Neurophysiologie Clinique/Clinical Neurophysiology (2019) 49, 235—242

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com/en

ORIGINAL ARTICLE

Temporal Characteristics of Attentional Disengagement from Emotional Facial Cues in Depression

Qiangfeng Zhao[a,1], Xiong Jiao[a,b,1], Yingying Tang[b], Shan Chen[a], Shanbao Tong[a,c], Jijun Wang[b,c,d,**], Junfeng Sun[a,c,*]

[a] *Shanghai Med-X Engineering Research Center, School of Biomedical Engineering, Shanghai Jiao Tong University, 200030 Shanghai, China*
[b] *Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China*
[c] *Brain Science and Technology Research Center, Shanghai Jiao Tong University, Shanghai, China*
[d] *Bio-X Institutes, Key Laboratory for the Genetics of Developmental and Neuropsychiatric Disorders (Ministry of Education), Shanghai Jiaotong University, 200030 Shanghai, China*

Received 4 September 2018; accepted 4 March 2019
Available online 19 March 2019

KEYWORDS
Depression;
Attentional disengagement;
ERP;
Contingent negative variation

Summary
Objectives. — Studies have reported that depressed patients have difficulties in disengaging attention from negative information, but knowledge of the temporal characteristics of this disengagement is still rudimentary. Our objective is to reveal the temporal characteristics of attentional disengagement from emotional facial cues in depression.
Methods. — We recruited 22 depressed patients and 22 healthy controls to participate in a cued target-response task with emotional facial expressions (happy, natural, and sad) as cues and three types of cue-target intervals (CTIs: 350 ms, 1000 ms, and 1500 ms). Both behavioral and electroencephalography (EEG) data were collected from each subject while performing the task. Then, both behavioral results and event-related potentials (ERPs) were analyzed across groups (depressed patients and normal controls), emotional types of facial cues (happy, natural, and sad), and CTIs.
Results. — Both depressed patients and healthy controls had shorter response times in the conditions of CTI = 1000 ms and 1500 ms than in the condition of CTI = 350 ms but had no significant difference in response time between the conditions of CTI = 1000 ms and CTI = 1500 ms.

* Corresponding author at: School of Biomedical Engineering, Shanghai Jiao Tong University, Shanghai, China.
** Co-corresponding author at: Shanghai Key Laboratory of Psychotic Disorders, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai, China.
E-mail addresses: jijunwang27@163.com (J. Wang), jfsun@sjtu.edu.cn (J. Sun).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.neucli.2019.03.001
0987-7053/© 2019 Elsevier Masson SAS. All rights reserved.

The contingent negative variation (CNV), a well-documented ERP marker of cue-induced expectation of the forthcoming target, clearly appeared about 1000 ms following cue onset for normal controls and 1300 ms following cue onset for depressed patients. Statistical analysis by repeated-measures Anova showed that a main group effect exists for the average amplitudes of ERPs at electrode Cz 930 ms after cue onset, while there was no main effect of cue or interaction effect between cue and group.

Discussion. — These results suggest that normal controls complete their attentional disengagement from emotional facial expression between 350 ms to 1000 ms after cue offset, while depressed patients complete their attentional disengagement later than that of normal controls but earlier than 1500 ms from the perspective of CNV onset, though the two groups have no significant difference in response time in the conditions of CTI = 1000 ms and CTI = 1500 ms respectively.

© 2019 Elsevier Masson SAS. All rights reserved.

Introduction

Depression is one of the most prevalent psychiatric disorders, characterized by sustained negative affect and loss of pleasure [1]. Cognitive theories of depression suggest that depressed patients exhibit biases in emotional material processing [13]. Beck proposed a theory that long-term memory representations lead individuals to filter information from their environment [2]. Furthermore, the memory representations of depressed patients were speculated to contain themes of loss, separation, failure, worthlessness and other negative features; thus, depressed patients will exhibit a systematic bias in their processing of environmental information related to these negative themes [2]. In addition, another study found that the theme-processing bias in depression was influenced by promoting the salience of negative material and reducing the salience of positive material [16].

Related to the prediction of specific theme-processing bias, studies have examined negative attentional bias, where depressed patients, compared with healthy controls, showed enhanced attention towards negative material rather than neutral material [6,11,14,15,19,24]. For example, in a dot-probe task using emotional faces as cues, Gotlib et al. found that depressed participants, compared with non-depressed participants, more easily directed their attention selectively to negative faces (presented for 1000 ms) than to non-negative faces [14]. Later, in a meta-analysis of 12 dot-probe experiments, Peckham et al. found a significant difference in the magnitude of the attentional bias between depressed and control participants [25]. In recent years, eye-tracking technology, which allows continuous monitoring of focus of gaze and provides indicators of attention, has been used to investigate attentional bias. Eizenman et al. found that depressed patients had significantly longer average glance durations for pictures with themes of sadness and failure, compared with non-depressed controls [10]. In another eye-tracking study, Caseras et al. found that depressed patients were not more likely than non-depressed controls to shift their attention toward negative expressions, but spent significantly more time looking at negative expressions once their attention was focused on them [4]. These findings suggest that depressed patients are characterized by having difficulties in disengagement from negative information rather than orienting attention toward negative information [13]. Moreover, it has been claimed that the assessment of attentional disengagement is important in interpreting the attentional bias in depression [21].

