ORIGINAL RESEARCH

Emotional face recognition deficit in amnestic patients with mild cognitive impairment: behavioral and electrophysiological evidence

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Abstract: Amnestic mild cognitive impairment (MCI) has been conceptualized as a transitional stage between healthy aging and Alzheimer's disease. Thus, understanding emotional face recognition deficit in patients with amnestic MCI could be useful in determining progression of amnestic MCI. The purpose of this study was to investigate the features of emotional face processing in amnestic MCI by using event-related potentials (ERPs). Patients with amnestic MCI and healthy controls performed a face recognition task, giving old/new responses to previously studied and novel faces with different emotional messages as the stimulus material. Using the learning-recognition paradigm, the experiments were divided into two steps, ie, a learning phase and a test phase. ERPs were analyzed on electroencephalographic recordings. The behavior data indicated high emotion classification accuracy for patients with amnestic MCI and for healthy controls. The mean percentage of correct classifications was 81.19% for patients with amnestic MCI and 96.46% for controls. Our ERP data suggest that patients with amnestic MCI were still be able to undertake personalizing processing for negative faces, but not for neutral or positive faces, in the early frontal processing stage. In the early time window, no differences in frontal old/new effect were found between patients with amnestic MCI and normal controls. However, in the late time window, the three types of stimuli did not elicit any old/new parietal effects in patients with amnestic MCI, suggesting their recollection was impaired. This impairment may be closely associated with amnestic MCI disease. We conclude from our data that face recognition processing and emotional memory is impaired in patients with amnestic MCI. Such damage mainly occurred in the early coding stages. In addition, we found that patients with amnestic MCI had difficulty in post-processing of positive and neutral facial emotions.

Keywords: event-related potential, emotion, recognition memory, amnestic mild cognitive impairment, faces

Introduction

Amnestic mild cognitive impairment (MCI) frequently represents a transitional stage between normal aging and early Alzheimer's disease (AD).[1] Patients with amnestic MCI usually show normal cognitive ability and normal ability in activities of daily living. However, they are thought to be at high risk of developing AD.[2,3] Therefore, it would be useful to find a way of determining which patients with amnestic MCI will go on develop AD by investigating aspects of memory that are impaired and those that remain relatively intact.

Previous studies had shown that information with an emotional message may boost memory.[4] However, for patients with MCI, the amygdala, which is the key area of the brain for processing of emotional memory, may be damaged, as illustrated

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by significant elevation of neuritic plaques.[5] Currently, it remains controversial as to whether amnestic MCI shows an emotional superiority effect. Some studies have demonstrated impairment of emotional face recognition in patients with amnestic MCI.[6–9] However, others believe that the precedence effect of amnestic MCI memory encoding for emotional faces (beneficial effect) is damaged,[10] and the most recent study[11] showed that recognition memory for emotional faces is impaired in amnestic MCI.

Due to their high time and temporal resolution, event-related potentials (ERPs) are considered to be particularly useful in time process monitoring and processing of emotional faces. It is believed that three components of ERPs are related to earlier perception, ie, P100, N170, and P2. The P100 component is thought to reflect domain-general early visual processing and to be insensitive to face familiarity or correct recognition. The N170 component is considered to be an indicator of structural encoding of a face. In addition, a positive potential may emerge together with the N170 component in the frontocentral sites, such as the vertex positive potential (VPP).[12,13] Previous reports demonstrated that the amplitude of N170 was enhanced for personally familiar faces when compared with unfamiliar faces and for emotional faces when compared with neutral faces. The P2 component directly follows N170, and is thought to reflect visual processing linked to perceptual grouping, and is also considered to reflect an early recognition process. Moreover, P2 has been shown to be sensitive to emotional significance.[11] It was also described that ERPs were recorded while subjects performed a memory retrieval task that requires old/new judgments regarding visually presented old (previously studied) and new pictures.[14] This so-called ERP old/new effect consists of temporally and spatially dissociable subcomponents that have been associated with specific retrieval mechanisms and are evoked by a variety of stimuli. Two subcomponents were used in the current study. The first subcomponent was an early frontal old/new effect (300–500 milliseconds) that has often been associated with familiarity. A second subcomponent, the parietal old/new effect (500–800 milliseconds), has been associated with recollection.[15] Analysis of the ERP old/new effect in the early time window showed an early frontal old/new effect for negative faces but not for neutral faces. However, there is no difference in this regard between patients with amnestic MCI and healthy controls.[11] It has also been argued that negative emotion may boost familiarity due to enhanced conceptual or perceptual fluency for emotionally negative information,[16] and that emotional stimuli may be given priority for processing.[17,18] Similar behavioral test results have also been reported by a number of other research groups.[19–23]

Facial expressions inform how people feel and their action tendency. Six basic categories of emotional facial expressions have been identified, ie, happiness, sadness, anger, disgust, fear, and surprise,[24] Some involve signals of potential harm, whereas others convey signals of potential benefit. In prior behavioral research, happy facial expressions have been found to be more accurately and faster than other expressions.[25] In recent years, studies of emotional memory in younger and older adults have suggested that older adults may have reduced memory advantages for negative information,[26] and may in some instances demonstrate a positive bias, ie, a memory advantage for positive information.[27–30] However, the underlying cognitive mechanisms are not fully understood. It has found that emotion-induced memory enhancement is abolished and positivity-related recognition bias is preserved in patients with amnestic MCI,[10] but there have been no studies exploring the change in recognition memory of patients with amnestic MCI by performing ERP analysis.

In this study, we investigated whether recognition memory for positive emotional faces is impaired in patients with amnestic MCI, and if so, at what stage of memory recognition this impairment occurs, and whether it makes any difference if patients are tested for memory impairment using positive emotional faces or negative emotional faces. So far, all of these issues remain the subject of debate. We measured behavioral and ERP data in patients with amnestic MCI and in healthy controls to determine the time course of successful identification of emotional faces. We hypothesized that patients with amnestic MCI would show an early and late time window old/new effects deficit, and the changes in old/new effects in patients with amnestic MCI would be correlated with progression of amnestic MCI.

Materials and methods
Participants

All patients met Petersen's criteria[2] for amnestic MCI, which included the following: complaining of memory loss for more than 3 months; maintaining normal activities of daily living; presenting normal general cognitive function; showing objective impairment in one area of cognitive function as evidenced by scores >1.5 standard deviation of age-appropriate norms; and having a Clinical Dementia Rating score of 0.5.

The amnestic MCI and control groups were both required to meet the following conditions: no dementia; no significant

changes on brain imaging, such as cerebral infarct, hydrocephalus, or leukoaraiosis; right-handedness; no history or evidence of psychiatric or neurological disease, cardiovascular disease, diabetes, thyroid disease, vitamin B12 deficiency, or substance abuse; normal vision or corrected normal vision; and being native Chinese.

