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Abnormal Movements in Never-Medicated Indian Patients with Schizophrenia

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Background. Historical records suggest dyskinesia was observed in severely ill institutionalised patients with schizophrenia in the pre-neuroleptic era. More recent work has not found dyskinesia in never-medicated younger and middle aged patients. The present study complements this recent work and avoids the confounders of severity of illness and institutionalism by examining elderly patients in a wide variety of community settings.

Method. Movement disorders were examined in 308 elderly individuals in Madras, India, using the Abnormal Involuntary Movements Scale, the Simpson and Angus Parkinsonism Scale and the Barnes Akathisia Scale. Patients' mental state was assessed by the Positive and Negative Syndrome Scale.

Results. Dyskinesia was found in 15% of normal subjects (n=101, mean age 63 years), 15% of first degree blood relatives of younger schizophrenic patients (n=103, mean age 63 years), 38% of never medicated patients (n=21, mean age 65 years) and 41% of medicated patients (n=83, mean age 57 years). The respective prevalences for Parkinsonism were 6%, 11%, 24% and 36%; and for akathisia 9%, 5%, 21% and 23%. Dyskinesia was associated with negative schizophrenic symptoms.

Conclusions. Dyskinesia in elderly schizophrenic patients is an integral part of the illness and not associated with antipsychotic medication.

Kraepelin (1919), over 30 years before the introduction of antipsychotic medication, wrote:

> "the *spasmodic phenomena* in the musculature of the face and of speech which often appear are extremely peculiar disorders. Some of them resemble movements of expression, wrinkling of the forehead, distortion of the corners of the mouth, irregular movements of the tongue and lips, twisting of the eyes, opening them wide and shutting them tight, in short those movements which we bring together under the name of making faces or grimacing; they remind one of the corresponding disorders of choreic patients".

Such a description today would be taken for tardive dyskinesia (TD), considered a side-effect of antipsychotic drugs. More recent retrospective examination of case records of patients admitted to hospital in the pre-neuroleptic era found 15% had 'orofacial dyskinesia' (Fenton *et al*, 1994) and 28% 'movement disorders' (Turner, 1989). However, in a study from Morocco (Chorfi & Moussaoui, 1985) using the Abnormal Involuntary Movements Scale (AIMS) (U.S. Department of Health, Education and Welfare, 1976) no evidence of abnormal movements was found in never-medicated young schizophrenic patients (mean age 24 years, ill on average for 11.8 months). Also, in a study from Nigeria (McCreadie & Ohaeri, 1994), again using the AIMS, no evidence of abnormal movements was found in never-medicated middle-aged schizophrenic patients (mean age 42 years, ill on average for 12 years). In contrast, in a study from England abnormal movements were found in 53% of never-medicated elderly schizophrenic patients (mean age 67 years) (Owens *et al*, 1982). There are two principal differences between the studies that have and have not found movement disorders in never-medicated patients. Firstly, the former probably examined severely ill patients and are thus not representative of the whole range of schizophrenic patients. Secondly, those patients in the main were institutionalised; it has been suggested institutionalised patients have higher prevalence rates of 'spontaneous' dyskinesia (Casey & Hansen, 1984). However, disentangling institutionalism from severity of illness is difficult.

The present study complements the recent studies of young and middle aged patients by examining elderly schizophrenic patients. It avoids the two possible confounders of severity of illness and institutionalism by examining patients drawn from a wide range of community settings. It also compares the prevalence of movement disorders in

never-medicated with medicated patients, first degree blood relatives of schizophrenic patients and normal subjects.

Method

Background

The study was carried out in and around Madras in south east India. The principal language is Tamil, although many people also speak English. The population of Madras is nearly 5 million. There are about 120 psychiatrists, some working in state-run hospitals and the rest in private practice. There is one psychiatric hospital (1800 beds) serving the whole state (population 57 million) and three small in-patient units in general hospitals. In state-run hospitals which cater predominantly for lower socio-economic classes, antipsychotic medication is prescribed by the psychiatrist and supplied free. In other cases it is available only on prescription and has to be paid for. There are also a few non-governmental organisations catering to the needs of the mentally ill. One of them is the Schizophrenia Research Foundation (SCARF, India) which specialises in research and community care of schizophrenic patients.

