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Chapter 17

Incidence of dementia in subjects attending a memory clinic: Results of a two-year follow-up

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ABSTRACT

The present study evaluates changes in cognitive and affective functioning and in the incidence of dementia in a two-year follow-up of 65 patients visiting a specialized memory clinic. Six out of 47 patients who could be tested at follow-up (13%) appeared to have become demented, which is far more than expected on the basis of age alone (0.47 out of 47). Out of 24 patients who had received the diagnosis 'depression' at the first measurement, 10 had deteriorated at follow-up, without there being a change in the mean depression score. Eight out of this group of 24 subjects, however, had improved their cognitive scores and had better ratings of mood (i.e., less depression). It appeared that inferior cognitive scores at the time of the first assessment predicted cognitive decline in the follow-up assessment. The data should be considered with caution because the absolute numbers were small, and there was no control group. Yet, the results of the study underscore the notion that a population of elderly subjects with memory complaints may contain a substantial number of individuals who are in a prodrome of Alzheimer's disease (AD).

INTRODUCTION

There is an increase in the prevalence of healthy subjects who complain of forgetfulness as age increases, as shown in the MAAS–A_1 study (see Chapter 7). During the past decade, many patients with forgetfulness have attended health care facilities in order to find out whether their forgetfulness is an indication of incipient dementia or another pathological condition. Age-associated memory impairment, age-consistent

memory impairment and late life forgetfulness are terms proposed to describe this type of forgetfulness.

Up till now, it was not known to what extent cognitive complaints are a manifestation of incipient Alzheimer's disease: in other words, whether they are a prodrome of dementia. The differentiation of early AD is problematic when the clinical symptomatology is below the threshold for dementia. There is no consensus on the diagnostic criteria of the borderline states between the normal aging and frank dementia because there is limited knowledge about the crucial symptoms that accurately predict the development of dementia. A strategy has been recommended by which a range of variables are followed longitudinally, in the hope that time will show which symptoms are characteristic for the prodromes of dementia (Henderson & Huppert, 1984). In this chapter we describe an ongoing longitudinal project at the Memory Clinic of the University Hospital of Maastricht as a side arm study of MAAS. The major aim of this project is to collect data on a cohort of middle-aged and older patients who seek help for cognitive complaints in a specialized memory clinic (Verhey, Jolles, Ponds, Rozendaal, Plugge, de Veth, et al., 1993; Verhey, 1993), in order to establish the clinical characteristics of the prodromes of dementia. An additional aim is to determine optimal procedures for longitudinal research in the field of cognitive aging and for incidence studies of age-related cognitive deficits and psychopathology.

MATERIALS AND METHODS

Subjects

The cohort of this study consisted of 65 patients from the Maastricht Memory Clinic (MMC) of the University Hospital of Maastricht. Patients were 40 years or older, not demented, had a score on the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1977) of more than 24, and had no organic disorders. Patients fulfilling these criteria were contacted after two years to attend a follow-up assessment.

First assessment. The initial assessment included a detailed history provided by the patient and a significant other, a mental status (including psychiatric) examination, a physical (including neurological) examination, laboratory tests, and a CT scan. The MMSE, the Global Deterioration Scale (GDS; Reisberg, Ferris, de Leon, & Crook, 1982), the Hamilton Depression Rating Scale (HDRS; Hamilton, 1960) and the Blessed Dementia Scale (BDS; Blessed, Tomlinson, & Roth, 1968) were also administered. The diagnostic procedure of the MMC has been described elsewhere (Verhey et al., 1993).

Follow-up assessment. A medical history was taken as well as the MMSE and the Hamilton Depression Rating Scale (HDRS), the auditory verbal learning test (AVLT), the Revised Trail Making Test (R-TMT), the Stroop Color Word Test, and the Memory Scanning Task (MST) (see Section 4.3, for test descriptions). The neuropsychological tests were selected on the basis of literature showing that memory decline and cognitive slowing are among the first aspects of Alzheimer's disease and on the basis of previous results from our group concerning patients with age-associated memory impairment (Jolles, 1986; Houx, 1991).

Data analysis

The number of main variables was reduced to three by means of composite scores. The variables were: (1) Memory (Auditory Verbal Learning Test: maximum number of words recalled, number of words recalled, and number of words recalled in the delayed recall); (2) Sensorimotor speed (basic speed of memory scanning test; basic speed of concept shifting test (TMT-A), reading speed of Stroop test and memory scanning test, one letter), and (3) Cognitive speed (slope of memory scanning test; Stroop interference (Stroop-III), and concept shifting interference (TMT-C). The memory score was composed of parameters that were thought to represent different aspects of secondary memory. Sensorimotor speed was composed of those test variables that reflect the basic routine cognitive operations, such as visual scanning and reading. Cognitive speed consisted of variables that reflect the speed of mental processing. In order to form the composite scores, individual test scores were converted to standard *Z*-scores, using the means and standard deviations of the normative data of Houx (1991) and the MAAS study. The composite score of a given variable was regarded as impaired compared to that of the normative data when its value was below the arbitrary level of −2 standard deviations (*SD*). A decline in a given variable was defined as a decrease of 2 *SD* or more of the composite score of that variable, whereas an improvement was defined as an increase of 2 *SD* or more.