Presently, findings regarding impaired disengagement from negative material are mostly associated with visuospatial tasks which focus on attentional shifts in space. Studies on dysfunctional attentional inhibition to negative materials also used spatial distractor paradigms. For example, using a negative affective priming task, in which each trial consisted of two adjectives presenting as target and distractor respectively, Joormann et al. assessed the relations between inhibition and individual differences in the habitual use of rumination, reappraisal, and expressive suppression in depressed patients [19]. However, the study of the temporal characteristics of attentional disengagement in depression is rare. Human emotional facial expression is typically responsive to social interactions, and this responsiveness may be an indicator of effects on social function in depression [7]. Moreover, for depressed patients, knowledge of the consequences of continued attention to emotional facial expressions when processing a following target is still rudimentary. It has been reported that former visual expressions would influence subjects' response to subsequent stimuli, especially in the case of a short cue-target interval (CTI) (450∼500 ms) [9]. In our previous study, various CTIs (i.e., Exp. I: 17 ms, 350 ms and 1000 ms; Exp. II: 600 ms and 1500 ms) were used to investigate the influence of different emotional facial cues on the detection of subsequent visual digit targets [5]. The results showed that response time was faster as the CTI increased in both experiments, which suggested that attentional disengagement occurred between 350 ms and 1000 ms in healthy controls. Based on the results that depressed patients had difficulties

Table 1 The demographic data [mean (std)] of the subjects.

	MDD ($N=22$)	HC ($N=22$)	$T(38)/\chi^2$	P value
Age	31.68 (9.75)	33.91 (8.93)	−0.79	0.434
Gender[a] (males/females)	12/10	9/13	0.801	0.371
Education years	13.85 (2.46)	14.55 (3.33)	−0.756	0.454
HAMA	11.77 (2.22)	1.23 (1.02)	20.22	<0.001
HAMD	23.14 (3.71)	2.14 (2.25)	22.71	<0.001
SAS	55.50 (7.79)	32.14 (5.29)	12.51	<0.001
SDS	66.68 (9.29)	36.50 (6.47)	11.64	<0.001

MDD: major depressive disorder; HC: healthy controls; HAMA: Hamilton Rating Scale for Anxiety; HAMD: Hamilton Rating Scale for Depression; SAS: Self-rating Anxiety Scale; SDS: Self-rating Depression Scale; std: standard deviation.
[a] Chi^2 test were used for gender comparison.

in disengaging from negative information [13], we hypothesized that depressed patients need more time to disengage their attention from emotional facial cues than healthy controls. Thus, in this study, we adopted a similar cued target-response task with emotional facial expressions as cues, using three types of CTIs (i.e., 350 ms, 1000 ms and 1500 ms) to explore the temporal characteristics of attentional disengagement in depression.

In addition to the behavioral responses with respect to the different CTIs, the event-related potential (ERP) is a suitable tool to investigate the temporal characteristics of attentional disengagement, as it has high temporal resolution and can monitor the whole neural processes engaged in a cognitive function [7,23]. In a cued reaction time experiment, a negative ERP wave, called the contingent negative variation (CNV), is present in the period between the presentation of the warning stimulus and the response stimulus [27]. CNV has also been observed in other studies [3,12,18]. Generally, CNV is a well-documented ERP marker appearing over frontal—central areas that reflects motor preparation [27]. Moreover, CNV located within Broadmann's area 6 may also reflect attention and expectation [20]. Considering that adequate preparation for the forthcoming response indicates attentional disengagement from the former cues, we used CNV as a biomarker to monitor depressed patients' attentional disengagement from emotional facial cues in addition to the behavioral responses in this study.

Based on the previous studies, we hypothesized that healthy subjects would have their attentional disengagement from emotional facial expression during a particular period (possibly 350 ms to 1000 ms) after the end of cue presentation, while depressed patients may need more time to disengage their attention from emotional facial cues than healthy controls. Correspondingly, a CNV was expected to appear only in the condition of a CTI long enough to allow complete attentional disengagement. To examine this hypothesis and whether depressed patients have different temporal characteristics of disengagement from emotional facial cues compared with healthy controls, we recruited 22 depressed patients and 22 healthy controls to take a cued target-response task with emotional facial expressions as cues, using three types of CTIs (i.e., 350, 1000 and 1500 ms). EEG signals and behavioral responses were recorded during the experiment. ERPs (especially CNVs) were used to investigate the temporal characteristics of attentional disengagement from emotional facial expression in depression.

