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Self-reflection and positive schizotypy in the adolescent brain

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ABSTRACT

Clinical and phenomenological accounts of schizophrenia suggest that impairments in self-reflective processes significantly contribute to psychopathological expression. Recent imaging studies observe atypical cerebral activation patterns during self-reflection, especially around the cortical midline structures, both in psychosis-prone adults and individuals with schizophrenia. Given that self-reflection processes consolidate during adolescence, and that early transient expression of psychosis (positive schizotypy) also arises during this period, the present study sought to examine whether atypical cerebral activation during self-reflection task could be associated with early schizotypic expression during adolescence. Forty-two neurotypical adolescent participants (19 females) aged from 12 to 19 (15.92 ± 1.9) underwent a self-reflection task using functional neuroimaging (fMRI), where they had to evaluate trait adjectives (1 to 4 ratings) about themselves or their same sex best friend. The Schizotypal Personality Questionnaire (SPQ) was employed to assess positive schizotypic expression. Results showed that positive schizotypy in adolescents significantly correlated with cortical midline activation patterns in the dorsomedial prefrontal cortex (dmPFC) and the posterior cingulate cortex (PCC), as well as the dorsolateral PFC and the lingual gyrus. The results are consistent with previous imaging literature on self-reflection and schizophrenia. They further highlight that the relationship between self-reflection processes and positive schizotypy operates at the trait level of expression and can be observed as early as adolescence.

1. Introduction

Adolescence is often depicted as a critical developmental period for selfhood (Erikson, 1968), where questions such as "Who am I?" seek answers in both self-reflective and social cognitive processes (Pfeifer and Peake, 2012). Although psychiatric disorders involving anomalous self-experiences emerge during early adulthood, they are often preceded by subclinical symptom manifestations during adolescence (Rutter et al., 2006; Shiner, 2009). Schizophrenic spectrum disorders represent a good example of such developmental psychopathology. Indeed, cognitive-perceptual distortions such as transient hallucinatory, delusional and dissociative experiences during adolescence can, in some instances, be followed by adult onset of the disorder (Poulton et al., 2000; Dhossche et al., 2002; Dominguez et al., 2011). Importantly, these early cognitive-perceptual distortions, referred to as positive schizotypy (Dinn et al., 2002; Kerns, 2005; Debbané et al., 2009), can also be accompanied by social withdrawal, and together augment the risk of transitioning to clinical states commanding need for care (Miller et al., 2002). In this perspective, the cognitive processes sustaining reflective thinking about self and others during adolescence, even in those individuals that will not develop full-blown psychotic disorders, may provide critical information on the development of normative or clinical states of psychotic experiences.

Research on adolescent development has more recently involved structural and functional neuroimaging investigations (sMRI and fMRI), which are starting to uncover the profound cerebral modifications that characterize adolescent brain maturation (Fair et al., 2007; Shaw et al., 2008; Supekar et al., 2010). These studies have lead clinical neuroscientists to ask whether psychopathological conditions that typically arise during adulthood might be linked to atypical maturation during adolescent growth (Paus et al., 2008). Following this question, neuroimaging research involving "at-risk" youth samples seek to identify neuronal patterns signaling increased risk for severe adult psychopathology (Rotarska-Jagiela et al., 2010; Schneider et al., 2012). With regards to non-clinical positive schizotypy during adolescence, a few studies suggest that early schizotypic expression is associated with characteristic neural signature during task-free (Lagioia et al., 2010) as

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well as task-engaged states (Lagioia et al., 2011). In a sample of 33 adolescents, Lagioia et al. (2011) specifically investigated self-reflectivity in a source monitoring task, by asking participants to recollect the origin of previously studied word items amongst self-versus experimenter-generated items. In contrast to a context discrimination condition, origin discrimination recruited the medial prefrontal cortex (mPFC), and more specifically the activation of BA 10 during origin trials. Importantly, self-report ratings of positive schizotypy in this adolescent group were found to correlate with diminished BA 10 activation during origin discrimination. These results are among the first to bridge non-clinical and clinical expression of positive schizotypy in youth, as atypical activation of the mPFC and other cortical midline structures (CMS) such as the anterior cingulate (ACC), the superior frontal gyrus (SFG) and the posterior cingulate (PCC) cortices during self-reflective activity is also reported in subjects in the prodromal (Shim et al., 2010), first episode (Alonso-Solis et al., 2012) and chronic stages of schizophrenia (for a review, see (Nelson et al., 2009)). Together, this nascent body of literature suggests that self-reflective processes recruit neural areas often found to show atypical activation patterns in non-clinical to clinical states of the schizophrenic spectrum disease. Such patterns of activation should be studied as early as adolescence, where self-reflective processes are thought to consolidate in parallel to neuronal maturation (Pfeifer and Blakemore, 2012).

Adolescent neuronal maturation, much like adolescent schizotypy expression, exhibits important gender differences (Shaw et al., 2008; Raznahan et al., 2011). Both gray and white matter growth pattern differences between adolescent girls and boys may ultimately lead to differential developmental trajectories towards the equifinal outcome of interest (Cicchetti and Rogosch, 2002), here schizophrenia spectrum disorders. Interestingly, the expression of schizotypy during adolescence also yields gender differences, with females generally expressing more important positive schizotypic features (Fonseca-Pedrero et al., 2008). To date however, it remains unclear whether gender differences can be observed in neural correlates of adolescent self-reflective processes, and whether putative differences might be related to schizotypy expression.

In this context, the present fMRI investigation sought to characterize the potential relationships linking neural correlates sustaining adolescent self-reflective processes and adolescent positive schizotypy. To this end, we employed a well-known trait attribution fMRI paradigm, which recruits cerebral activity along the cortical midline structures (Murray et al., 2012). As reviewed above, atypical cortical midline activity has been conceptualized as the neural signature of anomalous self-reflective processing in schizophrenia (Nelson et al., 2009; van der Meer et al., 2010). In continuation with this line of research, we hypothesized that atypical cortical midline activity during a self-reflective task be associated to adolescent positive schizotypy expression. We further investigated gender differences in the neural correlates of self-reflective processes. Finally, we tested for gender-specific patterns of association between positive schizotypy and atypical neural activation during self and other trait attribution.

2. Methods

2.1. Participants

Forty-two healthy adolescents participated in this study (23 males, 19 females), aged between 12 and 19 years (M = 15.92, S.D. = 1.9). Participants were French-native speaking adolescents recruited throughout secondary schools of Geneva, Switzerland. Exclusion criteria were current psychiatric or neurological disease. Furthermore, participants filled out the Youth Self Report (YSR) questionnaire (Achenbach, 1991) or Adult Self Report (ASR) questionnaire (>18 years old) (Achenbach and Rescorla, 2003) to ensure that expression of internalizing (INT) and externalizing (EXT) problems was below clinical cutoff. Written informed consent was obtained from participants and their parents under protocols approved by the Institutional Review Board of the Department of Psychiatry of the University of Medicine, Geneva.

