The clinical phenomenon of akathisia

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SUMMARY The subjective and motor phenomena of neuroleptic-induced akathisia were studied in two different populations of psychiatric patients. Thirty nine (41%) of 95 patients attending community psychiatric centres and psychiatric day hospitals experienced a compulsion to move about, and 52 (55%) complained of restlessness of the body. Of 842 psychiatric in-patients 159 found to have marked hyperkinesia were divided into three groups; group 1 with motor restlessness, and a subjective desire to move about or marching on the spot (27 patients), group 2 with choreo-athetotic movements and motor restlessness (79 patients) and an indeterminate group 3 (53), bearing more similarities to group 1 than group 2. Motor disturbances associated with akathisia were repeated leg crossing, swinging of one leg, lateral knee movements, sliding of the feet and rapid walking.

Akathisia was a term initially used by Haskovec to describe an unusual mental state in which there is an inability to remain seated and a compulsion to move about.¹ He considered this to be due to psychological causes, and anxiety and hysteria were postulated as aetiological factors. Sicard described a similar syndrome in idiopathic and post-encephalitic Parkinson syndrome.² Sigwald was probably the first to recognise drug-induced akathisia when using promethazine in 1947.³ It was frequently reported in the 1950–1960s following use of neuroleptic drugs, the descriptions being similar to Haskovec's spontaneously occurring cases.⁴

Akathisia is now recognised as the principal cause of acute or chronic anti-psychotic-induced motor restlessness, but it has not been precisely distinguished from acute and tardive dyskinesias.⁵ Its association with post-encephalitic Parkinson syndrome, idiopathic Parkinson's disease and anti-psychotic drug therapy suggests that it should be categorised with other extrapyramidal movement disorders, with which it frequently coexists. However the pathogenesis is unknown; the most plausible current hypothesis implicates a competitive blockade of mesocortical post-synaptic dopamine receptors.⁶

There is no consensus of opinion on a definition or on diagnostic features of the disorder, because of the variable association of the subjective and objective

components. Some investigators have restricted the term to a subjective feeling of restlessness,⁷ others believe this aspect to be of major importance,⁸ whereas most have considered objective evidence of restlessness to be the prime feature. However, it is accepted that its classical evolution, whether as an immediate or delayed side-effect of therapy, follows a similar pattern.⁹ In the early stages subjective, often poorly defined, mental unease predominates. Some patients describe feelings of mounting inner tension, discomfort, dysphoria, anxiety or restless feelings in the legs that precede and later accompany the compulsion to move about. Feelings of fear and rage may also be reported. As with some forms of motor restlessness this state of mental unease may be confused with that seen in anxiety or delirium. Restless repetitive movements of limbs and trunk ensue and these are ultimately followed by continuous monotonous pacing behaviour or treading on the spot. In the sitting and lying positions there may be shifting of the body position and purposeless repetitive movements of the legs and feet.

Akathisia has been described after preoperative medication¹⁰ or within hours of starting treatment,⁷ but more often it takes some weeks to emerge. Once established it tends to persist for many years, but only rarely outlasts the duration of therapy.^{11 12} Its intensity fluctuates and it can resolve despite continued therapy.

In the early stages objective phenomena are absent; some patients are incapable of verbally expressing their feelings, while others with late-onset or persistent akathisia do not experience subjective discom-

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fort. Recrudescence of an underlying psychosis may be precipitated,¹³ or non-compliance with therapy can result.^{14 15} Occasionally puzzling forms of hyperactivity can develop in mentally retarded individuals^{16 17} and aggressive forms of agitation are described in other patients.¹⁸

In practice a tentative diagnosis depends on observing one of the few characteristic behaviour patterns,¹⁹ which may or may not be linked to a verbal expression of mental restlessness. In patients who are unable to express their subjective feelings the diagnosis must depend on the motor behaviour alone. The possibility of akathisia should always be considered in unexplained hyperkinetic states or peculiar behavioural syndromes.

There are two main shortcomings in the delineation of akathisia. Firstly the absence of precise diagnostic criteria makes it difficult to identify patients suffering from mild akathisia. Secondly the limited nature of phenomenological descriptions leads to difficulty in separating the disorder from other neuroleptic-induced dyskinesias. The most exacting differential diagnoses are tardive dyskinesia affecting the limbs,

illness-related motor restlessness and the restless legs syndrome. We have carried out two separate studies. In the first we have analysed the subjective phenomena of akathisia in psychiatrically stable neuroleptic-treated individuals, and in the second the motor phenomena which distinguish it from other neuroleptic-induced dyskinesias.