Methods

Participants

In this study, we enrolled 22 outpatients with major depressive disorder (MDD) and 22 healthy controls (HC), matched for age, gender, and education (Table 1). All the MDD subjects, recruited from Shanghai Mental Health Center, Shanghai, China, fulfilled ICD-10 diagnosis criteria for MDD and had no history of manic episodes. All the HCs, recruited from the local community in Shanghai, had no history of psychosis, substance or alcohol abuse. All the subjects had normal or corrected-to-normal vision. All the subjects agreed to participate in this study with written informed consent after complete description of the study, and were compensated for their time. Before the experimental session, all subjects took assessments of Hamilton Rating Scale for Anxiety (HAMA), Hamilton Rating Scale for Depression (HAMD), Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS) by attending doctors or senior doctors. All HCs received scores in the normal range (Table 1). Experimental protocols, proposed in compliance with the Helsinki Declaration, were reviewed and approved by the Ethics Committee of Shanghai Mental Health Center.

Materials

The cues used in this study included 12 happy, 12 neutral and 12 sad facial pictures, as well as 5 control pictures of neutral objects (e.g. desk). The emotional facial pictures were selected from the Nimstim facial picture set [26] by rating experiment. All the 171 facial pictures were converted into gray color with the same average luminance and the hair in each facial picture was cut off. Then, 10 healthy students from Shanghai Jiao Tong University rated the 171 facial pictures on dimensions of valence and arousal on a 9-point scale (1 = ''extremely negative valence, extremely low arousal'' to 9 = ''extremely positive valence, extremely high arousal''). For the selected pictures, happy and sad faces were matched for arousal ratings (6.62 ± 0.34 vs.

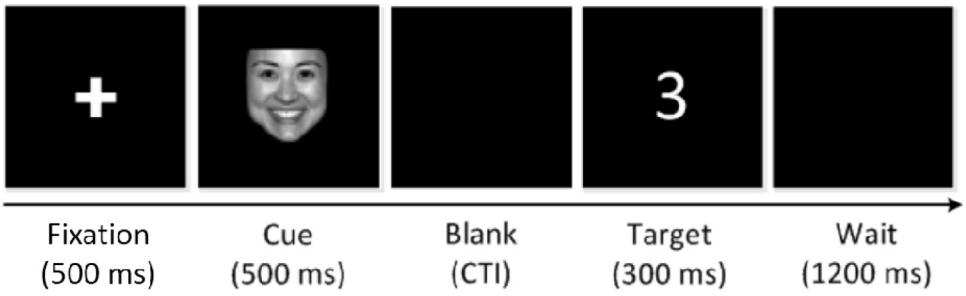

Figure 1 The cued target-response task with three types of cue-target intervals (CTIs), i.e., 350 ms, 1000 ms and 1500 ms.

6.79 ± 0.61, $P = 0.561$), which are higher than that of neutral faces (3.18 ± 0.23, $P < 0.001$). Additionally, the happy faces (7.51 ± 0.22), sad faces (2.02 ± 0.47), and neutral faces (4.43 ± 0.21, $P < 0.001$) were different from each other in valence ratings. Males and females were represented equally in the selected facial pictures.

Experiment Task and Procedure

The cued target-response task, modified from our previous study [5], was used (Fig. 1). In each trial, a cue consisting of a picture from one of the four types (i.e.,happy, sad, neutral, or control object) with equal probabilities was first presented at the center of screen for 500 ms, followed by a blank black screen which is called the cue-target interval (CTI). After CTI, a digit target (digit ''3'' or ''5'') appeared for 300 ms with equal probabilities. In each trial, participants were asked to pay attention to the emotional facial cue, and then respond to the target by pressing the left mouse button for digit ''3'' or the right mouse button for digit ''5'' as quickly as possible, but did not respond when a non-facial object cue was presented. Here, trials of non-facial neutral objects were used to ensure the participants' involvement during the experiment. Based on the behavioral results of healthy subjects reported in our previous study [5], we hypothesized that healthy subjects would have their attentional disengagement from emotional facial cues during the period from 350 ms to 1000 ms after the end of cue presentation, while depressed patients would need more time in disengaging their attention from emotional facial cues than healthy controls. Three different CTIs (i.e., 350 ms, 1000 ms, and 1500 ms) were used in different trials with equal probabilities. We expected that for healthy controls, there would be a significant difference in response time between the cases of CTI = 350 ms and CTI = 100 ms, but no significant difference in response time between the cases of CTI = 1000 ms and CTI = 1500 ms. On the other hand, for depressed patients we expected that there would be some difference in response time and/or ERPs from those of healthy controls in the cases of CTI = 1000 ms or CTI = 1500 ms, which would indicate their slower attentional disengagement from emotional facial cues. For each subject, the cognitive task consisted of 6 blocks of 120 trials with pseudo-randomized cue types and CTIs, resulting in 60 trials for each combination of the four different cue types and three CTIs.

Experiments were conducted in a sound-attenuated and electrically shielded room. For each subject performing the experiment, EEG signals of 32 channels were recorded continuously using an elastic cap (EasyCap, Brain Products, Germany) with sampling rate of 1000 Hz and skin impedance below 10 kΩ at each electrode. Horizontal and vertical electrooculograms (HEOG and VEOG, respectively) were recorded to help to remove artifacts and eye blinks in the following EEG signal pre-processing. All EEG signals were referenced to the tip of the nose and the AFz electrode was used as ground. Behavioral data (response time and accuracy) were also recorded during the experiment.

