Abstract Information

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Category :	Academic/Researcher
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Title :	Neuroinflammatory Mechanisms of Pain Hypersensitization in a Mouse Model of ADHD
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Abstract :

Attention-deficit/hyperactivity disorder (ADHD) is a common multifactorial neurodevelopmental disorder, with a prevalence of around 8% in children worldwide. This prevalence is increasing upon pollutant, especially plastics, contamination worldwide, making it a growing public health issue in the Mediterranean area.

ADHD is characterized by symptoms of inattention, hyperactivity, and impulsivity and is usually associated with cognitive, emotional, and behavioral deficits. Clinical studies suggest that pain hypersensitivity develops in subjects with ADHD. However, the mechanisms and neural circuits

involved in these interactions remain unknown.

Our team has previously validated a mouse model of ADHD obtained by neonatal 6-hydroxydopamine (6-OHDA) intracerebroventricular injection. We showed that 6-OHDA mice exhibited a marked sensitization to thermal and mechanical stimuli, suggesting that ADHD conditions increase nociception. Moreover, by combining different approaches, we also demonstrated that the anterior cingulate cortex (ACC) hyperactivity alters the ?ACC ? posterior insula (PI)? circuit, and triggers changes in spinal networks that underlie pain sensitization. We make the hypothesis that neuroinflammation is a major factor triggering ACC hyperactivity and the comorbidity between ADHD and pain.

By using immunofluorescence staining, we demonstrated changes in the morphology of microglia and astrocytes, indicative of their activation. With RT-qPCR, we have identified markers of inflammation and oxidative stress, in the cingulate and insular cortex. Through mass spectrometry and high-throughput phosphoproteomic assays, we

characterized deregulated kinase activity and signaling pathways under ADHD conditions. All

these changes lead to altered inflammatory pathways, which may underlie ADHD and its comorbid pain. The identification of shared mechanisms, engaging overlapping neuronal circuits and inflammation, and underlying both disorders, is key to better treatments.