The *Schizotypal Personality Questionnaire* (SPQ; (Raine, 1991)) was employed to assess the expression of schizotypy in our sample. It consists of a 74 dichotomous item instrument, yielding the three main following dimension scores: Positive (including unusual perceptual experiences, magical thinking, paranoid ideation, and ideas of reference; SPQpos), Negative (including social anxiety, constricted affects and no close friends; SPQneg) and Disorganisation (namely odd speech and behaviour; SPQdis). This scale has been validated in French-speaking adolescents (Badoud et al., 2011).

2.2. Experimental task

Stimuli were presented using the E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). During the block-designed fMRI paradigm, participants were asked to rate adjectives taken from the Anderson database (Anderson, 1968) referring to themselves (SELF condition), their same-sex best friend (OTHER condition) from 1 = “not at all” to 4 = “completely”. The control condition consisted in counting syllables of the word (CONTROL condition) from 1 = one syllable to 4 = four or more syllables. At the beginning of each block, a screen with the cue (“SELF”, “OTHER” or “SYLLABLE”) was shown for 3 seconds. Each block comprised 5 adjective ratings (with the cue remaining at the top of the screen) of 4 seconds with a 5-second resting period between blocks. Adjectives presented an equal number (55) of positive valence words (i.e. “nice” or “generous”) or negative valence word (i.e. “jealous” or “lazy”) and were translated to French by two independent translators. Non-concordant translations were solved by consensus. Total task time was approximately 16 minutes.

2.3. Data acquisition and imaging

Participants were scanned at the Brain Behavioral Laboratory at Geneva University, using a 3-Tesla Trio MRI system (Siemens, Erlangen, Germany). Stimuli were presented on a screen at the back of the MRI tube, reflected in a mirror placed on the 12-channels head coil above the participant's head. A vacuum cushion was place under the participants' head to contain head movement. High-resolution structural T1-weighted images were obtained in one volume of 192 slices [TR = 2500 ms, TE = 30 ms, slice thickness = 1.1 mm, flip angle = 8°, FOV = 220 mm]. Blood Oxygenation Level (BOLD) functional images consisted of 395 volumes of 38 slices [TR = 2400 ms, TE = 30 ms, slice thickness = 3.2 mm, flip angle = 85°, FOV = 235 mm] obtained in a descending order (from top to bottom) parallel to the AC-PC line.

2.4. Imaging analyses

Functional images were analyzed using SPM8 (Wellcome Trust Center for Neuroimaging, Department of Neuroscience, London, UK, http://www.fil.ion.ucl.ac.uk/spm/software/spm8/), running on Matlab 7.12.0 (R2011a). Functional images were realigned to correct for head movement, and any subject with values greater than 3 mm in translation or 3° in rotation was excluded from further analysis. We subsequently performed slice-timing using the middle slice as a reference to correct for acquisition time differences, standard normalization to the MNI (Montreal National Institute) space, and resampling to 2 mm^3. Finally, spatial smoothing was applied with a 8 mm FWHM Gaussian Kernel and a high pass filter was applied to remove low-frequency noise.

We modeled the following conditions of interest at the single subject level: SELF > CONTROL, OTHER > CONTROL, SELF > OTHER, OTHER > SELF, and added the 6 movement regressors (from the realignment step) as variables of no interest to the design matrix. We estimated brain activity for each condition by convolving the Hemodynamic Response Function (HRF) to the General Linear Model (GLM).

2.5. Statistical analyses

We analyzed the behavioral data using SPSS (www.ibm.com/software/analytics/spss/; version 20) to calculate means and standard deviations. We ran a two-sample *t*-test to compare ratings and RT between the female and male groups after checking for normal distribution of our data.

For fMRI group analyses, we first computed main effects contrasts of SELF versus OTHER and vice versa, as well as SELF versus CONTROL and OTHER versus CONTROL (thresholded at $p < .001$ at the peak and $p < .05$ FDR-corrected at the cluster level, $k = 20$). Subsequently, we conducted a series of two-sample *t*-test by comparing activity as derived by the above contrasts between females and males. These analyses did not reveal any significant sex-differences at the same statistical threshold. In a next step, we conducted a whole-brain regression analysis by correlating brain activity for SELF versus OTHER and vice versa, SELF versus CONTROL and OTHER versus CONTROL with SPQpos scores (thresholded at $p < .001$ uncorrected and $k = 20$). In order to do so, SPQpos scores were centered to avoid any problems of collinearity. We then ran a second regression analysis where we included 5 additional covariates to the model, namely SPQneg, SPQdis, INT, EXT, and Age. This was to make sure the effects found during the initial correlation analysis with SPQpos measures as the only covariate were specifically driven by SPQpos (this is particularly important regarding INT and EXT scores, because the latter have previously been reported to influence adolescent schizotypic expression; (Debbané et al., 2009; Dominguez et al., 2010; Debbané et al., 2012). Only voxels within initial clusters surviving this additional control step (at $p < .05$) were retained. Finally, we tested whether in the regions displaying a significant correlation with SPQpos scores, these relations were subject to sex-differences. This analysis was derived based on the above-mentioned two-sample *t*-test where we now added SPQpos as a covariate (ANCOVA). No significant effects were observed.

3. Results

3.1. Behavioral results

For all the variables included in Table 1, independent sample *t*-test mean comparisons were performed. The results showed that the SPQpos score was greater in the female than in the male adolescent group ($t = 2.755$, $df = 40$, $p = .009$, two-tailed). For the behavioral results of the fMRI paradigm, none of the ratings or reaction times yielded any significant group differences.

3.2. Functional MRI results

3.2.1. Main contrasts

Main effects contrasts of SELF versus OTHER and vice versa, as well as SELF versus CONTROL and OTHER versus CONTROL revealed the following results (at $p < .001$ at the peak and $p < .05$ FDR-corrected at the cluster level, $k = 20$). Whereas we did not find significantly increased activity during mentalizing about the SELF as compared to OTHER, the inverse contrast showed stronger blood-oxygen-level-dependent (BOLD) signal in the posterior cingulate cortex (PCC), ventromedial prefrontal cortex (vmPFC), anterior superior temporal gyrus (aSTG) and Brodman area 6 (BA 6; see Fig. 1 and Table 1). What is concerning the contrasts of SELF versus CONTROL and OTHER versus CONTROL, widespread and strongly overlapping activity was observed in cortical midline structures (medial prefrontal cortex, supplementary motor area, midcingulate and posterior cingulate cortex), amygdala, basal ganglia, thalamus, midbrain, medial temporal lobe and temporo-parietal junction (see Fig. 2 and Table 2). When subsequently testing

Table 1
For female and male adolescent group, variables describing age, schizotypal personality questionnaire scores, and YSR or ASR *t*-scores, as well as fMRI rating and reaction times means by condition.

