Autonomic dysfunction in sleep disorders: introduction to the series

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Sleep is a fascinating and enigmatic phenomenon occurring, with varying patterns, in virtually all known animal species. This issue of *Clinical Autonomic Research* features a series of manuscripts authored by renowned experts in the field which focus on the connections between the autonomic nervous system and sleep. Although sleep is not traditionally considered a function regulated by the autonomic nervous system, it is evident that there are overlapping areas in the central nervous system (CNS) that regulate both systems, resulting in interesting and relevant interactions that can potentially impact morbidity and mortality. These interactions are concisely summarized in the review by Fink and colleagues [6], which highlights how specific CNS nuclei play a critical role in regulating cardiovascular autonomic function during both rapid eye movement (REM) and non-REM sleep.

The sleep–autonomic interactions can occur, broadly speaking, under three different scenarios, which are not mutually exclusive and can overlap:

(1) A common etiology impairs both the autonomic and sleep systems. The α -synucleinopathies, disorders caused by the abnormal accumulation of misfolded α -synuclein, are a very good example of this scenario, as reviewed by Chiaro and colleagues in this issue [5]. Progressive α -synuclein-mediated neurodegeneration of specific brainstem nuclei can result in REM sleep behavior disorder (RBD), a distinctive parasomnia in which patients act out and scream in their dreams. Conversely, α -synuclein-related neurodegeneration of peripheral and central autonomic areas can result in autonomic failure. Consequently, the co-existence

of RBD and autonomic failure in patients with pure autonomic failure (PAF) [12], Parkinson disease (PD), dementia with Lewy bodies (DLB) and multiple system atrophy (MSA) is not infrequent. Interestingly, the presence of RBD and autonomic failure are now well-recognized prodromal markers of PD/DLB and MSA [2, 10]. Moreover, the coexistence of RBD and autonomic failure in patients without overt motor or cognitive deficits carries a very risk of phenoconversion to PD/DLB or MSA [10, 14]. Identifying sleep and autonomic abnormalities in patients is, therefore, highly relevant as the presence of these abnormalities has diagnostic, prognostic and therapeutic implications.

(2) Failure of sleep-related cardio-respiratory control mechanisms and impaired arousal response cause or aggravate autonomic dysfunction. In this context, autonomic dysfunction can occur in sleep apnea, as reviewed by Fink and colleagues [6], or in the sudden infant death syndrome, as explained by Horne in her authoritative review [9]. These disorders can potentially result in prolonged hypoxia during sleep, cardiac arrhythmias and death.

(3) A disorder in which autonomic dysfunction causes or aggravates a sleep disorder. Examples of this would be congenital central hypoventilation and familial dysautonomia (hereditary sensory and autonomic neuropathy type 3), the latter a rare genetic disease characterized by afferent baroreflex and chemoreflex failure and resulting in a very high incidence of sudden unexpected death during sleep [15]. Although rare, these genetic disorders represent interesting models to understand the interactions between sleep and the autonomic nervous system, which can be further studied in animal and cellular models of the disease [11].

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These mechanisms are not mutually exclusive. Not infrequently, patients with functional disorders affecting the

autonomic nervous system have sleep complaints without objective polysomnography abnormalities [13, 16]. Also, there are sleep disorders with autonomic dysfunction for which the exact nature of the relationship is yet to be fully understood. This is the case of narcolepsy, as reviewed by Berteotti and Silvani in this issue [3]. The fact that some patients with narcolepsy also have RBD but no cardiac sympathetic denervation [1], similarly to patients with MSA—also with RBD and preserved cardiac innervation [7]—is intriguing.

Another relevant topic is how to study the autonomic nervous system during sleep. For obvious reasons, routinely used techniques in the autonomic laboratory, such as the tilt-table test, cold pressor test or Valsalva maneuver, cannot be used while patients are sleeping. Some investigators are able to perform microneurography recordings or make catecholamine measurements on their subjects during sleep, but because virtually every polysomnography includes electrocardiography, heart rate variability has become the gold standard to study the autonomic nervous system during sleep, notwithstanding its limitations [8, 17]. In this issue, Bugalho and colleagues [4] report their measurements of heart rate variability during sleep in patients with RBD; their results appear to show that these patients have reduced vagal modulation compared to patients without RBD.

We hope this series is thought provoking and valuable to readers and that it is successful in its aim to broaden the interest of autonomic specialists in sleep disorders.

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Compliance with ethical standards

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