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Altered corticostriatal functional connectivity in individuals with high social anhedonia

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Background. Dysregulation of the striatum and altered corticostriatal connectivity have been associated with psychotic disorders. Social anhedonia has been identified as a predictor for the development of schizophrenia spectrum disorders. The aim of the present study was to examine corticostriatal functional connectivity in individuals with high social anhedonia.

Method. Twenty-one participants with high social anhedonia score and 30 with low social anhedonia score measured by the Chinese version of the Revised Social Anhedonia Scale were recruited from university undergraduates (age 17–21 years) to undergo resting-state functional MRI scans. Six subdivisions of the striatum in each hemisphere were defined as seeds. Voxel-wise functional connectivity analyses were conducted between each seed and the whole brain voxels, followed by repeated-measures ANOVA for the group effect.

Results. Participants with high social anhedonia showed hyper-connectivity between the ventral striatum and the anterior cingulate cortex and the insula, and between the dorsal striatum and the motor cortex. Hypo-connectivity in participants with high social anhedonia was also observed between the ventral striatum and the posterior cingulate cortex. Partial correlation analyses further showed that the functional connectivity between the ventral striatum and the pre-frontal cortex was associated with pleasure experience and emotional suppression.

Conclusions. Our findings suggest that altered corticostriatal connectivity can be found in participants with high levels of social anhedonia. Since social anhedonia has been considered a predictor for schizophrenia spectrum disorders, our results may provide novel evidence on the early changes in brain functional connectivity in at-risk individuals.

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Key words: Anhedonia, frontal lobe, functional connectivity, striatum.

Introduction

Schizotypy refers to a set of personality traits related to schizophrenia spectrum pathology, including magical ideation, odd behaviour, perceptual aberration as well as anhedonia (Nelson *et al.* 2013). Anhedonia, the reduced capacity to experience pleasure, is one of the core symptoms of major depressive disorder and also an important negative symptom of schizophrenia (Andreasen, 1982; APA, 2013). Social anhedonia refers to the phenomenon of reduced capacity to experience

pleasure in the social context, and has been considered a component of negative schizotypy and indicates an increased risk for psychosis (Meehl, 1990; Clardige & Beech, 1995). Previous studies have suggested that a high level of social anhedonia was observed not only in patients with schizophrenia and their unaffected first-degree relatives (Katsanis *et al.* 1990), but also in individuals prone to psychosis (Chan *et al.* 2012a). In addition, previous studies have also indicated that the level of social anhedonia reported by individuals with psychometrically defined schizotypy was not different from that reported by patients with schizophrenia (Wang *et al.* 2014). Longitudinal studies have shown that individuals with a high level of social anhedonia developed full-blown psychosis or schizophrenia with a higher probability in 5 and 10 years, whereas no difference was found on the probability

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of developing depression or bipolar disorder (Kwapil, 1998; Gooding *et al.* 2005). All these suggest that the level of social anhedonia could potentially be a predictor of schizophrenia spectrum disorders. Therefore, investigation of the neural correlates of social anhedonia may contribute to a better understanding of the development of psychosis.

The striatum has been identified as one of the key brain structures involved in reward processing. Recent studies have further suggested that the ventral and dorsal parts of the striatum play distinct roles; the former being related to reward expectation and the latter related to the maintenance of the meaning of the reward outcome (O'Doherty *et al.* 2004). These circuits have also been linked to schizophrenia and other disorders (Pantelis & Brewer, 1995, 1996; Gabbay *et al.* 2013). Di Martino *et al.* (2008) examined the resting-state functional connectivity of the striatum in healthy participants by dividing it into six subdivisions [including the nucleus accumbens (NAc), the ventral caudate, the dorsal caudate, the dorsal caudal putamen, the dorsal rostral putamen (DRP) and the ventral rostral putamen]. Their results described the different functional connectivity patterns of the subdivisions of the striatum. For example, the dorsal caudate is highly connected to the frontal lobe, while the ventral caudate is connected to the limbic areas, which correspond to the cognitive/affective divisions. Taken together, the existing findings suggest that examining corticostriatal connectivity may be an optimal approach.

Altered functional connectivity of the striatum has been found in individuals with psychosis. Fornito *et al.* (2013) adopted the seed-based approach and found reduced functional connectivity between the dorsal caudate and the prefrontal regions, and increased functional connectivity between the ventral caudate and the prefrontal regions in patients with first-episode psychosis and their unaffected first-degree relatives. Furthermore, the fact that this pattern was also observed in unaffected first-degree relatives suggests that it may be an endophenotype for psychosis (Fornito *et al.* 2013). Further work in individuals at ultra-high risk (UHR) for psychosis found reduced functional connectivity between the caudal caudate and the prefrontal cortex, and increased connectivity between the ventral putamen, and the frontal and the temporal lobes (Dandash *et al.* 2014), suggesting that these changes are apparent before psychosis onset. However, it is still not fully known whether functional connectivity between the striatum and the frontal lobe are disrupted in the whole spectrum of schizophrenic disorders, including individuals with schizotypal traits.

In addition, problems in emotional processing, especially reduced pleasure experience and expression,

have been found in patients with schizophrenia (Kring & Elis, 2013) and also in individuals at high-risk for psychosis (Phillips & Seidman, 2008). Although corticostriatal circuits are important in emotional processing, few studies have examined the association between altered corticostriatal connectivity and reduced pleasure experience and expression in patients with schizophrenia and individuals at-risk for psychosis. In the two studies mentioned above, reduced functional connectivity was associated with both positive and negative symptoms in patients with first-episode schizophrenia and UHR individuals (Fornito *et al.* 2013; Dandash *et al.* 2014), but the association between reduced emotional experience/expression and corticostriatal circuit in schizophrenia spectrum remains unclear.