Descriptive variables	*Females*		*Males*	
	Ratings (Mean)	*S.D.*	*Ratings (Mean)*	*S.D.*
Age	15.68	2.08	16.22	1.83
SPQ positive	11.26 **	6.87	5.95	5.62
SPQ negative	5.84	4.56	4.43	3.30
SPQ disorganized	6.73	4.41	5.30	3.88
YSR/ASR internalizing	52.32	11.45	48.26	8.81
YSR/ASR externalizing	56.11	9.84	54.7	10.02
fMRI task conditions	*Ratings (Mean)*	*S.D.*	*Ratings (Mean)*	*S.D.*
Self positive	2.91	0.43	2.90	0.37
Self negative	1.84	0.31	1.93	0.29
Other positive	2.85	0.48	2.96	0.35
Other negative	1.75	0.37	1.81	0.39
	Reaction times (ms)	*S.D.*	*Reaction times (ms)*	*S.D.*
Self–Positive	1556.48	355.80	1506.36	318.66
Self–Negative	1589.24	386.86	1580.73	353.94
Other–Positive	1512.43	319.59	1517.41	337.40
Other–Negative	1572.60	361.06	1602.14	370.62
Control–Positive	1548.28	459.05	1667.67	418.33
Control–Negative	1628.87	509.15	1690.80	386.43

** Indicates group difference at $p < 0.01$

for the presence of sex-differences in the main effects contrasts mentioned above, no significant effects were observed at the same statistical threshold.

3.2.2. Correlation analyses between positive schizotypy and trait adjective evaluation

After controlling for SPQneg, SPQdis, INT, EXT and age (see Methods), the following associations between SPQpos scores and brain activity during SELF versus OTHER (and vice versa), SELF versus CONTROL and OTHER versus CONTROL were observed (at $p < .001$ uncorrected and $k = 20$). SPQpos scores significantly negatively correlated with activity derived from the contrast SELF versus OTHER in the left lingual gyrus (LG, see Fig. 3 and Table 3). In turn, SPQpos scores significantly positively correlated with activity derived from the contrasts SELF versus CONTROL and OTHER versus CONTROL in the posterior cingulate cortex (PCC), dorsomedial prefrontal cortex (dmPFC) and dorsolateral prefrontal cortex (dlPFC; see Figs. 4 and 5 and Table 3). These associations between SPQpos scores and BOLD signal change were not subject to sex-differences.

4. Discussion

The present study evaluated the relationships between the neural correlates of self-reflective processes during a trait-evaluation task and psychometrically derived positive schizotypy scores in a sample of typically developing male and female adolescents. Neural activity observed during the trait attribution task was comparable to previously published studies using similar tasks with adolescent samples (Pfeifer et al., 2007, 2009; Schneider et al., 2012). Ascertainment of positive schizotypy was also consistent with a previous study involving a general population sample (Fonseca-Pedrero et al., 2008), where female adolescents were also found to report increased expression of positive schizotypy in comparison to male adolescents. Contrary to our initial hypothesis, the examination of potential gender differences in neural correlates sustaining self and other trait-evaluation failed to yield any significant differences. However, clear associations emerged linking adolescent positive schizotypy expression to atypical activation patterns during trait-evaluation. We found evidence for a relationship between positive schizotypy and self-reflective neural activation in the following regions: the left lingual gyrus (LG), the posterior cingulate cortex (PCC),

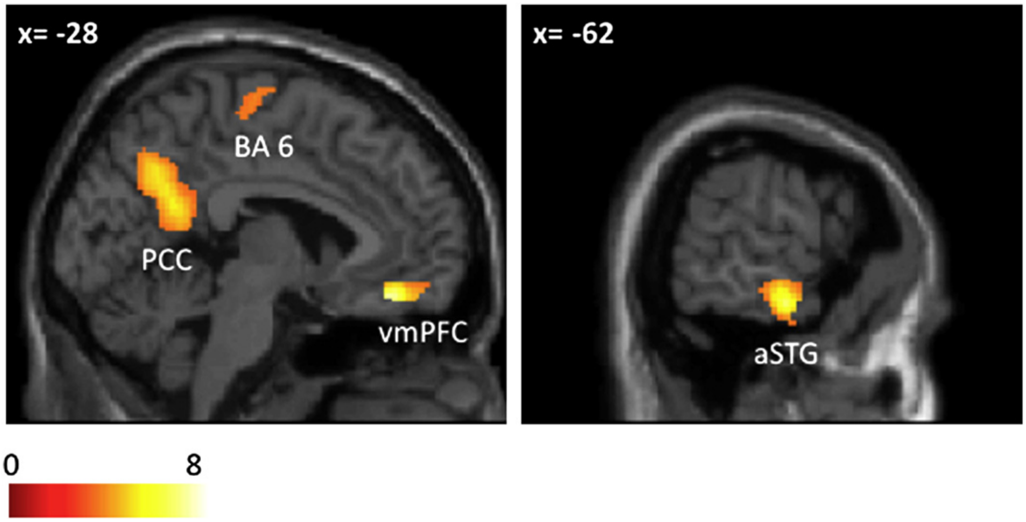

Fig. 1. Statistical parametric map depicting brain areas showing a significant main effect of OTHER versus SELF (at $p < .001$ uncorrected and $k = 20$ for illustration). Activation is overlaid on a single-subject anatomical T1 template.

the left dorsomedial prefrontal cortex (dmPFC) and the left dorsolateral prefrontal cortex (dlPFC). Note that none of these effects were driven by gender. These associations, observed in typically developing youths, are strikingly comparable to those found in previous studies involving adults expressing various degrees of psychotic pathology (Nelson et al., 2009; van der Meer et al., 2010). The results will be discussed in light such studies specifically examining self-referential processing in psychosis-prone and schizophrenic patients.

The trait-evaluation task employed in this study affords the opportunity to isolate specific neural activation during self as opposed to other trait-evaluation (SELF vs OTHER contrast). In isolating self-specific activation, we observed that LG activity negatively correlated with positive schizotypy in our sample. It is not surprising to find the implication of LG in this task, given its recognized implication in the visual recognition of words (Mechelli et al., 2000). In schizophrenic patients, low LG activation has been interpreted to underlie superficial perceptual processing of words (Ragland et al., 2005), and LG is part of a network implicated in the degree of insight patients may hold about their illness (Antonius et al., 2011). Given that the processing of lengthy words appears to modulate (increase) the activation of LG, it is possible that elevated positive schizotypy during adolescence is associated with a reluctance to engage in deep semantic processing of emotionally valenced words (Mechelli et al., 2000), particularly when they concern one's self. LG's association with adolescent positive schizotypy is still unclear, but the results here motivate further inquiry into the roles it may play in the processing, or lack thereof, of self-relevant information.

