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Autonomic dysfunction in Parkinson's disease

Abstract Autonomic dysfunction in patients with Parkinson's disease (PD) has been recognized since the original description by James Parkinson in 1817. Autonomic failure can be the clinical presentation of other diseases like pure autonomic failure (PAF) and multiple system atrophy (MSA). Both the central and peripheral autonomic nervous systems can be affected in PD. Rajput and Rozdilsky described cell loss and Lewy bodies within the sympathetic ganglia and antibodies to sympathetic neurons have been detected in PD patients. Lewy bodies can be seen in autonomic regulatory regions, including the hypothalamus, sympathetic (intermediolateral nucleus of the thoracic cord and sympathetic ganglia), and parasympathetic system (dorsal, vagal, and sacral parasympathetic nuclei). Lewy bodies were also found in the adrenal medulla and in the neural plexi innervating the gut, heart and pelvis. Symptoms of dysautonomia are variable, and include cardiovascular symptoms, gastrointestinal, urogenital, sudomotor and thermoregulatory dysfunction, pupillary abnormalities and sleep and respiratory disorders. They may represent a useful tool in the differential diagnosis of "atypical" or "complicated" parkinsonisms.

Key words Autonomic insufficiency • Parkinson's disease • Multiple system atrophy

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Introduction

Autonomic dysfunction in patients with Parkinson's disease (PD) has been recognized since the original description by James Parkinson in 1817. Symptoms of dysautonomia are variable, and include cardiovascular symptoms, gastrointestinal, urogenital, sudomotor and thermoregulatory dysfunction, pupillary abnormalities, and sleep and respiratory disorders (Chauduri, 2001; Siddiqui et al., 2002).

Autonomic failure can be the clinical presentation of other diseases such as pure autonomic failure and multiple system atrophy. Table 1 reports the main differences between the clinical presentation of autonomic dysfunction.

Brainstem autonomic centers include the ventrolateral medulla, nucleus tractus solitarius, and periaqueductal grey matter in the midbrain, the hypothalamus (via the pituitary and neuroendocrine system, and descending pathways to the intermediolateral cell columns or the reticular formation), the amygdale, and the cerebral cortex (insular and prefrontal). Dopamine is believed to play an important role in brainstem autonomic regulation, and recently investigators

Table 1 Clinical presentations of autonomic dysfunction (Niimi et al. 1999)

	Normal	PAF	AF-MSA	AF-PD
BP changes with HUT	→	↓	↓	↓
HR changes with HUT	↑	↑	→	↑
Basal plasma NE level	→	↓	→	→ or ↓
NE changes with HUT	↑	→	→	→
AVP changes with HUT	↑	↑	↑	↑
NE supersensitivity	-	++	- or +	+ or ++
Bladder disfunction	-	+	++	+
Urinary symptom			Obstructive	Irritative

PD, Parkinson's disease; *PAF*, pure autonomic failure; *MSA*, multiple system atrophy; *BP*, blood pressure; *HR*, heart rate; *NE*, norepinephrine; *AVP*, arginine vasopressin

have reported abundant dopamine immunoreactive fibers in the dorsal vagal complex, midline raphe nuclei, spinal trigeminal nucleus, and the lateral paragigantocellular nucleus of rats (Kitshama 2000).

Both the central and peripheral autonomic nervous systems can be affected in PD. Rajput and Rozdilsky described cell loss and Lewy bodies within the sympathetic ganglia and antibodies to sympathetic neurons have been detected in PD patients.

Lewy bodies can be seen in autonomic regulatory regions, including the hypothalamus, sympathetic system (intermediolateral nucleus of the thoracic cord and sympathetic ganglia), and parasympathetic system (dorsal, vagal, and sacral parasympathetic nuclei). Lewy bodies were also found in the adrenal medulla and in the neural plexi innervating the gut, heart, and pelvis.

Cardiovascular function

In PD patients, the prevalence of symptomatic orthostatic hypotension may be as high as 20%. The mechanisms of orthostatic hypotension in PD can be central, mediated through the degeneration of brainstem autonomic centers, and peripheral, due to post-ganglionic lesions. Symptoms resulting from orthostatic hypotension and impaired perfusion of organs include dizziness, visual disturbances, loss of consciousness, impaired cognition, angina pectoris, oliguria, weakness, and falls. Dopaminergic drugs may induce or worsen orthostatic hypotension. Cardiovascular investigations for autonomic failure include physiological and biochemical measurements. With physiological tests, autonomic failure can be diagnosed when at least two of tilt test, handgrip test, deep breathing, 30:15, and Valsalva maneuver, together with catecholamines dosage and sweating test are altered.