The aims of the present study were two-fold. First, we examined corticostriatal functional connectivity in individuals with high level of negative schizotypy (measured by the Social Anhedonia Scale), taking into account both the ventral and dorsal part of the striatum. Second, we examined the associations between emotional processing (including anticipatory/consummatory pleasure experiences and emotional expression) and corticostriatal functional connectivity. We hypothesized that individuals with high level of negative schizotypy would show reduced functional connectivity between the dorsal striatum and the frontal lobe and increased connectivity of the ventral part of striatum, a 'dorsal-to-ventral gradient of hypo- to hyper-connectivity with the prefrontal cortex'. In addition, the increased functional connectivity of the ventral striatum and the prefrontal cortex would be related to reduced anticipatory pleasure experience.

Method

Participants

There were two groups of participants in this study: individuals with high social anhedonia score (High SocAnh group) and those with low social anhedonia score (low SocAnh group). All participants were selected from a large sample pool from the Guangzhou Medical University based on their scores on the Chinese version of the Chapman Social Anhedonia Scale (CSAS; Chan *et al.* 2012a). The means and standard deviations (s.d.) from a previous study (Chan *et al.* 2012a) in Chinese college students ($n=887$) using the same scale (males: mean=9.40, s.d.=6.32; females: mean=7.61, s.d.=5.34) were used as reference in this study. Since previous meta-analysis has shown significant gender difference for the Chapman scales (Miettunen & Jaaskelainen, 2010), we calculated the cut-offs for males and females

Table 1. Demographic information and group comparison on scales

	Low SocAnh group (<i>n</i> = 30)	High SocAnh group (<i>n</i> = 21)	<i>t</i> / χ^2	<i>p</i>
Age, years, mean (s.d.)	19.3 (0.9)	19.3 (1.0)	0.054	N.S.
Gender (male female)	15:15	10:11	0.028	N.S.
IQ estimates, mean (s.d.)	116.43 (10.39)	115.86 (11.55)	0.186	N.S.
SocAnh total	3.07 (1.59)	15.19 (3.28)	15.69	<0.001
TEPS abstract anti	21.50 (2.22)	18.39 (3.13)	4.16	<0.001
TEPS contextual anti	20.17 (3.35)	16.06 (5.39)	3.09	<0.01
TEPS anti	41.67 (4.95)	34.45 (7.21)	4.2	<0.001
TEPS abstract cons	31.07 (3.05)	27.36 (4.55)	3.49	<0.01
TEPS contextual cons	18.53 (3.36)	15.69 (3.86)	2.80	<0.01
TEPS cons	49.60 (5.87)	43.05 (7.37)	3.53	<0.01
TEPS total	91.27 (9.83)	77.50 (12.33)	4.43	<0.001
EES expression	16.57 (4.20)	15.14 (4.00)	1.21	N.S.
EES suppression	46.33 (8.06)	38.52 (6.58)	3.66	<0.01
EES total	62.90 (11.19)	53.66 (7.88)	3.26	<0.01

SocAnh, The Chinese version of the Chapman Social Anhedonia Scale; TEPS, The Temporal Experiences and Pleasure Scales; anti, anticipatory factor of the TEPS; cons, consummatory factor of the TEPS; EES, Emotional Expressivity Scale.

separately. Participants whose scores were 0.5 s.d. above the mean of their own gender were recruited into the High SocAnh group (*n* = 21). Participants whose scores were 0.5 s.d. below the mean scores of their own gender were recruited into the low SocAnh group (*n* = 30). All participants were right-handed as assessed by the Annett Handedness Scale (Annett, 1970). They had no history of substance abuse, brain injury, neurological disorders and no personal and family history of mental disorders. The high SocAnh group had a mean age of 19.3 years (s.d. = 1.0) and consisted of 10 males. The low SocAnh group had a mean age of 19.3 years (s.d. = 0.9) and consisted of 15 males. Their IQ scores were estimated using the common-sense, arithmetic, similarity and digit span subtests of the Chinese Version of the Wechsler Adult Intelligence Scale – Revised (WAIS-R; Gong & Dai, 1984). The mean IQ estimates for the high SocAnh and the low SocAnh groups were 115.86 (s.d. = 11.55) and 116.43 (s.d. = 10.39), respectively. No significant difference was found between the two groups on age, gender and IQ estimates, as shown in Table 1. The present study was approved by the Ethics Committee of the Institute of Psychology, Chinese Academy of Sciences. Written informed consents were obtained from each participant prior to the study.

Measures

Chapman Social Anhedonia Scale (CSAS)

The Chinese version of CSAS was adopted from the original English version (Eckblad *et al.* 1982) after

undergoing a series of standard validation procedures (Chan *et al.* 2012a). The CSAS is a 40-item questionnaire assessing the reduced pleasure experiences induced by social interaction. For each item, participants were asked to report their own experience with a ‘true’ or ‘false’ answer. The total CSAS score was calculated for each participant. A higher total score indicates more severe anhedonia in social interactions.

Temporal Experiences and Pleasure Scales (TEPS)

The TEPS is a self-report questionnaire designed to measure individual trait dispositions in both anticipatory and consummatory experiences of pleasure. The original TEPS consists of a 10-item anticipatory and an 8-item consummatory pleasure scale (Gard *et al.* 2006). In this study, we adopted the validated Chinese version of the TEPS (Chan *et al.* 2012b), which includes 19 items and has a four-factor construct in the Chinese context, including abstract anticipatory, contextual anticipatory, abstract consummatory, and contextual consummatory factors.

Emotional Expressivity Scale (EES)

The EES, consisting of 17 items, was developed to capture individuals’ differences on the outward display of their emotion regardless of valence (Kring *et al.* 1994). Individuals rate themselves on a 6-point Likert scale from 1 (never) to 6 (always) on how often they express their emotions. The Chinese version of the EES has a two-factor construct with good internal consistency: whole scale (Cronbach’s α = 0.82), ‘suppression’ factor

(Cronbach's $\alpha=0.82$; e.g. 'I keep my feelings to myself') and 'expression' factor (Cronbach's $\alpha=0.78$; e.g. 'I display my emotions to other people') (Chan *et al.* 2010).

