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On the Pathogenesis of Abnormal Involuntary Movements in Lithium-Treated Patients with Major Affective Disorder

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Summary. Abnormal involuntary movements during long-term lithium treatment were investigated on two occasions, 7 years apart, in 37 outpatients with major affective disorder according to DSM-III. The patients had been on continuous lithium treatment for an average of 8.2 years when entering the study, and all had been exposed to neuroleptics. Psychiatric status and side effects were evaluated, and abnormal involuntary movements were assessed using the Abnormal Involuntary Movement Scale (AIMS). Signs of abnormal involuntary movements were age-dependent and seen in 8% of the patients at the initial investigation in 1980, and the proportion of affected individuals had increased to 16% by the end of the study in 1987. Women above the age of 50 (in which category the frequency of abnormal involuntary movements was 38%) were selected for further analysis. Severe abnormal involuntary movements in this category were associated with the early onset of affective illness, low body weight, the occurrence of dementia among first-degree relatives, and with high 12-h lithium levels.

Key words: Lithium – Abnormal involuntary movements – Long-term treatment – Major affective disorder – Point prevalence

Introduction

Abnormal involuntary movements, i.e. a variable mixture of orofacial dyskinesia, chorea, athetosis, dystonia, tics, and facial grimacing, is a phenomenon that may be permanent or transient. The term tardive dyskinesia (TD) was first used to describe these movements in patients treated with neuroleptics (Farbuye et al. 1964), and the disorder has been associated mainly with the administration of such drugs (American College of Neuropsychopharmacology 1973; Crane 1973; Kane and Smith 1982; Kane et al. 1982; Perris et al. 1979). Abnormal involuntary movements may, however, also occur spontaneously in patients never exposed to neuroleptics (Brandon et al. 1971; Delwaide and Desseilles 1977; Klawans and Barr 1982), and the causality of abnormal movements in psychiatric patients is not easily evaluated since many different factors, such as aspects or manifestations of the chronic psychotic process per se, may contribute to their development (Cunningham Owens et al. 1982; Cunningham Owens 1985). Abnormal involuntary movements are even known to vary with mood (Goswami et al. 1985; de Potter et al. 1983).

Several studies have reported high frequencies of abnormal involuntary movements, classified as TD, in patients with affective disorders (Davies et al. 1976; Rosenbaum et al. 1977; Rush et al. 1982; Yassa et al. 1984a), and there are indications of an increased vulnerability to TD in affectively ill patients as compared with patients with a diagnosis of schizophrenia (Yassa et al. 1984).

The aim of the present study was to investigate the point prevalence of abnormal involuntary movements on two separate occasions, 7 years apart, in patients with affective disorders who received continuous lithium treatment. The nature and severity of these abnormal movements were analysed in relation to a number of clinical and physiological variables in an attempt to discern distinct risk factors in this category of patient.

Materials and Methods

Patients

The participants in the study were outpatients at the University of Göteborg Department of Psychiatry at Lillhagen Hospital (Sweden) and had originally been selected for a research project focused on various aspects of long-term lithium treatment. Inclusion criteria for this part of the study were a DSM-III diagnosis of major affective disorder (American Psychiatric Association 1980), continuous lithium treatment for more than 1 year before entering the study in 1980, and adherence to lithium during the 7-year follow-up period. These criteria were met by a total of 37 patients, 12 men and 25 women. Patients who left the cohort during the follow-up period have been described in detail elsewhere (Nilsson and Axelsson 1989a). Discontinued participation could in no case be attributed to development of dyskinetic movements.

