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# Subjective memory complaints may announce dementia

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**Article abstract**—Whether subjective memory complaints in the absence of objective memory decline can predict future dementia has been investigated only in highly selected clinical and volunteer cohorts. Our study examines this question in a subsample of AMSTEL (Amsterdam Study of the Elderly), a longitudinal population study on cognitive decline and dementia. Subjects (aged 65 to 84 years;  $n = 357$ ) without dementia or other psychiatric disorders at baseline were followed for 3 years. After this interval, 16 of 203 re-examined patients developed a dementia. Logistic regression analyses indicated that memory complaints at baseline contributed a small but significant amount of diagnostic information. However, the most powerful predictor of future dementia was deficient memory performance. We conclude that subjective memory complaints may predict dementia within 3 years, particularly when there are objective signs of memory deterioration.

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Patients in the early stages of dementia generally have sufficient insight into their condition to be aware of memory failures.<sup>1,2</sup> Mild to moderate dementia patients report more memory complaints than do normal elderly people.<sup>3,4</sup> However, clinical and experimental studies of nondemented elderly subjects have not found memory complaints to be associated with performance on objective memory tests but rather with depression.<sup>5-11</sup> The sensitivity of

memory tests for subtle memory impairment is not perfect, however.<sup>12</sup> During the prodromal phase of dementia, self-perception may be more sensitive than objective assessment.

To date, subjective memory complaints have not been helpful in diagnosing dementia. In a clinical setting, self-assessment of memory function does not add to the discriminative power of objective tests for (cross-sectional) detection of dementia.<sup>13</sup> Follow-up

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studies of patients who were referred to memory clinics with subjective complaints but without objective signs of dementia found an increased risk of dementia in cases suffering from depression<sup>14,15</sup>; the depression (or its treatment with anticholinergic antidepressants or electroconvulsive therapy) and not the subjective complaints were the precursors of dementia, a finding supported by epidemiologic studies using case-control methods.<sup>16</sup> Prospective studies of small groups of elderly volunteers with subjective memory complaints but without objective signs of deterioration either found no change after 3 years<sup>17</sup> or only a small memory decline after 4 years.<sup>18</sup>

No longitudinal population studies exist on the predictive value of subjective memory complaints. The present study follows a group of elderly subjects not suffering from dementia or depression to determine whether subjective memory complaints predict the emergence of dementia over an interval of 3 years.

**Methods.** *Subjects.* Subjects participated in the Amsterdam Study of the Elderly (AMSTEL project), a two-phase population study on cognitive decline and dementia in community-dwelling elderly individuals. The design and sampling methods of the AMSTEL project are described in detail elsewhere.<sup>19,20</sup>

In brief, the study sample consisted of 4,051 subjects (aged 65 to 84 years) who were recruited from 30 general practices throughout Amsterdam. The sample was stratified in 5-year age groups. Of these 4,051 subjects, all persons with a score of less than 22 on the Mini-Mental State Examination (MMSE)<sup>21</sup> were invited to participate in a follow-up, together with age-stratified subsamples of subjects with a borderline (22 to 26) or good MMSE score (27 to 30). In total, 511 subjects agreed to participate in the follow-up. Of these volunteers, the following were excluded from the present analyses: 49 patients with dementia by DSM-III-R criteria,<sup>22</sup> 29 nondemented cases with a psychiatric disorder by CAMDEX (Cambridge Examination for Mental Disorders of the Elderly) criteria<sup>23</sup> (depressive syndrome [19], anxiety disorder [6], delirium [3], and schizophrenia [1]), and 76 cases with MMSE scores below 24. We report on the remaining 357 subjects not suffering from dementia or any psychiatric disorders.

*Measurements.* In phase 1, the participants ( $n = 4,051$ ) were visited at home by a trained lay interviewer. A structured interview was administered, consisting of questions on medical history, cognitive and emotional symptoms, risk factors for dementia, and the MMSE.