The second set of associations between neural activation and positive schizotypy concern two cortical midline areas (dmPFC and PCC). First, increased mPFC activation in elevated positive schizotypy is consistent with the only study involving non-clinical psychosis-prone adult participants, which reported a general pattern of increased activation in the medial frontal areas (Modinos et al., 2011). Moreover, in a recent meta-analytic review of 25 functional neuroimaging studies using trait adjective evaluation tasks, Murray et al. (2012) confirmed that left dmPFC activation significantly contributes to both self- and other-reflective processing. Interestingly, this meta-analysis quantified the distance between ventral and dorsal mPFC in trait evaluation tasks, and observed that thinking about self, close other, and unknown other

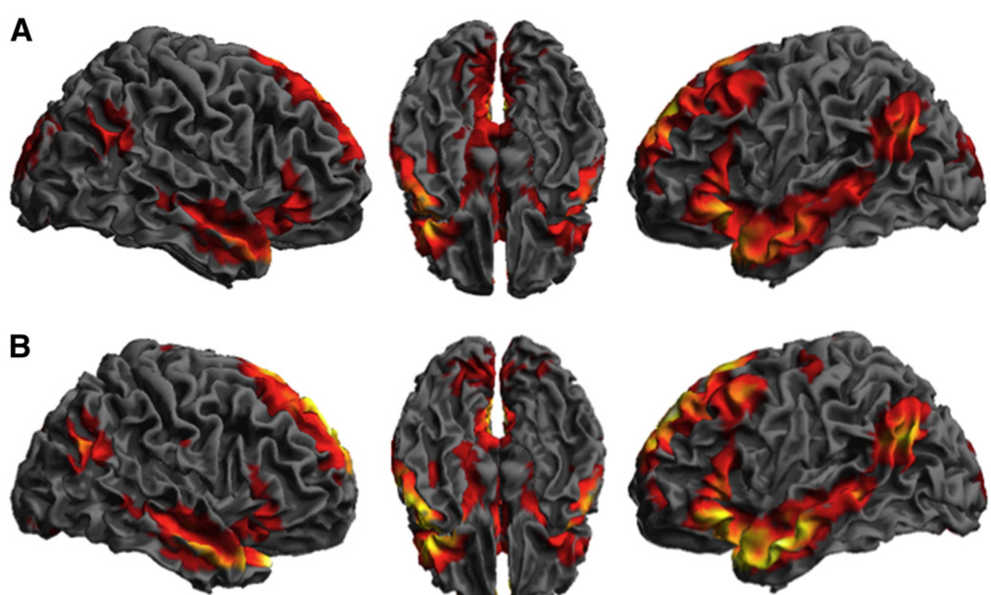

Fig. 2. Statistical parametric maps depicting brain areas showing a significant main effect of A) SELF versus CONTROL and B) OTHER versus CONTROL (at $p < .001$ uncorrected and $k = 20$ for illustration). Activation is overlaid on a single-subject anatomical T1 template.

Table 2
Main effects contrasts thresholded at $p < .001$ at the peak and $p < .05$ FDR-corrected at the cluster level. Coordinates are provided in MNI space. vmPFC = ventromedial prefrontal cortex, PCC = posterior cingulate cortex, aSTG = anterior superior temporal gyrus, BA = brodman area, TPJ = temporo-occipital junction, SMG = supramarginal gyrus, IPL = intraparietal lobule.

p FDR	*z*	*p Peak*	*x*	*y*	*z*	*Region*
OTHER versus SELF						
.019	6.31	< .001	0	36	−18	vmPFC
< .001	5.79	< .001	2	−52	22	PCC
.031	5.21	< .001	−62	−12	−18	aSTG left
.001	4.52	< .001	40	−10	60	BA 6 right
SELF versus CONTROL						
< .001	–	< .001	−10	−52	28	PCC
.015	7.15	< .001	−28	−82	−30	Cerebellum left
.001	6.91	< .001	0	−16	36	Cingulate
< .001	6.73	< .001	56	−64	32	TPJ/SMG right
.003	5.45	< .001	−2	−30	−30	Midbrain
.029	4.08	< .001	28	−12	−18	Amygdala right
OTHER versus CONTROL						
< .001	–	< .001	−2	−50	26	PCC
< .001	7.25	< .001	56	−64	28	TPJ/SMG right
.002	6.63	< .001	0	−14	38	Cingulate
.009	4.15	< .001	−34	−24	48	IPL left

Table 3
Areas showing significant correlations with SPQpos scores (at $p < .001$ uncorrected and $k = 20$) that remain significant after controlling for SPQneg, SPQdis, INT, EXT and Age (at $p < .05$). Coordinates are provided in MNI space. LG = lingual gyrus, PCC = posterior cingulate cortex, DLPFC = dorsolateral prefrontal cortex, DMPFC = dorsomedial prefrontal cortex.

z	*p Peak*	*x*	*y*	*z*	*Region*
SELF versus OTHER x SPQpos NEGATIVE					
3.85	< .001	−18	−68	−2	LG left
SELF versus CONTROL x SPQpos POSITIVE					
4.32	< .001	−8	−52	24	PCC
3.66	< .001	−38	16	50	DLPFC left
3.64	< .001	−12	56	36	DMPFC left
OTHER versus CONTROL × SPQpos POSITIVE					
4.39	< .001	−6	−52	24	PCC
3.66	< .001	−16	52	30	DMPFC left
3.62	< .001	−14	36	42	DMPFC left

appears to follow a ventral to dorsal gradient in the mPFC, where thinking about oneself activates more ventral mPFC in comparison to thinking about unknown others, which activates more dorsal mPFC regions. Importantly, the meta-analysis situates specific "unknown other vs control" activation around coordinates −6, 52, 33 of the dmPFC, which fall within the vicinity of dmPFC regions found to be associated with adolescent positive schizotypy in the present sample (SELF vs CONTROL; −12, 56, 36; OTHER vs CONTROL; −16, 52, 30). It thus appears remarkable that degree of positive schizotypy, when thinking about oneself or one's best friend, is associated with increased activation of an area usually devoted to evaluating trait-adjectives of "unknown others" in similar tasks. It could be worthwhile to further investigate how in individuals expressing to different degrees some positive symptoms of psychosis, thinking about a *familiar* person (self, best friend) recruits regions typically devoted to *unfamiliar* individuals.

Together with the mPFC, the PCC represents a cortical midline hub decisively involved in self and other-reflective processes (Denny et al., 2012; Qin et al., 2012). Adolescent positive schizotypy further correlates with increased activation in the PCC, both for SELF VS CONTROL and OTHER vs CONTROL contrasts. Increased PCC activation has been reported in self-trait attribution tasks performed by schizophrenic patients (van der Meer et al., 2010; Holt et al., 2011). Typically, increased PCC activation has been reported in functional imaging studies when contrasting different types of self-reflective stances, such as judging appearance characteristics (Moran et al., 2011), comparing present-self versus past-self processing (D'Argembeau et al., 2008), or opposing other- versus self-related processing (Modinos et al., 2011; van der Meer et al., in press). Furthermore, the PCC is recognized for supporting autobiographical memory, and recruiting features of past episodes (Wagner et al., 2005). From this perspective, an increased PCC activation associated with adolescent positive schizotypy might suggest a tendency to more readily rely on concrete observable details about their current selves (such as recent actions and behaviors) when performing self-trait judgments. This would be consistent with previous accounts of increased PCC activation in schizophrenic patients during self-reflective tasks, whose concrete reflective processing draws much less upon abstract, implicit, semantic knowledge about self (Holt et al., 2011; Shad et al., 2012).

