



Neurocognitive functioning as an intermediary variable between psychopathology and insight in schizophrenia



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ABSTRACT

Based on the neuropsychological deficit model of insight in schizophrenia, we constructed exploratory prediction models for insight, designating neurocognitive measures as the intermediary variables between psychopathology and insight into patients with schizophrenia. The models included the positive, negative, and autistic preoccupation symptoms as primary predictors, and activation symptoms as an intermediary variable for insight. Fifty-six Korean patients, in the acute stage of schizophrenia, completed the Positive and Negative Syndrome Scale, as well as a comprehensive neurocognitive battery of tests at the baseline, 8-weeks, and 1-year follow-ups. Among the neurocognitive measures, the Korean Wechsler Adult Intelligence Scale (K-WAIS) picture arrangement, Controlled Oral Word Association Test (COWAT) perseverative response, and the Continuous Performance Test (CPT) standard error of reaction time showed significant correlations with the symptoms and the insight. When these measures were fitted into the model as intermediaries between the symptoms and the insight, only the perseverative response was found to have a partial mediating effect – both cross-sectionally, and in the 8-week longitudinal change. Overall, the relationship between insight and neurocognitive functioning measures was found to be selective and weak.

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1. Introduction

Among the etiological models for the lack of insight into schizophrenia, the neuropsychological deficit model conceives the lack of awareness as the product of neurocognitive deficits. Some researchers have suggested that insight may be associated with some specific domains of cognition, rather than overall cognitive functioning (Shad et al., 2006); however, systematic meta-analysis studies on the relationship between the lack of insight and the overall performance in various cognitive domains have revealed significant (but weak) associations, ranging from $r=0.17$ to $r=0.20$ in patients with schizophrenia (Nair et al., 2014) and no difference in the mean effect size among the cognitive domains (Aleman et al., 2006).

On the other hand, executive functioning has earned much attention because links between self-monitoring and self-awareness have been found in many mental disorders (Stuss and Benson, 1988). Only about half of the studies that examined the

relationship between insight and executive functioning showed evidence of any association (Drake and Lewis, 2003). For example, only some studies have found significant associations between insight and the Wisconsin Card Sorting Test (WCST) indices, mostly with the perseverative response and the number of categories (Shad et al., 2006).

The delineation of associations between insight and neurocognitive functioning is further complicated by the confounding effects of psychopathology. In general, the relationship between insight and psychopathology seems to differ according to the stages of illness (acute, first-episode vs. chronic), and different symptom domains may show varying degrees of influence on specific neurocognitive functions (Mingrone et al., 2013; Heydebrand et al., 2004; Hughes et al., 2005; Heinrichs and Zakzanis, 1998; Strauss, 1993). It has been further suggested that these relationships may fluctuate during each episode of psychosis, and also undergo changes across the lifespan of the patient (Gerretsen et al., 2014). For example, a recent study found that the perseverative errors of a modified version of the WCST, and the psychopathological symptoms, correlated differently with insight at different stages of treatment, with the most drastic changes occurring during the acute stage (Chan et al., 2014).

In our previous studies, we discovered the mediating effects of

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the activation and anxiety/depression symptoms between the primary symptoms (i.e., positive, negative, and cognitive) and the insight, which changed according to the stages of illness (Hwang et al., 2009a,b). Likewise, certain neurocognitive functions may serve as intermediaries between the psychopathology and the insight, and the interactions between the symptoms and the neurocognitive functions are likely to undergo temporal changes.

In this study, we examined both the cross-sectional and longitudinal associations between insight, psychopathology, and a broad range of neurocognitive functioning, longitudinally, especially during the acute stage of illness. We also attempted to explore the possibility of constructing a broader causal model of insight by including neurocognitive predictors.

2. Methods

2.1. Subjects

Fifty-six Korean patients (male=62%) with a diagnosis of schizophrenia agreed to participate in this longitudinal study. All patients were recruited from the study conducted by Ahn et al. (2009), regarding the longitudinal changes in the neurocognitive functioning in patients, after starting or switching to amisulpride as a result of the onset or acute exacerbation of psychotic symptoms. The mean age, education level, and duration of illness in years at the baseline were 32.77 (SD=8.03, range=20.30–54.94), 12.43 (SD=2.49, range=6.00–18.00), and 6.73 (SD=6.13, range=0.20–25.60), respectively, with no significant difference between the genders in these variables. The mean medication dosages at the baseline, 8-month and 1-year assessments were 284.09 ± 144.58 , 477.27 ± 229.12 , and 529.55 ± 292.8 mg, respectively. All participants completed a written informed consent prior to any study procedure, which had been approved by the Board of Ethics Committee by the respective centers, as described in the original study (Ahn et al., 2009).

2.2. Measures

All patients were assessed by the clinicians using the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Among the items, the G12 “Lack of judgment and insight”, was used as the measure of insight. Factors from the five symptom domains derived from the previous study (Hwang et al., 2009a,b) were applied, namely positive, negative, autistic preoccupation, excitement/hostility, and anxiety/depression. These factors were similar in their composition to those obtained by White et al. (1997). In addition, the number of factors has been further supported by a recent study on the consensus five-factor model of the PANSS (Wallwork et al., 2012), where the proposed factor composition also mostly follows our model, with the exception of the disorganized factor, which includes fewer items compared to our model.

The patients also completed a comprehensive battery of tests designed to cover a wide range of neurocognitive domains, including general intelligence, working memory, executive function, verbal and non-verbal memory, attention, and psychomotor speed. All test procedures were carried out by a trained psychiatrist, or clinical psychologist, blind to the hypotheses of the study.

