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Subjective memory complaints, neuropsychological performance and psychiatric variables in memory clinic attendees: A 3-year follow-up study

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ABSTRACT

The aims were to evaluate the cognitive performance and clinical diagnosis in patients (<75 years) seeking help for subjective memory complaints, to determine the prevalence of certain psychiatric symptoms and to conduct follow-up examinations. At baseline 41% showed normal cognitive performance (subjective memory impairment; SMI), 37% fulfilled criteria for mild cognitive impairment (MCI) and 22% were classified as dementia. There were significant associations between the three groups and experiences of psychosocial stress and feelings of anxiety. The proportion of psychosocial stress was significantly higher in SMI vs. MCI and SMI vs. dementia. Feelings of anxiety were significantly higher in SMI vs. MCI. At the 3-year follow-up, 88% of the SMI patients remained stable SMI and 60% of the MCI patients remained stable. There was a significant reduction of psychosocial stress and moderate reduction of feelings of anxiety among the SMI patients. The findings indicate that the risk of patients with SMI developing dementia is small within a 3-year span. We propose that subjective memory complaints might be influenced by the presence of psychosocial stress and feelings of anxiety disturbing the memory processes and interfering with the patients' evaluation of their memory function.

1. Introduction

Subjective memory complaints are very common in the elderly but are also reported among middle-aged and young old patients. The complaints of poor memory might be associated with benign changes of healthy aging (DeCarli, 2003). However, memory complaints may also be associated with other conditions, especially MCI and dementia as well as depression and anxiety (Reisberg and Gauthier, 2008). The relationship between subjective memory complaints and objective performance in neuropsychological tests has been investigated (Jonker et al., 2000; Elfgren et al., 2003; Guarch et al., 2004; Lautenschlager et al., 2005; Vestberg et al., 2007, 2009; Gallassi et al., 2008). Some studies have found an association between subjective memory impairment and poor performance in memory tests, whereas others have failed to do so. It has been shown that the relationship between subjective memory complaints occurring in a sample drawn from the general population reporting the everyday irritation of minor forgetfulness is not the same as in a study recruiting subjects who seek help at a memory clinic (Jonker et al., 2000; Elberling et al., 2002; Mitchell, 2008). The evaluation of memory complaints in relation to objective test performance requires knowledge about how the choice of the sample affects the results.

Several studies have shown that depression and other psychiatric conditions such as anxiety and psychosocial stress may affect both the patients' perception of their own performance as well as their objective memory performance (Smith et al., 1996; Jonker et al., 2000; Comijs et al., 2002; Elfgren et al., 2003; Jorm et al., 2004). There are important and complex interrelationships between psychiatric conditions and cognitive impairment. In a study by Sinforiani et al. (2007) it was found that subjects with cognitive complaints but whose neuropsychological evaluation was within normal range were younger and presented higher scores of anxiety and depression. So far, there are only a few follow-up studies of patients with subjective memory complaints without objective memory impairment evaluating the influence of psychiatric variables. A recent study by Glodzik-Sobanska et al. (2007) has shown that the presence of subjective memory complaints was a predictor of future cognitive decline. Some subjects did however present as "unstable" over time fluctuating between decline and normal cognitive performance. These "unstable" subjects had a high intensity of memory complaints and more affective symptoms. A tentative conclusion from these findings is that the presence of even low levels of affective symptoms may have prognostic relevance and even treatment consequences in subjects with memory complaints (Reisberg and Gauthier, 2008).

In the current study the primary aim was to evaluate the cognitive performance, clinical diagnosis and duration of memory problems in patients (<75 years) seeking help for their subjective

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memory impairment at an out-patient memory clinic. The second aim was to determine the prevalence of certain psychiatric conditions (experiences of psychosocial stress, feelings of anxiety and depressed mood), which might influence the memory performance or the experience of memory deficits. A third aim was to conduct follow-up examinations after 3 years.

2. Patients and methods

2.1. Patients

Patients with subjective memory complaints, examined at the out-patient Memory clinic, University Hospital of Lund, Sweden, were recruited. The majority of the patients attending this Memory clinic are above 75 years but in the current study the focus was to examine patients younger than 75 years. The patients were either referred by their GP or attended of their own accord. Inclusion criteria were: (1) presence of memory complaints, (2) age between 35 and 75 years. Exclusion criteria were: (1) a previous diagnosis of organic dementia or other neurodegenerative brain disorder, (2) ongoing anti-dementia pharmacological treatment, (3) a prior history of stroke, (4) post-traumatic stress disorder, (5) long-term solvent exposure, long-term drug or alcohol abuse, (6) psychosis, bipolar disorder, significant depression or generalized anxiety disorder, (7) traumatic brain injury. Seventy-eight patients fulfilled the criteria. Nineteen of the 78 patients declined to participate resulting in a group of 59 (25 men, 34 women; age range, 35–73 years; mean age, 59.6 ± 8.2 years (±S.D.)). After 3 years, 43 patients were re-evaluated with the same neuropsychiatric and neuropsychological examinations as used at baseline. One patient had withdrawn consent and two were missing due to severe somatic disease. The patients diagnosed with dementia at baseline (n = 13) were followed clinically but not re-evaluated within the current study. There was one interim visit between baseline and the 3-year follow-up, however, not reported in this study.

