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Cultural differences and neural correlates of cognitive insight in schizophrenia

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ABSTRACT

Cognitive insight refers to a person's ability to examine their psychotic experiences and the inferences they draw from these experiences. Several studies suggest that cultural factors influence cognitive insight and the processes involved therein; a few studies have suggested differences between Western and Asian societies. However, there are no studies on cognitive insight and its neural correlates in non-Western populations. Hence, we examined factor structure of Beck's cognitive insight scale (BCIS) in a large sample of patients with schizophrenia (SCZ) and healthy volunteers (HV) from India and assessed the relationship between cortical thickness and cognitive insight. We recruited 240 participants (SCZ-140; HV-100). Of these, 58 participants (SCZ-33; HV-25) underwent magnetic resonance imaging. We found a three-factor structure for BCIS which is different from the original two factor structure; self-reflection (SR) of original two-factor structure was sub-divided into– SR1, introspection and SR2, openness to feedback. There was a significant difference between HV and SCZ in the new factors, SR1 and SR2 but not in the original SR factor. Difference was also seen on MRI analysis; while there was a significant positive correlation between original SR factor and thickness of right posterior cingulate cortex, SR2 was positively correlated with thickness of left ventrolateral prefrontal cortex. The difference in factor structure in Indian participants and their distinct neural correlates point to cultural differences in cognitive insight. While in western societies the constructs of introspection and openness to feedback might integrate, they might be separate entities in Asian population.

1. Introduction

Insight, a multifaceted construct, is impaired in individuals with psychosis and is considered a hallmark of schizophrenia (Amador et al., 1993; David et al., 1992). Though impairment in insight is characteristically seen with positive psychotic symptoms, insight does not necessarily improve with improvement in psychotic symptoms (McEvoy et al., 1989). Beck and colleagues conceptualized the construct of cognitive insight (Beck et al., 2004). Unlike clinical insight which focuses predominantly on awareness of the illness, cognitive insight assesses a person's ability to examine their psychotic experiences and the inferences they draw from these experiences. Beck's cognitive insight scale (BCIS) is frequently used to measure cognitive insight (Beck et al., 2004). The original study, as well as subsequent factor analyses from Western societies has delineated two major factors in BCIS – self-reflection (SR) and self-certainty (SC) (Beck et al., 2004; Riggs et al., 2012). SR refers to a person's ability and openness to observing their mental productions and considering alternative explanations for these and SC, reluctance to correct erroneous beliefs and overconfidence in the validity of said beliefs (Beck et al., 2004).

Interestingly, studies from Asian cultures have reported differences in the factor structure of BCIS compared to western societies. Two studies from East Asia that examined the factor structure of BCIS reported item loadings which were different from the original (Kao and Liu, 2010; Kim et al., 2007). A study from India examined cognitive insight using BCIS (Merlin et al., 2012) and reported a four - factor structure, different from the original two-factor structure (Merlin et al., 2012). This difference could be attributed to variations in cultural factors which influence processes contributing to cognitive insight such as introspection, evaluation of beliefs, and certainty about beliefs (Han and Northoff, 2009). For example, studies from non-Western societies have pointed out that individuals in these societies can simultaneously

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hold multiple contradictory disease models which may influence insight (Gater et al., 1991; Saravanan et al., 2007).

Emerging evidence suggests differences in the factor structure of BCIS between Asian and Western populations, however, it is not known whether this difference in factor structure is also associated with corresponding changes in brain structure or function. While the nature of relationship between brain structure and function is still being examined, a symbiotic relationship between brain structure and function is increasingly recognised by several studies (Batista-García-Ramó and Fernández-Verdecia, 2018; Honey et al., 2007; Meuli et al., 2009). A few studies have reported that cultural factors influence neural representations of self-related processing in healthy individuals (Han and Northoff, 2009; Zhu et al., 2007). Several studies in the past have reported significant associations between structural abnormalities in specific brain regions and symptom domains (Walton et al., 2018) including impaired insight in patients with schizophrenia (Bassitt et al., 2007; Buchy et al., 2011; Cooke et al., 2008; Emami et al., 2016; Ouzir et al., 2012; Sapara et al., 2007). On similar lines, several studies have examined the neural correlates of cognitive insight using structural imaging methods such as voxel based morphometry, cortical thickness measurements and structural covariance technique. (Buchy et al., 2010, 2016, 2018; Ćurčić-Blake et al., 2015; Gerretsen et al., 2014; Kuang et al., 2017; Orfei et al., 2013, 2017). These studies have reported significant associations between BCIS subscales and regional brain structure. One of the studies reported negative correlations between self-certainty and cortical thickness in the frontal, temporal, and parietal regions and posterior cingulate cortex (PCC) (Buchy et al., 2016, 2018). On the other hand, positive correlations between SR and thickness in the frontal, temporal, parietal, and occipital cortices have also been reported (Buchy et al., 2016).

