Journal of Psychiatric Research 68 (2015) 384–391

Contents lists available at ScienceDirect

Journal of Psychiatric Research

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

Reduced striatal activation in females with major depression during the processing of affective stimuli

Megan E. Connolly [a, *], Jackie K. Gollan [a], Derin Cobia [b], Xue Wang [c]

[a] Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 676 N. St. Clair St., Suite 1000, Chicago, IL 60611, USA
[b] Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 710 N Lake Shore Drive, Abbott Hall, Suite 1316, Chicago, IL 60611, USA
[c] Department of Radiology, Northwestern University Feinberg School of Medicine, 737 N Michigan Ave., Suite 1600, Chicago, IL 60611, USA

ARTICLE INFO

Article history:
Received 20 November 2014
Received in revised form
22 April 2015
Accepted 30 April 2015

Keywords:
Depression
Blunted affective reactivity
fMRI
Anhedonia
Striatum

ABSTRACT

The extent to which affective reactivity and associated neural underpinnings are altered by depression remains equivocal. This study assessed striatal activation in fifty-one unmedicated female participants meeting DSM-IV criteria for Major Depressive Disorder (MDD) and 61 age-matched healthy females (HC) aged 17–63 years. Participants completed an affective reactivity functional magnetic resonance imaging task. Data were preprocessed using SPM8, and region-of-interest analyses were completed using MarsBaR to extract caudate, putamen, and nucleus accumbens (NAcc) activation. General linear repeated measure ANOVAs were used to assess group differences and correlational analyses were used to measure the association between activation, depression severity, and anhedonia. Main effects of hemisphere, valence, and group status were observed, with MDD participants demonstrating decreased striatal activation compared with HC. Across groups and valence types, the left hemisphere demonstrated greater activation than the right hemisphere in the putamen and nucleus accumbens, whereas the right hemisphere demonstrated greater activation than the left in the caudate. Additionally, unpleasant stimuli elicited greater activation than pleasant and neutral stimuli in the caudate and putamen, and unpleasant stimuli elicited greater activation than neutral stimuli in the NAcc. There were no significant associations between activation, depression severity, and anhedonia. Overall, depression was characterized by reduced affective reactivity in the striatum, regardless of stimuli valence, supporting the emotion context insensitivity model of depression.

1. Introduction

Depression has been characterized by altered affective reactivity (Bylsma et al., 2008; Gollan et al., 2008; McFarland and Klein, 2009). However, there are conflicting theories related to the precise nature of affective reactivity in depression and associated neural underpinnings. Clarifying the underlying mechanisms of affective reactivity may elucidate the role of anhedonia, or amotivation, in depression.

Some research suggests that depression is associated with increased responsiveness to unpleasant or negative stimuli, suggesting such stimuli have a greater perceptual 'weight' (Gollan et al., 2008; Wenzlaff et al., 2001). Alternatively, the emotion context insensitivity (ECI) model proposes diminished reactivity to both pleasant/positive and unpleasant/negative stimuli in depression (Rottenberg et al., 2005), implying a dulled affect system. A recent meta-analysis supports the ECI model, demonstrating that depression is characterized by an inhibition of affective reactivity across valenced stimuli (Bylsma et al., 2008). Though consistent with the ECI model, the degree of blunted reactivity in depression may vary as a function of the stimuli. For example, blunted responsiveness is greater for pleasant compared with unpleasant stimuli (Bylsma et al., 2008). Further, some research supports the specific role of blunted reactivity to pleasant stimuli (Dunn et al., 2004; McFarland and Klein, 2009),

* Corresponding author. Affective Science and Treatment Lab, Asher Center for the Study & Treatment of Depressive Disorders, Department of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine, 676 N. St. Clair St., Suite 1000, Chicago, IL 60611, USA. Tel.: +1 312 926 7510; fax: +1 312 695 5502.
E-mail address: meganconnolly2016@u.northwestern.edu (M.E. Connolly).

http://dx.doi.org/10.1016/j.jpsychires.2015.04.025
0022-3956/

suggesting increased vulnerability of reward responsiveness in depression. Blunted reactivity to rewarding stimuli may be related to the presence of anhedonia in depression, or altered evaluation of a stimuli's hedonic value (Eshel and Roiser, 2010; McCabe et al., 2009; Pizzagalli et al., 2009b). Specifically, depression has been associated with altered processing of positive information, including decreased reactivity to and preference for reinforcing stimuli (Pizzagalli et al., 2005, 2009b). Collectively, this suggests that depression may be characterized by decreased responsiveness to pleasant stimuli rather than increased responsiveness to unpleasant stimuli.

