Spontaneous dyskinesia and parkinsonism in never-medicated, chronically ill patients with schizophrenia: 18-month follow-up

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Background Spontaneous dyskinesia and parkinsonism have been reported in never-medicated patients with schizophrenia but there has been no previous study of the natural history of these conditions.

Aims To determine the prevalence of spontaneous dyskinesia and parkinsonism in a group of never-medicated, chronically ill patients with schizophrenia on two occasions separated by an 18-month interval.

Method Dyskinesia was assessed by the Abnormal Involuntary Movements Scale using Schooler and Kane criteria for its presence; parkinsonism by the Simpson and Angus scale; and mental state by the Positive and Negative Syndrome Scale for schizophrenia.

Results Thirty-seven patients were examined on two occasions. Nine (24%) had dyskinesia on both occasions, 12 (33%) on one occasion and 16 (43%) on neither occasion. Twenty-one (57%) had dyskinesia on at least one occasion. Thirteen patients (35%) had parkinsonism on at least one occasion.

Conclusions Spontaneous dyskinesia and parkinsonism fluctuate over time. The former was found on at least one occasion in the majority of patients. It is an integral part of the schizophrenic disease process.

Declaration of interest None.

In a series of studies in south India (McCreadie *et al*, 1996, 1997, 2002) it was found that spontaneous dyskinesia, indistinguishable from 'tardive' dyskinesia, and parkinsonism are common in chronically ill, never-treated patients with schizophrenia living in south India. We abandoned attempts to assess akathisia, because the language spoken by villagers in south India, Tamil, does not clearly differentiate 'tension' from 'restlessness'. We have now examined 143 never-treated patients; the prevalence of dyskinesia was 35% and parkinsonism 15% (details available from the author upon request). These studies were cross-sectional. We now report the natural history of these abnormal movements through an 18-month follow-up study of patients who remained untreated. The study was designed to answer the following question: do spontaneous dyskinesia and parkinsonism persist, or do they fluctuate over time as do the milder forms of tardive dyskinesia (Bergen *et al*, 1989)?

METHOD

Patients

The study was conducted at the Schizophrenia Research Foundation, India (SCARF), a voluntary organisation involved in research and in the rehabilitation of people with schizophrenia in Chennai (Madras), south India. Patients live in the city, its suburbs and in outlying villages. Most are identified through outreach services, while others are recruited through the out-patient centre of SCARF, located in the city, and from the private consultation facility of the authors (R.T., R.P., T.N.S.), also located in the city. All patients fulfil DSM–IV criteria for schizophrenia (American Psychiatric Association, 1994). The diagnosis is made through mental state examination and history obtained from patients and relatives, and from case records where available. All patients and families who participate give consent.

The patients' lifetime exposure to medication is determined from a number of sources which include discussion with patients and relatives, and examination of case records and prescription sheets. None of our 'never-treated' patients had ever received antipsychotic medication. We also confirm that patients had not received any treatment from practitioners of indigenous systems of medicine. As we reported earlier (McCreadie *et al*, 1996), taking medication is an important and often expensive event in the lives of these patients and their families. We are confident of the accuracy of the medication histories. The participants in this study were drawn from a group of 108 patients who were assessed for a magnetic resonance imaging study (McCreadie *et al*, 2002). Attempts were made to trace and reassess these patients 18 months later.

Assessment

Dyskinesia at first assessment and follow-up was measured by the Abnormal Involuntary Movements Scale (AIMS), which examines seven areas of the body (US Department of Health, Education and Welfare, 1976). Dyskinesia was defined as probably present (Schooler & Kane, 1982) if movements were 'mild' in at least two areas, or 'moderate' in at least one. Parkinsonian symptoms were measured by the Simpson and Angus scale (Simpson & Angus, 1970); parkinsonism was defined as present if the mean score was greater than 0.3. One psychiatrist (R.G.M.) carried out all assessments of movement disorder with the help of an interpreter as required. He was blind to age at onset and duration of illness, mental state assessments (see below) and, at follow-up, to the assessment of movement disorders 18 months previously. The patients' mental state was assessed using the Positive and Negative Syndrome Scale (PANSS) for schizophrenia (Kay *et al*, 1987) by three of us (R.T., R.P., T.N.S.) trained in the use of the instrument and blind to the first assessment. This scale gives a total score, and scores on positive, negative and general psychopathology sub-scales.

