1999

Neuropsychiatry of movement disorders

Kevin J. Black  
*Washington University School of Medicine in St. Louis*

Jonathan W. Mink  
*Washington University School of Medicine in St. Louis*

Follow this and additional works at: [http://digitalcommons.wustl.edu/psych_facpubs](http://digitalcommons.wustl.edu/psych_facpubs)

Recommended Citation

[http://digitalcommons.wustl.edu/psych_facpubs/10](http://digitalcommons.wustl.edu/psych_facpubs/10)

This Article is brought to you for free and open access by the Department of Psychiatry at Digital Commons@Becker. It has been accepted for inclusion in Psychiatry Faculty Publications by an authorized administrator of Digital Commons@Becker. For more information, please contact engeszer@wustl.edu.
Neuropsychiatry of movement disorders

submitted for Current Opinion in Psychiatry 12(3), 1999

Kevin J. Black, M.D. (1,2,3)
Jonathan W. Mink, M.D., Ph.D. (2,4,5)

Departments of (1) Psychiatry, (2) Neurology and Neurological Surgery (Neurology), (3) Radiology, (4) Anatomy and Neurobiology, and (5) Pediatrics
Washington University School of Medicine, St. Louis, MO 63110

correspondence:
Kevin J. Black, M.D.
Campus Box 8134
4940 Children’s Place
St. Louis, MO 63110-1093
phone: 314 747-2013
fax: 314 362-0168 (attn: Dr. Black)
email: kevin@npg.wustl.edu

Acknowledgments:
Supported by NIH grants NS01808 and NS01898, a NARSAD Young Investigator award, the Tourette Syndrome Association, the American Parkinson Disease Association, the Charles A. Dana Foundation (The Dana Clinical Hypotheses Research Program), the McDonnell Center for Higher Brain Function, and Lilly Research Laboratories.
Summary

Movement disorders include both psychiatric illnesses with neurologic features and neurologic illnesses with frequent psychiatric complications. During 1998, neuropsychiatric progress was made on several fronts, notably in parkinsonism and tic disorders. This remains an exciting area for research, with many unsolved, clinically important problems, but increasing neurobiologic knowledge and sophistication.

Introduction

The term “movement disorders” is applied to a large and heterogeneous group of illnesses that affect the quality of volitional movement, produce unwanted excessive movements, or both. Phenomenologically, the abnormal movements include the parkinsonian syndrome, tremor, dystonia, chorea, myoclonus, hyperekplexia, and stereotypies. Many of these illnesses are often accompanied by disturbances of perception, memory, language, or mood. Additionally, several movement abnormalities have interested psychiatrists of their own right, including tic disorders, catatonia, the motor retardation of melancholic depression, odd movements as a feature of hysteria, and tardive movement disorders. During the past year, exciting new results have been reported in several of these areas.

Neuropsychiatry of parkinsonism

Cognition in parkinsonian disorders

A variety of cognitive deficits have been described in PD. The most well characterized are relatively subtle deficits that are usually attributed to dysfunction of frontal corticostriatal
circuits [1]. These include difficulties with shifting, sequencing, or maintaining behavioral set in the face of interfering stimuli. It has not been clear if the “frontal” dysfunction in PD is due to loss of dopamine innervation of frontal cortex, or to loss of the normal basal ganglia output to frontal cortex (via thalamus), or to a combination [2]. A recent study comparing patients with early PD to patients with damage to the left or right frontal lobes demonstrated clear differences between the groups [*3]. PD subjects showed an increased error rate as they performed successive trials, but not an increased time to switch between tasks. The authors suggested that intact dopamine neurotransmission is required to sustain cognitive and motor processes over prolonged time periods.

Another relatively common cognitive difficulty in PD is the development of dementia. It has been estimated that 10 - 20 % of patients with PD eventually become severely demented [4]. It is becoming increasingly clear, however, that dementia in PD is not due primarily to nigrostriatal dopamine loss, but is due instead to other mechanisms including coexistent Alzheimer’s disease, multi-system atrophy with loss of other subcortical nuclei, or diffuse Lewy body disease (DLBD) [5,6]. Churchyard and Lees [**7] examined the brains of 27 patients diagnosed during life with PD and compared them with 11 control brains. None of the subjects met clinical diagnostic criteria for DLBD, the Lewy body variant of Alzheimer's disease, or senile dementia of the Lewy body type. Five PD patients, 2 with moderate dementia and 3 with severe dementia, met pathological criteria for DLBD. There was no difference between PD brains and controls in measures of neuronal density, neurofibrillary tangles, or neuritic plaques in the hippocampus or amygdala. There was an increased density of Lewy bodies in hippocampal region CA2 in severely demented PD brains, but no correlation with severity of dementia.
However, increasing Lewy neurite densities in CA2 was related to worsening dementia as assessed by the mini-mental status exam and DSM-III criteria. The authors suggested that Parkinson’s disease and dementia with Lewy bodies overlap both clinically and pathologically.