The test battery was administered three times, at the baseline, 8-week and 1-year follow-up. The baseline data were obtained within 2 weeks of starting or switching to amisulpride, to secure cooperation and reliable test performance from patients in the acute stage.

The list of neurocognitive tests included in the battery is as follows:

1. **General intelligence:** The shortened version of the Korean-Wechsler Adult Intelligence Scale (K-WAIS) includes digit span, vocabulary, arithmetic, picture arrangement, and block design subtests (Yum et al., 1992; Wechsler, 1981). Among the measures, vocabulary, arithmetic, picture arrangement, and block design subtests were used to derive the full-scaled IQ score (Doppelt, 1956).
2. **Executive function and working memory:** Executive function and working memory were measured by a controlled oral word association test (COWAT), or letter fluency test, which assesses the ability of a person to think of words that begin with a specific letter (Benton et al., 1994), in a 1 min period. Three trials were administered, with three different letters (the English phonemic equivalents to “g”, “s” and “y”); the number of correct responses and perseveration were obtained (Summerall et al., 1997).
3. **Verbal and non-verbal memory function:** Verbal and non-verbal memory functions were assessed by administering the Rey-Kim memory test (Kim, 1999), consisting of the Auditory Verbal Learning Test (AVLT; Rey, 1964) and Rey’s Complex Figure Test (RCFT; Rey, 1941). The measures obtained from the AVLT were the sum of the words recalled in trials 1–5, delayed free recall (20 min) and delayed recognition. From the RCFT, copy, immediate and delayed recall scores were observed. The composite index of the memory function (MQ) was derived from the combination of the AVLT and RCFT measures.
4. **Attention:** The measures of attention were obtained by administering Conners’ Continuous Performance Test for Windows (CPT; Conners, 2004). The measures assessed were omission errors, commission errors, mean reaction time, standard error of reaction, and d-prime.
5. **Psychomotor speed:** Trail Making Test A was used to assess visuo-motor speed and accuracy and B (TMT-A and TMT-B) was used to assess set-shifting speed and accuracy, which is also considered as a part of executive functioning. The time required to complete Trail A and Trail B, as well as a number of errors, were recorded.

2.3. Data analysis

First, the neurocognitive variables significantly associated with insight were identified through a correlation analysis. Then, those neurocognitive variables were examined for their associations with psychopathology. Lastly, by applying the causal model of insight constructed in previous studies (Hwang et al., 2009a,b), they were fitted into the model as intermediary variables, and the validity of the resulting exploratory models was examined with a number of goodness-of-fit indices. All 56 patients completed both the baseline and the 8-week assessments, but since only 44 patients (males 57%) completed the 1-year assessment, the model construction did not include the results of the 1-year follow-up.

The assessment of the relative fitness of the models was carried out with various indices of goodness-of-fit, such as the significant χ^2 statistic (i.e., a probability value of less than 0.05 results in the rejection of the model), the adjusted goodness of fit index (AGFI), the comparative fit index (CFI), the Tucker–Lewis Index (TLI), and the root mean square error of approximation (RMSEA). For the AGFI, GFI, and TLI, the values close to 1 or above 0.95 indicate a good fit, but for the RMSEA, values below 0.06 are required (Bentler, 1990; Hu and Bentler, 1999). The lower (LO) and upper (HI) boundaries of a two-sided 90% confidence interval for the population RMSEA were also included. Amos 5.0 (Amos Development Corporation, Spring House, Pennsylvania, USA) was used for the model construction and validation. All other statistical analyses were carried out using SPSS 13.0 (SPSS Inc., Chicago, Illinois, USA) by applying a significance level of $p < 0.05$.

3. Results

3.1. Correlations between insight and neurocognitive functioning and their longitudinal changes

Presented on Table 1 are the results of the correlation analyses between insight and the neurocognitive variables, and their changes during the stabilizing (baseline to 8 weeks) and chronic (8 weeks to 1 year) stages. Here, the correlations between the change scores indicate the relationships between the directions of the changes so that the positive correlations imply changes toward the same direction, and negative correlations the opposite. At the baseline, the K-WAIS picture arrangement, the COWAT perseverance, and Conners' CPT SE reaction time were significantly correlated with the lack of insight. At 8-weeks, cross-sectional associations with insight were found with the K-WAIS picture arrangement, the estimated IQ, the AVLT 1–5 trials sum, the RCFT copy, immediate recall, delayed recall, and memory quotient (MQ), Conners' CPT omission, reaction time, and SE reaction time. In terms of longitudinal changes, a change in insight was significantly correlated with only the change in the COWAT perseverative responses (baseline–8 weeks), Conners' CPT reaction time (8 weeks – 1 year), and the TMT trail B time (baseline – 1 year).

3.2. Correlations among insight, psychopathology, and neurocognitive functioning and their 8 week longitudinal changes (Δ)

To examine the feasibility of fitting the neurocognitive functions into the causal model of insight, the cross-sectional and

longitudinal correlations between insight, psychopathology, and neurocognitive variables (i.e., K-WAIS picture arrangement, COWAT perseveration, and CPT SE reaction time) were further obtained (Table 2). At the baseline, only the COWAT perseverative response showed significant correlations with activation, positive, and autistic preoccupation factors of the PANSS, which were mostly consistent with the relationship between insight and the PANSS factors. The K-WAIS picture arrangement showed significant correlations with only activation and positive factors while the CPT SE reaction time was correlated with only the activation and autistic preoccupation factors. At the 8-week follow-up, only the CPT SE reaction time significantly correlated with the positive and autistic preoccupation factors. In terms of the longitudinal changes, the COWAT perseverative response was significantly correlated with negative, activation, and positive symptoms. Changes in the K-WAIS picture arrangement and the CPT SE reaction time, on the other hand, were not significantly correlated with changes in any symptom domains.