It may be useful to consider the *combination* of associations between adolescent positive schizotypy and the cortical midline regions of the dmPFC and PCC. In doing so, we first underline that the dmPFC/PCC are found for both the SELF vs CONTROL and the OTHER vs CONTROL contrasts. This suggests that the processes involved may participate in blurring the barrier between self and other, under circumstances devoted to thinking about oneself or a close other. Second, the dmPFC/PCC associations with positive schizotypy are not identical to what is observed in cortical midline activity of schizophrenic patients performing trait evaluation tasks. Indeed, self-reflective tasks with individuals meeting diagnostic criteria for schizophrenia have reported an "anterior to posterior shift" in neural activity, reflected

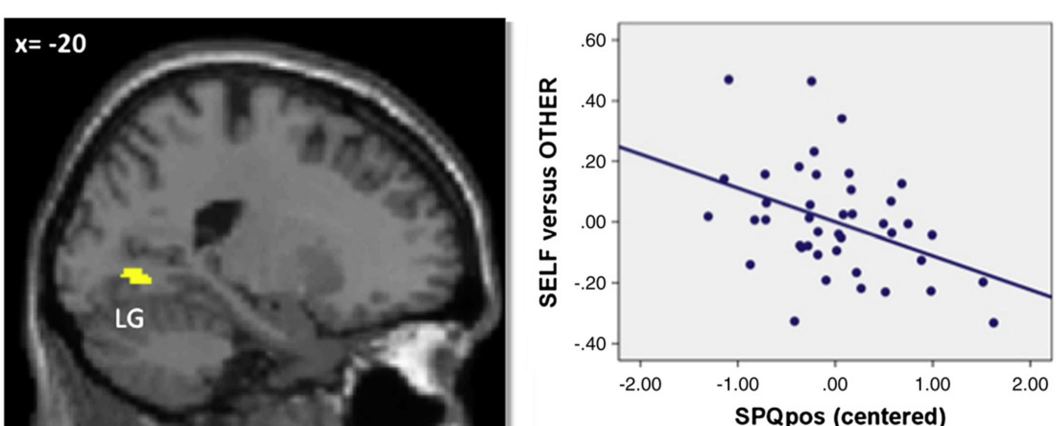

Fig. 3. Left: Statistical parametric map depicting the left lingual gyrus showing a significant negative correlation with SPQpos scores for the contrast SELF versus OTHER (at $p < .001$ uncorrected and $k = 20$) after controlling for SPQneg, SPQdis, INT, EXT and Age (at $p < .05$). Right: Graph depicting the negative relation (partial regression plot) between extracted beta values from the left lingual gyrus cluster (averaged across all voxels) and SPQpos. Activation is overlaid on a single-subject anatomical T1 template.

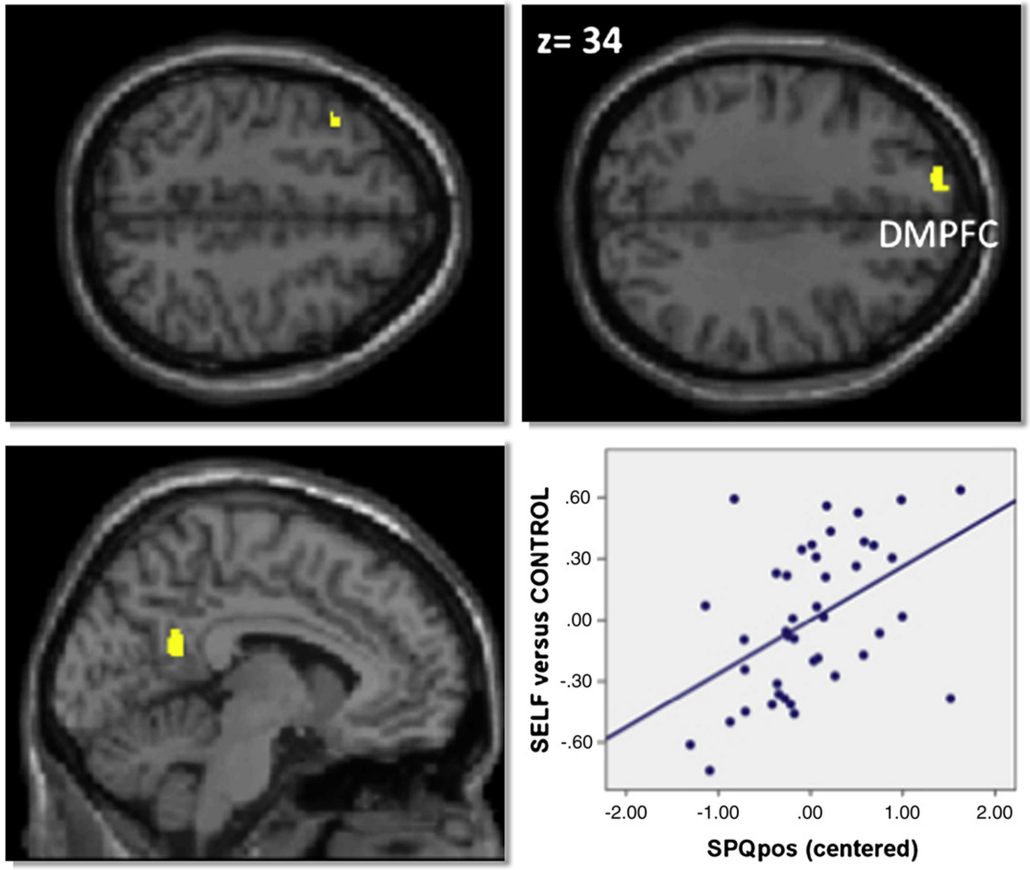

Fig. 4. Top: Statistical parametric map depicting brain areas showing significant positive correlations with SPQpos scores for the contrast SELF versus CONTROL (at $p < .001$ uncorrected and $k = 20$) after controlling for SPQneg, SPQdis, INT, EXT and Age (at $p < .05$), dorsomedial prefrontal cortex, dorsolateral prefrontal cortex, and extending to bottom left, posterior cingulate cortex. Bottom right: Graph depicting the positive relation (partial regression plot) between extracted beta values from the dorsomedial prefrontal cortex cluster (averaged across all voxels) and SPQpos. Activation is overlaid on a single-subject anatomical T1 template.

by hypoactivation in the mPFC and hyper activation in the PCC regions (Holt et al., 2011). In contrasts, the two studies with non-clinical subjects performing the trait-evaluation task failed to find hypoactivation in the mPFC (Modinos et al., 2011). Therefore, this discrepancy might signal one of the critical differences between non-clinical and clinical states in the way mPFC activation combines with PCC activation during self-reflective tasks. In support of this claim, a recent fMRI study, testing the effects of a psychedelic drug (psilocybin) during resting-state, suggests that anterior-posterior cortical midline connectivity is critically altered during drug-induced states (Carhart-Harris et al., 2012). This altered antero-posterior connectivity is notably observed in the default-mode network (DMN), a set of regions thought to sustain self-reflective introspective activity. Furthermore, this alteration in anterior-posterior midline connectivity is accompanied by an experiential shift where participants can describe dissolution of boundaries between self and others (Carhart-Harris et al., 2012). We may postulate that variations in dmPFC-PCC connectivity critically influences self-processing, but this requires to gather further empirical evidence. In this context, we may conjecture that normative positive schizotypy can already be observed as being associated with activation patterns in these two regions during self-reflection, while more clinical phenomena may altogether alter dmPFC-PCC interactions and sustain anomalous self experiences.

