Unraveling interrelationships among psychopathology symptoms, cognitive domains and insight dimensions in chronic schizophrenia

Rose Mary Xavier [a,*], Wei Pan [a], Jennifer R. Dungan [a], Richard S.E. Keefe [b,1], Allison Vorderstrasse [a,c,1]

[a] Duke University School of Nursing, 307 Trent Dr, Durham, NC 27710, United States
[b] Psychiatry and Behavioral Sciences, Duke University School of Medicine, United States
[c] Duke Center for Applied Genomics & Precision Medicine, United States

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ABSTRACT

Introduction: Insight in schizophrenia is long known to have a complex relationship with psychopathology symptoms and cognition. However, very few studies have examined models that explain these interrelationships.

Methods: In a large sample derived from the NIMH Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial (N = 1391), we interrogated these interrelationships for potential causal pathways using structural equation modeling. Using the NIMH consensus model, latent variables were constructed for psychopathology symptom dimensions, including positive, negative, disorganized, excited and depressed from the Positive and Negative Syndrome Scale (PANSS) items. Neurocognitive variables were created from five predefined domains of working memory, verbal memory, reasoning, vigilance and processing speed. Illness insight and treatment insight were tested using latent variables constructed from the Illness and Treatment Attitude Questionnaire (ITAQ).

Results: Disorganized symptoms had the strongest effect on insight. Illness insight mediated the relationship of positive, depressed, and disorganized symptoms with treatment insight. Neurocognition mediated the relationship between disorganized and treatment insight and depressed symptoms and treatment insight. There was no effect of negative symptoms on either illness insight or treatment insight. Taken together, our results indicate overlapping and unique relational paths for illness and treatment insight dimensions, which could suggest differences in causal mechanisms and potential interventions to improve insight.

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1. Introduction

Insight changes in schizophrenia were documented as early as 1906 as an important aspect of the illness (Kendler, 2016) and are associated with a multitude of adverse clinical outcomes (Lehrer and Lorenz, 2014). As such, several etiological models have been proposed to explain insight in schizophrenia. Most of these models have been discredited either due to inconsistent findings or failure to replicate, which have been primarily attributed to the complexity of insight (Osatuke et al., 2008). The clinical model of insight which posits insight changes as a primary feature of the illness, acknowledges this complexity. A closer examination of clinical insight does reveal that it has a multidimensional structure with variations observed in awareness of illness, symptoms, symptomatic attribution, treatment and consequences of the illness (Amador et al., 1993). The five dimensions of

insight, though independent, also seem to have some overlap. This finding is supported by neuroimaging literature which points to common as well as exclusive brain regions associated with insight dimensions (Shad and Keshavan, 2015). Intuitively, an individual needs to have some awareness of illness to have an awareness of the need for treatment.

Methodological issues such as the use of a variety of insight measures (Baier et al., 1998) have contributed to the inconsistencies in the associations between insight, symptoms and cognition. These measures likely assess different insight dimensions as discussed above or various forms of insight such as clinical insight versus cognitive insight - the ability to assess self-experiences and correctly interprets these experiences (Beck et al., 2004). Overly reductionist models that minimize or do not take into account other confounding or mediating factors have also lead to equivocal findings. For example, the neuropsychological deficit model of insight broadly conceptualizes insight as a result of cognitive dysfunction yet it fails to take into account the potentially distinct roles of different cognitive domains such as neurocognition, social cognition and metacognition with insight (Lysaker et al., 2013) or its changing relationship with psychopathology symptoms in different stages of the illness (Quee et al., 2010).

* Corresponding author.
E-mail addresses: rx13@duke.edu (R.M. Xavier), wei.pan@duke.edu (W. Pan), Jennifer.dungan@duke.edu (J.R. Dungan), richard.keefe@duke.edu (R.S.E. Keefe), allison.vorderstrasse@duke.edu (A. Vorderstrasse).
[1] Co-senior authors.

1.1. Insight and cognition

Cognitive (Aleman et al., 2006) and social cognitive measures are associated with insight and impairment in these areas interfere with development (Quee et al., 2014) and maintenance of insight (Lysaker et al., 2013). Though neurocognition and social cognition are often considered to be related, there is evidence to support that these are distinctly separate or independent dimensions of cognition (Van Hooren et al., 2008). Evidence for these associations comes not only from the neuropsychological literature but also from neuroimaging literature. Neuroimaging studies show that cortical and subcortical regions associated with neurocognition (Shad and Keshavan, 2015) and social cognition (Lee et al., 2006) are also associated with insight. Social cognition measured with multiple tasks (Lee et al., 2013) as well as neurocognitive measures including executive functioning (Mysore et al., 2007), memory (Chen et al., 2005) and attention, are associated with insight.

1.2. Insight and psychopathology symptoms

The relationship of insight to psychopathology symptoms varies by the symptom domain. Negative correlations between insight and the positive and negative symptoms have been reported whereas insight also has a positive correlation with the depressive symptoms (Mintz et al., 2003). As with the relationship between insight and cognition, these data are also inconsistent (Landi et al., 2016). Additionally, psychopathology symptoms (e.g. negative and depressive symptom domains) associated with insight are also associated with cognition, affirming the complexity of these relationships.