Image acquisition and preprocessing

All MRI scans were acquired on a Siemens Verio 3 T MR scanner (Siemens, Germany) at the Guangzhou First People's Hospital, Guangzhou, China. Resting-state fMRI data were acquired using a T2-weighted echo planar imaging (EPI) sequence; 200 whole-brain volumes were collected with slice thickness = 3.5 mm, echo time (TE) = 30 ms, repetition time (TR) = 2500 ms, flip angle = 90°, matrix size = 64 × 64, 42 slices in the coronal plane, field of view (FOV) = 200 mm, voxel size = 3.1 × 3.1 × 3.5 mm³, bandwidth = 2520 Hz/Px. Scans were screened by a radiologist to exclude any incidental clinical abnormalities before further analysis.

Preprocessing was performed using the Data Processing Assistant for Resting-State fMRI (DPARSF) software (Yan & Zang, 2010). The first 10 volumes were removed. Time delay in image acquisition and head motion were corrected. Two participants were excluded due to excessive head motion (>3 mm or 3°) prior to further analysis. The fMRI images were further spatially normalized to the Montreal Neurological Institute (MNI) EPI template, re-sliced to 3 mm cubic voxels and then smoothed using a 4 mm full-width at half maximum Gaussian kernel. Temporal band-pass filtering ($0.01 < f < 0.10$ Hz) was performed. The Nuisance covariates, including head motion parameters, global mean signal, white-matter signal and cerebrospinal fluid signal were regressed out. To exclude artifacts caused by head motion, we took the Friston 24-parameter model (Friston *et al.* 1996) as a regressor for the individuals' first-level analysis, which has been proved to be superior to the six-parameter model (Yan *et al.* 2013). We also calculated the mean framewise displacement (FD) (Power *et al.* 2012) of each participant. Although the group comparison did not show significant difference between the low SocAnh group (mean FD = 0.12, s.d. = 0.06) and high SocAnh group (mean FD = 0.10, s.d. = 0.04) ($t = 0.78$, $p > 0.1$), we still took the individuals' mean FD as a covariate in the second-level analysis as suggested by Yan *et al.* (2013).

Functional connectivity analyses

To examine the functional connectivity between seeds of the striatum and whole brain voxels, we first defined six seeds of the striatum in each hemisphere as described in a previous study (Di Martino *et al.* 2008), including the NAc (MNI coordinates: ± 9 , 9, -8), the ventral caudate (± 10 , 15, 0), the dorsal caudate (± 13 , 15, 9), the dorsal caudal putamen (± 28 , 1, 3), the

DRP (± 25 , 8, 6) and the ventral rostral putamen (± 20 , 12, -3). The radius of each seed was set at 4 mm. Voxel-wise functional connectivity analyses were conducted between brain activity of each seed and the whole brain voxels using a toolkit for resting-state functional MRI analysis (REST; Song *et al.* 2011).

Statistical analysis

Subjects were compared on age, gender, IQ estimates and scores on the CSAS, TEPS, and EES. One-sample *t* tests were conducted in both groups for functional connectivity analyses for all six pairs of seeds in the striatum. The results are illustrated in Supplementary Fig. S1. To examine the group effect in functional connectivity, correlation *r* maps were transformed to Fisher *z* maps and were analysed with repeated-measures ANOVA (two hemispheres by two groups) using the SPM8 software implemented in Matlab, with mean FD as a covariate in the general linear model. The clusters were considered significant if they reached a threshold of $p < 0.001$ with a cluster size of >50 voxels. We also extracted the transformed Fisher *z* values of the clusters that showed significant group effect and correlated these with the scores on the various scales to examine the associations between altered corticostriatal functional connectivity and emotion processing. Significance level was set as two-tailed $p < 0.05$.

Results

Demographics description and group differences in emotion processing

The two groups were matched in terms of age, gender and IQ estimates (see Table 1). The high SocAnh group reported lower pleasure experience in both anticipatory ($t = 4.20$, $p < 0.001$) and consummatory ($t = 3.53$, $p < 0.01$) components of the TEPS and lower EES suppression ($t = 3.66$, $p < 0.001$) and total scores ($t = 3.26$, $p < 0.01$).

Group effects in corticostriatal functional connectivity

A main effect of group was observed in the functional connectivity between the NAc and the right medial frontal gyrus [extending to the anterior cingulate cortex (ACC)] [BA (Brodmann area) 9/10/32], between the NAc and the left posterior cingulate gyrus (BA 31), between the ventral caudate and the left insula (BA 13), as well as between the DRP and the right superior frontal gyrus (supplementary motor area, BA 6). There was no interaction between group and the two hemispheres.

We then extracted the transformed z values of four significant clusters and compared them between the two groups. The results showed that compared to the low SocAnh group, reduced functional connectivity was observed in the high SocAnh group between the posterior cingulate cortex (PCC) and the bilateral NAc ($p=0.001$); while increased connectivity was found between the medial frontal gyrus and the bilateral NAc, between the insula and the ventral caudate, as well as between the superior frontal gyrus and the DRP (all p 's < 0.001) (see Fig. 1 for details).

Correlations between functional connectivity and self-reported scores

Taking age, gender and IQ estimates as covariates, the altered functional connectivity between the striatum subdivisions and cortical activity were correlated with the self-reported scores of scales capturing emotional processing. In the high SocAnh group, we found that both the TEPS anticipatory and consummatory scores were positively correlated with functional connectivity between the insula and the right ventral caudate ($r_s = 0.51$ for both, p 's < 0.05). EES suppression scores were negatively correlated with functional connectivity between the PCC and the left NAc ($r = -0.74$, $p < 0.001$) and positively correlated with functional connectivity between the superior frontal gyrus and the bilateral DRP (left DRP: $r = 0.57$, right DRP: $r = 0.54$; p 's < 0.05). In the low SocAnh group, significant negative correlations were found between the TEPS anticipatory subscale scores and functional connectivity between the medial frontal gyrus and the bilateral NAc (left NAc: $r = -0.49$; right NAc $r = -0.41$; p 's < 0.05) (see Fig. 2 and Table 3 for details).

