Cortical Thickness of Neural Substrates Supporting Cognitive Empathy in Individuals with Schizophrenia

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Abstract

Background—Cognitive empathy is supported by the inferior frontal gyrus (IFG), anterior mid-cingulate cortex (aMCC), insula (INS), supplementary motor area (SMA), medial prefrontal cortex (mPFC), right temporo-parietal junction (TPJ), and precuneus (PREC). In healthy controls, cortical thickness in these regions has been linked to cognitive empathy. As cognitive empathy is impaired in schizophrenia, we examined whether reduced cortical thickness in these regions was associated with poorer cognitive empathy in this population.

Methods—41 clinically-stable community-dwelling individuals with schizophrenia and 46 healthy controls group-matched on demographic variables completed self-report empathy questionnaires, a cognitive empathy task, and structural magnetic resonance imaging. We examined between-group differences in study variables using *t*-tests and analyses of variance. Next, we used Pearson correlations to evaluate the relationship between cognitive empathy and cortical thickness in the mPFC, IFG, aMCC, INS, SMA, TPJ, and PREC in both groups.

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Results—Individuals with schizophrenia demonstrated cortical thinning in the IFG, INS, SMA, TPJ, and PREC (all p<0.05) and impaired cognitive empathy across all measures (all p<0.01) relative to controls. While cortical thickness in the mPFC, IFC, aMCC, and INS (all p<0.05) was related to cognitive empathy in controls, we did not observe these relationships in individuals with schizophrenia (all p>0.10).

Conclusions—Individuals with schizophrenia have reduced cortical thickness in empathy-related neural regions and significant impairments in cognitive empathy. Interestingly, cortical thickness was related to cognitive empathy in controls but not in the schizophrenia group. We discuss other mechanisms that may account for cognitive empathy impairment in schizophrenia.

Keywords

Cortical Thickness; Empathy; Social Cognition; Schizophrenia

1. Introduction

Empathy encompasses the ability to understand the emotional perspective of others through mentalizing (i.e., cognitive empathy), and the capacity to share the same emotional state as others (i.e., affective empathy) (Shamay-Tsoory, 2011; Zaki and Ochsner, 2011). Cognitive empathy is impaired among individuals with schizophrenia based on self-report (Achim et al., 2011; Smith et al., 2012; Sparks et al., 2010), behavioral task performance (Derntl et al., 2009; Smith et al., 2014), and functional neuroimaging (Benedetti et al., 2009; Derntl et al., 2012; Lee et al., 2010; Smith et al., 2015). Furthermore, cognitive empathy impairments have been associated with deficits in social functioning among individuals with schizophrenia (Smith et al., 2014; Smith et al., 2012; Smith et al., 2015). Meanwhile, the literature is mixed regarding whether affective empathy is impaired in schizophrenia. Thus, we may gain a deeper understanding of how to develop targeted treatments aimed at enhancing social functioning by evaluating deficits in cognitive empathy.

Most studies suggest that cognitive empathy is supported by the medial prefrontal cortex (mPFC) (Meyer et al., 2012; Rameson et al., 2012; Schnell et al., 2011), right temporo-parietal junction (TPJ) (Hooker et al., 2008; Schulte-Ruther et al., 2007; Vollm et al., 2006), precuneus (PREC) (Farrow et al., 2001; Meyer et al., 2012; Nummenmaa et al., 2008) and supplemental motor area (SMA) (Keysers and Gazzola, 2009; Lamm et al., 2007). Together, these regions are thought to support self-referential representations, transient mental inference of others, and mentalizing (Shamay-Tsoory, 2011). Additionally, research suggests that cognitive empathy is supported by regions of the brain that process emotion, such as the inferior frontal gyrus (IFG), anterior mid-cingulate cortex (aMCC), and anterior insula (INS) (Gonzalez-Liencres et al., 2013). Collectively, these are some of the specific neural substrates that support cognitive empathy.

There is also a link between morphologic differences in regions supporting mentalizing and social information processing. Studies in healthy individuals have shown that gray matter volume (Banissy et al., 2012; Sassa et al., 2012; Takeuchi et al., 2014) and density (Mutschler et al., 2013) in neural regions supporting empathy are associated with measures of cognitive empathy. Other studies suggest individuals with neurodevelopmental disorders

(e.g., autism spectrum disorder) have cortical thinning in the mentalizing network that correlates with greater social impairment (Hadjikhani et al., 2006; Richter et al., 2015). Similarly, studies of individuals with schizophrenia have revealed cortical thinning in most, if not all, of the neural regions supporting empathy (Goldman et al., 2009; Kuperberg et al., 2003; Nesvag et al., 2008). However, the field has not yet evaluated whether cortical thinning in these regions is associated with impaired cognitive empathy.

