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A Clinical and Polysomnographic Comparison of Neuroleptic-Induced Akathisia and the Idiopathic Restless Legs Syndrome

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Summary: Neuroleptic-induced akathisia (NIA) is motor restlessness caused by dopamine receptor blocking antipsychotic agents. Nine patients with NIA and 11 patients with idiopathic restless legs syndrome (RLS) were studied polysomnographically. The sleep disturbances were milder in NIA than idiopathic RLS but increased numbers of awakenings and decreased sleep efficiencies were common to both groups. In addition, RLS patients demonstrated prolonged sleep latencies. Periodic movements in sleep (PMS) were present in only 5 of 9 patients with NIA but in all 11 patients with idiopathic RLS. In no NIA patient did we see the multiple, large amplitude, violent, resting myoclonic jerks of the legs that we saw during wakefulness in some of our more severe cases of idiopathic RLS. NIA patients tended to experience inner restlessness and idiopathic RLS patients tended to experience leg paresthesias as an antecedent to motor restlessness. Idiopathic RLS patients had symptoms that were worse at night and in repose far more frequently than patients with NIA. NIA and idiopathic RLS have similarities and differences. Because both NIA and idiopathic RLS are characterized by motor restlessness and sleep disturbances, the pharmacodynamics of antipsychotic medications may give clues as to both the cause and treatment of idiopathic RLS.
Key Words: Neuroleptic-induced akathisia—Restless legs syndrome—Sleep disturbances—Periodic movements in sleep—Myoclonus.

Neuroleptic-induced akathisia (NIA) is a motor restlessness caused by dopamine receptor blocking antipsychotic agents (1–5). Neuroleptic-induced akathisia can be divided into two types: (a) The acute type is due to ongoing neuroleptic exposure and it disappears on discontinuation of the neuroleptic; and (b) the tardive type is thought to be due to dopamine receptor hypersensitivity and it may persist for months to years after discontinuation of the neuroleptic (2). NIA and idiopathic restless legs syndrome (RLS) (6–12) share motor restlessness as a common feature. Therefore, in this study we looked at nine patients with NIA polysomnographically to determine if they also had other clinical features similar to those commonly found in idiopathic RLS such as sleep disturbances, periodic movements in sleep (PMS) and jerking movements of the legs during wakefulness (1). In addition, we gave our NIA patients a questionnaire to determine if any of them had clinical symptoms similar to those commonly found in idiopathic RLS such as leg paresthesias and a feeling of restlessness that is worse at night and at rest (1). A group of nonneuroleptic-exposed idiopathic RLS patients were also studied polysomnographically and given the questionnaire.

A previous polysomnographic study by Castaldo documented sleep disturbances in two patients with NIA, but there was no attempt to look for PMS (13). To our knowledge, ours is the first polysomnographic study to determine if PMS are present in NIA.

METHODS

Inclusion criteria. Patients with NIA were required to have a history of restlessness related to neuroleptic exposure. In order to qualify for the study they were required to have both a subjective sense of restlessness and objective signs of NIA such as floor pacing, body

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TABLE 1. *Neuroleptic-induced akathisia patients and their sleep parameters*

