Psychiatry Research: Neuroimaging 254 (2016) 127–136

Contents lists available at ScienceDirect

Psychiatry Research: Neuroimaging

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

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

Chao Yan [a,b], Yi Wang [b], Li Su [c], Ting Xu [b], Da-zhi Yin [d], Ming-xia Fan [e], Ci-ping Deng [a], Zhao-xin Wang [a], Simon S.Y. Lui [b,f], Eric F.C. Cheung [f], Raymond C.K. Chan [b,*]

[a] Key Laboratory of Brain Functional Genomics, Ministry of Education, Shanghai Key Laboratory of Brain Functional Genomics (MOE & STCSM), East China Normal University, Shanghai, China
[b] Neuropsychology and Applied Cognitive Neuroscience Laboratory, Key Laboratory of Mental Health, Institute of Psychology, Chinese Academy of Sciences, Beijing, China
[c] Department of Psychiatry, Cambridge Biomedical Campus, University of Cambridge, Cambridge, UK
[d] Institute of Neuroscience, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, China
[e] Shanghai Key Laboratory of MRI, East China Normal University, Shanghai, China
[f] Castle Peak Hospital, Hong Kong Special Administrative Region, China

ARTICLE INFO

Article history:
Received 28 January 2016
Received in revised form
9 May 2016
Accepted 23 June 2016
Available online 25 June 2016

Keywords:
Negative schizotypy
Positive schizotypy
fMRI
Reward anticipation
Reward consummation

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.

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

* Correspondence to: Institute of Psychology, Chinese Academy of Sciences, Room 526, South Building, 16 Lincui Road, Beijing, China.
E-mail address: rckchan@psych.ac.cn (R.C.K. Chan).

http://dx.doi.org/10.1016/j.pscychresns.2016.06.014
0925-4927/

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

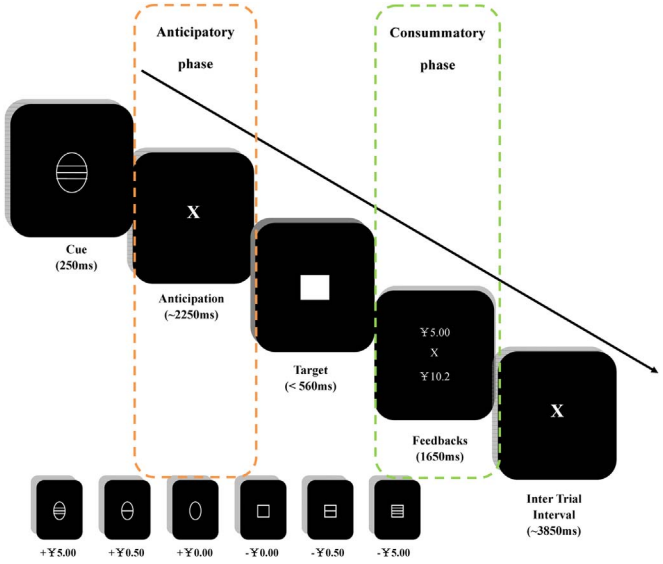

Fig. 1. Procedure of the Monetary Incentive Delay task. Each trial began with the presentation of a cue (circle/square), indicating the possible monetary reward/punishment. A fixation would appear for a pseudo-random period (2000–2500 ms) during the anticipatory phase. Then participants were required to respond to a white solid square by pressing a button as quickly as possible. A feedback was given to the participants about the money they had won/lost as well as their cumulative balance. The anticipatory phase (orange dotted square) began after the presence of cue and consummatory phase began when feedback is presented (green dotted square). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

version of the TEPS contains 20 items with six Likert-scales and has good internal consistency for the *anti*cipatory (Cronbach's α=.72) and consummatory subscales (Cronbach's α=.78). Higher score indicates stronger *anti*cipatory or consummatory pleasure. Physical and social anhedonia were measured using the Chapman Physical Anhedonia Scale (RCPAS, 61 items, Chan et al., 2012; Chapman et al., 1976) and the Chapman Social Anhedonia Scale (RCSAS, 40 items, Chan et al., 2012; Chapman and Chapman, 1978; Eckblad et al., 1982). The Chinese versions of these two scales have been shown to possess good psychometric properties (Cronbach's alpha coefficients $>$.75) (Chan et al., 2012). Higher scores indicate elevated physical or social anhedonia.

2.2.3. Imaging acquisition

All the participants were scanned in a 3-Tesla Siemens Trio magnetic resonance imaging scanner (Siemens Medical Solutions, Erlangen, Germany). The functional images were acquired by detecting BOLD signal with the following sequence: TR $=$2000 ms, TE $=$30 ms, field of view (FOV)$=$210 $\times$ 210 mm, flip angle $=$90 degree, slice number $=$32, resulting in voxel size of 3.3 $\times$ 3.3 $\times$ 4 mm. Participants viewed visual stimuli on a projector screen via a mirror fixed on the head coil and responded with the right index finger by pressing the button on a response glove fixed on their right hand. Following the first run of the MID task, high-resolution T1-weighted MPRAGE anatomy images were acquired (TR $=$2530 ms, TE $=$30 ms, FOV $=$256 $\times$ 256 mm, flip angle $=$7 degree, 192 continuous axial slice of 1-mm thickness, voxel size $=$1 $\times$ 1 $\times$ 1 mm).

2.3. Statistical analysis

2.3.1. Behavioural data analysis

Independent sample T-tests and chi-square tests were conducted to determine whether there were significant group differences in demographic information, IQ estimates and self-reported trait pleasure between controls and schizotypy individuals. One-way ANOVAs were performed to determine the differences between controls, PS, and NS in terms of those demographic information and scales scores. A series of two-way (Group x Magnitude) repeated measure ANOVAs were separately performed on valence and arousal rating during the anticipation of gain/loss and consummation of gain/loss outcomes. Group was considered as a between-subject factor containing two levels (controls and schizotypy) and magnitude was considered as a within-subject factor. Multiple comparisons were corrected using Bonferroni correction. Based on the a-priori hypothesis on the subtype of schizotypy (Kwapil et al., 2012; Wang et al., 2012), a K-means analysis with two clusters and 10 maximum iterations was performed on the three factors of the SPQ in individuals with schizotypy. One-way ANOVAs were simultaneously performed to test the differences on the scores of SPQ subscales between the subtypes.

2.3.2. Functional MRI data analysis

Functional images were analysed using SPM8 (Statistic Parametric Mapping, Wellcome Department of Neurology, London, UK, 2009). All the volumes were re-aligned to the mean volume, and corrected for differences in slice-time acquisition. Then, the structural 3D images were co-registered with the mean volume of functional images for each individual based on the algorithms by Collignon et al. (1995). The co-registered structural images were segmented using default tissue probabilities map and aligned to the International Consortium for Brain Mapping (ICBM) space template using mutual information affine registration. The transformation was subsequently applied to the functional images, followed by down-sampling to a resolution of 3 $\times$ 3 $\times$ 3 mm voxel size. The normalized images were smoothed with a Gaussian kernel (full width at half maximum $=$8 mm).