In phase 2, the selected participants ( $n = 511$ ) were visited at home by a research physician and a research nurse. The CAMDEX schedule<sup>23</sup> was used during these home visits, which were repeated every year. Subjects underwent a physical examination and a cognitive examination (CAMCOG: cognitive test section of the CAMDEX). In addition, their medical history was taken in greater detail. The CAMDEX variables of DSM-III-R dementia diagnosis,<sup>22</sup> severity rating of depressive symptoms, and the CAMCOG memory subscale were used in our analyses. The memory subscale is the most appropriate CAMCOG subscale for the detection of early signs of dementia and is more sensitive than the MMSE.<sup>24</sup>

**Table 1** Subjective Memory Complaints scale

Question	Score range	% With problems*	R(ir)†
1. Do you have any complaints concerning your memory?	0-3	39.8	0.60
2. Do other people find you forgetful?	0-2	14.4	0.39
3. Do you ever forget names of family members or friends?	0-3	12.8	0.41
4. Do you often forget where things are left?	0-3	40.5	0.55
5. Do you often use notes to avoid forgetting things?	0-2	38.4	0.27
6. Do you ever have difficulties in finding particular words?	0-1	39.2	0.34
7. Did you ever lose your way in your neighborhood?	0-1	3.8	0.12
8. Do you think more slowly than you used to?	0-2	22.9	0.43
9. Do your thoughts ever become confused?	0-2	7.0	0.43
10. Do you have concentration problems?	0-2	7.7	0.30

Scoring of items 1, 3, and 4: 0 = no; 1 = yes, but no problem; 2 = yes, problem; 3 = yes, serious problem. Scoring of items 2 and 5: 0 = no; 1 = yes, sometimes; 2 = yes, often. Scoring of items 6 and 7: 0 = no; 1 = yes. Scoring of items 8, 9, and 10: 0 = no; 1 = yes; 2 = yes, serious problem.

\* % with problems: % of total sample ( $N = 4,028$ ) indicating at least some problems with the item.

† R(ir): item-rest correlation.

*Data analysis.* Construction of a Subjective Memory Complaints scale (SMC). The phase I interview contained 10 questions on subjective memory complaints, which were derived from the CAMDEX. The data of the total sample ( $n = 4,051$ ) were used to construct a Subjective Memory Complaints scale (SMC; table 1). Cases with more than four missing answers were dropped ( $n = 23$ ). The rest of the missing answers were recoded into the maximum item score. An item score of zero indicates no complaint; higher item scores indicate presence of complaints.

Most complaints (~40% of the total sample;  $n = 4,028$ ) concerned misplacing things, making notes, difficulty in choosing the right word, and the general forgetfulness. The least frequent complaints (<8%) concerned losing one's way, confused thoughts, and concentration problems (table 1). The sum score of these items had an internal consistency of 0.72 (Cronbach's alpha;  $n = 4,028$ ). The mean correlation of the items with the sum of the remaining items was 0.38 (range 0.12 to 0.60; see table 1). Mean  $\pm$  SD SMC score was  $2.62 \pm 2.68$  (range 0 to 19).

*Predictive value of subjective memory complaints.* We performed a stepwise forward logistic regression analysis taking dementia status at year 3 (yes/no) as the dependent variable to assess whether subjective memory complaints add any predictive power over and above age (as the main

**Table 2** Age, gender, and baseline scores on MMSE, SMC, CAMCOG Memory subscale, and CAMDEX Depression severity rating broken down by dementia status after three years

	Normal, n = 187	Demented, n = 16	Died, n = 36	Dropped out, n = 118	Significance
Men/women	82/105	6/10	16/20	45/73	
Age (yr)	74.0 (5.5)	80.6 (3.3)***	76.6 (5.1)**	76.1 (5.6)**	0.0001
MMSE	27.0 (1.8)	25.9 (1.1)*	26.3 (1.9)*	26.3 (1.8)**	0.003
SMC	2.5 (2.4)	4.4 (2.9)**	2.6 (3.2)	2.7 (2.8)	0.04
CAMCOG Memory	22.0 (2.7)	16.9 (4.8)***	21.8 (2.4)	21.0 (3.6)**	0.0001
CAMDEX Depression	0.14 (0.48)	0.19 (0.40)	0.33 (0.59)**	0.21 (0.54)	0.05

Significance is overall level of significance by ANOVA or Kruskal-Wallis test (Depression).