3.3. Construction of the modified causal model of insight, with neurocognitive functioning variables

From the above correlation analysis, we constructed the modified versions of the causal model of insight that included the neurocognitive variables. Specifically, in order to examine the mediation effects of the neurocognitive variables between psychopathology and the lack of insight, the cognitive variables were added to our causal model of insight by designating the K-WAIS picture arrangement, the COWAT perseverative response, and the

Table 1
Cross-sectional and longitudinal (Δ) correlations between lack of insight (G12) and neurocognitive functioning measures.

Measures	Variables	Baseline (N=56)	8-week (N=56)	1-Year (N=44)	B – 8 week (Δ) (N=56)	8 week – 1 Year (Δ) (N=44)	B – 1 Year (Δ) (N=44)
K-WAIS	Digit Span	–0.08	0.04	0.22	0.16	0.23	–0.12
	Vocabulary	–0.02	–0.16	0.06	0.16	0.25	0.23
	Arithmetic	–0.19	–0.15	–0.09	0.16	–0.05	0.23
	Picture Arrangement	–0.33*	–0.28*	–0.18	–0.14	0.09	–0.24
	Block Design	–0.15	–0.23	–0.25	0.06	0.10	–0.23
	Estimated IQ	–0.12	–0.26*	–0.05	0.13	0.13	0.02
COWAT	Correct Response	–0.09	0.01	0.11	0.09	0.19	0.07
	Perseveration	0.45***	0.19	0.12	0.28*	–0.08	0.21
AVLT	1-Trials Sum	–0.14	–0.32*	0.03	–0.01	0.08	0.02
	Delayed Recall	–0.16	–0.16	0.05	0.12	–0.22	–0.02
	Recognition	–0.11	–0.18	–0.07	0.08	–0.02	0.13
RCFT	Copy	–0.15	–0.35*	–0.16	–0.04	0.25	0.08
	Immediate Recall	–0.14	–0.29*	–0.16	0.05	–0.08	0.05
	Delayed Recall	–0.18	–0.33*	–0.16	–0.04	–0.03	–0.11
	Memory Quotient(MQ)	–0.06	–0.27*	–0.03	0.02	0.04	0.03
CPT	Omission	0.24	0.39**	0.22	–0.11	0.16	–0.17
	Commission	0.16	0.24	0.22	0.22	–0.03	0.03
	Reaction Time	0.24	0.28*	0.24	–0.19	0.35	–0.02
	SE Reaction Time	0.27*	0.33*	0.04	0.05	0.05	0.25
	D-prime	–0.18	–0.24	–0.30	–0.11	–0.26	–0.14
TMT	Trail A Time	0.15	–0.08	–0.06	0.02	0.19	0.08
	Trail A Error	0.08	0.08	0.08	0.03	–0.25	0.02
	Trail B Time	0.03	0.05	0.12	–0.18	0.13	–0.34*
	Trail B Error	–0.11	0.07	0.15	–0.08	0.01	–0.29

K-WAIS=Korean Wechsler Adult Intelligence Scale, COWAT=Controlled Oral Word Association Test, AVLT=Auditory Verbal Learning Test, RCFT=Rey's Complex Figure Drawing Test, CPT=Conner's Continuous Performance Test, and TMT=Trail Making Test.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$, Δ =change in score

Table 2
Correlations among insight, psychopathology, and target neurocognitive variables and their 8 week longitudinal changes.

Lack of Insight (G12)					PANSS Factors														
		Lack of Insight (G12)			PANSS Factors					PANSS Factors					PANSS Factors				
		Baseline	8-Week	Δ	Baseline	8-Week	Δ	Baseline	8-Week	Δ	Baseline	8-Week	Δ	Baseline	8-Week	Δ	Baseline	8-Week	Δ
					NEG	ACT	POS	AUT PRE	ANX/DEP	NEG	ACT	POS	AUT PRE	ANX/DEP	NEG	ACT	POS	AUT PRE	ANX/DEP
Lack of Insight	Baseline				0.52***	0.58***	0.43**	0.36**	0.03	0.06	0.24	0.06	0.23	−0.09	−0.46***	−0.38**	−0.39**	−0.21	−0.09
	8-Week	0.48***			0.21	0.51***	0.11	0.17	−0.11	0.28*	0.34*	0.23	0.45**	−0.03	0.07	−0.24	0.02	0.18	0.06
	Δ	−0.62***	0.39**		−0.35**	−0.15	−0.36**	−0.22	−0.14	0.18	0.06	0.14	0.16	0.07	0.55***	0.18	0.43**	0.38**	0.15
K-WAIS Picture Arrangement	Baseline	−0.33***	−0.17	0.20	−0.23	−0.39**	−0.28*	−0.12	−0.10	−0.16	−0.04	−0.11	−0.17	0.04	0.08	0.34*	0.21	0.00	0.10
	8-Week	−0.35***	−0.28*	0.12	−0.17	−0.36**	−0.30*	−0.19	−0.11	−0.17	−0.09	−0.11	−0.21	0.07	0.01	−0.28	0.24	0.04	0.12
	Δ	0.03	−0.12	−0.14	−0.02	0.03	0.00	0.12	0.00	−0.10	−0.04	−0.01	−0.03	−0.04	−0.08	−0.06	0.00	0.10	0.03
COWAT Perseveration	Baseline	0.45***	0.31**	−0.20	0.14	0.41**	0.31*	0.28*	−0.04	−0.11	0.03	−0.04	0.14	−0.24	−0.25	−0.37**	−0.33*	−0.20	−0.14
	8-Week	0.16	0.19	−0.00	0.10	0.07	0.17	0.22	−0.03	0.10	0.03	0.03	0.13	0.15	0.00	−0.04	−0.15	−0.14	0.13
	Δ	−0.31*	−0.05	0.28*	−0.12	−0.22	−0.19	−0.06	0.08	0.15	0.19	0.22	0.16	0.33*	0.28*	0.34*	0.31*	0.20	0.18
CPT SE Reaction Time	Baseline	0.27*	0.27	−0.07	0.15	0.39**	0.24	0.32*	0.04	0.21	0.12	0.31*	0.29*	0.12	0.07	−0.28*	−0.06	−0.12	0.06
	8-Week	0.31*	0.33*	−0.02	0.12	0.49***	0.29*	0.29*	−0.06	0.16	0.15	0.31*	0.31*	0.08	0.04	−0.35**	−0.11	−0.06	0.10
	Δ	−0.10	−0.08	0.05	−0.18	−0.08	0.02	−0.08	0.02	−0.08	0.01	0.18	−0.14	0.10	0.10	0.08	0.09	−0.02	0.06

