Facial Emotion Recognition Deficit in Amnestic Mild Cognitive Impairment and Alzheimer Disease

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Objectives: A deficit in facial emotion recognition was described in patients with Alzheimer disease (AD). However, this issue has been underexplored in subjects with amnestic mild cognitive impairment (a-MCI). Thus, the authors aimed to determine whether a deficit in facial emotion recognition is present in a-MCI phase and whether this is intensity dependent. A secondary aim was to investigate relationships between facial emotion recognition and cognitive performances. Design: Case-control study. Setting: Memory clinic. Participants: Fifty a-MCI patients, 50 mild AD patients, and 50 comparison subjects (COM) were enrolled. Measurements: Information about facial emotion recognition was obtained from Penn Emotion Recognition Test. The Mental Deterioration Battery was used to measure cognitive impairment. Results: Mild AD patients were more impaired in the recognition of almost all emotional stimuli of all intensities than a-MCI and COM subjects. However, there was an increased progression only in low-intensity facial emotion recognition deficit from COM to a-MCI to mild AD patients. In particular, a-MCI subjects differed significantly from COM in low-intensity fearful face recognition performance. This deficit in a-MCI patients was explained by the short-term verbal memory impairment, whereas the same deficit in mild AD patients was explained by the long-term verbal memory impairment. Conclusions: Emotion recognition progresses from a deficit in low-intensity fearful facial recognition in a-MCI phase to a deficit in all intensities and emotions in mild AD. This could be an effect of the progressive degeneration of brain structures modulating emotional processing. An early detection of emotional impairment in MCI phases of dementia may have clinical implications. (Am J Geriatr Psychiatry 2008; 16:389–398)

Key Words: Facial emotion recognition, Alzheimer disease, amnestic mild cognitive impairment, cognition
Alzheimer disease (AD) is a chronic and multidimensional neurodegenerative disorder. Classical expressions usually considered during the clinical assessment are cognitive deficits, functional impairment, and behavioral disorders. However, a different and potentially relevant contributing factor observed in patients with AD may be a deficit in processing some or all facial expressions of emotions. In particular, in AD patients, there is evidence that impaired facial emotion recognition ability, rather than deterioration of general cognition, influences interpersonal behavior. Thus, the social cognition approach, which takes into consideration the environmental–cognitive relationship with particular attention on what is going on in the minds of other people during specific stimuli of emotional valence, could contribute to the deepening of the knowledge of this complex disorder.

However, the relationship between facial emotion recognition impairment and cognitive deficits in AD patients still remains unclear. On the one hand, there are studies describing independence of facial emotion recognition ability from face processing cognitive performance, therefore suggesting a distinct role of systems involved in emotional and visuospatial processing. On the other hand, some authors describe that facial emotion recognition deficit is linked to cognitive impairment, specifically to visual–perceptual performances. A possible explanation for these controversial findings may be that these studies used different emotion recognition tests, several types of cognitive tasks and samples of patients with different severity of illness. In particular, emotional recognition of faces is a complex process that activates different cerebral structures (e.g., occipitotemporal cortex, amygdala, orbitofrontal cortex, right parietal cortex, etc.); thus, it involves a number of cognitive abilities that are differentially impaired during the course of dementia. Therefore, it may be interesting to clarify whether, and to what extent, facial emotion recognition impairment is linked to memory decline, which is the clinical and neuropsychological hallmark of AD from its preclinical stage.

Because facial emotion recognition impairment has been found to increase during the progression of dementia, we wonder if it is also present in patients with mild cognitive impairment (MCI), which is a transitional zone between normal cognitive functioning and probable AD. This preclinical syndrome describes people who do not fulfill a diagnosis of dementia, but have a high risk of conversion in dementia in the following few years and a quite intact functional life style. Many subtypes of MCI exist. According to a four-group classification scheme, the “amnestic single domain MCI” (a-MCI) is characterized by a selective deficit in memory performance, the “amnestic multiple domain MCI” presents impairment in memory and at least one other cognitive domain, the “nonamnestic single domain MCI” is associated with impairment in one nonmemory domain, and the “nonamnestic multiple domain MCI” is associated with impairment in two or more nonmemory domains. Research in MCI patients has focused on neuropsychological deficits and behavioral disorders, whereas there is limited information on facial emotion recognition. Only a very recent study explored this issue in a small sample of 9 subjects with a-MCI, 14 subjects with amnestic multiple domain MCI, and 68 normal elderly participants. Results suggested that facial emotion recognition may be impaired in amnestic multiple domain MCI and not in a-MCI. The authors wonder whether the small sample size influenced these results. Therefore, focusing on illness stage, studies found that facial emotion recognition impairment is present in patients with multiple domain MCI and in AD of mild degree, whereas the occurrence of this deficit in the earliest preclinical stage of dementia still remains uncertain. Patients who present impairment in memory and other cognitive domains (i.e., amnestic multidomain MCI) seem to be clinically very close to AD of mild degree. In contrast, there is evidence that a-MCI represents the first stage of dementia, from both a neuropsychological and a neuropathologic point of view. On the basis of Braak and Braak staging, precocious structural changes in patients with memory complaints can be expected in cerebral regions involved in memory and emotional processing such as hippocampus, parahippocampal gyrus, amygdala, and other limbic structures, and there is evidence that histopathology hallmarks are present in these regions in MCI patients. However, atrophy seems to be selectively delimitied to amygdala, hippocampus, and enthorinal cortex only in a-MCI patients, compared with multidomain MCI subgroups. In particular, an amnestic multidomain MCI sub-
group has been found to show a more widespread pattern of gray matter loss, involving also posterior lateral and basal temporal lobes, posterior cingulate, anterior insula, and medial frontal lobe, and this pattern of degeneration is also typical of mild AD.

