Spectrum of the autonomic nervous system degeneration in multiple system atrophy

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Background: Multiple system atrophy (MSA) is an adult-onset neurodegenerative disease that presents clinically with autonomic nervous system dysfunction characterized by orthostatic hypotension, dysuria, sweating disorder, gastrointestinal dysfunction, and respiratory disturbance. The lesions responsible for autonomic dysfunction in MSA patients achieve widespread distribution in the central nervous system. Accumulation of phosphorylated alpha-synuclein in the central nervous system is considered as an essential step in the MSA disease process. Aim and Methods: To update the information on the anatomical bases of autonomic dysfunction in MSA, recent papers that provided new, and important information regarding the autonomic nervous system degeneration in MSA are reviewed. Results: Accumulating evidence indicates that pathological involvements of the preganglionic neurons in the sympathetic and parasympathetic nervous systems are responsible for the autonomic dysfunction in MSA patients. However, recent reports that patients with MSA exhibited postganglionic denervation have highlighted the need for further investigations regarding the involvements of peripheral nerves and visceral organs in MSA. The leading hypothesis is that there is propagation of the alpha-synuclein pathology in a prion-like fashion in the vulnerable regions of MSA. Based on this, the autonomic nervous system is considered as a potential candidate for the pathway of alpha-synuclein transmission in MSA. Conclusion: The pathological involvement of the autonomic nervous system in MSA may extend to postganglionic nerves. Therefore, to fully determine the MSA disease process, it is crucial that detailed investigations of the extended spectrum of autonomic dysfunction aspects be undertaken.

Effect of autonomic dysfunction on survival in multiple system atrophy

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Background: Multiple system atrophy (MSA) is a rapidly progressing disorder with a mean survival of 6 to 10 years, and the factors associated with the survival have been investigated in many studies.
Aim and Methods: To review the effect of autonomic dysfunction on the survival in MSA, retrospective and prospective studies on the survival of MSA were reviewed. In addition, reports on MSA patients with unusually long or short disease duration were reviewed with special attention to autonomic dysfunction.
Results: The presence of severe autonomic dysfunction (urinary incontinence, urinary catheterization, and symptomatic orthostatic hypotension) and the early onset of autonomic dysfunction, but not the presence of autonomic dysfunction at disease onset or autonomic onset were associated with shorter survival. In addition to survival, early onset of autonomic dysfunction was associated with the rapid disease progression as measured by the time to aid-requiring walking, confinement to a wheelchair, and bedridden state. Negative effect of autonomic dysfunction on survival is also suggested by the later development of autonomic dysfunction in MSA patients with prolonged survival and the early development of autonomic dysfunction in patients with ‘minimal-change’ MSA with short disease duration. Interestingly, autonomic dysfunction has been associated with shorter survival in other synucleinopathies including Parkinson disease, Parkinson disease dementia, and dementia with Lewy body.
Conclusion: Autonomic dysfunction negatively impacts the prognosis in patients with MSA in terms of disease progression as well as survival. Whether early proper interventions on autonomic dysfunction benefit these patients should be investigated in future studies.

New insights into autonomic dysfunction and sleep disorder in MSA

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Early and severe autonomic failure, primarily including urogenital and cardiovascular dysfunction, is a key feature of MSA and represents major determinant of impaired quality of patient's life. The natural history of autonomic disturbances in MSA shows that erectile dysfunction is the earliest feature, followed by urinary disturbances, and finally by orthostatic hypotension (Jecmenica-Lukic et al. 2012). The early presence of orthostatic hypotension and/or severe bladder dysfunction with early incontinence could point towards a diagnosis of MSA and can be useful in the early differential diagnosis with others parkinsonian syndromes. Dysfunctions of autonomic and cardiovascular control have been related to shortened survival and implicated in sudden death in MSA.
Sleep dysfunctions are frequently seen in MSA populations, some of these overlap across the other parkinsonism disorders while other ones are either unique to or far more prevalent in this disease. Sleep disorders include reduced and fragmented sleep, excessive daytime sleepiness, REM sleep behaviour disorder (RBD) and sleep-disordered breathing.
Evidence increasingly suggests that non-motor features, such as autonomic failure, respiratory problems and sleep disorders might precede the classic motor features by several years but these symptoms can overlap with others neurodegenerative disorders, in particular PD and Pure Autonomic Failure (PAF) (Jecmenica-Lukic et al. 2012).
The timecourse of autonomic failure might help to differentiate between MSA and PAF.
In conclusion, sleep and autonomic disorders can shed light on the specific neuropathology and pathophysiology of MSA providing additional clues in the differential diagnosis of parkinsonian disorders. Further, these disorders represent an early marker of neurodegeneration and would allow testing new disease-modifying strategies to delay or stop the disease progression in the pre-motor phase.