For each participant, a general linear model (GLM) (Friston et al., 1994) was used to estimate the BOLD response for each condition containing six regressors for anticipation of gain and loss (0 RMB, .50 RMB, 5.00 RMB), six regressors for gain and loss outcome (0 RMB, .50 RMB, 5.00 RMB), three for gain omission outcome (i.e. receiving 0 RMB for the three magnitudes), three regressors for loss avoidance outcome ($-$0 RMB under three magnitudes), and six regressors for head movement parameters. Regressors of interest were also convolved with a canonical haemodynamic response function combined with time derivatives. For the anticipatory phase, we included the contrast of potential monetary gain (.50 RMB $+$5.00 RMB) versus non-gain (0 RMB) and the contrast of potential monetary loss (.50 RMB $+$5.00 RMB) versus non-loss (0 RMB), resulting in a T statistic for each voxel. For the consummatory phase, we included the contrast of gain outcomes (.50 RMB $+$5.00 RMB) versus non-gain outcomes (0 RMB) and the contrast of loss outcomes (.50 RMB $+$5.00 RMB) and non-loss outcomes (0 RMB), resulting in T maps for each voxel.

At the second level of analysis, we performed one sample T-tests for each contrast in controls and schizotypy individuals. To examine between-group effects, we separately performed two-sample T-tests on the four contrasts mentioned above between controls and schizotypy individuals. We used a voxel-wise threshold of $p<.001$ for T-values. At this voxel-wise threshold, a Monte Carlo simulation indicated that a minimum cluster size of 19 voxels was required to achieve a significance level of $p<.05$, corrected for multiple comparisons (AlphaSim correction) over the whole brain.

2.3.3. Region of interest definition and correlation analysis

Functional regions of interest (ROIs) were determined based on previous meta-analysis indicating the involvement of the bilateral VS, the right anterior insula, the right putamen, the MPFC and the right thalamus in reward anticipation as well as involvement of the medial prefrontal cortex, the right caudate, the left amygdala

and the left putamen in reward consummation (Knutson and Greer, 2008). They were identified by drawing sphere with a 8 mm radius under their MNI coordinates using MarsBar (Brett et al., 2002) (see supplementary material). Contrast coefficient maps of ROIs were compared in these *t* tests for gain/loss anticipation and consummation contrasts.

The percentages of BOLD signal change for the contrasts were extracted for the 10 a-priori ROIs using MarsBar. Pearson correlation analyses were performed to determine the relationships between anhedonia scores in schizotypy individuals (i.e. TEPS, RCPAS, RCSAS) and the percentage of signal change in the a-priori ROIs using SPSS version 17.0. Shapiro-Wilk tests were performed

Table 1
Demographic information and self-report scales scores for the individuals with schizotypy and healthy control.

	Controls		Schizotypy						Control vs. Schizotypy			Control vs. PS vs. NS		Multiple comparisons
	(N = 22)		All (N = 33)		PS (N = 18)		NS (N = 15)		t/χ^2	*p*	Cohen's *d*	F/χ^2	*p*	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD						
Age	19.78	.80	19.30	1.19	19.28	1.18	19.33	1.23	1.79	.08	.46	1.76	.22	Controls vs. PS: $p=.342$; Controls vs. NS: $p=.531$; PS vs. NS: $p=1$
Gender (Male: Female)	11: 11		17: 16		9: 9		8: 7		.012	.91		.049	.98	Controls vs. PS: $p=1$; Controls vs. NS: $p=.842$; PS vs. NS: $p=.849$
IQ estimated	126.27	8.59	126.73	8.48	125.67	9.06	128.00	7.86	−.19	.85	−.05	.32	.73	Controls vs. PS: $p=1$; Controls vs. NS: $p=1$; PS vs. NS: $p=1$
TEPS_T	88.32	11.78	87.39	10.39	89.50	10.81	84.87	9.61	.31	.76	.08	.79	.46	Controls vs. PS: $p=1$; Controls vs. NS: $p=1$; PS vs. NS: $p=.690$
TEPS_Ant	39.09	5.31	36.73	5.38	37.67	5.34	35.60	5.38	1.61	.11	.44	1.91	.16	Controls vs. PS: $p=1$; Controls vs. NS: $p=.169$; PS vs. NS: $p=.819$
TEPS_Con	45.36	7.97	47.06	6.39	47.78	6.60	46.20	6.24	−.87	.39	−.24	.58	.56	Controls vs. PS: $p=.869$; Controls vs. NS: $p=1$; PS vs. NS: $p=1$
SPQ_T	16.36	4.41	40.91	4.40	40.22	4.24	41.73	4.59	−20.25	< .001	−5.57	205.38	< .001	PS > Controls: $p<.001$; NS > Controls: $p<.001$; PS vs. NS: $p=.993$
SPQ_Co_Pe	8.32	3.29	18.52	4.46	21.11	3.16	15.40	3.78	−9.18	< .001	−2.53	71.50	< .001	PS > Controls: $p<.001$; NS > Controls: $p<.001$; PS > NS: $p<.001$
SPQ_Int	5.82	3.23	15.55	4.22	12.78	3.21	18.87	2.56	−9.16	< .001	−2.52	83.03	< .001	PS > Controls, $p<.001$; NS > Controls, $p<.001$; NS > PS, $p<.001$.
SPQ_Diso	3.36	2.34	10.61	2.55	10.33	2.66	10.93	2.46	−10.66	< .001	−2.93	56.49	< .001	PS > Controls, $p<.001$; NS > Controls, $p<.001$; PS vs. NS: $p=1$
RCSAS	5.18	2.97	11.52	6.99	11.56	7.09	11.47	7.11	−4.62	< .001	−1.10	7.88	.001	PS > Controls, $p=.003$; NS > Controls, $p=.006$; PS vs. NS: $p=1$
RCPAS*	12.38	6.46	16.09	7.15	14.41	6.48	18.00	7.61	−1.92	.06	−.54	2.99	.059	Controls vs. PS: $p=1$; Controls vs. NS: $p=.055$; PS vs. NS: $p=.429$

Note: TEPS = Temporal Experience of Pleasure Scale; T = Total Score; Ant = Anticipatory subscale score; Con = Consummatory subscale score; SPQ = Schizotypal Personality Questionnaire; Co-Pe = Cognitive – perceptual factor; Int = Interpersonal factor; Diso = Disorganized factor; RCSAS = Revised Chapman Social Anhedonia Scale; RCPAS = Revised Chapman Physical Anhedonia Scale. *: 21 controls and 32 schizotypy (including 17 positive schizotypy (PS) and 15 negative schizotypy (NS)) finished RCPAS. Multiple corrections were performed using Bonferroni correction.

on all the variables included in the correlation (see Supplementary Table 1). If the data did not follow the normal distribution, Spearman correlation was performed instead. Multiple comparisons were corrected with a significance level of $p < .0083$ (correcting for six ROIs, .05/6) during the anticipatory phase and $p < .0125$ (correcting for four ROIs, .05/4) during the consummatory phase.