\*  $p < 0.05$ , \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$ ; two-tailed significance of planned comparisons comparing subgroup with normals by  $t$  test or Mann-Whitney test (Depression).

MMSE = Mini-Mental State Examination; SMC = Subjective Memory Complaints scale.

risk factor associated with dementia) and depressive symptoms (as a possible confounding variable). Age, SMC score, and the CAMDEX Depression severity rating at baseline were used as independent variables.

This analysis was repeated, including the CAMCOG Memory score at baseline, to test the predictive value of subjective memory complaints when objective memory performance is taken into account.

**Results.** *Incidence of dementia, mortality, and dropout.* After 3 years, 16 subjects (7.9%) from the group we re-examined were suffering from dementia. Thirty-six died before a diagnosis could be made, and 118 dropped out of the study (refused further cooperation or left Amsterdam).

*Characteristics of follow-up sample at baseline.* Table 2 presents the demographic characteristics, mean test scores at baseline of the follow-up sample, and the numbers of those who died or dropped out. Analysis of variance showed significant differences on all variables except gender (chi-square test). Planned comparisons of the normal group with each of the other groups showed that the subgroup of dementia patients had more subjective memory complaints than did the normal subgroup. Those suffering from dementia and those who died or dropped out of the study were older and had lower MMSE and CAMCOG memory scores than subjects who did not suffer from dementia. The subgroup that died within 3 years had significantly more symptoms of depression. Severity of depressive symptoms correlated 0.20 ( $p < 0.0001$ ) with SMC score at baseline in the total follow-up sample ( $n = 357$ ).

This pattern of results was largely the same after 1 and 2 years (not shown), despite the attrition.

*Predictive value of subjective complaints.* Table 3 lists the results of the stepwise logistic regression analysis with dementia status (demented versus nondemented) after 3 years as dependent variable. Age, the SMC score, and the CAMDEX Depression rating were used as independent variables. Age was entered first, followed by the SMC score. The CAMDEX Depression rating was not included in the model. Table 3 also shows the odds ratios and partial correlations after adjustment for the remaining variable. Age predicts dementia better than subjective complaints, but once age is accounted for, the complaints still add to the prediction.

Table 4 shows that memory performance is a more powerful predictor of future dementia. In this analysis, the CAMCOG Memory subscale was entered first, followed by age. (Four nondementia patients were dropped because of incomplete CAMCOG data.) The CAMDEX Depression rating and the SMC score were not included in this model.

**Table 3** Results of logistic regression analyses (stepwise forward) to predict dementia after three years using age, SMC scale, and CAMDEX Depression rating as independent variables

	OR	(95% CI)	R	Significance
Age (yr)	1.28	(1.12–1.46)	0.31	0.0003
SMC scale	1.25	(1.03–1.52)	0.16	0.027
Depression	Not included			
No. normal/demented	187/16			

SMC = Subjective Memory Complaints scale; OR (95% CI) = odds ratio with 95% confidence interval; R = partial correlation of variable concerned with dementia status after correction for the other variable; Significance = level of significance of the partial correlation.

**Table 4** Results of logistic regression analyses to predict dementia after three years using age, SMC scale, CAMDEX Depression rating, and CAMCOG Memory scale as independent variables

	OR	(95% CI)	R	Significance
CAMCOG-M	0.73	(0.62–0.86)	–0.34	0.0001
Age (yr)	1.22	(1.06–1.41)	0.22	0.007
SMC scale	Not included			
Depression	Not included			
No. normal/demented	183/16			

SMC = Subjective Memory Complaints scale; OR (95% CI) = odds ratio with 95% confidence interval; R = partial correlation of variable concerned with dementia status after correction for the other variable; Significance = level of significance of the partial correlation.

