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Correlation of neurological soft signs and neurocognitive performance in first episode psychosis

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ABSTRACT

Neurological soft signs and neurocognitive impairments are commonly observed in first episode psychosis but the correlation of these factors remains controversial. Here, we evaluated 30 patients with remitted first episode psychosis and 30 healthy controls for the presence and severity of neurological soft signs (using the Neurological Evaluation Scale - NES) and for neurocognitive impairments (using seven subtests of the Cambridge Neuropsychological Test Automated Battery - CANTAB). NES score was higher in patients compared to controls. Neurocognitive impairment was evident in patients in the following domains: working memory, spatial recognition memory, attention set shifting, planning and inhibition. The NES revealed significant correlations with spatial working memory performance and Intra-Extra Dimensional Set Shifting (as a component of executive function). These correlations were observed both in patients and in controls. Planning and inhibition showed correlation with the total NES score and the sequencing of complex motor acts in both groups. In addition, spatial span and spatial recognition memory showed significant correlation with total NES score and the sequencing of complex motor acts in controls. The correlation between sequencing of complex motor acts and specific domains of neurocognitive tasks suggests that similar neuroanatomical substrates might be implicated in these processes.

1. Introduction

Schizophrenia is a chronic disease with deterioration of function in many domains including cognition (Green, 1996; Green et al., 2000). Neurocognitive deterioration constitutes a wide range of impairments from intact cognition to severe deficits (Perez-Iglesias et al., 2010; Keefe, 2007). Deficit has been found in most domains of cognition, but it is reported as more prominent in specific aspects such as visuomotor processing, semantic memory and verbal learning (Albus et al., 2006) and are attributed to some neurological disorders (Liddle, 1987). Many neurological soft abnormalities are found in patients with schizophrenia in excess of their prevalence in general population (Rossi et al., 1990). In spite of this, the evidence for the prevalence of Neurological Soft Signs (NSS) and their specificity is not consistent across the literature; although, there are reports of specific impairments of function (Buchanan and Heinrichs, 1989), compared to hard signs, these soft signs are often non-specific, not well localized and reflect generalized neurological impairments (Quitkin et al., 1976). Similarly, some reports show general correlation between the presence of NSS and the overall cognitive dysfunction (Kolakowska et al., 1985; Liddle, 1987), while others indicate a more selective correlation between NSS and specific domains of neurocognition (Mohr et al., 1996; Flashman et al., 1996). Mohr et al. (2003) examined this correlation in patients with first episode psychosis and found that NSS are predictive of neuropsychological performance in general with no specificity. Arango et al. (1999) found that the neurological signs are predictive of global cognitive impairment with the sensory integration score being the best predictor of neuropsychological performance. Flashman et al. (1996) found that soft signs in patients with schizophrenia were a predictor of localized cognitive performance deficit; they best predicted the deterioration of motor speed, coordination and sequencing, but not a global decline in performance. Chan et al. (2009) show a modest to moderate association between NSS and executive attention, verbal memory and visual memory in patients with schizophrenia while limited associations were found within normal controls.

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There is also mix evidence for the timing and occurrence of neurocognitive deteriorations. Some investigations indicate that the largest portion of cognitive deterioration occurs before developing psychosis (Becker et al., 2010). In contrast, others show that neurocognitive deficit is linked to the duration of untreated psychosis (Amminger et al., 2002; Barnes et al., 2000), with further reports of progressive structural brain damage observed during the transition to psychosis (Borgwardt et al., 2007; Pantelis et al., 2003a). While the NSS are more prevalent in chronic severely ill schizophrenic patients (Mohr et al., 1996), they can be observed in first episode psychosis (Gupta et al., 1995). It is not clear in the literature how the duration of the psychosis may impact the prevalence or severity of NSS. Some studies showed that NSS, particularly in the motor coordination domain, is present in first episode psychosis and persist or deteriorate with time during the course of schizophrenia (Dazzan and Murray, 2002). Yet, other studies report an improvement in total neurological signs, and motor coordination in particular, with improvement in positive symptoms, 6 months after the first presentation of psychosis (Whitty et al., 2003). Similarly, Emsley et al. (2005) observed that the motor sequencing domain improved with improvement in psychopathology 12 months after the first presentation. Other investigations provide support for the link between NSS and psychopathological symptoms across the course of the disease: Prikryl et al. (2012) showed that the total Neurological Evaluation Scale (NES) score as well as specific subtypes of NSS, such as sensory integration and sequencing of motor acts, decreased in those who fulfilled the remission criteria, while total NES increased in other patients who did not reach the point of remission. They also found a link between negative symptoms and NSS. Bachmann et al. (2005) showed that NSS varies with the clinical course, and its decrease during the course of the disease is more obvious in those who have a favorable outcome. NSS score was also associated with some anatomical indices in the brain: NSS inversely correlated with the volume of the right cerebellar hemisphere (Bottmer et al., 2005) and therefore may exhibit further changes over time in relation to changes in the cerebellar volume.