3. Results

3.1. Demographic information and anhedonia scores

Table 1 summarizes the demographics and scale scores of individuals with schizotypy and controls. There were no significant differences in age, IQ, and gender proportion between schizotypy individuals and controls. No significant differences in the anticipatory and the consummatory factor scores on the TEPS were found between these two groups. However, individuals with schizotypy reported significantly higher scores on the RCSAS ($p < .001$). In addition, the PS group and the NS group had elevated scores on the RCSAS (PS: $p = .003$; NS: $p = .006$), but comparable scores on the RCPAS and the anticipatory and consummatory subscales on the TEPS compared with controls.

3.2. Behavioural performance in the MID task

For subjective affective rating, there were no significant group (schizotypy vs. control) effect or group × magnitude interaction on valence or arousal rating during gain and loss anticipation and during gain and loss outcome consummation (all $ps > .05$). As expected, a significant main effect of magnitude was observed on valence and arousal ratings during both the anticipatory and the consummatory phase, indicating increasing pleasantness/unpleasantness and arousal level with increase in gain/loss magnitudes (all $ps < .001$, see complete statistic in Supplementary Table 2 and Fig. 2).

In addition, the PS and the NS group reported no difference in anticipatory or consummatory pleasure compared with controls, reflected by the non-significant main effect of group and group × magnitude interaction (all $ps > .05$, see Supplementary Fig. 1 and Supplementary Table 1).

As for the payments by MID, there was no significant difference in the personal finances provided by MID between individuals with schizotypy and controls ($t(53) = -.159$, $p = .874$). Similarly, no significant difference was observed between controls, the PS and the NS groups ($F(2, 52) = .359$, $p = .70$).

3.3. Brain activations in schizotypy individuals and controls

3.3.1. Gain versus non-gain outcomes

In the consummatory phase, "gain vs. non-gain outcomes" activated foci in the MPFC, the ACC, the left dorsolateral prefrontal cortex, the right precuneus and the left dorsal striatum in both controls and schizotypy individuals. Besides, controls showed prominent activation in the left superior parietal lobe, the right VS, the inferior parietal lobe and the left fusiform gyrus, but the schizotypy group exhibited significant activation in the left hippocampus and the left angular gyrus (see Supplementary Table 3). However, there was no significant group difference in brain activation between controls and schizotypy individuals as a whole. Even with ROI analysis, no significant group differences were observed in the MPFC, the right caudate, the left amygdala and the left putamen.

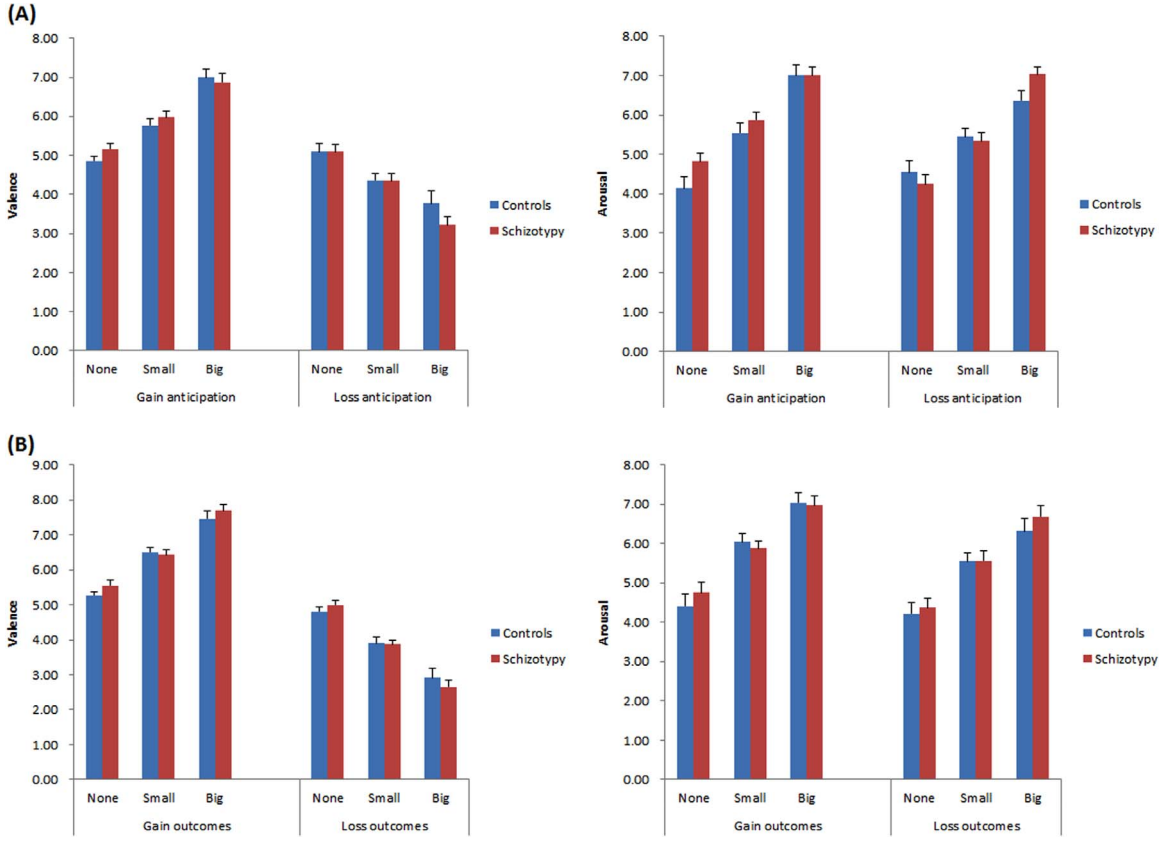

Fig. 2. Mean valence and arousal ratings during gain/loss anticipation (A) and consummation of gain/loss outcomes (B) in the MID task in schizotypy individuals and controls. Error bars represent standard errors.

