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Decreased response inhibition to sad faces during explicit and implicit tasks in females with depression: Evidence from an event-related potential study

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ABSTRACT

The present study aimed to investigate neural substrates of response inhibition to sad faces across explicit and implicit tasks in depressed female patients. Event-related potentials were obtained while participants performed modified explicit and implicit emotional go/no-go tasks. Compared to controls, depressed patients showed decreased discrimination accuracy and amplitudes of original and nogo-go difference waves at the P3 interval in response inhibition to sad faces during explicit and implicit tasks. P3 difference wave were positively correlated with discrimination accuracy and were independent of clinical assessment. The activation of right dorsal prefrontal cortex was larger for the implicit than for the explicit task in sad condition in health controls, but was similar for the two tasks in depressed patients. The present study indicated that selectively impairment in response inhibition to sad faces in depressed female patients occurred at the behavior inhibition stage across implicit and explicit tasks and may be a trait-like marker of depression. Longitudinal studies are required to determine whether decreased response inhibition to sad faces increases the risk for future depressive episodes so that appropriate treatment can be administered to patients.

1. Introduction

Depression is one of the most common psychiatric disorders and a leading cause of disability worldwide (Goodwin et al., 2006). Studies suggest that at least 20% of adolescents experience a depressive episode before adulthood, which is associated with high morbidity and mortality (Brent and Birmaher, 2006). Women show a younger age of onset and higher rate of recurrence of depression than men (Kessler et al., 2005; Schuch et al., 2014). Repeated negative thoughts are considered a hallmark of depression (Koster et al., 2011), and are related to impaired cognitive control over negative information (Ochsner and Gross, 2008; Wager et al., 2008). Response inhibition is an important component of this cognitive control system; depressed individuals are unable to inhibit their response to negative information (De Raedt and Koster, 2010; Gotlib and Joormann, 2010), which is also observed in unmedicated offspring of depressed mothers (Joormann et al., 2007).

Sad facial expressions are one type of negative social stimulus. In social interactions, inhibiting inappropriate negative emotions conveyed by sad faces is an indispensible social skill. Depression patients show attentional bias to sad faces and are unable to prevent being troubled by sad expressions (Gollan et al., 2008; Gur et al., 1992; Sylvester et al., 2015). In one study, depressed adolescents and those who developed depression at follow-up made more commission errors for sad than for happy faces (Kilford et al., 2015). Moreover, unmedicated offspring of depressed mothers showed greater pupil dilation compared to controls, which was associated with greater depression risk (Burkhouse et al., 2015). Neuroimaging studies have found that depressed individuals exhibit higher activity in the amygdala in response to sad faces, whereas control subjects show higher activity in response to happy faces (Suslow et al., 2010). Depression patients also show less differential activation of the insular cortex in response to sad vs. happy faces as compared to healthy controls; the difference in activation is negatively correlated with depression severity (Henje Blom et al., 2015). These results suggest that depressed individuals show facilitated negative bias in the processing of sad

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faces. Exerting cognitive control over sad emotions is critical for the remission of depression, and understanding the neural correlates of response inhibition to sad faces in depression can enable the initiation of appropriate interventions.

In explicit processing, facial expressions are within the scope of voluntary attention and are directly processed, whereas in implicit processing they occur outside the scope of voluntary attention and are incidentally processed. As such, attentional resources for stimulus processing differ between the two conditions. Implicit and explicit facial processing serve different functions (Taylor et al., 2003) and have distinct neural substrates (Linden et al., 2010; Valdes-Conroy et al., 2014; Winston et al., 2003), and subjects have reported different emotional intensities associated with facial expressions processed explicitly vs. implicitly. For instance, rating pictures was associated with reduced intensity of sadness as compared to passive viewing, likely because the rating task reduced the activation of brain regions related to emotional experiences (Taylor et al., 2003). Psychiatric patients show different responses to explicit and implicit emotional stimuli. For example, schizophrenia and depression patients exhibit greater automatic amygdala responses to implicit sad faces than controls, in the former, these responses were positively correlated with the negative subscale of the Positive and Negative Syndrome Scale (Rauch et al., 2010). We previously found that response inhibition was modulated by sad facial information at the action inhibition stage when facial expressions are processed explicitly as opposed to implicitly (Yu et al., 2014). Moreover, individuals with generalized anxiety disorder showed impaired response inhibition to sad faces in an explicit but not in an implicit task (Yu et al., 2015). However, it is not known whether depression patients exhibit deficits in response inhibition across implicit and explicit conditions.

To address this issue, we developed a modified emotional go/no-go paradigm consisting of two sections. In the task-related section, participants made their go/no-go decision according to recognition of facial expressions; that is, the emotional expression was explicitly processed. In the task-irrelevant section, participants responded or inhibited their response based on identification of the gender of the face; that is, the emotional processing was implicit. We used the same set of stimuli in the two sections to exclude interference from additional factors. We hypothesized that response inhibition deficits in depression are reflected by lower discriminating accuracy and shorter response time to sad stimuli across explicit and implicit tasks.