Discussion

In this study, we examined resting-state functional connectivity in individuals with high levels of negative schizotypy, which may be a vulnerability trait marker for psychosis. Adopting the seed-based approach, we used six subdivisions of the striatum and calculated functional connectivity between each seed of the striatum and the rest of the brain. Compared to individuals with low level of social anhedonia, the high SocAnh group showed reduced connectivity between the PCC and NAc. Increased connectivity was observed between the dorsomedial prefrontal cortex and NAc, between the insula and ventral caudate, and between the superior frontal gyrus (supplementary motor area) and the DRP.

The idea of taking into account the subdivisions of the striatum is based on empirical findings that the ventral and dorsal striatum play different roles in

reward processing. The ventral part is a key brain structure in the reward circuit, and has been suggested to be specifically related to reward expectation. It receives inputs from the prefrontal cortex, including the orbitofrontal cortex, the medial prefrontal cortex and the dorsal ACC, and projects to the ventral pallidum, then back to the prefrontal cortex through the thalamus, constituting the frontal-basal ganglia circuit in reward processing. Through this circuit, sensory information, personal expectation, beliefs and memory could be integrated and goal-directed plans would then be generated (Haber & Knutson, 2010). Our finding of increased functional connectivity between the ventral striatum and the medial prefrontal cortex, the ACC and the insula in individuals with high level of social anhedonia suggests that decreased pleasure experience in social interaction may be related to dysfunction of this frontal-basal ganglia circuit. Reduced pleasure experience has been observed in schizophrenia patients, their unaffected relatives and high-risk populations (Katsanis *et al.* 1990; Burbridge & Barch, 2007; Wang *et al.* 2014). Patients with schizophrenia have been shown to have deficits in anticipatory pleasure, but not consummatory pleasure. Strauss *et al.* (2013) proposed that this specific pattern may be due to the low-pleasure beliefs and reduced estimation of past and future pleasure. Similar to previous findings, individuals with social anhedonia in the present study also showed lower anticipatory pleasure than controls (Shi *et al.* 2012). Using partial correlation analysis, we found significant associations between TEPS anticipatory scores and functional connectivity between the ventral striatum and the dorsomedial prefrontal cortex/ACC in the low SocAnh group. At the same time, functional connectivity between the ventral caudate and the insula was associated with both TEPS anticipatory and consummatory subscale scores in the high SocAnh group. Hence, our study showed that reduced anticipatory pleasure, which has been found in patients with schizophrenia, is also observed in individuals with high level of social anhedonia. Furthermore, this reduced pleasure experience may be related to dysfunction of the reward system, especially functional connectivity between the ventral striatum and the medial prefrontal cortex and the insula.

We also found reduced functional connectivity between the NAc and PCC. Di Martino *et al.* (2008) reported a connection between the NAc and PCC, both of which are regions involved in emotion processing. A previous study has shown that abnormalities of the PCC may be related to novelty seeking and may be linked to the behavioural activation system (Lei *et al.* 2014). Although the PCC is an important midline cortical structure in the default mode network and its

