Published in final edited form as:
Acta Neuropsychiatr. 2010 October ; 22(5): 262–263. doi:10.1111/j.1601-5215.2010.00484.x.

Involuntary movements and their correlates in first-episode psychoses

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Involuntary movements (IMs) are seen in schizophrenia and are widely considered to be side-effects of neuroleptic medications (1,2). Although dopamine-blocking antipsychotics may be related to IMs, IMs are often manifested in medication-naïve patients and were frequently reported in the preneuroleptic era (3–5). IMs are reported in medication-free chronically ill (6–8) and medication-naïve first-episode patients (9–14). Previous studies report IMs in neuroleptic-naïve psychosis up to 14% (5), suggesting that IMs could be state-independent, core features. It, however, remains unclear whether IMs represent medication-induced phenomena or whether they are the core phenotypic trait-related features of schizophrenia (15).

Some studies suggest that the severity of IMs may correlate with the degree of negative (3,16) or positive symptoms (10), albeit inconsistently (17). Working memory impairments and negative symptoms may correlate with IMs in patients treated for chronic schizophrenia 18), suggesting a role for frontostriatal neural systems in the pathophysiology of IMs. Although the relationship between IMs, negative symptoms and neurocognitive deficits, one of the core features of schizophrenia (19), has not been studied previously in untreated patients with first-episode psychoses, those studies examining IMs in untreated schizophrenia patients are limited by a small sample size (10,14) and by the lack of standardised assessment scales (13).

We examined IMs in a relatively large group of medication-free first-episode psychosis patients and studied their relationships to positive and negative symptoms and executive function (Box 1). We hypothesised that the patients will have IMs and these would correlate with more severe negative symptoms as well as executive function impairment.

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Box 1. Involuntary Movements in Medication-free First-episode Psychosis Patients and Their Relationship to Positive and Negative Symptoms and Executive Functions

Methods

The subjects included individuals who were involved in a longitudinal study of first-episode psychosis [for details of the methods see Keshavan et al. (20)]. About 178 previously untreated patients with psychosis were evaluated with a thorough medical, neurological and psychiatric evaluations. Of these, 162 were diagnosed with schizophrenia or schizoaffective disorder (104 males; 24.8 + 7.81 years), and 16 were diagnosed with other psychotic disorders (12 males; 34.72 ± 9.24 years). Patients were recruited from the in-patient and out-patient services of the Western Psychiatric Institute and Clinic, Pittsburgh. All subjects were interviewed by experienced clinical raters (Debra Montrose PhD, Kevin Eklund RN or Elizabeth Radomsky PhD) using the Structured Clinical Interview for Diagnostic and Statistical Manual, fourth edition (DSM-IV) (21). Diagnoses were derived by consensus diagnostic evaluations and were formally confirmed after at least 6 months follow-up. These patients were aged 15–45 years, had minimal prior exposure to neuroleptics, and met the DSM-IV criteria for a non-organic psychotic disorder. Exclusion criteria were significant neurological or medical illness, mental retardation as diagnosed by DSM-IV, head injury with loss of consciousness, current substance abuse or substance dependence within the previous 6 months. All participants provided informed consent after full explanation of the study. The study was approved by the University of Pittsburgh Institutional Review Board.

Involuntary movements were evaluated by an experienced clinician Kevin Eklund, RN), trained by the senior investigator (Matcheri S Keshavan) using abnormal involuntary movements scale (AIMS). Executive dysfunction was examined using the perseverative errors on the Wisconsin Card Sort Test (WCST). The Scale for the Assessment of Negative Symptoms and the Scale for the Assessment of Positive Symptoms were completed close to the time of the neuropsychological evaluations without knowledge of the findings from cognitive investigations. Similarly, neuropsychological testing was done blind to knowledge of clinical ratings. Correlational analyses were conducted using Spearman rank-order correlations.

Results

AIMS scores were elevated (0.43 ± 1.6) in the schizophrenia patients compared to the other psychoses (0.25 ± 1). We found the rate of involuntary movements (score of 1 or more on any of the anatomical item of AIMS) to be 10.49% in the subset of 162 patients with first-episode Schizophrenia, which contrasts with 6.25% in the group with other Psychoses. No correlation was found between the AIMS scores and the positive symptoms ($\rho = 0.11$, $p = 0.13$) or the neurological soft signs ($\rho = 0.92$, $p = 0.36$). The negative symptoms showed a strong correlation with the AIMS total score ($\rho = 0.24$, $p = 0.001$), which is in consonance with the results found in previous studies (5). The AIMS total score was positively correlated to the perseverative errors on the WCST, in those patients in whom ($n = 136$) the data were available ($\rho = 0.19$, $p = 0.04$). This correlation remained significant if only patients with a diagnosis of schizophrenia or schizoaffective disorder were included in the analyses ($\rho = 0.17$, $p = 0.047$).

We found increased AIMS scores in a small proportion of previously untreated patients with first-episode psychoses suggesting that IMs might be at least partially, a disease-induced state-dependent change, independent of the effect of antipsychotic medications. AIMS scores were correlated with negative symptoms (but not positive symptoms) consistent with

prior literature (9); a novel observation is that IMs correlated with increased perseverative errors on the WCST. The perseverative errors in the WCST and their relationship to IMs (albeit small but significant) point towards the possible involvement of the prefrontal and striatal structures (which are implicated in the executive function deficits) in the pathogenesis of the IMs in psychotic disorders.

The strengths of this study include a relatively large sample of minimally treated patients with first-episode psychosis who were well characterised with psychopathologic and neurocognitive assessments. However, our study was limited by the absence of AIMS data in a group of well-matched controls. Future studies need to confirm these observations and systematically examine the relationship between IMs and neurobiological indices of frontostriatal pathology in the early course of psychiatric disorders.

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