Differential mesolimbic and prefrontal alterations during reward anticipation and consummation in positive and negative schizotypy

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ABSTRACT

Schizotypy is associated with anhedonia. However, previous findings on the neural substrates of anhedonia in schizotypy are mixed. In the present study, we measured the neural substrates associated with reward anticipation and consummation in positive and negative schizotypy using functional MRI. The Monetary Incentive Delay task was administered to 33 individuals with schizotypy (18 positive schizotypy (PS),15 negative schizotypy (NS)) and 22 healthy controls. Comparison between schizotypy individuals and controls were performed using two-sample T tests for contrast images involving gain versus non-gain anticipation condition and gain versus non-gain consummation condition. Multiple comparisons were corrected using Monte Carlo Simulation correction of $p < .05$. The results showed no significant difference in brain activity between controls and schizotypy individuals as a whole during gain anticipation or consummation. However, during the consummatory phase, NS individuals rather than PS individuals showed diminished left amygdala and left putamen activity compared with controls. We observed significantly weaker activation at the left ventral striatum during gain anticipation in NS individuals compared with controls. PS individuals, however, exhibited enhanced right ventral lateral prefrontal activity. These findings suggest that different dimensions of schizotypy may be underlied by different neural dysfunctions in reward anticipation and consummation.

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1. Introduction

Schizotypy is characterized by a set of stable traits including cognitive-perceptual (i.e. perceptual alteration), disorganized (i.e. eccentric behaviour) and interpersonal dimensions (i.e. anhedonia), which may be observed in the general population (Raine, 2006). Theoretically, schizotypy can be sub-divided into positive schizotypy (PS) and negative schizotypy (NS), which are separately associated with cognitive-perceptual and interpersonal dysfunctions and resemble positive and negative symptoms of schizophrenia (Kwapil et al., 2012; Wang et al., 2012). Schizotypy also shows overlap with schizophrenia across behavioural, brain structural and functional as well molecular domains (Ettinger et al., 2014), suggesting a relationship between schizotypy and schizophrenia. Anhedonia, the inability to experience pleasure, is one of the major dysfunctions in schizotypy (Blanchard et al., 2009; Chan et al., 2012; Meehl, 1962). Over the past decade, a number of neuroimaging studies have examined the neural substrates of anhedonia in schizotypy, which may facilitate our understanding of schizophrenia spectrum disorders, and may provide more objective biomarkers for the early detection and prevention of this disorder (Cohen et al., 2015; Radua et al., 2015).

Substantial evidence from both animal and human studies has suggested that reward processing can be classified into reward anticipation and reward consummation, which are associated with distinct neural circuits (Gard et al., 2006; Knutson and Greer, 2008; Kringelbach and Berridge, 2009). For example, reward anticipation has been associated with neural activation and dopamine release in the ventral striatum (VS), the insula and the

orbitofrontal cortex (Kringelbach and Berridge, 2009; Salimpoor et al., 2011). Reward consummation has been associated with neural activities and opioid and cannabinoid release in the medial prefrontal cortex (MPFC), the amygdala, and the striatal regions (Knutson and Greer, 2008; Kringelbach and Berridge, 2009).

Based on this framework, an increasing number of fMRI studies have investigated the neural substrates of consummation of reward or positive events in schizotypy. However, findings from these studies are relatively mixed. For example, Hooker et al. (2014) reported a decreased ventral lateral prefrontal response to positive facial expressions in people with high trait social anhedonia. Similarly, when viewing positively-valenced pictures, individuals with elevated trait anhedonia/schizotypy have also shown reduced neural activity in the MPFC and the rostral anterior cingulate cortex (ACC) (Harvey et al., 2010). However, other studies have suggested intact or even enhanced prefrontal, ACC and amygdala activations in individuals with schizotypy or those at high risk of developing psychosis while processing rewards or positively-valenced stimuli (de Leeuw et al., 2015; Harvey et al., 2007; Huang et al., 2013; van Buuren et al., 2011; Wotruba et al., 2014). The heterogeneous findings might be a result of the different subtypes of schizotypy (PS and NS) recruited in these studies (Kwapil et al., 2012; Shi et al., 2012). For example, PS is characterized by thought disorder, suspiciousness, but intact positive affect; while NS is characterized by social dysfunctions and decreased positive affect (Kwapil et al., 2012; Shi et al., 2012). Previous neuroimaging studies have also suggested that different neural substrates of emotional dysfunction are associated with different dimensions of schizotypy (Harvey et al., 2007; Rapp et al., 2010; Soliman et al., 2011; Wang et al., 2015) and different clinical symptoms (positive vs negative symptoms) (See Radua et al. (2015) for a meta-analysis). It is possible that individuals with negative schizotypal features would show reduced neural activation in response to reward or positive events, and when positive schizotypy individuals were recruited, they might display intact brain activation. However, few studies have addressed this possibility.