Another recent study used MRI volumetric analysis to investigate the relationship between hippocampal size and deficits on verbal, visual, or spatial memory or set-shifting ability in non-demented PD subjects [8]. The authors found an inverse relationship between performance on visual or verbal memory tasks and hippocampal volume. There was no relationship between performance on spatial working memory or set-shifting tasks and hippocampal volume. They concluded that memory deficits in PD are due to hippocampal atrophy. These results appear to differ with those of Churchyard and Lees [**7] who reported no hippocampal atrophy in demented PD subjects. However, the volume loss as seen with MRI may not be due to change in neuronal density.

**Mood disorders in PD**

One important complication of PD and its treatment is the development of mood fluctuations which parallel plasma levodopa levels. Maricle and colleagues have reported several studies of this phenomenon, confirming that this is most likely a direct cerebral effect of levodopa [9,10]. They have now shown that earlier in PD, patients show smaller fluctuations in mood [**11]. This fits well with the hypothesis that mood fluctuations in advanced PD are similar in etiology (though probably different in functional neuroanatomy) to motor fluctuations.

A large minority of PD patients have persistent major depression. Unfortunately, there is little sound data on treatment; one review found no published study with adequate methodology
Psychosis in PD

Psychosis is a frequent complication of PD and probably a substantial risk for nursing home placement and death [17,18]. However, 46 years after chlorpromazine, there is still no peer-reviewed, methodologically adequate trial of any antipsychotic in this population. Perhaps the best published study was the 1996 report on olanzapine, but in that study raters were aware of treatment assignment [19]. Fortunately, we will not have to wait much longer. A presentation at the 1998 American Academy of Neurology meeting described a multicenter, double-blind, placebo-controlled study of clozapine in PD [**20]. Also, several small case series suggested that initial enthusiasm about risperidone, olanzapine and quetiapine must be tempered by the fact that they can occasionally cause significant worsening of parkinsonism in this population [21,22,*23,24,25,26,27,28]. More rigorous data are required before we can decide the merits of any of the newer antipsychotics in PD.

The neurobiology of psychosis in PD is still largely unknown, but a pilot study by Goetz and colleagues [*29] confirms clinical evidence that levodopa-induced hallucinations are a long-term rather than immediate effect of levodopa. Two recent phenomenological studies [*30,*31] show that PD patients who develop psychosis early in their course may comprise a different
group than patients who develop psychosis only in late PD, often accompanied by dementia or depression. However, the suggestion [*29] that psychosis early in the course of parkinsonism requires a diagnosis other than idiopathic PD seems premature, pending (1) studies in which parkinsonian etiology is ascertained blind to presence of psychosis, and (2) firmer consensus on the nosology of diffuse Lewy body disease and parkinsonism with Alzheimer’s disease. Auditory hallucinations are less common than visual hallucinations but clearly occur in PD patients [32].

**Huntington’s Disease**

One simple but clever study attempted to “determine why patients with Huntington disease (HD) are apparently unaware of their involuntary movements” [*33]. The results support the view that patients have a form of anosognosia rather than dementia or psychologically motivated denial.

Two reports address the question of whether cognitive deficits can be identified in asymptomatic gene carriers for HD. Clinically unaffected carriers showed no significant cognitive deficits in one study [*34]. In a larger study [**35], logical and verbal memory test performance was worse in neurologically normal at-risk individuals who later were found to have abnormal versus normal number of CAG repeats in the huntingtin gene. Additionally, gene carriers with higher repeat numbers tended to do worse on several tests. These studies show that there are statistically significant, but clinically subtle, cognitive disturbances before development of abnormal neurological signs in HD. However, motor abnormalities below the neurological exam threshold may precede these cognitive abnormalities.
Psychological symptoms in dystonia

An interview study of 44 adult patients with cervical dystonia found frequent panic disorder, major depression, and OCD [*36]. The 66% frequency of diagnosable psychiatric illness in this group implies that, contrary to suggestions in the literature [37], the presence of preexisting mental illness is unreliable as an indicator of atypical or “psychogenic” dystonia.