Patient and neuroleptic at time of study	Age	Sex	Sleep complaints[a]	Sleep onset latency (min)	Sleep efficiency (%)[b]	Percent stage 3 and 4 sleep[c]	REM latency (min)	Percent REM sleep[c]	No. of awakenings[d]	PMS/hr sleep
1 Thiothixene	36	M	2+ DIMS	Δ^2 14.87	Δ^4 88	Δ^1 4.90	35.2	26.20	Δ^6 11.5	—
2 Fluphenazine	40	M	1+ DIMS	Δ^0 15.17	Δ^1 82	Δ^0 4.40	Δ^0 85.1	Δ^2 14.20	Δ^3 13.5	25.3
3 Trifluoperazine	40	M	None	0.50	93	Δ^0 6.00	Δ^1 120.0	Δ^0 19.40	Δ^5 18.0	—
4 Thiothixene	58	M	1+ DIMS	Δ^1 26.64	Δ^2 81	7.00	Δ^0 98.8	21.30	Δ^6 16.5	21.4
5 Thioridazine	63	M	None	6.25	Δ^2 73	Δ^0 0.00	13.3	Δ^1 17.40	Δ^4 23.5	93.3
6 None	41	M	2+ DIMS/EDS	4.73	Δ^1 80	14.10	Δ^1 115.6	Δ^2 12.00	Δ^7 21.0	5.3
7 None	50	F	3+ DIMS/EDS	Δ^6 41.23	Δ^3 69	Δ^0 8.80	55.7	27.16	Δ^1 8.0	—
8 None	53	M	None	11.18	Δ^2 83	12.60	Δ^0 87.1	Δ^0 20.90	Δ^9 23.0	—
9 None	57	M	3+ DIMS	Δ^1 32.88	Δ^7 61	Δ^0 0.90	73.0	Δ^0 19.60	Δ^{21} 44.0	20.4
Mean	49			17.05	79	6.52	76.0	19.86	19.9	33.1

Note: All figures are averages of values from two nights of polysomnographic recording. REM = rapid eye movement; DIMS = disorder of initiating and maintaining sleep; PMS = periodic movements in sleep; EDS = excessive daytime somnolence.

[a] 1+ = Mild sleep complaints; 2+ = moderate sleep complaints; 3+ = severe sleep complaints.

[b] $p < 0.05$ by chi square.

[c] Percent stage 3 and 4 sleep and percent REM sleep are calculated as a percentage of sleep period time.

[d] $p < 0.01$ by chi square.

Δ = Relative to mean for age and sex, patient has increase (in sleep latency, REM latency, number of awakenings) or decrease (in sleep efficiency, percent stage 3 and 4 sleep, percent REM sleep). Superscript next to Δ indicates number of standard deviations value deviates from mean for age and sex.

rocking, or marching-in-place (1–5). So as not to bias results in favor of sleep disturbance, we sought NIA patients for the study who did not come to us with a primary sleep complaint. Patients with idiopathic RLS were required to have idiopathic motor restlessness. Patients with idiopathic RLS were a self-selected population in the sense that they were actively seeking medical attention for moderate to severe sleep disturbances.

Exclusion criteria. Patients with medical or neurological problems known to be associated with motor restlessness or PMS were excluded from the study as were NIA patients with a family history of idiopathic RLS (1). Patients who were still actively psychotic were also excluded from the study as were NIA patients with prominent neuroleptic-induced involuntary movements other than NIA.

Methodology. Eleven patients with idiopathic RLS (8 men and 3 women, ages 40–69) and 9 patients with schizophrenia in remission and a current history of NIA (8 men and 1 woman, ages 36–63) were selected for the polysomnographic portion of the study. Five NIA patients were taking neuroleptics at the time of the study (Table 1) and four were not. By definition the four patients who had motor restlessness that persisted beyond the time the neuroleptics were stopped had tardive neuroleptic-induced akathisia (1–5).

At least 6 days prior to the polysomnographic study, patients were taken off all medications known to cause PMS, such as tricyclic antidepressant agents (1). Only 1 patient (#6 of the NIA group) was on tricyclics prior to the polysomnographic study. According to the literature, the half-life of the tricyclic in question, trimipramine, is 24 hr (14). Therefore, this medication should have been out of the bloodstream by the time the studies were done.

Prior to their first polysomnographic study, the 9 NIA patients were asked to rate their usual sleep disturbances as follows: Disorders of initiating and maintaining sleep (DIMS) and excessive daytime somnolence (EDS) were rated as none = no sleep complaints, 1 = mild sleep complaints, 2 = moderate sleep complaints and 3 = severe sleep complaints.

The 9 NIA patients and the eleven RLS patients were then studied polysomnographically by previously described methods (7–11) for two nights wherever possible. The records were then scored by previously described methods (7–11,15). The polysomnographic data for idiopathic RLS has been previously published in part (9–11).