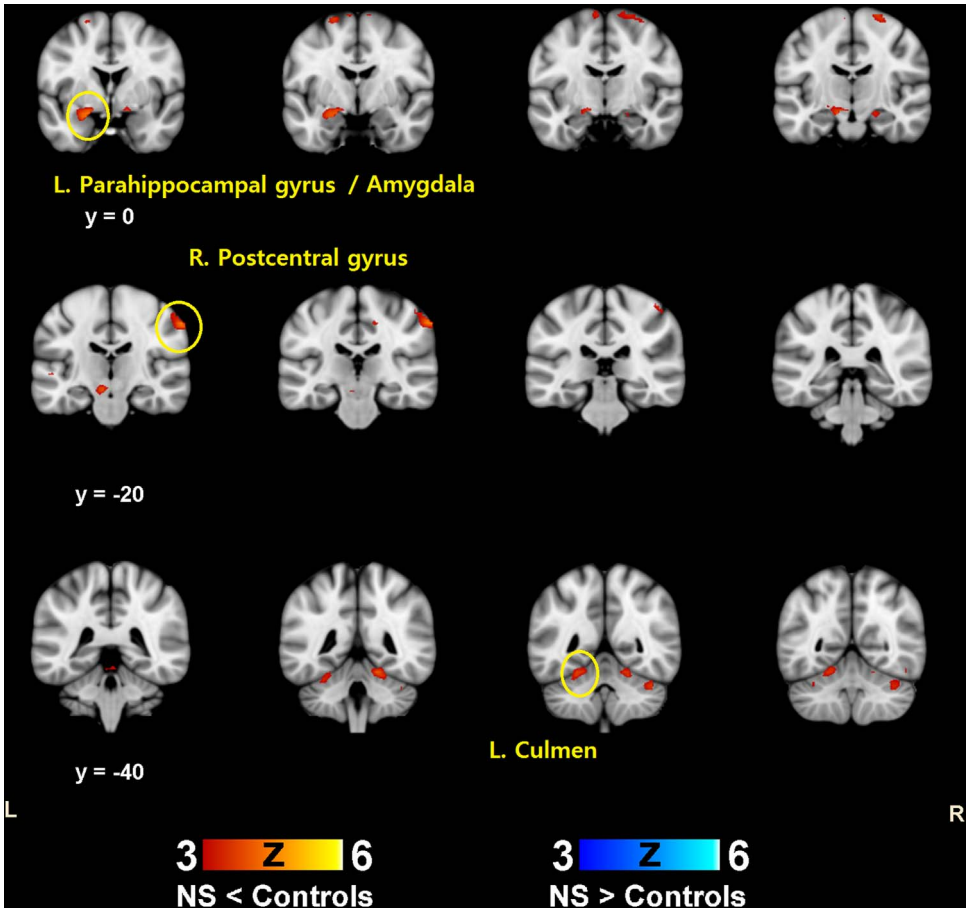

Fig. 3. Difference in brain activations for the contrast of gain versus non-gain outcomes consummation between negative schizotypy and control groups. Multiple comparisons were adjusted by using AlphaSim correction at $p < .05$.

Table 2
Group differences in whole brain activations during the reward anticipation and consummation between the NS and control group ($p_{\text{AlphaSim corrected}} < .05$).

Contrast	Group comparisons	Label	BA	Cluster size	peak Z	MNI Coordinates		
						X	Y	Z
Gain vs. Non-gain Anticipation	Controls > NS	L. Cerebellar tonsil		28	4.73	−30	−48	−42
		R. Cerebellar tonsil		26	3.97	12	−99	0
					3.21	0	−90	−3
		L. MTG	21	19	3.47	−63	−36	−6
		L. VS		23	3.44	−15	21	−3
					3.25	−15	27	−12
	NS > Controls	n.s.						
Gain vs. Non-gain Outcomes	Controls > NS	R. Postcentral Gyrus		31	4.47	66	−21	45
		L. Parahippocampal gyrus/Amygdala		73	3.91	−18	0	−15
					3.77	−6	−18	−15
		L. Culmen		21	3.54	−21	−51	−18
	NS > Controls	n.s.						

Note: reported are the two-sample T results for the contrasts of "Gain versus Non-gain anticipation" and "Gain versus Non-gain outcomes consummation" between 15 individuals with NS and 22 controls with Brodmann area (BA), cluster size, z-value, MNI coordinate for the whole brain. R. = Right; L. = Left; MTG = middle temporal gyrus; VS = ventral striatum; NS = Negative schizotypy.

To further investigate the neural responses in subtypes of schizotypy, two-sample *t*-tests were performed between the PS, the NS and control groups at the whole brain level. It was found that the NS group exhibited weaker activation in the right postcentral gyrus, the left parahippocampus gyrus/amygdala and the left culmen compared with the control group (see Fig. 3 and Table 2). ROI analysis revealed attenuated left putamen activation ($t(35)=2.403$, $p=.0109$) in the NS group compared with controls. There was no significant group difference between the PS and the control group.

Furthermore, the NS group displayed reduced brain activations in the right postcentral gyrus, the left culmen, the left precuneus, the bilateral precentral gyrus, and the left parahippocampal gyrus/amygdala compared with the PS group (see Supplementary Table 5). Apart from the left amygdala, ROI analysis did not reveal different activations in the other regions concerned between the NS and the PS group.

3.3.2. *Loss versus non-loss outcomes*

Loss versus non-loss outcomes consummation activated foci in the medial frontal cortex (MFC) and the insula in both the control

and the schizotypy groups. In addition, individuals with schizotypy showed prominent activations in the ACC and the right parahippocampal gyrus (see Supplementary Table 3). However, both whole brain analysis and ROI analysis did not reveal any significant group difference in brain activation between individuals with schizotypy as a whole and controls and between subtypes of schizotypy and controls.

3.3.3. *Gain versus non-gain anticipation*

Anticipation of gain versus non-gain activated the bilateral VS, the dorsal anterior cingulate cortex (dACC) and the right lingual gyrus in both controls and schizotypy individuals. In addition, control participants exhibited prominent activations in the right insula, the dorsal striatum (i.e. the right putamen and the medial globus pallidus), the MPFC and the parietal and occipital lobes (see Supplementary Table 4). However, group comparison using whole brain analysis and ROI analysis did not reveal any significant group difference in brain activation.

To further investigate brain activations in schizotypy subtypes, we performed two-sample *t*-tests between these groups across the whole brain. We found that individuals with PS displayed hyperactivation in the right ventral lateral prefrontal cortex compared with controls (see Fig. 4). The NS group, in contrast, showed significantly weaker activations in the left ventral striatum, the left middle temporal gyrus, and the bilateral cerebellar tonsil compared with controls (See Fig. 4 and Table 2). Apart from the left VS, ROI analysis did not find any significantly different activation in the other regions of interest between the NS and the control group.

In addition, compared with the PS group, the NS group showed weaker activation in the right VS extending to the ACC, the MPFC, the MFC, the left superior temporal gyrus, the right lingual gyrus, the right fusiform gyrus, and the left MTG using whole brain approach (see Supplementary Table 5). Using ROI approach, we only observed weaker activation in the right VS in the NS group compared with the PS group.

3.3.4. *Loss versus non-loss anticipation*

Anticipation of loss versus non-loss activated foci in the bilateral VS, the thalamus and the left precuneus in both controls and schizotypy individuals. The control group also showed prominent brain activations in the right red nucleus, the left lingual gyrus and the MFC, while the schizotypy group showed prominent activations in the bilateral precentral gyrus, the left parahippocampal gyrus, the middle cingulate cortex and the left declive (see Supplementary Table 4). However, group comparison with both whole brain analysis and ROI analysis did not reveal any significant difference in brain activation between controls and schizotypy individuals as a whole and between subtypes of schizotypy and controls.

3.3.5. *Correlations between % BOLD signal at ROIs and anhedonia in schizotypy*

During gain anticipation, right anterior insula activation was correlated with the severity of social anhedonia in schizotypy individuals (i.e. higher social anhedonia scores were associated with higher activation in the right anterior insula during gain anticipation; r =.58, p <.001), especially in the NS group (r =.70, p =.005) (see Fig. 5). No other significant correlation was observed between anhedonia scores and neural activities in the ROIs in schizotypy individuals.