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Patient Variables in 1980

At the start of the study in 1980, the age range of the 37 participants was 30–71 years (mean 52), and their body weight was 46–125 kg (mean 77 kg). The duration of lithium treatment was, on average, 8.2 years (1.6–13.2 years). A sustained-release preparation of lithium was given as sulphate (Lithionit; ASTRA, Södertälde, Sweden) to 26 patients (70%) and as citrate (Litarex; DUMEX, Helsingborg, Sweden; Köpenhamn, Denmark, manufacturer) to 1 (3%). Ten patients (27%) received a conventional release preparation (Lithium-karbonat; ACO, Solna, Sweden). All were on divided dose schedules with doses ranging from 12 to 41 mmol/day (mean dose 28.1 mmol/day). The mean daily weight-related dose was 0.38 mmol/kg (0.13–0.59 mmol/kg). The mean 12-h plasma lithium concentration was 0.61 mmol/l (0.23–0.96 mmol/l) on the day of investigation.

Concomitant medication on the day of investigation in 1980 is presented in Table 1. Four women were on thyroxine substitution and all of them were euthyroid. Every patient had accumulated more than 3 months of neuroleptic exposure before entering the study.

Any change in medication during the follow-up period (1980–1987) was determined according to clinical need by independent psychiatrists in charge of treatment. Lithium dosages were continuously adjusted to maintain a 12-h serum level of approximately 0.5–0.9 mmol/l.

Patient Variables in 1987

When re-examined in 1987, the patients were 37–79 years old (mean 59), and their body weight ranged from 46–130 kg (mean 77 kg). The average duration of lithium treatment was 15.4 years (8.9–20 years). Lithium in sustained-release preparation was given as sulphate (Lithionit) to 31 of the patients (84%) and as citrate (Litarex) to 6 (16%). All but 2 patients were on divided dose schedules with doses ranging from 6 to 42 mmol/day (mean 20.4 mmol/day). The daily weight-related dose was 0.27 mmol/kg (0.09–0.46 mmol/kg). The mean 12-h plasma lithium concentration was 0.56 mmol/l (0.30–0.85 mmol/l) on the day of investigation.

The concomitant medication at the reinvestigation in 1987 is given in Table 1. Eight women (22%) were on thyroxine substitution, and all were euthyroid. A thyroid-stimulating hormone (TSH) value above 60 IU/l, an unbound thyroxine (F-T_4) concentration of 3 pmol/l, and clinical signs of hypothyroidism were, however, found in a woman without thyroxine substitution. She showed no dyskinetic movements on either occasion.

Design of the Study

The patients were submitted to thorough psychiatric, physical, and laboratory investigations upon entering the study in 1980 and at the end of the study in 1987. The procedures were exactly the same in 1980 as in 1987, and if not otherwise stated, the same analyses and investigations were completed on both occasions.

Analyses and Functional Tests

Blood Tests. Sodium and potassium were determined in 1980 and 1987. The TSH, F-T_4, calcium, phosphate, and magnesium levels were calculated only in 1987.

Lithium Parameters. The 12-h plasma lithium concentration was determined in 1980 and in 1987, and ratios were calculated between the lithium plasma level and the weight-related dosage (li-plasma level/li-dose $\times$ kg^{-1}). In 30 patients, the approximate elimination half-life of lithium was estimated according to a previously described method (Nilsson and Axelsson 1989b).

Anamnestic Data

The number of first-degree relatives affected with dementia or with a psychiatric disorder other than dementia was recorded in each case on the basis of reports given by the patients in 1980 and 1987. This information was used for calculation of "familial scores", one for dementia and one for other psychiatric disorders. The sta-

Table 1. Concomitant psychotropic medication in 37 patients in long-term lithium treatment