In this study, we examined the relationship between cortical thickness in regions thought to subserve cognitive empathy and both self-reported and performance-based measures of cognitive empathy. We examined this relationship in individuals with schizophrenia and healthy controls. Based on our review of the literature, we had three primary hypotheses. First, we expected that individuals with schizophrenia would have cortical thinning in frontal, temporal, and parietal substrates of empathy relative to controls. Second, we hypothesized that individuals with schizophrenia would demonstrate deficits in performance-based and self-reported measures of cognitive empathy relative to controls. Third, we hypothesized that cortical thickness would correlate with both performance-based and self-reported measures of cognitive empathy in both individuals with schizophrenia and controls.

2. Materials and Methods

2.1 Sample

Individuals with schizophrenia (*n*=41) and healthy controls (*n*=46) were group-matched for age (18–50 years), gender, ethnicity, parental socioeconomic status and handedness (Table 1). Individuals with schizophrenia were recruited using advertisements placed in outpatient clinics at an academic medical center, community mental health clinics in local and surrounding neighborhoods, and on local National Alliance for Mental Illness websites. Controls were recruited from the same geographic areas as the individuals with schizophrenia using paper and online advertisements. Participants were excluded if they: 1) met DSM-IV criteria for current substance abuse or dependence within the past six months; 2) had a severe medical condition; or 3) sustained a head injury with neurological sequelae. Controls were further excluded if they had a lifetime history of any DSM-IV Axis I disorder or a first-degree biological relative with a psychotic disorder. Written informed consent procedures were conducted with all participants. The Institutional Review Board at Northwestern University approved all study procedures.

2.2 Measures

2.2.1 Demographic and Clinical Measures—Demographic and clinical measures were collected using the Structured Clinical Interview for DSM-IV (SCID-IV) (First et al., 2002), which was administered by trained Masters- and PhD-level research staff. A diagnosis of schizophrenia was validated via consensus between a semi-structured psychiatrist interview and SCID ratings. Recent alcohol and cigarette consumption were assessed using a semi-structured interview adapted from the Lifetime Alcohol Consumption Assessment Procedure (Skinner, 1982). Antipsychotic medication dosages were converted into chlorpromazine equivalents using a standardized method (Andreasen et al., 2010). Psychopathology was

assessed in schizophrenia subjects using the global ratings from the Scale for the Assessment of Positive Symptoms (Andreasen, 1983b) and the Scale for the Assessment of Negative Symptoms (Andreasen, 1983a). We measured parental socioeconomic status using the Barratt Simplified Measure of Social Status (Barratt, 2005).

2.2.2 Cognitive Empathy Task—Cognitive empathy was assessed using the Emotional Perspective-Taking Task (EPT) (Derntl et al., 2009; Smith et al., 2014). Participants viewed sixty 4-second scenes showing two Caucasian individuals involved in social interactions meant to portray five basic emotions, and neutral scenes (10 stimuli per condition). The face of one individual was masked. Participants were asked to infer the corresponding emotional expression of the masked face by selecting between two different emotional facial expressions or a neutral expression presented after each scene. One option was correct, while the incorrect option was selected at random from all other choices.

2.2.3 Cognitive Empathy Questionnaires—Participants also completed the perspective-taking subscale of the Interpersonal Reactivity Index (IRI) (Davis, 1983) and the cognitive empathy subscale of the Questionnaire of Cognitive and Affective Empathy (QCAE) (Reniers et al., 2011). The IRI is the most widely used self-report questionnaire that assesses empathy as a multidimensional construct. The 7-item perspective taking subscale includes first-person statements such as, "Before criticizing somebody, I try to imagine how I would feel if I were in their place." Participants rate their response to the degree to which the statement describes them on a 5-point Likert scale ("Does not describe me well" to "Describes me very well"). The IRI perspective-taking subscale had an acceptable-to-low alpha reliability in controls (α=0.74) and individuals with schizophrenia (α=0.55), respectively.

