



Psychiatric symptoms mediate the effects of neurological soft signs on functional outcomes in patients with chronic schizophrenia: A longitudinal path-analytic study

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ABSTRACT

Neurological soft signs (NSS) in motor coordination and sequencing occur in schizophrenia patients and are an intrinsic sign of the underlying neural dysfunctions. The present longitudinal study explored the relationships among NSS, psychiatric symptoms, and functional outcomes in 151 Chinese patients with chronic schizophrenia across a 6-month period. The participants completed neurological assessments at baseline (Time 1), psychiatric interviews at Time 1 and 3-month follow-up (Time 2), and self-report measures on daily functioning at 6-month follow-up (Time 3). Two possible (combined and cascading) path models were examined on predicting the functional outcomes. Direct and indirect effects of Time 1 NSS on Time 3 functional outcomes via Time 2 psychiatric symptoms were evaluated using path analysis under bootstrapping. Motor coordination and sequencing NSS did not have significant direct effects on functional outcomes. Motor coordination NSS exerted significant and negative indirect effects on functional outcomes via psychiatric symptoms. These results contribute to a better understanding of the determinants of functional outcomes by showing significant indirect pathways from motor coordination NSS to functional outcomes via psychiatric symptoms. That motor sequencing NSS did not affect functional outcomes either directly or indirectly may be explained by their trait marking features.

1. Introduction

Schizophrenia is an intricate neuropsychiatric disorder associated with deficits in cognitive, affective, and neurological domains (Heinrichs and Zakzanis, 1998). Neurological soft signs (NSS), defined as subtle neurological abnormalities in sensory integration, motor coordination and sequencing of complex motor acts (Heinrichs and Buchanan, 1988), occur consistently in patients with schizophrenia (Emsley et al., 2005). A meta-analysis (Bachmann et al., 2014) among schizophrenia patients reveals a declining trend in NSS together with remission of psychopathological symptoms in remitting patients. Other studies (Chen et al., 2000; Prikryl et al., 2012) have found deteriorations in NSS for non-remitting patients with a chronic course. A recent study (Chan et al., 2016) reveals an abnormally flat and elevated life-span trajectory of NSS in schizophrenia patients. These results suggest that NSS comprise both state- and trait-like features and vary in the clinical course of schizophrenia.

Schizophrenia patients have been found to exhibit significantly more NSS than healthy subjects and patients with other psychiatric disorders (Chan et al., 2010; Wang et al., 2016). Their unaffected first-degree relatives also display higher NSS compared to healthy controls (Xu et al., 2016). Kong et al. (2012) have linked persistent and heightened NSS with progressive cerebral changes in schizophrenia patients. Given the linkage between NSS and genetic variants and neural abnormalities in brain regions (Zhao et al., 2014; Hirjak et al., 2016), NSS have been suggested as a potential endophenotype for schizophrenia. The relative ease of assessment of NSS implies that NSS could be used to monitor progression of the disorder or to identify subjects at risk to develop chronic schizophrenia.

NSS have been advocated (Sewell et al., 2010; Chan et al., 2015, 2016) as outcome predictors of essential features of the disorder such as psychopathological severity and functional outcomes. Previous studies have established significant and positive associations between NSS and psychiatric symptoms such as positive symptoms (Chan et al.,

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2010), negative symptoms (Prikryl et al., 2012; Mittal et al., 2014; Chan et al., 2015), and disorganized symptoms (Basso et al., 1998; Bombin et al., 2005) in schizophrenia patients. Both NSS and psychiatric symptoms are associated with poor functional outcomes in schizophrenia. NSS have been correlated with worse functional outcomes (Behere, 2013; Papiol et al., 2016) in the form of social functioning (Jahn et al., 2006), and global functioning (Peralta et al., 2014). Similarly, psychiatric symptoms have been found to contribute to long-term comorbidity and worse functioning (Milev et al., 2005; Chan et al., 2015; Strassnig et al., 2015).

Nevertheless, few researchers have simultaneously investigated the relationships among NSS, psychiatric symptoms, and functional outcomes in schizophrenia patients. A better understanding of these relationships is essential to devise effective interventions that facilitate patients' recovery and enhance their overall functioning. Path-analytic approaches are preferred and suitable to explore these patterns. A meta-analysis by Ventura et al. (2009) demonstrates that negative symptoms mediate the relationship between neurocognition and functional outcomes. Findings from other studies (Lin et al., 2013; Mehta et al., 2014) support such a mediating role for psychiatric symptoms. Apart from direct effects from NSS to functional outcomes, it is plausible that NSS might have indirect effects on functional outcomes through indirect pathways via psychiatric symptoms. Further research is warranted to elucidate the roles of NSS and psychiatric symptoms in predicting functional outcomes.