	Patients with abnormal involuntary movements in 1980 and/or in 1987 ($n = 7$)	Patients without abnormal involuntary movements in 1980 and in 1987 ($n = 30$)	Significance of difference between groups
Examination in 1980			
Number of CPZ equivalents	*Mean* 84[a]	*Mean* 37[b]	
	Range 0–450	*Range* 0–400	NS
Change in neuroleptic dose < 2 weeks before examination	Decreased dose in 1 patient	Decreased dose in 5 patients, increased in 1	NS
Other psychotropic medication	Antiepileptics in 1 patient	Antidepressants in 4 patients antiepileptics in 1, bensodiazepines in 1	NS
Examination in 1987			
Number of CPZ equivalents	*Mean* 72[c]	*Mean* 76[d]	
	Range 0–250	*Range* 0–400	NS
Change in neuroleptic dose < 2 weeks before examination	0	Decreased dose in 4 patients, discontinued in 1	NS
Other psychotropic medication	Antiepileptics in 1 patient	Antidepressants in 6 patients, bensodiazepines in 1	NS

[a] 2 patients had no chlorpromazine (CPZ) equivalents
[b] 16 patients had no chlorpromazine (CPZ) equivalents
[c] 4 patients had no chlorpromazine (CPZ) equivalents
[d] 13 patients had no chlorpromazine (CPZ) equivalents

NS, Not significant

tistical method for calculating familial scores has been described by Axelsson and Odén (1989).

Medical records were used to calculate the total accumulated dose of lithium given prior to entering the study and that given during the follow-up period as well as the total treatment time with lithium in each case. The duration of affective illness when entering the study was calculated from patient statements regarding age at the first affective episode. All 12-h serum lithium values recorded during the 7-year follow-up were collected from the medical records, giving an average of 17 recordings per patient, and the mean 12-h lithium value was calculated for every patient. Body weights recorded within a week before the start of lithium treatment were collected from the medical records.

The numbers of hospital admissions and inpatient days during the follow-up were calculated from the medical records, as were the number of episodes of depression and hypomania/mania treated in the outpatient clinic and/or hospital during the 7-year follow-up. The definition of an episode was a change in mood leading to sick-leave, hospitalization, or other treatment adjustments.

Information regarding number of treatment days with high-dose and/or low-dose neuroleptics, antidepressants, benzodiazepines and other sedatives in addition to lithium during the follow-up was obtained from the medical records and used to measure exposure to other psychotropic drugs during the period. Chlorpromazine (CPZ) equivalents, calculated as described by Davis (1976), were used as a measure of exposure to neuroleptics on the day of investigation in 1980 and in 1987. The year when the patient was exposed to neuroleptics for the first time was also traced through the medical records in each case.

Assessment of Clinical Status

Movement Disorders. A global assessment of movement disorders with ratings of 1 for mild, 2 for moderate, 3 for severe, and 0 for no abnormal movements was used in the evaluations in 1980 and 1987. At the reinvestigation in 1987, such disorders were also assessed by means of a more standardized method, i.e. the Abnormal Involuntary Movement Scale (AIMS) (Guy 1976).

Extrapyramidal Symptoms. The Simpson-Angus rating scale (Simpson and Angus 1970) was used for evaluation of extrapyramidal symptoms at the reinvestigation in 1987. The investigation in 1980 included only a global assessment scale with a score of 1 for mild, 2 for moderate, 3 for severe, and 0 for no extrapyramidal symptoms.

Other Side Effects. A comprehensive check-list containing common side effects seen during treatment with neuroleptics, lithium, and other psychotropic drugs was used as described in a previous paper (Nilsson and Axelsson 1989a). Side effects were rated 0–3 on the basis of subjective reports and objective signs of side effects. The same rating procedure was used in 1980 and in 1987.

Psychiatric Status. The psychiatric status in 1980 and 1987 was assessed by means of the Comprehensive Psychopathological Rating Scale (CPRS) (Åsberg et al. 1978); a preliminary version (1975) was obtained by courtesy of the authors, which differs from the final version only in a few instances (Axelsson et al. 1982). In the analysis of psychiatric status, the total CPRS score as well as clusters of scores for items seen in depression (CPRS Σ22), in organic brain syndrome, and in mania were used as described elsewhere (Nilsson and Axelsson 1989c).

