Behavioural Brain Research 294 (2015) 111–122

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Behavioral and neural correlates of visual emotion discrimination and empathy in mild cognitive impairment

Simone Pernigo[a,*], Giuseppe Gambina[c], Valeria Valbusa[a,b], Maria Teresa Condoleo[a,b], Elisabetta Broggio[a,b], Alberto Beltramello[c], Giuseppe Moretto[b], Valentina Moro[a,*]

[a] NPSY.Lab-Vr, Department of Philosophy, Education and Psychology, University of Verona, Lungadige Porta Vittoria 17, 37129 Verona, Italy
[b] USO Centro Alzheimer e Disturbi Cognitivi, Neurologia d.O, Azienda Ospedaliera Universitaria Integrata, 37126 Verona, Italy
[c] UOC Neuroradiologia, d.O. Azienda Ospedaliera Universitaria Integrata, 37126 Verona, Italy

HIGHLIGHTS

- Orbitofrontal atrophy and executive deficits are associated with lack of EEF in MCI.
- MCI patients lack emotional enhancement effect specifically for facial stimuli.
- Lower cognitive empathy in MCI is associated with fusiform and cerebellar atrophy.
- Reduced interpersonal functioning is independent from implicit emotional deficits.
- Implicit and explicit measures of empathy in Mild Cognitive Impairments.

ARTICLE INFO

Article history:
Received 10 May 2015
Received in revised form 18 July 2015
Accepted 23 July 2015
Available online 26 July 2015

Keywords:
Mild cognitive impairment
Emotion recognition
Empathy
Medial prefrontal cortex
Executive functions
Voxel-based morphometry

ABSTRACT

Emotional and social cognitive deficits were investigated in a group of 24 individuals with mild cognitive impairment (MCI) and 24 healthy controls. Empathic and visual emotional responses were collected, analyzed and correlated to brain structural imaging data by means of: (i) a pictorial matching-to-sample task with facial and non-facial stimuli; (ii) self-reported questionnaires for cognitive and affective emotional components, and alexithymia; (iii) in-depth assessment of cognitive functions. Results indicated that visual processing of faces in MCI individuals did not benefit from fearful emotional content which in healthy controls facilitates stimulus' recognition (emotional enhancement effect). This implicit visuo-emotional disorder was specific for the faces, did not generalize to other categories, and did not correlate to explicit measures of empathy. Thus, our main finding indicates that in MCI individuals, deficits in visual recognition of facial emotions may arise already in the earliest stages of memorization, during the visual encoding of facial emotions. Voxel-based morphometry revealed its association with atrophy in frontal and occipito-temporal regions, mostly involving the anterior medial prefrontal cortex ($P < 0.05$, multiple-comparison correction). Neural evidences were corroborated by clinical scores showing significant correlation between reduction of Emotion Enhancement Effect and deficits in frontal/executive functions. Crucially, the disorder did not appear to be related to the number of impaired cognitive domains (single or multiple-domain MCI) but rather to the involvement of frontal brain networks and frontal/executive functions. This suggests that in prodromal stages of dementia, frontal symptoms may represent a significant signal of emotional recognition disorders.

1. Introduction

The ability to recognize emotions from facial expressions is a fundamental prerequisite for successful interaction in everyday life. Being able to infer what others are feeling enables individuals to anticipate events, respond appropriately, avoid conflict and regulate their own emotions [1]. Clinical and experimental evidence

* Corresponding authors at: Department of Philosophy, Education and Psychology,University of Verona.Lungadige Porta Vittoria 17, 37129 Verona, Italy.
E-mail addresses: simone.pernigo@gmail.com (S. Pernigo), valentina.moro@univr.it (V. Moro).

http://dx.doi.org/10.1016/j.bbr.2015.07.047
0166-4328/

indicates that the vulnerability of social cognition mechanisms may increase with aging [2,3], particularly in the presence of dementia [4,5].

Although emotional and social disorders are mainly described as a prominent feature of fronto-temporal degeneration [6–8], it has been proposed that specific social cognition tasks may be particularly useful when identifying the earliest symptoms in other forms of dementia [9]. In particular, deficits in emotion recognition may reflect the progression of neuro-degeneration from the entorhinal cortex and hippocampus toward the lateral temporal cortex which underlies the transition from amnestic Mild Cognitive Impairment (MCI) to early dementia [10]. Indeed, in Alzheimer's disease (AD), deficits in the visual recognition of faces expressing anger [10,11], surprise [12], disgust [10], sadness, fear and happiness [11,13], have been shown. In contrast, MCI results are to date far from being conclusive [14], indicating that emotion recognition deficits may be absent [10,15], general [13,16,17], specific to negative expressions [11,18,19], or present only in multiple-domain MCI [13,17,20].

A reduction in the Emotional Enhancement Effect (EEF) has been reported in amnestic MCI [21,22] and multiple-domain MCI [74]. EEF is described as the consequence of the emotional contents of a stimulus, which, being consciously or unconsciously encoded, significantly increase the probability that the information is remembered over time [23,24]. Since MCI mainly affects the medial temporal and frontal structures normally involved in encoding emotional stimuli, a reduction in EEF would be expected. Nevertheless, neuroanatomical [25,26] and behavioral findings are still controversial [22,27–30], possibly due to the different methodologies employed.

