A Comparison between Subjective Memory Complaints and Objective Memory Deficits in Elderly Patients with Depression or Mild Cognitive Impairment

Berker DUMAN¹, Erguvan Tuğba ÖZEL KIZIL², Zeynel BARAN³, Sevinç KIRICI⁴, Engin TURAN⁵

SUMMARY

Objective: Since depression in the elderly is usually accompanied by memory complaints and may impair memory functions, differential diagnosis of cognitive impairment is quite difficult. This study aimed to investigate the discrepancy between subjective memory complaints (SMC) and objective memory deficits in elderly patients with major depressive disorder (MDD) and mild cognitive impairment (MCI).

Method: The study sample consisted of 30 elderly patients with a diagnosis of MCI (according to Petersen-Mayo criteria) and 29 with a diagnosis of DSM-IV-TR MDD who were treated at the outpatient geriatric psychiatry clinic. The control group consisted of 30 healthy elderly volunteers. Turkish versions of the Mini Mental State Examination (MMSE), Clock Drawing Test (CDT), ADAS-Cog, Subjective Memory Complaints Questionnaire (SMCQ) and Geriatric Depression Scale (GDS) were administered to all participants.

Results: The SMCQ scores of both the MDD and MCI group patients were higher than those of the healthy control (HC) group. However, there was no difference between the HC and MDD groups in terms of the MMSE, the CDT and the ADAS-Cog scores.

Conclusion: In elderly patients, subjective memory complaints do not seem to differentiate between depression and cognitive impairment. However, the discrepancy between SMC and cognitive performances suggests depression rather than cognitive impairment. Further longitudinal studies should investigate the role of SMC in cognitive impairment for elderly patients with depression.

Keywords: episodic memory, depression, mild cognitive impairment

INTRODUCTION

In Turkey, as well as throughout the world, the elderly population is increasing. According to the 2013 data of the Turkish Statistical Institute, the elderly constitute 7.7% of the general population in Turkey, and by 2050 this is expected to be 20.8% (Turkish Statistical Institute 2014). Together with an ageing population, memory complaints are observed more often and the frequency of dementia is increasing (Prince et al. 2013). Therefore, the evaluation of cognitive impairments in patients presenting with memory complaints and differential diagnosis has become increasingly important in daily clinical practice.

The concept of ‘subjective memory complaints’ (SMC) is defined as the complaint of forgetfulness and corresponds to situations where the memory performance, which is evaluated with neuropsychological tests, could either be preserved or impaired. In some studies, SMC has been evaluated with a single question (are you forgetful?), while in others evaluation has been attempted either with a group of questions or a scale. However, there is no consensus on how SMC should be measured and therefore it is not possible to compare the results obtained in different studies (Abdulrab and Heun 2008). The most frequently used way of evaluating SMC is the Subjective Memory Complaints Questionnaire, developed by Youn et al.
SMC is observed frequently in the geriatric population (Ponds et al. 1997; Mitchell, 2008; Balash et al. 2010). Besides SMC, cognitive impairments such as mild cognitive impairment (MCI) and depression may be seen in healthy elderly individuals (Mitchell, 2008). In previous epidemiological studies, SMC has been determined to be 40-80% in the community (Balash et al. 2010; Begum et al. 2012). Although SMC has often been reported in community studies, the rates of people seeking clinical help for these complaints have been reported to be between 18.6%-26.1% (Waldorff et al. 2008, Jorm et al. 2004, Begum et al. 2012).

SMC is significant as it could be an indicator of early stage cognitive disorder. However, when this symptom occurs at a later stage, it is debatable as to what extent this is a routine part of cognitive disorder (Begum et al. 2012). In addition, clinical meaning of SMC, whether or not it requires further evaluation and whether or not there are differentiating features, has not yet been fully revealed. In a study by Chin et al (2014), it was determined that in patients presenting with SMC with healthy memory performance, depressive symptoms and attention to themselves played a role in SMC. Lehrner et al (2014) showed that depressive symptoms increased SMC, regardless of the status of cognitive performance.

No definitive consensus has been reached yet on the extensive group which encompasses those between healthy ageing with MCI and early stage dementia (Kelley and Petersen, 2009). According to the scales used, there is a great variation, with prevalence of MCI previously reported at 4%-70% in the elderly population (Kochan et al. 2010). In a previous meta-analysis, the annual rate of MCI cases developing dementia was reported as 6.7%, and the total five-year transformation to dementia as 38.2% (Mitchell and Shiri-Feski, 2009).

