative and flexible in nature. When needed, more than 250 simple tasks are given to the subject, ranging from tests for simple and complex motor acts via perceptual, language, and memory functions to tests for higher cognitive functions. Total administration time is 1–2 h. In essence, Luria’s method is aimed at generating hypotheses concerning specific disabilities, and then testing these hypotheses by a proper choice of small tasks. For instance, with respect to memory functions, Luria differentiates between memory for visual forms (“draw the figures that you saw”) and verbal material (“write the words you saw”). The learning performance is measured, as well as the sensitivity to interference by homogeneous material or heterogeneous material. In addition, the formation of a stable intention to memorize or to associate is measured in addition to several other aspects of memory function (Luria, 1976). Luria used his method originally to investigate brain-injured subjects, and the tests have provided important information in assessing the location of brain injuries and in planning rehabilitation programs. More recently, it appeared effective in assessing ‘functional’ psychiatric illness from ‘organic’ patients (Purish et al., 1978) and also in the assessment of AD (Ernst et al., 1970; Sulkava and Amberla, 1982).

Luria’s investigation is essentially behavioral neuropsychology. The administration of the tasks is systematic but non-structured. Its main advantage is the fact that the assessment schedule is based upon a theory of brain–behavior relationships. This allows for an interpretation with respect to the specific aspect or part of a ‘functional system’ which is affected. This approach gives rise to a wealth of data which has more coherence than the data which arise from a battery of standard psychometric tests. An important disadvantage of the procedure is its qualitative nature which necessitates extensive observer training and reduces the interobserver reliability. In addition, the lack of quantifiable data prohibits the use of the paradigm in the assessment of treatment efficacy and cognitive decline in individual subjects. However, used in combination with psychometric tests and information processing tasks, it can provide important information on the selective nature of cognitive deficits in elderly subjects and AD. Recently, attempts have been directed at quantifying Luria’s neuropsychological investigation. Unfortunately, the Luria-Nebraska battery (Golden et al., 1979) which is a structured and semi-quantitative test series, has lost the flexibility and richness of the original method. In addition, it has several other shortcomings (Adams, 1984).

Behavioral and cognitive testing; an integrated approach

Both the psychometric, the information processing and the behavioral neurological approach have their strengths and weaknesses. A combination of them may be fruitful in the early assessment of AD and related disorders. The assessment procedure used for this purpose in our clinic is a combination of a qualitative behavioral neurological investigation and quantitative methods derived from psychometrics and information processing paradigms. The procedure is, first, to get a qualitative impression on the total range of cognitive functions. When signs are present which may indicate a deficit, a more detailed investigation is performed in that direction: other qualitative tests are used in order to test the hypothesis that something is wrong and to find out the specific nature of the deficit. These tests are then followed by quantitative methods which ‘measure’ the deficit and relate it to existing norms. This approach has several advantages: (1) it is possible to make a profile of cognitive functioning in all its different aspects — for instance, it is fairly easy to indicate those aspects of cognition which do not show deficiencies; (2) many observations are done, increasing the reliability of the final interpretation; (3) the duration of the neuropsychological investigation has been decreased as a result of the relatively shorter duration of the qualitative tests;
(4) some kind of hypothesis testing is performed; the hypotheses are based upon a thorough knowledge of brain–behavior relationships, and (5) much emphasis is placed on 'pathognomonic signs' which are clear-cut signs that pathology is present. The psychometric tradition usually does not give attention to these signs.

The test series used in the assessment of early dementia in our clinic consists of the following tests and tasks: (1) the Luria-Christensen test battery; (2) 'fifteen word learning test' (which provides information on the use of active coding strategies, on consolidation versus retrieval, on the rate of retrieval, on sensitivity to interference; Luria, 1976; Brand and Jolles, 1986); (3) 'Utrecht memory comparison task' (rate of perception and motor output, rate of memory comparison; Jolles and Gaillard, 1984; Brand and Jolles, 1986); (4) 'Stroop interference task' (naming: retrieval of words and colornames, color-word interference; Lezak, 1983); (5) 'Utrecht trail making test' (rate of perception, retrieval of letters, flexibility towards concept shift; Vink and Jolles, 1985); (6) 'road map test' (left-right discrimination; evaluation; mental rotation; Lezak, 1983); and (7) 'symbol digit modalities test' (general speed of perception and motor output; Lezak, 1983). In addition to this test series many other tests are performed to better localize a specific deficit, if found. These tests are chosen from standard batteries (e.g. 'tapping test' from HRNTB or 'block design' from WAIS) or experimental tasks (e.g. an experimental task for the assessment of decision speed, a test for the assessment of tactile functions or the dichotic listening task).