However, to the best of our knowledge, the neural correlates of cognitive insight have not been examined in a non-Western population. In this study, we aimed to examine the factor structure of BCIS and its relationship to cortical thickness in individuals with schizophrenia from India. We hypothesized that (i) the BCIS factor structure would differ from the original structure in the Indian population (ii) the new factors will have different neural correlates in the Indian population.

2. Materials and methods

2.1. Subjects and clinical assessments

We recruited 240 participants, 140 patients with a diagnosis of DSM-IV schizophrenia or schizoaffective disorder (SCZ) and 100 healthy volunteers (HV). Of these, 58 male participants (33 SCZ and 25 HV) also underwent magnetic resonance imaging (MRI). We recruited patients from the inpatient and outpatient services at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore, India, between 2013 and 2017. Out of the 140 patients recruited, 98 were outpatients and 42 were inpatients. One hundred and thirty three patients had a diagnosis of schizophrenia and 7 had a diagnosis of schizoaffective disorder. Healthy volunteers were recruited from the same geographical area via flyers, word of mouth and announcements.

A board certified psychiatrist established the clinical diagnosis and it was confirmed using the Structured Clinical Interview (SCID-I) for DSM-IV (First et al., 2002). We excluded patients with lifetime substance dependence/abuse except nicotine, ongoing comorbid axis I disorder, and treatment with electro convulsive therapy in the previous six months; and HV with life time history of any axis I psychiatric disorder or family history of psychosis in a first degree relative. We also excluded participants with history of head injury, claustrophobia, or other contraindications for MRI such as presence of metal implants in the body. All participants provided written informed consent to participate in the study. The human ethics committee at the National Institute of Mental Health and Neurosciences, Bangalore approved the study. After obtaining necessary permissions, BCIS (Beck et al., 2004) was translated to Kannada, an Indian language. It was administered either in Kannada or English based on the language preference of the participant and proficiency in the language (162 individuals preferred English and 78, Kannada). We measured the severity of clinical symptoms using positive and negative syndrome scale (PANSS) (Kay et al., 1987). BCIS and clinical scales were administered on same day and within one week of conducting the scan. The mean delay between clinical assessments and MRI scan was 2.47 ± 5.67 days.

2.2. Image acquisition and analysis

We acquired magnetic resonance images using a 3 T MRI scanner. We acquired a 3-D MPRAGE sequence with the following scan parameters: TR/TE = 2200/2.45 msec; matrix size = 256 × 256; voxel size = 1 × 1 × 1 mm^3; number of slices = 176; flip angle = 8°.We used BrainVoyager QX version 20.4 (Brain Innovation Maastricht, Netherlands) (Goebel et al., 2006) for pre-processing and cortical thickness analysis of the images. After advanced segmentation, we separated the two hemispheres using a high-resolution cortical mapping approach (Frost and Goebel, 2012; Goebel et al., 2002, 2004). We then transformed the folded cortical representations to spherical representations for across subject alignment while preserving the curvature information of the folded mesh surfaces. We conducted cortical thickness analysis built on an automated Laplacian method (Jones et al., 2000) to quantify the cortical thickness of individual segmented hemispheres in the volume space [forming volume maps (VMPs)]. We projected each individual cortical thickness value onto the cortex mesh of the corresponding hemisphere. We then used this projected surface map (SMP) to perform group level investigations on predefined regions of interest (ROIs). We obtained the ROIs for the current study after reviewing previous studies on this topic and those regions which were found to be associated with cognitive insight in at least two studies were selected (Buchy et al., 2010, 2015, 2016, 2018; Caletti et al., 2017; Ćurčić-Blake et al., 2015; Gerretsen et al., 2014; Kuang et al., 2017; Orfei et al., 2013, 2017; Pu et al., 2013; Van Der Meer et al., 2013) (details in Supplementary Table S4). Based on this literature, we selected the following ROIs in both hemispheres; posterior cingulate cortex (PCC) [Brodmann area (BA) 31], precuneus (BA 7), superior frontal cortex (BA 9), orbitofrontal cortex (OFC) (BA 10,11, 47) ventrolateral prefrontal cortex (VLPFC) (BA 44), inferior frontal gyrus (IFG) (BA 47) inferior temporal cortex (BA20), and temporal pole (BA 38). We extracted the BA constituting each ROI using the AtlasBrains module within BrainVoyager and used it for further statistical analysis.