Patients

Patients were recruited from a variety of settings: (1) out-patients and day patients attending the SCARF centre in Madras city; (2) in-patients in a short stay rehabilitation unit, run by SCARF on the outskirts of Madras; (3) attenders at a day centre run by families of schizophrenic patients; (4) residents of three homes for the elderly, one in the slums of Madras, two in the suburbs; (5) out-patients at a rural outreach facility, run by SCARF 40 km south of Madras; (6) out-patients attending psychiatrists in private practice. The minimum age for inclusion was 50 years. All patients fulfilled DSM–IV criteria for schizophrenia (American Psychiatric Association, 1994). The diagnosis was made through mental state examination (see below) and history obtained from patients, relatives and case records where available.

Control subjects

There are two types of control subjects: firstly, first degree blood relatives of schizophrenic patients; these were mainly fathers and mothers of younger schizophrenic patients attending facilities (1), (3) and (5) (see above). Secondly, normal subjects were recruited: these were husbands and wives of schizophrenic patients; day attenders and residents at facility (4) and who were not mentally ill; staff at (1), (2) and (4); and community mental health workers attached to (5). Again the minimum age for inclusion was 50 years.

Assessment

Dyskinesia in patients and control subjects was assessed by the Abnormal Involuntary Movements Scale (AIMS), Parkinsonism by the Simpson & Angus Scale (Simpson & Angus, 1970) and akathisia by the Barnes Akathisia Scale (Barnes, 1989). All assessments of movement disorders were carried out by one psychiatrist (RGMcC) who was blind to the medication status of patients and, in the vast majority of cases, blind also as to who was a patient and who a control subject. Assessments where necessary were carried out with the help of an interpreter (SL). The patient's mental state was assessed by the Positive and Negative Syndrome Scale (PANSS; Kay *et al*, 1987) by three psychiatrists (RT, SK, RP) who were fluent in both Tamil and English and who had been trained in the use of the scale for a multi-centred drug study.

Medication

The patients' lifetime exposure to antipsychotic medication was determined through discussion with patients and relatives, and examination of case records and prescription sheets. Taking antipsychotic medication is an important, and often expensive event in the lives of schizophrenic patients and their relatives in Madras. We are satisfied that accurate medication histories were obtained, especially in the case of those who had never had such medication. The latter were drawn mainly from the slums and from the rural outreach centre (see above).

Other information

The following additional information about patients and control subjects was recorded: age, gender, marital status; and for patients, age of onset of illness, and length of illness.

Results

In all, 308 individuals were assessed: 21 never-medicated patients, 83 medicated patients, 103 relatives and 101 normal subjects. Table 1 shows social, demographic and clinical data. Medicated patients were significantly younger than the other three groups (analysis of variance: $F=12.94$, $P<0.0001$). Never-medicated patients had higher

Table 1
Demographic, social and clinical data

	Normal subjects (n=101)	Relatives (n=103)	Never-medicated patients (n=21)	Medicated patients (n=83)
Gender				
Male	47 (47%)	50 (48%)	9 (43%)	39 (47%)
Female	54 (53%)	53 (52%)	12 (57%)	44 (53%)
Age (years)				
Mean (s.d.)	63 (8)	63 (8)	65 (8)	57 (6)
Marital status				
Single	10 (10%)	4 (4%)	1 (5%)	6 (7%)
Married	67 (66%)	72 (70%)	14 (67%)	58 (70%)
Widowed	20 (20%)	24 (23%)	4 (19%)	12 (15%)
Divorced/separated	4 (4%)	3 (3%)	2 (9%)	7 (8%)
Duration of illness (years)				
Mean (s.d.)	–	–	14 (11)	19 (11)
<5 years	–	–	8 (38%)	15 (18%)
5–10 years	–	–	2 (10%)	6 (7%)
>10 years	–	–	11 (52%)	62 (75%)
PANSS scores (mean (s.d.))				
Positive symptoms	–	–	17.6 (7.1)	11.1 (4.9)
Negative symptoms	–	–	12.6 (7.1)	14.4 (6.0)
General psychopathology	–	–	23.7 (5.0)	23.2 (10.6)