Pathophysiology of Tics

The prevailing hypothesis of tic pathophysiology involves increased dopamine activity in basal ganglia circuits. This idea is variably supported by neurochemical, functional imaging, and clinical pharmacologic data [38]. Recent support comes from functional MRI findings of BOLD signal changes in basal ganglia and thalamus that correlated inversely with tic severity during attempts to suppress the tics [39]. One prediction of this hypothesis is that dopamine depletion should decrease or eliminate tics. However, a recent report of 4 individuals with tics beginning in childhood and Parkinson’s disease beginning in later adulthood found that tics neither decreased with onset of PD nor worsened with dopamimetic treatment [*40]. This suggests that tics are not exclusively due to functional overactivity of the dopamine system, but must involve other systems as well.

Over the past several years, there has been increasing evidence for a post-infectious or immune-mediated mechanism in some individuals with tics or TS. It has long been known that neurologic illness, especially Sydenham (rheumatic) chorea, can follow group A beta-hemolytic streptococcal (GABHS) infections [41]. Less well-known is that obsessions, compulsions, inattentiveness, tics, and even mania can accompany Sydenham chorea [41,42]. Thus, it may not
be surprising that some individuals develop obsessive-compulsive disorder (OCD), tics (including Tourette syndrome), or both in close temporal relationship to an antecedent GABHS infection. Post-infectious onset of tics or OCD has been an area of active research by several investigators [**43]. Although tics associated with infections other than strep have been reported, including Lyme disease [44], the strep association appears to be the most convincing. A group at the NIMH has coined the term PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal infection) and has recently published a description of their first 50 patients [*45]. They define PANDAS by abrupt childhood onset of OCD or tics, temporally related to GABHS infection, with neurologic signs (hyperactivity, choreiform movements, tics) during an exacerbation.

Support for PANDAS as a possible etiology of tics comes from several independent lines of evidence, as reviewed recently by Kurlan [**43]. Two lines of evidence will be discussed here. One is the presence of antineuronal antibodies in subjects with TS. Singer et al. [**46] found increased levels of antibodies against putamen in 41 children with TS compared to 39 age-matched controls. However, there was substantial overlap. In TS subjects, these antibodies were more common in those with serologic evidence of GABHS infection. There was no association between elevated antineuronal antibodies and age of tic onset, tic severity, sudden onset of tics, presence of OCD, or presence of ADHD.

The second line of evidence concerns the presence of markers associated with acute rheumatic fever in individuals without rheumatic fever, but with tics or OCD. One such marker is a B cell surface marker called D8/17. This marker had is present in 90 - 100% of subjects with rheumatic fever and virtually absent in controls [47]. In a study by Murphy et al. [48], patients
with either TS or OCD, but without rheumatic fever, had an elevated average percentage of B cells expressing D8/17. All patients but only one control were considered D8/17 positive.

Another study investigated the frequency of D8/17 positive individuals among groups of 27 children with PANDAS, 9 children with Sydenham chorea, and 24 healthy controls [49]. They found that 85% of the PANDAS group, 89% of the Sydenham chorea group, and 17% of the control group were D8/17 positive. Thus, some individuals with tics or OCD appear to share a genetic marker with individuals who are susceptible to developing rheumatic fever. This lends support to the notion that in some predisposed individuals, tics or OCD may be a manifestation of post-streptococcal immune-mediated disease.

Although many studies have suggested an autosomal dominant inheritance of TS, attempts to identify a specific gene have been unsuccessful, as reviewed recently [*50]. One approach has been to test candidate genes in neurotransmitter systems thought to be involved in TS. Previous studies have suggested that the dopamine receptor D2, D3, or D4 loci might be implicated in TS, but other studies have not confirmed those findings [*50]. A recent report using single stranded conformational polymorphism analysis of the D1 receptor gene failed to demonstrate any mutations in subjects with TS [51].