The study was approved by the ethics committee at the First Hospital of Hebei Medical University. Before the experiments, all tested subjects were informed regarding the purpose of this study and signed consent forms.

The study included 24 patients with amnestic MCI and 24 age-matched healthy controls recruited as volunteers from Shijiazhuang City, People's Republic of China between May 2012 and February 2014. Demographic data and results for neuropsychological assessments are shown in Table 1.

Stimulus materials

Three hundred pictures of faces were chosen from the China Faces Emotions Materials database for this study.[31] One third of the selected pictures (n=100) were positive faces, one third were neutral faces, and one third were negative faces. The pictures selected were evenly divided between men and women. All pictures were of uniform size, background, and color, and were presented in the center of a 17-inch flat screen monitor with a gray background.

Three types of pictures matched in a pleasant degree of polarization (positive, 7.44±0.31; neutral, 5.03±0.22; negative, 2.45±0.28). The arousal of three types of pictures was consistent (positive, 5.54±0.47; neutral, 4.48±1.37; negative, 5.44±0.40).

Procedure and design

Using a learning-recognition paradigm, we divided our experiments into two steps, ie, a learning phase and a test phase. In the learning phase, subjects were presented with pictures depicting each of the three types of emotional face

(there were 50 pictures for each type of emotion, with a total of 150 pictures presented). In response to presentation of each emotional picture, the test subjects were asked to type in a corresponding key. Each picture was presented four times in order to increase familiarity, and in a randomized order. The tests were started 40 minutes later after completion of the learning period, with recording of an electroencephalogram. Before the start of the learning phase, participants were asked to carefully observe and remember the presented faces. Forty minutes later, some novel faces were presented in order to test the ability to distinguish and memorize faces. During the learning stage, the subjects were required to focus on the point for 500 msec, after which a picture of a face was presented for 3 seconds and the subjects were required to make category judgments (positive, neutral, or negative) by pressing specific keys. Presentation of each picture was separated by a 1,000 msec blank screen. For the recognition phase, the three types of learned emotional faces and novel faces were mixed first, and then presented to the subjects, who made decisions regarding their familiarity with the faces.

The details of the testing procedure used in our study are as follows: at the beginning of each test, a "+" sign appears at the focus point for 500 msec, a picture of a face then appears for up to 2,000 msec, and the subject is asked to make the decision about the familiarity of the tested faces (learned or novel). A blank screen appears for 2,000 msec between each picture presentation. The guidance language used by the investigators was standardized after 12 practice trials before performing the recognition experiments.

Electrophysiological recording

An electroencephalogram was recorded continuously for each subject by means of a Neuroscan amplifier SynAmps2. The electrodes were placed according to the international 10/20 placement system using a 64-lead electrode cap. A unilateral

Table 1 Demographic and neuropsychological assessment data

	Amnestic MCI group (n=24)		Control group (n=24)		t	P-value
	Mean	SD	Mean	SD		
Sex (male/female)	10/14		12/12			
Age (years)	71.50	4.53	71.79	3.74	−0.244	0.809
Education (years)	8.20	4.12	9.33	3.55	−1.013	0.317
MMSE score	26.583	1.863	28.791	1.382	−4.663	0.000
Montreal Cognitive Assessment score	21.750	3.300	27.708	1.301	−8.228	0.000
Activities of daily living score	20.666	2.277	20.166	0.637	1.036	0.306
CES-D	1.8750	5.33497	2.125	5.735	−0.156	0.876

Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; MMSE, Mini-Mental State Examination; MCI, mild cognitive impairment; SD, standard deviation.

reference electrode was placed in the mastoid of the left ear. Vertical and horizontal electro-oculographic activity was recorded with additional electrodes located above and below the left eye and outside the outer canthi of both eyes. Connections were also placed at the midpoint frontoparietal zone and at the frontal zone. Electrical activity was amplified with a bandpass filter from 0.01 to 100 Hz and at a sampling rate of 500 Hz. In offline analysis, the data were intercepted into single sweep recordings from 100 msec before each stimulus onset to 800 msec after the stimulus. The baseline was corrected by averaging the signal during the 100 msec preceding the onset of the stimulus. All epochs with ocular artifacts greater than 75 µV were automatically rejected by a regression method with a bandpass filter of 0.05–40 Hz. The resistance between each electrode and the scalp was less than 5 KΩ. Electroencephalographic data were analyzed with Scan 4.5 software. E-Prime software was used to collect the stimulus and behavioral data.

Neuropsychological tests

All study subjects underwent a series of neuropsychological tests one day before implementation of the ERP test. The main tests used were the Mini-Mental State Examination[32] and the Beijing version of the Montreal Cognitive Assessment.[33] Assessment of daily activity was done using the activities of daily living.[34] The Center for Epidemiologic Studies Depression Scale[35] was used to identify depression.

Data analyses
Behavioral data

In the learning phase, we analyzed how often the subjects classified the different types of emotional pictures correctly. In the subsequent recognition phase, we analyzed four indicators as follows: the percentage of subjects correctly recognizing pictures of happy, neutral, and angry faces (hits); the percentage of erroneously recognized faces (false positives); discrimination accuracy, calculated as (Pr = p [hits] − p [false positives]); and recognition bias, ie, the probability of saying "yes" to an item when uncertain, calculated as (Br = p [false positives]/p [1− Pr]).[36]

ERP data

ERP data were analyzed from 800 msec after the stimulus onset. The baseline was taken for the time window of 100 msec before the stimulus onset. As in previous studies, ERP data were analyzed on the basis of the early components (P100, N170/VPP, P200), which were quantified by mean amplitude, and the late old/new effect (early frontal old/new

effect, parietal old/new effect). The range of peak value and latency were selected based on the total averaged figure.

Three-factor repeated measures analysis of variance was performed for the peak latency of each early component (P100, N170/VPP, P200). The three factors were group (healthy control, amnestic MCI), emotion (positive, neutral, negative), scalp position (P100 at 90–140 msec for O1 and O2; N170 at 160–240 msec for PO8 and PO7; VPP at 160–240 msec for the frontal zone and the central zone; P2 at 240–380 msec for PO8 and PO7). The average amplitude of the early components (P100, N170/VPP, P200) were similarly analyzed, with the corresponding three factors being groups (normal, amnestic MCI), emotion (positive, neutral, negative), and scalp position (left [P07] and right [P08]). The average amplitude detection range was at 80–130 msec for P1, 130–200 msec for N170/VPP, and 240–380 msec for P2.