Table 2
AIMS assessment of dyskinesia in patients and control subjects

	Normal subjects (n=101)	Relatives (n=103)	Never-medicated patients (n=21)	Medicated patients (n=83)
Schooler & Kane criteria				
Dyskinesia	15 (15%)	15 (15%)	8 (38%)	34 (41%)
No dyskinesia	86 (85%)	88 (85%)	13 (62%)	49 (59%)
Global assessment				
Absent	77 (76%)	72 (70%)	8 (38%)	31 (37%)
Minimal	7 (7%)	8 (8%)	4 (19%)	10 (12%)
Mild	15 (15%)	21 (20%)	5 (24%)	23 (28%)
Moderate	2 (2%)	1 (1%)	3 (14%)	15 (18%)
Severe	–	1 (1%)	1 (5%)	4 (5%)
Orofacial dyskinesia				
Mean score (s.d.)	0.96 (1.75)	1.17 (1.88)	2.91 (3.39)	2.84 (3.11)
Distal dyskinesia				
Mean score (s.d.)	0.12 (0.52)	0.17 (1.13)	0.43 (0.81)	0.66 (1.70)

PANSS scores for positive symptoms when compared with medicated patients ($t=4.94$, $P<0.0001$).

Table 2 shows various AIMS ratings for the four groups: the presence of dyskinesia as defined by Schooler & Kane criteria (Schooler & Kane, 1982), that is, dyskinesia was present if movement disorders were rated as 'moderate' in at least one or 'mild' in at least two of the seven individual areas assessed; global assessment; and scores separately for orofacial and distal dyskinesia. It can be seen that the prevalence of dyskinesia as assessed by Schooler & Kane criteria is very similar in never-medicated and medicated patients (38% and 41% respectively), and that it is significantly higher in patients when compared with relatives (15%) and normal controls (15%) ($\chi^2=26.0$, d.f.$=3$, $P<0.0001$). The severity of dyskinesia, as assessed by the global scale, was greater in patients than in

controls (22% and 1% respectively had moderate or severe dyskinesia: $\chi^2 = 38.0$, d.f. = 1, $P < 0.0001$). There were no significant differences in the severity of orofacial and distal dyskinesia between never-medicated and medicated patients, but orofacial dyskinesia was more severe in patients than in controls (analysis of variance: $F = 10.56$, $P < 0.05$).

As medicated patients were significantly younger than the other three groups a further analysis was carried out only in those aged over 60 years. The prevalence of dyskinesia in normal subjects ($n = 57$), relatives ($n = 53$), medicated patients ($n = 23$) and never-medicated patients ($n = 14$) was respectively 21%, 28%, 43% and 43% (patients *v.* normals: $\chi^2 = 3.8$, d.f. = 1, $P = 0.05$).

Patients with and without dyskinesia were compared on the basis of gender, age, length of illness, total length of time on antipsychotic medication and PANSS ratings; and control subjects with and without dyskinesia on gender and age (Table 3). The only significant differences were that normal subjects and relatives with dyskinesia were older than those without dyskinesia (normals: $t = 4.3$, $P < 0.0001$; relatives: $t = 3.8$, $P = 0.0002$); that more medicated patients with early onset schizophrenia (ill more than 10 years) had dyskinesia compared with late onset patients (ill less than five years) ($\chi^2 = 4.1$, d.f. = 1, $P = 0.04$); and that medicated patients with dyskinesia had more severe negative symptoms than those without dyskinesia ($t = 2.7$, $P = 0.009$) (a similar difference in never-medicated patients was not statistically significant).