2.3. Factor analysis

After assessing the suitability of the data for factor analysis and sampling adequacy with Kaiser-Meyer-Olkin measure and Bartlett's test of sphericity, we performed factor analysis of BCIS items using principal component analysis with varimax rotation and Kaiser normalization. To determine the number of factors to be retained, we used parallel analysis (Horn, 1965) using SPSS syntax (O'Connor, 2000). Parallel analysis is a data driven method originally proposed by Horn (1965). This method determines the number of factors by comparing the eigenvalues extracted from the data, to eigenvalues derived from random data having the same number of variables and sample size. This method is reported to be better than the popular methods for determining the number of factors based on eigenvalues or the scree plot as the latter methods tend to over or underestimate the number of factors to be extracted (Crawford and Koopman, 1979; Gaskin and Happell, 2014; Hayton et al., 2004; Zwick and Velicer, 1986).

2.4. Statistical analysis

To compare the differences between SCZ and HV groups in BCIS, we used Analysis of Covariance (ANCOVA) with age and education as

covariates since we found these variables to be significantly different between groups. We also used the average global cortical thickness as a covariate in the cortical thickness analysis to account for individual variations. We examined the relationship between BCIS – subscales and clinical severity symptom scores and cortical thickness using Pearson product moment correlation. We ran separate analyses for the new factors extracted through factor analysis as well as the original BCIS factors; SR and SC subscales. While the correlation between BCIS and clinical severity was examined only in patients, the relationship between BCIS and cortical thickness was examined with SCZ and HV together. We ran regression analyses for those variables which were found to be significantly correlated in the BCIS- cortical thickness analyses, with patient status and age as additional predictors. We carried out all statistical tests using the IBM Statistical Package for the Social Sciences (SPSS) version 24.

3. Results

3.1. Participant characteristics

The socio-demographic and clinical characteristics of the full sample are shown in Table 1.

3.2. Factor analysis

KMO measure of 0.62 in Bartlett's test (chi-square = 438.07, $p < 0.0001$) indicated sampling adequacy of the data. While Cattel's scree plot (Fig. S1) indicated three or four factors to be extracted, parallel analysis suggested three. Hence, we decided to extract 3 components. Table 2 shows the varimax rotated factor solution. The first factor corresponded to SC subscale (items 2, 7, 9, 10, 11, & 13). The items on the original SR scale were distributed across 2 newly identified factors SR1 (items 1, 3, 4, & 5) and SR2 (items 6, 8, 12, 14, 15). Items on SR1 corresponded with constructs of self-reflection and introspection. The items on SR2 were related to the construct of openness to feedback (Merlin et al., 2012).

3.3. Comparison between HV and SCZ on BCIS

We found significant difference between SCZ and HV on BCIS-SC (HV – 9.18 + 2.93; SCZ – 10.77 + 3.69; F = 6.83; $p = 0.01$) and BCIS Composite scores (HV – 3.38 + 4.59; SCZ – 1.41 + 6.02; F = 6.16; p = 0.01) but not BCIS-SR (HV – 12.56 + 3.04; SCZ – 12.21 + 5.14; F = 1.06; $p = 0.30$). On examination of the difference between SCZ and HV using the new factors obtained on factor analysis (SR 1 and SR2); there was a significant difference between SCZ and HV in both SR subscales (SR1 - HV – 3.56 + 2.23; SCZ – 4.92 + 2.76; F = 3.86; $p = 0.05$; SR2 - HV – 9.00 + 2.22; SCZ – 7.28 + 3.53; F = 10.04; $p = 0.002$) (Fig. 1).