Taking these considerations into account, the first aim of the present study was to verify in a large group of subjects whether facial emotion recognition impairment characterizes a-MCI phase. Because medial-temporal lobe regions, which represent important structures both in memory and emotional processes, are precociously affected in mild AD and a-MCI patients, we hypothesized that early emotional impairment precociously manifests in a-MCI patients, and in particular, we expected the presence of a progression in severity and/or extension of emotion recognition deficit from normal elderly comparison (COM) subjects to a-MCI to mild AD patients.

Schizophrenia studies have shown that accuracy of identifying facial emotions is dependent on the intensity of the cues. Thus, here we used a specific approach to measure emotion recognition impairment on the basis of the different intensity (mild to extreme) of emotional cues. Our hypothesis was that low-intensity faces, which are much more frequent in daily life interactions but presumably more difficult to recognize, can be precociously more impaired than high-intensity ones, especially in the preclinical stage of AD.

Finally, we investigated the relationship between facial emotion recognition ability and cognitive performance in COM participants, a-MCI, and mild AD patients. We hypothesized that memory impairment would be associated with facial emotion recognition in a-MCI subjects as well as in AD patients.

**METHODS**

Fifty people with a diagnosis of a-MCI, 50 patients with a diagnosis of probable AD of mild degree, and 50 COM subjects, 50 to 90 years old, were recruited in this study. The three groups were well matched for age, educational level, and gender.

**Specific Inclusion and Exclusion Criteria for a-MCI, AD and COM**

Specific inclusion criteria for a-MCI were 1) diagnostic evidence of a-MCI consistent with Petersen guidelines: i) complaint of defective memory, ii) normal activities of daily living, iii) normal general cognitive function, iv) abnormal memory function for age, and v) absence of dementia; and 2) a Mini-Mental State Examination (MMSE) score ≥23.

Specific inclusion criteria for mild AD were 1) diagnostic evidence of probable AD consistent with the NINCDS-ADRDA criteria, and 2) a MMSE score ≥18. A specific exclusion criterion for AD was the lack of a “reliable” caregiver, defined as someone able to ensure the patient’s compliance with assessment procedures and to contact the patient at least twice weekly, with one contact being a personal visit.

Both a-MCI and mild AD patients were recruited from three outpatient clinics of central Italy. These patients were at the onset of their cognitive impairment; they were drug naive and had undergone their first clinical examination for the diagnosis of AD or a-MCI.

A specific inclusion criterion for COM required that all neuropsychological scores were above the cutoff scores, corrected for age and educational level, identifying normal cognitive level in the Italian population. The volunteers included in the COM group were recruited from the general population of the same geographic region as the patients.

**Common Inclusion and Exclusion Criteria for a-MCI, AD and COM**

Common inclusion criteria for a-MCI, mild AD, and COM were 1) vision and hearing sufficient for compliance with testing procedures; and 2) laboratory values within the appropriate reference intervals or considered to be clinically insignificant by the investigators. Common exclusion criteria were 1) major medical illnesses, e.g., diabetes (not stabilized), obstructive pulmonary disease, or asthma; hematologic and oncologic disorders; vitamin B12 or folate deficiency as evidenced by blood concentrations below the lower limits of the reference intervals; pernicious anemia; clinically significant and unstable active gastrointestinal, renal, hepatic, endocrine, or cardiovascular system disease; newly treated hypo-
thyroidism; 2) comorbidity of primary psychiatric or neurologic disorders (e.g., schizophrenia, major depression, stroke, Parkinson disease, seizure disorder, head injury with loss of consciousness) and any other significant mental or neurologic disorder; 3) known or suspected history of alcoholism or drug dependence and abuse during lifetime; 4) MRI evidence of focal parenchymal abnormalities; and 5) MRI evidence of neoplasm.