Four of the 103 relatives were in fact relatives of patients in the study. One relative but not the corresponding patient had dyskinesia; one patient but not the relative had dyskinesia; and two patients and their relatives had no dyskinesia.

Parkinsonism, defined as a score of more than 0.3 on the Simpson & Angus scale, was present in 6% of normal subjects, 11% relatives, 24% never-medicated patients and 36% medicated patients ($\chi^2 = 34.1$, d.f. = 3, $P < 0.0001$). Within the never-medicated group the prevalence of dyskinesia in those with Parkinsonism was similar to that in those without Parkinsonism. Of those in the never treated group with Parkinsonism ($n = 5$) all had rigidity but only one had a tremor. Akathisia, defined as a score of at least 2 on the global scale, was found in 9% of normal subjects, 5% relatives, 21% never-medicated patients, and 23% medicated patients ($\chi^2 = 17.2$, d.f. = 3, $P = 0.0006$). Only three patients, all on medication, had objective evidence of akathisia.

Discussion

Western readers may be surprised that a minimum age of 50 years was chosen to define the 'elderly'.

Table 3
Patients and control subjects with and without dyskinesia

	Normal subjects (n=101)		Relatives (n=103)		Never-medicated patients (n=21)		Medicated patients (n=83)	
	Dyskinetic subjects (n=15)	Non-dyskinetic subjects (n=86)	Dyskinetic relatives (n=15)	Non-dyskinetic relatives (n=88)	Dyskinetic patients (n=8)	Non-dyskinetic patients (n=13)	Dyskinetic patients (n=34)	Non-dyskinetic patients (n=49)
Gender								
Male	3	44	7	43	3	6	17	22
Female	12	42	8	45	5	7	17	27
Age (years)								
Mean (s.d.)	72 (11)	62 (7)	70 (7)	62 (8)	69 (8)	63 (8)	58 (7)	56 (5)
Length illness (years)								
Mean (s.d.)	–	–	–	–	13 (13)	14 (9)	19 (10)	18 (12)
<5 years	–	–	–	–	4	4	2	13
5–10 years	–	–	–	–	0	2	4	2
>10 years	–	–	–	–	4	7	28	34
Length of time on medication (years)								
Mean (s.d.)	–	–	–	–	–	–	11 (9)	11 (10)
PANSS scores (mean (s.d.))								
Positive symptoms	–	–	–	–	18 (8)	18 (7)	11 (5)	11 (5)
Negative symptoms	–	–	–	–	15 (10)	11 (5)	16 (6)	13 (5)
General psychopathology	–	–	–	–	26 (7)	23 (3)	23 (7)	21 (6)

However, average life expectancy in India is 58 years. If we had chosen a minimum age of, say, 65 years, adequate recruitment of both controls and patients would have been impossible. Elderly treated schizophrenic patients were the most difficult to find; only two of the 83 patients were aged over 70 years. Schizophrenic patients in the West die earlier than normal subjects (Morgensen & Juel, 1990); the same may well be true in India.

General impressions

We comment below on the significance of the AIMS results. However, quantitative scores can not describe adequately the movement disorders shown by the patients, especially those who had never had antipsychotic medication. Repeatedly, when the rater who assessed movement disorders (RGMcC, a psychiatrist who has personally carried out more than 1500 ratings using the AIMS scale) was told afterwards that a patient had never had medication, he said, "It was just like classic TD". By this he meant, for example, chewing movements, pursing and smacking of the lips, and writhing movements and protrusion of the tongue. A follow-up is planned and we hope then to make video-recordings.

Interpretation of findings

The prevalence of dyskinesia in control subjects, 15%, is similar to that found in other studies of normal elderly subjects: 10% (Varga *et al*, 1982) and 18% (Bourgeois *et al*, 1980). There was no difference in the prevalence of dyskinesia in normal subjects and first degree blood relatives, mainly fathers and mothers of younger schizophrenic patients. Although presumably the relatives share many of the genes of their ill offspring, our findings suggest that the illness must become manifest before the prevalence of dyskinesia rises.