PANSS=Positive and Negative Syndromes Scale, NEG=Negative, ACT=Activation, POS=Positive, AUT PRE=Autistic Preoccupation, ANX/DEP=Anxiety/Depression, K-WAIS=Korean Wechsler Adult Intelligence Scale, COW-AT=Controlled Oral Word Association Test, CPT=Conner's Continuous Performance Test, and SE Reaction Time= Standard Error of Reaction Time.

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$, Δ=Change in Score

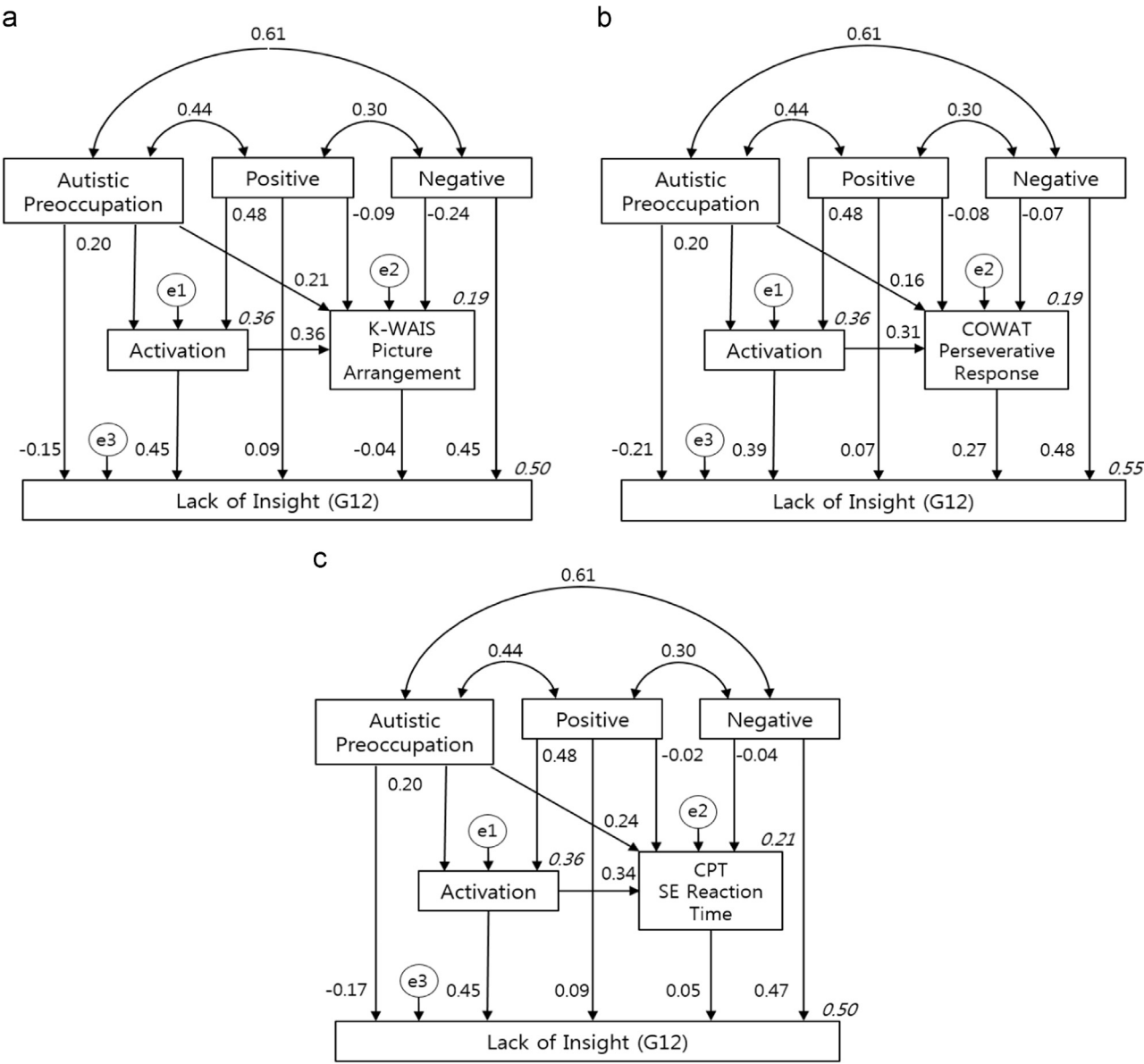


Fig. 1. Modified causal model of insight with (a) K-WAIS picture arrangement, (b) COWAT perseverative response, and (c) CPT SE reaction time at the baseline. The values associated with the bi-directional arrows are correlation coefficients. The values associated with the unidirectional arrows are standardized regression coefficients. The values in italics at the box corners are R^2 values. "e" denotes error variances; K-WAIS=Korean Wechsler Adult Intelligence Scale, COWAT=Controlled Oral Word Association Test, and CPT=Conner's Continuous Performance Test.