Twenty NIA patients (8 from the polysomnographic group and 12 others, 18 men and 2 women, ages 27–72, 8 tardive and 12 still on neuroleptics) were given a questionnaire asking about leg paresthesias, about an inner sense of restlessness and about whether their symptoms were worse at night and in repose. A similarly aged population of 20 patients with idiopathic RLS (6 from the polysomnographic group and 14 others, 11 men and 9 women, ages 37–78) were also given the questionnaire.

All statistics for the polysomnographic and questionnaire portions of the study were done by chi square and a p value was derived from the chi square statistic. For sleep parameters, the NIA and RLS groups were each compared against the means for age- and sex-matched normal populations from the literature (16) and a one sample chi square statistic was obtained. The number of patients who had PMS in the NIA and

RLS groups was compared against the number that would be expected in age-matched normal populations from the literature (17) and a one sample chi square statistic was obtained. For the questionnaire concerning paresthesias, inner restlessness and the effect of night and body position on symptoms, the NIA and RLS groups were compared against each other to obtain a two sample chi square statistic with one degree of freedom.

RESULTS

Sleep complaints

Six of our 9 NIA patients who were studied polysomnographically complained of sleeping difficulties (Table 1), but with the exception of two patients who rated them as severe, these disturbances were generally said to be mild to moderate and sleep disturbance was not a primary complaint of any of the patients. Sleep disturbances in our NIA patients included both DIMS and EDS (Table 1). Sleep complaints seemed to be equally distributed between those akathitic patients still taking neuroleptics and those no longer taking neuroleptics (tardive akathisia) (Table 1).

The idiopathic RLS patients all had serious complaints of sleeping difficulties as they were a self-selected group of patients seeking medical attention for moderate to severe DIMS, EDS or both.

Polysomnography

Following are the results of polysomnographic studies in the 9 patients with NIA and the 11 patients with idiopathic RLS.

Sleep disturbances. Compared to the mean for age and sex (16), all the NIA patients from the polysomnographic group had more awakenings ($p < 0.01$) (Table 1) and 8 of the 9 had lower sleep efficiency ($p < 0.05$) (Table 1). There were no differences in sleep parameters between those akathitic patients still on neuroleptics and those akathitic patients previously on neuroleptics (Table 1). NIA patients' subjective ratings of their usual sleeping difficulties correlated well with sleep efficiency as patients 7 and 9 who rated their sleep disturbances as severe has sleep efficiencies of 69% and 61%, respectively (Table 1).

Sleep disturbances tended to be more severe in RLS than NIA. Compared to the mean for age and sex (16), idiopathic RLS patients from the polysomnographic group also showed statistically significant increases in the number of awakenings ($p < 0.05$) and statistically significant decreases in sleep efficiency ($p < 0.01$), but they also showed statistically significant prolongations in sleep onset latencies ($p < 0.05$), statistically significant prolongations in rapid eye movement (REM) onset latencies ($p < 0.05$) and statistically significant decrements in the percentage of REM sleep ($p < 0.01$) (Table 2).

Periodic movements in sleep. Periodic movements in sleep (PMS) were present in five of nine NIA patients studied polysomnographically and were present in those akathitic patients still on neuroleptics as well as those no longer taking neuroleptics. Because PMS exist in 5% of the normal population aged 30–50 and in 29% of the normal population over age 50 (17), we should expect $(5 \times 0.05) + (4 \times 0.29) = 1.41$ NIA patients our of 9 instead of 5 out of 9 to have PMS. However, this difference was not statistically significant. For the polysomnographic idiopathic RLS group all had PMS (2.95 of 11 expected) ($p < 0.01$) (Table 2).

Involuntary movements during wakefulness other than motor restlessness. In three of our NIA patients studied polysomnographically, a few repetitive, rhythmical bursts of 0.5–2 cps activity were present in the legs during wakefulness as documented by the electromyograph (EMG). These bursts were characterized by cocontractions of agonist and antagonist muscles. Such EMG patterns have been described previously in tardive dyskinesia (18). In no NIA patient did we see the multiple, large amplitude, violent, resting myoclonic jerks of the legs that we saw during wakefulness in some of our more severe cases of idiopathic RLS.