Diagnostic and Cognitive Examination

Prior to the beginning of the study, the interviewers had been trained by means of didactic instruction, live interviews, and a review of diagnostic rating. The nature and purposes of this study were presented to both patients (and their responsible caregivers) and COM subjects, and written informed consent was obtained before beginning detailed screening activities. Trained clinical neurologist (N = 1) and psychologists (N = 3) interviewed patients and caregivers using the NINCDS-ARDRA criteria for the diagnosis of AD, and Petersen criteria for the diagnosis of a-MCI. Acceptable interrater reliability for the present study was defined as $k \geq 0.80$. All interviewers achieved this level between them. To confirm cognitive deficits required for AD and a-MCI diagnosis, and to enroll control subjects, the below-mentioned neuropsychological battery was used.

To obtain a global index of cognitive impairment, we administered the MMSE. It is an amply used neuropsychological screening test measuring orientation, language, verbal memory, attention, visuospatial function, and mental control. It is composed of 16 items, with scores ranging from 30 (no impairment) to 0 (maximum impairment).

To assess single cognitive domains, we administered the Mental Deterioration Battery (MDB) and other cognitive tests. The MDB is a standardized and validated neuropsychological battery, comprising seven neuropsychological tests, from which eight performance scores can be derived. Of the eight total scores, four pertain to the elaboration of verbal stimuli and four to visuospatial materials. The tests were selected to provide information about the functionality of different cognitive domains such as verbal memory (MDB Rey’s 15-word Immediate Recall and Delayed Recall); short-term visual memory (MDB Immediate Visual Memory); logical reasoning (MDB Raven’s Progressive Matrices 47); language (MDB Phonological Verbal Fluency, and MDB Sentence Construction); simple constructional praxis (MDB Copying Drawings, and MDB Copying Drawings with Landmarks). In addition to the MDB, we administered additional tests listed below to assess other cognitive domains such as long-term visual memory (Delayed Recall of Rey-Osterrieth picture); complex constructional praxis (Copy of Rey-Osterrieth picture); and frontal abilities of attentive shifting and control (Stroop test Interference time). Finally, to measure visual–perceptual abilities that could interfere with emotion recognition visual tasks, we administered the Benton Facial Recognition Test (BFRT). BFRT is a validated and standardized instrument that contains a 27-item short form and a 54-item long form. The subject is asked to find the target face among six alternatives, by matching identical front views, front views to roughly three-fourths profile view and faces under different lighting conditions. This test examines facial recognition without interference of memory abilities. We administered the short form with scores ranging from 0 to 27.

Emotion Recognition Examination

To assess facial emotion recognition ability, we administered a standardized and validated instrument: the Penn Emotion Recognition Test. It is a computer-based test including 96 color photographs of facial expressions of evoked or felt emotions, i.e., happy, sad, angry, fearful, disgusted, and nonemotional or neutral. There were 8 low-intensity and 8 high-intensity expressions of each emotion and 16 neutral expressions. Across emotional categories, stimuli were balanced for poser’s gender. Participants were asked to rate the emotional valence of each expression without time limit for responses.

In addition to specific emotion subscores and total emotion score, we used an “intensity-based approach” by calculating low-intensity and high-intensity subscores, to explore if there were differences in performances related to emotion intensity, i.e., how many faces were recognized exactly when the stimuli were extreme or when they were mild.

Statistical Analyses

Comparison among mild AD, a-MCI and COM diagnostic groups on gender variable was performed.
using the χ² test. Comparisons among mild AD, a-MCI and COM diagnostic groups on sociodemographic characteristics (i.e., age and educational level), global cognitive level (i.e., MMSE scores), facial visual perceptual abilities (BFRT), and global facial emotion expression recognition (i.e., total [high plus low intensity], high intensity, low intensity, and neutral scores) were performed using factorial analysis of variance (ANOVA) followed by Fisher’s Protected Least Significant Difference (PLSD) post-hoc test.

Univariate factorial ANOVAs followed by PLSD post-hoc tests were also used to detect differences in means among mild AD, a-MCI and COM diagnostic groups for each cognitive domain and each facial emotion expression. In the case of facial emotion expression recognition, we separately analyzed the total scores, the high-intensity scores and the low-intensity scores.

To minimize the likelihood of type-I error, univariate ANOVAs of cognitive domains, total scores of facial emotion expression recognition, high-intensity scores of facial emotion expression recognition and low-intensity scores of facial emotion expression recognition were preceded by overall multivariate analyses of variance (MANOVAs) using all the continuous categories considered in each of the four analyses as dependent variables.

Cognitive predictors of emotion recognition level, separately in mild AD, a-MCI and COM groups, were assessed by using stepwise multiple regression analyses, using a forward procedure and an F to enter of 4.

The level of statistical significance was defined as p < 0.05.