4. Discussion

In the present study, we did not find any significant difference in brain activations during gain/loss anticipation or consummation between the schizotypy group as a whole and the control group. As expected, NS individuals exhibited weaker activation in the left amygdala and the left putamen during gain consummation compared with controls. There was no significant difference in brain activation between the PS group and controls. As for gain anticipation, attenuated left VS activations were observed in NS individuals compared with controls. In contrast, individuals with PS demonstrated enhanced activation at the right VLPFC compared with controls. More severe social anhedonia in the NS group was associated with enhanced brain activations in the right anterior insula during gain anticipation.

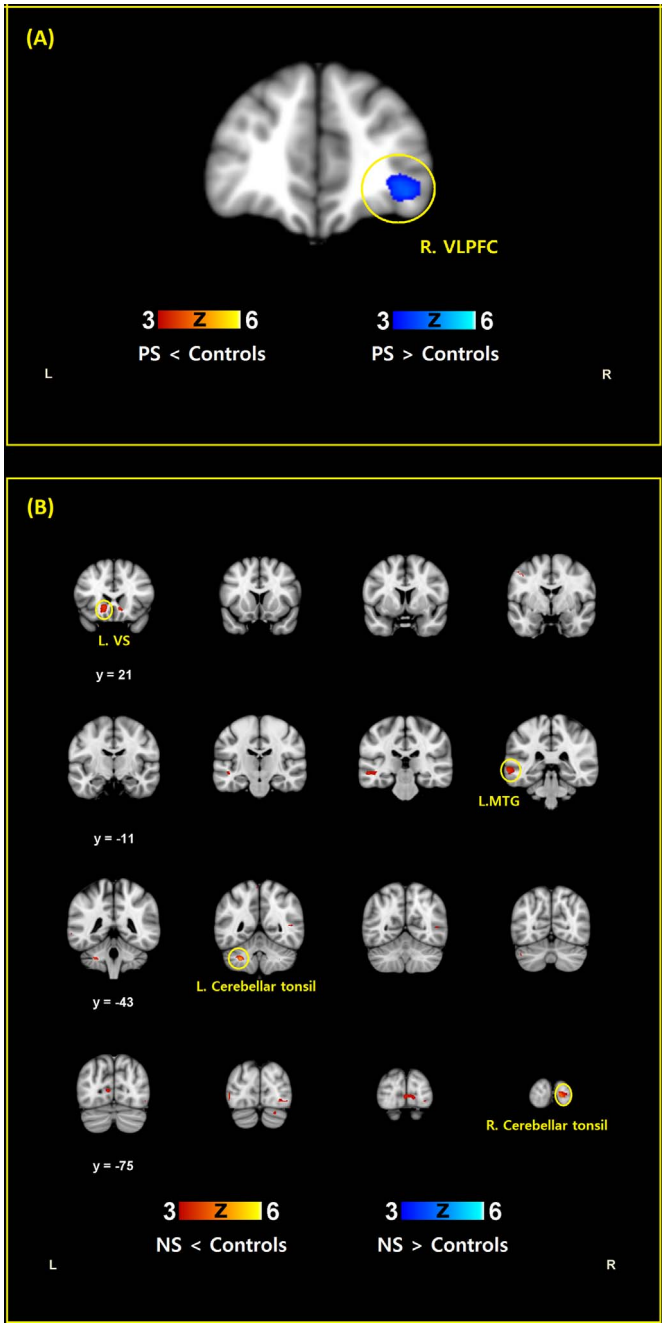

Fig. 4. Difference in brain activations for the contrast of gain versus non-gain anticipation between subtypes of schizotypy (the positive schizotypy (A) and negative schizotypy (B)) and control groups, respectively. Multiple comparisons were adjusted by using AlphaSim correction at $p < .05$.

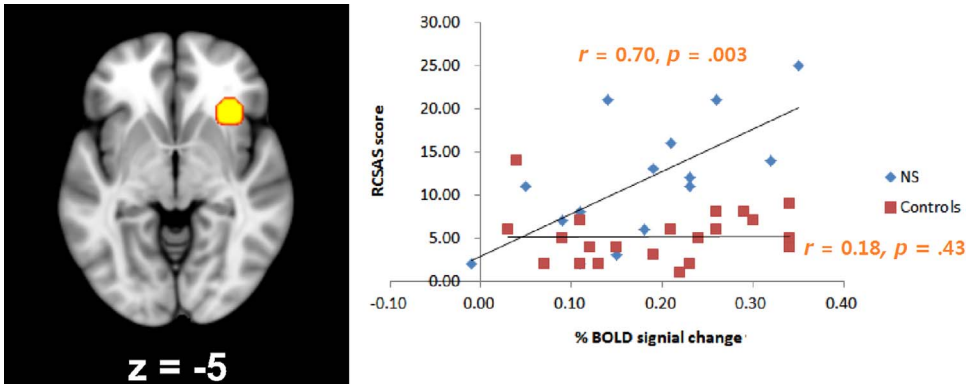

Fig. 5. Significant correlation between % BOLD signal change at the right anterior insula and social anhedonia scores in negative schizotypy (NS) and controls. The left panel of the figure presents location of the right anterior insula (x/y/z: 33/23/−5, MNI space transformed, Knutson and Greer, 2008). The right panel of figure shows scatter plot of correlations between averaged % BOLD signal changes for the contrast of gain versus non-gain anticipation and Chapman Social anhedonia scores in the controls, and the NS group. Multiple comparison were corrected at $p < .0083$ (.05/6 (number of ROI)) during anticipatory phase.

4.1. Reduced amygdala activation during reward consummation in individuals with negative schizotypy

In this study, we did not observe any significant difference in brain activation associated with gain consummation between the schizotypy group as a whole and the controls. Our results are consistent with the study by Wotruba et al. (2014), which employed the same paradigm and did not observe any altered brain activation during consummation of monetary reward outcome in individuals with ultra-high risk compared with healthy controls. However, other studies have reported that schizotypy may be associated with hypo-activations in the MPFC, the VLPFC, and the ACC (Harvey et al., 2010; Hooker et al., 2014). One explanation for the heterogeneous findings may be related to the dimensions of schizotypy investigated. Consistent with our hypothesis, we observed that the NS group differed from the PS group in left amygdala/hippocampal gyrus activations during the consummation of gain outcomes, which supports the hypothesis that there are distinct psychopathologies and emotional dysfunctions in positive and negative schizotypy (Kwapil et al., 2012; Loas et al., 2014; Wang et al., 2012). When directly compared with the control group, the NS rather than the PS group displayed reduced left amygdala activation, which is consistent with previous meta-analyses suggesting diminished amygdala activity with emotional processing in schizophrenia (Anticevic et al., 2012; Yan et al., 2015). Unfortunately, we did not observe any altered prefrontal and ACC activation during consummation of reward outcomes in either the PS or the NS groups, which differed from the results of some previous studies (Harvey et al., 2007; Huang et al., 2013). As suggested by Cohen et al. (2015), hyper-activation in the prefrontal cortex and the ACC may play a role in up-regulating activity in the limbic system during passive affective processing. Insufficient engagement of the limbic system during consummation of reward outcomes might reflect a failure of prefrontal and ACC up-regulating activity in schizotypy individuals. This may partially explain why we did not observe any hyper-activation in the prefrontal cortex and the ACC. Taken together, studies recruiting NS rather than PS individuals would more likely produce abnormal limbic activation, which may partially explain the previous mixed findings on the neural correlates of reward outcome consummation in schizotypy.