Nine of our patients with idiopathic RLS who underwent polysomnography had jerking movements of the legs during wakefulness (Table 2). Some of these were of the myoclonic type just described and were characterized by repetitive flexions of the hips, knees, ankles and toes and some were less rapid and of smaller amplitude characterized by simple repetitive dorsiflexions of the ankles and toes. In some cases the jerking of the legs during wakefulness took the form of periodic movements while awake (PMWA) similar in their periodicity to PMS (e.g. an involuntary movement every 5–120 seconds) (8). In other cases they were aperiodic or clustered and sometimes the jerking movements involved the arms as well as the legs. The jerking movements during wakefulness were quantitated in idiopathic RLS (Table 2). A striking feature of the jerking movements during wakefulness was that they tended to be present when the patients were trying to sit still or lie still, but they tended to temporarily disappear during actions such as shifting body position in bed or walking.

Questionnaire results

Following is a summary of the results of a questionnaire administered to 20 patients with NIA and 20 patients of similar age with idiopathic RLS.

TABLE 2. *Idiopathic restless legs patients and their sleep parameters*

Patient	Age	Sex	Sleep onset latency[e] (min)	Sleep efficiency[a] (%)	Percent stage 3 and 4 sleep[b]	REM latency[e] (min)	Percent REM sleep[a,b]	No. of awakenings[e]	PMS/hr sleep[a]	Jerking movements legs/hr awake
1	69	M	7	Δ^4 61	15	Δ^2 162	Δ^3 11	Δ^0 10	226	126
2	69	M	Δ^2 25	Δ^7 37	7	Δ^3 202	Δ^4 6	Δ^6 30	117	0
3	62	M	Δ^{12} 100	Δ^5 52	10	Δ^6 333	Δ^3 12	Δ^8 38	85	13
4	61	F	Δ^1 41	Δ^9 4	Δ^0 1	NA	Δ^5 0	Δ^1 8	Present	139
5[c]	68	M	Δ^0 10	Δ^3 68	Δ^0 2	Δ^1 144	Δ^2 15	Δ^4 25	112	84
6	65	M	Δ^{11} 91	Δ^9 23	Δ^0 0	Δ^2 196	Δ^6 1	7	38	80
7	67	M	Δ^{10} 85	Δ^6 42	5	Δ^1 144	Δ^4 6	Δ^1 13	120	121
8[d]	65	M	Δ^8 70	Δ^{11} 12	Δ^0 0	NA	Δ^6 0	2	238	Clustered myoclonus
9	40	M	Δ^0 13	93	18	Δ^0 96	Δ^1 15	Δ^1 9	44	11
10	59	F	9	Δ^0 87	21	Δ^0 91	Δ^1 17	Δ^3 12	33	Not scored
11	68	F	Δ^0 19	Δ^1 78	15	65	Δ^0 20	Δ^7 20	59	39
Mean	63		43	51	9	159	9	16	107	68

Note: The figures are averages of values from two nights of polysomnographic recording where possible. REM = rapid eye movement; PMS = periodic movements in sleep; NA = not applicable.

Δ = Relative to mean for age and sex, patient has increase (in sleep latency, REM latency, number of awakenings) or decrease (in sleep efficiency, percent stage 3 and 4 sleep, percent REM sleep). Superscript next to Δ indicates number of standard deviations value deviates from mean for age and sex.

[a] $p < 0.01$ by chi square.

[b] Percent stage 3 and 4 sleep and percent REM sleep are calculated as a percentage of sleep period time.

[c] Patient 5 slept so little that a meaningful figure for PMS/hr could not be obtained although they were present.

[d] Patient 8 had hundreds of jerking movements of the legs during wakefulness that were solely of the tightly clustered type. The interval between jerks was so short that a meaningful quantitation of their number could not be obtained.

[e] $p < 0.05$ by chi square.

Paresthesias versus inner restlessness. Five of 20 patients with NIA had paresthesias (25%). These were generally described as mild and in no case could the patients definitely attribute their motor restlessness to the paresthesias. The other 15 NIA patients had an inner sense of restlessness (75%). In a group of 20 patients of similar age with idiopathic RLS, 19 of 20 had generally moderate to severe leg paresthesias (95%) that they said were the cause of their motor restlessness. The remaining RLS patient had inner restlessness (5%). These differences were statistically significant at the $p < 0.0001$ level.