The main aim of this study is to investigate deficits in the discrimination of emotional stimuli in MCI subjects using an integrated approach that compares implicit responses to emotional visual stimuli with explicit reports concerning the subjects' emotional reactivity and empathy. MCI has been proposed as the pre-clinical stage of dementia when cognitive impairment is beyond what is considered normal for the age in question, but not of a magnitude to warrant a diagnosis of dementia [31]. As this constitutes a prodromal phase of Alzheimer disease (AD) and dementia [32], devising specific instruments for diagnosis and interventions in MCI represents a scientific priority [33–35] .

A matching-to-sample task was implemented in order to investigate the visual abilities of MCI people in the discrimination of emotional or neutral images in four different categories: human faces and bodies, animals (dog faces) and inanimate objects (knives).

It was thus possible to establish whether deficits in the discrimination of emotions may be selective for specific categories of stimuli and in particular for social information (faces and bodies). Moreover, differences in performance concerning the discrimination of stimulus morphology (identity discrimination) and emotional information (emotional discrimination) enabled us to control for eventual general disorders in visual discrimination.

A comparison between the experimental results and the subjects' responses in three validated interviews concerning empathy and emotional reactivity (IRI, BEES and TAS20) provided information on potential dissociations between explicit and implicit measures of emotional behavior. In addition, we used the Voxel Based Morphometry (VBM) to explore any correlations between deficits in the discrimination of emotions and cerebral areas of atrophy, as showed by Magnetic Resonance Imaging (MRI). Finally, these explicit and implicit measures were correlated with the subjects' performance in neuropsychological tests, particularly focusing on executive functions. It was thus possible to identify any correlations between emotional responses and cognitive functions.

2. Materials and methods

2.1. Participants

30 right-handed subjects affected by MCI [36] were recruited at the Alzheimer's Disease Center, University Hospital of Verona. They agreed to participate in the study. Subsequently, three of them developed evident signs of mental deterioration and another three refused to conclude the experimental protocol. The final group included 24 MCI individuals (women, 13; mean age, 74.4; SD, 5.9; range, 63–85). 24 age-, gender- and education-matched healthy subjects served as controls (mean age, 73.8; SD, 5.9; range, 64–86). These did not report subjective memory complaints and performed within the normal range (score $\geq$ 22) at the Montreal Cognitive Assessment (MOCA) [37,38]. The MCI subjects met the diagnostic Mayo criteria [31]: (i) reports of cognitive impairment described by the patient, relatives or both; (ii) specific cognitive impairment identified by means of a neuropsychological test battery (the Carlesimo & Caltagirone Battery [36] assessing attention, verbal memory, verbal fluency, constructive praxis) interpreted in conjunction with the first criterion and the personal history of the patient; (iii) no impairment in daily activities [39,40]; (iv) absence of global deterioration (Mini-Mental State Examination, corrected score $\geq$ 24/30) [41] and dementia, as defined by the Diagnostic and Statistical Manual of mental disorders criteria (DSM-IV-American Psychiatric Association, 2000). In fact, although all the MCI subjects performed over the cut-off for global mental deterioration (MOCA and MMSE), they complained cognitive impairment and performed under cut-off in at least one of the test of the neuropsychological battery used for screening [36]. Impact on everyday activities was evaluated and excluded by means of the Clinical Dementia Rating (CDR) scale and two clinical interviews, administered to both the patient and the informant (Instrumental Activities of Daily Living and Basic Activities of Daily Living [39,40]).

After the initial screening, an in depth neuropsychological assessment focused on executive functions, in particular tests of executive speed (Digit Symbol-Coding test of the Wechsler Adult Intelligence Scale [42]), verbal working memory (Listening Span Test, [43]), attentional flexibility (Trail Making Test – Part B [44]; Visual Elevator Task, subtest of the Test of Everyday Attention, Italian Version [45]), planning (Tower of London, [46]), and Verbal Judgments [47] were administered. Sustained and divided attention was investigated by means of the Dual Task [48], the Trail Making Test – Part A [44]) and Attentional Matrices [49]. The Rivermead Behavioural Memory Test [50] was used as a measure of memory capacities in daily life context. Finally, language abilities were controlled by means of the Aachener Aphasia Test's subtests of Comprehension, Denomination and Repetition [51].

The assessment indicates that ten of the MCI subjects presented with a single impairment in memory (7 subjects) or executive functions (3 subjects); 13 people suffered from multiple-domain amnestic MCI, and 1 presented with multiple-domain non-amnestic MCI. Globally, the functions most frequently compromised were memory (20 subjects), executive functions (12 subjects), and attention (10 subjects). Only 4 subjects failed in verbal fluency, and two in constructive praxis.

All participants underwent a comprehensive assessment including medical and neurological examinations. Structural brain imaging excluded the presence of relevant cerebrovascular lesions, and standard laboratory blood tests (thyroid function, complete blood count, blood chemistry, folic acid and vitamin B12, homocysteine, and blood lipid profile) ruled out any reversible causes of cognitive impairment. Other criteria of exclusion were: (i) current neurological and systemic diseases (included serious ocular causes of visual impairment) or a history of head injury with loss of consciousness; (ii) history or symptoms of psychosis or major