RESULTS

After a mean follow-up time of 25.0±3.6 months, 47 patients (74%) could be retested (28 men and 19 women). The mean age was 57.5±11.0 years. Thirty-three patients had received a psychiatric diagnosis according to DSM-III-R at the initial assessment: major depression (12) dysthymia (12), personality disorder (4), anxiety disorder (2), adjustment disorder (2), and post-traumatic stress disorder (1). Fifteen patients had no psychiatric diagnosis.

There were no differences in age, level of education, and the initial scores on the MMSE between those patients who were tested in year two and

Table 17.1.
Means and standard deviations for clinical and cognitive measures.

Measure	Year 0			Year 2			Difference		
	n	*Mean*	(*SD*)	*n*	*Mean*	(*SD*)	(%)	*df*	p^1
HDRS score	46	9.9	(5.7)	45	6.5	(5.5)	−34	43	<.001
MMSE score	40	28.3	(1.7)	45	27.5	(1.9)	−3	37	<.01
Memory	47	−8.5	(6.8)	45	−9.5	(7.8)	−12	44	ns
Sensorimotor speed	45	−7.3	(5.9)	43	−7.0	(6.2)	4	40	ns
Cognitive speed	39	−5.9	(5.2)	40	−4.1	(3.0)	31	35	<.01

Note. Values for the Verbal Learning Test represent number of items. Values for the other cognitive measures represent seconds. For MMSE and the verbal Learning Test, high scores indicate a good performance, whereas for all other measures high scores indicate a poor performance. [1] *T*-test for paired samples, two-tailed.

those who were not. The only variable that was different between the two groups was the initial score on the HDRS (9.9±5.7 in the retested group, versus 13.3±5.5 in the group that was tested only once (Wilcoxon rank sum test, two-tailed, $p<0.05$). Thus, there was some selective attrition in this study: the patients who could not be retested had a higher level of depressive symptomatology than the entire cohort.

Table 17.1 shows the number of observations, the means, and the standard deviations for the clinical and composite cognitive measures at the initial assessment and at follow-up for the 47 patients who attended the follow-up assessment. Some data are missing, because a number of patients found the tests too tiring and wanted to stop prematurely, despite encouragement by the test assistant. As a consequence, a composite score could not be obtained. Table 17.2 shows the number of patients with impaired and unimpaired composite scores at the initial assessment and the development of these scores at follow-up. The memory score was initially impaired in 36 (80%) of the patients who were tested. Memory appeared to have deteriorated at follow-up in more than 50% of these patients. In contrast, most of the patients who initially had impaired scores of sensorimotor and cognitive speed did not appear to have declined further at follow-up, but were unchanged (44%) or improved (22%).

At the time of follow-up, four patients were found to have become clearly demented, while one patient was diagnosed as questionably demented. One patient was diagnosed as demented by one specialist and as questionably demented by the other. The other 41 patients were not found to have become demented at follow-up. Thus, the two raters showed

Table 17.2.
Cognitive composite scores classified by impairment status at initial assessment and follow-up: absolute numbers (%).

		Initial assessment	Follow-up assessment		
			Decline	No change	Improvement
Memory	impaired	36 (80)	20 (56)	3 (8)	13 (36)
	not impaired	9 (20)	3 (33)	4 (44)	2 (22)
Sensomotoric speed	impaired	36 (88)	11 (31)	14 (39)	11 (31)
	not impaired	5 (12)	1 (20)	3 (60)	1 (20)
Cognitive speed	impaired	31 (86)	2 (6)	15 (32)	14 (61)
	not impaired	5 (14)	1 (20)	4 (80)	0 (0)

100% agreement when the two categories of dementia and questionably demented were combined. None of the patients had cerebrovascular symptoms in the follow-up period, nor any other somatic abnormalities. Therefore, these six subjects were thought to suffer from probable Alzheimer's disease.

