Neuropsychologia 67 (2015) 100–110

Contents lists available at ScienceDirect

Neuropsychologia

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

The neural basis of social risky decision making in females with major depressive disorder

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ARTICLE INFO

Article history:
Received 4 September 2014
Received in revised form
29 November 2014
Accepted 7 December 2014
Available online 9 December 2014

Keywords:
Major Depressive Disorder
Social cognition
Risky decision making
Anterior insula
Dorsal putamen
Prefrontal regions

ABSTRACT

Recent evidence indicates that Major Depressive Disorder (MDD) may be associated with reduced tendency of committing noncompliant actions during social decision-making even when the risk of being punished is low. The neural underpinnings of this behavioral pattern are unknown, although it likely relates to compromised functioning of the lateral prefrontal-striatal/limbic networks implicated in executive control, emotion regulation and risk/value-based instrumental behaviors. We employed a modified trust game (TG) that provided explicit information on the risk levels of cheating behaviors being detected and punished. Behavioral and neuro-image data were acquired and analyzed from 14 first-episode female MDD patients and 15 age- and gender-matched controls performing the role of trustee in the TG. Relative to controls, MDD patients exhibited less behavioral switching to making cheating choices under low risk, and reduced activity in the dorsal putamen, anterior insula and dorsolateral prefrontal cortex (DLPFC) during making low-risk cheating versus benevolent choices, with limited evidence indicating abnormal bilateral inferior frontal gyrus activities of patients when making high-risk cheating versus benevolent choices. Patients' left dorsal putamen/anterior insular signals correlated positively with their frequency of low-risk cheating. MDD patients' symptom severity correlated positively with their signals in the lateral prefrontal networks during decision-making. A psychophysiological interaction analysis provided tentative evidence for the recruitment of IFG-striatal/limbic circuitry among the control participants, but greater frontopolar-striatal/limbic connectivity among the MDD patients, during low-risk decision-making. We propose that making risky social decisions based on the balancing of self-gain and other's welfare relies on the functioning of the integrated lateral prefrontal-striatal/limbic networks, which are less efficient and dysregulated among MDD patients compared with controls, impacting negatively on the patients' social capacity and highlighting a key therapeutic target for MDD.

1. Introduction

Major Depressive Disorder (MDD) is a devastating condition accompanied by impaired social functioning (Segrin, 2000) and less fulfilling social interactions (Nezlek et al., 1994), with patients often benefiting from good social support during symptom recovery (Brugha et al., 1997). It is hence of high theoretical and clinical significance to understand the neural underpinnings of the impaired social decision-making process in MDD. One component of social interaction that plays important roles in evolutionary human survival is trust, which is based on presumed reciprocity and social promise among multiple parties (Rilling and Sanfey, 2011). Nevertheless, a trust relationship is unstable and can be broken by cheating behaviors from any involved parties, which may in turn be detected and punished by the (adversely) affected parties (de Quervain et al., 2004). Therefore, adaptive social functioning involves the balancing of self-gain and other's welfare based on considerations of the risk of cheating detection, which processes might be altered in MDD (Zhang et al., 2012).

Abbreviations: MDD, Major Depressive Disorder; TG, Trust Game; DLPFC, dorsolateral prefrontal cortex; IFG, inferior frontal gyrus; VLFPC, ventrolateral prefrontal cortex; BDI-II-C, the Chinese version of Beck Depression Inventory; BOLD, Blood-Oxygen-Level-Dependent; SVC, small volume correction; VBM, voxel-based morphometry; PSC, percentage signal change; PPI, psycho-physiological interaction

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http://dx.doi.org/10.1016/j.neuropsychologia.2014.12.009
0028-3932/

Previous research conducted on healthy populations has employed the multi-round trust game (TG), in which 2 players performed the roles of 'investor' and 'trustee' while engaging in a number of interactions involving investment and return (King-Casas et al., 2005). Focusing on the trustee, the TG measures both social reciprocity (benevolence), when the trustee returns a satisfactory share to the investor and keeps a social promise, and social non-reciprocity (cheating), when the trustee returns less than the investor's expectation and breaks a social promise. While benevolence or compliance might be the normative response, cheating or defiance could be motivated by interest in self-gain and/or in punishing the investor for ungenerous behavior (de Quervain et al., 2004). In a recent study involving both healthy and MDD samples (Zhang et al., 2012), different risk levels were incorporated into the modified TG by systematically manipulating the probability that the trustee's cheating behavior would be detected by the investor and punished, since the capacity to accurately evaluate risk and act accordingly is critical to adaptive decision-making (Shao and Lee, 2014). Zhang et al.'s (2012) findings indicate that while non-depressed participants switched to giving more cheating responses when the risk was low, MDD patients showed less of such behavioral switching, suggesting (relative) lack of integration of risk information to social decision-making.

