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Executive function in first-episode schizophrenia: A three-year prospective study of the Hayling Sentence Completion Test

Kevin K.S. Chan [1], J.Q. Xu, Kristy C.M. Liu [2], Christy L.M. Hui, Gloria H.Y. Wong, Eric Y.H. Chen *

Department of Psychiatry, The University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong

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ABSTRACT

In recent decade, deficits in the mechanism of Supervisory Attentional System (SAS) have become increasingly influential in explaining the nature of dysexecutive syndrome experienced by schizophrenic patients. The SAS model is characterized by having a detailed sub-classification of specific executive function components, among which semantic inhibition has been investigated using the Hayling Sentence Completion Test (HSCT). Several studies thus far have indicated that schizophrenic patients show impairment in HSCT performance. However, HSCT data concerning first-episode patients is still scarce. Besides, as previous HSCT studies were all cross-sectional in nature, they were not able to assess changes in HSCT performance over time. In order to address the paucity of knowledge about the longitudinal trajectories and correlates of semantic inhibition deficits in early schizophrenia, this paper reports a three-year prospective study of HSCT performance in medication-naïve, first-episode patients with schizophrenia-spectrum disorders. HSCT performance was assessed in 34 patients at four times over a period of three years, while the 34 healthy controls were assessed once. We found that medication-naïve patients demonstrated impairment in the inhibition condition in HSCT as compared to controls, but not in the initiation condition. Such HSCT impairment gradually improved in the three years following the first psychotic episode; however, HSCT performance did not predict improvement in negative or positive symptoms over the three-year period. The present findings suggest that semantic inhibition impairment is a specific deficit in schizophrenia that may require early intervention efforts, with the goal of facilitating more successful verbal communication and thereby better interpersonal functioning.

1. Introduction

One of the most robust and central neurocognitive deficits associated with schizophrenia is executive impairment (Fioravanti et al., 2005), which affects various cognitive processes, including initiation, sustained attention, online updating, switching and flexibility, disinhibition, and attention allocation and planning (Chan et al., 2006a, b). Consistent with the link between the dysexecutive syndrome and frontal dysfunction in schizophrenia (Morice and Delahunty, 1996), studies have demonstrated that schizophrenic patients tend to perform more poorly than healthy controls in neuropsychological tests sensitive to frontal lobe lesions, such as Wisconsin card sorting, verbal fluency, and trail making (Chan et al., 2006a,b). However with respect to the longitudinal trajectory of executive functioning in schizophrenia, the findings have not been consistent. A recent meta-analysis (Szoke et al., 2008) found that while some studies have demonstrated longitudinal stability, others have found decline or improvement. It has been argued that the inconsistent findings in the literature might be accounted for by several methodological and conceptual inconsistencies across studies. Most importantly, given the diverse range of executive function tests that have been developed and used in schizophrenia research and the lack of research on the psychometric properties of each (namely, construct validity and criterion validity; Donohoe and Robertson, 2003), it is not surprising that varied findings have been reported. Additionally, it may be that the measures probe different aspects of executive functions (Evans et al., 1997) and that the temporal change of these components differs. Therefore, the ultimate problem in executive function research continues to be the lack of sophisticated theoretical and methodological approaches to the fractionation of the executive system (Burgess, 1997).

In light of the importance of detailing the different components of executive functioning in schizophrenia, Norman and Shallice (1986) have proposed a model of the supervisory attentional system (SAS) to explain the nature of dysexecutive syndrome experienced by schizophrenic patients. Under this framework, the SAS is responsible for regulating goal-directed behaviors in non-routine and novel situations; however, disruption of this system may give rise to the inability to formulate a goal, to plan, and to choose between alternative

* Corresponding author. Tel.: +852 2255 4488; fax: +852 2255 1345.
E-mail address: eyhchen@hku.hk (E.Y.H. Chen).
[1] Current address: Department of Psychology, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong.
[2] Current address: Department of Psychology, The University of Hong Kong, Pokfulam Road, Hong Kong.

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sequences of behavior in order to attain a specific goal (Norman and Shallice, 1986). The SAS model is characterized by having a detailed sub-classification of specific executive function components (Burgess and Shallice, 1996a,b; Stuss et al., 1995). In accordance with this, the SAS has been fractionated into different executive processes in several empirical studies. For instance, using the Six Elements Test, the Sustained Attention to Response Task, and the Hayling Sentence Completion Test, Chan et al. (2004) have found that executive function in schizophrenic patients could be fractionated into output generation, action/attention inhibition, and semantic inhibition.

Among these factors, semantic inhibition, which refers to the executive control of prepotent speech activation in semantic memory, has been considered to make important implications for successful verbal communication in real-life settings (Chan et al., 2010). In this connection, the Hayling Sentence Completion Test (HSCT; Burgess and Shallice, 1996a) was specifically developed to measure semantic inhibition capacities. In this test, test-takers are presented with sentences in which the last word is missing but is strongly cued by the rest of the sentence. To correctly perform this task, test-takers must suppress the activated word and its semantic associates. In this sense, HSCT could capture the regulation of the non-routine element from the supervisory attentional perspective. Several neuroimaging studies have further highlighted the executive nature of HSCT by showing the association of response inhibition in this task with increased activation in a network of left prefrontal areas (e.g., Collette et al., 2001). Moreover, HSCT has been shown to be sensitive to semantic inhibition deficits in individuals with different psychiatric and neurological disorders, including Alzheimer's disease (Belleville et al., 2006), Parkinson's disease (Bouquet et al., 2003), major depressive disorder (Gohier et al., 2009), obsessive–compulsive disorder (Van der Linden et al., 2005), and schizophrenia.