Night-time exacerbation of symptoms. Six of 20 patients with NIA had night-time exacerbation of their symptoms (30%), which they generally attributed to evening intake of neuroleptics whereas 18 of 20 patients with idiopathic RLS reported nighttime worsening of their symptoms (90%) ($p < 0.0004$).

Effect of body position on symptoms. Three of 20 patients with NIA reported that the symptoms were worst while lying down (15%) whereas 16 of 20 patients with idiopathic RLS reported that their symptoms were worst on lying (80%) ($p < 0.0001$). Furthermore, 14 of these 16 RLS patients reported that symptoms were worse on sitting than standing.

There were no differences in responses to any of the questions on the questionnaire between the akathitic patients still taking neuroleptics and those no longer taking neuroleptics. Table 3 lists the most prominent features of NIA and idiopathic RLS.

TABLE 3. *Most prominent features of NIA and idiopathic RLS*

NIA	RLS
1. Inner restlessness	1. Paresthesias associated with an urge to move
2. Motor restlessness as manifested by floor pacing, body rocking and marching-in-place, leg jiggling, abduction/adduction of the thighs	2. Motor restlessness as manifested by floor pacing, tossing and turning in bed, foot rubbing, leg stretching, leg flexions, deep knee bends and occasionally body rocking and marching-in-place[a]
3. Sleep disturbance (may be mild)	3. Resting leg dyskinesias while awake [periodic (PMWA) or aperiodic][b]
	4. PMS
	5. Sleep disturbance (often severe)
	6. Worse at rest/repose
	7. Worse at night
	8. Neurological examination normal
	9. Age of onset childhood to senescence, often progressive (severe >50 years of age), there may be spontaneous remissions
	10. Autosomal dominant family history

Most prominent features of NIA (neuroleptic-induced akathisia) and RLS (restless legs syndrome) are listed below the condition in question.

[a] Body rocking and marching-in-place are not universally present in cases of idiopathic RLS and occur only intermittently and usually at night.

[b] PMWA = periodic movements while awake.

DISCUSSION

NIA and idiopathic RLS show both similarities and differences (Table 3). Based upon the current study and previous studies of ourselves and others we can now summarize these differences and similarities as follows:

1) Inner restlessness versus paresthesias. In a previous comparison of NIA and RLS, Blom and Ekbom noted that paresthesias could occur in both conditions (6). However, others have found that a sense of inner restlessness is the usual antecedent to motor restlessness in NIA (1–5) and leg paresthesias are the usual antecedent to motor restlessness in idiopathic RLS (1,6–12). Our study confirms these findings. It is generally assumed that NIA patients move to relieve their sense of inner restlessness and RLS patients move to relieve their paresthesias (1–5, 7–12, 19, 20). RLS patients describe the paresthesias as cramping, aching, painful, burning, creeping, crawling, tingling, pins and needles or sometimes as "indescribable" (1, 6–12). Occasionally RLS patients experience paresthesias in the arms as well (19, 20).

2) Motor restlessness. The characteristic features of motor restlessness in NIA are floor pacing, marching-in-place while standing, body rocking while seated, abduction-adduction movements of the legs while seated or jiggling of one foot while one leg is crossed over the other (1–5). The characteristic features of motor restlessness in idiopathic RLS are floor pacing, tossing and turning in bed, foot rubbing, leg stretching, leg flexions and deep knee bends (1,6–12,21). Patients may also take baths to relieve the paresthesias in idiopathic RLS. Although most patients with NIA have marching-in-place (1–5), our previous work has shown that marching-in-place and body rocking are not universally present in cases of idiopathic RLS and that in idiopathic RLS they tend to occur only intermittently and mostly at night (7,21).