For a diagnosis of MCI, it is recommended that mild impairment in standardized neuropsychological tests is confirmed by the patient’s relatives as MCI if there is minimal or no impairment in daily life activities (O’Brien, 2008). According to the MCI diagnostic scale recommended by the Mayo Clinic Alzheimer’s Disease Research Centre, for confirmation of forgetfulness by selected informed patients, there should be objective memory impairment according to age and education, protection of general cognitive functions, normal daily living activities and absence of dementia (Andreas cu and Aizenstein, 2009). In the DSM-5 which was published in 2013, under the heading of ”Mild Neurocognitive Impairment”, MCI is defined as impairment in one or more cognitive fields at a level not affecting daily living activities (American Psychiatric Association 2013). Neuropsychological tests are not sufficient alone for the diagnosis of MCI, largely because of the effect of sociodemographic elements. The observation of psychiatric disorders such as anxiety and depression in the course of MCI and since these disorders affect the clinical appearance, makes differential diagnosis more difficult (O’Brien, 2008).

Depressive symptoms are seen in 10%-15% of elderly individuals. According to the DSM-IV-TR criteria, the incidence of major depressive disorder (MDD) has been reported at 3% in the elderly (Baldwin 2008). Confusion in the clinical picture of objective memory deficits in depression in old age makes it difficult to differentiate between different clinical pictures in terms of treatment and prognosis (Lahr et al. 2007). However, as much as there may be objective cognitive defects in depression, no strong association has been observed between objective disorders in neuropsychological tests and SMC. Generally, SMC has been reported as severe and objective cognitive deficits as relatively mild (Lahr et al. 2007).

In this study, by comparing the samples of patients with MCI, MDD and healthy elderly individuals using a standardized evaluation tool for SMC, we aimed to determine the characteristics of SMC and evaluate its relationship with objective memory deficits. The main hypothesis of the study was that elderly patients with MDD would differ from the MCI group in that there would be no relationship between SMC and objective memory performance.

**MATERIAL and METHODS**

The study sample was comprised of a total of 59 patients over 60 years in age who were evaluated as outpatients with an accompanying relative at the Geriatric Psychiatric Unit of the university hospital and were diagnosed according to the DSM-IV-TR diagnostic criteria (American Psychiatric Association 2000) with MDD (n=29) or according to the Petersen-Mayo diagnostic criteria (Peteren 2004) with amnestic-type MCI (n=30). A control group consisted of 30 healthy (with no neurological or psychiatric disease) elderly volunteers from residential homes in the Ankara region. Any patients with hearing, visual, neurological or orthopedic disabilities, those with less than 5 years of education, and those with any other major neurological or psychiatric disease, which could inhibit the evaluation, were excluded from the study.

The MCI diagnosis was made by a detailed neuropsychiatric examination (including orientation, short-term memory, attention, verbal fluency, judgement, abstraction, resemblances, copying shapes, calculations, praxis, and language functions) which was applied by a physician working in the field of geriatric psychiatry. The patients diagnosed with MCI and MDD as a result of the neuropsychiatric evaluation and the healthy control subjects were administered the following tests by a psychologist: Standardized Mini Mental Test (SMMT), the ADAS-cog (Alzheimer’s Disease Assessment Scale Cognitive subscore), the Clock Drawing Test (CDT), the Subjective
The Scales

The Standardized Mini Mental Test (SMMT) is a scale of 30 items, which is useful in the evaluation of various cognitive functions such as orientation, long-term memory, recall, attention, calculation and language (Folstein et al. 2011). Low points indicate cognitive loss. Since it is a practical scale which can be applied in a short time, it is in widespread use as a scanning tool for dementia. Validity and reliability studies were applied by Güngen et al (2002) for the Turkish version of the form for educated patients.

The Alzheimer’s Disease Assessment Scale–Cognitive Subscore (ADAS-Cog) was developed by Rosen et al in 1984. The ADAS-Cog has 11 subtests including word recall, naming, commands, constructional praxis, ideational praxis, orientation, word recognition, language, comprehension, word finding difficulty and remembrance of test instructions (Maviöglu et al. 2006). In the study by Can et al (2010), three evaluation methods were compared, and the scoring method developed by Shulman et al. was shown to have the highest sensitivity and specificity for dementia diagnosis. In this method, the participants are requested to place clock numbers and hands inside a circle to show ten minutes past 11:00 and scoring is ranges from 0 (uncertain) to 5 (perfect clock). In the current study, this aformentioned method of CDT was applied.