Table 1
Socio-demographic and clinical characteristics of SCZ and HV.

Characteristics	SCZ (n = 140)	HV (n = 100)	t/χ^2	P
	Mean (S.D)	Mean (S.D)		
Age (years)	32.60(6.60)	28.10 (5.43)	3.29	<0.001
Sex (M:F)	119:21	63:37	15.40	<0.001
Education (years)	13.49 (3.07)	17.31(2.79)	2.94	<0.001
Duration of illness (years)	7.85 (5.48)			
PANSS total	53.46(16.80)			
PANSS positive	11.97(5.55)			
PANSS negative	13.47(5.71)			
PANSS general psychopathology	24.67(6.98)			

SCZ – patients with schizophrenia; HV – healthy volunteers; t – independent *t*-test; PANSS: Positive and Negative Symptom Scale.

3.4. Correlation between BCIS sub-scales and PANSS scores

In the original BCIS sub-scales, there was a positive correlation between SC and PANSS positive subscale ($r = 0.035$; $p = 0.001$) and PANSS total score ($r = 0.221$; $p = 0.02$) and a negative correlation between SR and PANSS total score ($r = -0.251$; $p = 0.006$). The BCIS - composite score negatively correlated with PANSS positive sub-scale ($r = -0.360$; $p < 0.001$), PANSS general psychopathology ($r = -0.314$; p = 0.001) and PANSS total score ($r = -0.347$; p < 0.001). In the new factor structure, there was a negative correlation between SR2 (openness to feedback) and PANSS total score ($r = -0.256$; $p = 0.005$). Item P1 in PANSS which measures the severity of delusions was positively correlated with SC ($r = 0.318$; $p < 0.001$) and negatively correlated with BCIS - composite score ($r = 0.310$; p = 0.001).

3.5. Group difference between SCZ and HV in Cortical thickness

In the subgroup of participants who underwent MRI scan, there was a significant difference in age (SCZ - 31.24 ± 6.84; HV- 26.85 ± 4.71; $t = 2.752$; $p = 0.008$), education (SCZ - 15.27 ± 2.17; HV - 17.48 ± 2.87; $t = 3.336$; $p = 0.002$) and global cortical thickness (SCZ - 5.81 ± 0.36; HV - 6.01 ± 0.36; $t = 2.157$; $p = 0.035$) between SCZ and HV (Table S1). Hence these variables were used as covariates in further group level analysis. As we compared multiple ROIs (eighteen considering both hemispheres), we applied Bonferroni correction for multiple comparisons and considered $p < 0.002$ as significant. We considered *P* values <0.05 as trend towards significance. There was a significant difference between groups in the right IFG (HV - 3.44 ± 0.36; SCZ -3.13 ± 0.23; F = 13.34; $p < 0.001$) and a trend level difference in the right precuneus, right OFC, right VLPFC, left PCC, and left IFG ($p < 0.05$). In all these regions, SCZ had thinner cortices compared to HV (Fig. 2 and Supplement Table S2).

3.6. Relationship between BCIS sub-scales and cortical thickness

We conducted correlation analyses to examine associations between BCIS sub-scales and cortical thickness in selected ROIs. The significance level was set at 0.01 following the method described by Curtin and Schulz (1998) for multiple correlation analyses. When the original BCIS sub-scales were used, SR was found to be positively correlated with the right precuneus ($r = 0.0347$; p < 0.001). On the other hand, with the new factor structure, we found a significant positive correlation between SR2 (openness to feedback) and left VLPFC ($r = 0.336$; $p = 0.010$). BCIS- composite score positively correlated with the right precuneus ($r = 0.383$; p < 0.001), right VLPFC ($r = 0.393$; p = 0.002) and left inferior temporal cortex ($r = 0.348$; p = 0.008) (Table S3). In the subsequent regression analysis, which also included age and diagnostic status as predictors, the associations found in the correlation analyses remained significant (Fig. 3; Table S4).