The QCAE is a more recently developed scale of cognitive and affective components of empathy that integrates the strengths of several validated empathy questionnaires including the IRI. The cognitive empathy subscale contains 9 first-person statements ("I sometimes try to understand my friends better by imagining how things look from their perspective"). Participants rate the degree to which they agree with each statement on a 5-point Likert scale ("Strongly disagree" to "Strongly agree"). The QCAE cognitive empathy subscale had strong reliabilities in controls (α=0.87) and individuals with schizophrenia (α=0.84).

2.2.4 MRI Acquisition and Data Processing—Magnetic resonance imaging (MRI) scans were acquired on a 3T Tim Trio scanner (Siemens Medical Systems) and collected using an MPRAGE sequence (TR = 2400 mms, TE = 3.16 ms, flip angle = 8°, TI = 1000 ms, ACQ-2, Matrix = 256 × 256, FOV = 22 cm, scanning time = 17 min) with 1mm × 1 mm × 1 mm isotropic resolution. Scans were then analyzed and processed using FreeSurfer (FS, http://surfer.nmr.mgh.harvard.edu) release 5.1.0 (Dale et al., 1999). Inaccuracies were corrected using a combination of automatic and manual methods (Fischl et al., 1999). Manual editing was done according to established guidelines (Segonne et al., 2007). Reconstruction of white and pial surfaces was required for estimation of cortical measures.

We selected 12 *a priori* regions of interest (ROI), 6 per hemisphere, based on previous research implicating these specific regions in cognitive empathy ability (Farrow et al., 2001;

Hooker et al., 2008; Keysers and Gazzola, 2009; Lamm et al., 2007; Meyer et al., 2012; Nummenmaa et al., 2008; Rameson et al., 2012; Schnell et al., 2011; Schulte-Ruther et al., 2007; Vollm et al., 2006). ROI definitions were based on modifications to the standard FS parcellation atlas (Desikan et al., 2006), and include the IFG, INS, aMCC, SMA, TPJ, and PREC. Estimated cortical thickness was calculated using embedded FS algorithms.

2.3 Data Analysis

Schizophrenia and control group demographics were compared using t- and χ^2 tests for continuous and categorical variables, respectively. We used one-tailed t-tests to evaluate differences in cortical thickness, given prior evidence that individuals with schizophrenia have thinner cortical regions compared to controls (Goldman et al., 2009; Kuperberg et al., 2003). Finally, we examined whether cortical thickness in each ROI was associated with measures of cognitive empathy using partial correlations that covaried for any observed between-group differences and age, due to the association between age and cortical thickness (Lemaitre et al., 2012). We conducted one-tailed correlations between measures of cortical thickness and cognitive empathy, given that brain structure has been associated with empathic ability among healthy individuals (Banissy et al., 2012; Cheng et al., 2009; Mutschler et al., 2013; Sassa et al., 2012; Takeuchi et al., 2014) and individuals with clinical conditions characterized by empathic deficits (Hadjikhani et al., 2006; Meda et al., 2012). Corrections for multiple comparisons for the correlations were handled using the false discovery rate of 0.05 (Benjamini et al., 2001).

3. Results

Individuals with schizophrenia and controls did not differ with respect to age, parental socioeconomic status, handedness, or past year alcohol consumption (Table 1). Three individuals with schizophrenia reported past year alcohol consumption greater than 3 standard deviations above the mean and were excluded as outliers. Individuals with schizophrenia reported smoking more cigarettes per day in the past year compared to controls ($p<0.01$). Thus, we evaluated cigarette consumption as a covariate in our subsequent analyses. However, this variable was a non-significant covariate and was removed from the analyses to optimize statistical power.

When compared to the control group, schizophrenia subjects demonstrated significantly lower accuracy rates and higher response times during their performance on a cognitive empathy task (both $p<0.001$) and reported lower levels of cognitive empathy on both the QCAE and IRI (both $p<0.01$, Table 2).

We observed significant between-group differences in cortical thickness (Table 3), where schizophrenia subjects demonstrated greater thinning in the IFG (left: $p=0.01$; right: $p=0.07$ (trend)); aMCC (right: $p=0.09$); INS (both left and right: $p<0.05$); SMA (right: $p<0.01$; left: $p=0.07$ (trend)); TPJ (right: $p<0.05$; left: $p=0.07$ (trend)); and PREC (left: $p=0.07$ (trend)). Group differences in cortical thickness were not found in the mPFC, left aMCC, and right PREC.