## RESULTS

### Sociodemographic Variables

Sociodemographic characteristics of COM, a-MCI and mild AD are given in Table 1. The three groups did not differ significantly for age, level of education, and gender.

### Global Cognitive, Facial Visual-Perceptual, and Facial Emotion Recognition Variables

Table 2 shows differences among COM, a-MCI and mild AD groups for global cognitive level, facial visual–perceptual performance, and global facial emotion recognition ability (i.e., total, high-intensity, low-intensity scores, and neutral score). ANOVA results indicate that the three groups differed for all the

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**TABLE 1. Sociodemographic Characteristics of 50 COM, 50 a-MCI, and 50 Mild AD Outpatients**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>COM (N = 50)</th>
<th>a-MCI (N = 50)</th>
<th>AD (N = 50)</th>
<th>χ² or F</th>
<th>df</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender male (n, %)</td>
<td>22, 44</td>
<td>27, 54</td>
<td>25, 50</td>
<td>1.014</td>
<td>2</td>
<td>0.602</td>
</tr>
<tr>
<td>Age (years ± SD)</td>
<td>71.84 ± 7.35</td>
<td>71.20 ± 7.49</td>
<td>72.68 ± 6.89</td>
<td>0.524</td>
<td>2</td>
<td>0.593</td>
</tr>
<tr>
<td>Educational level (years ± SD)</td>
<td>9.06 ± 4.18</td>
<td>9.78 ± 4.60</td>
<td>7.88 ± 4.55</td>
<td>2.328</td>
<td>2</td>
<td>0.101</td>
</tr>
</tbody>
</table>

**Notes:** COM: comparison subjects; a-MCI: amnestic mild cognitive impairment; AD: Alzheimer disease; SD: standard deviation; df: degrees of freedom.

**TABLE 2. Global Cognitive Level and Global Recognition of Facial Emotions in 50 COM, 50 a-MCI, and 50 Mild AD Outpatients**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>COM (Mean ± SD)</th>
<th>a-MCI (Mean ± SD)</th>
<th>AD (Mean ± SD)</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>COM vs. a-MCI</th>
<th>COM vs. AD</th>
<th>a-MCI vs. AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>27.82 ± 1.75</td>
<td>26.68 ± 2.50</td>
<td>22.04 ± 3.32</td>
<td>69.155</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.030</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total emotion score</td>
<td>46.92 ± 6.99</td>
<td>44.04 ± 8.08</td>
<td>36.72 ± 7.53</td>
<td>24.278</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.058</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Low-intensity emotion score</td>
<td>20.64 ± 3.85</td>
<td>18.62 ± 4.08</td>
<td>16.22 ± 4.45</td>
<td>14.327</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.016</td>
<td>&lt;0.0001</td>
<td>0.004</td>
</tr>
<tr>
<td>High-intensity emotion score</td>
<td>26.28 ± 4.08</td>
<td>25.42 ± 4.99</td>
<td>20.5 ± 4.01</td>
<td>25.324</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.528</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Neutral score</td>
<td>9.80 ± 3.74</td>
<td>10.70 ± 4.01</td>
<td>7.08 ± 4.30</td>
<td>10.969</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.265</td>
<td>0.0009</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BFRT</td>
<td>21.04 ± 2.25</td>
<td>21.10 ± 2.62</td>
<td>17.86 ± 3.19</td>
<td>23.328</td>
<td>2</td>
<td>&lt;0.0001</td>
<td>0.912</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Notes:** MMSE: Mini-Mental State Examination; BFRT: Benton Facial Recognition Test; COM: comparison subjects; a-MCI: amnestic mild cognitive impairment; AD: Alzheimer disease; SD: standard deviation; df: degrees of freedom.
Facial Emotion Recognition Deficit

variables investigated. Post-hoc pairwise comparisons revealed that MMSE scores increased continuously from mild AD to a-MCI patients and from a-MCI to COM subjects.

Total, high-intensity, neutral facial emotion recognition global scores and BFRT scores of mild AD patients were significantly lower than those of all other groups, whereas they did not differ between a-MCI and COM groups. Similarly, low-intensity facial emotion recognition recognition scores of mild AD patients were significantly lower than those of all other groups. However, an interesting result emerged. Indeed, the low-intensity facial emotion recognition score of a-MCI patients was significantly lower than that of COM group. Thus, there was an increased progression in global facial emotion recognition deficit from COM to a-MCI to mild AD patients, but the only emotion variable that discriminated between a-MCI and COM subjects was the low-intensity facial emotion recognition.

Individual Cognitive Variables

Table 3 shows the cognitive data of COM, a-MCI, and mild AD groups.