ERP old/new effect

The ERP old/new effect was analyzed using data collected from 12 factors (F5, FZ, F6, C5, CZ, C6, P5, PZ, P6, CB1, OZ, CB2). The time window for analysis was 300–500 msec for the early frontal old/new effect and 500–800 msec for the parietal old/new effect. Five-factor repeated-measures analysis of variance was performed for the ERP old/new effect from two recorded brain areas. These five factors were: factors region (frontal [F5, FZ, F6] versus central [C5, CZ, C6] versus parietal [P5, CZ, P6] versus occipital [CB1, OZ, CB2], hemisphere (left [F5, C5, P5, CB1] versus midline [FZ, CZ, PZ, OZ] versus right [F6, C6, P6, CB2]), old/new response, emotion, and between-subject factor group. The *P*-value for analysis of variance was corrected using the Greenhouse–Geisser method.

Results
Behavioral data
Study session

The accuracy of emotion classification was high in both groups. The mean (± standard deviation) percentage of correct classifications was 81.19%±12.7% for the amnestic MCI group and 96.46%±8.3% for the control group. The percentage of correct classifications was higher for healthy controls than for patients with amnestic MCI (*F*=5.26, *P*=0.028). There were no differences in or interactions between the emotional categories.

Test session

Parameters of recognition performance are displayed in Table 2. In this study, the average error rate was 30.56%

Table 2 Recognition of emotional faces by patient with amnestic MCI and control subjects

Face type	Control group (n=24)		Amnestic MCI group (n=24)		Group difference	
	Mean	SD	Mean	SD	t	P-value
Angry						
Hits	0.764	0.198	0.655	0.218	1.818	0.076
False positives	0.155	0.110	0.244	0.165	−2.203	**0.033**
Accuracy (Pr)	0.610	0.186	0.411	0.258	3.052	**0.004**
Bias (Br)	0.437	0.267	0.432	0.205	0.080	0.937
Neutral						
Hits	0.591	0.233	0.545	0.183	0.774	0.443
False positives	0.223	0.156	0.416	0.213	−3.577	**0.001**
Accuracy (Pr)	0.368	0.180	0.129	0.154	4.959	**0.000**
Bias (Br)	0.380	0.258	0.471	0.211	−1.340	0.187
Happy						
Hits	0.752	0.190	0.688	0.161	1.271	0.210
False positives	0.211	0.149	0.413	0.231	−3.602	**0.001**
Accuracy (Pr)	0.541	0.190	0.274	0.257	4.085	**0.000**
Bias (Br)	0.471	0.267	0.556	0.208	−1.241	0.221

Notes: Hits – the effects within the group were significant ($F=17.013$, $P<0.001$). Further analysis with multiple comparisons indicated an angry versus neutral MD of 0.141 ($P=0.001$) and a neutral versus happy MD of −0.152 ($P=0.000$). The interaction was not significant ($F=0.697$, $P=0.5030$). False positives – the effects within the group were significant ($F=11.753$, $P=0.000$). Further multiple comparison indicated an angry versus neutral MD of −0.121 ($P=0.000$) and an angry versus happy MD of −0.007 ($P=0.000$). The interaction was not significant ($F=2.625$, $P=0.084$). Accuracy (Pr) – the effects within the group were significant ($F=25.150$, $P=0.000$). Further multiple comparison indicated an angry versus neutral MD of 0.262 ($P=0.000$), a neutral versus happy MD of −0.159 ($P=0.000$), and an angry versus happy MD of 0.103 ($P=0.000$). The difference between the groups was significant ($F=−0.170$ ($P=0.000$)). The interaction is not significant ($F=2.772$, $P=0.103$). Bias (Br) – the effects within the group were significant ($F=5.278$, $P=0.026$). Further multiple comparison indicated a neutral versus happy MD of −0.088 ($P=0.001$). The interaction was not significant ($F=1.772$, $P=0.190$).
Abbreviations: MCI, mild cognitive impairment; MD, mean difference; SD, standard deviation.

and the error rate for all subjects was 19.55%–43.55%. The error rates during the test are listed in Table 3.

ERP data

In this analysis, we only included electroencephalographic data from tests with correct rejections (CR), ie, the "old" response to faces we researched in this study (hits) and the "new" response to novel faces (CR). The total mean ERPs evoked by hits and CR for negative, positive, and neutral faces are presented in Figures 1–3, respectively.

P100 component

Four-factor repeated-measures analysis of variance was performed for the amplitude and peak latency of P100. The four factors were group (healthy control, amnestic MCI), emotion (positive, neutral, negative), scalp position (01, 02), and old/new effect (hits, CR). The results are summarized in Table 4. The data indicate that there were no significant differences between the two groups of subjects (amplitude [$F=0.437$, $P=0.512$], latency [$F=0.187$,

Table 3 Error rates during tests for different emotional faces

	Control group (n=24)	Amnestic MCI group (n=24)
Angry	19.55%	29.45%
Neutral	31.60%	43.55%
Happy	22.95%	36.25%

Abbreviation: MCI, mild cognitive impairment.

