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Patología del Sueño: de la Neurobiología a las manifestaciones sistémicas

Sleep disorders: from Neurobiology to Systemic Consequences

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ABSTRACT

Disfunción adenosinérgica: el nexo entre las alteraciones de glutamato y dopamina en el trastorno de Movimientos Periódicos y en el Síndrome de Piernas Inquietas

Adenosine dysfunction: the link between dopamine and glutamate alterations in PLMs and RLS.

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We recently showed that rodents with brain iron deficiency (BID), a pathogenetic animal model of Restless Legs Syndrome (RLS), is associated with a hypoadenosinergic state, with downregulation of adenosine A1 receptors (A1R).

Using an optogenetic-microdialysis approach, we demonstrated that A1R downregulation leads to hypersensitive striatal glutamatergic terminals in the rodent with BID, which could represent a main pathogenetic factor in RLS.

In fact, the dopaminergic agonists pramipexole and ropinirole and the $\alpha 2\delta$ ligand gabapentin, used in the initial symptomatic treatment of RLS, completely counteracted optogenetically-induced glutamate release from BID-induced hypersensitive corticostriatal glutamatergic terminals.

We have obtained preclinical and clinical evidence that indicates that inhibitors of nucleoside equilibrative transporters, such as dipyridamole, by increasing the tonic A1R activation mediated by endogenous adenosine, represent a new alternative therapeutic strategy for RLS.

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