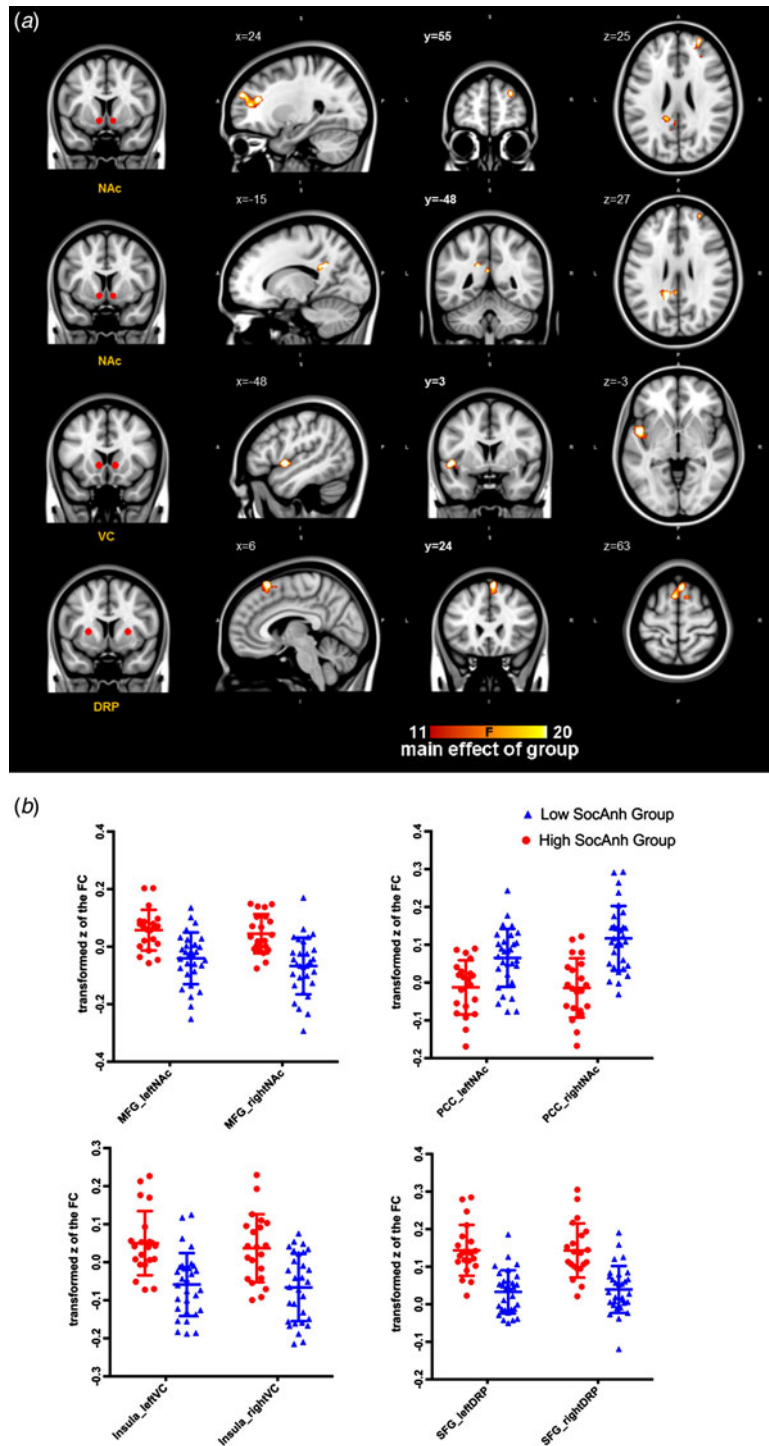


Fig. 1. Significant group effect of high and low social anhedonia on the functional connectivity (FC) of the striatum. Repeated-measures ANOVA was conducted. Results are displayed at $p < 0.001$, cluster size > 50 voxels, uncorrected. See Table 2 for details. NAc, Nucleus accumbens; VC, ventral caudate; DRP, dorsal rostral putamen; MFG, medial frontal gyrus; PCC, posterior cingulate gyrus; SFG, superior frontal gyrus.

dysconnectivity has been reported in patients with schizophrenia and individuals with familial risk (Peeters *et al.* 2015), little is known whether this is also the case in individuals with schizotypy. In the

present study we also found a strong correlation between EES suppression and functional connectivity between the NAc and PCC in the high SocAnh group. This finding suggests that the PCC and its connection

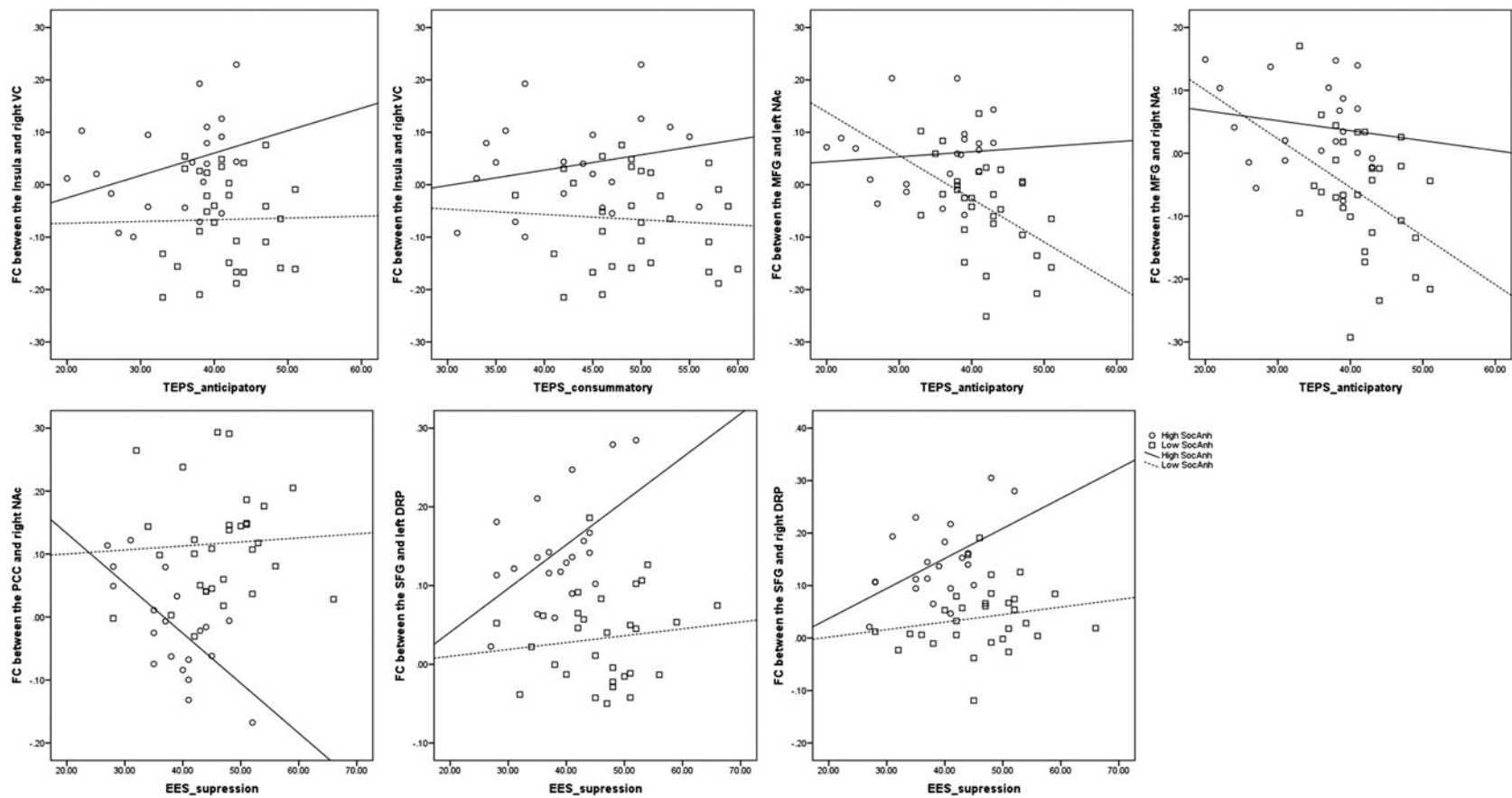


Fig. 2. Partial correlations between functional connectivity (FC) of the striatal seeds and the self-reported scale scores. SocAnh, Chinese version of the Chapman Social Anhedonia Scale; TEPS, Temporal Experiences and Pleasure Scale; EES, Emotional Expressivity Scale. PCC, posterior cingulate cortex; VC, ventral caudate; SFG, superior frontal gyrus; DRP, dorsal rostral putamen; MFG, medial frontal gyrus; NAc, nucleus accumbens.