Table 3
Goodness-of-fit indices of the causal models constructed with PANSS G12.

Measures	χ^2	df	P	AGFI	CFL	TLI	RMSEA	LO	HI
COWAT Perseveration	0.02	1	0.892	0.998	1.000	1.144	0.000	0.000	0.166
K_WAIS Picture Arrangement	-0.02	1	0.893	0.998	1.000	1.153	0.000	0.000	0.166
CPT SE Reaction Time	-0.02	1	0.893	0.887	1.000	1.232	0.000	0.000	0.166

COWAT=Controlled Oral Word Association Test, K-WAIS=Korean Wechsler Adult Intelligence Scale, CPT=Conner's Continuous Performance Test, and SE Reaction Time=Standard Error of Reaction Time.

CPT SE reaction time as the intermediary variables between insight and negative, positive, autistic preoccupation, and activation factors, respectively.
The constructed modified causal models of insight are

presented in Fig. 1. The model that included the COWAT perseverative response explained the greatest variance of insight ($R^2=0.55$), and it had a markedly higher predictive power on insight, with the standardized regression coefficient β of 0.27,

than did the K-WAIS picture arrangement ($\beta = -0.04$) and the CPT SE reaction time ($\beta = 0.05$). In essence, the inclusion of the COWAT perseverative response into the model caused the β coefficients of the autistic preoccupation, positive, and activation symptoms to decrease from -0.21 to -0.17 , 0.10 to 0.07 , and 0.48 to 0.39 , respectively. The total variance (R^2) of insight, explained without the inclusion of COWAT perseverative response, was 0.47 . These results clearly demonstrated the partial mediating role of the COWAT perseverative response between these symptoms and insight. On the other hand, the β coefficient of the negative symptoms did not show much difference (i.e., increase from 0.47 to 0.48). Hence, although all three modified models of insight indicated a satisfactory level of model fit (see Table 3), in essence, only the COWAT perseverative response contributed significantly to predicting insight, when considered along with psychopathology.

3.4. Modified longitudinal causal model of insight with COWAT perseverative response

The changes (Δ) in scores between the baseline and the 8 week follow-up were used to construct the longitudinal causal model of insight. Here, only the COWAT perseverative response was applied, as it was the only variable in which the changes in the scores correlated with the changes in the symptom severity, as measured by the PANSS factors. As Fig. 2 shows, the variance of the perseverative response, explained by the symptoms, was only modest ($R^2 = 0.09$), and the standardized regression coefficient from the perseverative response to the lack of insight was small ($\beta = 0.05$). The mediating effect of the perseverative response between psychopathology and insight, in terms of their longitudinal changes, appeared to be minimal, since the total variance (R^2) of insight explained with the inclusion of COWAT perseverative response increased by merely 0.02 . Otherwise, the goodness-of-fit indices showed the inadequacy of the model ($\chi^2 = 6.805$, $df = 1$, $P = 0.009$; AGFI = 0.216 ; CFI = 0.927 ; TLI = -0.099 ; RMSEA = 0.325 ,

LO = 0.130 , HI = 0.574).

4. Discussion

This study examined both cross-sectional and longitudinal data pertaining to insight, psychopathology, and various domains of neurocognitive functioning. We used a homogeneous sample of patients with schizophrenia, who started on – or switched to – amisulpride, which eliminated confounding effects resulting from a variation in medication (such as side effects). The overall analysis of the results suggest a lack of associations between insight and neurocognitive functioning variables in general, except for a few key variables.

In our study, the COWAT perseverative response played significant roles in predicting insight, both cross-sectionally and longitudinally. While most studies regarding insight, that have included the measure of the perseverative response in their design applied the WCST, rather than the COWAT, it is questionable whether perseverative errors in the COWAT and the WCST can be considered to be equal measures. Perseverative errors in the WCST have been positively correlated with the severity of poor insight in 12/15 studies, in one review (Drake and Lewis, 2003), but the link between the COWAT perseveration response and insight has not been examined as of yet. A recent study by Chan et al. (2014) found the baseline WCST perseverative errors to predict improvement in insight, but our study showed the baseline COWAT perseveration to be significantly correlated with lack of insight at the 8-week follow-up, but not with the change. The perseverations in these two measures, therefore, are likely to reflect different cognitive processes, since the WCST involves processing the negative feedback and updating new rules (Prentice et al., 2008) while the COWAT relies on the patients' working memory, involving selective retention of the instruction and the list of self-generated words. A recent study has reported a positive association between working memory and an awareness of mental illness, in schizophrenia patients with cognitive deficits (Pegoraro et al., 2013). A future study, comparing differences in perseverative errors in various neurocognitive function tests, may be helpful to understand discrete components of cognitive deficits in schizophrenia.