One-tailed Pearson partial correlations (with age as covariate) revealed significant relationships between cortical thickness and performance-based cognitive empathy in the control group (Table 4). Specifically, cognitive empathy task performance was positively correlated with cortical thickness in the following bilateral ROIs: mPFC (left: r= 0.43, p=0.002 and right: r=0.41, p =0.003) and INS (left: r= 0.41, p=0.003 and right: r=0.35, p=0.012) as well as in the right IFG (r= 0.37, p=0.008) and left aMCC (r= 0.31, p=0.023). The IRI and QCAE measures of cognitive empathy did not correlate with any measures of cortical thickness among controls. No significant correlations between cortical thickness and measures of cognitive empathy were observed in the schizophrenia group; even when controlling for antipsychotic medication (all p>.10).

4. Discussion

In this study, we detected reduced cortical thickness in individuals with schizophrenia relative to controls in regions supporting empathy, which is consistent with prior studies evaluating cortical thickness in schizophrenia (Ehrlich et al., 2012; Hartberg et al., 2011; Nesvag et al., 2012). Individuals with schizophrenia also demonstrated deficits in cognitive empathy as measured by self-report and behavioral performance, which was consistent with the findings of the larger sample from which they were drawn (Michaels et al., 2015; Smith et al., 2014). Although we observed correlations between regions supporting empathy and cognitive empathy performance in controls, we did not observe significant correlations among the individuals with schizophrenia.

Specifically, we found that individuals with schizophrenia were characterized by reduced cortical thickness of the right IFG, which is implicated in the functional support of emotion processing and triggers insular responses to facial expressions (Jabbi and Keysers, 2008; Liakakis et al., 2011). We also observed reduced cortical thickness bilaterally in the INS, which is thought to support a cognitive-evaluative form of empathy (Fan et al., 2011), and in the right SMA, which is involved in perceiving and processing action behaviors (Etkin et al., 2011; Keysers and Gazzola, 2009; Smith et al., 2015). Differences in cortical thickness were also noted in the TPJ, which is thought to be important for differentiating the mental state of others from oneself (Decety and Lamm, 2007; Saxe and Kanwisher, 2003).

In regard to the relationship between cortical thickness and cognitive empathy performance, we observed several correlations in controls. Consistent with prior studies of brain structure and empathy, these correlations predominantly involved the mPFC, IFG, INS, and aMCC (Banissy et al., 2012; Cheng et al., 2009; Mutschler et al., 2013; Sassa et al., 2012; Takeuchi et al., 2014). Specifically, we found that better cognitive empathy performance correlated with thicker left and right mPFC, which supports internal representation of others (i.e., mentalizing) (Rameson et al., 2012). In addition, we observed a correlation between cognitive empathy and left aMCC, which is thought to be involved in emotion discrimination, empathy for pain, and preparing behavioral responses to stressful situations (Bruneau et al., 2012; Torta and Cauda, 2011; Vogt, 2005). We also observed correlations between cognitive empathy performance and the right IFG and bilateral INS (functionally described above), which were regions that demonstrated reduced cortical thickness in the schizophrenia group.

Although we observed brain-behavior correlations among controls, we did not observe any significant correlations among the individuals with schizophrenia. We considered the possibility that changes in cognitive empathy or brain structure related to having schizophrenia may have reduced the variance in these measures, which could make it more difficult to detect correlations, but this was not the case given the observed standard deviations (Tables 2 and 3). There are several potential explanations for our negative findings. One possibility, is that schizophrenia is characterized by altered white matter pathways (Ellison-Wright and Bullmore, 2009; Karlsgodt, 2016), which may be accounting for the observed impairment in cognitive empathy in schizophrenia. Thus, Diffusion Tensor Imaging (DTI, e.g., fiber tractography) could be one possible tool to measure the complex integration of networks supporting cognitive empathy. Also, there is increasing evidence that schizophrenia is a disorder of functional disconnectivity (Anticevic et al., 2015), and network integrity involving the regions subserving empathy (and probably others), rather than reduced cortical thickness alone, contribute to empathic deficits in schizophrenia (Ioannides et al., 2004). In the context of observed social functioning deficits, the lack of a specific relationship between empathy-related regions and cognitive empathy in the schizophrenia group could reflect functional reorganization associated with abnormal neurodevelopment (Vertes and Bullmore, 2015).