4. Discussion

To the best of our knowledge, this is the first study to examine the relationship between cognitive insight and cortical thickness in the Indian population. The results of the study suggest that (a) the factor structure of BCIS in the Indian population is different from that in Western populations; while the Western studies have reported only two factors, we identified three factors (b) the original SR subscale scores did not differ between SCZ and HV, but the new subscales (SR1 and SR2) showed significant difference between the two groups (c) there was a significant difference in the cortical thickness of regions involved in cognitive insight between the groups; SCZ had lower cortical thickness compared to HV (d) there was a difference in the neural correlates of the original SR sub-scale and SR2 sub-scale, as measured using cortical thickness; while there was a significant positive correlation between original SR factor and thickness of right posterior cingulate cortex, SR2

Table 2
Varimax rotated factor loading for the fifteen BCIS items, Eigen values for each component and total variance explained.

BCIS item no[a]	Factor 1	Factor 2	Factor 3
(13) I can trust my own judgment at all times	**0.690**	−0.143	0.005
(2) My interpretations of my experiences are definitely right	**0.684**	0.051	0.008
(11) I cannot trust other people's opinion about my experiences	**0.578**	−0.051	0.130
(7) If something feels right, it means that it is right.	**0.549**	0.188	−0.242
(10) When people disagree with me, they are generally wrong	**0.542**	0.247	−0.174
(9) I know better than anyone else what my problems are	**0.366**	0.009	0.252
(5) Some of my experiences that have seemed very real may have been due to my imagination	0.067	**0.706**	0.108
(4) I have jumped to conclusions too fast	0.080	**0.672**	0.021
(3) Other people can understand the cause of my unusual experiences better than I can	0.087	**0.597**	−0.226
(1) At times, I have misunderstood other people's attitudes towards me	−0.036	**0.449**	0.184
(14) There is often more than one possible explanation for why people act the way they do	0.103	0.027	**0.656**
(8) Even though I feel strongly that I am right, I could be wrong	−0.119	0.024	**0.617**
(12) If somebody points out that my beliefs are wrong, I am willing to consider it	0.030	−0.080	**0.570**
(15) My unusual experiences may be due to my being extremely upset or stressed	0.048	0.193	**0.563**
(6) Some of the ideas I was certain were true turned out to be false	−0.206	0.471	**0.493**
Eigen value	2.23	2.17	1.56
Total variance explained	14.87	14.48	10.33

The bold signifies the highest factor loading for that item. This is as per the convention
[a] Numbers in parentheses refer to item number in original BCIS (Beck et al., 2004); Factor 1 – Self-Certainty (SC); Factor 2 – Self-Reflection sub-scale 1; Factor 3 – Self-Reflection sub-scale I2 (openness to feedback).

was positively correlated with thickness of left ventrolateral prefrontal cortex.

Most of the studies from Western populations have replicated the original two factor structure that Beck et al. proposed in their study (Beck et al., 2004; Riggs et al., 2012) However, factor analysis in our data demonstrated a three-factor model. All items from the original SC subscale loaded on a single factor in our analysis. This is in line with previous research where, compared to SR, items on SC have tended to consistently load on a single factor (Beck et al., 2004; Kim et al., 2007; Konsztowicz et al., 2018; Uchida et al., 2009). However, the items on the original SR subscale segregated into two factors which we termed SR subscales - SR1 and SR2. SR1 comprised of items related to introspection and self-reflection while SR2 included items reflecting the construct of openness to feedback. To ensure that the difference in factor structure was not due to translation of the scale to Kannada, we conducted a factor analysis including only those participants for whom BCIS was administered in English ($n = 164$). The factor structure remained the same except for one item (item 7) which could be attributable to the small sample size (details in Supplement, Table S5). A previous study done in India also had reported a 4-factor structure with openness to feedback as one of the factors (Merlin et al., 2012). Our findings replicate the difference in factor structure of BCIS and processes involved in cognitive insight in Asian and Western populations. In contrast to western cultures which emphasize the uniqueness of the individual, the concept of self in Indian and other Asian cultures depends not only on the individual but also their significant others (Han and Northoff, 2009; Markus and Kitayama, 1991). That is, while the individual traits are invariant across different social contexts in western cultures, the concept of self in Asian cultures is interdependent on others and the social context. While in western societies the constructs of introspection and openness to feedback might integrate, they might be separate entities in our study population. These findings point to the importance of incorporating therapeutic elements that address cultural differences while developing interventions to improve cognitive insight. Only a few studies have compared cognitive insight in SCZ patients with healthy controls. These studies reported differences in SC but not in SR between SCZ and HV (Engh et al., 2007; Warman et al., 2007). Our findings were similar when the original two factor structure was considered. However, when the three-factor structure was considered, there was a significant difference between SR1 and SR2 across the groups. While SCZ had higher scores on SR1, HV had higher scores on SR2. It is possible that the directional differences negate each other when these two factors are combined resulting in absence of significant difference between groups on total SR scores.