A MANOVA using all cognitive scores as dependent variables (Wilks’ λ = 0.19; F = 14.47, df = 24,272, p <0.0001) and a series of follow-up one-way ANOVAs indicated that the severity of impairment of all cognitive domains was different among COM, a-MCI, and mild AD patients. Post-hoc pairwise comparisons revealed that all cognitive domains of mild AD patients were significantly more impaired than those of the other two groups. As expected by the diagnostic selection, a-MCI patients performed worse than COM subjects on all the memory tests, except IVM, and no difference between the two groups of subjects was found in all the remaining cognitive domains.

Individual Facial Emotion Recognition Variables

Table 4 shows total (i.e., high plus low intensity) scores of each facial emotion in COM, a-MCI, and mild AD groups.

A MANOVA using total scores of each facial emotion as dependent variables (Wilks’ λ = 0.66; F = 5.47, df = 12,284, p <0.0001) and a series of follow-up one-way ANOVAs indicated that there were significant differences among groups on all the emotions here considered. Post-hoc pairwise comparisons re-

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TABLE 3. Individual Cognitive Scores in 50 COM, 50 a-MCI, and 50 Mild AD Outpatients

<table>
<thead>
<tr>
<th>Neuropsychological Tests</th>
<th>COM (Mean ± SD)</th>
<th>a-MCI (Mean ± SD)</th>
<th>AD (Mean ± SD)</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>COM vs. a-MCI</th>
<th>COM vs. AD</th>
<th>a-MCI vs. AD</th>
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<tbody>
<tr>
<td>Verbal memory</td>
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<tr>
<td>RAVLTIR</td>
<td>42.42 ± 8.44</td>
<td>28 ± 7.91</td>
<td>19.32 ± 6.09</td>
<td>119.513</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td>RAVLTDR</td>
<td>9.28 ± 2.42</td>
<td>3.28 ± 2.55</td>
<td>1.30 ± 1.98</td>
<td>159.304</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td>Longterm visual memory</td>
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<tr>
<td>ROPDR</td>
<td>11.81 ± 5.85</td>
<td>7.43 ± 5.22</td>
<td>2.42 ± 3.07</td>
<td>46.649</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
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<tr>
<td>Short term visual memory</td>
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<tr>
<td>IVM</td>
<td>19.20 ± 2.35</td>
<td>19.12 ± 2.17</td>
<td>14.84 ± 3.85</td>
<td>37.304</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.890</td>
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<td>Logical reasoning</td>
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<tr>
<td>PM47</td>
<td>24 ± 5.85</td>
<td>24.42 ± 5.03</td>
<td>17.48 ± 5.92</td>
<td>23.992</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.709</td>
<td>&lt;0.0001</td>
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<tr>
<td>Language</td>
<td></td>
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<tr>
<td>PVF</td>
<td>30.22 ± 10.70</td>
<td>26.94 ± 11.92</td>
<td>16.92 ± 8.15</td>
<td>22.286</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.116</td>
<td>&lt;0.0001</td>
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<tr>
<td>SC</td>
<td>16.66 ± 6.06</td>
<td>15.04 ± 6.51</td>
<td>8.66 ± 6.06</td>
<td>23.154</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.194</td>
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<tr>
<td>Simple constructional praxis</td>
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<td></td>
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<tr>
<td>CD</td>
<td>9.32 ± 1.96</td>
<td>9.36 ± 1.66</td>
<td>7.42 ± 2.47</td>
<td>14.465</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.923</td>
<td>&lt;0.0001</td>
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<tr>
<td>CDL</td>
<td>65.88 ± 5.09</td>
<td>63.48 ± 5.46</td>
<td>55.74 ± 10.65</td>
<td>24.881</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.112</td>
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<td>Complex constructional praxis</td>
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<tr>
<td>CROP</td>
<td>30.09 ± 4.31</td>
<td>28.1 ± 6.82</td>
<td>18.79 ± 10.14</td>
<td>32.505</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.186</td>
<td>&lt;0.0001</td>
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<td>Attention abilities</td>
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<tr>
<td>ST Interference time</td>
<td>47.88 ± 15.06</td>
<td>55.94 ± 21.87</td>
<td>85.82 ± 43.05</td>
<td>28.239</td>
<td>2,147</td>
<td>&lt;0.0001</td>
<td>0.170</td>
<td>&lt;0.0001</td>
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</tbody>
</table>

Notes: COM = comparison subjects; a-MCI = amnestic mild cognitive impairment; AD = Alzheimer disease; SD = standard deviation; df = degrees of freedom; RAVLTIR = MDB Rey’s 15-word Immediate Recall; RAVLTDR = MDB Rey’s 15-word Delayed Recall; ROPDR = Rey-Osterrieth Picture Delayed Recall; IVM = MDB Immediate Visual Memory; PM47 = MDB Raven’s Progressive Matrices ‘47; PVF = MDB Phonological Verbal Fluency; SC = MDB Sentence Construction; CD = MDB Copying Drawings; CDL = MDB Copying Drawings with Landmarks; CROP = Copy of Rey-Osterrieth picture; ST = Stroop Test.
revealed that mild AD patients differed significantly from COM subjects on all emotion variables. Furthermore, mild AD patients differed significantly from a-MCI subjects on all variables with the exception of disgusted scores. Finally, there were no significant differences between mild AD and a-MCI groups on all the variables considered with the exception of disgusted scores (Table 5).