Data Pre-processing

Trials were excluded when response time was shorter than 200 ms or longer than 800 ms, with the considerations that: (i) response time shorter than 200 ms would imply an erroneous response in the trial, as previous studies have suggested that the response time is generally at least 200 ms; (ii) response time longer than 800 ms would indicate delayed response or inadequate involvement in the trial, as it is out of the range of two standard deviations of response time over all trials. The EEG data were pre-processed offline with Brain Vision Analyzer 2.0 (Brain Products, Germany). The raw data was first digitally filtered using a zero phase-shift, 0.5—100 Hz bandpass filter (24db/Oct) and a 50 Hz notch filter. The EEG data was then re-referenced to an average reference of all electrodes and ocular artifacts were corrected using ICA algorithm. Artifact-free data was then segmented into epochs. For the trials of CTI = 1000 ms, EEG epochs from 200 ms pre-cue to 1500 ms after cue onset were extracted, and for the trials of CTI = 1500 ms, EEG epochs from 200 ms pre-cue to 2000 ms after cue onset were extracted. Trials with artifacts greater than 100 μV after EOG correction were rejected. Finally, 20 MDD patients and 20 HCs, who had more than 40 valid trials for each type of cue in each CTI condition, were included for further analysis. For the retained subjects, the numbers of valid trials were 49.8 ± 6.5, 49.1 ± 6.2, 49.4 ± 6.5 for happy, neutral, and sad faces in MDD group respectively, and 49.5 ± 7.2, 50.1 ± 7.8, 50.4 ± 6.9 for happy, neutral, and sad faces in HC group respectively.

To explore the temporal characteristics of attentional disengagement from emotional facial cues, we focused on the onset of the CNV component, which was typically observed over fronto—central areas preceding the target

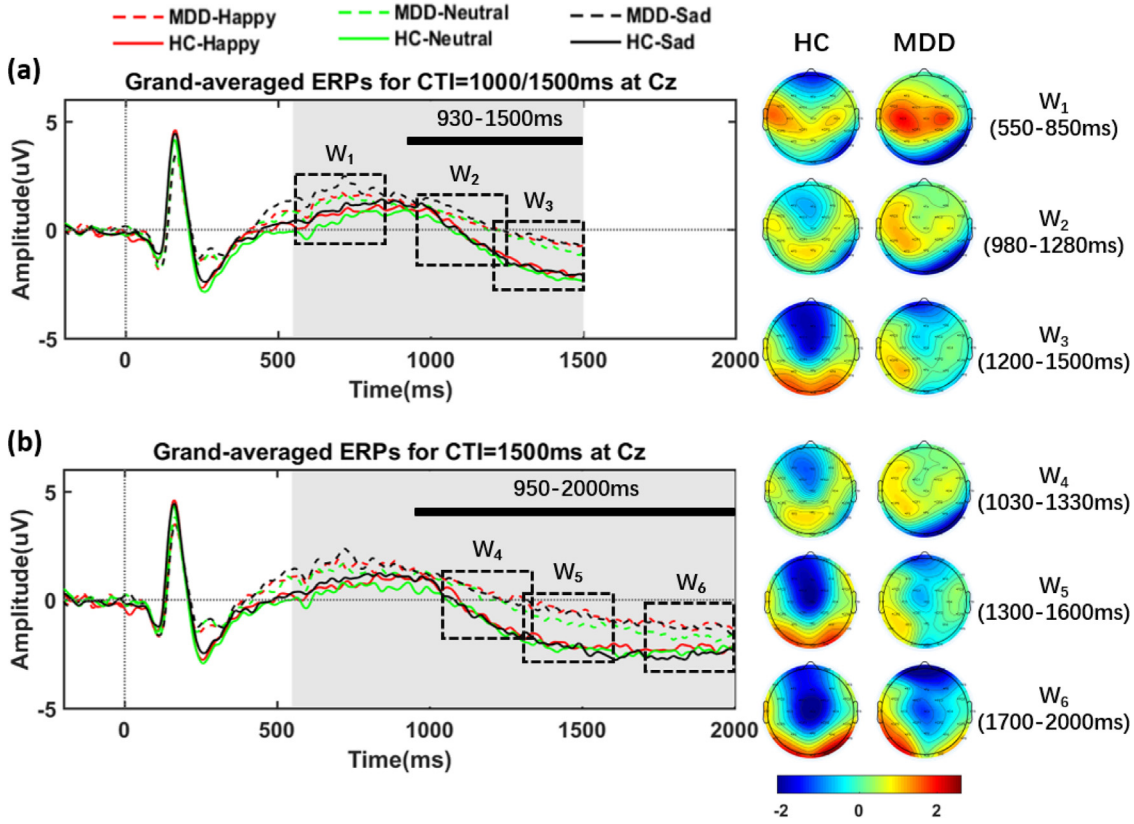

Figure 2 Grand-averaged ERPs elicited by happy, neutral and sad facial cues in depressed patients (MDD) and healthy controls (HC) in the pooled trials of CTI = 1000 ms and CTI = 1500ms (a), and the trials of CTI = 1500 ms (b) at electrode Cz, and the topographies of average amplitudes of ERPs at all electrodes in the six selected windows (i.e., W_1, W_2, W_3, W_4, W_5, and W_6) in healthy controls and depressive patients respectively. The horizontal bars marked the periods in which there were main effects of group on the average amplitudes of ERPs in sliding windows at electrode Cz in statistical analysis by repeated-measures Anova.