Gastrointestinal dysfunction

Disorders of the enteric nervous system may result in motor, secretor, inflammatory, or immune dysfunction. Loss of enteric neurons causes abnormal motility and suppression of secretor responses. Tests of colon and anorectal function suggest that both delayed colonic transit (abnormal motility of the colon) and defecatory dysfunction (dyscoordinate activity in the pelvic floor and sphincter muscles) contributes to the development of symptoms. Lewy bodies have been identified in autonomic neurons supplying the gastrointestinal tract, as well as in the enteric nervous system of the esophagus and colon. Constipation and difficult defecation are the most-common gastrointestinal symptoms among PD patients. Other symptoms include sialorrhea, dysphagia, gastroparesis, nausea, changes in appetite, and weight loss. Sialorrhea is a common complaint in PD, attributed to both overproduction and infrequent swallowing of saliva.

Urinary and sexual dysfunction

The pathology of PD involves brain regions normally involved in detrusor control, such as the substantia nigra, basal ganglia, hypothalamus, and locus coeruleus. Detrusor hyperactivity occurs in the majority of PD patients, due to loss of inhibition from the basal ganglia and substantia nigra. Most-frequent urinary symptoms in PD usually include difficulty in voiding, nocturnal urinary frequency, sensation of urgency, urge incontinence, diurnal urinary frequency, enuresis, and urinary retention.

Sexual dysfunction has been reported with high frequency in PD patients (Singer 1992); men complain of the inability to maintain an erection and women of the inability to achieve orgasm. There is an apparent relationship between sexual dysfunction and the duration and severity of PD disease.

Thermoregulatory dysfunction and skin changes

The hypothalamus plays an important role in the maintenance of normal core body temperature; other central neural systems important in the regulation of body temperature are found in the cerebral cortex, thalamus, brainstem, and spinal cord.

Peripheral sweat gland function is regulated by the sympathetic nervous system. Sympathetic skin responses have been studied in PD patients to evaluate autonomic dysfunction. Patients with PD often complain about increased sweating on their face, neck, arms, and back, and seborrhea on face and head (Mano 1994). This overexcretion of sebum has been attributed to hyperactivity of the parasympathetic component of the autonomic nervous system. Male PD subjects had the highest excretion rate, suggesting a possible role for androgens.

Pupillary changes

The size and reactivity of the pupils are controlled by the sympathetic and parasympathetic components of the autonomic nervous system. Constriction of the pupils is mediated via the parasympathetic fibers of the third cranial nerve that arise from the Edinger-Westphal nucleus of the midbrain. Pupillary dilatation is mediated via the sympathetic pathways. Micieli et al. (1991) found abnormally slow pupil-

lary responses to light and pain in PD patients. Similarly, Korczyn et al. studied pupillary responses in PD and found that resting diameters were normal, but the response to changes in light were less. Application of pharmacological agents to the eye demonstrated the peripheral autonomic nervous system to be intact in these PD patients; pupillary abnormalities resulted from central autonomic dysfunction centered in the parasympathetic Edinger-Westphal nucleus of the midbrain.

Sleep and respiratory disorders

Sleep disturbances and sleep-related respiratory dysrhythmias are common in patients with PD. Sleep, breathing, and the autonomic nervous system are closely linked, and the nucleus tractus solitarius contains the medullary respiratory and lower brainstem hypnogenic neurons. Sleep problems in PD include insomnia, hypersomnia, parasomnia, and circadian rhythm sleep disorders. Obstructive, central and mixed apneas have been described in PD. The spectrum of sleep-related respiratory dysrhythmias in PD includes sleep apnea-hypopnea, hypoventilation, Cheyne-Stokes and Cheyne-Stokes variant pattern of breathing, dysrhythmic breathing and nocturnal stridor. Another important sleep disturbance is REM behavior disorder.

Suggested reading

Chauduri KR (2001) Autonomic dysfunction in movement disorders. Curr Opin Neurol 14:505–511

Kitshama K, Nagatau I et al (2000) Distribution of dopamine-immunoreactive fibers in the rat brainstem. J Clin Neuroanat 18:1–9

Mano Y, Nakamuro T, Takayanagi T et al (1994) Sweat function in Parkinson's disease. J Neurol 241:573–576

Mathias CJ, Bannister R (1999) Autonomic failure. A textbook of clinical disorders of the autonomic nervous system. Oxford Medical Publications, Oxford

Micieli G, Tassorelli C, Martignoni E et al (1991) Disordered pupil reactivity in Parkinson's disease. Clin Auton Res 1:55–58

Niimi Y, Ieda T, Hirayama M et al (1999) Clinical and physiological characteristics of autonomic failure with Parkinson's disease. Clin Auton Res 9:139–144

Rajput AH, Rodzdilski C (1976) Dysautonomia in parkinsonism: a clinicopathological study. J Neurol Neurosurg Psychiatry 39:1092–1100

Siddiqui MF, Rast S, Lynn MJ et al (2002) Autonomic dysfunction in Parkinson's disease: a comprehensive symptom survey. Parkinsonism Relat Disord 8:277–284

Singer C, Weiner WJ, Sanchez-Ramos JR (1992) Autonomic dysfunction in men with Parkinson's disease. Eur Neurol 32:134–140