4.2. Reduced VS activation during reward anticipation in individuals with negative schizotypy

In the present study, we did not observe altered neural activation during reward anticipation in the schizotypy group as a whole. However, individuals with NS exhibited decreased ventral striatal activity during reward anticipation compared with controls and individuals with PS, which has rarely been reported in previous studies (see Cohen et al. (2015)). Two previous behavioural studies had investigated the relationship between anticipatory pleasure deficit and the negative dimension of schizotypy. Shi et al. (2012) have found that anticipatory pleasure deficit measured by the TEPS was present in individuals with NS rather than PS. Loas et al. (2014) observed that the negative dimension of schizotypy was characterized by both *anti*cipatory and consummatory pleasure deficits. Our results suggest that diminished VS activation during reward anticipation may be specifically associated with the negative dimension of schizotypy.

Moreover, our findings are also consistent with a number of imaging studies suggesting that patients with schizophrenia (Gradin et al., 2011; Walter et al., 2009; Waltz et al., 2009; White et al., 2015) and people at risk of developing psychosis (de Leeuw et al., 2015; Grimm et al., 2014; Wotruba et al., 2014) exhibited similar ventral and dorsal striatal activity reduction during reward anticipation. Two recent imaging meta-analyses have summarized that both the ventral and dorsal striatum might be the underlying neural substrate of anticipatory pleasure deficit in schizophrenia (Radua et al., 2015; Yan et al., 2015). Taken together with our findings, we believe that the negative dimension of schizotypy might share neural substrates of reward dysfunctions with schizophrenia and population at risk for schizophrenia. Indeed, ventral striatal activity reduction during reward anticipation may be a potential biomarker of schizophrenia spectrum disorders.

Within the NS group, interestingly, we observed significant positive correlations between the severity of social anhedonia and right anterior insula activity during reward anticipation. Indeed, previous studies had also reported positive correlations between anhedonia severity and activities of the right insula and the ventral MPFC with emotional processing (Harvey et al., 2007; Wang et al., 2015). There is evidence suggesting the presence of a strong functional connectivity between the insula and the VS during reward processing such as monetary reward anticipation (Cho et al., 2013), aggressive behaviour avoidance (Buades-Rotger et al., 2015) and joyful music (Koelsch and Skouras, 2014). The increased activity in the insula may play a role in compensating the attenuated VS activity during reward anticipation in NS individuals.

4.3. Increased right VLPFC activity during reward anticipation in individuals with positive schizotypy

We found that individuals with PS displayed enhanced activity in the right VLPFC compared with controls during reward

anticipation. Previous studies have also reported exaggerated prefrontal activity during emotional processing in population at high familial risk for psychosis (de Leeuw et al., 2015; Li et al., 2012; Myin-Germeys and van Os, 2007; van Buuren et al., 2011), ultra-high risk populations (Seiferth et al., 2009; Wotruba et al., 2014) and healthy people with schizophrenia risk-associated gene (Radulescu et al., 2013). For example, van Buuren et al. (2011) have found that unaffected siblings of schizophrenia showed exaggerated activity in the MPFC, the ACC and the insula when viewing both positive and negative pictures compared with healthy controls. Some have also noted that the enhanced prefrontal activity associated with reward/hedonic processing might compensate for neural anomalies in the VS and the amygdala (Cohen et al., 2015; Harvey et al., 2007; Raine, 2006; Wang et al., 2015). Since there is evidence that the VLPFC upregulates activity in the limbic and mesolimbic system (Harvey et al., 2010; Tupak et al., 2014), it is possible that hyper-activation of the prefrontal cortex in PS individuals may be related to intact engagement of neural activation in the VS, the insula, the thalamus and the putamen during reward anticipation.

4.4. Limitation and conclusion

The present study has several limitations. First, we only recruited psychometrically-defined schizotypy individuals. The recruitment of individuals with high familial risk of developing psychosis and people in the prodrome of psychosis should be considered in future studies. Secondly, our study used reinforcement stimuli (i.e. money) to elicit pleasure experience. Since social dysfunction is one of the major features of schizotypal personality disorder (Blanchard et al., 2009; Raine, 2006), it is not clear whether reinforcement stimuli with more social content would lead to the same results. Thirdly, our findings were also limited by the small sample size regarding the number of individuals with PS ($n = 18$) and NS ($n = 15$). Considering the fact that previous studies have suggested fMRI studies with typical subject number ($n = 10$ to 20) might be underpowered (Desmond and Glover, 2002; Murphy and Garavan, 2004), the relatively small sample size ($n < 20$) of individuals with schizotypy subtypes in the present study might limit statistical power. Finally, the PS and NS samples were drawn from the same group of psychometrically-defined schizotypal individuals, which may be not an independent procedure. There are alternative procedures to independently identify schizotypy subtypes from the general population. For example, a median split procedure or principal component analysis of the Chapman Perceptual Aberration/ Magical Ideation scale and RCSAS/RCPAS have been used to independently identify high positive (and low negative) schizotypes as well as high negative (and low positive) schizotypes (Leonards and Mohr, 2009; Wang et al., 2013). These procedures could be employed to identify PS and NS from the general population in future studies.

In conclusion, our findings suggest that different dimension of schizotypy may differentially contribute to altered striatal-limbic-prefrontal activities during reward anticipation and consummation.

Contributor

Yan C. designed the study, analysed the data, and wrote the paper. Wang Y., Su L. and Xu T. analysed the data and interpreted the data. Yin DZ, Fan MX, Deng C. P., Wang Z. X. collected the data. Cheung E.F.C. interpreted the data and commented. Chan R.C.K. generated the idea, supervised the study, and commented significantly on the first draft of the manuscript. All authors read and commented on the final version of the paper.

Conflict of interest

Declaration of Conflicts: The authors declare no conflicts in authorship and publication for this paper.

Competing financial interests: The authors declare no competing financial interests.

Acknowledgements

This study was supported by grants from the National Science Fund China (81088001, 81571317, 91132701 and 31500894), the Strategic Priority Research Programme (B) of the Chinese Academy of Sciences (XDB02030002), the Beijing Training Project for Leading Talents in S & T (Z151100000315020), and a grant from the initiation fund of the CAS/SAFEA International Partnership Programme for Creative Research Team (Y2CX131003). These funding agents had no role in the study design, collection, analysis, and interpretation of the data, writing of the manuscript or decision to submit the paper for publication.

Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.pscychresns.2016.06.014.

References

Anticevic, A., Van Snellenberg, J.X., Cohen, R.E., Repovs, G., Dowd, E.C., Barch, D.M., 2012. Amygdala recruitment in schizophrenia in response to aversive emotional material: a meta-analysis of neuroimaging studies. Schizophr. Bull. 38, 608–621.

Blanchard, J.J., Collins, L.M., Aghevli, M., Leung, W.W., Cohen, A.S., 2009. Social anhedonia and schizotypy in a community sample: the Maryland longitudinal study of schizotypy. Schizophr. Bull.

Brett, M., Anton, J.-L., Valabregue, R., Poline, J.-B., 2002. Region of interest analysis using the MarsBar toolbox for SPM 99. NeuroImage 16, S497.

Buades-Rotger, M., Brunnlieb, C., Munte, T.F., Heldmann, M., Kramer, U.M., 2015. Winning Is not enough: ventral striatum connectivity during physical aggression. Brain Imaging Behav.

Chan, R.C.K., Wang, Y., Yan, C., Zhao, Q., McGrath, J., Hsi, X., Stone, W.S., 2012. A study of trait Anhedonia in non-clinical Chinese samples: evidence from the chapman scales for physical and social anhedonia. PLoS One 7, e34275.

Chan, R.C.K., Wang, Y., Huang, J., Shi, Y., Wang, Y., Hong, X., Ma, Z., Li, Z., Lai, M.K., Kring, A.M., 2010. Anticipatory and consummatory components of the experience of pleasure in schizophrenia: cross-cultural validation and extension. Psychiatry Res. 175, 181–183.

Chapman, L.J., Chapman, J.P., 1978. Revised Physical Anhedonia Scale. Department of Psychology, 1202 West Johnson Street, University of Wisconsin, Madison.

Chapman, L.J., Chapman, J.P., Raulin, M., 1976. Scales for physical and social anhedonia. J. Abnorm. Psychol. 85, 374–382.

Chen, W.J., Hsiao, C.K., Lin, C.C., 1997. Schizotypy in community samples: the three-factor structure and correlation with sustained attention. J. Abnorm. Psychol. 106, 649–654.

Cho, Y.T., Fromm, S., Guyer, A.E., Detloff, A., Pine, D.S., Fudge, J.L., Ernst, M., 2013. Nucleus accumbens, thalamus and insula connectivity during incentive anticipation in typical adults and adolescents. NeuroImage 66, 508–521.

Cohen, A.S., Mohr, C., Ettinger, U., Chan, R.C., Park, S., 2015. Schizotypy as an organizing framework for social and affective sciences. Schizophr. Bull. 41 (Suppl. 2), S427–S435.

Collignon, A., Maes, F., Delaere, D., Vandermeulen, D., Suetens, P., Marchal, G., 1995. Automated Multi-Modality Image Registration Based on Information Theory. Kluwer Academic Publishers, Dordrecht, The Netherlands.

Desmond, J.E., Glover, G.H., 2002. Estimating sample size in functional MRI (fMRI) neuroimaging studies: Statistical power analyses. J. Neurosci. Methods 118, 115–128.

Eckblad, M., Chapman, L.J., Chapman, J.P., Mishlove, M., 1982. The Revised Social Anhedonia Scale. University of Wisconsin, Madison (unpublished manuscript).

Ettinger, U., Meyhöfer, I., Steffens, M., Wagner, M., Koutsouleris, N., 2014. Genetics, cognition, and neurobiology of schizotypal personality: a review of the overlap with schizophrenia. Front. psychiatry 5, 18.

Friston, K.J., Holmes, A.P., Worsley, K.J., Poline, J.P., Frith, C.D., Frackowiak, R.S.J., 1994. Statistical parametric maps in functional imaging: a general linear