Subjects and methods

Subjective aspects of motor restlessness were assessed by interview in 95 patients, (54 men and 41 women) aged 19–64 years, with schizophrenia and attending community psychiatric clinics or day hospitals at 2–4 weekly intervals for long-acting intramuscular neuroleptic injections; four other patients declined interview. All of them had attended the clinics for more than one year; 50 (52.6%) had required neuroleptic medication for over 10 years. None had required hospital admission in the previous year; all lived independently in the community and some were employed. The variety of intramuscular depot neuroleptics and their fortnightly equivalent doses were: fluphenazine decanoate (moderate) 25–100 mg, flupenthixol decanoate (depixol) 10–100 mg, clopenthixol decanoate (clonixol) 200–400 mg, haloperidol decanoate (haldol) 50–150 mg and fluspirilene 8 mg. Forty (42.1%) patients did not take anticholinergic drugs and 55 (57.9%) did. These were orphenadrine (50–300 mg daily), procyclidine (5–20 mg daily) or benzhexol (5–15 mg daily). In addition some patients took haloperidol (60 mg daily), chlorpromazine (250–1000 mg daily), trifluoperazine (8–30 mg daily) and lithium carbonate (800 mg). The other prescribed drugs were benzodiazepines and antidepressants; diazepam, flurazepam, lorazepam, amitriptyline and tranylcypromine. A questionnaire on aspects of motor restlessness was completed at an informal interview, which allowed a greater explanation of the questions and clarification of the answers, so that random answering and non-specific complaints were reduced to a minimum. The data were processed using the Statistical Package for the Social Sciences (SPSS). After validation, contingency tables were established for the different grades of outcome against the different values for the various parameters. The null hypothesis, that there was no relationship between each variable and outcome, was tested using a chi squared statistic. The results of this test were summarised as being significant if *p* was less than 0.05 for the null hypothesis and highly significant if *p* was less than 0.01.

The motor behaviour of 171 in-patients at Friern Hospital was also studied in the standard clinical setting of the psychiatric ward. These patients were selected from a total of 842 using two criteria; (1) in-patient psychiatric care in excess of one year and (2) the presence of prominent hyperkinetic movements. Patients with isolated choreic orofacial dyskinesia or mild hyperkinesia were not included. Each patient was observed for a period of ten minutes, within which time all the observed hyperkinetic movements were noted (table 1). Patients were scored once for each set of movements. Abnormal hand and leg movements demonstrated by walking related only to those with abnormal gaits. Patients who chose to walk during the observation period were asked about their subjective desire to do so, whereas patients who

Table 1 *Hyperkinetic movements observed in inpatients. The movement patterns are often continuous, repetitive or alternating.*

Sitting
Head and trunk
Head nod, flick, shake
Neck writhing
Rocking trunk; forward, backwards, side to side, round, swaying
Sitting up or straightening up motions of trunk
Shifting body or trunk
Arms and hands
Arms crossing and uncrossing
Rubbing, caressing or shaking arms or hands
Rubbing or caressing face and head, including hair
Fidgeting of hands, wrists, fingers
Legs and feet
Lateral movements of knees, abduction-adduction of legs
Crossing-uncrossing at knees or ankles
Crossed leg—swinging or kicking
—plantarflexion-dorsiflexion of foot
—lifting movements of fore or rear part of foot
—crablike movements of opposite leg
Lifting fore or rear part of foot with bouncing, tapping or crablike movement
Sliding foot backwards, forwards, laterally
Inversion, eversion and writhing of ankle and foot, and writhing of foot and toes
Others—gesticulations (1), rhythmic jolt of body (1), treading of feet (1).
Standing
Walking or marching on the spot
Changing stance, shifting weight, slow treading, turning
Flexion of knees
Swaying
Walking
Pacing like caged beast or fast, striding, repetitive walk or slower, small steps or wandering
Prominent hand clasp
Hands fidgeting
Excessive leg lift
Others—walking sideways (3), exaggerated arm swing (3), head bashing (1).