Post-hoc pairwise comparisons indicated that mild AD patients differed significantly from COM subjects for all variables except disgust. In addition, mild AD patients differed from a-MCI subjects for sad, angry, and fearful scores. There were no significant differences between a-MCI and COM subjects on all the high-intensity emotional scores.

A MANOVA using low-intensity scores of each facial emotion as dependent variables (Wilks’ $\lambda = 0.78; F = 5.068, df = 10,286, p < 0.0001$) and a series of follow-up one-way ANOVAs indicated that there were significant differences among COM, a-MCI and mild AD groups on all the variables considered with the exception of disgusted scores (Table 6).

Post-hoc pairwise comparisons revealed that low-intensity fearful score was the only variable that discriminated between a-MCI and COM subjects. In addition, mild AD patients differed significantly from a-MCI subjects for sad and happy scores. Lastly, mild AD patients differed significantly from

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**Table 4. Total Emotion Recognition Scores in 50 COM, 50 a-MCI, and 50 Mild AD Outpatients**

<table>
<thead>
<tr>
<th>Emotion</th>
<th>COM (Mean ± SD)</th>
<th>a-MCI (Mean ± SD)</th>
<th>AD (Mean ± SD)</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>COM vs. a-MCI</th>
<th>COM vs. AD</th>
<th>a-MCI vs. AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy</td>
<td>14.92 ± 1.35</td>
<td>14.64 ± 2.03</td>
<td>13.3 ± 2.96</td>
<td>7.635</td>
<td>2.147</td>
<td>0.0007</td>
<td>0.528</td>
<td>0.0004</td>
<td>0.003</td>
</tr>
<tr>
<td>Sad</td>
<td>9.38 ± 2.99</td>
<td>8.82 ± 5.18</td>
<td>6.94 ± 2.84</td>
<td>9.042</td>
<td>2.147</td>
<td>0.0002</td>
<td>0.355</td>
<td>&lt;0.0001</td>
<td>0.002</td>
</tr>
<tr>
<td>Angry</td>
<td>7.12 ± 2.22</td>
<td>6.96 ± 2.14</td>
<td>5.14 ± 2.19</td>
<td>12.716</td>
<td>2.147</td>
<td>&lt;0.0001</td>
<td>0.714</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fearful</td>
<td>8.34 ± 3.13</td>
<td>7.44 ± 2.83</td>
<td>5.90 ± 2.43</td>
<td>9.614</td>
<td>2.147</td>
<td>0.0001</td>
<td>0.112</td>
<td>&lt;0.0001</td>
<td>0.007</td>
</tr>
<tr>
<td>Disgusted</td>
<td>7.16 ± 2.69</td>
<td>6.18 ± 2.84</td>
<td>5.44 ± 3.04</td>
<td>4.543</td>
<td>2.147</td>
<td>0.0122</td>
<td>0.089</td>
<td>0.003</td>
<td>0.198</td>
</tr>
</tbody>
</table>

**Notes:** COM: comparison subjects; a-MCI = amnestic Mild Cognitive Impairment; AD = Alzheimer Disease; SD = standard deviation; df = degrees of freedom.

**Table 5. High-Intensity Emotion Recognition Scores in 50 COM, 50 a-MCI, and 50 Mild AD Outpatients**

<table>
<thead>
<tr>
<th>Emotion</th>
<th>COM (Mean ± SD)</th>
<th>a-MCI (Mean ± SD)</th>
<th>AD (Mean ± SD)</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>COM vs. a-MCI</th>
<th>COM vs. AD</th>
<th>a-MCI vs. AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy-high</td>
<td>7.72 ± 0.57</td>
<td>7.56 ± 1.03</td>
<td>7.16 ± 1.57</td>
<td>3.234</td>
<td>2.147</td>
<td>0.0422</td>
<td>0.482</td>
<td>0.015</td>
<td>0.080</td>
</tr>
<tr>
<td>Sad-high</td>
<td>5.08 ± 1.80</td>
<td>4.92 ± 2.14</td>
<td>3.80 ± 1.62</td>
<td>6.991</td>
<td>2.147</td>
<td>0.0013</td>
<td>0.669</td>
<td>0.0008</td>
<td>0.003</td>
</tr>
<tr>
<td>Angry-high</td>
<td>5.78 ± 1.31</td>
<td>5.68 ± 1.48</td>
<td>4.16 ± 1.88</td>
<td>16.725</td>
<td>2.147</td>
<td>&lt;0.0001</td>
<td>0.750</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fearful-high</td>
<td>5.06 ± 1.99</td>
<td>4.94 ± 1.80</td>
<td>3.34 ± 1.71</td>
<td>13.696</td>
<td>2.147</td>
<td>&lt;0.0001</td>
<td>0.744</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Disgusted-high</td>
<td>2.64 ± 1.58</td>
<td>2.52 ± 1.42</td>
<td>2.04 ± 1.55</td>
<td>1.947</td>
<td>2.147</td>
<td>0.1644</td>
<td>0.295</td>
<td>0.051</td>
<td>0.359</td>
</tr>
</tbody>
</table>