$P=0.667$]), or between different scalp positions (amplitude [$F=0.103$, $P=0.749$] and latency [$F=0.836$, $P=0.365$]). Similar results were found for old/new effect (amplitude [$F=0.275$, $P=0.603$] and latency [$F=0.320$, $P=0.547$]), and emotional effect (amplitude [$F=1.024$, $P=0.317$] and latency [$F=2.085$, $P=0.130$]). No significant difference was found with regard to interaction (amplitude [$F=0.254$, $P=0.776$] and latency [$F=1.181$, $P=0.311$]).
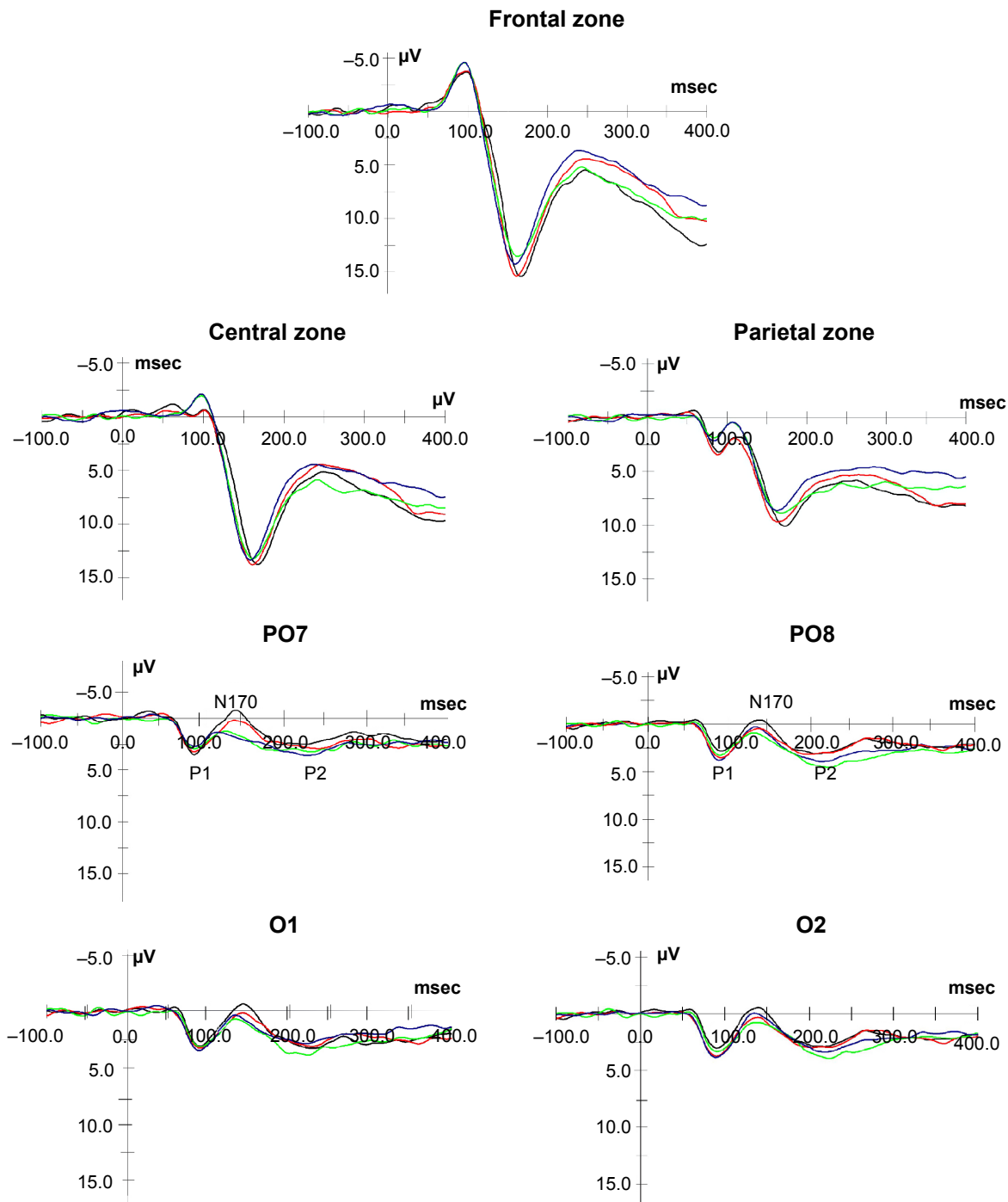
N170/VPP component

Four-factor repeated-measures analysis of variance was performed for the amplitude and peak latency of N170. The four factors were group (healthy control, amnestic MCI), emotion (positive, neutral, negative), scalp position (P07 and P08), and old/new effect (hits, CR). Compared with the healthy control group, the peak latency of N170 for the amnestic MCI group was clearly prolonged ($t=5.57$, $P<0.01$). For the control group, at the P08 recording position, the amplitude of hits for negative faces was larger than the amplitude for CR ($t=5.61$, $P<0.01$). Similar results were observed for positive faces ($t=3.11$, $P<0.05$), but no difference was observed for neutral faces. For the control group, the amplitude of N170 in the hits condition was enhanced for both positive faces ($t=12.36$, $P<0.001$) and negative faces ($t=15.26$, $P<0.001$). The difference was significant compared with neutral faces. For the amnestic MCI group, the amplitude of N170 did not

