TABLE 1. *Neurologic signs of the neurodegenerative disorders*

	AD	CBGD	DLBD	MSA			PD	PSP
				OPCA	SDS	SND		
Autonomic failure	+	+	++	++	++++	++	++	+
Cerebellar signs	+	+	0	++++	+	++	0	+
Cognitive dysfunction	++++	++	++++	++	+	++	++	+++
Dysarthria	++	+++	++	+++	+	+++	++	+++
Dysphagia	++	+	++	++	+	++	++	+++
Involuntary movements	+	++	+++	++	+	+	+++	+
Oculomotor impairment	+	++	++	+++	+	+	++	++++
Parkinsonism	++	++++	++++	++	+++	++++	++++	++++
Peripheral neuropathy	+	+	0	++	+	+	0	+
Pyramidal signs	+	++	+	++	+	++	0	++

0, none; +, uncommon or unusual; ++, common or moderate; +++, frequent or marked; ++++, present in nearly all cases or severe; AD, Alzheimer's disease; CBGD, corticobasalganglionic degeneration; DLBD, diffuse Lewy body disease; MSA, multiple system atrophy; OPCA, olivopontocerebellar degeneration; PD, Parkinson's disease; PSP, progressive supranuclear palsy; SDS, Shy–Drager syndrome; SND, striatonigral degeneration.

ous descriptions in the literature of "atypical" presentations that unmask our professional bias.

It is interesting to speculate on the forces that promote reductionism in medicine. Desire for mastery coupled with frustration with ignorance motivates physicians to make a specific diagnosis. To a lesser extent, the enhanced recognition and compensation accorded to specialists may underlie this inclination. Nonetheless, if the motive is clarity and candor, when confronted with a patient with an insidious progression of levodopa-nonresponsive parkinsonism and dementia, our current state of knowledge would support a simple diagnostic description of a *neurodegenerative disorder involving the basal ganglia and cerebral cortex.* The reliance on more specific diagnostic labels rather than the neurodegenerative process is misleading to physicians and patients alike. Simple descriptors highlight the preeminence of the neurodegenerative process and the relative vulnerability of the different regions of the brain to neuronal injury. Consider the confusion that would result from disparate names for different forms of cancer, rather than the accepted usage of cancer of the lung, cancer of the breast, and so on.

It is worthwhile to question whether a need for precision and nonambiguity has driven us to embrace and expound a misleading concept of neurodegenerative disease: the view that the different manifestations of neurodegeneration are unique entities. Although significant gains in our understanding of the neurodegenerative disorders have arisen from the current approach, it is valuable to recognize its limits. Academic clinical subspecialists do not regularly consult on patients representing the spectrum of neurodegenerative disease (e.g., parkinsonism, primary dementia, motor neuron disease). Few training fellowships encompass the variable manifestations of the neurodegenerative process. Educational symposia for the "dementiologists" and "parkinsonologists" are generally segregated, and there is inadequate cross-pollination of ideas between subspecialists. Speculative articles that address unifying hypotheses for the cause of neurodegenerative disorders are few (7). Patterns and trends may be obscured by unnecessarily narrow scrutiny. The merits of the current approach are undisputed, but while the jury is still out on the true nature of neurodegenerative disease, the potential benefits of a broader, more comprehensive perspective remain unappreciated.

"The advance of medical knowledge is, in general, toward causation; it often leads to redefinition of diseases, disorders of structure or of function displacing syndrome, and causation in turn displacing these as defining characteristics. It is thus inevitable that diagnostic terms of these various sorts coexist in current nosology. Unless the differing factual implications of the names of diseases defined in these various ways are recognized, confusion is inevitable" (8).

Lisa M. Shulman
Parkinson's Disease and Movement Disorders Center
Department of Neurology
University of Miami School of Medicine
Miami, Florida, U.S.A.

References

1. Skinner HA. *The origin of medical terms.* 2nd ed. Baltimore: Williams & Wilkins, 1961:143.
2. *Stedman's Medical Dictionary.* 17th ed. Baltimore: Williams & Wilkins, 1949:340.
3. *Stedman's Medical Dictionary.* 21st ed. Baltimore: Williams & Wilkins, 1966:456.
4. *Stedman's Medical Dictionary.* 22nd ed. Baltimore: Williams & Wilkins, 1972:358.
5. *Dorland's Medical Dictionary.* 19th ed. Philadelphia: WB Saunders, 1943:441.
6. Quinn N. Multiple system atrophy. In: Marsden CD, Fahn S, eds. *Movement disorders 3.* Oxford: Butterworth-Heinemann, 1994: 262–281.
7. Appel SH. A unifying hypothesis for the cause of amyotrophic lateral sclerosis, parkinsonism, and Alzheimer's disease. *Ann Neurol* 1981;10:499–505.
8. Scadding JG. Health and disease: what can medicine do for philosophy? *J Med Ethics* 1988;14:118–124.