Table 17.3 shows the characteristics of those patients who became demented in the follow-up period and those who did not. The demented subjects were on average 10 years older and had significantly worse memory scores, both at the initial and at the follow-up assessment, than the non-demented subjects. Sensorimotor speed was worse in the dementing group at follow-up. The two groups did not differ significantly with regard to the initial and the follow-up scores on the HDRS and the MMSE. Within the group of the patients who developed dementia, none of the variables had changed significantly. It should be noted, however, that the number of patients who developed dementia was small (n=6), and that, additionally, several values were missing. The mean cognitive speed of the non-dementing group had improved significantly. Twenty-four patients had received a diagnosis of depression (including dysthymia) at the initial assessment and 19 of them also had impaired memory scores. Ten of these 24 patients had deteriorated at follow-up, but their mean depression score had not changed significantly (HDRS 13.0±6.6 initially and 12.1±7.6 at follow-up). In contrast, the memory scores of 8 of these 24 patients had improved, and so had their depression ratings (initial HDRS score 12.5±3.3 and 7.8±4.6 at follow-up). Of the six patients who subsequently developed (clear or questionable) dementia, three had received a psychiatric diagnosis at the initial assessment: one had been diagnosed as having major depression, one as having dysthymia and one as having an anxiety disorder.

Table 17.3.
Clinical measures and composite scores by diagnosis of dementia at follow-up.

	Dementia at follow-up (n=6)					P within group	No dementia at follow-up (n=41)					P within group	P between group	
													initial	follow-up
	n	M_1	(sd)	M_2	(sd)	p^1	n	M_1	(sd)	M_2	(sd)	p^1	p^2	p^2
Clinical measures														
Initial age (years)	6	66.0	9.4				41	55.8	10.5				<.05	
HDRS score	6	9.7	3.3	6.6	4.6	ns	40	9.9	5.9	6.8	5.9	<.001	ns	ns
MMSE score	5	28.2	1.3	27.2	1.7	ns	35	28.4	1.8	27.5	1.9	<.01	ns	ns
Composite scores														
Memory	6	−14.8	6.9	−16.6	5.4	ns	41	−7.5	6.3	−8.3	7.5	ns	<.01	<.01
Sensorimotor speed	5	−5.8	4.6	−13.0	13.6	ns	40	−8.2	8.1	−6.7	6.1	ns	ns	<.05
Cognitive speed	3	−6.5	6.8	−5.6	6.8	ns	37	−5.8	4.7	−4.6	3.4	<.05	ns	ns

Note. [1] T-test for paired samples, one-tailed, for comparisons within groups. [2] T-test for independent samples, one-tailed, for comparisons between groups.

DISCUSSION

This study has several limitations that should be considered before the possible implications of the results are discussed. A substantial number of patients did not take part in the follow-up: almost 30% of the original cohort could not be retested. Some patients refused because they found the tests too tiring, others gave no reason for their refusal. Because a tendency to get stressed and an increased exhaustibility may occur early in the development of dementia, the patients who dropped out of the study probably represent a group that is more at risk of becoming demented than those who participated. As a consequence, the results obtained with the retested group probably underestimate the real level of deficits in the entire cohort. Quite a few patients could not finish all the neuropsychological tests, especially those tests that demanded relatively more mental effort. For instance, composite scores for cognitive speed could not be obtained in 23% of the patients who were retested. This is another cause of selective attrition effects in this study. Since a control group was not studied in parallel to the study group, the study does not allow for comparisons between the patient group and the general population. Because of these methodological problems, the results of these study should be interpreted with due consideration.

Six of the 47 patients who were tested (13%) were thought to have become demented at the two-year follow-up. Given the fact that the mean age of the population under study was quite low and that the time of follow-up was short, this number is much higher than expected on the basis of known incidence rates. Estimating the incidence rate in a given group on the basis of the age distribution, the expected number of patients who would develop dementia in two years would be less than one (0.47) in our study population. Thus, the rate observed in this study was much higher than expected. However, the figures presented here give only a global indication and should be considered with caution, because the absolute number of patients was small and we did not study a control group. Nevertheless, these results clearly illustrate the methodological value of services such as the Maastricht Memory Clinic for research into the very early manifestations of dementia. The MMC –in comparison to other memory clinics– is unique in that the mean age of the patients is low (below 60) and only one-third of the patients is demented. The majority of the patients have cognitive complaints, are not demented, and potentially suffer from a prodrome of dementia. A follow-up period longer than the two years used in our study would probably have detected more cases of dementia, as there were several patients who showed a decline of cognitive functions but who were not thought to have become demented. The number of patients who subsequently developed dementia would have been 50% lower if psychiatric disorders had been an exclusion criterion in our study. Changes in affectivity and personality may be among the earliest features of dementia. Therefore, patients with cognitive complaints who also demonstrate psychopathological symptoms may represent a population of particular interest with respect to the early detection of dementia.

Because of the limitations mentioned above, the findings of the present study cannot be considered as conclusive with regard to the early cognitive changes of Alzheimer's disease. The present study will be extended by reassessing the patients of this study after another two years, parallel to a control group of normal subjects, in order to enable comparisons between the patients' course and that of normal subjects. The results of this study do underscore the notion that a population of elderly subjects with memory complaints may contain individuals who are in a prodrome of Alzheimer's disease. A longitudinal follow-up of the MAAS study will be performed in order to evaluate this hypothesis.

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