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Recognition of Facial Emotional Expression in Amnesic Mild Cognitive Impairment

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Abstract

We examined whether recognition of facial emotional expression would be affected in amnesic mild cognitive impairment (aMCI). A total of 50 elderly persons met the initial inclusion criteria, 10 were subsequently excluded (Geriatric Depression Score >5). 22 subjects were classified with aMCI based on published criteria (single domain aMCI [SD-aMCI], $n = 10$; multiple domain aMCI [MD-aMCI], $n = 12$); 18 subjects were cognitively normal. All underwent standard neurological and neuropsychological evaluations as well as tests of facial emotion recognition (FER) and famous faces identification (FFI). Among normal controls, FFI was negatively correlated with MMSE and positively correlated with executive function. Among patients with aMCI, FER was correlated with attention/speed of processing. No other correlations were significant. In a multinomial logistic regression model adjusted for age, sex, and education, a poorer score on FER, but not on FFI, was associated with greater odds of being classified as MD-aMCI (odds ratio [OR], 3.82; 95% confidence interval [CI], 1.05–13.91; $p = 0.042$). This association was not explained by memory or global cognitive score. There was no association between FER or FFI and SD-aMCI (OR, 1.13; 95% CI, 0.36–3.57; $p = 0.836$). Therefore, FER, but not FFI, may be impaired in MD-aMCI. This implies that in MD-aMCI, the tasks of FER and FFI may involve segregated neurocognitive networks.

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Keywords

assessment of cognitive disorders/dementia; cognitive aging; emotion; mild cognitive impairment; neuropsychiatric symptoms

INTRODUCTION

The abilities to recognize facial emotional expressions and famous faces are important aspects of social behavior. Deficits in these skills may contribute to difficulties in social communication, including the interaction between patients and caregivers. Both these skills are associated with temporal lobe function. However, facial emotion recognition (FER) and famous face identification (FFI) may depend on different neural networks. FER is associated with medial temporal lobe structures, i.e., hippocampus, amygdala, and adjacent cortex [1], which are affected early in the course of Alzheimer disease (AD). FFI is presumed to be governed by lateral structures, i.e., fusiform gyrus [2] and superior temporal sulcus [3]. These structures have been proposed to be affected later in the course of the disease as the pathological process spreads beyond the hippocampus, as described by Braak staging [4]. Recognition of facial identity is related to occipital gyri which have extensive connections with temporal lobes [5]. Decision about familiarity may occur later on when the temporal lobe connects with the orbitofrontal cortex [6], the area well known to govern executive functions [7]. FER and FFI are differently related to hemisphere dominance. Whereas FER is connected with non-dominant temporal lobe [8], FFI needs bilateral cooperation and, if naming of the recognized faces is used, then the left hemisphere is critically involved [9].

Mild cognitive impairment (MCI) is defined as an intermediate stage between normal cognitive aging and dementia [10]. MCI is further classified into amnesic MCI (aMCI) and non-amnesic MCI (naMCI). As the name implies, aMCI primarily involves memory impairment whereas memory impairment is not substantial in naMCI. We used the modified Petersen criteria to diagnose and classify patients with MCI [11].

Impairment in FER was reported in patients with dementia [12, 13]; however, it may also help identify patients with MCI [14-16]. Examining emotion recognition in aMCI and AD, two studies [17, 18] found aMCI patients to be deficient in recognizing emotions, particularly negative emotions, while AD patients had difficulties in recognizing all emotions. In another study, only the multiple domain aMCI patients were impaired in FER while single domain aMCI patients were not [19]. Bedieu et al. [20], using a small sample of aMCI patients among a wider range of participants with various diagnoses, found no impairment of FER in aMCI patients. Results of these studies were summarized in a review [21], concluding that the majority of the studies report worse FER in individuals with MCI compared to cognitively normal older adults.

Neuroimaging [22] and neuropathological [23, 24] studies have implicated the hippocampus in the pathogenesis of aMCI. Besides that, bilateral damage of the amygdala has been associated with difficulty in recognizing facial emotion [1, 25]. Furthermore, there is an extensive reciprocal connection between the hippocampus and the amygdala [26]. Therefore, FER impairment in aMCI patients may implicate amygdala and associated networks [27]. Despite the fact that FFI depends on the lateral neocortex, face identification may be impaired in MCI, although detailed studies are lacking. Therefore, we sought to examine FER and FFI in single- and multiple-domain MCI in comparison with cognitively normal controls.

