Toward a central origin of nociceptive hypersensitivity in adult rats after a neonatal maternal separation

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Abstract

Early life adversities alter the development of a still maturing nervous system and can have long-term consequences on its function at adult age. This include nociceptive circuits that are critical to shape an adaptive pain response to protect our organism from potentially damaging insults. As such, adult rats with a history of neonatal maternal separation (NMS) display a visceral and somatic nociceptive hypersensitivity and inefficient analgesic responses to stress. In this study, we have characterized the consequences of NMS on wide dynamic range neurons (WDR) in the spinal cord of anesthetized adult rat during the nociceptive processing of hot and cold noxious information. We found that WDR neurons of NMS rats display an excessive coding of mechanical and thermal information applied at the rat hindpaws. This nicely explains the hypernociceptive behaviors seen after noxious mechanical, cold and hot peripheral stimulation. A peripheral change in the expression of molecular transducers for these stimuli (i.e. TRPV1, TRPM8, TRPA1) does not seem to account for this general hyperexcitability. Instead, a decreased chloride-mediated inhibitory tone on WDR neurons may play a role as indicated by the abnormal elevated of the type 1 Na-K-Cl cotransporter transcripts. Altogether, we propose that long-term consequences of NMS is associated with a reduced spinal cord inhibition favoring the expression of pain hypersensitivity. We cannot exclude that this phenomenon is also present at supraspinal sites as other NMS-associated symptoms include also excessive anxiety and impaired sociability.

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