RLS – Advances in brain imaging: iron, dopamine, connectivity, volume, spectroscopy

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Several imaging studies have shed light on the pathophysiology of restless legs syndrome (RLS), however there have been some discrepancies in the findings, and divergence in the interpretations offered. These studies essentially include nuclear medicine techniques, which have mainly evaluated the dopaminergic pathway, and magnetic resonance imaging (MRI) studies, which have employed various techniques to evaluate several putative components of the pathophysiology of this disorder. Structural MRI studies using voxel-based morphometry and diffusion tensor imaging have reported contrasting and inconclusive results. Functional and metabolic impairment seems to be the pathophysiological core, tied to a single or multiple-connected brain networks, via neurotransmitter modifications. Positron emission and single positron emission computed tomography studies support a dysfunction of dopaminergic pathways, involving not only the nigrostriatal but also mesolimbic pathway. Furthermore, a possible role of serotonergic neurotransmission has been suggested. Functional MRI studies have demonstrated in RLS patients a pathologic activation of cerebral areas belonging to both the sensorimotor and the limbic networks. Proton magnetic resonance spectroscopy has confirmed abnormality of the limbic system and suggested the presence of a glutamatergic pathology. Finally, MRI studies using iron-sensitive sequences have demonstrated reduced iron content in several regions of the brain of RLS patients. A convergent pathophysiological interpretation of the results of all current imaging studies can be attempted.