Based on previous literature [14-16, 27], we hypothesized that FER, but not FFI, would be poor in subjects with aMCI as compared to controls. MCI subtypes are classified based on the type and number of cognitive domains involved [11]; therefore, we also examined the association of FER with neuropsychological test performances.

METHODS

Participants

This was a case-control study in which participants were older adults recruited from the Memory Disorders Clinic at 2nd Faculty of Medicine, Charles University and Motol University Hospital in Prague, Czech Republic. Patients were referred to the clinic by general practitioners, neurologists, psychiatrists, and geriatricians. Referral to the memory clinic was triggered by a memory complaint expressed by a patient or a caregiver. In the memory clinic, the patient was evaluated by a neurologist who obtained a medical history from the patient and caregiver, and performed the Mini-Mental State Examination (MMSE), Hachinski Ischemic Scale, and a neurological examination. Research assistants and study coordinators gathered other data including Geriatric Depression Scale, Activities of Daily Living, and additional personal and family history information. Laboratory studies were performed including a chemistry group, blood cell count, sedimentation rate, vitamin B12, thyroid stimulating hormone, syphilis, and Lyme serology. All patients underwent 1.5T magnetic resonance brain imaging.

Standard protocol approvals, registrations, and patient consents

The study was approved by the institutional ethics committee. Written informed consent was obtained from all subjects participating in the study.

Neuropsychological battery

All participants underwent a neuropsychological evaluation. The psychometric battery covered the following cognitive domains: 1) memory – measured with the Auditory Verbal Learning Test trials 1–6 and the Auditory Verbal Learning Test Delayed Recall [28], the Benton Visual Retention Test [29], and the Free and Cued Selective Reminding Test (free recall and total recall) [30]; 2) attention/processing speed – measured with the Digit Span Backwards [31] and Trail Making Test A [32]; 3) frontal/executive function – measured with the Trail Making Test B [32] and Controlled Oral Word Association [32, 33]; 4) language – measured with the Boston Naming Test [34]; and 5) visuospatial function – measured with the Rey-Osterreith Complex Figure [35].

The score for each domain was expressed as a mean of z-scores from the relevant tests. The Trail Making Test subtasks, which are expressed in seconds to completion, were reverse scored before the means were generated. Rey-Osterreith Complex Figure and Boston Naming Test scores were used only for MCI patient classification. The MMSE [36] and the Czech version of Addenbrooke's Cognitive Screening [37] were administered to measure global cognitive function.

Definition of cases and controls

Clinical criteria for the diagnosis of aMCI included: memory complaints reported by patient or caregiver, evidence of memory dysfunction on neuropsychological testing, generally intact activities of daily living, and absence of dementia [11]. Patients with a Hachinski Ischemic Scale score >4 or with a history of other neurological or psychiatric disorders were excluded from the study.

The sample consisted of 31 patients with aMCI [single domain aMCI (SD-aMCI; $n = 12$) and multiple domain aMCI (MD-aMCI; $n = 19$)] and 19 controls matched on age, sex and education. Patients with SD-aMCI had isolated memory deficits. Cognitive impairment in attention and executive functions, language skills, or visuospatial skills in addition to memory impairment were used to classify subjects as having MD-aMCI. The control subjects did not report any memory complaints, scored normal on neuropsychological tests, had normal magnetic resonance imaging and blood tests, had no history of neurological or psychiatric disease, and did not take any psychiatric medications.

Ten participants (9 subjects with aMCI and 1 cognitively normal person) with a Geriatric Depression Scale [38] score >5 were excluded, resulting in the final sample of 10 subjects with SD-aMCI, 12 subjects with MD-aMCI, and 18 normal controls.