Luria used a syndrome analysis to describe the profile of cognitive strengths and weaknesses of his subjects. Such a syndrome appeared specific to involvement of particular brain structures. For instance, an involvement of 'frontal areas' could be observed in many different functional systems, such as a perseveration in motor function, a proactive memory interference, a flat learning curve on a word learning test, an inability in concept shifting, etc. A similar syndrome analysis appears to be important when test methods are used such as described in this paragraph.

In fact, a cognitive profile emerges which is a description of the cognitive strengths and weaknesses of a certain subject at a certain moment. Such a profile analysis is an attempt to simplify the picture which might otherwise contain too much information to be intelligible. Some examples of such an approach are given in Jolles (1985). The large amount of data gathered per individual subject appears to allow a fairly reliable description of individual cases.

The neuropsychology of aging and dementia

Similarities and differences between aging and AD

Neuropsychological research in aging and dementia has primarily focussed on memory processes although it is obvious that other cognitive functions are impaired as well. The quantity of research on memory may thus give the wrong impression that memory is the major function involved. There is an obvious need for further studies of information processing, language, perception and planning/organization/coding processes. There exists a parallel with biological research on aging and dementia, which focusses on the structure and function of the hippocampus (involved in memory function; Newcombe, 1980). The emphasis on memory and hippocampus tends to obscure the fact that other cognitive functions (information processing, language, perception, problem solving) and other brain areas (other neocortical and limbic/subcortical) are involved as well. The neuropsychological knowledge discussed so far does not provide any indication that there is more than a gradual difference between 'normal' aging and AD. Of course, when demented patients are compared to age-matched controls, the demented patients perform worse on all test parameters. But, generally, there is not a different pattern of cognitive deficits in aged and AD subjects. Thus, as pointed out in the preceding paragraphs, a relative deficit is seen in the areas of intelligence,
language functions, memory, problem solving, perception, coding processes etc. This indicates that — on the basis of behavioral observation and neuropsychological tests alone — senile dementia might be considered 'exaggerated aging'. It is important to note that this is a controversial issue (see for instance Whitehouse et al., 1983). Several authors have proposed a similar view on the basis of (neuro)biological data (e.g. Terry and Wisniewsky, 1975), whereas others have stated that the cerebral processes underlying 'normal' aging are different from those underlying senile dementia.

The possible cerebral substrate underlying aging. Neuropsychologically, a clear pattern is visible in the cognitive deficits in normal aging. One common element refers to aspects of cognition which have been related to frontal lobe functioning: in this sense, stimulus persistence, proactive interference, lack of behavioral planning, deficient memory search and other deficits can be indicative of less efficient frontal lobe functioning (Luria, 1973, 1980; Fuster, 1980). Interestingly, morphological evidence is available to show that areas in the frontal lobes degenerate already in people aged 40–50 (Haug, 1985). With respect to memory consolidation, limbic areas must be involved on the hippocampal and diencephalic level (Newcombe, 1980; Luria, 1966). It remains to be seen whether a general decrease in the rate of information processing has to do specifically with the ascending fiber system, as would be hypothesized on the basis of Luria's model of brain–behavior relationships (1973, 1966).

The cerebral substrate possibly underlying AD: a neuropsychological hypothesis. The nature of the memory disorders which are associated with aging and dementia suggest that limbic/subcortical structures are involved, especially those involving the hippocampus. This notion evolves from the consideration that the memory deficits are modality-aspecific, and that there seems to be an impairment in the consolidation of new information. However, another important aspect of memory processes which is frequently overlooked, concerns the impairment in encoding processes; the search in memory is less effective, with a consequent impairment in active recall (with preservation of passive recognition); there is also less efficient planning and programming. These cognitive deficits in both aged and demented patients suggest that frontal neocortical structures may be involved. Likewise, the (relative) lack of inhibition, the stimulus persistence, the lack of flexibility, the deficits in planning (problem solving behavior) and other cognitive dysfunctions are in line with this notion.

The data which have been gathered by clinical and experimental neuropsychological research are suggestive of frontal cortex dysfunctions: this hypothesis is based upon the brain–behavior model of Luria (1973, 1976, 1966), who differentiated between three types of frontal syndromes (see also Fuster, 1980).