The K-WAIS picture arrangement and Conners' CPT SE reaction time are significantly correlated with insight at the baseline. Though the models that included these variables did not show significant increase in the variance of insight explained when fitted into the model, they effectively exemplified the divergent interaction effects of psychopathology and neurocognitive functioning on insight. The picture arrangement task has been previously identified as constituting a social cognition construct (Allen and Barchard, 2009), so the increase in negative, autistic preoccupation, and activation symptoms would contribute to poor performance on this task. In terms of the positive relationship between the activation factor and the variability in the reaction time, our results were mostly consistent with a previous study (Vinogradov et al., 1998), concerning medication-free schizophrenia patients, that found the variability of reaction time on the lexical choice reaction task to show a unique covariation with positive, disorganized and tension/hostility symptoms, after controlling for the mean reaction time. These results demonstrated the need for future studies to take into account the intermediary role of the activation symptoms, when examining the relationships between psychopathology and neurocognitive functioning.

Aside from the above findings, this study showed an overall lack of association between insight and neurocognitive variables, especially at the acute stage of illness. The appearance of significant correlations between insight and measures of IQ, memory,

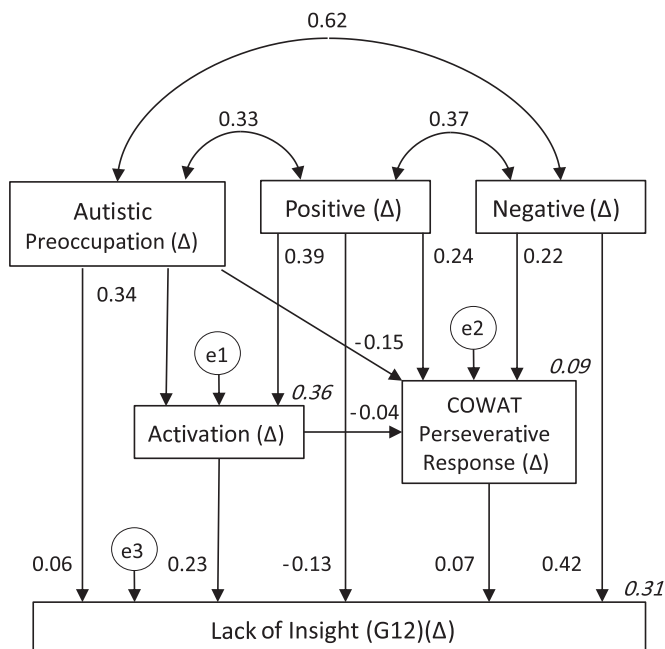


Fig. 2. Modified causal model of insight with COWAT perseverative response applying 8-week longitudinal changes (Δ) in score. The values associated with the bi-directional arrows are correlation coefficients. The values associated with the unidirectional arrows are standardized regression coefficients. The values in italics at the box corners are R^2 values. "e" denotes error variances; COWAT = Controlled Oral Word Association Test.

and attention at the 8 week follow-up, which were not evident at the baseline, strongly suggests that the relationship between insight and these cognitive variables may be somewhat orthogonal, varying according to the stages of illness. Insight may be determined mostly by the severity of psychopathology, at the acute stage, but may be influenced more by cognitive ability, such as procedural learning and working memory, as symptoms become more stabilized. For example, verbal memory has been found to be strongly sensitive to practice effects (Benedict and Zgaljardic, 1998), and patients with schizophrenia, with prior exposure over repeated trials, have shown practice effects at weeks 10 and 14, with the California Verbal Learning Test (Hawkins and Wexler, 1999). However, the relationship between insight and individual differences in this cognitive ability has been left largely unexamined as of yet.

Additionally, we found a lack of significant associations between insight and neurocognitive variables in their longitudinal changes (Δ) and poor goodness-of-fit of the longitudinal model that included the COWAT perseverative response. These results were not unrelated to those of a recent meta-analysis study on insight (Nair et al., 2014), which found significant- but small- associations of clinical insight with IQ, memory, and executive functions, especially set-shifting ability, as measured by the WCST or the Trail Making Test B (Diez-Martin et al., 2014; Gerretsen et al., 2014). Taken together, it is difficult to claim any specific neurocognitive deficit as the primary etiological factor of poor insight. On the other hand, although beyond the scope of this study, very recent studies have sought to identify the links between neurocognitive deficits and insight, in a broader context of social cognition (Konstantakopoulos et al., 2014; Lam et al., 2014; Lysaker et al., 2013; Vaskinn et al., 2013) and meta-cognition (Briki et al., 2014; Konstantakopoulos et al., 2014; David et al., 2012; Nicolò et al., 2012; Lysaker et al., 2011). Studies of this nature may help to further complement our understanding of the complex interplay between psychopathology, neurocognition and insight in schizophrenia.

Lastly, some limitations of our study warrant consideration when interpreting our results. We have used a single item of insight (G12 of the PANSS), rather than multi-dimensional measure like the Scale to Assess Unawareness of Disease (SUMD: Amador et al., 1993) which may limit the generalizability of our results. It is noteworthy however that a recent study by the authors of the SUMD (Michel et al., 2013) has obtained significant correlations ranging from 0.501 to 0.682 between the factors of the abbreviated version of the SUMD and G12. In particular, “aware of disease” factor ($r=0.676$, $p<0.01$) and “aware of positive symptoms” factor ($r=0.682$, $p<0.01$) were highly correlated with G12. While some overlap of results can be expected using the SUMD, future studies should further examine the specific dimensions of insight to confirm the results of the present study. Also, the number of subjects in our study was relatively small for entering all neurocognitive variables simultaneously in a prediction model, since using sample size of at least 10 cases per parameter is recommended (Kline, 2011). Future longitudinal studies should benefit by including a bigger sample and neurocognitive variables of a specific domain, e.g. executive functioning, to examine their relative effects.

Conflicts of interest

All of the authors of this manuscript hereby declare that there is no conflict of interest.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found in the online version at <http://dx.doi.org/10.1016/j.psychres.2015.11.004>.