Past research has generated valuable findings on neural responses elicited by social decision-making on trust and reciprocity, among both healthy participants and patients with emotion or affective disorders (Delgado et al., 2005; Krueger et al., 2007; King-Casas et al., 2008; Sripada et al., 2009). Making trust decisions in healthy participants were associated with activations of the striatum and dorsal prefrontal regions (Delgado et al., 2005; Krueger et al., 2007), and dorsal striatal activities in the trustees delivered prediction-error-like signals that encoded the behavioral patterns of the investor in a multi-round TG (King-Casas et al., 2005). These findings are consistent with existing evidence indicating important roles of the dorsal striatal regions in instrumental learning and actions (Balleine et al., 2007; Haruno and Kawato, 2006). On the other hand, patients with social anxiety disorders exhibited reduced prefrontal activities in the superior and inferior frontal gyri (IFG) when making trust decisions compared with control participants (Sripada et al., 2009), implicating possible deficits in executive control and affect regulatory processes (Grecucci et al., 2013; Miller and Cohen, 2001; Yamasaki et al., 2002). Specifically, the inferior frontal gyri (IFG) is a critical area for action implementation based on emotive and value information, through connections with limbic areas via the insula and with motor cortices (Carr et al., 2003). Thus, IFG dysfunction may lead to compromised capacity in making goal-directed decisions under inhibitory and regulatory control of prefrontal networks (Gotlib et al., 2005). Furthermore, both healthy participants and patients with borderline personality disorder exhibited signals in the anterior insula that negatively predicted their reciprocity in a trust game (King-Casas et al., 2008), consistent with evidence implicating this region in risky decision-making and behaviors (Clark et al., 2008; Kuhnen and Knutson, 2005; Paulus et al., 2003). The IFG, anterior insula and dorsolateral prefrontal (DLPFC) areas were all involved in social promise breaking (Baugmgartner et al., 2009), and in non-reciprocal trustee behavior in a multi-round anonymous TG (Bereczkei et al., 2013), possibly due to the greater demand on executive control and emotion regulatory processes when committing the more risky actions that violate social norm (Spencer et al., 2001).

MDD is associated with functional deficiencies in the striatal/limbic circuitries (Dichter et al., 2009; Gotlib et al., 2010; Smoski et al., 2009) and associated lateral prefrontal networks (Gotlib et al., 2005; Mayberg, 1997; Ochsner and Gross, 2005). The rostral dorsal putamen is a key region involved in instrumental actions based on expected reward value (Haruno and Kawato, 2006; Lerchner et al., 2007; McClure et al., 2003) and punishment (Bjork et al., 2008; Voon et al., 2010), through functional connections with lateral prefrontal, sensori-motor, limbic and other striatal networks (Postuma and Dagher, 2006). MDD patients show reduced left putamen and insular activities during reward anticipation and selection (Gotlib et al., 2010; Smoski et al., 2009), with the former normalized following treatment (Dichter et al., 2009). As such MDD individuals typically exhibit altered sensitivity to reward and punishment (Mogg et al., 1995; Pizzagalli et al., 2008; Von Gunten et al., 2011), as well as to risk (Corwin et al., 1990; Smoski et al., 2008), during decision-making. Previous research also indicates that MDD individuals show abnormal activities of the lateral prefrontal networks, such as the IFG, during emotion regulatory processes (Gotlib et al., 2005; Ochsner and Gross, 2005). As making defiant social decisions requires regulating prosocial emotions such as guilt and empathy (Elliott et al., 2011; O'Connor et al., 2007), MDD individuals who are less capable of resolving those emotions may experience difficulties in deciding to cheat, even when the risk of such behavior being detected is low (Thayer et al., 2003; Pulcu et al., 2013; Zhang et al., 2012). Furthermore, MDD is associated with impaired executive functioning such as working memory (Landro et al., 2001), mental flexibility (Beats et al., 1996) and inhibitory control (Dunkin et al., 2000), along with abnormal DLPFC activities during executive performance (Fales et al., 2008; Okada et al., 2003; Siegle et al., 2007). It was proposed that MDD individuals' elevated DLPFC activations compared with controls may serve as a compensatory mechanism for their reduced prefrontal functional efficiency (Harvey et al., 2005; Wagner et al., 2006).

In the present study, we aimed to investigate the neural basis of MDD patients' reduced tendency of making low-risk cheating choices in the modified TG. Such investigation would give insights on a social cognitive/affective model of MDD, elucidate on the underlying neural mechanism of the disorder, as well as informing intervention techniques targeted at improving social efficacy and/or regulating the functioning of key neural circuitries (e.g. Dichter et al., 2009; Young et al., 2006). We included only patients with first MDD episode in order to avoid the confounding effect of disorder recurrence and longitudinal disorder severity (Harvey et al., 2004). Only female participants were included, as females are more representative of the total MDD population (Kessler et al., 2003), and previous evidence showed gender differences in risk-taking tendency (Byrnes et al., 1999) and in social decision-making preference (Andreoni and Vesterlund, 2001). We hypothesized that, based on previous findings (Zhang et al., 2012), MDD individuals would exhibit less behavioral switching from benevolent to cheating responses when the risk level changed from high to low. At the neural level, depressed individuals would show reduced functional activities in neural circuitries implicated in risk/value-based instrumental behaviors such as the anterior insula and dorsal putamen, as well as in DLPFC networks implicated in executive control, during making the critical low-risk cheating versus benevolent responses compared with non-depressed controls, corresponding to their behavioral differences. Also, MDD patients would show elevated IFG activities during making cheating relative to benevolent responses compared to controls, particularly when the risk was high, which situation was expected to elicit the maximal level of negative affect.

2. Materials and methods

2.1. Participants

Ethical approval was granted by The University of Hong Kong and the Hospital Authority of Hong Kong West Cluster. Thirty-four