Frontal zone

Central zone

Parietal zone
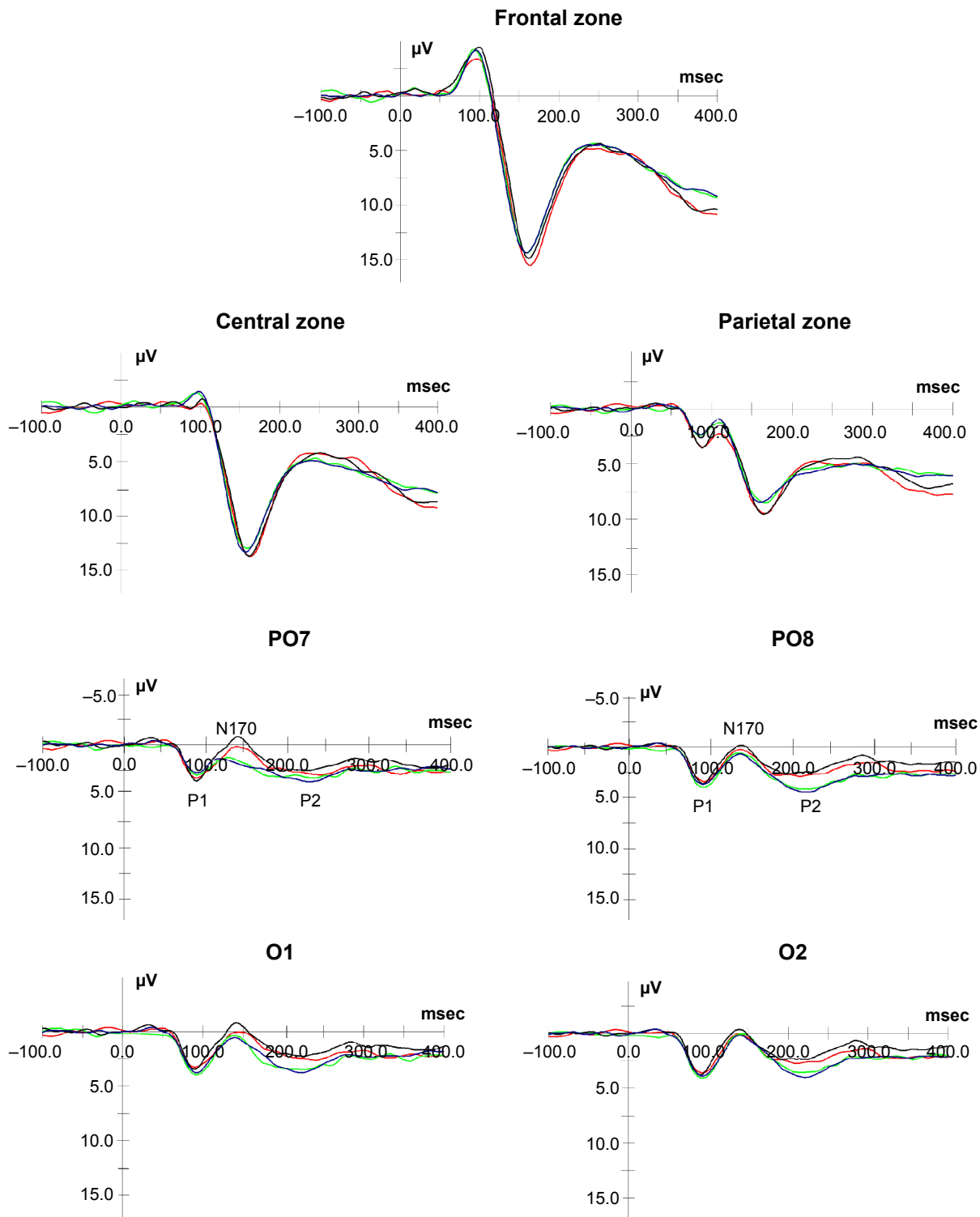
PO7

PO8

O1

O2

Figure 1 Total mean ERPs evoked by hits and CR for negative faces at electrodes FZ, CZ, PZ, P07, P08, O1, and O2 for healthy controls and patients with amnestic MCI. The corresponding conditions are color-coded, respectively: hits, amnestic MCI (green); CR, amnestic MCI (blue); hits, control; and CR, control (red).
Abbreviations: CR, correct rejections; ERPs, event-related potentials; MCI, mild cognitive impairment; msec, milliseconds; FZ, frontal zone; CZ, central zone; PZ, parietal zone.

change for old/new effect. However, for the presentation of novel faces, the difference was significant for the different emotional faces. Compared with neutral faces, the amplitude of N170 was decreased for negative faces in both recording electrodes for P08 ($t=6.01$, $P<0.01$) and P07 ($t=7.73$, $P<0.01$, Table 5).

Four-factor repeated-measures analysis of variance was also performed for the amplitude of VPP. The four factors were group (healthy control, amnestic MCI), emotion (positive, neutral, negative), scalp position (frontal zone, central zone), and old/new effect (hits, CR). The results indicated that the amplitude of negative hits in the amnestic MCI

Frontal zone

Central zone

Parietal zone
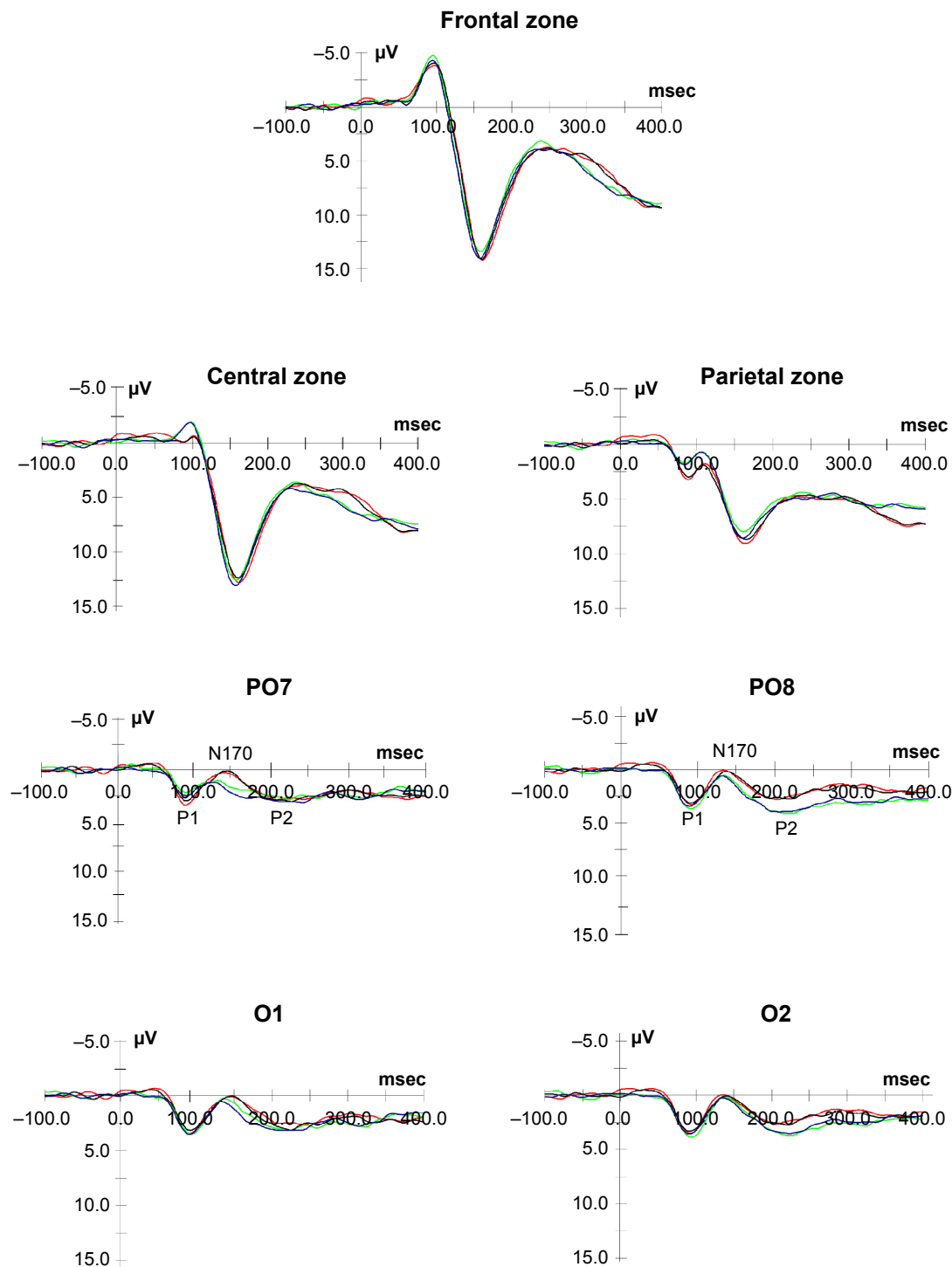
PO7

PO8

O1

O2

Figure 2 Total mean ERPs evoked by hits and CR for positive faces at electrodes FZ, CZ, PZ, P07, P08, O1, O2 for healthy controls and patients with amnestic MCI. The corresponding conditions are color-coded, respectively: hits, amnestic MCI (green); CR, amnestic MCI (blue); hits, control; and CR, control (red).
Abbreviations: CR, correct rejections; ERPs, event-related potentials; MCI, mild cognitive impairment; msec, milliseconds; FZ, frontal zone; CZ, central zone; PZ, parietal zone.

group was increased (t=13.30, $P<0.001$) when compared with the CR for negative faces in the healthy control group. No significant differences were observed with the rest of the dimensions (Table 6).