onset. It has been reported that CNV would take several hundreds of milliseconds (about 500-600 ms) after the offset of cue to appear [12]. In order to examine the CNV component, ERPs were first calculated with the trials of CTI = 1000 ms and of CTI = 1500 ms pooled together to improve signal-to-noise ratio. To further examine the CNV component in a longer duration (i.e., 550 ms to 2000 ms from cue onset), ERPs were calculated with only the trials of CTI = 1500 ms. For the estimated ERPs, we further calculated the average amplitudes of ERPs in sliding windows (window width: 300 ms; moving step: 10 ms) starting from 550 ms from cue onset for each electrodes, and examined whether the average amplitude of ERP at electrode Cz in each sliding window was statistically smaller than zero by left-tailed one sample *t*-test. If the average amplitude of ERP at Cz in a certain window was smaller than zero and the topography of average amplitudes of ERPs for all electrodes showed a typical CNV pattern, i.e., negative average amplitudes of ERPs in the frontal—central electrodes (see the ERP topography of window W_6 in Fig. 2 for example), then we would claim that the CNV component appeared in the window. Here, the time window and electrode selection for CNV were based on literature and topographical distribution [3,18,22,27]. Note that the early ERP components (i.e. P1 and N170) of this experiment have been used to examine the early perceptual anomaly of negative facial expression in depression in another study [28].

Statistical Analysis

T-test and Chi^2 test were used to compare demographic data between MDD patients and healthy subjects respectively. Behavioral data, including response time and accuracy, were analyzed using repeated-measures Anova across emotion (three levels: happy face, neutral face, and sad face) and CTI (three levels: 350 ms, 1000 ms, and 1500 ms) with two groups (two levels: MDD, HC). A two-factor [emotion (three levels: happy face, neutral face, sad face) and X group (two levels: MDD, HC)] repeated-measures Anova was performed on the average amplitudes of ERPs at electrode Cz in each sliding window. All the Anovas were corrected for violations of the sphericity assumption using the Greenhouse—Geisser epsilon correction, and all post hoc *t*-tests were corrected by Bonferroni correction for multiple comparisons. The alpha level of significance was set at 0.05 throughout.

Results

Behavioral Results

Analyses of accuracy showed no main effects of group, emotion or CTI [$F(1,38) = 1.202$, $P = 0.280$; $F(2,76) = 2.958$, $P = 0.060$; $F(2,76) = 2.865$, $P = 0.074$]. The mean accuracy was

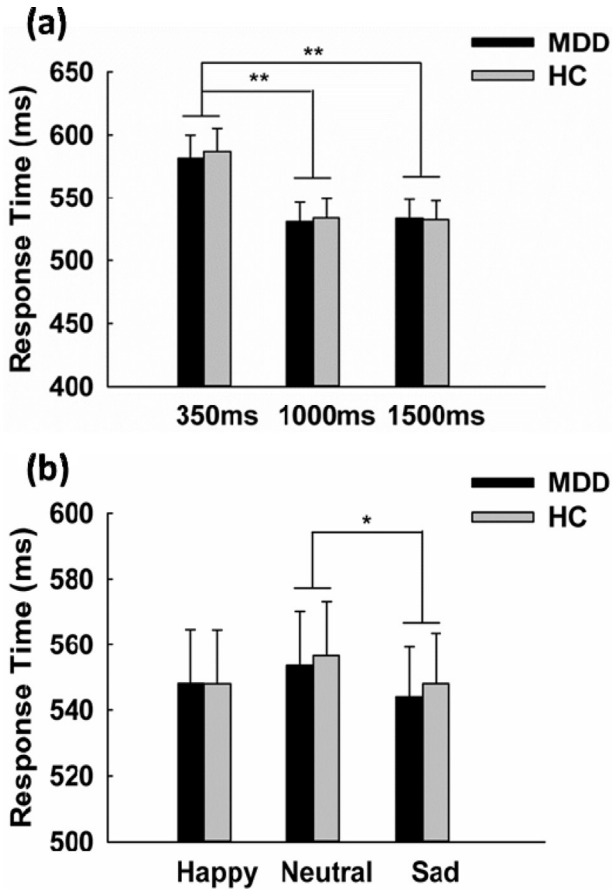

Figure 3 Response time for (a) conditions of CTI = 350 ms, 1000 ms and 1500 ms, and for (b) conditions of happy, neutral and sad facial cues in depressed patients and healthy controls. * indicates $P < 0.05$, and ** indicates $P < 0.01$. The error bars indicate mean ± SEM.

