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Phosphorylation of the GluN1 subunit in dorsal horn neurons by remifentanil: a mechanism for opioid-induced hyperalgesia

C. Zhang, S.S. Li, N. Zhao and C. Yu

Chongqing Key Laboratory for Oral Diseases and Biomedical Sciences, The Affiliated Hospital of Stomatology, Chongqing Medical University, Chongqing, China

Corresponding author: C. Yu
E-mail: yucongab@sina.com

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ABSTRACT. Remifentanil (an ultra-short acting μ-opioid receptor agonist) use has been associated with acute opioid tolerance and hyperalgesia. Previous electrophysiological studies have shown that remifentanil elicits rapid and prolonged upregulation of N-methyl-D-aspartate receptor (NMDAR) currents. However, the effect of remifentanil on the levels of the GluN1 subunit of the NMDAR in dorsal horn neurons (DHNs) has not been reported. We investigated the effect of remifentanil, along with ketamine (NMDAR antagonist) and naloxone (μ-opioid receptor antagonist), on GluN1 mRNA levels and the amount of phosphorylated GluN1 in primary cultures of embryonic rat DHNs. DHNs were isolated from 18-19-day rat embryos and treated with remifentanil or vehicle for 1 h. GluN1 mRNA and protein levels, determined by real time reverse transcription polymerase chain reaction (RT-PCR) and Western blot, respectively, were significantly and persistently increased by remifentanil exposure compared with the control group ($P < 0.05$). These results may partially account for the

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mechanism of remifentanil-induced hyperalgesia. This increase was prevented by ketamine (NMDAR antagonist) and naloxone (μ-opioid receptors antagonist), thus providing a potential therapeutic mechanism for the prevention of opioid-induced hyperalgesia.

Key words: Remifentanil; Opioid-induced hyperalgesia; NMDA receptor; μ-Opioid receptor

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