**Comorbidity in Tourette Syndrome**

Although TS is defined solely by tics, many TS patients find other symptoms more problematic, especially obsessions, compulsions, or impaired attention or learning. An important unanswered question is whether comorbid psychological symptoms define a clinically meaningful subgroup of TS.
In a multicenter German family study of TS and OCD, obsessions and compulsions (OC symptoms) were more frequent in relatives of TS patients who themselves had OC symptoms [*52]. However, OC symptoms in relatives were most likely caused by the same gene(s) as tics, as they were usually accompanied by tics (in male relatives). Also, if OC symptoms were present, their severity, including the diagnostic threshold for OCD, was irrelevant to heritability of either tics or OC symptoms. These findings support the concept that the presence or absence of OC symptoms may be a biologically meaningful clinical feature of TS. This study also reports several other clinically relevant findings, including the observation that five relatives had otherwise typical tic syndromes but definitely dated tic onset to after age 21.

Another report also supports the validity of subdividing TS by presence or absence of OC symptoms. A group from Harvard [*53] examined 61 patients with TS, OCD, or both (TS-OCD) for various other psychiatric syndromes. The rates for most mood and anxiety disorders did not differ between the TS-only group and the OCD-only group. However, the 3 groups differed significantly in rates of bipolar disorder, social phobia, body dysmorphic disorder (BDD), trichotillomania, attention deficit hyperactivity disorder (ADHD), and substance abuse. To summarize, the TS+OCD group had the highest frequency of comorbidity, ADHD segregated with tics, and (surprisingly) BDD also seemed more closely related to TS. The authors conclude that TS+OCD has more substantial comorbidity than either diagnosis alone, and that this group is probably linked more closely to TS than to OCD.

In this study, three of 20 patients with both TS and OCD met criteria for bipolar disorder [*53]. Given a population prevalence for bipolar disorder of <1%, the 15% prevalence here is remarkable. However, a study from Spain found that 12% of 90 consecutively examined patients
with TS had either bipolar disorder or schizoaffective disorder, and an additional 21% had bipolar II disorder or cyclothymia [54]. The majority of these patients (80%) also had OCD, and many of them reported fewer tics during depressive episodes and more with manic episodes [54]. This surprising prevalence of manic illness in TS+OCD patients is probably not due to excessive symptom reporting in general, as this group reported less panic disorder or agoraphobia than the other groups [**53]. Further studies of this difficult to treat subgroup are warranted.

**Tardive movement disorders**

Molho et al [**55] contrasted clinical features of torticollis patients with presumed tardive or primary etiologies. Contrary to clinical lore, several clinically useful distinctions were found. Another large report on tardive cervical dystonia also found frequent retrocollis [*56]; although the disease was chronic, stopping neuroleptics could clearly help the dystonia.

A large prospective study on the incidence of tardive dyskinesia (TD) in the elderly found staggeringly high cumulative rates of 25% and 53% after 1 and 3 years of total antipsychotic treatment, respectively [**57]. Surprisingly, a past history of electroconvulsive therapy treatment was a strong risk factor for later development of TD; whether this reflects diagnosis, severity of illness, or other symptomatic features remains to be shown. A meta-analysis of vitamin E treatment of TD concludes that a subgroup of patients shows statistically meaningful but clinically modest benefit without substantial side effect risk [58]. However, methodological flaws in several of the studies reviewed render these conclusions tentative. In a randomized study, fully informed consent regarding TD risk did not negatively affect antipsychotic compliance [59].

The availability of a direct genetic test for HD allowed a study of 12 patients with
presumed senile chorea to conclude that six had Huntington’s disease with a negative family history [60]; this has implications for prior studies of “spontaneous” dyskinesias in the elderly. On the other hand, the existence of abnormal movements in never-treated subjects with schizotypal personality disorder [61] or schizophrenia suggests that movement disorder may be an integral part of these illnesses [62]. However, in this study and in prior reports on untreated schizophrenia, the abnormal movements observed are often complex and are generally not the orofacial stereotypies with tongue protrusion which are typical of tardive dyskinesia.

**Catatonia and neuroleptic malignant syndrome**

Two interesting reports on the genetics of periodic catatonia, an illness marked by relapsing and remitting catatonic episodes, involved 83 probands [63,64]. The authors found evidence for a single major gene effect with genetic anticipation and a 27% risk to first-degree relatives. There was a trend (p < 0.10) for paternal transmission of illness to be associated with younger age of onset in the probands. These results are preliminary but may be consistent with a triple repeat mechanism.