References

- Ahn, Y.M., Lee, K.Y., Kim, C.E., Kim, J.J., Kang, D.Y., Jun, T.Y., Choi, J.S., Chung, I.W., Kim, S.H., Hwang, S.S., Kim, Y.S., 2009. Changes in neurocognitive function in patients with schizophrenia after starting or switching to amisulpride in comparison with the normal controls. *J. Clin. Psychopharmacol.* 29, 117–123.
- Aleman, A., Agrawal, N., Morgan, K.D., David, A.S., 2006. Insight in psychosis and neuropsychological function: meta-analysis. *Br. J. Psychiatry* 189, 204–212.
- Allen, D.N., Barchard, K.A., 2009. Identification of a social cognition construct for the WAIS-III. *Appl. Neuropsychol.* 16 (4), 262–274.
- Amador, X.F., Strauss, D.H., Yale, S.A., Flaum, M.M., Endicott, J., Gorman, J.M., 1993. Assessment of insight in psychosis. *Am. J. Psychiatry* 150 (6), 873–879.
- Benedict, R.H., Zgaljardic, D.J., 1998. Practice effects during repeated administrations of memory tests with and without alternate forms. *J. Clin. Exp. Neuropsychol.* 20, 339–352.
- Bentler, P.M., 1990. Comparative fit indices in structural models. *Psychol. Bull.* 107, 238–246.
- Benton, A.L., Hamsher, K., Sivan, A.B., 1994. *Multilingual Aphasia Examination* (3rd ed.). AJA Associates, Iowa City, IA, US.
- Briki, M., Monnin, J., Haffen, E., Sechter, D., Favrod, J., Netillard, C., Cheraitia, E., Marin, K., Govyadovskaya, S., Tio, G., Bonin, B., Chauvet-Gelinier, J.C., Leclerc, S., Hodé, Y., Vidailhet, P., Berna, F., Bertschy, A.Z., Vandel, P., 2014. Metacognitive training for schizophrenia: a multicentre randomised controlled trial. *Schizophr. Res.* 157 (1–3), 99–106.
- Chan, S.K., Chan, K.K., Hui, C.L., Wong, G.H., Chang, W.C., Lee, E.H., Tang, J.Y., Chen, E.Y., 2014. Correlates of insight with symptomatology and executive function in patients with first-episode schizophrenia-spectrum disorder: a longitudinal perspective. *Psychiatry Res.* 216 (2), 177–184.
- Conners, C.K., MHS Staff., 2004. *Conners' Continuous Performance Test for Windows (CPTII)*. Multi-Health Systems Inc., Toronto, Canada.
- David, A.S., Bedford, N., Wiffen, B., Gilleen, J., 2012. Failures of metacognition and lack of insight in neuropsychiatric disorders. *Philos. Trans. R. Soc. B: Biol. Sci.* 367 (1594), 1379–1390.
- Diez-Martin, J., Moreno-Ortega, M., Bagney, A., Rodriguez-Jimenez, R., Padilla-Torres, D., Sanchez-Morla, E.M., Santos, J.L., Palomo, T., Jimenez-Arriero, M.A., 2014. Differential relationships between set-shifting abilities and dimensions of insight in schizophrenia. *Psychopathology* 47 (2), 86–92.
- Doppelt, J.E., 1956. Estimated the full scale score on the Wechsler Adult Intelligence Scale from scores on four subtests. *J. Consult. Psychol.* 20, 63–66.
- Drake, R., Lewis, S.W., 2003. Insight and neurocognition in schizophrenia. *Schizophr. Res.* 62, 165–173.
- Gerretsen, P., Plitman, E., Rajji, T.K., Graff-Guerrero, A., 2014. The effects of aging on insight into illness in schizophrenia: a review. *Int. J. Geriatr. Psychiatry* 29 (11), 1145–1161.
- Hawkins, K.A., Wexler, B.E., 1999. California verbal learning test practice effects in a schizophrenia sample. *Schizophr. Res.* 39, 73–78.
- Heinrichs, R.W., Zakzanis, K.K., 1998. Neurocognitive deficit in schizophrenia: a quantitative review of the evidence. *Neuropsychology* 12, 426–445.
- Heydebrand, G., Weiser, M., Rabinowitz, J., Hoff, A.L., DeLisi, L.E., Csernansky, J.G., 2004. Correlates of cognitive deficits in first episode schizophrenia. *Schizophr. Res.* 68, 1–9.
- Hu, L., Bentler, P.M., 1999. Cutoff criteria for fit indexes in covariance structure analysis: conventional criteria versus new alternatives. *Struct. Equ. Model.* 6, 1–55.
- Hughes, C., Kumari, V., Das, M., Zachariah, E., Ettinger, U., Sumich, A., Sharma, T., 2005. Cognitive functioning in siblings discordant for schizophrenia. *Acta Psychiatr. Scand.* 111, 185–192.
- Hwang, S.S., Chang, J.S., Lee, K.Y., Ahn, Y.M., Kim, Y.S., 2009a. The causal model of insight in schizophrenia based on the Positive and Negative Syndrome Scale factors and the structural equation modeling. *J. Nerv. Ment. Dis.* 197, 79–84.
- Hwang, S.S., Chang, J.S., Lee, K.Y., Kim, S.H., Ahn, Y.M., Kim, Y.S., 2009b. Causal model of insight and psychopathology based on the PANSS factors: 1-year cross-sectional and longitudinal revalidation. *Int. Clin. Psychopharmacol.* 24, 189–198.
- Kay, S., Fisbein, A., Opler, L., 1987. The Positive and Negative Syndrome Scale for Schizophrenia. *Schizophr. Bull.* 13, 261–276.