Tests of facial emotional recognition (FER) and famous faces identification (FFI)

Recognition of facial emotions—Pictures from the Ekman and Friesen series [39] representing six basic emotions, i.e., happiness, anger, sadness, fear, surprise, and disgust were used to measure recognition of facial emotions. Each category of the six emotions was presented by using four pictures of different faces. The description of each emotion was printed under each picture in a random order in multiple choices. The participants were asked to name or point to the emotion which correlated best with the facial expression shown above. There were 24 trials (four for each emotion) with possible scores ranging from 0–24. The emotions were randomly presented and no target picture was used more than once.

Identification of pictures of famous persons—FFI was assessed with pictures of 10 highly famous faces (politicians, actors, musicians, etc.) and 10 unfamiliar faces, presented in a fixed pseudo-random order. We used pictures of famous people from visual media. For each face, the participant was asked to decide whether or not the person was familiar. The performance was measured by the number of faces correctly recognized as familiar or unfamiliar (correct rejections) with possible scores ranging from 0–20. Only spontaneously named pictures were accepted as the correct answer. The test was adapted from the Keane's study [40] and adjusted for a Czech population [41]. The battery of famous faces was composed only of Czech personalities.

Statistical analysis

Initially, we correlated FER and FFI scores with cognitive scores separately in controls and patients with aMCI to examine the interrelation between FER and FFI performance and cognitive abilities within each group. For the main analyses, scores for FER and FFI were transformed into z-scores and reversed (more errors = greater score) to facilitate result interpretation. We used multinomial logistic regression [42] within a generalized logits model in SAS® (SAS Institute, Inc., Cary, NC) to assess whether FER or FFI could reliably distinguish patients with SD-aMCI or MD-aMCI from the cognitively normal participants, independent of age, sex, and education. We carried out the following specific steps: we defined FER and FFI scores to be independent variables; then, the groups, i.e., SD-aMCI, MD-aMCI, and controls, were entered as three levels of the outcome, with the control group serving as the reference category. We examined three regression models, i.e., a model adjusted for age, sex, and education (Model 1), and models with additional adjustments for global cognitive functioning (MMSE; Model 2) and memory scores (Model 3) in order to partition FER/FFI performance from cognitive abilities. Results are expressed as odds ratios (OR) and 95% confidence intervals (CI) which correspond to a two-tailed 0.05 level of significance.

RESULTS

Descriptive information is presented in Table 1. The patients with MD-aMCI were older and had significantly worse scores on the MMSE, memory, attention/processing speed, executive function, and FER than normal controls. As expected, the patients with SD-aMCI had poorer performance on memory testing as compared to cognitively normal persons. As shown in Table 2, among normal controls, FFI was negatively correlated with MMSE and positively correlated with executive function. Among patients with aMCI, FER was correlated with attention/speed of processing. No other correlations were significant.

Facial emotion recognition (FER) and amnesic mild cognitive impairment (aMCI) group classification

Results of the multinomial logistic regression analyses are presented in Table 3. After controlling for age, sex, and education, the association between poorer FER and being classified as SD-aMCI (as compared to cognitively normal) was not significant. However, scoring 1 standard deviation below the mean on the FER test was associated with almost 4 times greater odds of being classified as MD-aMCI compared to cognitively normal (OR, 3.82; $p = 0.042$). FFI scores could not reliably distinguish patients with SD-aMCI and MD-aMCI from normal controls.

To assess whether the association between poor FER and classification as MD-aMCI might be a function of general cognitive dysfunction, we added the MMSE score (Model 2) and MMSE plus memory scores (Model 3) into the model already adjusted for demographic characteristics. The association between poor FER and classification as MD-aMCI remained significant, indicating about 6.5 times greater odds of being classified with MD-aMCI when scoring 1 standard deviation below the mean on FER in the fully adjusted model.

DISCUSSION

We found significant deficits in FER, but not in FFI, among subjects with MD-aMCI, confirming previous suggestions that separate neurocognitive processes may govern these tasks [43, 44]. The finding could not be explained by age, sex, education, or the performance on MMSE or memory.