96.5% for MDD and 97.7% for HC, respectively, which showed that participants were engaged with the cued target-response task. Repeated-measures Anova on response time revealed significant main effects of CTI [$F(2,76) = 72.216$, $P < 0.001$]. Post-hoc pairwise comparisons showed that response time of CTI = 350 ms (583.75 ± 83.82 ms) was longer than those of CTI = 1000 ms (532.58 ± 67.85 ms, $P < 0.001$) and CTI = 1500 ms (533.15 ± 66.52 ms, $P < 0.001$) respectively, but there was no significant difference on response time between the conditions of CTI = 1000 ms and CTI = 1500 ms ($P = 0.982$) (Fig. 3a). The Anova also showed a significant main effect of emotion [$F(2,76) = 5.243$, $P = 0.007$]. Post-hoc pairwise comparisons indicated that response time of sad cues (546.09 ± 68.13 ms) was shorter than that of neutral cues (555.15 ± 72.99 ms, $P = 0.011$, Fig. 3b).

ERP results

The contingent negative variation (CNV), which is typically observed over fronto—central areas preceding the target onset, is a well-documented ERP marker of cue-induced expectation of the forthcoming target [3,18,27]. The appearance of CNV indicates that participants have prepared for the forthcoming targets. Correspondingly for the cognitive task in this study, the appearance of CNV may indicate that the subject accomplished their attentional disengagement from emotional facial cues.

ERPs were calculated with pooled trials of CTI = 1000 ms and of CTI = 1500 ms (Fig. 2a). Statistical analysis by repeated-measures Anovas (two factors: emotional cue X group) showed a main effect of group [$F(1,38) = 3.94$, $P = 0.0495$] on the average amplitudes of ERPs at electrode Cz in sliding windows starting from 930 ms after cue onset (marked by a black horizontal bar in Fig. 2a). However, there was no main effect of cue or interaction effect between cue and group. For the healthy controls (HC), left-tailed one-sample *t*-test showed that the average amplitudes of ERPs at Cz was smaller than zero in sliding windows starting from 980 ms after cue onset (i.e., W_2 in Fig. 2a, $P = 0.0165$), and typical CNV pattern began to appear in the ERP topography (i.e., negative average amplitudes of ERPs in the frontal—central electrodes such as Fz, Cz, FC1, and FC2) from window W_2 and lasted to 1500 ms after cue onset, suggesting that CNV appeared in HC from 980 ms after cue onset. On the other hand, for the MDD group, the average amplitude of ERPs at Cz in sliding windows was not significantly smaller than zero during the period from 550 ms to 1500 ms after cue onset, and the ERP topography also showed no typical CNV pattern during this period, indicating that CNV did not appear in the MDD group during this period. The ERP topography in a window (W_1) prior to window W_2 is given as a reference in Fig. 2a. Obviously, the ERP topography in window W_1 showed no typical CNV pattern.

To find the onset of CNV component for the MDD group, ERPs were further calculated with only the trials of CTI = 1500 ms (Fig. 2b). Statistical analysis by repeated-measures Anovas (two factors: emotional cue X group) showed a main effect of group [$F(1,38) = 4.15$, $P = 0.0439$] on the average amplitudes of ERPs at electrode Cz in sliding windows starting from 950 ms after cue onset (marked by a black horizontal bar in Fig. 2b). However, there was no main effect of cue or interaction effect between cue and group. For the HC group, left-tailed one-sample *t*-test showed that the average amplitudes of ERPs at Cz were significantly smaller than zero in sliding windows starting from 1030ms after cue onset (i.e., W_4 in Fig. 2b, $P = 0.0088$), and typical CNV pattern appeared in the ERP topography from window W_5 to 2000 ms after cue onset, suggesting that CNV appeared in the HC group from 1030 ms after cue onset. While for the MDD group, the average amplitudes of ERPs at Cz were smaller than zero in sliding windows starting from 1300 ms after cue onset (i.e., W_5 in Fig. 2b, $P = 0.0004$), and typical CNV pattern began to appear in the ERP topography from this window. In sliding windows later than window W_5, the typical CNV pattern in the MDD group became more evident, just as that demonstrated in window W_6 (Fig. 2b). These results suggested that the CNV appeared in the MDD group 1300 ms after cue onset, which was later than the time when CNV appeared in the HC group.

Discussion

The aim of this study was to investigate the temporal characteristics of attentional disengagement from emotional facial

expression in depressed patients, from the perspectives of response time and the onset latency of CNV. Results showed that both the MDD and HC groups had shorter response times in the conditions of CTI = 1000 ms and 1500 ms than in the condition of CTI = 350 ms, but had no significant difference in response time between the conditions of CTI = 1000 ms and CTI = 1500 ms (Fig. 3). These results suggested that a former emotional facial cue would influence the response to the following target which was presented after the cue offset, that is, attention would be maintained on the cue for a certain period, and it might take the subject some time to disengage and respond to the subsequent target. Thus, the longer response time for the case of CTI = 350 ms suggested that subjects had not entirely disengaged from the emotional facial cue at 350 ms after cue offset, while no difference in response time between the cases of CTI = 1000 ms and CTI = 1500 ms suggested that subjects had completed their attentional disengagement from emotional facial cue in 1000 ms after cue offset. These results implied that attentional disengagement from emotional facial expression was completed at a time point between 350 ms to 1000 ms after cue offset, which is consistent with the results (around 500 ms after cue offset) in healthy subjects reported in previous studies [5,9,12].