3) Sleep disturbances. It is common for patients with idiopathic RLS to present to a sleep disorders center with a primary complaint of sleeping difficulty but uncommon for patients with NIA to present similarly. This alone would suggest that sleep disturbances are more severe in idiopathic RLS than in NIA. None of the NIA patients we selected for our study had a primary sleep complaint. However, in NIA both subjective and objective evidence of sleep disturbance were common. NIA and idiopathic RLS patients shared complaints of DIMS and EDS and both groups demonstrated evidence of increased numbers of awakenings and decreased sleep efficiency. In addition, RLS patients had prolonged sleep onset latencies. As would be predicted, the changes were less profound in NIA than RLS patients. Polysomnographic evidence of sleep disturbance in NIA has been confirmed in a previously published smaller study (13) and in an as yet unpublished study of another 9 patients (J. F. Lipinski et al., personal communication) completed since the publication of our original abstract (22).

There is no evidence from our data that the presence of sleep complaints or the increased number of awakenings or decrements in sleep efficiency in our NIA patients were directly related to the presence of PMS as NIA patients without PMS also had sleep complaints and an increased number of awakenings and decreased sleep efficiencies (Table 1). Moreover, we do not suspect that the sleep complaints and abnormalities in sleep parameters were related to schizophrenia. Nonetheless, we cannot exclude this possibility and the complaints of DIMS and EDS as well as the decreases in sleep efficiency and the increased number of awakenings we observed in our NIA patients (Table 1) can also be seen in schizophrenic but nonakathitic patients (23,24). However the sleep abnormalities in schizophrenia tend to disappear after the psychosis dissipates (23,24) and none of our NIA patients were actively psychotic at the time of the study. Furthermore, decrements in stage 3 and 4 sleep as well as shortened REM latencies are also common in schizophrenia (23,24). Only one of our NIA patients had a decrease in stage 3 and 4 sleep one standard deviation below the mean for age and sex (patient 1) and only three of our NIA patients showed shortened REM latencies one standard deviation below the mean for age and sex (patients 1, 5, and 7) (16).

4) Periodic movements in sleep. Involuntary movements during sleep were common in NIA and took the form of periodic movements in sleep (PMS) in five of nine patients. An as yet unpublished study (J. F. Lipinski et al., personal communication) found PMS in only one of nine NIA patients. Taken as a whole these two studies suggest that although PMS can occur in NIA, they do not occur in the majority of patients. As has been confirmed by this study and by many other authors, most severely affected idiopathic RLS patients have PMS (1,7–12,21). PMS usually take the form of discrete, repetitive flexions at the hips, knees, ankles, toes and less frequently the arms that recur at regular intermovement intervals of between 5 and 120 sec (8,21) in stages 1 and 2 of nonREM sleep (12). They are usually 0.5–5 sec in duration (8) and thus they are rarely as brief in duration as true myoclonus (8,21,25). Hundreds of PMS may occur per night and in idiopathic RLS the PMS may awaken the patients (1,12).

5) Jerking movements of the legs during wakefulness. In no case of NIA did we observe any of the multiple, large amplitude, violent, resting myoclonic jerks of the legs that are sometimes seen during wakefulness in severe cases of idiopathic RLS (1,7,21). This study and previous studies by ourselves and others (1,7,12,21,26)

confirm that jerking movements of the legs can occur during wakefulness in idiopathic RLS. In more severe cases of idiopathic RLS, hundreds of these movements can occur per night. They usually take the form of flexion jerks of the hips, knees, ankles, toes and sometimes the arms that occur during wakefulness when the patients lie down and they may interfere with sleep onset (1,7,21). Occasionally they may occur while patients are sitting quietly. We have called these involuntary movements resting dyskinesias while awake (DWA) (1,7,21). They may be periodic (periodic movements while awake or PMWA) forming a continuum with PMS or they may be aperiodic or clustered. In some cases of idiopathic RLS, the DWA may be of smaller amplitude, more prominent in the ankles and toes and less rapid than true myoclonus. In idiopathic RLS the resting DWA occur at rest and generally temporarily disappear when the patient voluntarily moves or ambulates. However, in some secondary forms of RLS, e.g., that associated with uremia, action myoclonus may be seen as well (27–29).

