

## Correspondence

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### Letter to the Editor

#### **Movement disorders should be a criterion for schizophrenia in DSM-V**

Movement disorders are common in schizophrenia. The relationship between psychosis and spontaneous movement disorders was established more than a century ago. Bleuler and Kraepelin in particular made meticulous descriptions of dyskinesia, dystonia, and parkinsonism in patients with psychosis (Bleuler, 1916).

After the introduction of antipsychotics, there was a revival of interest in movement disorders, first in acute syndromes such as parkinsonism, and later in the tardive syndromes as well, particularly in tardive dyskinesia. Since most psychiatric publications about movement disorders focused on movement disorders related to antipsychotics, the DSM-IV-TR classified tardive dyskinesia and parkinsonism under medication-induced movement disorders, thereby dismissing the link between movement disorders and schizophrenia identified by the 'founders' of the psychiatric disease classification before the advent of antipsychotics.

Recently Papa & Dazzan (2009), in their excellent meta-analysis, have rekindled the notion that antipsychotic-naive patients with first-episode schizophrenia display dyskinesia and parkinsonian symptoms. Their study strongly suggests that movement disorders are pathogenetically related to psychosis and schizophrenia. Our group published another meta-analysis on movement disorders in antipsychotic-naive patients, their non-ill first-degree family members, and a healthy control group. Consistent with Papa & Dazzan's analysis, we found that dyskinesia was closely associated with schizophrenia and parkinsonism compared to healthy controls. Moreover, first-degree family members displayed more dyskinesia and parkinsonian signs than the healthy control group, a finding which corroborates that these symptoms are genetically related to schizophrenia (Koning *et al.* 2008).

The relationship between schizophrenia and movement disorder is consistent. This suggests that deliberation about whether to make movement disorders a criterion in the classification of schizophrenia and consequently about whether to add them in the next edition of DSM is in order.

Criteria for psychiatric illnesses are usually selected on the basis of an adequate prevalence base rate and of inter-rater reliability. Although there is no specific DSM agreed-upon minimum base rate for inclusion as a criterion, a minimum prevalence rate of around 10% is suggested; more than 30–40% is ideal (Widiger, 1994). In schizophrenia, high prevalence rates are found for A criteria such as delusions and hallucinations, but not for A criteria such as formal thought disorder, catatonic behaviour, and abnormalities in affect are far less common and their prevalence may be in the same range as those reported for movement disorders in both meta-analyses (John *et al.* 2003; Koning *et al.* 2008; Pappa & Dazzan, 2009). Furthermore, several studies, in which movement disorders were measured instrumentally, have found a higher prevalence than studies using clinical rating scales. These instrumental measurements in antipsychotic-naive patients with schizophrenia report prevalence rates of 13–20% for dyskinesia and 18–28% for parkinsonian signs, respectively, rates which approach the ideal base rate for an A criterion (Cortese *et al.* 2005).

Other than an adequate base rate, aspects such as (i) predictive value, (ii) a biological basis, or (iii) the specificity of the symptom add to the value of a criterion.

With regard to the predictive value, only in schizophrenia and possibly schizotypal personality disorder do antipsychotic-naive patients exhibit movement disorders. To our knowledge, there are no reports of movement disorders in patients with other psychiatric diseases who were naive for agents with D<sub>2</sub> antagonistic properties. (Neurological disorders such as Huntington's, Morbus Parkinson's, and Wilson's diseases, in which dyskinetic and parkinsonian symptoms are present, must be ruled out.) Dyskinetic symptoms may also be present in older people in the general population but this should not negatively impact on their predictive value because the diagnosis of schizophrenia typically takes place in early adulthood.

The biological origin of schizophrenia and movement disorders is likely to reside in a shared dysfunction in the dopamine system. Despite the fact that schizophrenia exhibits a wide clinical variability and heterogeneous genetic architecture, dysfunction in the dopamine system seems to be the final common pathway (Howes & Kapur, 2009). A twin study reported that the unaffected co-twins of patients had increased caudate D<sub>2</sub> density compared to healthy twin-pair controls, a finding that implies that D<sub>2</sub>

receptor up-regulation is related to the liability for schizophrenia (Hirvonen *et al.* 2005). Similarly, in respective SPECT and PET studies of patients with schizophrenia receiving antipsychotic therapy, evidence indicated that a subgroup of patients with D<sub>2</sub> receptor up-regulation may be characterized by pronounced parkinsonism, poor drug response (Schroder *et al.* 1998), and the development of tardive dyskinesia (Silvestri *et al.* 2000)

Another factor that supports the inclusion of movement disorders in antipsychotic-naive patients with schizophrenia as an A criterion for schizophrenia is that it is highly specific. All other DSM criteria of schizophrenia are non-specific and non-pathognomic, i.e. many symptoms are also prevalent in affective disorders.