Table 2 Analysis of subjective aspects of motor restlessness in outpatients

Questions	Yes	No	Missing
1. Do you have a compulsion to move?	39 (41%)	56 (59%)	—
2. From where does the feeling emanate?			
from the mind?	14 (16%)	69 (79%)	12
or from the body?	22 (24%)	64 (71%)	9
or from the legs?	9 (10%)	76 (85%)	10
3. Does your mind feel restless?	44 (47%)	49 (52%)	2
4. Does your body feel restless?	52 (55%)	42 (44%)	1
5. Do your limbs feel restless?	31 (33%)	63 (67%)	1
6. Does your mind feel tense?	30 (32%)	63 (68%)	1
7. Does your body feel tense?	35 (37%)	60 (63%)	—
8. Do your limbs feel tense?	26 (28%)	68 (72%)	1
9. Do you have limb discomfort?	30 (32%)	65 (68%)	—
10. Do you have trouble falling off to sleep?	43 (48%)	45 (51%)	7
11. Do you tend to feel anxious?	22 (38%)	29 (50%)	44
12. Do you tend to feel depressed?	20 (34%)	29 (49%)	46

failed to stand and walk were asked to. Techniques for augmenting mental and motor concentration or stress were not used as they could not be consistently applied and performed by all the patients. Patients were divided into three categories on the basis of the presence or absence of oral tardive dyskinesia, subjective akathisia and walking on the spot. Group one, the definite akathisia group, comprised 27 patients with motor restlessness associated with a subjective desire to move about or that were observed to walk on the spot. They did not have orofacial dyskinesia. Group two, the tardive dyskinesia group, comprised 79 patients with motor restlessness and orofacial dyskinesia. They did not demonstrate walking on the spot or a subjective desire to move. Group three, an indefinite group, consisted of 53 patients with restlessness but without orofacial dyskinesia, or a subjective desire to move or walk on the spot. The remaining 12 patients could not be categorised and were excluded. The principle diagnoses were schizophrenia in 117 (73.6%), dementia in 36 (22.6%) and affective disorder in 6 (3.8%).

Results

Subjective features

In the study of subjective features of akathisia among outpatients 14 questions were used for analysis (table 2). Missing data relating to questions not asked or not answered are reported in column 3. Thirty-nine (41.1%) patients had a compulsion to move; of these, 22 were men and 17 were women. Fifty-two (54.7%) patients complained of a restless body. Compulsion to move was present in 39% of patients prescribed neuroleptic drugs for less than 5 years, 48% in those treated for 5–15 years and 26% in those treated for more than 15 years. There was no difference in the frequency between those on neuroleptics alone (40%) and those also taking an anticholinergic drug (41.8%). No clear correlation with neuroleptic dosage was found. The feeling of compulsion to move emanated from the mind and/or body and/or legs in 45.2%, 64.7% and 27.3% respectively.

Restlessness of the body was associated with restless limbs, tense body, limb discomfort and insomnia

($p = 0$), tense limbs ($p < 0.005$), restless mind and depression ($p < 0.05$). Tense mind and anxiety were not significantly associated.

Compulsion to move was associated with restless body and restless limbs ($p = 0$); with limb discomfort and insomnia ($p = 0.0001$); and with restless mind, tense body and tense limbs ($p < 0.01$). It was not significantly associated with tense mind, anxiety and depression. Fourteen patients who complained that compulsion-to-move emanated from the mind were excluded from analysis, but probability values were not changed.

Anxiety was related to depression ($p = 0.005$) and to sex of patient ($p < 0.05$). Seventy-three per cent of anxious patients were female (52% of the total females and 22% of the males). Restless mind was associated with restless limbs, tension of mind ($p < 0.001$), tense limbs ($p < 0.005$), tense body ($p < 0.01$), limb discomfort and depression ($p < 0.05$). Limb discomfort was associated with insomnia ($p = 0$), tense body, tense limbs ($p < 0.001$), restless limbs and depression ($p < 0.005$).

Motor disturbances

In the study of motor phenomena among inpatients all observed movements were recorded, so the numbers in some movement categories were too small to be analysed statistically (table 3). One patient from group one, 18 from group two and four from group three were not prescribed neuroleptic medication at the time of study. No attempt was made to relate age or sex of patient and neuroleptic dose to the movement disorder.

Sitting, head and trunk There were no significant inter-group differences in the frequency of head nodding, neck writhing, rocking of the trunk, sitting up or shifting body movements. They tended to occur more frequently in group two.

Arms and hands Rubbing movements of the hands were significantly more frequent in group two ($p < 0.05$), but there was no difference in the frequency of