Analytical Methods

The plasma lithium concentration values were analysed by flame emission spectrometry. Standard hospital procedures were used for all blood tests.

Statistics

Pitman's permutation test (Bradley 1968) with two-tailed levels of significance was used in the statistical analyses unless otherwise stated.

Results

Prevalence of Abnormal Involuntary Movements in 1980

Signs of abnormal involuntary movements were noted in 3 female patients at the initial examination in 1980. The youngest of these women (aged 43 years) showed no detectable trace of abnormal movements at the reinvesti-

Table 2. Severity and type of abnormal involuntary movements in 1980 and 1987 and ratings of extrapyramidal symptoms in 1987 in 7 patients on long-term lithium treatment

Case	Sex	Age in 1980	Global rating score		AIMS[a] score in 1987								Total Simpson-Angus score in 1987
					Item number:							Total score	
			1980	1987	1	2	3	4	5	6	7		
1[b]	F	63	1	3	1	2	4	2	2	4	3	18	3
2[c]	F	68	0	1.5	0	2	0	2	0	0	0	4	3
3[c]	F	54	0	1	1	1	2	1	0	0	0	5	2
4[c]	F	56	0	1	0	1	0	0	0	0	0	1	7
5[b]	F	65	2	3	1	1	3	2	3	1	2	13	2
6[d]	F	43	1	0	0	0	0	0	0	0	0	0	1
7[c]	M	59	0	1	0	0	0	2	0	0	0	2	2

Item: 1 Muscles and facial expression, 2 Lips and perioral area, 3 Jaw, 4 Tongue, 5 Upper extremities, 6 Lower extremities, 7 Trunk movements

[a] Abnormal Involuntary Movement Scale
[b] Abnormal Involuntary Movements in 1980 and 1987
[c] Abnormal Involuntary Movements only in 1987
[d] Abnormal Involuntary Movements only in 1980

gated in 1987, while a further progress of symptoms was noted in the 2 older women (aged 63 and 65) (Table 2). No significant difference was seen in psychotropic medication between patients with and without abnormal movements (Table 1).

Severity of Abnormal Involuntary Movements in 1980

The severity of the abnormal involuntary movements according to the global scale used at the beginning of the study is given in Table 2.

Prevalence of Abnormal Involuntary Movements in 1987

Signs of abnormal involuntary movements were found in 6 of 37 patients at the reinvestigation in 1987, making the overall prevalence of involuntary movements 16% by the end of the study. The disorder was seen in 5 of 25 women and in 1 of 12 men, which is not a statistically significant sex difference. Signs of involuntary movements were present in 20% of the female participants in 1987, and since all the affected women were above the age of 50 when entering the study, the prevalence of abnormal involuntary movements in this age group of women was 5 of 13 (38%) by the end of the study. The affected male patient was also older than 50 years, which made the total prevalence of involuntary movements in patients above 50 years of age 6 of 19 (32%), while the corresponding figure in patients below the age of 50 years was 0 of 18. At the examination in 1987, a significant positive relationship was revealed between the presence of abnormal involuntary movements and age ($P < 0.05$). No significant difference in concomitant psychotropic medication was found between patients with and without abnormal involuntary movements (Table 1).

Severity of Abnormal Involuntary Movements in 1987

The AIMS ratings for each patient with abnormal involuntary movements are given in Table 2. Four of the women above 50 years (31%) had AIMS ratings satisfying the Research Diagnosis for Probable Tardive Dyskinesia (Schooler and Kane 1982).

Relationship Between Total AIMS Score in 1987 and Variables Investigated in Women Above the Age of 50 Years

In view of the significant relationship between age and abnormal involuntary movements, and since these movements were more frequently seen in women, we chose to limit the final study group to women above the age of 50. This final population included 5 women with and 8 women without detectable signs of abnormal involuntary movements throughout the entire study period. The findings in this group of 13 women are presented below.