- Kim, H.K., 1999. Rey-Kim Memory Test. Doschoolpan Shinkyungshimli, Seoul, Korea.
- Kline, R.B., 2011. Principles and Practice of Structural Equation Modeling, 3rd ed. The Guildford Press, New York, USA.
- Konstantakopoulos, G., Ploumpidis, D., Oulis, P., Patrikelis, P., Nikitopoulou, S., Papadimitriou, G.N., David, A.S., 2014. The relationship between insight and theory of mind in schizophrenia. *Schizophr. Res.* 152 (1), 217–222.
- Lam, B.Y., Raine, A., Lee, T.M., 2014. The relationship between neurocognition and symptomatology in people with schizophrenia: social cognition as the mediator. *BMC Psychiatry* 13 (14), 138.
- Lysaker, P.H., Erickson, M., Ringer, J., Buck, K.D., Semerari, A., Carcione, A., Dimaggio, G., 2011. Metacognition in schizophrenia: the relationship of mastery to coping, insight, self-esteem, social anxiety, and various facets of neurocognition. *Br. J. Clin. Psychol.* 50 (4), 412–424.
- Lysaker, P.H., Vohs, J., Hasson-Ohayon, I., Kukla, M., Wierwille, J., Dimaggio, G., 2013. Depression and insight in schizophrenia: comparisons of levels of deficits in social cognition and metacognition and internalized stigma across three profiles. *Schizophr. Res.* 148 (1–3), 18–23.
- Michel, P., Baumstarck, K., Auquier, P., Amador, X., Dumas, R., Fernandez, J., Lancon, C., Boyer, L., 2013. Psychometric properties of the abbreviated version of the scale to assess unawareness in mental disorder in schizophrenia. *BMC Psychiatry* 22 (13), 229.
- Mingrone, C., Rocca, P., Castagna, F., Montemagni, C., Sigauco, M., Scalese, M., Rocca, G., Bogetto, F., 2013. Insight in stable schizophrenia: relations with psychopathology and cognition. *Compr. Psychiatry* 54 (5), 484–492.
- Nair, A., Palmer, E.C., Aleman, A., Davis, A.S., 2014. Relationship between cognition, clinical and cognitive insight in psychotic disorders: a review and meta-analysis. *Schizophr. Res.* 152 (1), 191–200.
- Nicolò, G., Dimaggio, G., Popolo, R., Carcione, A., Procacci, M., Hamm, J., Buck, K.D., Pompili, E., Buccione, I., Lagrotteria, B., Lysaker, P.H., 2012. Associations of metacognition with symptoms, insight, and neurocognition in clinically stable outpatients with schizophrenia. *J. Nerv. Ment. Dis.* 200 (7), 644–647.
- Pegoraro, L.F., Dantas, C.R., Banzato, C.E., Fuentes, D., 2013. Correlation between insight dimensions and cognitive functions in patients with deficit and non-deficit schizophrenia. *Schizophr. Res.* 147 (1), 91–94.
- Prentice, K.J., Gold, J.M., Buchanan, R.W., 2008. The Wisconsin Card Sorting impairment in schizophrenia is evident in the first four trials. *Schizophr. Res.* 106, 81–87.
- Rey, A., 1964. L'examen Clinique en Psychologie. Press Universitaire de France, Paris.
- Rey, A., 1941. L'examen Psychologique Dans les cas D'encéphalopathie Traumatique. *Arch. Psychol.* 28, 286–340.
- Shad, M.U., Tamminga, C.A., Cullum, M., Haas, G.L., Keshavan, M.S., 2006. Insight and frontal cortical function in schizophrenia: a review. *Schizophr. Res.* 86, 54–70.
- Strauss, M.E., 1993. Relations of symptoms to cognitive deficits in schizophrenia. *Schizophr. Bull.* 19, 215–231.
- Stuss, D.T., Benson, D.F., 1988. The Frontal Lobes. McGraw Hill, New York, US.
- Summerall, S.W., Timmons, P.L., James, A.L., Ewing, M.J., Oehlert, M.E., 1997. Expanded norms for the Controlled Oral Word Association. Test. *J. Clin. Psychol.* 53, 17–21.
- Vaskinn, A., Sundet, K., Ueland, T., Agartz, I., Melle, I., Andreassen, O.A., 2013. Social cognition and clinical insight in schizophrenia and bipolar disorder. *J. Nerv. Ment. Dis.* 201 (6), 445–451.
- Vinogradov, S., Poole, J.H., Willis-Shore, J., Ober, B.A., Shenaut, G.K., 1998. Slower and more variable reaction times in schizophrenia: what do they signify. *Schizophr. Res.* 32, 183–190.
- Wallwork, R.S., Fortgang, R., Hashimoto, R., Weinberger, D.R., Dickinson, D., 2012. Searching for a consensus five-factor model of the Positive and Negative Syndrome Scale for schizophrenia. *Schizophr. Res.* 137, 246–250.
- Wechsler, E., 1981. WAIS-R Manual. The Psychological Corporation, New York, US.
- White, L., Harvey, P.D., Opler, L., The PANSS Study Group, Lindenmayer, J.P., 1997. Empirical assessment of the factorial structure of clinical symptom in schizophrenia. A multisite, multimodel evaluation of the factorial structure of the positive and negative syndrome scale. *Psychopathology* 30, 263–274.
- Yum, T.H., Park, Y.S., Oh, K.J., Kim, J.G., Lee, H.Y., 1992. The Manual of Korean-Wechsler Adult Intelligence Scale. Korean Guidance Press, Seoul, Korea.