A case-control of study neuroleptic malignant syndrome (NMS) confirmed previously reported risk factors for development of NMS, including parenteral administration of neuroleptics and catatonia, and also revealed risks for agitation, parkinsonism, akathisia, and neuroleptic dosing [*65]. Another study [66] examined the relationship between catatonia, NMS, and low serum iron, an acute phase reactant which had previously been found in NMS [67]. Low serum iron was found in every instance of “malignant catatonia” (NMS-like without neuroleptic exposure), and these patients had a high risk of NMS upon exposure to neuroleptics. Some
catatonic patients without malignant features also had low serum iron, but these patients did not
tend to develop NMS. These interesting results may indicate a clinically meaningful subdivision
of catatonia, and deserve confirmation in prospective studies.

Conclusion

Important advances were reported in 1998 in the neuropsychiatry of movement disorders.
We should soon see the long-awaited publication of adequate treatment studies of psychosis in
Parkinson’s disease. Also, increasing evidence supports the hypothesis that some cases of
Tourette syndrome or OCD may be caused by autoimmune responses to streptococcal infections.
However, at our current stage of knowledge, it remains appropriate to study TS using several
different approaches, including genetic and neuroimaging studies. Exciting research opportunites
remain in this field of medicine.

Reference List

1. Brown RG, Marsden CD. Cognitive function in Parkinson's disease: from

2. Mink JW. The basal ganglia: Focused selection and inhibition of

Dissociating executive mechanisms of task control following frontal lobe damage
* This is a report of different deficits among patients with frontal lobe lesions or
Parkinson's disease in a task-switching paradigm. The Parkinson's disease patients
showed an increase in error rate as they performed succesive trials, but not an
increased time to switch between tasks. The authors suggest that intact dopamine
neurotransmission is required to sustain cognitive and motor processes over
prolonged time periods.


** The authors examined the brains of 27 patients who had been diagnosed with Parkinson's disease during life. The severity of cognitive impairment was correlated with the density of Lewy neurites in region CA2 of the hippocampus. The authors suggest that Parkinson's disease with dementia and dementia with Lewy bodies are overlapping clinical and pathological entities.


** This is a carefully executed study of levodopa-induced mood fluctuations in Parkinson's disease which extends the authors' earlier work to patients with milder disease and shorter treatment histories.

* A survey of neurologists from the Parkinson's Study Group found that a quarter of their patients were being treated with an antidepressant, but of these almost half were taking tricyclic agents. As dose was not specified and many respondents reported they chose tricyclics in part for their hypnotic effects, the adequacy of treatment in many depressed PD patients is suspect.

* Selegiline (an MAO-B inhibitor at the doses used) was found to confer additional benefit when added to moclobemide (a reversible MAO-A inhibitor) in treating depressed patients with PD. However, these results will need confirmation in a blinded, randomized allocation study, and comparison to the simpler strategy of using a nonselective MAO inhibitor or a higher dose of selegiline, before this treatment option has clear utility.

* Twenty-five depressed PD patients treated with electroconvulsive therapy (ECT) were compared retrospectively to 25 non-PD ECT patients matched for age and gender. ECT was clearly effective as an antidepressant, but nearly half their patients developed confusion on days between treatments.


**This is only an abstract, but represents the first successful, methodologically adequate study of this clinically very important illness. Low-dose clozapine successfully treated positive symptoms without worsening of parkinsonism. One of 60 patients experienced transient leukopenia.**


**The author describes his clinical experience with olanzapine in several parkinsonian patients with psychosis. The majority had improvement of psychosis, but several patients developed delirium or clinically significant worsening of parkinsonian motor signs. The reply from Wolters et al reminds us that the methodologically best published study found no significant motor deterioration with olanzapine, and suggests that in their experience, younger, nondemented PD patients without agonist treatment may do better with olanzapine.**


   * Five PD patients with hallucinations during the ordinary course of treatment received 1.5mg/kg levodopa intravenously, in addition to their usual oral medications. Not one patient experienced hallucinations, although patients had clear motor effects and adequate plasma levodopa levels. The authors conclude that "visual hallucinations do not relate simply to high levels of [levodopa] or to sudden changes in plasma levels."


   * This phenomenological study of psychosis in PD confirms earlier evidence that psychosis is less common with levodopa than with dopamine agonists.