Abnormal Involuntary Movements in Women Above 50 Years

Anamnestic Variables. Table 3 gives anamnestic data for each of the 13 women included in this part of the study. The total AIMS score was negatively correlated to age at the onset of affective illness ($P < 0.05$), but not to duration of affective illness (mean 24.8 ± 12.0 years) or of lithium treatment.

Heredity. A close positive relationship was found between the total AIMS score in 1987 and the familial score calculated for dementia ($P < 0.005$). Four patients with abnormal involuntary movements had first-degree relatives with dementia, while the corresponding figure in the group without abnormal movements was 0 of 8. The familial score for psychiatric illness other than dementia did not vary with the total AIMS score (Table 3). Data on first-degree relatives were unavailable for 1 woman with involuntary movements who was adopted and had no information about her biological family.

Laboratory Data. The sodium, potassium, calcium, phosphate, and magnesium values were all within normal limits in each patient. The total AIMS score in 1987 showed no variation with the sodium and potassium values recorded in 1980 or 1987. Neither the calcium nor the phosphate values obtained in 1987 varied with the AIMS score, but a negative relationship was seen between AIMS score and magnesium values in 1987 (mean 0.8 ± 0.06 mmol/l) ($P < 0.04$). AIMS scores did not vary with F-T_4 (mean 16 ± 3.3 pmol/l) or TSH values (mean 3.1 ± 3.4 mU/l).

Body Weight. The body weight recorded before initiation of lithium therapy showed a close negative relationship to the AIMS score ($P < 0.01$). This relationship was demonstrated at the start of the study in 1980 ($P < 0.006$) and at the reinvestigation in 1987 ($P < 0.002$) (Table 3). No female patient with abnormal involuntary movements had a recorded body weight of more than 70 kg, while 5 of 8 female patients without such movements weighed more than 70 kg.

Lithium Parameters (Table 4). The total AIMS score was positively correlated to the plasma lithium values on the day of investigation in 1987 ($P < 0.04$). The total AIMS score did not vary with the total accumulated dose of lithium (mean 87.8 ± 37.7 mol) given before the study or during the follow-up period, nor with the li-plasma level/li-dose $\times$ kg^{-1} ratios (mean $2.4 \pm 0.9\,kg^{-1}$). The total AIMS score was not correlated to the elimination half-life of lithium in 1980 (mean 31 ± 9 h), or 1987 (mean 42 ± 27 h), or to the change in this parameter during the study period.

Psychopathology. There was no significant correlation between the total AIMS score and the number of episodes of mania or depression treated in hospital or outpatient clinic during the 7-year follow-up. Nor was the AIMS score correlated to the number of hospital admissions (mean 1.6 ± 2.0 admissions) or number of days in hospital during the same period (mean 66.5 ± 111 days; see Table 3).

A remarkable finding among the female patients with abnormal involuntary movements was, however, that

Table 3. Anamnestic variables in 13 female patients above the age of 50 on long-term lithium treatment

	Case number													Correlation to AIMS[b] score (1987)
	1[a]	2[a]	3[a]	4[a]	5[a]	8	17	21	25	28	31	32	36	
Age in 1980 (years)	63	68	54	56	65	71	59	61	63	61	62	66	61	NS
Age at onset of affective illness (years)	20	23	29	38	–	–	44	22	42	49	50	45	39	$P<0.05$
Body weight (kg):														
Before start of lithium treatment	44	66	66	67	53	84	59	–	72	55	85	87	70	$P<0.02$
In 1980	46	66	56	70	54	–	62	64	70	62	87	90	82	$P<0.006$
In 1987	46	60	57	65	52	70	68	60	64	69	83	85	72	$P<0.002$
Familial score:														
Dementia	9.7	7.3	8.1	–	8.1	4.7	3.8	3.8	4.4	4.4	3.5	4.1	4.1	$P<0.005$
Other mental disorder	7.3	2.0	2.0	–	5.8	3.4	6.2	6.2	10.0	3.0	6.3	2.7	11.0	NS
Total number of recurrences (1980–1987)														
Mania	3	2	4	0	0	1	1	1	0	0	0	0	2	NS
Depression	0	0	0	0	0	4	7	0	2	2	4	0	1	NS

