Psychiatry Research 230 (2015) 792–799

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

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

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ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form
30 July 2015
Accepted 2 November 2015
Available online 9 November 2015

Keywords:
Insight
Schizophrenia
Psychopathology
Neurocognitive functioning
Executive functioning

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.

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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http://dx.doi.org/10.1016/j.psychres.2015.11.004
0165-1781/

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 X^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 $p < 0.05$.