The study was approved by the Research Ethical Committee and written consent was obtained from all participants.

2.2. Neuropsychiatric examination

The neuropsychiatric examinations were conducted by experienced psychiatrists (UP, LG). The assessments included a clinical interview with the patient, a standardized psychiatric assessment including the mini-mental state examination (MMSE), a physical/neurological examination and routine electrocardiogram (Folstein et al., 1975). The presence of depressive symptoms was rated in accordance with the Montgomery–Asberg depression scale (MADRS; Montgomery and Asberg, 1979). In the clinical interview the psychiatrists ascertained the presence of depressed mood and/or feelings of anxiety. Subjects were judged as having depressed mood if the ratings according to MADRS ≥7 and/or if they reported "feeling sad" regularly over the last month and/or if the clinical interview indicated sadness (Snaith et al., 1986). Feelings of anxiety were based on the patient's own report as well as clinical signs. Furthermore, the presence of psychosocial stress at work and/or at home was recorded if the patient reported experiences of daily stress over the last 3 months.

2.3. Neuropsychological examination

All subjects were evaluated using eight neuropsychological tests chosen from the Betula study, Sweden (Nilsson et al., 1997). The Betula study is a prospective cohort study on memory, health and aging. Verbal functions were examined through a multiple-choice vocabulary test and two tests of verbal fluency (the Betula study). Four tests of verbal episodic memory were used: test (a) free immediate recall of 16 imperative sentences that were read aloud for the patients to follow and to memorize; test (b) 16 similar sentences, also read aloud but with visible text which then had to be memorized. Delayed cued recall of nouns from the previously learned and performed sentences (tests (c) and (d)) was tested after 30–40 min (the Betula study). Visuo-spatial construction ability was examined using block design (the Betula study; Wechsler, 1992). Besides the Betula tests, there was a test of visual episodic memory, the immediate recall of Rey complex figure test (RCFT; Meyers and Meyers, 1995). The neuropsychological test results for the Betula tests were compared with the age scaled normative data from the Betula study (Nilsson et al., 1997). The data used was from the first wave of 1000 subjects of the Betula study. The test result of the RCFT test was compared with the normative standard groups given in the manual (Meyers and Meyers, 1995).

2.4. Diagnostic procedure

Based on the neuropsychiatric and neuropsychological examinations, the patients were classified into three groups: patients with no significant memory deficits on the neuropsychological testing hereafter referred to as patients with SMI, patients with MCI and patients with a dementia disorder. The patients were classified into the SMI and the MCI groups on the basis of the neuropsychological test results. The operational criteria for SMI were (1) subjective memory complaint, (2) no significant deficits in any of the tests of episodic memory, verbal function or visuospatial construction ability. The criteria for MCI were (1) subjective memory complaint, (2) impaired memory function documented by the results of the neuropsychological memory tests, the scores of which should be 1.5S.D. or more, below age and estimated premorbid level of intellectual function. The premorbid level, as determined by a neuropsychologist's judgment, was based on the results of the test of vocabulary and on the years of education of the patient, (3) preserved general cognitive abilities, allowing for some cognitive impairment but diagnosed as no dementia by the psychiatrist, (4) essentially normal activities of daily living as determined by a clinical interview with the patient, and (5) not sufficiently impaired, cognitively and functionally, to meet either the DSM IV criteria for dementia or the criteria for Alzheimer's disease (AD), established by NINCDS-ADRDA (McKhann et al., 1984; APA, 1994). The MCI criteria included two clinical subtypes of MCI: (1) Amnestic MCI (aMCI) with objective memory impairment and absence of other cognitive disorders, (2) Multiple domains MCI (mdMCI) with objective memory impairment and a slight impairment in other cognitive domains (Petersen, 2004). Patients with a dementia disorder were diagnosed according to DSM IV criteria for dementia, NINCDS-ADRDA and consensus criteria for frontotemporal dementia (McKhann et al., 1984; APA, 1994; Brun et al., 1994). The diagnostic procedure also incorporated a standard battery of screening blood tests, CT or MRI scans, EEG and single photon emission computed tomography (SPECT).

2.5. Statistical analysis

Statistical analyses were conducted using SPSS version 14.0. Dichotomous variables were analyzed using McNemar test, χ^2-test and Fisher exact test. Parametric ANOVA (with a post hoc Bonferroni) was used to test differences regarding age, years of education, duration of memory complaints and scores on MMSE. Group comparisons for small subgroups (aMCI vs. mdMCI) were performed using Mann–Whitney U-test.