However, the CNV component indicated that there is a difference in the temporal characteristics of attentional disengagement from emotional facial expression between the MDD group and the HC group. The CNV component clearly appeared from about 1300 ms after cue onset for the MDD group and from about 1000 ms (980 ms in window W_2 and 1030 ms in window W_4) after cue onset for the HC group (Fig. 2). In addition, the average amplitudes of ERPs at electrode Cz in the MDD group were weaker than those in the HC group in windows from about 930 ms after cue onset (Fig. 2). For the HC group, the onset latency of CNV (about 1000 ms after cue onset) suggested that normal controls may complete their attentional disengagement from emotional facial expression just around 1000 ms after cue offset, which is in agreement with the temporal characteristics of attentional disengagement suggested by response time (i.e., completion of attentional disengagement between 350 ms to 1000 ms after cue offset). On the other hand, for the MDD group, the onset latency of CNV (1300 ms after cue onset) suggested that depressed patients may not complete their attentional disengagement from emotional facial cues before 1000 ms after cue offset, which is not consistent with the completion of attentional disengagement between 350 ms to 1000 ms after cue offset, suggested by response time.

Some studies have investigated the relationship between CNV and response time; however results are generally inconsistent and no evident relationships have been revealed [17]. Only a few studies have paid attention to the onset of CNV. In a study on patients with deficit schizophrenia (DS) and patients with bipolar I disorder (BP I), Li and his colleagues defined the period from the instant of target onset to the crossing point of ERP to baseline as the onset latency of CNV, and reported that the DS group had a longer onset latency of CNV than BP I group and healthy controls, and both the DS and BP I groups had significantly smaller CNV amplitude and longer reaction time than healthy controls [22]. Hillyard showed that only five of the ten subjects had a statistically significant negative correlation between CNV amplitude and response time [17]. In a study on post-traumatic stress disorder (PTSD), the subjects with PTSD had significantly larger CNV amplitude and more response errors than the subjects without PTSD, while the two groups had no statistically significant difference in response time [8]. In this study, we considered the first window in which the average amplitude of ERP at Cz was significantly smaller than zero at the instant of CNV onset, so as to average out the possible random effects that may be induced by fluctuations of ERP when it crosses the baseline. Based on the information in existing studies, we cannot demonstrate an evident relationship between CNV and response time and would like to propose that CNV and response time may characterize the process of attentional disengagement from different perspectives.

Studies have suggested that depressed patients may have greater difficulties in disengaging from negative information. For example, using eye-tracking technology, Eizenman et al. and Caseras et al. found that when focusing on negative cues, depressed patients spent significantly more time looking at them compared with non-depressed controls [4,10]. Note that the paradigms used in these two studies were based on visual spatial attention, while in our study with cued target-response paradigm, cues and targets were both presented at the center of screen. In order to explore the temporal characteristics of attentional disengagement, we set three types of CTI (i.e. 350 ms, 1000 ms, and 1500 ms), taking about 45 minutes to complete the experiment. For each condition, only 60 trials of EEG data were collected, and about 50 trials were retained for ERP/CNV analysis after data pre-processing. The limited number trials may result in a poorer signal-to-noise ratio, which makes it difficult to detect the underlying interaction. If the spatial attention paradigm was performed with the three CTIs, it would take about 90 minutes to perform the whole experiment for each subject. Considering the tolerance and engagement of the subjects (especially for depressed patients) in the experiment, we adopted the cued target-response paradigm in this study. The different tasks may account for the different results, as the response task may be too easy in cued target-response paradigm so that the depressed patients may complete it just as well as the controls. Nevertheless, we would suggest adopting the visual spatial attention paradigm with two CTIs (e.g., with the CTIs of 500 ms and 1500 ms) to further explore attentional disengagement from different emotions in depression in the future.

Disclosure of interest

The authors declare that they have no competing interest.

Acknowledgements

This work was supported by grants from National Key R&D Program of China (N0. 2017YFC0909200), National Natural Science Foundation of China (61673267, 60901025), Shanghai Key Laboratory of Psychotic Disorders (13dz2260500), Natural Science Foundation of Shanghai (16ZR1446600), Shanghai Science and Technology Committee (134119b0300), Advanced Appropriate Technology Promotion Projects of Shanghai Health System (2013SY003),

Shanghai Municipal Commission of Health and Family Planning (201640050), and Med-X Research Fund of Shanghai Jiao Tong University (YG2015ZD12, YG2016MS36).