Table 2. Effect of the high and low social anhedonia groups on corticostriatal functional connectivity

Seed	Cluster size	x	y	z	F	Brain region	Hemi	BA
Nucleus accumbens	64	-15	-48	27	29.77	PCC	L	31
Nucleus accumbens	86	27	54	24	29.19	dmPFC/ACC	R	9/10/32
Ventral caudate	51	-48	3	-3	39.21	insula	L	13
Dorsal rostral putamen	117	6	24	63	32.55	SMA	R	6

Hemi, Hemisphere; BA, Brodmann area; R, right; L, left; PCC, posterior cingulate cortex; dmPFC, dorsomedial prefrontal cortex; ACC, anterior cingulate cortex; SMA, supplementary motor area.

Threshold at $p < 0.001$, cluster size > 50 voxels.

Table 3. Partial correlations between functional connectivity of regions of interest and self-reported scales

	High SocAnh group				Low SocAnh group			
	TEPS_anti	TEPS_cons	EES_exp	EES_sup	TEPS_anti	TEPS_cons	EES_exp	EES_sup
PCC_left NAc	0.43 ($p = 0.073$)	-0.09	0.00	-0.16	-0.12	-0.09	0.30	0.03
PCC_right NAc	0.05	0.11	-0.08	-0.74	0.19	-0.01	0.27	0.08
MFG_left NAc	0.14	0.04	-0.10	-0.30	-0.49	-0.17	-0.07	-0.08
MFG_right NAc	-0.23	-0.08	-0.25	-0.06	-0.41	-0.21	-0.01	0.10
Insula_left VC	0.01	0.25	0.05	-0.27	-0.07	-0.16	0.06	-0.03
Insula_right VC	0.51	0.51	0.17	-0.06	-0.01	-0.06	-0.20	-0.06
SFG_left DRP	0.07	-0.20	-0.13	0.57	-0.18	-0.09	0.07	0.16
SFG_right DRP	-0.10	-0.20	-0.02	0.54	-0.16	-0.21	0.29	0.20

TEPS, Temporal Experiences and Pleasure Scales; EES, Emotional Expressivity Scale; anti, anticipatory factor; cons, consummatory factor; exp, expression factor; sup, suppression factor; PCC, posterior cingulate cortex; NAc, nucleus accumbens; MFG, medial frontal gyrus; VC, ventral caudate; SFG, superior frontal gyrus; DRP, dorsal rostral putamen.

Age, gender and estimated IQ were taken as covariates; numbers in bold indicate the significant correlations with $p < 0.05$ as threshold, two tailed.

with the ventral striatum may be related to emotion regulation and needs to be carefully examined in the future.

We also found increased functional connectivity between the dorsal striatum and the supplementary motor cortex (BA 6). The dorsal striatum is involved in motor control, which is the basic function of the basal ganglia. Both human and non-human studies have shown that the dorsal striatum and its connections to the sensorimotor or associative cortex are important in the learning of action-reward association (Balleine *et al.* 2007). The reduced pleasure experience and greater suppression of emotion observed in individuals with high social anhedonia in the present study is consistent with this. We also found an association between emotion suppression and functional connectivity between the dorsal striatum and supplementary motor area, suggesting that dysconnectivity of the dorsal striatum may be a neural correlate underlying abnormal emotion processing in individuals with high risk for psychosis. Individuals with high levels of

social anhedonia may have problems in the initiation of behaviour that induces pleasure experience, which further affects their beliefs and estimation of pleasure, as well as action-reward association.

In Fornito *et al.*'s (2013) study, the authors examined the resting-state functional connectivity of the striatum in patients with schizophrenia and their unaffected first-degree relatives. They found a reduced functional connectivity between the dorsal striatum and the prefrontal cortex, and increased functional connectivity between the ventral striatum and the orbitofrontal cortex/dorsolateral prefrontal cortex and the insula in schizophrenia patients, i.e. a 'dorsal-to-ventral gradient of hypo- to hyper-connectivity with the prefrontal cortex' (Fornito *et al.* 2013). Similar patterns were also observed in unaffected first-degree relatives. Furthermore, in a study of UHR individuals, Dandash *et al.* (2014) also found reduced functional connectivity between the dorsal striatum, the prefrontal cortex and the thalamus; as well as increased functional connectivity between the ventral putamen and the superior

temporal gyrus and the insula. Our results are consistent with these findings in terms of the hyperconnectivity between the ventral striatum and the prefrontal cortex and the insula in the high SocAnh group. However, the high SocAnh group in our study also exhibited increased connectivity at the dorsal striatum and reduced connectivity at the ventral striatum. This may be related to the fact that our sample was recruited from well-functioning college students screened by self-reported Social Anhedonia Scale, who are likely to be different from the unaffected relatives of schizophrenia patients and UHR individuals with psychotic-like symptoms in previous studies. For example, a previous study has shown that higher levels of positive symptoms predicted lower connectivity at the dorsal striatum and stronger connectivity at the ventral striatum (Dandash *et al.* 2014). It is not clear if this reversed connectivity pattern of the dorsal striatum is related to the more severe positive symptoms in high-risk individuals. Future research is needed to clarify this issue.

In the present study, we recruited college students, whose age ranged from 17 to 21 years. This period is important in examining the development of psychosis, since psychosis usually emerges in late adolescence or early adulthood with a peak age between 18 and 25 years. Existing findings have shown that the human brain continues to develop until young adulthood, especially the prefrontal cortex (Gogtay *et al.* 2004). A very recent study examined the age-related changes of intrinsic functional connectivity to middle adulthood and found decreasing connection strength between the ventral striatum and the ACC and the insula (Porter *et al.* 2015). In particular, there is a quick drop in connection strength from young to middle adulthood between the ventral striatum and the ACC. In the context of this finding, individuals with high negative schizotypy in our study showed hyperconnectivity between the ventral striatum and the ACC, suggesting an association between abnormal cortico-striatum connectivity and negative schizotypy.