Event-related potentials (ERPs) were recorded during the evaluation of behavioral measures. The main advantage of this non-invasive method is the high time resolution that reflects the time course of brain activity (Otten and Rugg, 2004); it has been frequently used to explore the neural basis of response inhibition (Fabiani et al., 2000), which comprises two different cognitive processes—namely, conflict monitoring and action inhibition (Sehlmeyer et al., 2010). No-go N2 reflects the former, while no-go P3 is associated with conflict resolution and behavioral inhibition (Donkers and van Boxtel, 2004; Kropotov et al., 2011). Neuroimaging studies have revealed that the right inferior prefrontal cortex (rIFC) plays a crucial role in response inhibition to emotional stimuli (Berkman et al., 2009; Goldstein et al., 2007; Ochsner et al., 2004; Padmala and Pessoa, 2010; Shafritz et al., 2006); ERP measurements have shown that response inhibition is impaired in individuals with anxiety (Hum et al., 2013). Depression patients showed decreased no-go N2 amplitudes in a modified auditory go/no-go task (Kaiser et al., 2003; Katz et al., 2010). However, another study in which participants performed a cued emotional conflict task revealed differences between depression patients and controls only during the late N450 time window (Vanderhasselt et al., 2012). These inconsistent findings may be due to variations in experimental paradigms and patient inclusion criteria in these studies. Although depression disrupts response inhibition, the neural basis of this effect is not well understood. It has been suggested that depression is linked to a reduced ability to monitor conflict or to apply active inhibition (Aarts and Pourtois, 2010; Berggren and Derakshan, 2013; Botvinick et al., 2001).

The present study investigated the neural substrates of response inhibition to sad faces across implicit and explicit tasks in depression patients based on ERP recordings. We hypothesized that depression patients would show deficits in response inhibition to sad faces across both tasks, and would therefore show decreased accuracy in discerning sad faces as well as a shorter response time to sad faces relative to control subjects. For ERP recordings, we expected decreased N2 and P3 amplitudes in inhibition-related brain areas such as the rIFC in both tasks. We also examined the correlation between behavioral measures, ERP components, and clinical parameters to determine whether decreases in N2 and P3 are markers of depression. We recruited only women in this study since response inhibition and patterns of brain activation show gender differences (Yuan et al., 2009) and the incidence of depression is higher among females (Kessler et al., 2005; Schuch et al., 2014).

2. Materials and methods

2.1. Participants

Female unipolar depression outpatients (n=20; age: 17–46 years) were recruited from the depression disorder clinic in Anhui Mental Health Center. Diagnostic assessments were independently completed by two psychiatrists based on DSM-IV criteria. DSM-IV is the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM) which has been praised for standardizing psychiatric diagnostic categories and criteria (American Psychiatric Association, 1994). The manual includes all currently recognized mental health disorder and thus is usually used by mental health professionals to describe the characteristics of a given mental disorder to distinguish the disorder from other, similar problems. In addition, patients included in the study scored > 14 on the Hamilton Depression Rating Scale (HAMD)-17 which is used for adults and to rate the depression severity by probing mood, feeling of guilt, suicide ideation, agitation, retardation, anxiety, weight loss, and somatic symptom. The scale showed high inter-rater reliability as 0.9 for 70 patients (Hamilton, 1960). Exclusion criteria were as follows: any history of mania, psychosis or any other Axis I disorders; a history of neurological conditions; substance abuse; and current use of psychotropic medication. Patients had never had behavioral or drug treatment for depression or had suspended treatment for at least two months prior to the study. Age-matched female adults (n=21) screened for current and past psychiatric and neurological disorders were recruited through internet postings. All participants had normal or corrected-to-normal vision and HAMD-17 scores < 7. Control tests and characteristics of the study population are shown in Table 1. This study was carried out in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of Anhui Medical University. All participants completed the experiment on a voluntarily basis with receiving RMB50 yuan.

Table 1
Group characteristics of the DEP group and CON group.

	DEP Group	CON Group	Between group comparison
	Mean (SD)	Mean (SD)	P-value
Age(years)	30.6(9.4)	25.9(6.2)	t_{39}=1.84, P=0.084
Education(years)	13.7(3.4)	13.9(0.9)	t_{39}=0.25, P=0.80
BDI	18.5(4.5)	4.9(2.1)	t_{39}=12.42, P < 0.001
SAI	50.2(10.3)	36.0(6.9)	t_{39}=5.37, P < 0.001
TAI	57.3(8.5)	34.4(6.7)	t_{39}=9.64, P < 0.001

Abbreviations: DEP, depression; CON, control; BDI, Beck Depression Inventory. SAI, State Anxiety Inventory; TAI, Trait Anxiety Inventory.