It may be the case that several dysfunctions which are found in the earlier stages of the dementing process are a result of cerebral dysfunctions in the medial zones of the frontal lobe. This applies especially to memory disturbances, confabulation tendencies, orientation disturbance and loss of flexibility. Similarly, the deficits in emotional control and impulsivity which are noted in these stages, may depend on basal/orbital and medial zones. In later stages, involvement of secondary cortical areas (lateral convex structures of the frontal lobe) may become apparent in disturbances in the organization and planning of the motor functions, perseverative tendencies, general inertia and adynamic speech regulation. This argument is described in Jolles and Hijman (1983) and is based upon Luria (1973, 1966) and Fuster (1980).

Parallel to the development of symptoms involving the tertiary (association) areas on the lateral aspect of the frontal neocortex, similar observations can be done with respect to cognitive functions which depend on proper functioning in the tertiary areas in the posterior neocortex. For instance the higher order integration between sensory modalities breaks down earlier than the cognitive functions which depend on secondary areas (e.g. language functions, figure background...
discrimination) or the primary projection areas. In fact, the temporal sequence of the development of cognitive deficits in AD suggest that there may be a gradual increase in the number of neocortical areas involved, the tertiary association areas degenerating before the secondary areas and the primary areas staying relatively intact until very late in the disease process. This is suggested by the fact that performance of simple motor acts is preserved (activity of the primary motor cortex) as is the use of syllables and phonemes (but not words) in undirected babbling, which severely demented patients are still capable of. Support for this view also comes from histological investigations in which it was found that several cortical areas are indeed relatively spared in the course of this disease (Brody and Vijayashankar, 1977; Hanley, 1974). In addition, it has been known for some time that there is a correlation between extent of cortical degeneration (senile plaques) and poor test performance (e.g. Blessed et al., 1968). If the notion that tertiary, secondary and primary cortical areas degenerate in that order is true, this degeneration is exactly the reverse of the ontogenetical development (primary projection areas develop before secondary, and these before tertiary areas; "law of the hierarchical structure of the cortical zones", Luria, 1973, 1966). This would suggest that the processes underlying aging and dementia are reversed compared to those in ontogenesis. Several investigators address this interesting possibility (e.g. Heiman, 1985; De Ajuriaguerra et al., 1967).

With respect to the question "What are the very first signs of decreasing abilities in AD?", one is tempted to hypothesize that the cognitive deficits associated with neocortical degeneration are secondary to dysfunctions in the subcortical systems. The neuropsychological findings suggest that the very first symptoms of decreasing abilities might depend upon dysfunctions of ascending fibers and fronto-limbic connections. These symptoms seem to be evident especially in speed factors, general activity and aspects of memory processes. This neuropsychological hypothesis agrees with current neurobiological findings on the importance of cholinergic fibers originating in the basal forebrain (e.g. nucleus basalis of Meynert) and projecting onto the neocortex and hippocampus. However, it is not clear whether the degeneration of these subcortical fibers is itself secondary to degeneration of structures located deeper in the brain (as would be a prediction based upon neuropsychological data alone), or secondary to a corticofugal influence.

Summary and conclusions

Elderly subjects perform worse than young persons on virtually all cognitive and behavioral functions that are tested. Thus, performance decrements in intellectual functions, memory, perception, behavioral organization and motor functions have been noted. However, elderly people are not inferior in tasks in which they can rely on well-established skills and knowledge. With respect to AD, the pattern of cognitive deficits seems to be similar to that seen in 'normal' aging but the dementing subject is also characterized by deficiencies in verbal functions and recognition memory. Other forms of dementia such as multifacet dementia and Pick's disease appear to have another pattern of cognitive strengths and weaknesses. This knowledge of the age-associated cognitive decline and of deficits in the different forms of dementia has recently been used to propose the use of new methods in the assessment of early stages in dementia: most of the methods which until now have been used in the assessment of early stages of dementia have their drawbacks. It appears that the use of a combination of psychometric tests with techniques based upon information processing paradigms and behavioral neurology may be a fruitful approach. Future developments will almost certainly be in the direction of techniques that are more sensitive, and give more insight into the nature of the cognitive deficits. Information processing tasks such as those proposed by several authors (Poon, 1983; Branconnier and DeVitt, 1984; Jolles, 1985; Brand and Jolles, 1986) will contribute, provided that some relation is estab-
lished between the cognitive functions and the underlying cerebral substrate, and provided that tasks will be constructed which have ecological validity.