Risperidone-Induced Tardive Dyskinesia and Parkinsonism

Risperidone is widely believed to have little risk of extrapyramidal side effects and is not believed to be associated with

A videotape segment accompanies this article.

Received December 18, 1995, and in revised form March 18, 1996. Accepted March 18, 1996.

tardive dyskinesia. We report, with videotape accompaniment, a patient who developed parkinsonism and involuntary oral-buccal-lingual dyskinesias while undergoing treatment for manic-depressive disorder with risperidone. This case emphasizes the importance of vigilance regarding the risks for involuntary movement disorders in patients on neuroleptics, including patients being treated with atypical neuroleptics such as risperidone.

Case Report

A 69-year-old man with a long history of bipolar disorder presented to our clinic with complaints of "tremors, inside and out." He had been admitted to the state psychiatric hospital ~11 months earlier, with what was described as a manic episode, and was treated with valproic acid 250 mg b.i.d., lorazepam 1 mg q.i.d., buproprion hydrochloride 75 mg t.i.d., trihexyphenidyl 5 mg b.i.d., and risperidone 3 mg b.i.d. There were no involuntary movements or gait difficulties at the time of that admission. His mood disorder improved, and he was discharged. However, a few months after discharge, he developed involuntary mouth movements, tremor, slowness, and difficulty with gait. The patient was treated with risperidone for a total of 10 months, at which point both the risperidone and trihexyphenidyl were discontinued. However, the movements and parkinsonism persisted, and he was seen initially in our clinic 3 weeks after the risperidone had been discontinued. Past medical history was significant for exposure to thiothixene hydrochloride (Navane) 10 years earlier, with no movement disorders during or following that treatment. The patient was edentulous, but had no involuntary oral movements prior to institution of the risperidone. Medications at the time of both of our evaluations included valproic acid 250 mg b.i.d., lorazepam 1 mg t.i.d, and buproprion hydrochloride 75 mg t.i.d.

Initial examination revealed a thin Caucasian gentleman. He appeared anxious, but mental status was otherwise normal. Cranial nerve examination revealed mild masked facies. The patient was edentulous and wearing loose fitting dentures. There were marked to severe continuous oral-buccal-lingual dyskinesias (Segment 1). Motor examination was significant for mild rigidity of the neck and moderate rigidity of all extremities with cogwheeling. There was moderate rest tremor of both upper extremities, which was symmetric. Rapid alternating movements were moderately slowed, with breakdown of movement bilaterally. Gait examination revealed short step height and length, with mild stooped posture and bradykinesis. No other abnormalities were noted. The last follow-up examination in our clinic was done 4 weeks later. Severe oral-buccal-lingual dyskinesias persisted (Segment 2). No rigidity was noted in the neck or in the extremities. No rest or action tremor was seen. Rapid alternating movements were minimally slowed. Ability to rise from a chair and gait were normal. Thereafter, attempts at follow-up failed, despite repeated efforts, and the person at the patient's previous residence reported that the patient had been readmitted to a psychiatric facility in a nearby state, following a gambling spree.

Discussion

Although this patient had a remote history of exposure to neuroleptics, symptoms of parkinsonism and dyskinesias did not emerge until the patient was treated with risperidone. Additionally, although the patient is edentulous, these movements did not precede risperidone treatment, making it unlikely that the movements represent involuntary oral movements, which can be seen in the edentulous elderly, without other cause. It is likely that this patient's parkinsonism and tardive dyskinesia were induced by risperidone.

A recent advance in pharmacotherapy has been the development of newer antipsychotic medications, such as clozapine and risperidone, which are felt to cause relatively few extrapyramidal symptoms (EPS) (1,2,3). It is known, however, that risperidone can worsen parkinsonism in patients with Lewy body dementia (4) and can induce parkinsonism (5). Additionally, clozapine can cause tremor, bradykinesia, and oculogyric crises (6,7). It remains possible that the acute EPS seen in these cases is separate from any risk of tardive dyskinesia (TD), although there may be a relationship between susceptibility to EPS and TD (8).