**Notes:** COM: comparison subjects; a-MCI = amnestic mild cognitive impairment; AD = Alzheimer disease; SD = standard deviation; df = degrees of freedom.

**Table 6. Low-Intensity Emotion Recognition Scores in 50 COM, 50 a-MCI, and 50 Mild AD Outpatients**

<table>
<thead>
<tr>
<th>Emotion</th>
<th>COM (Mean ± SD)</th>
<th>a-MCI (Mean ± SD)</th>
<th>AD (Mean ± SD)</th>
<th>F</th>
<th>df</th>
<th>p</th>
<th>COM vs. a-MCI</th>
<th>COM vs. AD</th>
<th>a-MCI vs. AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Happy-low</td>
<td>7.20 ± 1.11</td>
<td>7.08 ± 1.17</td>
<td>6.14 ± 1.74</td>
<td>8.982</td>
<td>2.147</td>
<td>0.0002</td>
<td>0.662</td>
<td>0.0002</td>
<td>0.0008</td>
</tr>
<tr>
<td>Sad-low</td>
<td>4.50 ± 1.63</td>
<td>3.90 ± 1.76</td>
<td>3.14 ± 1.76</td>
<td>5.866</td>
<td>2.147</td>
<td>0.0035</td>
<td>0.247</td>
<td>0.001</td>
<td>0.029</td>
</tr>
<tr>
<td>Angry-low</td>
<td>1.34 ± 1.36</td>
<td>1.28 ± 1.21</td>
<td>0.98 ± 0.98</td>
<td>1.300</td>
<td>2.147</td>
<td>0.2756</td>
<td>0.802</td>
<td>0.134</td>
<td>0.212</td>
</tr>
<tr>
<td>Fearful-low</td>
<td>3.28 ± 1.60</td>
<td>2.50 ± 1.50</td>
<td>2.56 ± 1.56</td>
<td>4.236</td>
<td>2.147</td>
<td>0.0163</td>
<td>0.010</td>
<td>0.017</td>
<td>0.841</td>
</tr>
<tr>
<td>Disgusted-low</td>
<td>4.52 ± 1.76</td>
<td>3.86 ± 1.86</td>
<td>3.40 ± 2.00</td>
<td>4.493</td>
<td>2.147</td>
<td>0.0128</td>
<td>0.081</td>
<td>0.003</td>
<td>0.223</td>
</tr>
</tbody>
</table>

**Notes:** COM: comparison subjects; a-MCI = amnestic Mild Cognitive Impairment; AD = Alzheimer disease; SD = standard deviation; df = degrees of freedom.
COM subjects for sad, disgusted, fearful, and happy scores.

With these results in mind and taking into consideration that recognition of low-intensity fearful faces was the only emotional characteristic that was impaired in a-MCI subjects in comparison with COM subjects, we performed a series of three stepwise multiple regression analyses to clarify the cognitive predictors of impairment in recognition of low-intensity fearful faces. In these analyses, the low-intensity fearful face recognition score was the dependent variable, and all the cognitive scores here investigated were the independent variables.

No statistical significant cognitive predictor of recognition of low-intensity fearful faces was found in COM subjects.

Interestingly, the only statistically significant predictor of recognition of low-intensity fearful faces in a-MCI was Rey’s 15-word Immediate Recall score. The resulting equation was significant ($F = 4.952$, $df = 1,48$, $p = 0.0308$) and explained 9.4% ($r^2$) of the overall variance of the low-intensity fearful face recognition score. In particular, lower Rey’s 15-word Immediate Recall score predicted the lower fearful facial emotion recognition score (standard coefficient: 0.306).

In mild AD patients, the statistically significant predictor of recognition of low-intensity fearful faces was Rey’s 15-word Delayed Recall score. The resulting equation was significant ($F = 5.306$, $df = 1,48$, $p = 0.0256$) and explained 10% ($r^2$) of the overall variance of the low-intensity fearful facial recognition score. In particular, lower Rey’s 15-word Delayed Recall score predicted the lower fearful facial emotion recognition score (standard coefficient: 0.315).