Recognition of FER seems to be mediated by the amygdala. For example, bilateral damage of the amygdala was associated with impairment of FER but not of FFI [25]. Among the few relevant studies pertaining to facial emotion processing in patients with AD and MCI, a recent study by Teng et al. also reported deficits in facial emotion processing among patients with MD-aMCI when compared to patients with SD-aMCI and to controls [19]. Our findings are similar despite using different scales to measure facial emotion processing, i.e., the Florida Affect Battery facial affect discrimination subtest (subtest 2) [45] was used in the previous study and we used pictures from the Ekman and Friesen series [39]. Gender-specific facial emotion processing had been observed previously [46]. Teng et al. noted such a gender-specific difference in their study as well, i.e., men in the MD-aMCI group performed worse than women, whereas we found no gender differences in our study.

In one study, the difference in performance on FER between patients with MCI and normal controls only approached significance, whereas significant differences were noted only for patients with dementia in comparison with normal controls [47]. This differs from our findings; and there are several possible explanations to account for the difference. The authors used a different subset of photographs than we did. Their study was specifically designed to test the ability to recognize a threat in pre-dementia and dementia subjects and to explore the relationship between threat perception, cognitive impairment, and emotion

recognition. On the other hand, we measured a spectrum of emotions, as specified in the Ekman and Friesen series test.

Current literature contains a few studies on deficits in FER in MCI and AD [17-19, 21, 47], but there is little evidence with regard to deficits in the FFI and cognitive impairment in general. Using patients with AD, Roudier et al. suggest that both FER and FFI performance may be impaired [12], whereas studies using patients with MCI suggest that, for FFI, only the completion time becomes longer with such impairment, but performance remains intact when compared to normal controls [48, 49]. Using functional magnetic resonance imaging, Teipel et al. also found the use of compensatory mechanisms to retain face-matching ability.

In our study, FFI was not impaired in patients with SD-aMCI or MD-aMCI. This might be explained by the design of the face recognition test we used. Only spontaneously verbally named personalities were accepted as recognized. This process required the involvement of different structures for FER and for FFI. The lateral temporal neocortex and dominant verbal hemisphere were predominantly involved in FFI processing, whereas medial temporal structures in the non-dominant hemisphere likely played a key role in FER processing.

As expected from the definition, both SD-aMCI and MD-aMCI subjects were impaired on memory tests. However, FER performance only correlated with attention/speed of processing among patients with aMCI while correlations with FER were weaker and non-significant for memory and executive function. It may be that FER is implicated in various structures and is not necessarily limited to the medial temporal lobe structures [44]; for example, FER may also implicate the orbitofrontal network [1]. Alternatively, it is possible that the wide variety of impairment in aMCI does not allow for a strong enough correlation with one cognitive domain. Finally, the small sample size may have affected these results. In addition, in a post-hoc analysis adjusted for age, sex, and education, we found a somewhat greater memory impairment in MD-aMCI than in SD-aMCI, although the result did not reach the pre-specified threshold for statistical significance. This trend may point to a more advanced impairment of the mediotemporal lobe in patients with MD-aMCI than SD-aMCI [50].

Among normal controls, FFI correlated negatively with MMSE and positively with executive function while correlations with memory and attention/speed of processing were not significant. Given the small sample size and the relative similarity within the control group with respect to cognitive function, it is possible that even the significant correlations were only spurious.

Our study excluded participants with GDS 5 and higher as the mood disturbance might interfere with the assessment of positive (joy) and negative (anger, sadness, disgust, fear, surprise) emotions. However, we did not collect data on other common symptoms in MCI represented, for example, by apathy and anxiety, as assessed by the Neuropsychiatric Inventory Questionnaire [51] or the Beck inventory [52].

Our study findings should be interpreted in light of the limitations of the study. This is a case-control study; therefore, we cannot make an argument for a cause-effect association. On the other hand, the limitations of our study are comparable to weaknesses noted in similar studies in the field. For example, only one study group [53] reported neuroimaging correlates of FER in MCI as measured by the Ekman and Friesen facial affect series. The authors reported fear and surprise recognition to be related to the integrity of white matter in the left uncinate fascicle [53].

Our study has potential implications for future research. FER impairment has been associated with deficits in social behavioral competence [54] and interpersonal problems in

patients with dementia [55, 56]. Future studies should investigate the associations of FER deficit in the day-to-day life of patients with MCI. Further work is needed to understand the structural basis of emotion recognition in aMCI patients.