The results speak to some of the *reflective* processes that might already sustain the expression of positive schizotypy during adolescence. Some authors, however, argue that positive schizotypy represents a secondary, phenotypical manifestation of a more fundamental, *pre-reflective* disturbance in the basic sense of self (Meehl, 1962; Parnas et al., 2005). This pre-reflective dimension was not tested in our study, but its implications will be discussed with reference to our results. Parnas and colleagues argue that a basic self disturbance constitutes the core feature of schizophrenic spectrum disorders (Parnas, 2003; Sass and Parnas, 2007). Originating from the tradition phenomenology in continental philosophy, these authors define three distinct levels of selfhood, the last of which carries reflective features such as an individual's characteristics traits, attitudes, motivations and habits. This reflective, conceptual self naturally relies on the integrity of the pre-reflective, minimal and basic level of selfhood. Crucially, the notion of pre-reflective self draws attention to the implicit awareness embedded in subjective experience, each individual thus living experience as *one's own* experience. Northoff and colleagues suggest that the cortical midline sustain the minimal self functions (Northoff and Bermpohl, 2004; Northoff et al., 2006, 2011), and that atypical patterns of CMS activations may be somehow connected to disturbances in the pre-reflective self (Nelson et al., 2009), although this requires further research.

With regards to our own results, it may thus be fruitful to integrate a phenomenological perspective to our neurocognitive account of the significant associations found between adolescent positive schizotypy and dmPFC/PCC activations. The phenomenological descriptions of diminished self-affection have recently been researched in relation to the schizophrenia prodrome (Nelson et al., 2008, 2012a, 2012b), and may also be relevant to adolescent positive schizotypy. Diminished self-affection is thought to result from a type of sustained self-focus that objectifies self-experience (Sass and Parnas, 2003). We may hypothesize that decreased LG activity, together with increased dmPFC/

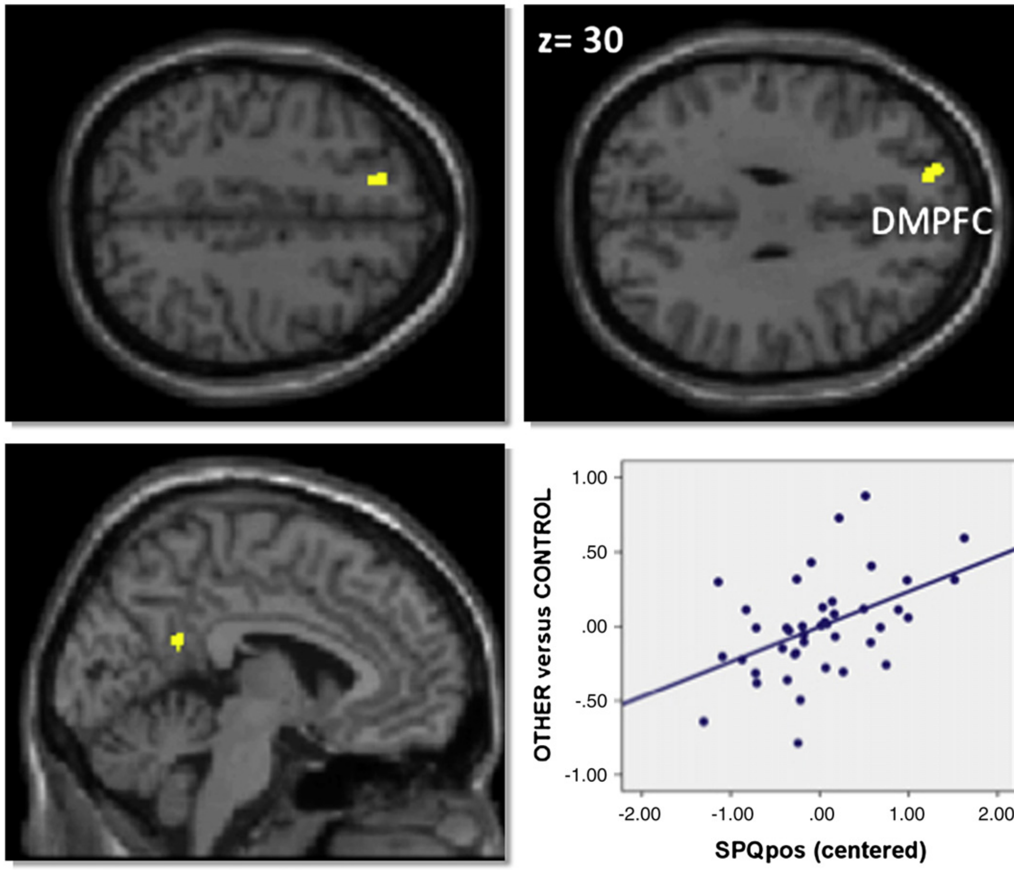

Fig. 5. Top: Statistical parametric map depicting brain areas showing significant positive correlations with SPQpos scores for the contrast OTHER versus CONTROL (at $p < .001$ uncorrected and $k = 20$) after controlling for SPQneg, SPQdis, INT, EXT and Age (at $p < .05$), dorsomedial prefrontal cortex, dorsolateral prefrontal cortex, and extending to bottom left, posterior cingulate cortex. Bottom right: Graph depicting the positive relation (partial regression plot) between extracted beta values from the posterior cingulate cortex cluster (averaged across all voxels) and SPQpos. Activation is overlaid on a single-subject anatomical T1 template.

PCC activations in association to positive schizotypy may sustain such diminished self-affection. In other words, the self-reflective processes by which self-traits are superficially processed (low LG), evaluated on the basis of concrete and observable criteria (increased PCC) and evaluated as unfamiliar to self (increased dmPFC) may operate, to a degree, within a phenomenological dimension of experiencing the present self as an *other*. Put differently, self-trait evaluations on such a combination of reflective processes may be characteristic of diminished self-affectation in adolescents reporting increased positive schizotypy. It remains open to question however, whether the observed self-reflective profile associated to adolescent schizotypy conduces to faulty self-development and/or anomalous self-experiences such as those observed in adults suffering from schizophrenia (Parnas, 2003). Further qualitative and empirical research on positive schizotypy and self-reflexivity during adolescence, especially using longitudinal designs, will be required to assess its developmental links to atypical experiences of the self, and to potential risk for schizophrenic spectrum disorders during adulthood.

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Author contribution

Authors M.D., D.S. and S.E. designed the study and wrote the protocol. Authors D.B. and M.L. managed the data collection and analyses. Authors M.D., P.V. and M.L. undertook the statistical analysis, and author M.D. wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

None of the authors have any conflict of interest to report

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References

Achenbach, T.M., 1991. Manual for the Youth Self-Report and 1991 Profile. University of Vermont, Department of Psychiatry, Burlington, VT.

Achenbach, T.M., Rescorla, L.A., 2003. Manual for the ASEBA adult forms and profiles. University of Vermont, Research Center for Children, Youth, and Families, Burlington.

Alonso-Solis, A., Corripio, I., de Castro-Manglano, P., Duran-Sindreu, S., Garcia-Garcia, M., Proal, E., Nunez-Marin, F., Soutullo, C., Alvarez, E., Gomez-Anson, B., Kelly, C., Castellanos, F.X., 2012. Altered default network resting state functional connectivity in patients with a first episode of psychosis. Schizophr. Res. 139 (1–3), 13–18.