P2 component

In the amnestic MCI group, the tested subjects showed strong effects of recognition with negative faces, but no effects with neutral faces or positive faces. In this study,

Figure 3 Grand mean ERPs evoked by hits and CR for neutral faces at electrodes FZ, CZ, PZ, P07, P08, O1, O2 for healthy controls and patients with amnestic MCI. The corresponding conditions are color-coded, respectively: hits, amnestic MCI (green); CR, amnestic MCI (blue); hits, control; and CR, control (red).
Abbreviations: CR, correct rejections; ERPs, event-related potentials; MCI, mild cognitive impairment; msec, milliseconds; FZ, frontal zone; CZ, central zone; PZ, parietal zone.

four-factor repeated-measures analysis of variance was performed for P2 amplitude. The four factors were group (healthy control, amnestic MCI), emotion (positive, neutral, negative), scalp position (P07 and P08), and old/new effect (hits, CR). In the control group, the P2 amplitude in the hits situation was significantly larger than that of the CR with negative faces (t=6.09, P<0.01), and was similar with positive faces (t=7.33, P<0.01). However, for hits in the control group, the P2 amplitude for recognition of negative faces was much higher than that for recognition of neutral faces

Table 4 Amplitude and latency of p100 component

	Amplitude (µV)				Latency (msec)			
	Control		Amnestic MCI		Control		Amnestic MCI	
	01	02	01	02	01	02	01	02
Negative								
Hit	3.273	3.495	3.209	3.231	92	89	88	92
CR	2.907	3.107	3.588	3.493	91	91	90	91
T1	1.704	1.086	−1.797	−0.330	1.733	−0.096	−1.528	0.683
P-value	0.095	0.283	0.079	0.743	0.090	0.924	0.133	0.498
Neutral								
Hit	3.278	3.497	3.273	2.921	97	94	97	96
CR	3.473	3.026	3.025	2.923	95	97	92	95
T2	−1.907	1.545	1.528	0.799	1.400	−0.912	0.111	1.722
P-value	0.063	0.129	0.133	0.428	0.168	0.366	0.912	0.092
Positive								
Hit	2.924	3.028	2.885	3.270	92	89	92	88
CR	3.329	2.928	3.278	3.228	88	93	91	92
T3	1.820	0.330	−1.911	0.521	1.632	−1.197	1.310	−0.125
P-value	0.075	0.743	0.062	0.605	0.109	0.237	0.197	0.901
F3	0.254				1.181			
P-value	0.776				0.311			

Abbreviations: CR, correct rejetions; msec, milliseconds; MCI, mild cognitive impairment.

(t=5.17, $P<0.01$) and positive faces (t=3.36, $P<0.05$), and the difference was significant. In the amnestic MCI group, at the P08 recording electrode, the peak hits for negative faces was more positively shifted than the CR peak for negative faces (t=6.60, $P<0.01$), but no statistically significant differences were observed for P2 peak latency ($F<0.81$, $P>0.05$, Table 7). This result suggests that when the tested subjects tried to recognize negative faces, they could distinguish easily between studied faces and unstudied faces. The participants retained the negative face recognition effect, and had a more accurate memory for negative faces. P2 is believed to be more sensitive to emotional information,[37–39] and our results suggest that negative emotional information improves face information processing during the learning period.

Table 5 Amplitude and latency of N170 component

	Amplitude (µV)				Latency (milliseconds)			
	Control		Amnestic MCI		Control		Amnestic MCI	
	P07	P08	P07	P08	P07	P08	P07	P08
Negative								
Hit	3.463	3.683	3.346	3.745	156	147	166	157
CR	2.250	1.505	3.525	3.726	151	152	158	152
T1	0.393	5.610	−0.962	1.243	1.762	−0.513	1.419	1.749
P-value	0.696	0.000	0.341	0.22	0.085	0.61	0.163	0.087
Neutral								
Hit	2.495	2.044	2.047	2.657	152	145	162	158
CR	2.944	2.576	2.73	2.933	154	156	157	161
T2	−0.89	−0.258	−0.78	−0.03	−0.981	−0.981	0.289	−0.571
P-value	0.378	0.797	0.439	0.976	0.331	0.331	0.774	0.571
Positive								
Hit	3.534	3.496	3.262	3.594	149	154	151	158
CR	2.047	2.622	3.534	3.384	144	150	153	166
T3	1.5	3.115	−1.12	0.393	0.464	0.834	−0.018	−0.313
P-value	0.14	0.013	0.268	0.696	0.645	0.408	0.986	0.756
F3	13.127				11.125			
P-value	0.001				0.002			

Abbreviations: CR, correct rejections; MCI, mild cognitive impairment.

Table 6 Amplitude and latency of VPP component

	Amplitude (μV)				Latency (msec)			
	Control		Amnestic MCI		Control		Amnestic MCI	
	FZ	CZ	FZ	CZ	FZ	CZ	FZ	CZ
Negative								
Hit	15.44	14.800	15.229	14.152	163	160	163	153
CR	14.358	13.342	13.106	13.172	161	156	153	162
T1	0.644	0.153	13.30	0.213	1.817	1.699	0.21	−0.331
P-value	0.523	0.879	0.000	0.832	0.076	0.096	0.835	0.742
Neutral								
Hit	13.323	13.729	13.197	13.129	152	162	162	157
CR	14.152	13.187	12.152	13.187	161	155	159	162
T2	−0.122	0.417	1.117	−1.591	−1.439	0.168	0.469	−0.204
P-value	0.903	0.679	0.27	0.118	0.157	0.867	0.641	0.839
Positive								
Hit	15.057	14.438	14.162	13.687	147	157	165	163
CR	14.197	14.687	15.197	13.242	163	149	163	155
T3	1.421	−0.043	−0.033	1.258	−1.772	0.213	0.968	1.354
P-value	0.162	0.966	0.974	0.215	0.083	0.832	0.338	0.182
F3	17.272				0.154			
P-value	0.000				0.697			

Abbreviations: CR, correct rejections; MCI, mild cognitive impairment; CZ, central zone; FZ, frontal zone; VPP, vertex positive potential; msec, milliseconds.