In conclusion, our results suggest the hypothesis that the tasks of FER and FFI may involve segregated neurocognitive networks in prodromal stages of Alzheimer's disease. Future research is needed to test this hypothesis. Ultimately, FER could be a useful early diagnostic tool of mediotemporal impairment in MCI as well as of social maladaptation of individuals at risk of AD.

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REFERENCES

- [1]. Adolphs R. Recognizing emotion from facial expressions: psychological and neurological mechanisms. *Behavioral and Cognitive Neuroscience Reviews*. 2002; 1:21–62. [PubMed: 17715585]
- [2]. Kanwisher N, McDermott J, Chun MM. The fusiform face area: a module in human extrastriate cortex specialized for face perception. *J Neurosci*. 1997; 17:4302–4311. [PubMed: 9151747]
- [3]. Hoffman EA, Haxby JV. Distinct representations of eye gaze and identity in the distributed human neural system for face perception. *Nat Neurosci*. 2000; 3:80–84. [PubMed: 10607399]
- [4]. Braak H, Braak E. Neuropathological staging of Alzheimer-related changes. *Acta Neuropathol (Berl)*. 1991; 82:239–259. [PubMed: 1759558]
- [5]. Bruce V, Young A. Understanding face recognition. *Br J Psychol*. 1986; 77(Pt 3):305–327. [PubMed: 3756376]
- [6]. Gainotti G, Marra C. Differential contribution of right and left temporo-occipital and anterior temporal lesions to face recognition disorders. *Front Hum Neurosci*. 2011; 5:55. [PubMed: 21687793]
- [7]. Collins A, Koechlin E. Reasoning, learning, and creativity: frontal lobe function and human decision-making. *PLoS Biol*. 2012; 10:e1001293. [PubMed: 22479152]
- [8]. Adolphs R, Damasio H, Tranel D, Cooper G, Damasio AR. A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *J Neurosci*. 2000; 20:2683–2690. [PubMed: 10729349]
- [9]. Griffith HR, Richardson E, Pyzalski RW, Bell B, Dow C, Hermann BP, Seidenberg M. Memory for famous faces and the temporal pole: functional imaging findings in temporal lobe epilepsy. *Epilepsy Behav*. 2006; 9:173–180. [PubMed: 16766230]
- [10]. Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. *Arch Neurol*. 1999; 56:303–308. [PubMed: 10190820]
- [11]. Petersen RC, Ivnik RJ, Boeve BF, Knopman DS, Smith GE, Tangalos EG. Outcome of clinical subtypes of mild cognitive impairment. *Neurology*. 2004; 62:A295.
- [12]. Roudier M, Marcie P, Grancher AS, Tzortzis C, Starkstein S, Boller F. Discrimination of facial identity and of emotions in Alzheimer's disease. *J Neurol Sci*. 1998; 154:151–158. [PubMed: 9562305]
- [13]. Bucks RS, Radford SA. Emotion processing in Alzheimer's disease. *Aging Ment Health*. 2004; 8:222–232. [PubMed: 15203403]
- [14]. Lyketsos CG, Lopez O, Jones B, Fitzpatrick AL, Breitner J, DeKosky S. Prevalence of neuropsychiatric symptoms in dementia and mild cognitive impairment: results from the Cardiovascular Health Study. *JAMA*. 2002; 288:1475–1483. [PubMed: 12243634]