Anderson, N.H., 1968. Likableness ratings of 555 personality-trait words. J. Pers. Soc. Psychol. 9 (3), 272–279.

Antonius, D., Prudent, V., Rebani, Y., D'Angelo, D., Ardekani, B.A., Malaspina, D., Hoptman, M.J., 2011. White matter integrity and lack of insight in schizophrenia and schizoaffective disorder. Schizophr. Res. 128 (1–3), 76–82.

Badoud, D., Chanal, J., Eliez, S., Van Der Linden, M., Debbané, M., 2011. Validation study of the french Schizotypal Personality Questionnaire in an sample of adolescents; a confirmatory factor analysis. L'Encéphale 37, 299–307.

Carhart-Harris, R.L., Erritzoe, D., Williams, T., Stone, J.M., Reed, L.J., Colasanti, A., Tyacke, R.J., Leech, R., Malizia, A.L., Murphy, K., Hobden, P., Evans, J., Feilding, A., Wise, R.G., Nutt, D.J., 2012. Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. Proc. Natl. Acad. Sci. U. S. A. 109 (6), 2138–2143.
Cicchetti, D., Rogosch, F.A., 2002. A developmental psychopathology perspective on adolescence. J. Consult. Clin. Psychol. 70 (1), 6–20.
D'Argembeau, A., Feyers, D., Majerus, S., Collette, F., Van der Linden, M., Maquet, P., Salmon, E., 2008. Self-reflection across time: cortical midline structures differentiate between present and past selves. Soc. Cogn. Affect. Neurosci. 3 (3), 244–252.
Debbané, M., Van der Linden, M., Gex-Fabry, M., Eliez, S., 2009. Cognitive and emotional associations to positive schizotypy during adolescence. J. Child Psychol. Psychiatry 50 (3), 326–334.
Debbané, M., Van der Linden, M., Balanzin, D., Billieux, J., Eliez, S., 2012. Associations among metacognitive beliefs, anxiety and positive schizotypy during adolescence. J. Nerv. Ment. Dis. 200 (7), 620–626.
Denny, B.T., Kober, H., Wager, T.D., Ochsner, K.N., 2012. A meta-analysis of functional neuroimaging studies of self- and other judgments reveals a spatial gradient for mentalizing in medial prefrontal cortex. J. Cogn. Neurosci. 24 (8), 1742–1752.
Dhossche, D., Ferdinand, R., Van der Ende, J., Hofstra, M.B., Verhulst, F., 2002. Diagnostic outcome of self-reported hallucinations in a community sample of adolescents. Psychol. Med. 32 (4), 619–627.
Dinn, W.M., Harris, C.L., Aycicegi, A., Greene, P., Andover, M.S., 2002. Positive and negative schizotypy in a student sample: neurocognitive and clinical correlates. Schizophr. Res. 56 (1–2), 171–185.
Dominguez, M.D., Saka, M.C., Lieb, R., Wittchen, H.U., van Os, J., 2010. Early expression of negative/disorganized symptoms predicting psychotic experiences and subsequent clinical psychosis: a 10-year study. Am. J. Psychiatry 167 (9), 1075–1082.
Dominguez, M.D., Wichers, M., Lieb, R., Wittchen, H.U., van Os, J., 2011. Evidence that onset of clinical psychosis is an outcome of progressively more persistent subclinical psychotic experiences: an 8-year cohort study. Schizophr. Bull. 37 (1), 84–93.
Erikson, E.H., 1968. Identity: youth and crisis. W.W. Norton & Company, New York.
Fair, D.A., Dosenbach, N.U., Church, J.A., Cohen, A.L., Brahmbhatt, S., Miezin, F.M., Barch, D.M., Raichle, M.E., Petersen, S.E., Schlaggar, B.L., 2007. Development of distinct control networks through segregation and integration. Proc. Natl. Acad. Sci. U. S. A. 104 (33), 13507–13512.
Fonseca-Pedrero, E., Lemos-Giraldez, S., Muniz, J., Garcia-Cueto, E., Campillo-Alvarez, A., 2008. Schizotypy in adolescence: the role of gender and age. J. Nerv. Ment. Dis. 196 (2), 161–165.
Holt, D.J., Cassidy, B.S., Andrews-Hanna, J.R., Lee, S.M., Coombs, G., Goff, D.C., Gabrieli, J.D., Moran, J.M., 2011. An anterior-to-posterior shift in midline cortical activity in schizophrenia during self-reflection. Biol. Psychiatry 69 (5), 415–423.
Kerns, J.G., 2005. Positive schizotypy and emotion processing. J. Abnorm. Psychol. 114 (3), 392–401.
Lagioia, A., Van de Ville, D., Debbané, M., Lazeyras, F., Eliez, S., 2010. Adolescent resting state networks and their associations with schizotypal trait expression. Front. Syst. Neurosci. 35 (4), 1–12.
Lagioia, A., Eliez, S., Schneider, M., Simons, J.S., Van der Linden, M., Debbane, M., 2011. Neural correlates of reality monitoring during adolescence. NeuroImage 55 (3), 1393–1400.
Mechelli, A., Humphreys, G.W., Mayall, K., Olson, A., Price, C.J., 2000. Differential effects of word length and visual contrast in the fusiform and lingual gyri during reading. Proc. Biol. Sci. R. Soc. 267 (1455), 1909–1913.
Meehl, P.E., 1962. Schizotaxia, schizotypy, schizophrenia. Am. Psychol. 17, 827–838.
Miller, P., Byrne, M., Hodges, A., Lawrie, S.M., Owens, D.G., Johnstone, E.C., 2002. Schizotypal components in people at high risk of developing schizophrenia: early findings from the Edinburgh High-Risk Study. Br. J. Psychiatry 180, 179–184.
Modinos, G., Renken, R., Ormel, J., Aleman, A., 2011. Self-reflection and the psychosis-prone brain: an fMRI study. Neuropsychology 25 (3), 295–305.
Moran, J.M., Lee, S.M., Gabrieli, J.D., 2011. Dissociable neural systems supporting knowledge about human character and appearance in ourselves and others. J. Cogn. Neurosci. 23 (9), 2222–2230.
Murray, R.J., Schaer, M., Debbane, M., 2012. Degrees of separation: a quantitative neuroimaging meta-analysis investigating self-specificity and shared neural activation between self- and other-reflection. Neurosci. Biobehav. Rev. 36 (3), 1043–1059.
Nelson, B., Yung, A.R., Bechdolf, A., McGorry, P.D., 2008. The phenomenological critique and self-disturbance: implications for ultra-high risk ("prodrome") research. Schizophr. Bull. 34 (2), 381–392.
Nelson, B., Fornito, A., Harrison, B.J., Yucel, M., Sass, L.A., Yung, A.R., Thompson, A., Wood, S.J., Pantelis, C., McGorry, P.D., 2009. A disturbed sense of self in the psychosis prodrome: linking phenomenology and neurobiology. Neurosci. Biobehav. Rev. 33 (6), 807–817.
Nelson, B., Thompson, A., Yung, A.R., 2012a. Basic self-disturbance predicts psychosis onset in the ultra high risk for psychosis "prodromal" population. Schizophr. Bull. 38 (6), 1277–1287.