The Clock Drawing Test (CDT) is a measurement scale with many different applications and forms of scoring, which is useful in the evaluation of several different cognitive functions such as attention, memory, motor functions and primarily visual and spatial functions (Cangöz et al. 2006). In the study by Can et al (2010), three evaluation methods were compared, and the scoring method developed by Shulman et al. was shown to have the highest sensitivity and specificity for dementia diagnosis. In this method, the participants are requested to place clock numbers and hands inside a circle to show ten minutes past 11:00 and scoring is ranges from 0 (uncertain) to 5 (perfect clock). In the current study, this aformentioned method of CDT was applied.

The Geriatric Depression Scale (GDS) is a questionnaire in the form of 30 Yes/No questions. Total score range from 0-30, with high points indicating increasing severity of depressive symptoms. The psychometric features of the GDS were researched by Sağduyu (1997). The test-retest reliability was defined as high (r=0.87) and internal consistency was sufficient (Cronbach alpha =0.72). A high correlation was determined with the Hamilton Depression Scale, and it was able to differentiate elderly with depression. When the cut-off score of 13-14 points was taken, sensitivity of 0.90 and specificity of 0.97 were reported in the determination of depression (Sağduyu 1997).

Statistical Analysis

All statistical analyses were carried out by SPSS software. The continuous variables (age, education level, SMCQ, ADAS-cog, SMMT, CDT, and GDS) of the three groups in this study were compared using the One-Way ANOVA test. The LSD test was used for post hoc analysis.

RESULTS

The patients with major depressive disorder consisted of eighteen females and eleven males. The patients with mild cognitive impairment consisted of ten females and twenty males and the healthy control group was comprised of thirteen females and seventeen males. No statistically significant difference was found between the groups in respect to gender (p>0.05). The mean ages and education levels of the patients are shown in Table 1. No statistically significant difference was found between the groups in respect to age or educational level.
The total score of the ADAS-Cog, the mean scores of the subtests and statistical comparisons of the three groups are shown in Table 2. No statistically significant difference was found between the groups in respect to the subtest scores for commands, constructional praxis, remembrance of the instructions, language and comprehension. A statistically significant difference was found between the groups in respect to total ADAS-Cog scores and the mean points of the subtests of word recall, naming, ideational praxis, orientation, word recognition and word finding difficulty. In the post-hoc analyses, the total ADAS-Cog scores of the MCI group were statistically significantly higher than those of the control group and the MDD group (p<0.001). No statistically significant difference was found between the control group and the MDD group (p=0.25).

The comparison of the mean scores of the SMCQ, SMMT, CDT and GDS of the three groups is shown in Table 3. A statistically significant difference was found between the groups in respect to the mean scores of the SMCQ (p<0.001). In the post hoc analyses, the total SMCQ scores of the MCI group were statistically significantly higher than those of the control group (p<0.001), but no significant difference was found with those of the MDD group (p=0.685). The scores of the MDD group were determined to be statistically significantly higher than those of the control group (p<0.001).

A statistically significant difference was found between the groups in respect to the SMMT scores (p=0.004). In the post hoc analyses, the SMMT points of the MCI group were statistically significantly lower than those of the control group (p=0.001). No statistically significant difference was found between the MDD group, the MCI group and the control group.

A statistically significant difference was found between the groups in respect to the CDT scores (p=0.016). In the post hoc analyses, the CDT points of the MCI group were statistically significantly lower than those of the control group and the MDD group (p=0.13, p=0.012). No statistically significant difference was found between the MDD group and the control group (p=0.977).

A statistically significant difference was found between the groups in respect to the total GDS scores (p<0.001). The total GDS scores of the MDD group were determined to be statistically significantly higher than those of the MCI group and the control group (p<0.001). The total scores of the MCI group were determined to be statistically significantly higher than those of the control group (p=0.004).