To the best of our knowledge, no existing studies have explored the potential mediating role of psychiatric symptoms on the relationship between NSS and functional outcomes. The present study adopted a path-analytic approach to evaluate the temporal relationships among NSS, psychiatric symptoms, and functional outcomes in schizophrenia patients across a 6-month period. Fig. 1 depicts the conceptual model of the present study, where psychiatric (positive, negative, and disorganized) symptoms are posited as potential mediators of the relationships between NSS (deficits in motor coordination and motor sequencing) and functioning outcomes (IADL and ADL). This study examined two possible path models on predicting functional outcomes in schizophrenia patients – a combined model, comprising both direct and indirect effects of NSS on functional outcomes, and a cascading model, where NSS predicted functional outcomes solely by indirect effects via psychiatric symptoms. We hypothesized that the combined path model would provide a better fit than the cascading path model and that psychiatric symptoms would mediate the associations between NSS and functional outcomes.

2. Methods

2.1. Participants

The present study is a secondary analysis of data from a random-

ized controlled trial (Ho et al., 2016) on the effectiveness of Tai-chi and physical exercise in schizophrenia patients. The study sample comprised 151 chronic schizophrenia patients recruited from a mental health rehabilitation complex in Hong Kong from September 2013 to January 2014. The patients were receiving long-term residential care in the hostel. Inclusion criteria were fulfillment of the DSM-IV TR criteria for schizophrenia according to a psychiatrist's diagnosis, aged between 18 and 65 years, and ability to understand and speak Cantonese. Exclusion criteria included acute schizophrenia requiring hospitalization, presence of unstable schizophrenic symptoms (such as persistent withdrawal) that limit interaction in an assessment interview, a history of brain trauma or organic mental disorders, and presence of physical disabilities or severe illnesses that could impair cognitive or visuomotor functioning.

At baseline (Time 1), the participants completed neurological assessments on NSS. They underwent structural clinical interviews on psychiatric symptoms at Time 1 and at 3-month follow-up (Time 2) from the same rater. At 6-month follow-up (Time 3), the participants completed self-report measures on functional outcomes. Written informed consent was sought from the participants and the study protocol was approved by the institutional ethics committee of the University of Hong Kong (HKCTR-1453). Demographic and clinical information such as duration of the disorder and type of antipsychotic medications were obtained via medical record reviews.

2.2. Assessments

2.2.1. Neurological soft signs

Two subscales of the Neurological Evaluation Scale (NES) (Buchanan and Heinrichs, 1989) were used to evaluate the participants' NSS in motor coordination and sequencing of complex motor acts. Compared to the Cambridge Neurological Inventory (Chen et al., 1995) and Heidelberg Scale (Schröder et al., 1991), the NES was widely used among longitudinal studies on NSS in schizophrenia (Bachmann et al., 2014). Neurological deficits for motor coordination consist of six items, namely, tandem walk, rapid alternating movements (for dominant and non-dominant hand), finger/thumb opposition (for dominant and non-dominant hand), and finger-to-nose test. Neurological deficits for sequencing in complex motor acts comprise three items, namely, fist-ring test, fist-edge-palm test, and Ozeretski test.

Participants' performance on each item was rated on a 3-point scale based on the number of mistakes they made. Each item score was summed up to produce a subscale score for motor and sequencing deficits, with higher scores indicating greater levels of NSS. The Chinese version of the NES showed marginal internal consistency for sequencing deficit (Cronbach's $\alpha=0.59$) and good internal consistency for motor deficit ($\alpha=0.80$) subscales in a previous study (Fong et al., 2015). In the present study, assessment of NSS was conducted by three professional raters who had a medical-related background and had

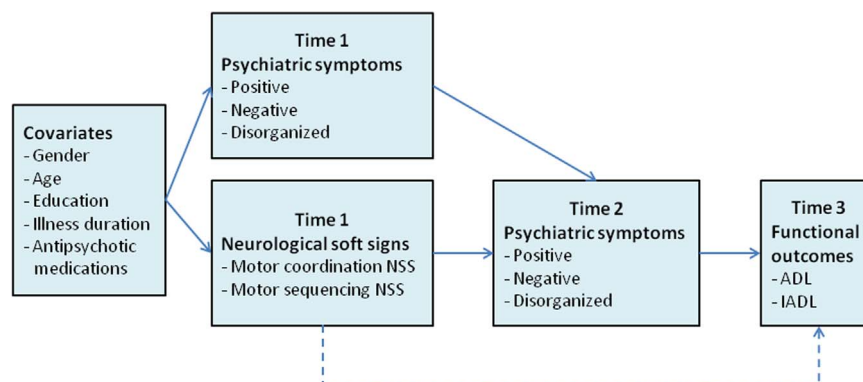


Fig. 1. Hypothesized path model on neurological soft signs, psychiatric symptoms and functional outcomes in the present study. Note: Pathways for the cascading model are denoted by solid lines, whereas the dashed line indicates the direct effects from neurological soft signs to functional outcomes.

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