   * Parkinsonian patients who develop hallucinations early in the course of illness show clear clinical differences when contrasted to patients who develop hallucinations only after years of illness and treatment.


   * HD patients underestimated the severity of their movement disorder, but accurately reported the consequences, such as falling or knocking over a glass of water. If patients had psychologically motivated denial they would deny both. Unawareness of chorea did not correlate with dementia. Although other interpretations are possible, the authors conclude reasonably that patients have a form of anosognosia. The study bears replication in other forms of chorea and in tardive dyskinesia.

* Asymptomatic carriers with normal neurological examination results showed no significant differences and performed only minimally worse on any of several cognitive tests compared to non-gene-carrying relatives of HD patients. However, asymptomatic individuals with abnormal neurologic exams did somewhat worse on verbal memory and response inhibition tasks, and clearly worse on several motor tasks, than genotypically normal at-risk individuals. The study had low power due to group size.


** In this fairly large study from the Salpêtrière, there were statistically significant differences in neuropsychological test results between neurologically normal at-risk individuals who later were found to have abnormal versus normal number of CAG repeats in the huntingtin gene. Logical and verbal memory was most affected. Additionally, there were significant correlations of several tests with repeat number within the gene carrier group, including response inhibition, memory (Wechsler paired associates), and digit symbol tests.


* In this interview study of 44 adult patients with cervical dystonia, panic disorder, major depression, and OCD were especially common, although no comparison group was examined simultaneously. Most patients with major depression said it antedated the torticollis, suggesting that it was not simply a response to pain, disability or embarrassment.


* This is a report of 4 individuals with tics since childhood, who met historical criteria for Tourette Syndrome who developed Parkinson's disease in adulthood. There was no change in the tics associated with the onset of parkinsonian symptoms (follow-up 3 mos. to 11 yrs.). Further, in the three patients who were treated with l-dopa (the 4th refused treatment), there was no change in tics associated with l-dopa therapy. This report suggests that tics are not due exclusively to dopaminergic mechanisms.


** The author reviews the concept that a spectrum of childhood neurobehavioral disorders can follow infection with group A beta-hemolytic streptococcus and discusses the possible relationship between tic disorders and antecedent strep infections. This is one of the most thorough rigorous reviews on the subject to date.

** This is a study of serum antineuronal antibodies in 41 children with Tourette syndrome and 39 age-matched controls. The authors report increased antibodies against putamen. Among subjects with elevated antistreptolysin O or
antideoxyribonuclease B titers, a significantly larger group of TS subjects had elevated antineuronal antibodies. Although the TS subjects had increased antineuronal antibodies as a group, several control subjects had increased antibodies and several TS subjects did not have increased antibodies as measured by ELISA optical density.


* A review of the the progress and obstacles in the search for specific genes involved in Tourette Syndrome


** This family study of Tourette syndrome (TS) was carefully executed; diagnosis in 75% of 267 first degree relatives came from examination of patient and/or parental interview. There were several clinically relevant findings, but the results are most important for their implications for the nosology of obsessive-compulsive symptoms in TS patients.
** Patients in 3 groups (TS alone, OCD alone, or both) differed significantly in rates of several comorbid psychiatric illnesses. Primarily this was due to higher rates of comorbidity in the TS+OCD group compared to the OCD group, but the TS+OCD group also had higher rates than the TS-only group, except for ADHD. After Bonferroni correction for multiple comparisons, the group difference in prevalence of body dysmorphic disorder remained statistically significant.


** Patients with cervical dystonia were retrospectively divided into tardive and idiopathic groups on clinical grounds. The tardive patients had more extracervical involvement, retrocollis, and dystonic head movements; head tremor and dystonia in relatives were found exclusively in the idiopathic group, and torticollis, laterocollis, hypertrophy of neck muscles, and sensory tricks were more common in the idiopathic group.

* A retrospective review which underscores the serious and chronic nature of this illness. The dystonia was more likely to improve in patients in whom stopping neuroleptics was possible.

** A final report from a large, prospective study of tardive dyskinesia (TD) in older patients. The risk of TD after 3 years of neuroleptic treatment was over 50%.


   *This study identified clinical as well as pharmacologic risk factors for NMS in patients treated with neuroleptics: psychomotor agitation, confusion, disorganized behavior, and catatonia; parkinsonism, dystonia, and akathisia; and neuroleptic dose, recent dose increases, and parenteral administration.*