- [15]. Geda YE, Roberts RO, Knopman DS, Petersen RC, Christianson TJ, Pankratz VS, Smith GE, Boeve BF, Ivnik RJ, Tangalos EG, Rocca WA. Prevalence of neuropsychiatric symptoms in mild cognitive impairment and normal cognitive aging: population-based study. *Arch Gen Psychiatry*. 2008; 65:1193–1198. [PubMed: 18838636]
- [16]. Geda YE, Knopman DS, Mrazek DA, Jicha GA, Smith GE, Negash S, Boeve BF, Ivnik RJ, Petersen RC, Pankratz VS, Rocca WA. Depression, apolipoprotein E genotype, and the incidence of mild cognitive impairment: a prospective cohort study. *Arch Neurol*. 2006; 63:435–440. [PubMed: 16533972]
- [17]. Spoletini I, Marra C, Di Iulio F, Gianni W, Sancesario G, Giubilei F, Trequattrini A, Bria P, Caltagirone C, Spalletta G. Facial emotion recognition deficit in amnesic mild cognitive impairment and Alzheimer disease. *Am J Geriatr Psychiatry*. 2008; 16:389–398. [PubMed: 18403572]
- [18]. Weiss EM, Kohler CG, Vonbank J, Stadelmann E, Kemmler G, Hinterhuber H, Marksteiner J. Impairment in emotion recognition abilities in patients with mild cognitive impairment, early and moderate Alzheimer disease compared with healthy comparison subjects. *Am J Geriatr Psychiatry*. 2008; 16:974–980. [PubMed: 19038896]
- [19]. Teng E, Lu PH, Cummings JL. Deficits in facial emotion processing in mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2007; 23:271–279. [PubMed: 17351319]
- [20]. Bediou B, Ryff I, Mercier B, Milliery M, Henaff MA, D'Amato T, Bonnefoy M, Vighetto A, Krolak-Salmon P. Impaired social cognition in mild Alzheimer disease. *J Geriatr Psychiatry Neurol*. 2009; 22:130–140. [PubMed: 19321881]
- [21]. McCade D, Savage G, Naismith SL. Review of emotion recognition in mild cognitive impairment. *Dement Geriatr Cogn Disord*. 2011; 32:257–266. [PubMed: 22222774]
- [22]. Jack CR Jr, Petersen RC, Xu Y, O'Brien PC, Smith GE, Ivnik RJ, Boeve BF, Tangalos EG, Kokmen E. Rates of hippocampal atrophy correlate with change in clinical status in aging and AD. *Neurology*. 2000; 55:484–489. [PubMed: 10953178]
- [23]. Petersen RC, Parisi JE, Dickson DW, Johnson KA, Knopman DS, Boeve BF, Jicha GA, Ivnik RJ, Smith GE, Tangalos EG, Braak H, Kokmen E. Neuropathologic features of amnesic mild cognitive impairment. *Arch Neurol*. 2006; 63:665–672. [PubMed: 16682536]
- [24]. Jicha GA, Parisi JE, Dickson DW, Johnson K, Cha R, Ivnik RJ, Tangalos EG, Boeve BF, Knopman DS, Braak H, Petersen RC. Neuropathologic outcome of mild cognitive impairment following progression to clinical dementia. *Arch Neurol*. 2006; 63:674–681. [PubMed: 16682537]
- [25]. Young AW, Hellawell DJ, Van De Wal C, Johnson M. Facial expression processing after amygdalotomy. *Neuropsychologia*. 1996; 34:31–39. [PubMed: 8852691]
- [26]. Mesulam MM. From sensation to cognition. *Brain*. 1998; 121:1013–1052. [PubMed: 9648540]
- [27]. Poulin SP, Dautoff R, Morris JC, Barrett LF, Dickerson BC. Amygdala atrophy is prominent in early Alzheimer's disease and relates to symptom severity. *Psychiatry Res*. 2011; 194:7–13. [PubMed: 21920712]
- [28]. Schmidt, M. *Rey Auditory Verbal Learning Test : a handbook*. Western Psychological Services; Los Angeles, LA: 1996.
- [29]. Sivan, AB. *Benton Visual Retention Test*. Psychological Corporation; San Antonio: 1992.
- [30]. Grober E, Buschke H. Genuine memory deficits in dementia. *Dev Neuropsychol*. 1987; 3:13–36.
- [31]. Wechsler, D. *Wechsler Memory Scale*. The Psychological Corporation; San Antonio; Toronto: 1997.
- [32]. Reitan, RM.; Wolfson, D. *The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation*. Neuropsychology Press; South Tucson: 1993.
- [33]. Borkowski JG, Benton AL, Spreen O. Word fluency and brain damage. *Neuropsychologia*. 1967; 5:135–140.
- [34]. Kaplan, E.; Goodglass, H.; Brand, S. *Boston Naming Test*. Lea & Febiger; Philadelphia: 1983.
- [35]. Osterrieth PA. The test of copying a complex figure: a contribution to the study of perception and memory. *Arch Psychologie*. 1944; 30:286–356.