Ethical considerations

Many untreated patients assessed by SCARF remain untreated, owing to their refusal of the offer of free antipsychotic medication.

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There is no question of compulsory administration of psychotropic medication in community-dwelling patients.

RESULTS

Patients

At follow-up, of the 108 patients assessed 18 months previously, 8 were dead and 36 had received antipsychotic medication. Twenty-seven could not be traced, even though letters were sent and home visits made; these patients lived in the city, most of them in the slum areas. Thirty-seven patients remained untreated and were reassessed. Of this group, 16 (43%) were men and 21 (57%) women. Their mean age was 52 years (s.d. 13 years, range 20–72 years) and the mean length of illness (estimated from the first appearance of psychotic symptoms) was 17 years (s.d. 8 years, range 4–32 years).

The patients who were reassessed did not differ from the others in gender distribution or in numbers with dyskinesia at first assessment. However, those reassessed were older: mean age 52 (s.d. 13) years *v.* 38 (s.d. 15) years, $t=3.45$, d.f.=106, $P=0.008$; had been ill longer: mean 17 (s.d. 8) years *v.* 7 (s.d. 7) years, $t=4.93$, d.f.=106, $P<0.0001$; and had lower scores on the PANSS general psychopathology sub-scale: mean 23 (s.d. 11) *v.* 29 (s.d. 11), $t=2.69$, d.f.=106, $P=0.008$.

Dyskinesia

Dyskinesia, defined by Schooler and Kane criteria, was present in 17 (46%) patients at first assessment and in 13 (35%) at follow-up. Nine patients had dyskinesia on both occasions; 8 at first assessment but not at follow-up; 4 at follow-up but not at first assessment; 16 did not have dyskinesia on either occasion. Therefore 21 (57%) had dyskinesia on at least one occasion. When those who had dyskinesia on both occasions ($n=9$) were compared on social, demographic and clinical findings to those who had dyskinesia on neither occasion ($n=16$), the only significant between-group difference was that patients with dyskinesia had higher scores on the follow-up rating of parkinsonism (mean 0.41 (s.d. 0.37) *v.* 0.12 (s.d. 0.29); $t=2.19$, d.f.=21, $P=0.04$).

Parkinsonism

Parkinsonism symptoms were not assessed in 3 patients at first assessment and another 3 at follow-up. Parkinsonism was present in 7 (21%) patients at first assessment and in 12 (35%) at follow-up. Five patients had parkinsonism on both occasions; 2 at first assessment but not at follow-up; 6 at follow-up but not at first assessment; 17 did not have parkinsonism on either occasion. Therefore 13 of the 37 patients (35%) had parkinsonism on at least one occasion.

Mental state assessment

When the PANSS scores at first assessment and follow-up were compared, there was no significant change in mean positive and negative symptom sub-scale scores. Mean scores on general psychopathology and total scales decreased, indicating an improvement in mental state: paired *t*-test, mean total score 61 (s.d. 19) *v.* 52 (s.d. 16), $t=2.49$, d.f.=36, $P=0.02$. There was no significant correlation between scores at first assessment and at follow-up on positive, general psychopathology and total scales. There was a significant correlation in negative symptom sub-scale scores (Pearson's $r=0.45$, $P=0.006$).

There was no significant correlation between, on the one hand, change in total scores on the AIMS between first assessment and follow-up, and, on the other hand, change in either parkinsonism, positive symptom, negative symptom, general psychopathology or total PANSS scores (Pearson's r ranged from 0.08 to 0.27).

DISCUSSION

Of the 108 patients originally identified, only 37 were reassessed. However, 75% were traced in what is a constantly changing, large Indian city. The fact that 36 patients were not reassessed as they had agreed to take antipsychotic medication is not a drawback but a probable health gain. The patients who were reassessed were older and had been ill longer. Our findings therefore may not be generalisable to all chronically ill, never-treated patients.