In addition, it is possible that changes in cortical thickness may influence cognitive empathy, but only as evidenced by associated behavioral processes, such as social information processing deficits. Empathic processing is modulated by many other factors, including cognitive abilities, personality factors, context and motivation (Engen and Singer, 2013; Han et al., 2009). Moreover, empathy is a multifaceted construct, dependent on integration among various social information processing networks which are disrupted in schizophrenia (Green et al., 2015). For example, empathic responding requires intact self-other distinction, or the capacity to correctly distinguish between one's own affective representations and those of another (Lamm et al., 2016), which are impaired in schizophrenia (Ebisch and Gallese, 2015; Liepelt et al., 2012). While these explanations are purely speculative, the absence of a correlation between cortical thickness and impaired cognitive empathy contributes incrementally to the understanding of the neurobiological mechanisms that underlie emotional processing deficits seen in schizophrenia. As such, future studies could evaluate these alternative hypotheses as explanations for the lack of relationship between cognitive empathy and cortical thickness.

While this study provides insights into the relationship between the integrity of the neural circuitry supporting empathy and measures of cognitive empathy performance, the results must be interpreted in the context of some limitations. First, individuals with schizophrenia in this sample had lived with the illness for well over a decade. Thus, our results may not generalize to individuals in earlier or later stages of illness. Second, the cross-sectional study conducted does not allow for inference of a causal relationship between cortical thickness and cognitive empathy in either the control or schizophrenia group. Third, the self-reported measures of cognitive empathy were unrelated to cortical thickness in both of the control and schizophrenia groups. This finding raises an important question about whether self-report measures of cognitive empathy assess the same phenotypes as performance-based measures of cognitive empathy.

In conclusion, observed patterns of cortical thinning in empathy-related neural regions found in this study are consistent with the larger schizophrenia literature. Our correlation analyses suggest that there is an important, widespread relationship between cortical thickness and cognitive empathy performance in healthy individuals. However, this relationship was not found in individuals with schizophrenia. Thus, we conclude that cognitive empathy impairment in schizophrenia may not be related to alterations in cortical thickness in empathy-related brain regions. Abnormal neural synchrony, irregular connectivity between local and or distal brain regions, problems with integration, or other mechanisms may better account for performance on measures of cognitive empathy in schizophrenia. Future studies that combine functional imaging paradigms to probe cognitive empathy with the examination of structural connectivity using estimates of white matter integrity and fiber tractography are recommended to further elucidate this question.

Acknowledgments

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Table 1

Participant characteristics

	Healthy Controls (n = 46)	Individuals with Schizophrenia (n = 41)	Test statistic
	Mean (SD) or %		t or χ^2
Demographics			
Age	31.79 (8.56)	32.91 (6.59)	0.69
Gender (% male)	52.20	65.90	1.67
Non-Hispanic Caucasian (%)	45.70	39.00	1.44
African American (%)	39.10	51.20	
Other ethnicity (%)	15.20	9.80	
Parental socioeconomic status[a]	28.18 (9.78)	25.10 (9.40)	−1.47
Alcohol and tobacco use			
Mean (SD) alcohol use in grams, past year[b]	1248.93 (2147.34)	688.72 (1735.64)	−1.30
Mean (SD) cigarette consumption, past year[b]	281.47 (873.00)	1794.54 (2808.63)	3.23***
Clinical Measures			
Duration of illness in years	--	12.87 (7.58)	
Years 1st generation antipsychotic treatment	--	0.38 (1.51)	
Years 2nd generation antipsychotic treatment	--	4.61 (3.70)	
Dosage of current antipsychotic medication (converted to milligrams of chlorpromazine)	--	510.79 (431.10)	
Hallucinations	--	2.90 (2.00)	
Delusion	--	3.10 (1.88)	
Bizarre behavior	--	1.56 (1.87)	
Positive formal thought disorder	--	2.24 (1.56)	
Affective flattening	--	3.29 (1.50)	
Alogia	--	2.49 (1.70)	
Avolition	--	3.43 (1.45)	
Anhedonia	--	3.21 (1.39)	
Attention	--	2.22 (1.85)	