1.3. Interrelationships of insight, cognition and symptoms

Though there is a wealth of literature examining the interrelationships between insight, psychopathology and cognition, such studies have been primarily correlational. Very few studies have focused on identifying causal models of these complex relationships. One such study conducted in a sample of patients with acute psychosis found that neurocognition had only a weak selective effect on insight with perseverative responses exerting a partial mediating effect between insight and psychopathology (Hwang et al., 2015). It is not clear if this holds true in the chronic phase of the illness. Further, there are far fewer studies that have examined the interrelationships of psychopathology symptoms and cognition with different insight dimensions. Given that insight serves as an important predictor of a range of adverse outcomes, including treatment refractory outcomes which are tied to both good and impaired insight, such knowledge would be informative in developing precise, clinically meaningful interventions. Thus, we set out to simultaneously assess the interrelationships of insight dimensions with psychopathology symptom domains and cognitive domains to determine if there are causal relational pathways, in a sample of patients with chronic schizophrenia. Our approach was to test for direct and indirect effects between variables in the model depicted in Fig. 1. Specifically, we tested (i) whether insight into illness mediated the relationship between psychopathology symptom dimensions and treatment insight and (ii) whether cognitive domains (neurocognition and social cognition) independently mediated the relationship between psychopathology symptoms and insight dimensions.

2. Methods

This study utilized baseline data from the Clinical Antipsychotic Trial of Intervention Effectiveness (CATIE) schizophrenia study which was a large randomized controlled trial conducted between 2001 and 2004, funded by the National Institute of Mental Health to compare the effectiveness of a representative typical antipsychotic, perphenazine, and the atypical antipsychotic medications available at that time. Confer Stroup et al. (2003), for study details. Sample selection criteria and sample characteristics are described elsewhere (Lieberman et al., 2005). Briefly, 1493 patients between the ages of 18–65 with chronic schizophrenia (with the exclusion of treatment resistant patients), who had the ability to take oral medications and who demonstrated decisional capacity
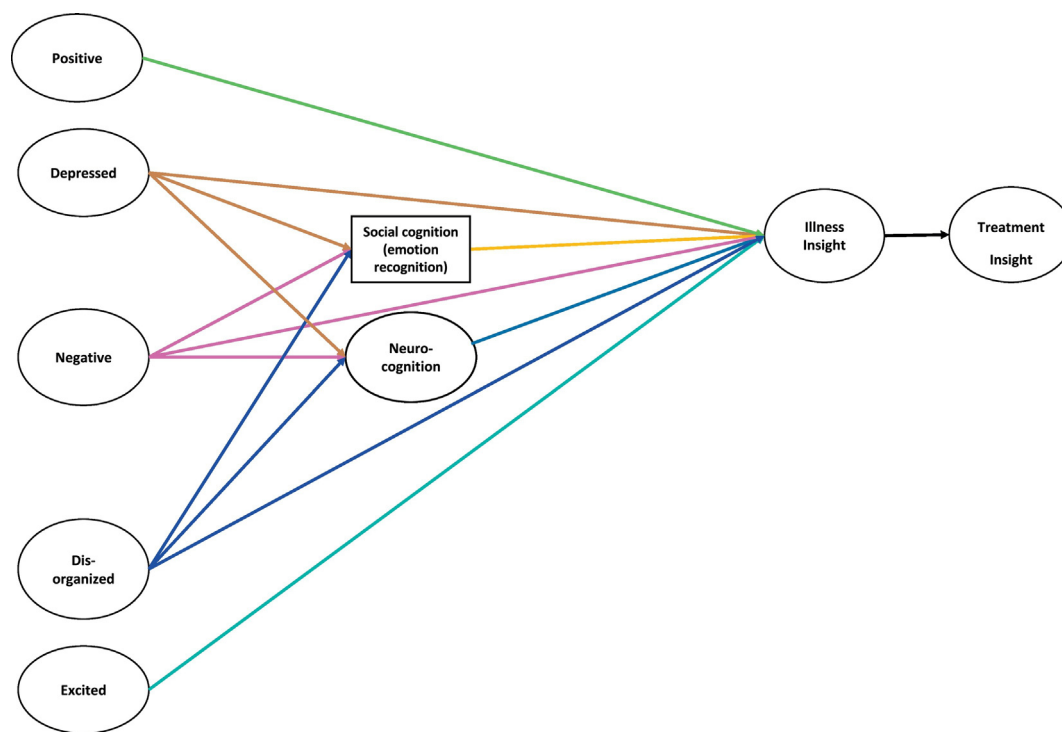

Fig. 1. Structural model depicting hypothesized relationships between psychopathology symptoms (positive, depressed, negative, disorganized and excited) neurocognition, social cognition and insight dimensions (illness insight and treatment insight). Direct paths were hypothesized from all variables in the model to treatment insight, but are not shown in the figure.