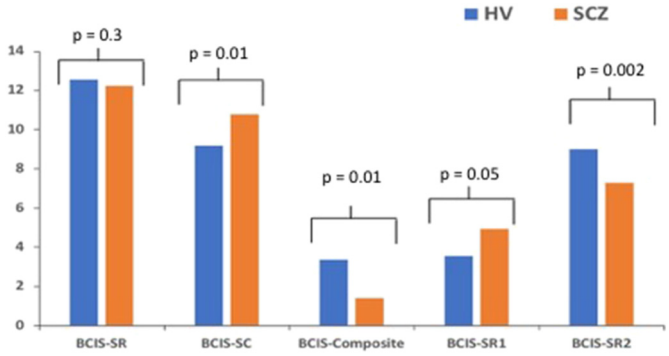

Fig. 1. Group differences in BCIS scores between SCZ and HV; 1A – differences between groups in original BCIS scores; 1B – differences between groups with new factors – SR1 (introspection) and SR2 (openness to feedback). BCIS – Beck's Cognitive insight scale; BCIS-SR – Self- reflection sub scale of BCIS; BCIS_SC – Self certainty sub scale of BCIS; BCIS_SR1 – Introspection sub-scale of BCIS; BCIS_SR2 – Openness to feedback subscale of BCIS.

Another important finding of the study is the relationship between BCIS sub-scales and cortical thickness. When the original factor structure was considered, there was a significant positive relationship between SR and cortical thickness in the right PCC. However, when new SR-sub scales were considered, there was a positive relationship between SR2 (openness to feedback) and cortical thickness in left VLPFC. PCC along with other cortical midline structures has been consistently associated with self-referential processes in healthy and SCZ (Buchy et al., 2016, 2018; Northoff et al., 2006). One of the important functions ascribed to VLPFC is selecting goal relevant cognitive representations among competing sources information (Thompson-Schill et al., 2005). Openness to feedback involves an individual's ability to modify currently held beliefs by considering alternative explanations and external feedback. This indicates that VLPFC may play a significant role in processes involved in SR2 but not in SR1. The regression analysis including age and diagnostic status as additional variable in the model the associations found in the correlation analyses remained significant. We also performed multiple regressions separately for SCZ and HV. However, the findings were different for sub-group analysis compared to the combined analysis (Supplement Table S10), possibly due to the small sample in sub-groups. While we have examined the association between the BCIS factors and brain structure, it is important to note that same brain regions may sub-serve several cognitive functions. Also, multiple factors may influence brain structure, in addition to the reorganization