ERP old/new effect

In the control group, the average amplitude of the negative face hits was greater than the average CR amplitude in the early time window. This effect appeared in F5 (t=6.65, $P<0.01$), the frontal zone (t=7.07, $P<0.01$), and the central zone (t=5.33, $P<0.01$). The result was similar for recognition of positive faces at recording electrodes in the frontal zone (t=3.17, $P<0.05$) and central zone (t=13.80, $P<0.001$). In the control group, when compared with neutral face recognition, the peak for angry face hits was more positively shifted. This emotional effect was found only in the frontal zone (t=6.01, $P<0.01$) and central zone (t=6.82, $P<0.01$). In the amnestic MCI group, the average hits amplitude was larger than the average CR amplitude. This emotional effect occurred in the frontal zone (t=5.14, $P<0.01$) and the central zone (t=3.78, $P<0.05$). Compared with the control group, the amplitude of hits for angry faces was more positively offset than that for neutral faces. This emotional effect was found in the

Table 7 Amplitude and latency of P2 component

	Amplitude (μV)				Latency (msec)			
	Control		Amnestic MCI		Control		Amnestic MCI	
	P07	P08	P07	P08	P07	P08	P07	P08
Negative								
Hit	3.935	3.944	3.317	3.307	223	241	235	212
CR	2.553	2.246	3.163	3.597	231	221	241	242
T1	0.364	6.091	0.468	6.603	−0.611	0.068	−0.221	−1.229
P-value	0.717	0.000	0.642	0.000	0.544	0.946	0.826	0.225
Neutral								
Hit	3.194	3.177	2.315	2.993	215	235	247	229
CR	2.782	2.750	2.847	2.946	233	226	241	231
T2	1.249	0.617	−0.061	1.788	−0.31	0.458	0.88	−1.027
P-value	0.218	0.54	0.952	0.08	0.758	0.649	0.383	0.31
Positive								
Hit	3.415	3.534	3.438	3.858	215	217	237	241
CR	3.024	3.265	2.912	2.633	224	241	223	222
T3	0.311	7.332	1.769	1.091	−1.729	−1.613	1.813	1.172
P-value	0.757	0.000	0.083	0.281	0.090	0.113	0.076	0.247
F3	17.021				3.49			
P-value	0.000				0.068			

Abbreviations: CR, correct rejections; MCI, mild cognitive impairment; msec, milliseconds.

Table 8 Old/new effect in early time window

	Negative				Neutral				Positive			
	Hit	CR	T1	P-value	Hit	CR	T2	P-value	Hit	CR	T3	P-value
Frontal												
Control	3.934	3.27	2.534	0.015	3.032	3.010	1.405	0.167	3.597	3.369	2.218	0.031
Amnestic MCI	2.763	2.544	0.278	0.782	2.376	2.239	0.014	0.989	2.484	2.140	0.905	0.37
Central												
Control	3.814	2.474	3.994	0.000	3.017	2.644	0.341	0.735	3.809	3.346	2.332	0.024
Amnestic MCI	2.614	1.979	0.783	0.438	3.582	3.380	0.75	0.457	3.727	3.119	−0.725	0.472
Parietal												
Control	3.400	4.688	−3.707	0.001	3.369	3.177	0.228	0.821	4.178	3.579	2.258	0.029
Amnestic MCI	3.499	2.054	1.013	0.316	3.248	3.164	0.571	0.571	3.068	2.954	0.264	0.793
Occipital												
Control	3.928	3.624	0.748	0.458	3.391	3.234	0.761	0.451	3.833	3.048	1.146	0.258
Amnestic MCI	3.142	2.988	2.113	0.040	3.009	2.812	0.361	0.72	3.536	2.944	0.244	0.809
Left												
Control	3.784	3.127	2.681	0.010	3.331	2.025	0.703	0.486	3.834	3.799	0.157	0.876
Amnestic MCI	3.036	2.647	0.089	0.929	2.992	2.317	1.402	0.168	2.923	2.354	−0.192	0.849
Midline												
Control	4.334	2.488	2.645	0.011	3.052	2.422	0.319	0.751	3.429	3.286	2.025	0.049
Amnestic MCI	3.229	2.302	0.417	0.679	2.253	2.369	−0.66	0.512	2.559	2.334	−1.725	0.091
Right												
Control	2.983	2.080	0.088	0.931	2.296	2.098	1.068	0.291	3.471	3.192	−0.546	0.587
Amnestic MCI	3.221	3.026	1.053	0.298	2.110	2.339	−0.294	0.77	3.211	3.130	0.944	0.35

Abbreviations: CR, correct rejections; MCI, mild cognitive impairment.

frontal zone (t=6.90, P<0.01) and central zone (t=12.41, P<0.001, Table 8).

In the control group, the hits amplitude for positive faces was greater than the CR amplitude in the late time window. The main electrodes showing this phenomenon were at the central zone (t=14.69, P<0.001) and parietal zone (t=15.28, P<0.001). Similar results were also obtained with negative faces at the main electrodes of the central zone (t=7.02, P<0.01) and parietal zone (t=5.33, P<0.01). In the control group, the hits amplitude for negative faces was greater than

Table 9 Old/new effect in late time window

	Negative				Neutral				Positive			
	Hit	CR	T1	P-value	Hit	CR	T2	P-value	Hit	CR	T3	P-value
Frontal												
Control	3.511	3.462	0.041	0.967	3.332	2.827	1.815	0.076	3.347	3.267	2.716	0.009
Amnestic MCI	3.132	3.287	−0.036	0.971	1.770	2.702	−1.737	0.089	2.912	2.109	0.122	0.904
Central												
Control	3.690	3.117	4.317	0.000	3.122	2.387	1.652	0.105	3.297	2.727	2.179	0.034
Amnestic MCI	2.142	2.887	−0.138	0.891	3.273	2.019	1.582	0.12	2.747	2.832	−0.040	0.968
Parietal												
Control	3.797	3.527	3.456	0.001	3.622	3.027	1.562	0.125	3.228	1.409	1.967	0.055
Amnestic MCI	3.357	3.162	1.130	0.264	2.102	2.222	−1.16	0.252	3.512	2.467	1.116	0.27
Occipital												
Control	3.421	2.742	−1.361	0.18	2.059	2.027	1.059	0.295	2.672	1.777	1.267	0.211
Amnestic MCI	3.102	3.146	−1.565	0.124	3.452	3.471	−0.925	0.36	2.019	2.131	−1.705	0.095
Left												
Control	2.767	2.022	0.982	0.331	2.489	2.537	−0.901	0.372	2.247	2.927	−0.671	0.506
Amnestic MCI	2.014	2.308	−0.727	0.471	3.252	2.523	−0.622	0.537	2.342	2.429	−1.704	0.095
Midline												
Control	3.629	3.650	−2.123	0.039	2.297	2.177	0.491	0.626	2.539	2.877	−3.850	0.000
Amnestic MCI	2.422	2.152	0.467	0.643	2.537	3.262	0.317	0.753	2.279	2.752	−1.411	0.165
Right												
Control	2.997	2.408	0.008	0.994	2.527	3.47	0.223	0.825	2.976	2.752	1.880	0.066
Amnestic MCI	2.899	2.377	0.373	0.711	2.898	2.932	−1.815	0.076	2.252	2.049	0.583	0.563

Abbreviations: CR, correct rejections; MCI, mild cognitive impairment.

that for either positive faces ($t=6.38$, $P<0.01$) or neutral faces ($t=4.72$, $P<0.05$). However, in this late time window, no significant difference of old/new effect was observed in the amnestic MCI group (Table 9).