Table 3 Analysis of hyperkinetic movements observed in inpatients

Sets of movements	Group 1 (27)	Group 2 (79)	Group 3 (53)
<i>Sitting</i>			
Head and trunk:			
Head nod	1 (3.7%)	5 (6.3%)	2 (3.5%)
Neck writhing	0	3 (3.8%)	0
Rocking trunk	3 (11.1%)	14 (17.7%)	6 (11.3%)
Sitting up	2 (7.4%)	4 (5.0%)	1 (1.9%)
Shifting body	2 (7.4%)	8 (12.7%)	4 (7.5%)
Arms and hands:			
Arms crossing	1 (3.7%)	0	1 (1.9%)
Rubbing arms	3 (11.1%)*	24 (30.4%)	8 (15.1%)*
Rubbing face	4 (14.8%)*	10 (12.7%)	4 (7.5%)
Fidgeting hands	5 (18.5%)	30 (38.0%)	13 (24.5%)
Legs and feet:			
Lateral knee movement	5 (18.5%)	6 (7.6%)	6 (11.3%)
Repeated knee crossing	7 (25.9%)	13 (16.4%)	9 (17.0%)
Swinging leg	7 (25.9%)*	6 (7.6%)	15 (28.3%)*†
Plantar flexion of crossed foot	7 (25.9%)	15 (19%)	10 (18.9%)
Forefoot lift	8 (29.6%)	13 (16.4%)	7 (13.2%)
Sliding foot	5 (18.5%)	7 (8.9%)	1 (1.9%)
Writhing foot movements	4 (14.8%)*	29 (35.4%)	5 (9.4)*‡
<i>Standing</i>			
Walking on spot	7 (25.9%)	0	0
Changing stance	7 (25.9%)	10 (12.7%)	8 (15.1%)
Knee flexion	1 (3.7%)	2 (2.5%)	2 (3.8%)
Swaying	2 (7.4%)	3 (3.8%)	2 (3.1%)
<i>Walking</i>			
—type			
Spontaneous pacing	1 (3.7%)	0	6 (11.3%)
Fast walk	13 (48.0%)*‡	5 (6.3%)	33 (62.3%)*‡
Slower walk	5 (18.5%)	20 (25.3%)	0
Wandering	0	7 (8.9%)	2 (3.8%)
Hands together	6 (31.6% of walkers)	7 (21.9%)	4 (9.8%)
Hands fidgeting	3 (15.8%)	7 (21.9%)	7 (17.1%)
Excessive leg lift	0	5 (15.6%)	1 (2.4%)

*†‡ indicate significant differences between groups 1 and 3 and groups 2 ($p < 0.05$, $p < 0.0027$, $p < 0.001$).

rubbing of the face. Fidgeting movements of hands and arms were also more frequent in group two, but the significance level was below 5%.

Legs and feet Swinging of one leg crossed on another was significantly more common in group one ($p < 0.05$) and group three ($p < 0.0027$); lateral knee movements, crossing of knees or ankles, plantarflexion of crossed feet, forefoot lift or sliding feet were more frequently seen in group one. Writhing movements of the feet occurred significantly more frequently in group two than group one ($p < 0.05$) or three ($p < 0.001$).

Standing

The criteria for grouping patients included walking on the spot as a major feature of group one patients. Changing body stance was also more common in this group.

Walking

Abnormally fast walking was more frequent in groups one and three ($p < 0.001$). Wandering behaviour was not observed in group one.

Discussion

All the patients in whom subjective phenomena were

analysed were stabilised on chronic regular medication. Although 38% complained of suffering from anxiety and 34% from intermittent depression, in the majority the subjective restlessness was assumed to be due to drug-induced akathisia. We believe the 41% with compulsion to move have akathisia. In support of this contention it is notable that anxiety was not significantly associated with any aspect of motor restlessness. Furthermore the exclusion of 14 patients in whom compulsion to move emanated from the mind did not alter probabilities. Depression was associated with restless body, but insignificantly with compulsion to move. This introduces the possibility that a proportion of patients in the restless body group belong to those with illness-related movement disorder, in whom an association with depression has been noted.¹⁹

Prevalence rates of akathisia varying from 3%²⁰ to 49%¹³ have been reported in psychiatric patients. A multi-centre double-blind study which investigated antipsychotic reactions in newly treated schizophrenics²¹ reported figures of 5.5%, 5.7% and 12.1% in groups of 88–91 patients taking thioridazine, fluphenazine and chlorpromazine respectively. In a placebo group 4% were also thought to have akathisia, showing that restlessness of the

feet, the major guideline for diagnosis in this study, can be non-specific. A low prevalence of 3–7%, depending on the drug used, has also been found in 5000 patients.²⁰ Recently a higher prevalence of 25% was observed among 109 acute psychiatric inpatient admissions treated with a variety of antipsychotic drugs and followed for 23 days.¹⁹

Studies of patients treated for long periods show considerable variation in prevalence rates,^{22–23} but most show figures of at least 20%.²⁴ The diagnosis in the study by Ayd,²⁴ as in others, relied on complaints of restlessness or observations of persistent motor activity, such as shifting of the legs or tapping of the feet when sitting, shifting weight from foot to foot when standing, or pacing the floor. Motor restlessness was found in 38% of male and female patients on trifluoperazine for longer than 3 years,²⁵ and recently in another study an unusually high rate of 49% was found, when the diagnosis depended on improvement in restlessness after intramuscular biperiden, rather than placebo.¹³ We suggest that the greater number of patients in our putative akathisia group, compared with many studies which have depended mainly on objective features, is due to the incorporation of mild cases of akathisia.