Anhedonia or reward processing is important since it is a key symptom not only for schizophrenia spectrum disorders, but also for some other mental disorders, such as depression. A prior study examined the striatum-based circuitry in adolescents with major depressive disorder and found that the anhedonia severity in patients with major depression showed positive correlations with functional connectivity between the caudate and supplementary motor area, the precuneus, the middle frontal gyrus, and the subgenual ACC, as well as negative correlations with functional connectivity between the NAc and the subgenual ACC (Gabbay *et al.* 2013). Similar findings have also been found in other psychiatric disorders. Gabbay *et al.*

(2013) suggested that abnormal functional connectivity of the striatum related to anhedonia may be independent of the major depressive disorder diagnosis. In the present study, however, we adopted the psychologically defined 'schizotypy' approach, and found a link between higher levels of social anhedonia and hyper- or hypo-connectivity of the striatum. All these findings support the Research Domain Criteria (RDoC) proposed by the National Institute of Mental Health (NIMH) (Cuthbert & Insel, 2013) that examining anhedonia and its underlying circuits across different disorders might be a helpful step in understanding mental disorders.

There are several limitations in this study. First, we recruited a convenience sample from college students and the categorization of the two comparison groups was based on scores from a self-reported scale. A more rigorous approach adopting an interview-based measure and behavioural tasks to capture emotion processing should be incorporated in future studies. Second, because we focused on anhedonia in the present study, the potential effect of positive symptoms was not examined. The possibility that the reverse pattern of ventral striatum connectivity may be related to positive symptoms needs to be further clarified. Last, since the present study was conducted in relatively well-functioning college students and was exploratory in nature, we did not correct for multiple comparisons in the functional connectivity analyses.

In conclusion, we examined resting-state functional connectivity of the striatum by examining its ventral and dorsal subdivisions, in individuals with high levels of social anhedonia. We observed dysconnectivity between the ventral striatum and ACC, the insula and PCC, and between the dorsal striatum and motor cortex. These dysconnectivities were also associated with self-reported anticipatory pleasure experience and emotion suppression in individuals with high social anhedonia. These may be early changes in brain functional connectivity in the reward system associated with negative schizotypy (especially social anhedonia). Future studies on social anhedonia in UHR populations as well as first-episode schizophrenia patients could provide new evidence in the better understanding of the development of psychosis.

Supplementary material

For supplementary material accompanying this paper visit <http://dx.doi.org/10.1017/S0033291715001592>.

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Declaration of Interest

None.

References

- Andreasen NC** (1982). Negative symptoms in schizophrenia. Definition and reliability. *Archives of General Psychiatry* **39**, 784–788.
- Annett M** (1970). A classification of hand preference by association analysis. *British Journal of Psychology* **61**, 303–321.
- APA** (2013). *Diagnostic and Statistical Manual of Mental Disorders*, 5th edn (DSM-5). American Psychiatric Association: San Francisco, USA.
- Balleine BW, Delgado MR, Hikosaka O** (2007). The role of the dorsal striatum in reward and decision-making. *Journal of Neuroscience* **27**, 8161–8165.
- Burbridge JA, Barch DM** (2007). Anhedonia and the experience of emotion in individuals with schizophrenia. *Journal of Abnormal Psychology* **116**, 30–42.
- Chan RC, Shi YF, Lai MK, Wang YN, Wang Y, Kring AM** (2012a). The Temporal Experience of Pleasure Scale (TEPS): exploration and confirmation of factor structure in a healthy Chinese sample. *PLoS ONE* **7**, e35352.
- Chan RC, Wang Y, Li H, Shi Y, Wang Y, Liu W, Huang J** (2010). A 2-stage factor analysis of the Emotional Expressivity Scale in the Chinese context. *Psychologia* **53**, 44–50.
- Chan RC, Wang Y, Yan C, Zhao Q, McGrath J, Hsi X, Stone WS** (2012b). A study of trait anhedonia in non-clinical Chinese samples: evidence from the Chapman Scales for Physical and Social Anhedonia. *PLoS ONE* **7**, e34275.
- Clardige G, Beech T** (1995). Fully and quasi-dimensional constructions of schizotypy. In *Schizotypal Personality* (ed. A. Raine, T. Lencz and S. A. Mednick), pp. 192–216. Cambridge University Press: New York.
- Cuthbert BN, Insel TR** (2013). Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC Medicine* **11**, 126.
- Dandash O, Fornito A, Lee J, Keefe RS, Chee MW, Adcock RA, Pantelis C, Wood SJ, Harrison BJ** (2014). Altered striatal functional connectivity in subjects with an at-risk mental state for psychosis. *Schizophrenia Bulletin* **40**, 904–913.
- Di Martino A, Scheres A, Margulies DS, Kelly AMC, Uddin LQ, Shehzad Z, Biswal B, Walters JR, Castellanos FX, Milham MP** (2008). Functional connectivity of human striatum: a resting state fMRI Study. *Cerebral Cortex* **18**, 2735–2747.
- Eckblad ML, Chapman LJ, Chapman JP, Mishlove M** (1982). *The Revised Social Anhedonia Scale*, unpublished test. University of Wisconsin: Madison.
- Fornito A, Harrison BJ, Goodby E, Dean A, Ooi C, Nathan PJ, Lennox BR, Jones PB, Suckling J, Bullmore ET** (2013). Functional dysconnectivity of corticostriatal circuitry as a risk phenotype for psychosis. *JAMA Psychiatry* **70**, 1143–1151.
- Friston KJ, Williams S, Howard R, Frackowiak RS, Turner R** (1996). Movement-related effects in fMRI time-series. *Magnetic Resonance in Medicine* **35**, 346–355.
- Gabbay V, Ely BA, Li Q, Bangaru SD, Panzer AM, Alonso CM, Castellanos FX, Milham MP** (2013). Striatum-based circuitry of adolescent depression and anhedonia. *Journal of the American Academy of Child and Adolescent Psychiatry* **52**, 628–641.
- Gard D, Gard M, Kring A, John O** (2006). Anticipatory and consummatory components of the experience of pleasure: a scale development study. *Journal of Research in Personality* **40**, 1086–1102.
- Gogtay N, Giedd JN, Lusk L, Hayashi KM, Greenstein D, Vaituzis AC, Nugent TF, Herman DH, Clasen LS, Toga AW, Rapoport JL, Thompson PM** (2004). Dynamic mapping of human cortical development during childhood through early adulthood. *Proceedings of the National Academy of Sciences USA* **101**, 8174–8179.
- Gong YX, Dai XY** (1984). Application of the short forms of Wechsler Intelligence Scale. *Journal of Central South University (Medical Sciences)* **4**, 393–400.
- Gooding DC, Tallent KA, Matts CW** (2005). Clinical status of at-risk individuals 5 years later: further validation of the psychometric high-risk strategy. *Journal of Abnormal Psychology* **114**, 170–175.
- Haber SN, Knutson B** (2010). The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology* **35**, 4–26.
- Katsanis J, Iacono WG, Beiser M** (1990). Anhedonia and perceptual aberration in first-episode psychotic patients and their relatives. *Journal of Abnormal Psychology* **99**, 202–206.
- Kring AM, Elis O** (2013). Emotion deficits in people with schizophrenia. *Annual Review of Clinical Psychology* **9**, 409–433.
- Kring AM, Smith DA, Neale JM** (1994). Individual differences in dispositional expressiveness: development and validation of the Emotional Expressivity Scale. *Journal of Personality and Social Psychology* **66**, 934–949.
- Kwapil TR** (1998). Social anhedonia as a predictor of the development of schizophrenia-spectrum disorders. *Journal of Abnormal Psychology* **107**, 558–565.
- Lei X, Chen C, Xue F, He Q, Chen C, Liu Q, Moyzis RK, Xue G, Cao Z, Li J, Li H, Zhu B, Liu Y, Hsu ASC, Li J, Dong Q** (2014). Fiber connectivity between the striatum and cortical and subcortical regions is associated with temperaments in Chinese males. *NeuroImage* **89**, 226–234.
- Meehl PE** (1990). Toward an integrated theory of schizotaxia, schizotypy, and schizophrenia. *Journal of Personality Disorders* **4**, 1–99.