With respect to the potential contributions of neuropsychology, several points deserve to be mentioned. In the first place, modern neuropsychology is a neuroscience discipline trying to relate behavioral and cognitive functions to the underlying cerebral substrate. A brain-behavior model presents a working hypothesis which is essential to relate aspects of behavior and cognition which would otherwise never have been known to contain common elements (see for instance the different aspects of frontal involvement). A contribution based on neuropsychological theory predicts that the development of stages in the behaviorally observable deficits in the AD may be a manifestation of an underlying degeneration of subsequently (1) ascending fibers, (2) hippocampus and sensory non-specific neocortical association areas and (3) neocortical sensory association areas (Jolles and Hijman, 1983). Another theoretical contribution concerns the findings that — based on neuropsychological investigation alone — there is no qualitative but only a quantitative difference between aging and AD (Jolles and Hijman, 1983) and between presenile and senile forms of AD (Sulkava and Amberla, 1982). Human neuropsychology may thus provide testable hypotheses which deepen our insight into the nature of the underlying disease and its cerebral substrate.

A second important aspect of neuropsychology concerns the implications which emerge from a better behavioral and cognitive description of the deficits: for instance, the old subject seems to lose the ability to retrieve information which was consolidated some time ago. A consolidation deficit appears especially in dementia. Might it be the case that the underlying deficit is really a decreasing ability to cope with environmental stimuli? This notion could motivate changes in society such that older people get more opportunities to engage in new activities and actively plan their own behavior. Presently, there is a tendency in exactly the opposite direction, to take the responsibility out of the hands of the elderly subjects. This is especially true in psychiatric institutions. Patient rehabilitation and training based upon neuropsychological theory would suggest that subjects be trained to compensate for lost capabilities. In this respect, much emphasis must be given to activate behavior planning as opposed to passive perception. The strategy of 'enriched' environments which is known to have an effect on cortical thickness and neuronal connections in animals might have similar effects in man. Analogous to the muscular dystrophy in a diseased broken leg, there may be a brain atrophy because of lack of interaction of the organism with its environment (Jolles, 1985). This atrophy could — theoretically — be 'reversible' when assessed in the very early stages. Such a stimulation therapy — possible in combination with newly developed drugs — might be the treatment of choice in elderly people that are at risk of becoming demented.

References


Discussion

D. F. SWAAB: How long does it take to obtain a neuropsychological profile as you described from one patient, and how good are the chances to obtain a positive diagnosis of Alzheimer’s disease?

ANSWER: Generally, the neuropsychological investigation takes 1 to 2.5 h depending on the patient’s complaints and deficits. Deteriorated patients such as those with more advanced stages of AD cannot be subjected to psychometric tests. However, it is still possible to investigate such cases with behavioral neurological tests such as those described by Luria (see Jolles, 1986). It is possible to obtain a profile of cognitive functions. The validity and reliability of the profile thus obtained by behavioral neurology is increased, generally, by adding psychometric and information processing tests to the investigation in order to get more quantitative information on functions, studied qualitatively with the behavioral neurological procedure. The procedure described is able to find those patients who have been provisionally described as ‘Alzheimer’, but who appear to have a neuropsychological profile of deficits suggesting another disease (for example ‘normal pressure hydrocephalus’ (NPH)), alcoholic amnesia, depression or focal deficits related to multiinfarct dementia. With respect to the chances to obtain a positive diagnosis of AD; we do not have enough information yet on neuropathology in the patients we have seen, to answer that question.


J. M. RABEY: Could you give the neuropsychological profile of patients suffering from Parkinson’s dementia and NPH as obtained through your methods?

ANSWER: The neuropsychological investigation has been given to six patients with mild Parkinson’s disease. The profile of strengths and weaknesses was suggestive of deficits in motor functions (especially ‘dynamic organization’) and complex behavioral planning. Particularly interesting were findings with respect to defective initiation of motor patterns and motor integration. None of these patients had a profile suggestive of dementia: knowledge was usually completely intact although several of them were inferior with respect to mobilising this knowledge (which again may be a characteristic of a planning deficit). NPH patients are among the slowest subjects that we have tested with our methodology (even more than AD patients). When given the time, their performance appeared not to be due to general cognitive deficits. A group of NPH patients given a shunt dramatically improved in speed factors and in other cognitive functions such as concept shifting. This improvement was still present 6 months after the operation (Vanneste and Hijnaman, 1986).

W. VAN TILBURG: is the distinction between cortical and subcortical dementia useful from a neuropsychological point of view? Has it some validity?

ANSWER: The answer to this question is yes and no. Neuropsychological theory and practice have committed them-
selves especially to the higher cognitive functions, 'localized' in the
neocortex. It is of importance for neuropsychology and for
workers in this field that attention is given to subcortical
structures and their role in the cerebral mechanisms that
underly both complex and more elementary aspects of
behavior. It is relevant to know that subcortical dementia is a
classification derived from clinical observation by neurologists
(Cumming and Benson, 1964); it only states that patients show
slowness without higher cortical deficits such as aphasia,
agnosia and apraxia. In those cases a neuropsychological
investigation often shows minor signs of language dysfunctions
and other performance deficits.