approach. Hum. Brain Mapp. 2, 189–210.
Gard, D.E., Gard, M.G., Kring, A.M., John, O.P., 2006. Anticipatory and consummatory components of the experience of pleasure: a scale development study. J. Res. Pers. 40, 1086–1102.
Gong, Y.X., 1992. Wechsler Adult Intelligence Scale – Revised in China Version. Hunan Medical College, Changsha.
Gradin, V.B., Kumar, P., Waiter, G., Ahearn, T., Stickle, C., Milders, M., Reid, I., Hall, J., Steele, J.D., 2011. Expected value and prediction error abnormalities in depression and schizophrenia. Brain 134, 1751–1764.
Grimm, O., Heinz, A., Walter, H., Kirsch, P., Erk, S., Haddad, L., Plichta, M.M., Romanczuk-Seiferth, N., Pohland, L., Mohnke, S., Muhleisen, T.W., Mattheisen, M., Witt, S.H., Schafer, A., Cichon, S., Nothen, M., Rietschel, M., Tost, H., Meyer-Lindenberg, A., 2014. Striatal response to reward anticipation evidence for a systems-level intermediate phenotype for schizophrenia. JAMA Psychiatry 71, 531–539.
Harvey, P.O., Pruessner, J., Czechowska, Y., Lepage, M., 2007. Individual differences in trait anhedonia: a structural and functional magnetic resonance imaging study in non-clinical subjects. Mol. Psychiatry 12 (703), 767–775.
Harvey, P.-O., Armony, J., Malla, A., Lepage, M., 2010. Functional neural substrates of self-reported physical anhedonia in non-clinical individuals and in patients with schizophrenia. J. Psychiatr. Res. 44, 707–716.
Hooker, C.I., Benson, T.L., Gyurak, A., Yin, H., Tully, L.M., Lincoln, S.H., 2014. Neural activity to positive expressions predicts daily experience of schizophrenia-spectrum symptoms in adults with high social anhedonia. J. Abnorm. Psychol. 123, 190–204.
Huang, J., Wang, Y., Jin, Z., Di, X., Yang, T., Gur, R.C., Gur, R.E., Shum, D.H.K., Cheung, E.F.C., Chan, R.C.K., 2013. Happy facial expression processing with different social interaction cues: an fMRI study of individuals with schizotypal personality traits. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 44, 108–117.
Knutson, B., Greer, S.M., 2008. Anticipatory affect: neural correlates and consequences for choice. Philos. Trans. R. Soc. Lond. B Biol. Sci. 363, 3771–3786.
Knutson, B., Adams, C.M., Fong, G.W., Hommer, D., 2001. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. J. Neurosci. 21, RC159.
Koelsch, S., Skouras, S., 2014. Functional centrality of amygdala, striatum and hypothalamus in a "small-world" network underlying joy: an fMRI study with music. Hum. Brain Mapp. 35, 3485–3498.
Kring, A.M., Elis, O., 2013. Emotion deficits in people with schizophrenia. Annu. Rev. Clin. Psychol. 9, 409–433.
Kring, A.M., Barch, D.M., 2014. The motivation and pleasure dimension of negative symptoms: neural substrates and behavioral outputs. Eur. Neuropsychopharmacol. 24, 725–736.
Kringelbach, M.L., Berridge, K.C., 2009. Towards a functional neuroanatomy of pleasure and happiness. Trends Cognit. Sci. 13, 479–487.
Kwapil, T.R., Brown, L.H., Silvia, P.J., Myin-Germeys, I., Barrantes-Vidal, N., 2012. The expression of positive and negative schizotypy in daily life: an experience sampling study. Psychol. Med. 42, 2555–2566.
de Leeuw, M., Kahn, R.S., Vink, M., 2015. Fronto-striatal dysfunction during reward processing in unaffected siblings of schizophrenia patients. Schizophr. Bull. 41, 94–103.
Leonards, U., Mohr, C., 2009. Schizotypal personality traits influence idiosyncratic initiation of saccadic face exploration. Vision Res. 49, 2404–2413.
Li, H.J., Chan, R.C., Gong, Q.Y., Liu, Y., Liu, S.M., Shum, D., Ma, Z.L., 2012. Facial emotion processing in patients with schizophrenia and their non-psychotic siblings: a functional magnetic resonance imaging study. Schizophr. Res. 134, 143–150.
Loas, G., Verrier, A., Monestes, J.L., 2014. Relationship between anticipatory, consummatory anhedonia and disorganization in schizotypy. BMC Psychiatry 14, 211.
Meehl, P.E., 1962. Schizotaxia, schizotypy, schizophrenia. Am. Psychol. 17, 827–838.
Murphy, K., Garavan, H., 2004. An empirical investigation into the number of subjects required for an event-related fMRI study. NeuroImage 22, 879–885.
Myin-Germeys, I., van Os, J., 2007. Stress-reactivity in psychosis: evidence for an affective pathway to psychosis. Clin. Psychol. Rev. 27, 409–424.
Radua, J., Schmidt, A., Borgwardt, S., Heinz, A., Schlagenhauf, F., McGuire, P., Fusar-Poli, P., 2015. Ventral striatal activation during reward processing in psychosis: a neurofunctional meta-analysis. JAMA Psychiatry, 1243–1251.
Radulescu, E., Sambataro, F., Mattay, V.S., Callicott, J.H., Straub, R.E., Matsumoto, M., Weinberger, D.R., Marenco, S., 2013. Effect of schizophrenia risk-associated alleles in SREB2 (GPR85) on functional MRI phenotypes in healthy volunteers. Neuropsychopharmacology 38, 341–349.
Raine, A., 1991. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. Schizophr. Bull. 17, 555–564.
Raine, A., 2006. Schizotypal personality: neurodevelopmental and psychosocial trajectories. Annu. Rev. Clin. Psychol. 2, 291–326.
Rapp, A.M., Mutschler, D.E., Wild, B., Erb, M., Lengsfeld, I., Saura, R., Grodd, W., 2010. Neural correlates of irony comprehension: the role of schizotypal personality traits. Brain Lang. 113, 1–12.
Salimpoor, V.N., Benovoy, M., Larcher, K., Dagher, A., Zatorre, R.J., 2011. Anatomically distinct dopamine release during anticipation and experience of peak emotion to music. Nat. Neurosci. 14, 257–262.
Seiferth, N.Y., Pauly, K., Kellermann, T., Shah, N.J., Ott, G., Herpertz-Dahlmann, B., Kircher, T., Schneider, F., Habel, U., 2009. Neuronal correlates of facial emotion discrimination in early onset schizophrenia. Neuropsychopharmacology 34, 477–487.
Shi, Y.F., Wang, Y., Cao, X.Y., Wang, Y., Wang, Y.N., Zong, J.G., Xu, T., Tse, V.W., Hsi, X. L., Stone, W.S., Lui, S.S., Cheung, E.F., Chan, R.C., 2012. Experience of pleasure and emotional expression in individuals with schizotypal personality features. PLoS One 7, e34147.
Soliman, A., O'Driscoll, G.A., Pruessner, J., Joober, R., Ditto, B., Streicker, E., Goldberg, Y., Caro, J., Rekkas, P.V., Dagher, A., 2011. Limbic response to psychosocial stress in schizotypy: a functional magnetic resonance imaging study. Schizophr. Res. 131, 184–191.
Tupak, S.V., Dresler, T., Guhn, A., Ehlis, A.C., Fallgatter, A.J., Pauli, P., Herrmann, M.J., 2014. Implicit emotion regulation in the presence of threat: neural and autonomic correlates. NeuroImage 85 (Pt 1), 372–379.
van Buuren, M., Vink, M., Rapcencu, A.E., Kahn, R.S., 2011. Exaggerated brain activation during emotion processing in unaffected siblings of patients with schizophrenia. Biol. Psychiatry 70, 81–87.
Walter, H., Kammerer, H., Frasch, K., Spitzer, M., Abler, B., 2009. Altered reward functions in patients on atypical antipsychotic medication in line with the revised dopamine hypothesis of schizophrenia. Psychopharmacology 206, 121–132.
Waltz, J.A., Schweitzer, J.B., Gold, J.M., Kurup, P.K., Ross, T.J., Salmeron, B.J., Rose, E.J., McClure, S.M., Stein, E.A., 2009. Patients with schizophrenia have a reduced neural response to both unpredictable and predictable primary reinforcers. Neuropsychopharmacology 34, 1567–1577.
Wang, Y., Neumann, D., Shum, D.H., Chan, R.C., 2012. A cross-validation study of clustering of schizotypy using a non-clinical Chinese sample. Psychiatry Res. 200, 55–58.
Wang, Y., Liu, W.-h, Li, Z., Wei, X.-h, Jiang, X.-q, Neumann, D.L., Shum, D.H.K., Cheung, E.F.C., Chan, R.C.K., 2015. Dimensional schizotypy and social cognition: an fMRI imaging study. Front. Behav. Neurosci., 9.
Wang, Y., Neumann, D.L., Shum, D.H., Liu, W.H., Shi, H.S., Yan, C., Lui, S.S., Zhang, Q., Li, Z., Cheung, E.F., Chan, R.C., 2013. Cognitive empathy partially mediates the association between negative schizotypy traits and social functioning. Psychiatry Res. 210, 62–68.
White, D.M., Kraguljac, N.V., Reid, M.A., Lahti, A.C., 2015. Contribution of substantia nigra glutamate to prediction error signals in schizophrenia: a combined magnetic resonance spectroscopy/functional imaging study. npj Schizophr. 1, 14001.
Wotruba, D., Heekeren, K., Michels, L., Buechler, R., Simon, J.J., Theodoridou, A., Kollias, S., Rössler, W., Kaiser, S., 2014. Symptom dimensions are associated with reward processing in unmedicated persons at risk for psychosis. Front. Behav. Neurosci. 8, 382.
Yan, C., Yang, T., Yu, Q.-j, Jin, Z., Cheung, E.F.C., Liu, X., Chan, R.C.K., 2015. Rostral medial prefrontal dysfunctions and consummatory pleasure in schizophrenia: a meta-analysis of functional imaging studies. Psychiatry Res.: Neuroimaging 231, 187–196.