6) Daily variations in signs and symptoms. The manifestations of motor restlessness in NIA are present during the waking hours both day and night although there may be hourly fluctuations in the severity of motor restlessness depending on the time antipsychotics are given (1–5). Paresthesias and motor restlessness in idiopathic RLS are worse at night but they may be present during the day as well (1,6–12,21). The present work confirms these previously noted differences. The jerking movements of the legs during wakefulness also occur more at night in idiopathic RLS (7,21).

7) Effect of body position and state on signs and symptoms. As confirmed by the present work, the signs and symptoms in NIA are not particularly worse on lying in most patients. However, in idiopathic RLS the paresthesias, motor restlessness and jerking movements of the legs during wakefulness are exacerbated by lying or sitting still for prolonged periods in the majority of patients (1,6–12,21,30). Because patients lie down more at night than during the day, it is difficult to determine whether the nighttime exacerbation of signs and symptoms in idiopathic RLS is not simply a manifestation of repose. Our preliminary results from another study, however, suggest that idiopathic RLS is exacerbated by both night and repose (30).

8) Neurological examination. The neurological exam in NIA is frequently abnormal. This is because NIA is present both day and night and because other neuroleptic-induced movement disorders such as tardive dyskinesia, tardive dystonia or drug-induced parkinsonism often accompany NIA (1–5). Although involuntary movements can occur during the day in idiopathic RLS, they usually occur during the day only after prolonged sitting or lying. Therefore, the neurological examination is frequently normal in idiopathic RLS (6–12). In secondary forms of RLS, the neurological examination may show evidence of the primary condition, e.g. a peripheral neuropathy (1).

9) Clinical course. In NIA, symptoms may begin any time after neuroleptics are begun and may either disappear after neuroleptics are stopped as in the case of acute akathisia (1–5) or persist after neuroleptics are stopped as in the case of tardive akathisia (1–5). Idiopathic RLS is sometimes progressive and although it may occur at any age (31), the most severely affected patients are usually middle to older age (7). Spontaneous remissions sometimes occur (7).

10) Autosomal dominant family history. As has been noted by many authors, idiopathic RLS is often inherited in an autosomal dominant fashion (1,6–12,21,31). In a previous study, we asked 10 NIA and 10 idiopathic RLS patients questions about signs and symptoms of RLS in first degree relatives. Although family history was suggestive for RLS in eight patients with idiopathic RLS this was true of only one patient in the NIA group (7). This would suggest that most cases of NIA are not merely cases of familial RLS that are first precipitated by neuroleptics.

CONCLUSION

The current study has allowed us to further elucidate the clinical features of NIA and compare them with idiopathic RLS. NIA and idiopathic RLS show both similarities and differences. Motor restlessness and sleep disturbances can be seen in both NIA and idiopathic RLS, but periodic movements of sleep do not appear to occur as commonly in NIA as in idiopathic RLS. Myoclonus during wakefulness has been observed as a manifestation of neuroleptic exposure (32). However, in no case of NIA did we observe any of the multiple, large amplitude resting myoclonic flexion jerks of the hips, knees and ankles that are sometimes seen during relaxed wakefulness in severe cases of idiopathic RLS. Inner restlessness is the usual precipitant to motor restlessness in NIA and leg paresthesias the usual precipitant to motor restlessness in idiopathic RLS. Marching-in-place and body rocking are much more evident forms of motor restlessness in NIA than in RLS. Lastly, the symptoms are much more likely to be exacerbated by night and repose in RLS than in NIA. One interpretation of the results of this study is that neuroleptics create a condition similar but not identical to that caused by the genetic defect in idiopathic familial RLS. Because neuroleptics block the dopamine receptor, a logical hypothesis is that idiopathic familial RLS may be caused by a defect that either primarily or second-

arily alters dopamine synthesis or transmission. This hypothesis is further strengthened by the observation that dopamine agonists improve the symptoms of idiopathic RLS (11,33). However, both NIA (acute form) and idiopathic RLS have also been reported to respond to the opioids (3,4,9,10,34,35) and clonidine (36,37), suggesting that alterations in the endogenous opiate and adrenergic neurotransmitter system may be common to both conditions as well.

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