- [36]. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res.* 1975; 12:189–198. [PubMed: 1202204]
- [37]. Hummelová Z, Rektorová I, Sheardová K, Bartos A, Línek V, Ressler P, Zapletalová J, Vyhnálek M, Hort J. Czech adaptation of the Addenbrooke's cognitive examination. *Cesk Psychol.* 2009; 53:376–388.
- [38]. Brink TL, Yesavage JA, Lum O, Heersema PH, Adey M, Rose TL. Screening tests for geriatric depression. *Clin Gerontol.* 1982; 1:37–43.
- [39]. Ekman, P.; Friesen, WV. *Pictures of Facial Affect.* Consulting Psychologists Press; Palo Alto: 1976.
- [40]. Keane J, Calder AJ, Hodges JR, Young AW. Face and emotion processing in frontal variant frontotemporal dementia. *Neuropsychologia.* 2002; 40:655–665. [PubMed: 11792405]
- [41]. Bechyn K, Varjassová A, Lodinská D, Vyhnálek M, Bojar M, Brabec J, Petrovický P, Seidl Z, Schenk I, Hort J. The relation between amygdala atrophy and other selected brain structures and emotional agnosia in Alzheimer disease. *Cesk Slov Neurol Neurochir.* 2008; 71:675–681.
- [42]. Hosmer, DW.; Lemeshow, S. *Applied Logistic Regression.* Wiley; New York: 2000.
- [43]. Natu V, O'Toole AJ. The neural processing of familiar and unfamiliar faces: a review and synopsis. *Br J Psychol.* 2011; 102:726–747. [PubMed: 21988381]
- [44]. Adolphs R. The neurobiology of social cognition. *Curr Opin Neurobiol.* 2001; 11:231–239. [PubMed: 11301245]
- [45]. Blonder, L.; Bowers, D.; Heilman, K. *Florida Affect Battery.* Center for Neuropsychological Studies Department of Neurology; Gainesville, FL: 1998.
- [46]. Thayer JF, Johnsen BH. Sex differences in judgement of facial affect: a multivariate analysis of recognition errors. *Scand J Psychol.* 2000; 41:243–246. [PubMed: 11041306]
- [47]. Henry JD, Thompson C, Ruffman T, Leslie F, Withall A, Sachdev P, Brodaty H. Threat perception in mild cognitive impairment and early dementia. *J Gerontol B Psychol Sci Soc Sci.* 2009; 64:603–607. [PubMed: 19671637]
- [48]. Lim TS, Lee HY, Barton JJ, Moon SY. Deficits in face perception in the amnesic form of mild cognitive impairment. *J Neurol Sci.* 2011; 309:123–127. [PubMed: 21783204]
- [49]. Teipel SJ, Bokde AL, Born C, Meindl T, Reiser M, Moller HJ, Hampel H. Morphological substrate of face matching in healthy ageing and mild cognitive impairment: a combined MRI-fMRI study. *Brain.* 2007; 130:1745–1758. [PubMed: 17566054]
- [50]. Cenquizca LA, Swanson LW. Spatial organization of direct hippocampal field CA1 axonal projections to the rest of the cerebral cortex. *Brain Res Rev.* 2007; 56:1–26. [PubMed: 17559940]
- [51]. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. *Neurology.* 1994; 44:2308–2314. [PubMed: 7991117]
- [52]. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol.* 1988; 56:893–897. [PubMed: 3204199]
- [53]. Fujie S, Namiki C, Nishi H, Yamada M, Miyata J, Sakata D, Sawamoto N, Fukuyama H, Hayashi T, Murai T. The role of the uncinate fasciculus in memory and emotional recognition in amnesic mild cognitive impairment. *Dement Geriatr Cogn Disord.* 2008; 26:432–439. [PubMed: 18957848]
- [54]. Carton JS, Kessler EA, Pape CL. Nonverbal decoding skills and relationship well-being in adults. *Journal of Nonverbal Behavior.* 1999; 23:91–100.
- [55]. Chiu MJ, Chen TF, Yip PK, Hua MS, Tang LY. Behavioral and psychologic symptoms in different types of dementia. *J Formos Med Assoc.* 2006; 105:556–562. [PubMed: 16877235]
- [56]. Shimokawa A, Yatomi N, Anamizu S, Torii S, Isono H, Sugai Y, Kohno M. Influence of deteriorating ability of emotional comprehension on interpersonal behavior in Alzheimer-type dementia. *Brain Cogn.* 2001; 47:423–433. [PubMed: 11748898]