Risperidone, at a dose of 10 mg/day, has been implicated as the cause of tardive dyskinesia in a single patient previously (9). However, that patient complained of restlessness and stiffness, prior to risperidone treatment, suggesting preexisting neuroleptic-induced parkinsonism and akathesia (9). Furthermore, the onset of the dyskinesia was related to withdrawal of trifluroperazine, with the movements starting <6 months after trifluoperazine discontinuation (9). Our case demonstrates that tardive dyskinesia can occur with risperidone treatment, at doses as low as 6 mg/day. Although our patient had a history of neuroleptic exposure, that was >10 years earlier, making it a very unlikely cause of his dyskinesia.

The concurrent use of buproprion and risperidone at the time of our patient's admission to the outside hospital is worthy of further consideration. Buproprion inhibits norepinephrine uptake and has mild dopaminergic effects, although the exact mechanism of its antidepressant effect remains to be revealed (10). As a dopaminergic agent, buproprion is similar to but weaker than cocaine (10). Because dyskinesias and tics can be exacerbated or caused by cocaine (11), buproprion may also be capable of inducing involuntary movements. Buproprion has been described as worsening dystonia and tardive dyskinesias (12), and may be capable of causing dyskinesia (13). Interestingly, it may also mildly worsen parkinsonism (14). Because the patient was on buproprion at the time of both examinations, the possibility that it contributed to the movement disorder cannot be ruled out. However, the time course, including the improvement in parkinsonism, after risperidone discontinuation, suggests that risperidone, and not buproprion, is responsible for our patient's extrapyramidal syndrome.

The use of the anticholinergic trihexiphenidyl is also of interest in this patient, as anticholinergic medications have been shown to induce involuntary movements, which may be augmented by the concurrent use of dopaminergic agents (15). It is unlikely that the anticholinergic medication is responsible for this patient's symptoms, however, as they persisted well after that medication was discontinued.

The pathophysiology of neuroleptic-induced tardive dyskinesia remains to be fully characterized, although several theories exist. It has been proposed that neuroleptic use leads to dopamine receptor supersensitivity, particularly of the D2 receptor, and subsequent dyskinesias (8). Risperidone, like clozapine, blocks serotonin 5HT-2 receptors potently and D2 receptors relatively weakly (3). It has been proposed that this ratio could explain some of the valuable features of risperidone, including better efficacy for the negative symptoms of schizo-

phrenia and less risk of EPS and tardive dyskinesia (3,16). However, in a nonhuman primate study that tested compounds with a range of S2/D2 antagonism ratios, no significant difference in dose-related dystonia was seen between compounds (17). Other authors propose that TD is the result of damage to striatal cholinergic neurons, which could occur during chronic neuroleptic treatment, due to a release of these neurons from dopaminergic inhibition (18). It has been suggested that a difference in dopaminergic and muscarinic effects may be critical factors in the production of TD. Fluphenazine and clozapine, as well as risperidone, have an affinity for striatal dopamine receptors and may increase striatal dopamine receptor sensitivities (3,19). However, clozapine has an affinity for both dopamine and muscarinic receptors, and fluphenazine and risperidone have very little, if any, muscarinic affinity (3,19). It is possible that the cholinergic characteristics of clozapine, not the serotonergic, are responsible for its "atypical" features. If this is the case, then risperidone is more similar to "typical" neuroleptics and is able to induce tardive dyskinesia.

Risperidone has been a proposed treatment for tardive dyskinesia, especially for bucco-linguo-masticatory symptoms, and has been found to be more potent than haloperidol in suppressing the symptoms of TD (2). However, in this patient, risperidone not only induced parkinsonism, it also induced tardive dyskinesia. That risperidone suppresses TD does not imply that the drug is curative, nor even risk free, since traditional neuroleptics have the capacity to both produce and suppress TD. This case demonstrates that risperidone, in addition to other neuroleptics, should be used with great caution, especially in patients with a history of neuroleptic exposure, as it can induce, or possibly worsen, dyskinesia and/or parkinsonism. Although the risk of EPS may be lower with so-called nontraditional antipsychotics, such as risperidone, this case illustrates that one must maintain a high level of suspicion in order to determine the actual risk of such agents as they become more widely used.

Legends to Videotape

Segment 1. Three weeks after discontinuing risperidone. The patient has prominent oral-buccal-lingual dyskinesias consistent with tardive dyskinesia.

Segment 2. Seven weeks after discontinuing risperidone. The oral-buccal-lingual dyskinesias are persistent.