Taking the total GDS scores as a cofactor, when the SMCQ and ADAS-cog points were compared again, there continued to be a difference found between the three groups in the total SMCQ and ADAS-cog points (F=14.2, p<0.001; F=6.1, p=0.001). The interaction between the GDS and the SMCQ points was found to be significant (F=6.44, p=0.01), but

<table>
<thead>
<tr>
<th>Table 1. Comparison of the groups according to age and education</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCI</strong></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Education (year)</td>
</tr>
</tbody>
</table>

MCI, Mild Cognitive Impairment; MDD, Major Depressive Disorder; HE, Healthy Elderly
*By One-way ANOVA, p<0.05

<table>
<thead>
<tr>
<th>Table 2. Comparison of the groups according to the ADAS-Cog total and subtest mean scores</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MCI</strong></td>
</tr>
<tr>
<td>ADAS-Cog total score</td>
</tr>
<tr>
<td>Word recall</td>
</tr>
<tr>
<td>Naming</td>
</tr>
<tr>
<td>Commands</td>
</tr>
<tr>
<td>Constructional praxis</td>
</tr>
<tr>
<td>Ideational praxis</td>
</tr>
<tr>
<td>Orientation</td>
</tr>
<tr>
<td>Word Recognition</td>
</tr>
<tr>
<td>Language</td>
</tr>
<tr>
<td>Comprehension</td>
</tr>
<tr>
<td>Word finding difficulty</td>
</tr>
<tr>
<td>Remembrance of test instructions</td>
</tr>
</tbody>
</table>

MCI, Mild Cognitive Impairment; MDD, Major Depressive Disorder; HE, Healthy Elderly; ADAS-Cog, Alzheimer’s Disease Assessment Scale- Cognitive Subscore
*By One-way ANOVA, p<0.05
subjective memory complaints were found in both groups compared to the control group. In contrast to the ADAS-cog points used to evaluate objective memory deficits, the patients of the MCI group obtained significantly higher points than both the control group and the MDD group, thus demonstrating lower performance. In addition, no differences were observed between the control group and the MDD group in respect to the ADAS-cog points. In other words, although the subjective memory complaints of the MDD group were at the same level as those of the MCI patients, objective cognitive deficits were not determined. This can be explained by the conclusion previously reported by Lahr et al (2007), which says that, just as in other areas of their lives, patients with depression have a negative bias towards their own cognitive status.

The results obtained in this study of greater neuropsychological impairment of SMC in depression are similar to those indicated in previous studies (O’Connor et al. 1990; Dentone and Insua, 1997; Antikainen et al. 2001; Lahr et al. 2007).

The interaction with the ADAS-cog points was not (F=0.05, p=0.81).

The percentages of “Yes” responses of the three groups in relation to the 14 items of the SMCQ are shown in Table 4. It can be seen that apart from items one and two, the healthy control group subjects generally gave negative responses to the other items, and items three and eleven had no positive responses in this group. With the exception of item eleven, the responses of the MCI and MDD patients were seen to be similar to all the other items.

When evaluation was made with the Cronbach alpha coefficient for the 14 items of the SMCQ in the whole sample, the internal consistency was found to be high (0.829).

**DISCUSSION**

As a result of this study, as expected, the SMC measured with the SMCQ in the MCI patients was found to be similar to that of the MDD patients. A significantly greater level of subjective memory complaints were found in both groups compared to the control group. In contrast to the ADAS-cog points used to evaluate objective memory deficits, the patients of the MCI group obtained significantly higher points than both the control group and the MDD group, thus demonstrating lower performance. In addition, no differences were observed between the control group and the MDD group in respect to the ADAS-cog points. In other words, although the subjective memory complaints of the MDD group were at the same level as those of the MCI patients, objective cognitive deficits were not determined. This can be explained by the conclusion previously reported by Lahr et al (2007), which says that, just as in other areas of their lives, patients with depression have a negative bias towards their own cognitive status.

The results obtained in this study of greater neuropsychological impairment of SMC in depression are similar to those indicated in previous studies (O’Connor et al. 1990; Dentone and Insua, 1997; Antikainen et al. 2001; Lahr et al. 2007).
On the other hand, the fact that no statistically significant difference was found in the current study between the MDD group and the control group in respect to objective cognitive deficits is in conflict with the results of studies which reported objective cognitive losses in MDD (Den Hartog et al. 2003; Butters et al. 2004; Elderkin-Thompson et al. 2011; Begum et al. 2012). Different results obtained in different studies may be due to the means of evaluation of objective memory deficit or differences in the severity of depression.