NS, not significant

[a] Patients with abnormal involuntary movements

[b] Abnormal Involuntary Movement Scale

Table 4. Lithium parameters and concomitant psychotropic medication 1980–1987 in female patients above 50 years of age on long-term lithium treatment

Case number	Lithium dose in 1987 (mmol)	Plasma level of lithium in 1987 (mmol/l)	Total number of years on lithium	Total dose of lithium 1980–87 (mol)	CPZ equiv. in 1987	Number of treatment days 1980–1987 with:			
						Neuroleptics		Anti-depressants	Benso-diazepines
						High-dose	Low-dose		
1[a]	12	0.85	19.6	191.5	0	235	40	0	0
2[b]	18	0.51	17.8	131.3	10	1466	0	0	0
3[b]	24	0.40	19.6	155.2	0	1053	1531	100	0
4[b]	12	0.53	15.3	113.7	250	2478	0	0	0
5[a]	24	0.78	9.8	100.2	0	0	0	0	0
8	6	0.40	16.6	88.8	0	0		2220	1137
17	12	0.49	18.1	145.5	37.5	728	181	1656	1202
21	18	0.62	20.4	185.8	0	0	0	0	639
25	18	0.49	12.9	109.0	0	735	0	50	1099
28	24	0.75	15.1	191.0	0	391	0	2555	0
31	18	0.63	12.8	141.0	0	37	0	1557	1445
32	12	0.36	13.9	62.4	10	2555	0	0	0
36	18	0.60	16.0	182.5	0	19	1859	0	44
Correlation to total AIMS score 1987	NS	$P<0.04$	NS	NS	NS	NS	NS	NS	NS

NS, Not significant

[a] Abnormal involuntary movements in 1980 and 1987

[b] Abnormal involuntary movements in 1987

none had suffered a depressive recurrence during the 7-year study, while 6 of 8 female patients without abnormal movements had required treatment for depression (difference $P<0.04$; Fisher's exact test). The total AIMS score did not vary with psychiatric status, expressed as total CPRS score, in 1980 (mean 6.8 ± 5.0) or 1987 (mean 10.8 ± 9.4), or with the change in these scores during the follow-up. Nor were there any significant relationships between AIMS score and the CPRS clusters for depression (mean 3.5 ± 2.8 in 1980; 6.6 ± 6.6 in 1987), mania (mean 0.7 ± 1.3 in 1980; 1.2 ± 1.0 in 1987), or organic brain syndrome (mean 1.9 ± 1.3 in 1980; 3.0 ± 2.0 in 1987).

Other Side Effects. The total AIMS score did not vary with any of the other side effects investigated in 1980 and

1987. There were no significant correlations to the extrapyramidal symptoms assessed by the Simpson-Angus scale in 1987 (Table 2).

Concomitant Psychotropic Medication. At the reinvestigation in 1987, 3 of 5 patients with and 6 of 8 patients without abnormal involuntary movements were not on concomitant neuroleptic medication. During the last 2 weeks before the end of the study, no changes in neuroleptic medication had been made in the patients with abnormal movements, but 2 of the patients without such movements had been prescribed a decreased neuroleptic dosage and 1 patient had discontinued neuroleptic treatment during this period.

The total AIMS score was not significantly correlated to the number of CPZ equivalents on the day of investigation in 1980 or 1987, nor to the number of treatment days with either high- or low-dose neuroleptics, antidepressants, or bensodiazepines during the follow-up period (Table 4). The year of first exposure to neuroleptics (mean 1965 ± 2) showed no variation with the total AIMS score.