Discussion

In the current study, we investigated the time course of emotional face recognition in patients with amnestic MCI and in healthy controls by measuring behavioral and ERP data. Our main findings are summarized here. The accuracy of face recognition memory was lower in patients with amnestic MCI than in healthy controls, which supports the presence of damaged episodic memory in amnestic MCI.[2,11] Both patients with amnestic MCI and healthy controls showed an emotional preference for face memory. Compared with emotional faces (positive and negative), the hits rate was relatively low and the false positive rate was relatively high for neutral faces. The accuracy of face memory is clearly reduced for a neutral face. This finding indicates that emotional messages can improve episodic memory in amnestic MCI, which is supported by similar studies.[11,40,41]

P100 reflects visual processing, a positive going wave in the occipital lobe with its peak normally observed in the 100 milliseconds range post-stimulus onset.[42–44] P1 is one of the components of P100, and can be modulated by attention. In this study, we did not find a difference in P1 amplitude and latency between patients with amnestic MCI and healthy controls, indicating that early visual processing during face recognition was not damaged in patients with amnestic MCI. Schefter et al found that the amplitude of P100 for hits was increased compared with that for CR, independent of emotion or group.[11] However, we did not find similar results in our study. The difference between our current study and the previous one may reflect the fact that Schefter et al reused old studied faces in their test phase. The learning procedure and test producer are also different, such as test face presentation time when test session runs. All these factors could contribute to this discrepancy. However, this would not affect the conclusion of our study, since it is independent of emotion and group.

N170 is a negative wave that can be recorded in the temporal occipital region. The N170 component is thought to be related to face structural encoding.[45,46] In the current study, we found that N170 was delayed in patients with amnestic MCI when compared with healthy controls. The increase in N170 latency in patients with amnestic MCI indicates that the face structure encoding process may be slowed down by this disease. Similar results have been reported elsewhere.[11,47,48] In addition, with regard to N170 amplitude, the healthy

controls showed a recognition effect with negative faces and positive faces, but not with neutral faces. However, the patients with amnestic MCI did not show a face recognition effect, suggesting that emotional face recognition is impaired in patients with amnestic MCI in term of face structural encoding. Further analysis demonstrated that an emotion effect was present for hits but not for CR. However, previous studies of N170 have reported both a face familiarity effect[49,50] and a face emotion effect.[51,52] The interaction of these two face recognition effects over the right hemisphere has been reported. Hits can represent this interaction, yet CR does not share the characteristic of face familiarity. A candidate process driving this interaction effect could be attention because facial emotion can serve as a cue to attract attention to the face in order further to assist the process of face recognition.[51,53,54]

P2 showed a strong signal in the temporal and occipital sites, which is considered to reflect visual processing associated with perceptual grouping.[55] P2 is believed to be more sensitive to emotional information.[53–55] With regard to face recognition, P2 may reflect an early identification process.[49,56,57] Like N170, in healthy controls P2 showed a memory recognition effect for negative and positive faces, but not for neutral faces. Thus, our results strongly support the conclusion of previous studies, ie, that an emotional message can improve memory processing.[49,57] It has been suggested that within the context of face memory, P2 may reflect an early recognition process involved in personalized face recognition.[56] For patients with amnestic MCI, P2 demonstrated a memory recognition effect only with negative faces, but not with neutral or positive faces. Therefore, our results imply that in the early frontal processing stage, patients with amnestic MCI are still able to make personalized processing for negative faces, but not for neutral faces or positive faces. This indicates that emotional recognition and memory processing is impaired in patients with amnestic MCI and that these impairments in the early recognition process are selective for neutral and positive emotional faces. In other words, the advantageous negative emotional effect in the early recognition process is preserved in patients with amnestic MCI.

In addition, hits show an emotional effect on P2, since emotional stimuli can produce automatic visual attention.[56–58] Schefter et al[11] suggest that the recognition effect of hits with negative emotional faces might result from a one-way or reciprocal influence in the processing stage.

ERP old/new effect

ERPs are sensitive to neural activity underlying recognition. Measuring ERPs during the recognition test, a study/test

paradigm has been a fruitful research strategy when examining the effects of emotion on recognition memory. Generally correctly recognized "old" items elicit more positive moving waveforms than correctly rejected "new" items. This so-called "ERP old/new effect" consists of several temporally and spatially dissociable subcomponents.[58–61]

The first subcomponent is an early frontal old/new effect (300–500 milliseconds) that has often been associated with familiarity.[62–64] It has been suggested that the early frontal old/new effect may reflect implicit conceptual memory.[65–67] In young adults, the early frontal old/new effect is largely free from emotional stimuli,[68–72] but an early frontal old/new effect can be elicited by emotional stimuli in elderly people; neutral image cannot be drawn.[69]

In the early time window, an old/new effect could be observed with both negative and positive faces in the two tested groups, but not for neutral faces. For patients with amnestic MCI, no difference in frontal old/new effect was found in comparison with normal controls.

The second subcomponent is a parietal old/new effect (500–800 milliseconds), which is related to recollection.[14,64,73,74] Among the young subjects, compared with neutral stimuli, emotional stimuli would enhance this effect.[68–72,75,76] It has been pointed out that when tested subjects fail a recollection task, the old/new effect became weakened or absent.[77]

In the present study, emotional stimuli (positive faces and negative faces) led to a parietal old/new effect in the control group. However, neutral stimuli did not lead to the same effects, which is consistent with previous studies suggesting that non-emotional information has no parietal old/new effect.[78]

In the current study, we found that three types of stimuli (emotional and neutral faces) did not elicit any parietal old/new effect in patients with amnestic MCI. Since the parietal old/new effect is an indicator of recollection,[58–61] our results suggest impairment of recollection in patients with amnestic MCI. Previous behavioral data support the idea that recollection is impaired in patients with amnestic MCI.[19–21,23,79,80] This impairment may be closely associated with amnestic MCI, and the data strongly suggest that patients with amnestic MCI have difficulties in the late stage of emotional processing. Moreover, at this stage, the advantageous effect of negative face recognition even disappeared. This is not supported by a previous report[11] in which patients with amnestic MCI demonstrated a parietal old/new effect with negative faces. However, in that study, the old pictures were repeatedly presented in the learning stage, and the difference between that study and ours does suggest that a parietal old/new effect could be induced with intense stimuli in patients with amnestic MCI.

Conclusion

Our results show that in patients with amnestic MCI, face recognition was impaired for negative faces in terms of face structural encoding. However, emotional stimuli can enhance episodic memory in patients with amnestic MCI. The impairment of emotional face recognition in patients with amnestic MCI mainly occurred during the stage of structural encoding and in the early recognition stage when the stimuli were individualized. In addition, we found difficulties in the late stage of emotional processing in patients with amnestic MCI.

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Disclosure

The authors report no conflicts of interest in this work.

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