The compulsion to move and restless body group are closely associated with restless mind, tense body, restless and tense limbs, limb discomfort and insomnia, characteristics which we consider outline the akathisia condition. Most of those with compulsion to move had restless body, but one third (30.8%) with restless body did not complain of compulsion-to-move. Some of these may have illness-related restlessness, but as many as 50% of patients on chronic neuroleptic therapy could have mild akathisia. Study of patients with anxiety and depression is required, to allow comparison with the subjective phenomena of illness-related movement disorder. Whether they differ remains to be seen.

In the study on the motor components of akathisia the separation of the patients into three groups depended on the most basic features of akathisia and tardive dyskinesia. The use of these criteria resulted in a large group of indefinitely categorised patients. The possibility of observational bias, influenced by pre-conceived notions, was eliminated as far as possible by recording most abnormal movements, although the tables (tables 1 and 3) show that similar movements have been categorised, rather than exhaustively described. Only stereotyped movements and manic behaviour were not recorded.

Significant differences (table 3) between the groups were the presence of rubbing movements of the arms and squirming, jerky movements of the feet seen in the tardive dyskinesia group, and persistent swinging of the crossed leg and fast walking in the akathisia

and indefinitely categorised groups. Movements of head and trunk and fidgeting of hands and arms were more frequent in those believed to have tardive dyskinesia. Restless movements of legs and feet, except writhing movements of the feet were more common in the akathisia group. In general the indefinite group showed more features in common with akathisia. This emphasises that orofacial dyskinesia has greater potential for selecting patients with tardive dyskinesia than do either walking on the spot or subjective restlessness for selecting cases of akathisia. Akathisia and tardive dyskinesia appear to be divisible as two entities, although they often occur concomitantly in individual cases.

Buccolinguo-masticatory movements or orofacial dyskinesia were the first motor symptoms to be associated with antipsychotic medication.²⁶ Most authors agree that these constitute a core feature of the tardive dyskinesia syndrome and choreic lip, tongue, jaw and neck movements are characteristic.²⁷ It is accepted that “central” movements, as opposed to the peripheral limb movements of hyperkinesia, fulfil the need for an instantaneously recognisable sign of tardive dyskinesia. However it is tempting to link choreiform movements in limbs and trunk with this central syndrome. Distal limb chorea and axial hyperkinesia have gained an indefinite position as a syndrome either phenomenologically identical to or a variation upon orofacial dyskinesia.²⁸ In cases of chronic antipsychotic-induced movement disorder without orofacial dyskinesia a composite of trunk and limb movements may fail to distinguish tardive dyskinesia and akathisia. A group of patients has been identified with “peripheral movements” of limbs and trunk which cluster separately from patients with the central syndrome.²⁷ Consequently the concept of two subsyndromes has been proposed. Another study has outlined the following features; complaints of restless legs, accompanied by semipurposeful or purposeless normal leg and foot movements, myoclonic jerks of the feet, shifting trunk position while lying in bed or sitting in chair, inability to remain lying or seated, shifting weight from foot to foot, walking on the spot and pacing.¹⁹ In our study we have described the peripheral movements of patients and separated them into those occurring in akathisia and those occurring in tardive dyskinesia. The absence of a subjective component does not exclude the possibility of akathisia, as many patients, in particular those with late onset and persistent akathisia, do not express this.⁵ This point is supported by our indefinite group, which was similar to the akathisia group.

The restlessness of akathisia varies from repetitive limb movement to persistent pacing behaviour. The frustration of the mental and motor unease is uniquely demonstrated by walking on the spot. Our

akathisia group show that movements around the hip and knee are most frequent, while arm and trunk movements together with squirming of the feet and movements of the hands occur more frequently in the tardive dyskinesia group. This study does not attempt to distinguish on the basis of the movement disorder between patients with illness-related restlessness of anxiety and depression and those with neuroleptic-induced hyperkinesia. In practice these patients are distinguished by an overriding element of neurosis in the subjective component. A diagnosis of akathisia may determine whether neuroleptic medication should be reduced. Prominent subjective discomfort may be treated with anxiolytics such as benzodiazepines or β -adrenergic blockers such as propranolol, and anticholinergics may improve the motor restlessness.¹⁷

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