Dyskinesia

The finding that more than half of the patients had dyskinesia on at least one occasion supports our view that dyskinesia is an integral part of the disease process. We have recently gone further by proposing on the basis of magnetic resonance imaging findings (McCreadie *et al*, 2002) that there may be a subgroup of schizophrenia associated with dyskinesia and striatal pathology (namely, an enlarged lenticular nucleus, especially on the left side).

Of interest is the group of 12 patients in whom dyskinesia was present on one occasion only. This suggests that spontaneous dyskinesia may fluctuate over time. It has long been known that tardive dyskinesia, especially in its milder forms, shows temporal fluctuations (Bergen *et al*, 1989).

In our original study (McCreadie *et al*, 1996) we examined elderly patients in whom the prevalence of spontaneous dyskinesia was found to be 38%. We therefore suggested that antipsychotic drugs did not cause tardive dyskinesia, but rather brought forward in time a phenomenon that would occur inevitably when the illness had been present for decades, rather than years. We may need to revise that view, as in the present study more than half the group had dyskinesia even though they were not particularly elderly (mean age 52 years). It may be that spontaneous and tardive dyskinesia are indeed aetiologically different but phenomenologically similar. In this context it is noteworthy that we have recently found an excess of a dopamine D3 receptor gene variant in patients with tardive dyskinesia in Scotland (Steen *et al*, 1997) but not in never-treated patients with spontaneous dyskinesia in India (Løvlie *et al*, 2000). It may also be that what is taken to be 'tardive dyskinesia' in treated younger patients is in fact spontaneous dyskinesia, raising the question posed by Crow *et al* (1983): does tardive dyskinesia exist?

Parkinsonism

Parkinsonism was present in about a third of our patients on at least one occasion. As with dyskinesia, it fluctuated over time. The Simpson and Angus scale places considerable emphasis on rigidity. It was this rather than tremor that was most obvious in our patients; the latter was found in only 3 patients and was rated as mild. Patients with spontaneous dyskinesia had higher parkinsonism scores than those without dyskinesia; that is, there is probably an association between the two movement disorders, a finding similar to that in our larger study of 143 patients (details available from the author upon request).

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Over the 18 months between assessments not only did spontaneous dyskinesia and parkinsonism fluctuate, so also did the patients' mental state as measured by the positive and general psychopathology sub-scales of the PANSS. There was less change in negative symptoms. The fluctuations in different aspects of the illness appeared to be independent of each other.

Other studies of spontaneous dyskinesia and parkinsonism

Data from 14 studies of never-treated patients with schizophrenia were used to generate age-adjusted estimates of the prevalence of spontaneous dyskinesia (Fenton, 2000). Rates of 25% for those aged 30–50 years and 40% for those aged 60 years or older were estimated; these rates are similar to our follow-up rate of 35%. Apart from the present study, we know of no other longitudinal study of spontaneous dyskinesia.

Spontaneous parkinsonism has been described in never-treated patients experiencing their first episode of schizophrenia; prevalence rates have ranged from 4% (Puri *et al*, 1999) through 17% (Chatterjee *et al*, 1995) to 21% (Caligiuri *et al*, 1993). We know of no other reports, apart from our own, of parkinsonism in chronically ill, never-treated patients, from either cross-sectional or longitudinal studies.

We conclude that our findings in this longitudinal study provide further evidence that movement disorders, both dyskinesia and parkinsonism, are an integral part of the schizophrenic disease process. Our magnetic resonance imaging study (McCreadie *et al*, 2002) has suggested that there may be structural differences, namely striatal abnormalities, between the brains of those with and without spontaneous dyskinesia, and normal brains.

CLINICAL IMPLICATIONS

- Dyskinesia and parkinsonism are an integral part of the schizophrenic illness.
- Dyskinesia and parkinsonism in people with schizophrenia are not necessarily drug-related.
- The presence of dyskinesia and parkinsonism fluctuates over time, independently of changes in mental state.

LIMITATIONS

- Only a third of the patients originally identified were re-examined 18 months later.
- The patients re-examined were in the main middle-aged. Patterns of dyskinesia and parkinsonism may be different in younger people with schizophrenia.
- The scale used to assess parkinsonism gives great emphasis to rigidity.

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