For example, contradictory results were obtained in the current study related to SMMT, as the SMMT scores in the MDD group were not significantly different from those of the other two groups. In addition, the psychomotor speed and executive functions, which are reported to be often impaired in depression, may not be able to be adequately evaluated by the ADAS-cog. However, there was no difference between the control group and the patients with depression in the CDT results, where executive functions are evaluated. It was also clearly shown in this study that objective memory functions did not overlap with SMC in elderly patients with depression. However, the fact that the SMMT and CDT as neuropsychological tests used for scanning purposes may not provide detailed information should be considered as a limitation of this study.

The SMCQ is a valid and reliable tool which can be used in the evaluation of SMC in the elderly, with the advantages being that it can be applied quickly and evaluation is simple (Özel-Kızıl et al. 2013). In all groups, the SMCQ-1 (do you think you have a memory problem?) and SMCQ-2 (do you think your memory is worse than ten years ago?) questions were observed to generally receive a response of Yes.

Scanning for the presence of SMC as a diagnosis of MCI is controversial (Roberts et al. 2009). SMC, which can be seen in old age and in psychiatric impairments such as depression, is far from specific for a diagnosis of MCI. Those within the MCI group who were not aware of a cognitive defect have been reported as a group showing a more rapid development of dementia and low self-awareness (Roberts et al. 2009). Therefore, the questioning of SMC may be necessary for a diagnosis of MCI. However, when the presence of MCI is considered in terms of risk of transformation to dementia, SMC should be evaluated with a standard tool such as SMCQ in every elderly person.

In this study, a statistically significant difference was found between the groups in respect to depressive symptoms measured with the GDS. In the MCI group, it was observable that the depressive symptoms were greater than in the control group. This finding is consistent with the studies of Feldman et al (2004) and Hwang et al (2004), which showed depressive symptoms accompanying to MCI. However, the effect of depressive symptoms in the current study, was statistically controlled. In patients with major depressive disorders, neuropsychological evaluation during an episode is generally postponed until after treatment to remove the effect of depression. However, there have been studies that have reported that when a diagnosis of depression is made, there is a risk that the cognitive defects in the patient could predict Alzheimer’s disease in the future (Chodosh et al. 2007). Therefore, in MDD patients, the evaluation of both SMC and objective cognitive defects should not be postponed and should be repeated in high risk patients after an episode. In this study, in the patients with depression no objective memory deficit was found, however as the patient number was low, it would be incorrect to draw any conclusions.

As there are no Turkish forms of neuropsychological tests which can be applied to the elderly and as there are no normal values of the existing forms, MCI diagnosis is made by clinical examination. Therefore, the fact that objective neuropsychological test results were not used in the formation of the groups is a significant limitation of this study. However, a difference was found between the control group, the MDD group and the MCI group when comparing the neuropsychological tests widely used in Turkey to support the clinical diagnoses of those who did not have normal values for age in the MMSE, CDT and ADAS-cog, which were applied later. Only amnestic type MCI cases, and therefore probable pre-Alzheimer’s patients, were included in the study, so these results can not be generalised for other MCI groups. In addition, as the study was cross-sectional, there could be criticism that it did not have sufficient validity for both MCI and depression. Therefore, it can be said that there is a need for further, similar prospective studies to be conducted on a geriatric population. For MDD diagnosis, future studies should also focus on features such as the duration of the episode, the severity, the resistance to treatment and repeatability, which could affect both objective and subjective cognitive deficits.

Variables such as personality features or the level of anxiety, which could affect SMC, were not taken into consideration in this study (Steinberg et al. 2013; Balash et al. 2013). In addition, since the control group subjects with no informants were included, cognitive evaluation tools applied to the informants (IQCODE etc) were not used and therefore the informing of the relatives could not be taken into account (Özel-Kızıl et al. 2010).

In conclusion, the results of this study have shown that there could be a relationship between SMC and depression. Depressive symptoms must be considered in individuals presenting subjective memory complaints. In patients with major depressive disorder, it is necessary to evaluate both SMC and objective cognitive deficits. As a lack of the awareness of the memory deficit aspect of SMC is associated with a poor prognosis for MCI and dementia, SMC scanning with a valid test will be taken into consideration for both treatment and prognosis.