A number of studies thus far have shown that schizophrenic patients commit more errors in semantic inhibition than healthy controls (Chan et al., 2006a,b; Groom et al., 2008; Joshua et al., 2009; Marcezewski et al., 2001; Nathaniel-James et al., 1996; Nathaniel-James and Frith, 1996; Royer et al., 2009; Waters et al., 2003). In addition, some authors have found a significant correlation between semantic inhibition as measured by HSCT and several clinical features in schizophrenia, including auditory hallucinations (Waters et al., 2003) and social/impulsivity symptoms (Chan et al., 2004). These findings suggest that research into this relationship may link directly to our understanding of the psychopathological dynamics and may have a strong predictive power for the clinical course of the illness.

As previous HSCT studies were all cross-sectional in nature, they were not able to assess changes in semantic inhibition capacities over time. In order to address the paucity of knowledge about the longitudinal trajectories and correlates of semantic inhibition deficits in schizophrenia, this paper reports a three-year prospective study of HSCT performance in medication-naïve, first-episode patients with schizophrenia-spectrum disorders. We aim to address the following questions: (1) whether HSCT performance is impaired in patients; (2) how HSCT performance evolves over the three years after the first presentation of illness and; (3) whether HSCT performance is associated with demographics, clinical features, duration of untreated psychosis, or outcome in first-episode schizophrenia.

2. Methods

2.1. Participants

Participants were 34 medication-naïve patients with first-episode schizophrenia-spectrum disorders chosen from a larger cohort recruited for longitudinal studies by our research team (some of the baseline data has been reported by Chan et al., 2006b). The inclusion criteria were Cantonese-speaking, Han Chinese having primary diagnosis of schizophrenia, schizophreniform disorder, or schizoaffective disorder based on DSM-IV (American Psychiatric Association, 1994). Consensus clinical diagnoses were made by two experienced psychiatrists; an inter-rater agreement of 86% for diagnosis was obtained in an independent validation sample of 38 patients. Patients were excluded if they had significant medical illness or if they were clinically judged to have high risk of suicidal behavior. The healthy control sample consisted of 34 volunteers recruited from the general public. Potential participants with any personal or family history of psychiatric illness, history of brain trauma or neurological illness, mental retardation, or history of special group attendance were excluded from the present study. Approval of the relevant Institutional Review Boards was obtained prior to commencement of the study. All participants gave written informed consent after the procedure had been fully explained. Assessment of patients was carried out at the point of first contact (medication-naïve), after clinical stabilization, at the end of the first year and at the end of the third year. Healthy controls were assessed only once.

2.2. Assessments

2.2.1. Clinical assessments

The Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was used to assess the severity of symptoms in patients. The inter-rater reliability of the three raters was 0.83 for the PANSS (by intra-class correlation coefficient). The Interview for the Retrospective Assessment of the Onset of Schizophrenia (Hafner et al., 1992) was used to assess duration of untreated psychosis (DUP) and for obtaining data concerning education level.

2.2.2. Cognitive assessments

2.2.2.1. Intelligence. Intelligence was evaluated at the first assessment in both patients and healthy controls using the Information, Arithmetic, Digit Span, Digit Symbol and Block Design subtests of the Wechsler Adult Intelligence Scale-Revised, Cantonese version (Hong Kong Psychological Society, 1989).

2.2.2.2. Disinhibition. The Hayling Sentence Completion Test Part B (HSCT Part B; Burgess and Shallice, 1996a) was used for the assessment of the 'disinhibition' component of executive function. In this test, participants were presented with 15 sentences in which the last word is missing but is strongly cued by the rest of the sentence. They were required to give words that make no sense in the sentence context. The current study adopted the error classification and error scoring procedures suggested by Burgess and Shallice (1996a). Two possible types of errors in this task were: (A) direct (or slightly off but possible) completion of the sentence; and (B) generation of a word that is categorically or semantically related to the strongly cued word in the sentence. A total error score was computed according to the formulae: total error score = number of Type A errors X 3 + number of Type B errors (Burgess and Shallice, 1996a). Other performance measures comprised the numbers of correct items, Type A errors and Type B errors (Chan et al., 2004, 2010). The present study adopted the Chinese version of the task (Chan et al., 2004).

2.2.2.3. Other specific components of executive function. Participants were also administered other neuropsychological assessments capturing different domains of executive function with which to compare to the HSCT.

The Hayling Sentence Completion Test Part A (HSCT Part A; Burgess and Shallice, 1996a) (Chinese version, Chan et al., 2004) was used to assess the 'initiation' component of executive function. Unlike HSCT Part B, participants were required to appropriately complete the 15 sentences in this task. The number of correct items was recorded. HSCT Part A was originally developed to assess response