**Discussion.** In elderly people not suffering from dementia or any psychiatric disorders, subjective memory complaints may announce a dementia syndrome within 3 years. This finding is in accord with the reported relationship between subjective complaints and cerebral white matter lesions.<sup>25</sup> However, objective memory performance is a better predictor of future dementia when a more sensitive memory test than the MMSE, such as the CAMCOG Memory subscale, is used. In general, the predictive value of subjective memory complaints is inversely related to the quality of the objective memory assessment. After taking into account the results of a sufficiently thorough memory assessment, there is no contribution of subjective complaints in the prediction of future dementia. This corroborates the cross-sectional findings of McGlone et al.<sup>13</sup>

We draw the following clinically relevant conclusions. First, our findings show that subjective complaints in themselves may announce dementia within an interval of 3 years, even in seemingly healthy subjects who show no conspicuous signs of possible dementia. Second, this conclusion is also valid for subjects with mild symptoms of depression, because these symptoms did not influence the prediction. Thus, the clinician should be careful not to interpret subjective memory complaints as mere symptoms of depression, which will disappear as soon as the patient's mood improves, as suggested in clinical lore and small-scale studies.<sup>26</sup> From a longitudinal perspective, the patient's perception may be correct, and the memory complaints may indicate an impending dementia. On the other hand, subjective memory complaints may be symptoms of an organic depression, possibly prodromal to a dementia.<sup>15,27,28</sup> Third, an important implication of our findings is that we should not reassure a worried patient solely on the basis of a normal MMSE or other superficial memory examination. In such cases, the patient should be examined more thoroughly using sensitive neuropsychological tests. Once the patient has a clear dementia syndrome, however, he or she may stop complaining and develop an anosognosia, particularly when there are frontal symptoms.<sup>29-31</sup> The appraisal of the patient's relatives then becomes more informative than the self-report.<sup>13,32-34</sup> A collateral result of our study is the increased mortality risk in subjects with depressive symptoms (table 2). Although this is not a new finding,<sup>35,36</sup> it demonstrates that depressive symptoms are stronger predictors of death than of dementia. (Because we excluded cases with major psychiatric syndromes, we cannot draw conclusions about major depression.)

Some methodologic issues warrant discussion. At first glance, our findings seem to conflict with the negative results of follow-up studies using volunteers.<sup>17,18</sup> However, the subjects in these studies were significantly younger than ours (on average,  $\geq 60$  years). Moreover, they satisfied a long list of exclusion criteria concerning physical diseases and psychiatric history. Our subjects were almost 10 years

older, and our exclusion criteria were a low MMSE score and the presence of a psychiatric disorder. Therefore, the expected incidence of dementia was lower in these volunteer studies than in ours. In fact, the annual incidence was about 26 per 1000 in our sample, which is comparable with that in other population studies.<sup>37,38</sup>

The attrition due to mortality, geographic mobility, and noncompliance was somewhat selective. Subjects who died or dropped out of the study were older than the normal subjects, and their mean memory and mental status scores were also lower (table 2). In the subjects who died, this effect might be related to the phenomenon of "terminal drop."<sup>39</sup> The subgroup of nonresponders in our project was not only characterized by lower scores on cognitive tests but also by lower education and a greater frequency of mental and physical diseases.<sup>40</sup> Thus, the attrition may have caused an underestimation of the incidence of dementia in the cohort and reduced the power of the study. Without this attrition, the predictive effect of subjective memory complaints probably would have surfaced more prominently.

The subjective complaints scale is admittedly brief compared with published metamemory scales, but its item content is quite representative and its reliability is acceptable (see for a review, e.g., Gilewski and Zelinski<sup>41</sup>). Existing scales are too lengthy for application in a population survey. Some epidemiologic surveys use only one question on subjective memory complaints.<sup>4,42</sup> Only O'Connor et al<sup>3</sup> used a similar scale (seven items) to ours, also borrowing from the CAMDEX interview.

Forty percent of the total sample ( $n=4028$ ) had memory complaints evidenced by their affirmative answer to the first general question of the SMC. Dementia patients have almost twice as many subjective memory complaints than do normal elderly people (table 2), a figure comparable with other population studies.<sup>3,4</sup> Our finding of a significant correlation between subjective complaints and depressive symptoms (0.20) also agrees with those of numerous other studies (e.g., references 3-11, 42).

We conclude that patients with subjective complaints who show no conspicuous signs of memory deterioration do have an increased risk of developing dementia within 3 years. These memory complaints should serve as possible warning signs of impending dementia.

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