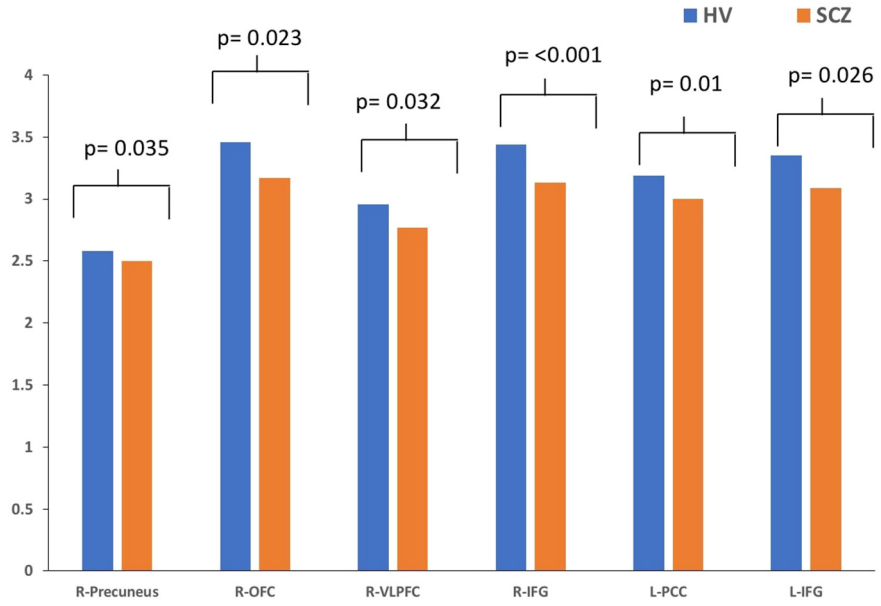

Fig. 2. Group differences between SCZ and HV in cortical thickness. OFC – Orbitofrontal cortex; VLPFC – ventrolateral prefrontal cortex; IFG – Inferior frontal gyrus; PCC – Posterior cingulate cortex.

due to functional dynamics. As similar cultural mechanisms may influence both cognitive functions and brain structure (Chee et al., 2011; Park and Huang, 2010), it is not possible to delineate the influence of cultural factors on individual cognitive functions and brain structure. Hence, the association between cognitive insight and cortical thickness seen in our study needs to be considered preliminary. Future multicentric studies using cross cultural design may be able to provide further insights.

We found associations between clinical severity scores and cognitive insight. As expected, patients with higher SC and lower SR had greater severity of the symptoms, particularly delusions. This is similar to earlier studies who also found association between cognitive insight and specific symptoms such as delusions (Engh et al., 2010; Warman et al., 2007). However, some earlier studies did not find any relationship between clinical symptom severity and cognitive insight (Riggs et al., 2012). The discrepancy between findings of previous studies and our study could be because of the differences in sample characteristics, as a considerable proportion of patients in the current study were in the acute stage of illness with higher positive symptom scores. Future studies need to include patients in both acute and maintenance phases of illness to examine the relation between symptom subtypes and cognitive insight.

The study results need to be interpreted in the background of following limitations. First, as the construct of cognitive insight is quantitatively but not qualitatively different between SCZ and HV, we included both

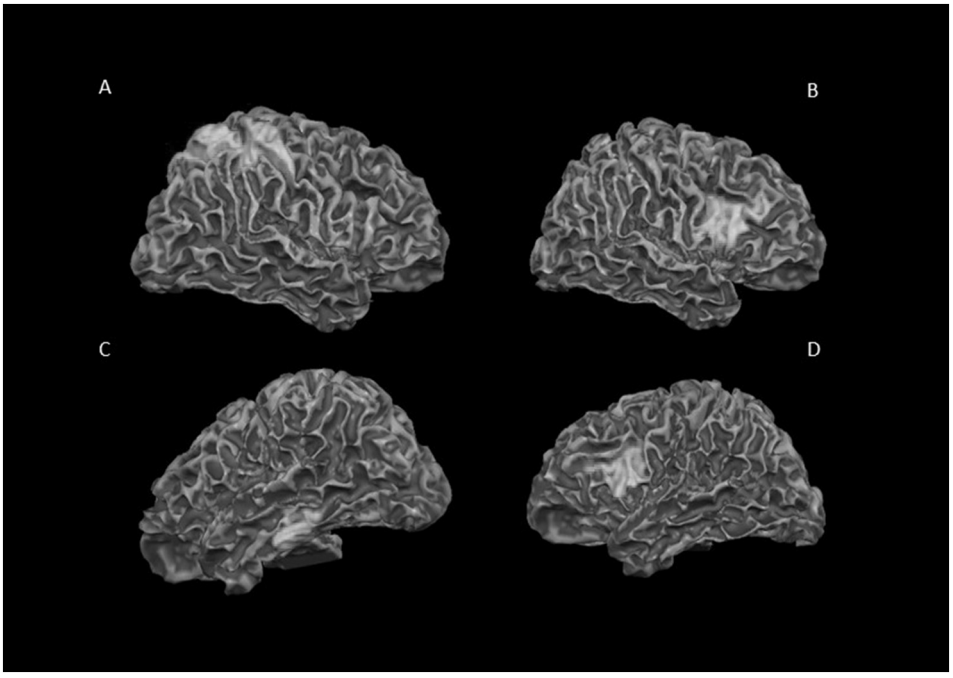

Fig. 3. ROIs with significant correlation between cortical thickness and BCIS subscales. A) Positive correlation between left precuneus with SR score. B) Positive correlation between right ventrolateral prefrontal cortex (VLPFC) with composite score. C) Positive correlation between left interior temporal cortex with composite score D) positive correlation between Left VLPFC with SR-2.