Although the presence of NSS is found to be somewhat independent of medication status (Rossi et al., 1990; King et al., 1991), the effect of prolonged exposure to drugs cannot be excluded. The majority of studies showed no relationship between NSS severity and antipsychotic dosage (Bombin et al., 2005) (but see Merriam et al., (1990) who reported that higher antipsychotic dosage are correlated with worse performance in prefrontal sign and better performance in parietal sign). Considering neuroleptic's side effect, Jahn et al. showed that neither the neuroleptic dose prescribed to the patient, nor scores for tardive dyskinesia and akathisia were significantly correlated with NSS (Jahn et al., 2006).

In summary, the evidence for the presence of NSS and their specificity is not entirely consistent across the literature, with most of the evidence coming from patients with schizophrenia. Till now there is ambiguity about whether NSS can predict a specific anatomical or cognitive abnormality or not. The present study aims to characterize the correlation of NSS and neurocognitive function both in general and for specific domains in patients with first episode psychosis compared to normal healthy controls. Are there specific cognitive deficits that correlate with specific domains of NSS? If so, does the identification of these domains help us to localize the anatomic/pathway correlates of the deficit in the brain. Focusing on patients with first episode psychosis eliminates the effect of prolonged duration of illness and minimizes the potential impact of medication, and allows better investigation of the direct correlations between the NSS and the neurocognitive dysfunctions.

2. Method

2.1. Subjects

Thirty patients were recruited. All patients presented with symptoms of psychosis for the first time in their life, affective or non-affective, and were consecutively admitted to Roozbeh hospital, a referral teaching psychiatric hospital in Tehran, Iran. Patients included in the study were between 18 and 50 years old. Those with mental retardation, any evident cognitive deterioration, any obvious neurological impairment, history of stimulant substance abuse, or those whose education were below 5 years were excluded from the study. Thirty controls were matched with the patients regarding their age, sex and education. We did not run a full IQ test on all participants. However, every participant (patient or control) was evaluated through a quick screening test. If borderline IQ was suspected, a more complex test was performed and the participant was excluded if the test confirmed an IQ that was lower than 90. Both groups gave an informed written consent before examination.

2.2. Measures

In order to obtain the diagnosis and confirm the psychotic state we used the information gathered from the history and the clinical evaluation by the attending psychiatrist and further validated the diagnosis by a semi-structured interview using Structured Clinical Interview for DSM-IV (SCID) (First et al., 1996; Sharifi et al., 2009). Patients with any psychotic disorder were included in the study. In order to minimize the impact of time of the disease period on NSS, we selected patients with first episode psychosis. To get better cooperation, the examination was performed after remission of the acute symptom.

Examination of the cognition and neurological signs were postponed until clinical remission was achieved. The remission was confirmed with Clinical Global Impression (CGI) scale ≤ 3 (Abbo et al., 2012; Guy, 1976). Neurological evaluations were done using Neurological Evaluation Scale (NES) (Mohr et al., 1996; Heinrichs and Buchanan, 1988). NES consisted of 26 signs classified in four subscales: (i) sensory integration, (ii) motor coordination, (iii) sequencing of complex motor actions, and (iv) other neurological impairments. The examination and rating were done by a senior resident of psychiatry (SA) who was trained in NSS evaluation. The soft signs were rated on a 0, 1, 2 scale which indicated normal, mild and marked impairment, respectively. Some items were assessed in both left and right side, and the scores were added in any special domain.

Neurocognitive assessments were derived from the Cambridge Neuropsychological Test Automated Battery (CANTAB) (Robbins et al., 1994). Four domains of neurocognition were selected and were tested by seven CANTAB subtests. The domains that were selected were as follows: (i) visual memory was assessed by Spatial Recognition Memory (SRM) and Pattern Recognition Memory (PRM). The variable of interest in these tests was percentage of correctly recalled location and pattern, respectively (Van der Molen et al., 2010). (ii) Working memory was assessed by Spatial Working Memory (SWM) and Spatial Span (SSP). Spatial Working Memory and Spatial Span, respectively represent working memory manipulation and maintenance. The variables which are included in the analysis were span length, total error and total usage error from SSP and total error and strategy from SWM (Summers and Saunders, 2012; Van der Molen et al., 2010). (iii) Response inhibition was assessed by Stop Signal Task (SST). Variables of interest in this test were median Go Reaction Time (GO RT), Stop Signal Reaction Time (SSRT) and total number of discrimination errors (Clark et al., 2005). (iv) Executive function was assessed by Intra-Extra Dimensional set shifting (IED) and Stockings Of Cambridge (SOC) (Van der Molen et al., 2010). IED assesses rule acquisition and flexibility of thinking. The variables of interest in this test were the number of completed stages, the total number of errors committed and the number of trials completed (Van der Molen et al., 2010). Spatial planning and problem solving abilities were assessed by SOC. The variable of interest was the number of problems solved with the minimum number of moves needed (Van der Molen et al., 2010). Motor Screening Task (MOT), Big/Little Circle (BLC) were done for training and screening. The CANTAB tests were administered in the following order: MOT, SSP, SWM, SOC, PRM, SRM, BLC, IED, and SST. In total, the entire test took approximately 100 min, including a 10 min break in the middle.

2.3. Statistics

Age, education level and gender were compared between groups using t and chi-square tests. Mann–Whitney U test was used to compare NES dimensions and total scores, and neurocognitive variables between the two groups. We used Spearman' rho to examine the correlation between the NES scores and the CANTAB subscale scores in the two groups. For all analyses, significance was considered at p value of 0.05.