On the other hand, some have suggested that impaired anticipation of future rewards might play an important role in understanding the nature of anhedonia in schizophrenia spectrum disorders (Kring and Barch, 2014; Kring and Elis, 2013). Previous imaging studies have consistently observed reduced VS activation during reward anticipation in populations with high familial risk for psychosis (de Leeuw et al., 2015; Grimm et al., 2014) and schizophrenia (See Radua et al. (2015) and Yan et al. (2015) for meta-analyses), suggesting a potentially reliable biomarker for anhedonia in people at risk of developing schizophrenia. However, few studies have addressed the neural substrates of reward anticipation in schizotypy and its various dimensions.

In the present study, we further investigated the neural correlates of reward anticipation and consummation in schizotypy and explored whether different dimensions of schizotypy were associated with different neural dysfunctions.

2. Materials and methods

2.1. Participants

All participants were recruited from 748 college students at the East China Normal University and the Shanghai Normal University. We adopted the categorical method in classifying individuals into schizotypy based on the manual of the Schizotypal Personality Questionnaire (Chinese version, Chen et al., 1997; SPQ, Raine, 1991). Individuals with schizotypy had a total SPQ score above the top 10th percentile of the sample, whereas individuals with scores at the bottom 50th percentile of the sample were classified as healthy controls. Thirty-three individuals with schizotypy (SPQ total score: Mean $=40.91$, SD $=4.40$) and 22 controls (SPQ total score: Mean $=16.36$, SD $=4.41$) were randomly selected from the schizotypy and control samples. No participant was excluded for the presence of a personal or family history of neurological and psychiatric disorders, a history of traumatic brain injury, substance abuse, upper body motor impairment, or metal implants in their body. All participants were right-handed, native Mandarin Chinese speakers. Individuals with schizotypy were further sub-classified into the positive (n $=18$) and negative (n $=15$) schizotypy groups based on clustering method of the factor scores of the cognitive-perceptual, the interpersonal and the disorganized subscales of the SPQ. This method has been successfully applied to classify subtypes of schizotypy in Chinese college students previously (Shi et al., 2012). Significant differences in scores in the cognitive perceptual and the interpersonal subscales were observed between the PS and the NS groups (Cognitive-perceptual: PS $>$ NS, F (1, 31)$=22.397$, $p < .001$; Interpersonal: PS $<$ NS, F (1,31)$=35.239$, $p < .001$; Disorganized: PS $=$ NS, $p > .05$). The study was approved by the Ethics Committee of the Institute of Psychology, the Chinese Academy of Sciences. Written informed consents were obtained from all participants. Each participant could withdraw from the study at any time.

2.2. Assessments and procedures

2.2.1. Monetary Incentive Delay task

We employed the Monetary Incentive Delay (MID) task, which was developed as an event-related paradigm by Knutson et al. (2001), to capture neural response during anticipation and consummation of monetary rewards and punishments. In the MID, there is a valence manipulation (gain or lose) and a magnitude manipulation (none (0 RMB), small (.50 RMB), big (5.00 RMB)). Each trial started with the presentation of a cue (circle/square, 250 ms), indicating the amount of money at stake (gain or lose). The line inside the cue reflected the amount of money (no line $=0$ RMB, one line $=.50$ RMB and three lines $=5.00$ RMB). Following a pseudo-random delay (2000–2500 ms) in the anticipatory phase, participants were required to respond to the target (a white solid square) that appeared for a variable length of time (110–560 ms) by pressing a button as quickly as possible using their right index finger. A feedback (1650 ms) was given on the screen in words to the participants about the amount of money they had won or lost, as well as their cumulative earnings. Participants could gain or avoid losing money if they pressed the button within the duration of the target. Finally, inter-trial interval was presented with a pseudo-random cross fixation (3000–4500 ms). In order to maximize the participants' engagement, task difficulty (duration of target presentation) was manually adjusted based on the performance of the participants so that the accuracy would approach 66% (see Fig. 1). Participants engaged in three runs and earned 16.9–56.7 RMB for the MID task.

After scanning, participants were immediately asked to provide their subjective ratings in terms of valence and arousal across all the conditions during the anticipatory and the consummatory phase. A nine-point bipolar scale was used to measure valence (1$=$extremely negative, 5$=$neutral, 9$=$extremely positive) and arousal (1$=$extremely calm, 9$=$extremely arousal).

2.2.2. Other assessments and questionnaires

The Chinese version of the Wechsler Adult Intelligence Scale-revised (WAIS-R, Gong, 1992) was administered to all the participants to estimate their IQ. The Temporal Experience of Pleasure Scale (TEPS, Chan et al., 2010; Gard et al., 2006) was used to measure *anti*cipatory and consummatory pleasure. The Chinese