Katrina A. Gwinn
John N. Caviness
Department of Neurology
Mayo Clinic Scottsdale
Scottsdale, Arizona, U.S.A.

References

1. Casey DE. Clozapine: neuroleptic-induced EPS and tardive dyskinesia. *Psychopharmacology (Berl)* 1989;99:S47–53.
2. Chouinard G. Effects of risperidone in tardive dyskinesia: an analysis of the Canadian multicenter risperidone study. *J Clin Psychopharmacol* 1995;15:36S–44.
3. Keltner NL. Risperidone: the search for a better antipsychotic. *Perspect Psychiatr Care* 1995;31:30–33.
4. McKeith I, Ballard CG, Harrison RWS. Neuroleptic sensitivity to risperidone in Lewy body dementia. *Lancet* 1995;343:699.
5. Mahmood T, Clothier EB, Bridgman R. Risperidone-induced extrapyramidal reactions. *Lancet* 1995;346:1226.
6. Dave M. Tardive oculogyric crises with clozapine. *J Clin Psychiatry* 1994;55:264–265.
7. Kurz M, Hummer M, Oberbauer H, Fleischhacker WW. Extrapyramidal side effects of clozapine and haloperidol. *Psychopharmacology (Berl)* 1995;118:52–56.
8. Andrew HG. Clinical relationship of extrapyramidal symptoms and tardive dyskinesia. *Can J Psychiatry* 1994;39:S70–80.
9. Addington DE, Toews JA, Addinton JM. Risperidone and tardive dyskinesia: a case report. *J Clin Psychiatry* 1995;56:484–485.
10. Ascher JA, Cole JO, Colin JN, et al. Buproprion: a review of its mechanism of antidepressant activity [Review]. *J Clin Psychiatry* 1995;56:395–401.
11. Cardoso FE, Jankovic J. Cocaine-related movement disorders. *Mov Disord* 1993;8:175–178.
12. LeWitt PA, Walters A, Henig W, McHale D. Persistent movement disorders induced by buspirone. *Mov Disord* 1993;8:331–334.
13. Strauss A. Pral dyskinesia associated with buspirone use in an elderly woman. *J Clin Psychiatry* 1988;49:322–323.
14. Hammerstad JP, Carter J, Nutt JG, Casten GC, Shrotriya RC, Alms DR, Temple D. Buspirone in Parkinson's disease. *Clin Neuropharmacol* 1986;9:556–560.
15. Hauser RA, Olanow CW. Orobuccal dyskinesia associated with trihexyphenidyl therapy in a patient with Parkinson's disease. *Mov Disord* 1993;8:512–514.
16. Owens DG. Extrapyramidal side effects and tolerability of risperidone: a review. *J Clin Psychiatry* 1994;55:29–35.
17. Casey DE. Serotonergic and dopaminergic aspects of neuroleptic-induced extrapyramidal syndromes in nonhuman primates. *Psychopharmacology (Berl)* 1993;112:S55–9.
18. Miller R, Chouinard G. Loss of striatal cholinergic neurons as a basis for tardive and L-dopa–induced dyskinesias, neuroleptic-induced supersensitivity psychosis and refractory schizophrenia. *Biol Psychiatry* 1993;34:713–38.
19. Friedman E, Gianutsos G, Kuster J. Chronic fluphenazine and clozapine elicit opposite changes in brain muscarinic receptor binding: implications for understanding tardive dyskinesia. *J Pharmacol Exp Ther* 1983;226:7–12.

Primary Sjögren's Syndrome Presenting as Progressive Parkinsonian Syndrome

Primary Sjögren's syndrome (pSS) is a common autoimmune disorder (1–3% of the general population) characterized by exocrine gland impairment (1). Numerous central nervous system manifestations have been described in pSS, including psychiatric disturbances; cognitive dysfunction; focal cerebral, brainstem, and cerebellar symptoms; epilepsy; acute and chronic myelopathy; stroke; aseptic meningoencephalitis; and optic neuritis, sometimes with remitting signs that mimic multiple sclerosis (1–6). Movement disorders such as tremor, dystonia, and pseudoathetosis have also rarely been reported (3,7).

We report a patient with pSS associated with bilateral parkinsonism. As far as we are aware, only one case of hemiparkinsonism in a patient with pSS has been reported previously (7).

Case Report

A 44-year-old female executive secretary was referred in June 1993 because of a progressive gait disorder. Her history

Received October 12, 1995, and in revised form January 25 and April 12, 1996. Accepted April 16, 1996.