With respect to the distinction between cortical and subcorti-
cal dementia: this dichotomy seems to suggest that in
'subcortical dementia' there is no involvement of the
neocortex and vice versa for the cortical dementias. In my
opinion there are many arguments to conclude that such a
statement is not true. For example, it seems very probable that
subcortical structures are involved in the early stages in AD,
and that in fact cortical degeneration may be secondary to
subcortical dysfunctions. Furthermore, several subcortical
dementias may be characterized by the fact that the subcortical
dysfunctions inhibit the efficient use of information which is
stored cortically.

E. DONCHIN: I was struck by the contrast between your
presentation which illustrated the ability of the psychologist to
give very detailed descriptions of behavior and Dr. Van Crevel
who reported that there are very few actions that the
neuropsychologist can take. If so, what would the neuropsychologist do with
all the information you provide?

ANSWER: A relevant part of the information on cognitive and
behavioral functions in aging and dementia has been obtained
in experimental studies, often using a group-comparison design.
This is why we know a lot on 'average aging' and 'average
AD'. It is a difficult story as to how to relate this knowledge to
diagnosis and care of individual patients. This is — in my
opinion — an important area of work for the neuropsycholo-
gist: to bridge the gap between theory and practice and to
translate the existing knowledge into assessment procedures
that will allow a differentiation of patients that the neurologists'
methods are not sensitive for. The neuropsychologist may be
able to (1) provide the neurologist with hypotheses on the
nature of the disease process and (2) give information on
cognitive functions and other psychological processes informa-
tion that may be important for an optimal choice of treatment
strategies and other interventions.

D. A. M. TWISK: The psychological tests you derived from
experimental psychology (like the Sternberg paradigm) usually
do require extensive training on behalf of the patient. Do the
modified tests you use also require a training session in clinical
practice?

ANSWER: We do not use a training session and we do not need
them. The original Sternberg tests as such cannot be used in the
clinic: they have been experimentally used in group-comparison
studies and are not applicable for individual diagnosis. We have
developed clinically applicable tasks that can be used for this
purpose. The tasks concern paper and pencil tasks which
appear to give results which are essentially similar to those
found by Sternberg and others with computer-aided apparatus.
In addition, new complex tasks were developed such as the
facial recognition task which also follows the 'additive factor
method' proposed by Sternberg (1975). The time needed per
task is about 3-4 min for the paper and pencil tests and 6-9
min for the computer tasks (including a short training).

L. BLOMERT: You showed that Alzheimer patients of
moderate severity showed language deficits of the following
kind: empty speech, circumlocutory speech, paraphasias,
amnesia. The same profile states that these patients have no
syntactic deficits. How is this possible in the light of the already
mentioned language disturbances?

ANSWER: The notion that both receptive and expressive
lexical aspects of language are deteriorating rapidly in advanced
stages of AD, while confrontation naming is only minimally
affected and syntactic processes are not affected, has been put
forward by L. Iragay and Broch (1973). Brannon and DeVitt
(1974) suggest that there is a breakdown of a conceptual
network (category generation) while the lexicon remains intact (confron-
tation naming) and give some experimental evidence in favor of
this notion.

R. S. SOHAL: Your data seem to imply that AD is merely an
accelerated form of aging. Is that correct?

ANSWER: When you state your question in this form: no. As a
neuropsychologist, looking at behavior and performance on
psychometric and other tests, I observe that the pattern of
deficits in aging and in Alzheimer type dementia is similar
even though the performance decrement is much greater in the
early and late stages in AD. Consequently, my statement was
that aging and AD do not seem to differ when seen from the
behavioral point of view. That does not imply that 'AD' is
merely an accelerated form of aging. Such a statement can
only be based upon a combination of arguments from the
neurobiological, the clinical and the behavioral point of view.

J. E. PISETSKY: Can the neuropsychological tests be used
for basal standards and tests which show changes with
medications? No tests have been sensitive enough to show
changes.

ANSWER: In principle they can. Presently, the tests that are
used for treatment evaluation are standard psychometric tests
that are often not usable for repeated testing. Generally, these
tests are not very sensitive. I favor the use of tests based upon experimental cognitive psychology (originally developed in the psychological laboratory) because timed measures are usually more sensitive and do allow repeated testing. The other neuropsychological tests described are useful as basal standards provided that they give quantitative (numerical) results.

References