A more practical advantage for including movement disorders as an A criterion is the ease with which dyskinesia and parkinsonian signs are assessed: no interview or extensive testing is required, merely a short physical examination. Furthermore, if instrumental measurement is used, inter-rater reliability is excellent without the necessity of extensive training (Cortese *et al.* 2005)

In conclusion, the sufficient base rate and the reliability, especially with instrumental measurements, combined with its predictive value and specificity, all suggest that movement disorders, should be an A criterion for schizophrenia.

#### Declaration of Interest

None.

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#### The authors reply

Spontaneous abnormal movements are part of a neurodysfunction intrinsic to the pathogenesis of schizophrenia (Pappa & Dazzan, 2009). In their letter, Van Harten and Tenback suggest that spontaneous movement disorders should be included as a criterion (A) for the diagnosis of schizophrenia in the next edition of DSM, on the basis of their adequate prevalence, reliability, predictive value and specificity. Indeed, movement disorders have been extensively documented in schizophrenia, and a proportion of abnormal movements, such as spontaneous dyskinesia and parkinsonism, are evident even before exposure to antipsychotic treatment (Torrey, 2002). Moreover, the prevalence of spontaneous dyskinesia and parkinsonism when measured electromechanically is even higher than that based on qualitative clinical,

observer-based evaluations (Caligiuri *et al.* 1993; Cortese *et al.* 2005). Finally, as suggested by Van Harten and Tenback, such motor abnormalities seem to be specific to schizophrenia. This body of evidence would suggest that spontaneous movement disorders may be intrinsic to the pathophysiology of schizophrenia and that antipsychotic medication may be acting by modifying the expression of disease-based motor dysfunctions (Pappa & Dazzan, 2009). On this basis, we would concur with the principles underpinning Van Harten and Tenback's proposal that movement disorders should be considered among criteria A for the diagnosis of schizophrenia. There are, however, factors that could potentially compromise the use of spontaneous movement disorders as a diagnostic criterion for schizophrenia in routine clinical practice. One of the main factors is that, to be of diagnostic utility, the evaluation should occur in antipsychotic-naive patients. However, in practice the majority of patients with psychotic symptoms presenting to health services is exposed to antipsychotic medication even at the very early illness stages, and this would significantly limit the application of movement disorders as a diagnostic criterion. Moreover, this patient group is frequently treated for a mood disorder before a diagnosis of schizophrenia or another psychosis is made. Drugs such as lithium, SSRIs and other antidepressants, can contribute to the development of parkinsonism and dyskinesia, thus confounding the clinical picture (Leo, 1996; Jiménez-Jiménez *et al.* 1997; Konitsiotis *et al.* 2005). Another potential limitation is that rates of spontaneous dyskinesia and parkinsonism are relatively low in patients with first-episode psychosis. Our review suggests a spontaneous dyskinesia median rate of 9% and a spontaneous parkinsonism median rate of 17% in this population (Pappa & Dazzan 2009). As Van Harten and Tenback rightly suggest, studies in which movement disorders are measured instrumentally have found a higher prevalence. However, the application of automated measures in a routine clinical setting in the evaluation of spontaneous movement disorders may prove troublesome. Finally, while the clinical assessment of spontaneous movement disorders is relatively easy, and the inter-rater reliability is satisfactory, there is unfortunately a lack of consensus around definitions of movement disorders, around the most appropriate scales, or around the operational criteria. So far, a variety of instruments have been used to evaluate abnormal movements and different threshold criteria for case definition applied across studies, often making the evaluation and interpretation of findings difficult. More work would need to be done in this area to achieve a consensus, if movement disorders were to be included as a diagnostic criterion.

The presence of spontaneous and drug-induced

movement disorders in patients with schizophrenia constitutes a complex and heterogeneous phenomenon. The inclusion of spontaneous movement disorders as a criterion A in schizophrenia is conceptually valid, but the reasons outlined above suggest it might be impractical in clinical practice and/or pragmatically limited to a minority of patients. Nevertheless, the evaluation and physical examination of spontaneous movement disorders should form an integral part of the clinical assessment of patients with psychosis and schizophrenia as it provides valuable information for the diagnostic formulation, enhances our understanding of the pathogenesis of the illness and its clinical presentation, and may well have significant treatment implications.

#### Declaration of Interest

None.

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