The prevalence and severity of dyskinesia was significantly greater in patients than in control subjects and dyskinesia was as common and as severe in never-medicated as in medicated patients. The medicated were younger than the never-medicated patients, but when only those aged over 60 years were considered, the prevalence of dyskinesia remained the same in both groups (43%) and significantly greater than in the control groups. We believe therefore that it is the illness *per se* and not antipsychotic medication that is associated with dyskinesia in elderly schizophrenic patients.

Two further factors within the patient groups were associated with dyskinesia. Firstly the type, or length of illness: those with early onset schizophrenia, ill for more than 10 years were more likely to show dyskinesia than those with late onset schizophrenia, ill for less than 5 years. Secondly, dyskinesia was associated with negative symptoms, an association statistically significant in medicated patients. This association has been shown before in most but not all studies (for a review, see Waddington, 1995).

Twenty-four per cent of never-medicated patients had Parkinsonism. This prevalence, lying between that of control subjects and medicated patients, is very similar to that in a previous study of newly diagnosed and never-medicated patients (21%; Caligiuri *et al*, 1993); that study found, as did ours, that rigidity was common, but tremor rare. Therefore muscle rigidity may also be a feature of the schizophrenic illness.

Akathisia was as common in never-medicated as in medicated patients and more common in patients than in control subjects. Akathisia as assessed by the Barnes scale has two components: an inner sense of restlessness and objective evidence of motor abnormalities. Only three patients, all receiving medication, had objective motor abnormalities. Our findings suggest an inner sense of restlessness may be a symptom of illness in some patients. However, our interpreter found it hard to convey to the patient the difference between restlessness and tension; she had a problem finding the appropriate equivalents for these terms in the Tamil language. It is possible therefore that some people may have been describing tension as part of anxiety rather than true akathisia.

Theoretical issues

How might dyskinesia be produced in elderly schizophrenic patients? The simplest explanation is that it is a non-specific effect of brain ageing or atrophy on the schizophrenic process. A more elaborate explanation (Davis *et al*, 1991; Fenton *et al*, 1994) invokes the current dopamine hypothesis which suggests that 'hypofrontality', low dopamine activity in the prefrontal cortex, may be associated with or indeed trigger increased dopamine activity in the striatal circuits of the mesolimbic system. It is suggested that the hypofrontal state is associated with negative symptoms and inferior cognitive performance and the hyperdopaminergic mesolimbic state is associated with positive psychotic symptoms and spontaneous dyskinetic movements. But why should dyskinesia be found in elderly but not in younger or middle aged patients? A possible explanation is that hypofrontality, which triggers off increased mesolimbic activity, only develops after many years of illness.

Conclusions

Our findings suggest that the illness of schizophrenia, measured perhaps in decades rather than years, is associated with dyskinesia and that this movement disorder is an integral part of the illness. We would suggest that antipsychotic medication brings forward in time a phenomenon, 'tardive dyskinesia', that would show itself in any case at a later stage of the illness. Our findings have medicolegal implications. If dyskinesia can occur in the absence of antipsychotic medication, then for any given individual, especially an elderly patient, it will be impossible to determine the specific cause of that movement disorder.

Clinical implications

- Dyskinesia occurs as frequently in elderly schizophrenic patients who have never received antipsychotic drugs as in medicated patients.
- Antipsychotic medication is not a risk factor for dyskinesia in elderly schizophrenic patients.
- Dyskinesia in the absence of antipsychotic medication has important medicolegal implications.

Limitations

- Rating scales such as the Abnormal Involuntary Movements Scale give quantitative but not qualitative information about dyskinesia.
- 'Elderly' individuals in India were defined as those aged over 50 years.
- Tamil speaking patients had difficulty in understanding the difference between the words 'restlessness' and 'tension'.

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