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Sympathetic Neurocirculatory Failure in Parkinson Disease: Evidence for an Etiologic Role of α -Synuclein

David S. Goldstein, MD, PhD, Sheng-Ting Li, MD, and Irwin J. Kopin, MD

National Institute of Neurological Disorders and Stroke, Bethesda, MD 20892-1620

TO THE EDITOR

In Parkinson disease, orthostatic hypotension reflects sympathetic neurocirculatory failure, characterized by cardiac sympathetic denervation (1). An Italian-American family has been shown to carry a mutation of the α -synuclein gene, with autosomal dominant transmission of Parkinson disease (2). We report neurogenic orthostatic hypotension and cardiac sympathetic denervation in an affected family member. Physical examination showed pill-roll tremor, bradykinesia, and cogwheel rigidity that improved with L-dopa-carbidopa. The patient had reproducible orthostatic hypotension without tachycardia. Speech and gait were approximately normal. Beat-to-beat blood pressure responses to the Valsalva maneuver indicated sympathetic neurocirculatory failure (3). The concentration of norepinephrine in antecubital venous plasma increased by only 50% during standing, compared with the normal doubling (4). This suggested neurogenic orthostatic hypotension from diffuse loss of sympathetic nerves.

Thoracic positron emission tomographic scanning after intravenous 6- ^{18}F fluorodopamine showed no detectable myocardial radioactivity, despite approximately normal perfusion on ^{13}N -ammonia scanning (Figure). This combination was consistent with loss of functional sympathetic nerves throughout the left ventricular myocardium.

Cardiac sympathetic denervation seems to characterize all patients with Parkinson disease and orthostatic hypotension. Such patients therefore have abnormal catecholamine function not only in the nigrostriatal dopamine system in the brain but also in the sympathetic norepinephrine system in the periphery. This case of orthostatic hypotension, sympathetic neurocirculatory failure, and cardiac sympathetic denervation in a patient with familial Parkinson disease associated with mutation of the α -synuclein gene supports the notion of a common pathogenic mechanism for motor and autonomic failure in Parkinson disease. Since Lewy bodies contain α -synuclein (4), and Lewy bodies have been identified not only in the substantia nigra but also in sympathetic ganglia and sympathetically innervated organs in patients with Parkinson disease (5), α -synuclein may play an etiologic role in both pathologic processes.

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Figure.

Thoracic positron tomographic emission scans after injection of ¹³N-ammonia (*top row*) and 6-[¹⁸F]fluorodopamine (*bottom row*).

Scans were done in a normal volunteer (*left*), a patient with sporadic Parkinson disease (*middle*), and a patient with familial Parkinson disease associated with mutation of the α -synuclein gene (*right*). White crosses indicate the left ventricular septum and chamber. Both patients with Parkinson disease have undetectable myocardial 6-[¹⁸F]fluorodopamine-derived radioactivity.