Discussion

The main aim of this study has been to explore abnormal involuntary movements in patients with major affective disorder and continuous lithium treatment. The study covers approximately 9–16 years of continuous lithium treatment. By conducting the study in an outpatient setting we were able to avoid bias due to institutionalization and an extremely chronic course of the affective illness.

A diagnosis of affective disorder is considered to be a risk factor associated with abnormal involuntary movements (Yassa et al. 1984a), and so is female sex (Kane and Smith 1982) and advanced age (Kane and Smith 1982; Smith and Baldessarini 1980). We controlled for these factors by limiting our final study group to women above the age of 50 with a diagnosis of major affective disorder, and this allowed us to investigate and evaluate further factors in relation to abnormal involuntary movements by the end of the study in 1987.

Neuroleptics have frequently been associated with the development of abnormal involuntary movements (American College of Neuropsychopharmacology 1973; Crane 1973; Kane and Smith 1982; Kane et al. 1982). All our patients had a history of at least 3 months of neuroleptic exposure before entering the study in 1980 (cf. Research Diagnosis for Tardive Dyskinesia; Schooler and Kane 1982). The ideal situation would obviously have been a study group never exposed to neuroleptics. It is, however, virtually impossible to find such a category of affectively ill patients as, for instance, manic recurrences frequently are treated with neuroleptics or a combination of lithium and neuroleptics. Various methods were employed to measure the exposure to neuroleptics in our study, and the fact that no correlation was found between the exposure variables and the total AIMS score agrees with the lack of such a relationship reported in several earlier studies (Brandon et al. 1971; Gibson 1978; Perris et al. 1979).

A few case reports have suggested lithium as a cause of extrapyramidal symptoms (Kane et al. 1978) or TD (Beitman 1978). The possibility that lithium may ameliorate TD has also been suggested and investigated in several studies, but the results have been contradictory (Cole et al. 1984; Gerlach et al. 1975; Jus et al. 1978; Mackay et al. 1980; Reda et al. 1975; Yassa et al. 1984b). Statistically significant beneficial effects have been reported in some studies, but their clinical importance has been slight (Gerlach et al. 1975; Reda et al. 1975). A matter that requires further investigation is the possibility of a causal relationship suggested by the correlation between the AIMS score and the 12-h lithium levels demonstrated in this study.

Our finding of a close correlation between low body weight and abnormal involuntary movements is interesting. There was even a correlation to the weight recorded immediately before the start of lithium treatment, possibly indicating a higher risk of developing abnormal movements in women with low body weight. One may, in view of this finding, speculate whether the sex difference seen in frequency of abnormal involuntary movements (Kane and Smith 1982) might be attributable merely to weight differences between the sexes.

The AIMS scores were not correlated to psychiatric status as assessed by the total CPRS score or by the CPRS clusters of items inherent in depression and mania. Our observation that no patient with abnormal movements had a depressive recurrence during the 7-year follow-up and the lack of significant correlation between the total AIMS score and the present psychiatric status disagree with reports on increased frequencies of hyperkinetic movements in depression (Casey 1984).

A finding of particular interest was the positive relationship between the AIMS score and the occurrence of dementia among first-degree relatives. This implies the possibility of an affinity between neuropsychiatric conditions, such as dementia, and an individual predisposition for the development of abnormal involuntary movements. However, we found no correlation between the AIMS score and the CPRS cluster for items seen in organic brain syndrome, and further studies are needed to elucidate these aspects.

In conclusion, the treating psychiatrist must be aware of the fact that abnormal involuntary movements may occur in patients with major affective disorder. Advanced age, low body weight, early onset of affective illness, and the familial occurrence of dementia were factors associated with the development of abnormal involuntary movements in female patients above the age of 50 with a diagnosis of major affective disorder and prophylactic lithium treatment. The relevance of these abnormal involuntary movements and their relationship with the TD syndrome requires further clinical evaluation.

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