References

[1] Association AP. Diagnostic and statistical manual of mental disorders: DSM-IV [M]. Washington DC: American Psychiatric Association; 1994.
[2] Beck AT. Cognitive therapy and the emotional disorders. Penguin; 1979.
[3] Brunia CH, Damen EJ. Distribution of slow brain potentials related to motor preparation and stimulus anticipation in a time estimation task. Electroencephalogr Clin Neurophysiol 1988;69:234—43.
[4] Caseras X, Garner M, Bradley BP, Mogg K. Biases in visual orienting to negative and positive scenes in dysphoria: An eye movement study. J. Abnorm Psychol 2007;116:491—7.
[5] Chen S, Sun J, Tong S. Delayed attentional disengagement from sad face: A study of alpha rhythm by event-related desynchronization. Conf Proc IEEE Eng Med Biol Soc 2012;2012: 6776—9.
[6] De Raedt R, Koster EH. Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. Cogn Affect Behav Neurosci 2010;10:50—70.
[7] Delle-Vigne D, Wang W, Kornreich C, Verbanck P, Campanella S. Emotional facial expression processing in depression: data from behavioral and event-related potential studies. Neurophysiol Clin 2014;44:169—87.
[8] Duan H, Wang L, Fernandez G, Zhang K, Wu J. Increased anticipatory contingent negative variation in posttraumatic stress disorder. Biol Psychol 2016;117:80—8.
[9] Duncan J, Ward R, Shapiro K. Direct measurement of attentional dwell time in human vision. Nature 1994;369: 313—5.
[10] Eizenman M, Yu LH, Grupp L, Eizenman E, Ellenbogen M, Gemar M, et al. A naturalistic visual scanning approach to assess selective attention in major depressive disorder. Psychiatry Res 2003;118:117—28.
[11] Gollan JK, Pane HT, McCloskey MS, Coccaro EF. Identifying differences in biased affective information processing in major depression. Psychiatry Res 2008;159:18—24.
[12] Gomez CA, Flores A, Ledesma A. Fronto-parietal networks activation during the contingent negative variation period. Brain Research Bulletin 2007;73:40—7.
[13] Gotlib IH, Joormann J. Cognition and depression: current status and future directions. Annu Rev Clin Psychol 2010;6:285—312.
[14] Gotlib IH, Krasnoperova E, Yue DN, Joormann J. Attentional biases for negative interpersonal stimuli in clinical depression. Abnorm Psychol 2004;113:121—35.
[15] Gotlib IH, McCann CD. Construct accessibility and depression: An examination of cognitive and affective factors. J Pers Soc Psychol 1984;47:427—39.
[16] Gotlib IH, Neubauer DL. Information-processing approaches to the study of cognitive biases in depression. In: Johnson SL, Hayes AM, Field TM, Schneiderman N, Mccabe P, editors. Stress Coping and Depression. Mahwah: Psychology Press; 2000. p. 117—43.
[17] Hillyard SA. Relationships between the contingent negative variation (CNV) and reaction time. Physiol Behav 1969;4:351—7.
[18] Hong X, Sun J, Bengson JJ, Mangun GR, Tong S. Normal aging selectively diminishes alpha lateralization in visual spatial attention. Neuroimage 2015;106:353—63.
[19] Joormann J, Gotlib IH. Emotion regulation in depression: relation to cognitive inhibition. Cogn Emot 2010;24:281—98.
[20] Knight RT, Grabowecky MF, Scabini D. Role of human prefrontal cortex in attention control. Adv Neurol 1995;66:21—34.
[21] Koster EH, De Raedt R, Goeleven E, Franck E, Crombez G. Mood-congruent attentional bias in dysphoria: maintained attention to and impaired disengagement from negative information. Emotion 2005;5:446—55.
[22] Li Z, Deng W, Liu X, Zheng Z, Li M, Li Y, et al. Contingent negative variation in patients with deficit schizophrenia or bipolar I disorder with psychotic features: Measurement and correlation with clinical characteristics. Nord J Psychiatry 2015;69:196—203.
[23] Luck SJ, Woodman GF, Vogel EK. Event-related potential studies of attention. Trends Cogn Sci 2000;4:432—40.
[24] Mathews A, Ridgeway V, Williamson DA. Evidence for attention to threatening stimuli in depression. Behav Res Ther 1996;34:695—705.
[25] Peckham AD, McHugh RK, Otto MW. A meta-analysis of the magnitude of biased attention in depression. Depress Anxiety 2010;27:1135—42.
[26] Tottenham N, Tanaka JW, Leon AC, McCarry T, Nurse M, Hare TA, et al. The NimStim set of facial expressions: judgments from untrained research participants. Psychiatry Res 2009;168:242—9.
[27] Walter WG, Cooper R, Aldridge VJ, McCallum WC, Winter AL. Contingent negative variation: An electric sign of sensorimotor association and expectancy in the human brain. Nature 1964;203:380—4.
[28] Zhao Q, Tang Y, Chen S, Lyu Y, Curtin A, Wang J, et al. Early perceptual anomaly of negative facial expression in depression: An event-related potential study. Neurophysiol Clin 2015;45:435—43.