Underlying neural correlates of affective reactivity include the striatum, a part of the mesolimbic dopamine system consisting of the caudate, putamen, and nucleus accumbens (NAcc). In addition to other functions, including motor performance, motivation, and learning (Liljeholm and O'Doherty, 2012), the striatum plays a unique role in the processing of emotional stimuli and is centrally involved in hedonic processing (Diener et al., 2012; Eppinger et al., 2012; Martin-Soelch, 2009; Monk, 2008; Nikolova et al., 2012; Reynolds and Berridge, 2002; Schultz, 2004). Indeed, depressed participants, relative to healthy controls, demonstrated reduced striatal activation while engaging in rewarding tasks or viewing pleasurable stimuli (Forbes and Dahl, 2012; Keedwell et al., 2005; Kumar et al., 2008; Robinson et al., 2012). Specifically, depressed participants exhibited reduced activation to pleasant stimuli (i.e. happy faces) in the right putamen (Surguladze et al., 2005), and reduced responsiveness to reward in the bilateral caudate, left putamen, and left NAcc (Pizzagalli et al., 2009a). Furthermore, anhedonia has been associated with decreased ventral striatal activation in response to happy faces (Keedwell et al., 2005). Perhaps more striking, participants with remitted depression displayed hypoactivation in the ventral striatum, though not in the caudate, in response to pleasant stimuli even when their subjective ratings matched those of healthy participants (McCabe et al., 2009), suggesting that striatal activation may be sensitive to past mood states in addition to current depression.

Though the striatum has been implicated in affective reactivity, research is inconsistent as to the direction of activation, laterality effects, and how the striatum may be differentially responsive to affective conditions within depressed and healthy participants. For example, in contrast to other findings, depressed adults have shown comparable NAcc activation relative to healthy controls in response to a monetary reward task (Knutson et al., 2008). Further, a meta-analysis of depression imaging studies highlighted laterality effects by showing that hypoactivation in the right caudate was specifically linked to the processing of pleasant stimuli (Diener et al., 2012). Yet another meta-analysis found both hypo- and hyperactivation in the striatum in depression with valence-specific findings (Groenewold et al., 2012). In healthy participants, the research is also mixed, with some studies demonstrating striatal reactivity to positive, but not negative, conditions (Hamann and Mao, 2002; Hare et al., 2005), and others indicating greater striatal activation in response to unpleasant compared with pleasant or neutral stimuli (Carretie et al., 2009). It is unclear, at this point, if the striatum responds to specific valence conditions in a similar pattern in depressed participants compared with healthy participants.

Together, these observations demonstrate the relevance of assessing specific striatal subregions, whether bilaterally or unilaterally, and prompt further exploration of their functioning in depression. In addition to elucidating inconsistencies in striatal subregion activation and lateralization, separately assessing left and right brain regions-of-interest (ROIs) has been effective in determining specificity of brain function associated with behavior (e.g., language and visuospatial processing) (Stephan et al., 2003; Szaflarski et al., 2002). The lateralization of emotional processes includes conflicting theories postulating right hemispheric superiority for the perception of emotion with the possible unique role of the left hemisphere in the processing of positive emotions (Heller, 1993; Root et al., 2006), compared with other findings that do not support general right-lateralization during emotional processing (Wager et al., 2003). It remains unclear how laterality impacts processing and whether proposed laterality in emotion extends to striatal functioning in depression. The aforementioned inconsistencies necessitate further investigation of bilateral striatal functioning in depression, as lateralized functional differences in affective reactivity may inform the pathophysiology of depression.

Despite the demonstrated relationship between the striatum and affective reactivity deficits seen in depression, the specific direction of this relationship has not been precisely identified, which may be a function of study design, the use of diverse samples, medicated participants, or varying tasks. Furthermore, few studies investigate how anhedonia specifically, in addition to depression severity, may impact striatal activation in depressed participants. Therefore, this study aimed to investigate the role of the striatum in affective reactivity by examining bilateral activation in an unmedicated sample of depressed and healthy participants during a functional magnetic resonance imaging (fMRI) affective reactivity task. The study assessed the extent to which depressed participants demonstrated differential striatal activation and explored the role of the striatum in affective reactivity (e.g., the presence of valence and laterality effects). This study also tested the extent to which neural activation was associated with dimensions of depression severity and anhedonia. Given recent meta-analytic support for the emotion context insensitivity model as well as the role of the striatum in affective reactivity, the primary hypothesis was that depressed participants, compared with healthy controls, would show hypoactivation in the caudate, putamen, and NAcc. Additional secondary hypotheses were that the striatum would demonstrate differential activation in response to valence conditions, differing by depression status and hemisphere, and that depression severity and anhedonia would be inversely correlated with striatal activation.

2. Methods and materials

2.1. Participants

Participants (17–63 years) enrolled in an institutional review board-approved study at Northwestern University Feinberg School of Medicine in the Department of Psychiatry and Behavioral Sciences, Chicago, IL (in accordance with the Declaration of Helsinki). Participants were recruited from community advertisements and screened for initial eligibility. During the first onsite assessment, prospective participants provided written informed consent, passed a urine toxicology screen, and completed clinical interviews and measures. Participants who met study criteria and passed safety requirements completed the fMRI visit. Participants were compensated and debriefed upon study completion.

Participants were English-speaking, right-handed, unmedicated females with no major medical conditions, and with normal or corrected-to-normal vision. Depressed participants met criteria for current and primary Major Depressive Disorder (MDD) based on the Structured Clinical Interview for the DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID; First et al., 2002) and The Inventory of Depressive Symptomatology-Clinician-Rated (IDS-C; Rush et al., 1986, 1996, 2000). Depressed participants meeting criteria for a comorbid anxiety disorder were included if depression was the primary diagnosis. Graduate students with bachelors or masters level degrees completed SCID training via training tapes