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Deficient manipulation of working memory in remitted depressed individuals: Behavioral and electrophysiological evidence

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HIGHLIGHTS

- Compared to the control participants, the remitted depressed (RMD) participants had higher sorting costs.
- A deficient manipulation of negative material was related to increased event related potential P3b and SW amplitudes in the RMD participants.
- The RMD participants were associated with unimpaired manipulation for positive material.

ABSTRACT

Objective: The study aimed to examine whether remitted depressed (RMD) individuals show a dysfunction of valence-dependent manipulation and its neurophysiological correlates.
Method: Event-related potentials were conducted on 25 individuals with remitted depression and 27 controls during a working memory manipulation task. The sorting costs and the P3b and slow wave (SW) amplitudes were analyzed.
Results: Compared to the control subjects, the RMD individuals revealed higher sorting costs, particularly when they were shown negative targets. The control individuals exhibited reduced P3b and SW amplitudes in response to the backward negative pictures, whereas the RMD participants exhibited increased central-parietal and lateral P3b and SW amplitudes in the backward condition. Both groups exhibited overall decreased P3b and SW amplitudes in response to the backward positive pictures.
Conclusions: RMD individuals are associated with a deficient manipulation for negative material and an unimpaired manipulation for positive material.
Significance: This study extends current knowledge that deficits in cognitive control persist after the remission of depressive symptoms.

1. Introduction

Over three-quarters of depressive individuals will experience more than one major depressive episode within the first 2 years of recovery (Boland and Keller, 2009). The high relapse rate indicates that there are specific factors that increase the possibility of repeated depressive episodes (Halvorsen et al., 2012). One of these specific factors, cognitive impairment, has been widely documented in major depressive disorder (MDD) (see Kircanski et al., 2012 for review). Cognitive impairment may not only affect the ability of the depressed individual to function socially during acute disease and remission (Jaeger et al., 2006) but also may have a long-term effect on the course of MDD (Hasselbalch et al., 2011). Moreover, deficits in cognitive capacities, including working memory (WM), persist into remission (Schöning et al., 2009; Kerestes et al., 2012; Levens and Gotlib, 2015).

WM, as a limited-capacity system, allows people to temporarily maintain and manipulate task-related information in complex cognitive activity (Baddeley and Logie, 1999). Maintenance and manipulation are processes in WM that have a functional rather than a neuroanatomical distinction (Veltman et al., 2003). Maintenance refers to the transfer, maintenance, and matching of information in WM (Fletcher and Henson, 2001), while manipulation

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is interpreted as the added re-organization or updating of information (Veltman et al., 2003). Given the capacity limitation of WM, it is significant that the contents of WM can be manipulated flexibly to respond to a rapidly changing environment. Investigators have documented that depression involves difficulties in expelling previously relevant negative material from WM (Berman et al., 2011; Joormann and Gotlib, 2008; Levens and Gotlib, 2010) and flexibly manipulating negative information in WM that has higher sorting costs (Joormann et al., 2011). In addition, neural evidence also supports this view. Some studies have found that difficulties in removing negative words from WM in MDD were related to increased activation in the left inferior frontal gyrus (Berman et al., 2011) and dorsal anterior cingulated cortex (Foland-Ross et al., 2013). Moreover, Yoon et al. (2014) proposed that deficits in expelling irrelevant negative words from WM may be specific to depression.

Behavioral and neural evidence has indicated that deficits in manipulating and updating emotional content in WM and executive control persist into remission when patients are euthymic and unmedicated (Levens and Gotlib, 2015; Vanderhasselt and De Raedt, 2009; Vanderhasselt et al., 2012). Less is known, however, regarding the persistence of deficits in the manipulation of negatively valenced material in WM after the depressive episode. Furthermore, the previous studies on manipulating or updating the content in WM used emotional words as stimulus material. However, the existent behavioral and electrophysiological evidence suggests that emotional pictures are processed with stronger and more widespread activation (Kensinger and Schacter, 2006). Therefore, this evidence was also concerned with whether the processing of emotional information in WM manipulation is different between emotional pictures and words.