- Miettunen J, Jaaskelainen E** (2010). Sex differences in Wisconsin Schizotypy Scales – a meta-analysis. *Schizophrenia Bulletin* **36**, 347–358.
- Nelson MT, Seal ML, Pantelis C, Phillips LJ** (2013). Evidence of a dimensional relationship between schizotypy and schizophrenia: a systematic review. *Neuroscience and Biobehavioral Reviews* **37**, 317–327.
- O’Doherty J, Dayan P, Schultz J, Deichmann R, Friston K, Dolan RJ** (2004). Dissociable roles of ventral and dorsal striatum in instrumental conditioning. *Science* **304**, 452–454.
- Porter JN, Roy AK, Benson B, Carlisi C, Collins PF, Leibenluft E, Pine DS, Luciana M, Ernst M** (2015). Age-related changes in the intrinsic functional connectivity of the human ventral vs. dorsal striatum from childhood to middle age. *Developmental Cognitive Neuroscience* **11**, 83–95.
- Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE** (2012). Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. *NeuroImage* **59**, 2142–2154.
- Pantelis C, Brewer W** (1995). Neuropsychological and olfactory dysfunction in schizophrenia: relationship of frontal syndromes to syndromes of schizophrenia. *Schizophrenia Research* **17**, 35–45.
- Pantelis C, Brewer WJ** (1996). Neurocognitive & neurobehavioural patterns & the syndromes of schizophrenia: role of frontal-subcortical networks. In *Schizophrenia: A Neuropsychological Perspective* (ed. C. Pantelis, H. E. Nelson and T. R. E. Barnes), pp. 317–343. John Wiley: London.
- Phillips LK, Seidman LJ** (2008). Emotion processing in persons at risk for schizophrenia. *Schizophrenia Bulletin* **34**, 888–903.
- Peeters SC, van de Ven V, Gronenschild EH, Patel AX, Habets P, Goebel R, van Os J, Marcelis M** (2015). Default mode network connectivity as a function of familial and environmental risk for psychotic disorder. *PLoS ONE* **10**, e0120030.
- Shi YF, Wang Y, Cao XY, Wang Y, Wang YN, Zong JG, Xu T, Tse VW, Hsi XL, Stone WS, Lui SS, Cheung EF, Chan RC** (2012). Experience of pleasure and emotional expression in individuals with schizotypal personality features. *PLoS ONE* **7**, e34147.
- Song XW, Dong ZY, Long XY, Li SF, Zuo XN, Zhu CZ, He Y, Yan CG, Zang YF** (2011). REST: a toolkit for resting-state functional magnetic resonance imaging data processing. *PLoS ONE* **6**, e25031.
- Strauss GP** (2013). The emotion paradox of Anhedonia in schizophrenia: or is it? *Schizophrenia Bulletin* **39**, 247–250.
- Wang Y, Lui SS, Zou LQ, Zhang Q, Zhao Q, Yan C, Hong XH, Tan SP, Cheung EF, Chan RC** (2014). Individuals with psychometric schizotypy show similar social but not physical anhedonia to patients with schizophrenia. *Psychiatry Research* **216**, 161–167.
- Yan CG, Cheung B, Kelly C, Colcombe S, Craddock RC, Di Martino A, Li Q, Zuo XN, Castellanos FX, Milham MP** (2013). A comprehensive assessment of regional variation in the impact of head micro-movements on functional connectomics. *Neuroimage* **76**, 183–201.
- Yan CG, Zang YF** (2010). DPARSF: a MATLAB toolbox for ‘pipeline’ data analysis of resting-state fMRI. *Frontiers in Systems Neuroscience* **4**, 13.