Table 1

Descriptive information

Characteristic	Controls (<i>n</i> = 18)	SD-aMCI (<i>n</i> = 10)	MD-aMCI (<i>n</i> = 12)	<i>p</i> -value [*]	<i>p</i> -value [†]
Age, yrs	69.3 (7.6)	74.0 (5.0)	77.8 (10.0)	0.174	0.016
No. of women	12	7	6	0.856	0.364
Education, yrs (<i>n</i>)					
Elementary	3	3	6	Reference	Reference
High school	8	2	3	0.223	0.087
College	7	5	3	0.738	0.119
Mini-Mental State Examination	29.3 (0.9)	28.4 (1.8)	26.8 (2.3)	0.166	0.021
Memory [‡]	0.4 (0.3)	−0.2 (0.4)	−0.6 (0.6)	0.019	0.003
Attention/processing speed [‡]	0.3(0.7)	0.3 (0.4)	−0.7 (0.7)	0.769	0.013
Frontal/executive function [‡]	0.5 (0.6)	0.2 (0.4)	−1.0 (0.6)	0.167	0.003
Facial Emotion Recognition	20.1 (2.5)	20.0 (1.6)	17.6 (2.9)	0.888	0.027
Famous Face Identification	18.3 (1.4)	18.5 (1.2)	17.8 (1.5)	0.664	0.309

P values are based on results from multinomial logistic regressions estimated separately for each variable presented in the column titled “Characteristic”; age, sex, and education were controlled in the analyses examining differences between the groups in each cognitive ability.

^{*} Cognitively normal participants versus patients with SD-aMCI.

[†] Cognitively normal participants versus patients with MD-aMCI.

[‡] Cognitive domains are expressed as z-scores.

Table 2

Correlations of Facial Emotion Recognition (FER) and Famous Faces Identification (FFI) with Cognitive Domain Scores

Variable	NC		aMCI	
	FER	FFI	FER	FFI
MMSE	0.21	−0.51 *	0.15	0.19
Memory	−0.09	−0.05	0.16	0.07
Attention/speed of processing	0.15	0.05	0.44 *	0.16
Frontal/executive function	0.04	0.47 *	0.28	0.23

Note: Spearman correlation coefficients are shown. NC = normal controls; aMCI = amnesic mild cognitive impairment; MMSE = Mini-Mental State Exam

* p<.05.

Table 3

Association between facial emotion recognition or famous faces identification and the odds of being a person with SD-aMCI or MD-aMCI compared to being a control

	SD-aMCI			MD-aMCI		
	OR	95% CI	<i>p</i> -value	OR	95% CI	<i>p</i> -value
Model 1 [*]						
Facial emotion recognition	1.13	0.36–3.57	0.836	3.82	1.05–13.91	0.042
Famous faces identification	0.78	0.30–2.01	0.606	1.08	0.43–2.72	0.867
Model 2 [†]						
Facial emotion recognition	1.17	0.35–3.95	0.799	5.40	1.09–26.71	0.039
Famous faces identification	1.01	0.37–2.78	0.986	1.98	0.59–6.61	0.266
Model 3 [‡]						
Facial emotion recognition	1.42	0.29–6.85	0.663	6.59	1.08–40.13	0.041
Famous faces identification	1.67	0.42–6.64	0.465	5.76	0.82–40.56	0.079

Participants in the control group were the reference category with the odds ratio set at 1.00.

^{*} Adjusted for age, sex, and education.

[†] Mini-Mental State Examination scores have been added.

[‡] Memory scores were added.