WM function in depressed patients can be examined through event-related potentials (ERPs) that are characterized by a high temporal resolution (Pelosi et al., 2000; Deldin et al., 2001). Pelosi et al. (2000) found that responses of depressed patients for all levels of memory load had different amplitude changes in the 375- to 840-ms epoch during the Sternberg WM paradigm. In a delayed matching to sample task, Deldin et al. (2001) demonstrated that MDD participants with increasing depressive symptoms had more negative slow wave (SW) amplitudes. Later, Lenartowicz et al. (2010) found that context activation and updating in WM are mostly related to the P3b component for the 400–700 ms in posterior areas, and they propose that the P3b component may indicate the activation of task-relevant posterior regions and context maintenance. In addition, Liu et al. (2010) found that the manipulation condition evoked significantly more positive ERPs from 400 to 750 ms in the frontal and central areas than those of the maintenance condition in healthy participants. These scholars suggested that manipulation includes the extra processes of reorganization or updating of information. Therefore, we questioned whether these ERPs during the WM manipulation task in remitted depressed patients were different from the ERPs of the control group.

The present study tested whether subjects who are in remission but who have a history of recurrent major depressive (RMD) episodes differed from control subjects in the manipulation of emotional pictures in WM. We adopted a WM manipulation paradigm with an affective modification, which was previously used by Joormann et al. (2011), to distinguish manipulation from maintenance in WM and to analyze the sorting costs of different valence material. Sorting costs represent the difficulties of depressed individuals in manipulating the material in WM (Joormann et al., 2011). Considering the previous results from a similar experimental paradigm in depressed individuals (Joormann et al., 2011), our hypotheses were as follows. (1) RMD participants would reveal a specific failure in manipulating the negative emotional pictures in WM, whereas the manipulation of positive emotional pictures would be unaffected by group status. (2) In the ERP data, the RMD participants would show different P3b and SW amplitudes of the manipulation effects compared to the control participants.

2. Methods

2.1. Participants

Twenty-seven RMD individuals and 27 control participants were initially included in the research. Two participants had to be excluded because of an inadequate number of correct artifact-free trials. Therefore, 25 RMD participants and 27 control subjects were involved in the final study. The two groups of participants did not differ significantly concerning gender, age, and years of education (see Table 1 for the demographic data).

The RMD participants were recruited from a local psychiatric hospital and advertisements. The participants who met the DSM-IV criteria for at least two previous major depressive episodes in their lives but did not meet the diagnostic criteria for current MDD or any other Axis I disorder were included in the RMD group. The diagnosis was confirmed by structured clinical interviews for the DSM-IV (SCID; Spitzer et al., 1995), which was administered by trained and experienced interviewers. Twenty-five control subjects were recruited from the respondents to advertisements that were posted in the community (e.g., university and internet bulletin boards). The control participants met neither the current nor past criteria for any psychiatric illness, and they did not have any first-degree relatives with a history of mental health disorders. Additionally, all enrolled subjects had not taken any psychiatric medication within the past 90 days. All subjects had corrected-to-normal eyesight and were right-handed, as indicated by a self-report.

To assess the current severity of depressive symptoms, the participants were administered the Hamilton Depression Rating Scale (HDRS-17; Hamilton, 1967) and the Beck Depression Inventory (BDI; Beck et al., 1961) on the same day as the experimental protocol. The participants needed to score less than 7 points on the HDRS-17 to be included. Table 1 presents the demographic features of the RMD and control subjects. The groups did not differ in age or years of education. The mood rating scale score did not differ between the groups. All subjects provided written informed consent, and the study procedures were approved by the local ethics boards.

2.2. Stimuli

Three hundred sixty pictures—120 positive, 120 negative and 120 neutral—were chosen from the International Affective Picture System (IAPS) Lang et al., 2008, which provides arousal and valence ratings on a 9-point scale. The mean valence ratings were 7.24 ($SD = 0.51$) for the positive pictures, 2.88 ($SD = 0.58$) for the negative pictures, and 5.14 ($SD = 0.42$) for the neutral pictures. The positive and negative pictures differed significantly in the valence dimension ($t\,(238) = 61.38$, $p < .001$) but not in the arousal ratings ($t\,(238) = -1.55$). In addition, the positive and neutral pictures differed significantly in the valence ($t\,(238) = 34.45$, $p < .001$) and arousal ratings ($t\,(238) = 14.71$, $p < .001$). The negative and neutral pictures also differed significantly in the valence ($t\,(238) = -34.11$, $p < .001$) and arousal ratings ($t\,(238) = 18.75$, $p < .001$). During the task (explained below), the pictures appeared on a black background in the center of a monitor and subsumed a visual angle of approximately $4.64 \times 4.64°$.