Nelson, B., Thompson, A., Yung, A.R., 2012b. Not all first-episode psychosis is the same: preliminary evidence of greater basic self-disturbance in schizophrenia spectrum cases. Early Interv. Psychiatry 7 (2), 200–204.
Northoff, G., Bermpohl, F., 2004. Cortical midline structures and the self. Trends Cogn. Sci. 8 (3), 102–107.
Northoff, G., Heinzel, A., de Greck, M., Bermpohl, F., Dobrowolny, H., Panksepp, J., 2006. Self-referential processing in our brain–a meta-analysis of imaging studies on the self. NeuroImage 31 (1), 440–457.
Northoff, G., Qin, P., Feinberg, T.E., 2011. Brain imaging of the self–conceptual, anatomical and methodological issues. Conscious. Cogn. 20 (1), 52–63.
Parnas, J., 2003. Self and schizophrenia: a phenomenological perspective. In: Kircher, T., David, A. (Eds.), The Self in Neuroscience and Psychiatry. Cambridge University Press, Cambridge, pp. 127–141.
Parnas, J., Moller, P., Kircher, T., Thalbitzer, J., Jansson, L., Handest, P., Zahavi, D., 2005. EASE: examination of anomalous self-experience. Psychopathology 38 (5), 236–258.
Paus, T., Keshavan, M., Giedd, J.N., 2008. Why do many psychiatric disorders emerge during adolescence? Nat. Rev. Neurosci. 9 (12), 947–957.
Pfeifer, J.H., Blakemore, S.J., 2012. Adolescent social cognitive and affective neuroscience: past, present, and future. Soc. Cogn. Affect. Neurosci. 7 (1), 1–10.
Pfeifer, J.H., Peake, S.J., 2012. Self-development: integrating cognitive, socioemotional, and neuroimaging perspectives. Dev. Cogn. Neurosci. 2 (1), 55–69.
Pfeifer, J.H., Lieberman, M.D., Dapretto, M., 2007. "I know you are but what am I?!": neural bases of self- and social knowledge retrieval in children and adults. J. Cogn. Neurosci. 19 (8), 1323–1337.
Pfeifer, J.H., Masten, C.L., Borofsky, L.A., Dapretto, M., Fuligni, A.J., Lieberman, M.D., 2009. Neural correlates of direct and reflected self-appraisals in adolescents and adults: when social perspective-taking informs self-perception. Child Dev. 80 (4), 1016–1038.
Poulton, R., Caspi, A., Moffitt, T.E., Cannon, M., Murray, R., Harrington, H., 2000. Children's self-reported psychotic symptoms and adult schizophreniform disorder: a 15-year longitudinal study. Arch. Gen. Psychiatry 57 (11), 1053–1058.
Qin, P., Liu, Y., Shi, J., Wang, Y., Duncan, N., Gong, Q., Weng, X., Northoff, G., 2012. Dissociation between anterior and posterior cortical regions during self-specificity and familiarity: a combined fMRI-meta-analytic study. Hum. Brain Mapp. 33 (1), 154–164.
Ragland, J.D., Gur, R.C., Valdez, J.N., Loughead, J., Elliott, M., Kohler, C., Kanes, S., Siegel, S.J., Moelter, S.T., Gur, R.E., 2005. Levels-of-processing effect on frontotemporal function in schizophrenia during word encoding and recognition. Am. J. Psychiatry 162 (10), 1840–1848.
Raine, A., 1991. The SPQ: a scale for the assessment of schizotypal personality based on DSM-III-R criteria. Schizophr. Bull. 17 (4), 555–564.
Raznahan, A., Lerch, J.P., Lee, N., Greenstein, D., Wallace, G.L., Stockman, M., Clasen, L., Shaw, P.W., Giedd, J.N., 2011. Patterns of coordinated anatomical change in human cortical development: a longitudinal neuroimaging study of maturational coupling. Neuron 72 (5), 873–884.
Rotarska-Jagiela, A., van de Ven, V., Oertel-Knochel, V., Uhlhaas, P.J., Vogeley, K., Linden, D.E., 2010. Resting-state functional network correlates of psychotic symptoms in schizophrenia. Schizophr. Res. 117 (1), 21–30.
Rutter, M., Kim-Cohen, J., Maughan, B., 2006. Continuities and discontinuities in psychopathology between childhood and adult life. J. Child Psychol. Psychiatry 47 (3–4), 276–295.
Sass, L.A., Parnas, J., 2003. Schizophrenia, consciousness, and the self. Schizophr. Bull. 29 (3), 427–444.
Sass, L.A., Parnas, J., 2007. Explaining schizophrenia: the relevance of phenomenology. In: Chung, M.C., Fulford, K.W.M., Graham, G. (Eds.), Reconceiving Schizophrenia. Oxford University Press, New York, pp. 63–96.
Schneider, M., Debbane, M., Lagioia, A., Salomon, R., d'Argembeau, A., Eliez, S., 2012. Comparing the neural bases of self-referential processing in typically developing and 22q11.2 adolescents. Dev. Cogn. Neurosci. 2 (2), 277–289.
Shad, M.U., Keshavan, M.S., Steinberg, J.L., Mihalakos, P., Thomas, B.P., Motes, M.A., Soares, J.C., Tamminga, C.A., 2012. Neurobiology of self-awareness in schizophrenia: an fMRI study. Schizophr. Res. 138 (2–3), 113–119.
Shaw, P., Kabani, N.J., Lerch, J.P., Eckstrand, K., Lenroot, R., Gogtay, N., Greenstein, D., Clasen, L., Evans, A., Rapoport, J.L., Giedd, J.N., Wise, S.P., 2008. Neurodevelopmental trajectories of the human cerebral cortex. J. Neurosci. 28 (14), 3586–3594.
Shim, G., Oh, J.S., Jung, W.H., Jang, J.H., Choi, C.H., Kim, E., Park, H.Y., Choi, J.S., Jung, M.H., Kwon, J.S., 2010. Altered resting-state connectivity in subjects at ultra-high risk for psychosis: an fMRI study. Behav. Brain Funct. 6, 58.
Shiner, R.L., 2009. The development of personality disorders: perspectives from normal personality development in childhood and adolescence. Dev. Psychopathol. 21 (3), 715–734.
Supekar, K., Uddin, L.Q., Prater, K., Amin, H., Greicius, M.D., Menon, V., 2010. Development of functional and structural connectivity within the default mode network in young children. NeuroImage 52 (1), 290–301.
van der Meer, L., Costafreda, S., Aleman, A., David, A.S., 2010. Self-reflection and the brain: a theoretical review and meta-analysis of neuroimaging studies with implications for schizophrenia. Neurosci. Biobehav. Rev. 34 (6), 935–946.
van der Meer, L., de Vos, A.E., Stiekema, A.P., Pijnenborg, G.H., van Tol, M.J., Nolen, W.A., David, A.S., Aleman, A., 2013. Insight in schizophrenia: involvement of self-reflection networks? Schizophr. Bull. (in press).
Wagner, A.D., Shannon, B.J., Kahn, I., Buckner, R.L., 2005. Parietal lobe contributions to episodic memory retrieval. Trends Cogn. Sci. 9 (9), 445–453.