Effects of Dopamine-Agonist Treatment on Heart Rate Variability during Sleep in Restless Legs Syndrome

Marco Zucconi,1 Mauro Manconi,1 Raffaele Ferri,2 Francesco Rundo,2 Alessandro Oldani,1 Luigi Ferini-Strambi1

1Sleep Disorders Center, Department of Neuroscience, Scientific Institute and University Ospedale San Raffaele, Vita-Salute University, Milan; 2Sleep Research Centre, Department of Neurology I.C., Oasi Institute (IRCCS), Troina, Italy.

Restless legs syndrome (RLS) is a sensorimotor disorder characterized by both a discomfort of and urge to move the legs, primarily during rest or inactivity. There is partial or total relief of symptoms with movement, and symptoms are present or worsen exclusively in the evening. The majority of patients with RLS present periodic leg movements during sleep (PLMS), which are coupled with cortical and autonomic activations. Dopamine agonists are the first-line treatment in RLS; however, little is known on the impact of dopamine-agonist treatment on the autonomic function during sleep. For this reason, a prospective, polysomnographic, single-blind, placebo-controlled study was carried out in 23 patients with RLS. Basal spectral analysis of heart rate variability (HRV) and transient heart rate (HR) changes during PLMS in patients were compared with those of 10 healthy subjects and, subsequently, before and after pramipexole or placebo treatment, in the RLS group. Regarding basal sympathovagal balance outside of PLMS sequences, no differences were found between RLS and controls and, in the RLS group, before and after treatment. The mean amplitude of PLMS-related HR changes were significantly higher in patients than in controls. Pramipexole suppressed the number of PLMS and normalized the PLMS-related HR response in subjects with RLS. The repetitive abnormal autonomic response to PLMS might play a role in the increased cardiovascular risk observed in RLS patients. Pramipexole significantly reduced the number of PLMS and the autonomic response to the residual PLMS, without effects on the basal sympathovagal regulation during PLMS-free periods. D3 receptors in the sympathetic pre-ganglionic neurons of the spinal intermediolateral columns might represent the target of pramipexole. The normalization of the HR reaction to PLMS may be relevant in reducing the risk of cardiovascular diseases in RLS.