groups together in the factor analysis. Sub-group analysis conducted separately for SCZ and HV were underpowered to draw definitive conclusions (details in Supplement Tables S7 and S8). A larger sample size would enable separate factor analysis for HV and SCZ to examine differences between the groups if any in the future. Second, the sample size for cortical thickness analysis was modest, and the findings need to be considered preliminary until it is replicated in a bigger sample. Considering the small sample size, we conducted the cortical thickness analysis on an exclusively male sample to avoid confounding effects of sex on structural brain measures, but this limits the generalizability of results. Findings need to be replicated with larger samples including both male and female participants. Third, all patients were on treatment with antipsychotic medications which may have confounded the cortical thickness measures. Future studies involving drug-naïve SCZ subjects are needed to overcome this limitation. Fourth, the SCZ and HV groups were not matched on age, gender and years of education which may influence the findings. While it is ideal to match the groups on these demographic variables, several studies in the past have reported that patients with schizophrenia tend to have lower scholastic achievement compared to age matched healthy volunteers (Frissen et al., 2015; Welham et al., 2009). Matching the groups on age and years of education may decrease the generalizability of findings as it will not be representative of the distribution of these variables in the community. Hence, our sample is more representative of real-world scenario. Nonetheless, we statistically controlled for age and education in the analysis. There was no significant relationship between gender and cognitive insight in our study (details in supplement) similar to a previous study (Kao et al., 2013). Hence, we did not use gender as an additional covariate. Sixth, as several factors may influence the construct of cognitive insight as well as the neural correlates of cognitive insight, multi-centric studies examining the cross-cultural differences in cognitive insight and their neural correlates are needed in future. While we speculate that cultural differences could be the reason for differences in factor structure, one cannot rule out the influence of other differences in subject characteristics. Multi-centric studies with uniform study methodology across all centres are required to definitively address this issue, Seventh, while we have used BCIS in the current study, it is important to remember the limitations of BCIS for measurement of insight. Insight in schizophrenia is a multi-dimensional construct and both clinician administered and self-administered scales will be required to measure all dimensions of insight (Konsztowicz et al., 2018). In the current study, we used a self-administered measure of insight. Future studies need to include clinician administered scale as well as other measures in addition to BCIS to further understand the construct of insight in different cultural contexts. Finally, we could not use DSM 5 criteria for diagnosis as structured clinical interview for DSM5 was not available at the time of start of the study. Considering the similarities between DSM-IV and DSM5 criteria for diagnosis of schizophrenia, we believe that the findings will be replicable even in patients with DSM5 diagnosis of schizophrenia (American Psychiatric Association, 2013).

In summary, the three-factor structure of BCIS found in our study and the difference between SCZ and HV in self-reflection and openness to feedback, suggest that cultural factors may influence cognitive insight and the underlying cognitive processes. The distinct neural correlates of SR2 provide further support for this hypothesis. Since cognitive insight has a significant influence on adherence to treatment and functional outcome in schizophrenia it is important to develop specific strategies to treat impairments in cognitive insight in schizophrenia. Such treatment strategies to improve cognitive insight need to take cultural differences into consideration.

Conflict of interest

The authors report no conflict of interest.

Contribution

NPR was involved in the conceptualization design of the study, interpretation of results and manuscript preparation. SV, GV, MP, RDB were involved in the design of the study, interpretation of results and manuscript preparation. AAJ and AS were involved in data collection, data analysis, interpretation of results and writing the first draft of the manuscript. UT, BN, DMC, CH, PD, VK, AD, MK were involved in data collection and data analysis.

AAJ, AS and NPR wrote the first draft of the manuscript and all authors contributed to revisions. All authors have approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.schres.2019.05.010.

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