**CONCLUSIONS**

This study explored facial emotion recognition ability in a-MCI patients, mild AD patients, and COM subjects. Our study achieved at least three original findings. The main result was found in patients in the preclinical phase of dementia. Indeed, despite a quite preserved performance in global facial emotion recognition, a-MCI group differed significantly from COM group on low-intensity face recognition total score, and particularly on low-intensity fearful face recognition score. As both neutral faces identification and BFRT performance were not impaired in a-MCI subjects, the low-intensity fearful facial emotion recognition deficit is unrelated to a more general facial visual-perceptual deficit. Second, in a-MCI patients the deficit in low-intensity fearful face expression recognition was explained by the short-term verbal memory impairment, which is the diagnostic neuropsychological hallmark of this stage of the illness. Third, we found that facial emotion recognition is impaired in mild AD patients for all emotions with the exception of disgust, giving further validation to the assertion that facial emotion recognition impairment strongly characterizes AD patients of very mild degree. Finally, an emotion intensity-based approach may be more useful and sensitive to detect facial emotion recognition impairment in MCI patients.

We can explain the finding that facial emotion recognition impairment in dementia seems to progress from a deficit in low-intensity fearful face recognition in a-MCI phase and subsequently it extends to mild AD, as a possible effect of the well-described progressive degeneration of brain structures modulating emotion processing, such as amygdala and other limbic and paralimbic structures. Even though amygdala has been found to respond to a range of facial emotion expressions, it seems to play a critical role in perceiving fear and in particular, for recognition of ambiguous, unconscious, or low-intensity fearful cues. Notably, deterioration of the amygdala can explain both mildly fearful expression recognition deficit and precocious memory impairment in a-MCI patients, because of its projections to prefrontal cortex and hippocampal complex, forming the neural network for emotional memory. Indeed, the role of amygdala is also well established in consolidation of memory of fearful cues, and is suggested by studies supporting the cholinergic model in AD. In this context, it is of interest that amygdala receives a major cholinergic projection from the nucleus basalis of Meynert. In addition, acetylcholinesterase activity in the amygdala is significantly reduced in AD patients, and this reduction is positively related to global cognitive deficit. Remarkably, after stroke or transient ischemic attack, amygdala volume is significantly reduced in those subjects with dementia and MCI of vascular type, in comparison to subjects without cognitive impair-
ment; and amygdalar atrophy is related to visual memory deficit. Thus, it could be assumed that corticodlimbic system degeneration underlies facial emotional recognition impairment as well as memory deficit, since from the preclinical stage of dementia. Further studies are needed to substantiate this hypothesis.

Finally, amygdala is considered as an essential "social structure" because one of its functions is the modulation of the neural system underlying social cognition, that is the basis of ability to interpret nonverbal communication (such as facial emotion expressions) and to respond to emotional cues with appropriate interpersonal behaviors. Thus, we explain the result that facial emotion recognition deficit in a-MCI patients is specific for low-intensity levels of fear hypothesizing that mild emotions are more subtle and more difficult to recognize, and therefore require greater social cognition ability than high-intensity ones. But, low-intensity facial expressions are more frequently encountered in daily life. Thus, this type of impairment can have practical consequences in social interactions in the MCI phase, because deficits in processing fearful emotions may probably affect nonverbal communication, interpersonal relatedness, and consequently quality of life. Future study should confirm this hypothesis.

The major strengths of this study are the careful selection of the participants, the use of internationally standardized MCI diagnostic criteria, and the large sample sizes. Some limitations of this study should be taken into account for the generalization of the results. First, as previously discussed by other authors, static facial photographs lack important dynamic information that individual uses in natural contexts to interpret facial expressions (for instance, speech prosody). However, the three-dimensional nature of the stimuli in the Penn Emotion Recognition Test provides a more "real" effect of the facial emotion, than one-dimensional face photographs.

Second, our samples have not been matched for living conditions, overall functioning, and socioeconomic status, and it could be argued that these variables may have a potential confounding effect on facial emotion recognition performance. On the other hand, there is no evidence in literature on socioeconomic correlates of facial emotion recognition in dementia, or in other clinical populations. This issue should be considered in upcoming research.

Finally, our study is cross-sectional in design, and longitudinal studies should be employed to clarify the progression, as well as the predictors, of facial emotion recognition deficit from normal elderly people, a-MCI, and AD patients. Taking these issues into account, upcoming studies should aim to better characterize the deficits in emotional processing in a-MCI patients and AD. An early detection of facial emotion recognition impairment during the preclinical phase of dementia may have clinical implications, to permit a preventive intervention on the increasing decline in cognitive performance, interpersonal behavior, and social ability, improving the quality of life of both patients and caretakers.

This work was supported by the RC/05A grant from Italian Ministry of Health.

References

Facial Emotion Recognition Deficit