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Reporting the latest news in Molecular Surgery

Role of spinal microglia in the development of morphine-induced hyperalgesia

Contributed by Francesco Ferrini[1] and Yves De Koninck[2,3]

[1]*Department of Veterinary Sciences, University of Turin,10095 Grugliasco, Turin, Italy*
[2]*Institut universitaire en santé mentale de Québec, QC, G1J 2G3, Canada*
[3]*Department of Psychiatry and Neuroscience, Université Laval, Québec, QC, G13 7P4, Canada*

Morphine-induced hyperalgesia and tolerance dramatically limit the use of morphine, especially in chronic diseases. By definition, morphine tolerance is a reduced antinociceptive effect for a given morphine dose, while morphine-induced hyperalgesia is a state of nociceptive sensitization observed in morphine-treated patients.[1,2] It is therefore tempting to postulate that antinociceptive tolerance is set by the decrease in nociceptive threshold due to the hyperalgesia.[3] However, this common view appears to be in contrast with clinical evidence indicating that while increasing the morphine dose can effectively counteract morphine tolerance, the same approach can backfire and worsen pain symptoms in patients with morphine-induced hyperalgesia.[1] In our recent study published in *Nature Neuroscience,*[4] we demonstrated that morphine hyperalgesia and morphine tolerance are mechanistically distinct and that morphine induces hyperalgesia by recapitulating the same maladaptive mechanisms in the spinal cord observed in pathological pain syndromes.

In particular, we addressed the question whether microglia drive morphine-induced hyperalgesia, as the communication between neurons and microglia in the spinal dorsal horn plays a central role in the development of neuropathic pain.[5] The role of microglia in diseases can be tested by using pharmacological tools, such as minocycline, which have been proved to inhibit microglia function.[6] However, the specificity of such approaches to target microglia is debated and direct effects on neuronal activity cannot be ruled out.[7] Therefore, we decided to perform intrathecal injections of a saporin-conjugated antibody against the *(continued on page 6)*

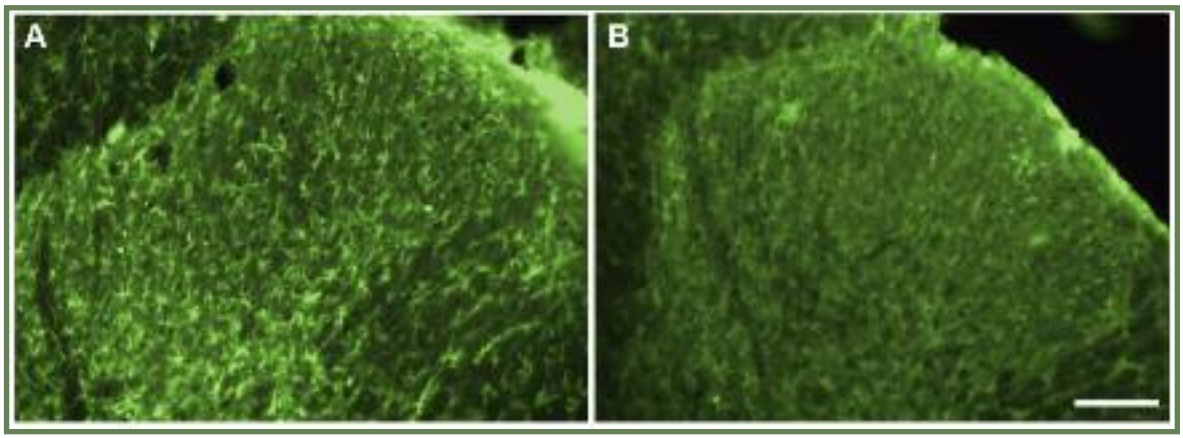

Figure 1. Microglia depletion in the lumbar region of the spinal cord after intrathecal injections of Mac-1-SAP. Microglia are immunohistochemically identified by a mouse CD11b antibody, clone OX-42 (1:500). A) A representative cervical spinal dorsal horn section obtained from a rat which was subcutaneously injected with morphine for 10 days (10 mg/kg) and intrathecally injected with Mac-1-SAP (20 µg) during the last 3 days. B) A representative lumbar spinal dorsal horn section from the same rat showing the decrease in OX-42 staining after Mac-1-SAP treatment. Scale bar 50 µm.

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Denise Higgins, Editor

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