[a] completed by N=44 CON and N=40 SCZ

[b] completed by N=45 CON and N=39 SCZ

p<0.001***

Table 2

Between-group differences in cognitive empathy

	Healthy Controls ($n = 43$)	Individuals with Schizophrenia ($n = 39$)	Test statistic
Performance-based cognitive empathy			
EPT task accuracy	0.85 (0.08)	0.74 (0.10)	t = −5.34 ***
EPT response time (sec)	1.42 (0.27)	1.67 (0.39)	t = 3.28 **
Self-Reported cognitive empathy			
QCAE cognitive empathy total score[a]	61.11 (8.49)	55.29 (9.21)	t = 2.77 **
IRI perspective-taking	20.79 (4.74)	16.48 (4.76)	t = 4.10 ***

Note. EPT, emotional perspective-taking; QCAE, questionnaire for cognitive and affective empathy; IRI, interpersonal reactivity index;

[a] n=36 healthy controls and n=35 individuals with schizophrenia completed the QCAE.

** p<0.01;

*** p<0.001.

Table 3

Between-group differences in cortical thickness (mm) in neural regions associated with cognitive empathy

	Cortical thickness (mm)		*t*	*df*	*p*
	Healthy Controls (*n* = 46)	Individuals with Schizophrenia (*n* = 41)			
Frontal Regions					
mPFC, left, mean (SD)	2.44 (0.15)	2.43 (0.23)	−0.46	85	0.32
mPFC, right, mean (SD)	2.35 (0.14)	2.31 (0.22)	−1.04	85	0.15
IFG, left, mean (SD)	2.61 (0.12)	2.57 (0.15)	−1.48	85	0.07
IFG, right, mean (SD)	2.62 (0.14)	2.55 (0.14)	−2.35 [**]	85	0.01
aMCC, left, mean (SD)	2.71 (0.22)	2.71 (0.25)	−0.18	85	0.43
aMCC, right, mean (SD)	2.50 (0.23)	2.57 (0.24)	1.34	85	0.09
INS, left, mean (SD)	3.08 (0.16)	3.00 (0.15)	−2.10 [*]	85	0.02
INS, right, mean (SD)	3.07 (0.21)	3.00 (0.12)	−1.78 [*]	85	0.03
SMA, left, mean (SD)	2.63 (0.18)	2.58 (0.13)	−1.50	85	0.07
SMA, right, mean (SD)	2.62 (0.16)	2.55 (0.13)	−2.46 [**]	85	0.008
Temporo-Parietal Regions					
TPJ, left, mean (SD)	2.61 (0.17)	2.56 (0.12)	−1.48	85	0.07
TPJ, right, mean (SD)	2.66 (0.16)	2.60 (0.14)	−1.91 [*]	85	0.03
PREC, left, mean (SD)	2.45 (0.14)	2.41 (0.12)	−1.51	85	0.07
PREC, right, mean (SD)	2.44 (0.15)	2.42 (0.11)	−0.72	85	0.24

Note. mPFC, medial prefrontal cortex; IFG, inferior frontal gyrus; aMCC, anterio-mid cingulate cortex; INS, insula; SMA, supplementary motor area; TPJ, temporo-parietal junction; PREC, precuneus.

[*]
p<0.05;

[**]
p<0.01;

Table 4

Partial correlations between cortical thickness and cognitive empathy (covaried with age)

	Cognitive empathy task accuracy			
	Healthy Controls (*n* = 43)	**p-value**	**Individuals with Schizophrenia (*n* = 39)**	**p-value**
mPFC, left	.43	.002	.00	.493
mPFC, right	.41	.003	−.09	.299
IFG, left	.22	.085	.14	.194
IFG, right	.37	.008	.11	.254
aMCC, left	.31	.023	−.12	.235
aMCC, right	.25	.055	−.19	.133
INS, left	.41	.003	.20	.119
INS, right	.35	.012	−.05	.374
SMA, left	.04	.405	.13	.220
SMA, right	.01	.481	.14	.196
TPJ, left	.27	.043	.06	.353
TPJ, right	.14	.188	.12	.234
PREC, left	.12	.223	.04	.413
PREC, right	.25	.056	.16	.165

Note: mPFC, medial prefrontal cortex; IFG, inferior frontal gyrus; aMCC, anterio-mid cingulate cortex; INS, insula; SMA, supplementary motor area; TPJ, temporo-parietal junction; PREC, precuneus.