

**The role of the descending ‘diffuse noxious inhibitory control’ (DNIC) in patients with Restless Legs Syndrome: a study with laser evoked potentials (LEPs)**

*Angela Sandri*<sup>1</sup>, E. Antelmi<sup>1</sup>, G.M. Squintani<sup>2</sup>, M. Lippolis<sup>2</sup>, S.M. Cartella<sup>1</sup>, M. Tinazzi<sup>1</sup>

<sup>1</sup>Neurology Unit, Parkinson Disease and Movement Disorders Division, Department of Neurosciences, Biomedicine and Movement Sciences, University of Verona, Verona, Italy

<sup>2</sup>UOC Neurologia A, Department of Neurosciences, AOUI, Verona, Italy

*Introduction:* Restless legs syndrome (RLS) is a complex sensorimotor disorder occurring with a typical circadian fashion [1]. Symptoms worsen towards evening and at rest, and they are temporarily relieved by movement [2]. Symptoms are perceived as painful in up to 45% of cases [3], and nociception seems involved also given the opioids’ efficacy and the physiologic dopamine-pain control link [4].

*Objective:* To assess the descending diffuse noxious inhibitory control (DNIC) in RLS patients.

*Methods:* 22 RLS patients (mean age: 58±16 years; 11 females) and 20 matched controls (mean age: 55±11 years; 12 females) underwent a conditioned pain modulation protocol. Cutaneous heat stimuli were delivered via Laser evoked potentials (LEPs) on the dorsum of the right hand (UL) and foot (LL). N2/P2 amplitude and pain ratings (NRS) were recorded before (baseline), during (DNIC), and after (post) the application of a heterotopic noxious conditioning stimulation, where subjects submerged their left foot into an ice water bath (0°C).

*Results:* Non-parametric analyses in both RLS patients and controls show a physiological (N2/P2 amplitude) and subjective (NRS) reduction during the DNIC condition in both UL and LL in comparison to baseline and post conditions (all,  $p < 0.002$ ). For the N2/P2 amplitude, the post conditions were significantly lower in both groups with respect to the baselines (all,  $p < 0.002$ ), but not for NRS ratings. Between groups comparisons revealed a significant difference at the N2/P2 amplitude during the DNIC condition only for the LL ( $p = 0.011$ ), with RLS patients having a lower amplitude reduction than controls.

*Conclusions:* The lower physiological reduction during the DNIC condition at LL in RLS patients suggest a defect in the endogenous inhibitory pain system. Further studies should clarify the causal link with these findings also investigating the circadian modulation of this paradigm.

**References:**

- [1] Manconi et al., 2021. Nat Rev Dis Primers; 7:80.
- [2] Allen et al., 2014. Sleep Med; 15:860-873.
- [3] Bassetti et al., 2001. Eur Neurology; 45:67–74.
- [4] Millan, 2002. Progress Neurobio; 66:355–474.