Reviewer’s report

Title: Antinociceptive tolerance to NSAIDs in the anterior cingulate cortex is mediated via endogenous opioid mechanism

Version: 1 Date: 11 Oct 2017

Reviewer: Ahmet Ulugol

Reviewer’s report:

This manuscript is a nicely performed study with clear and interesting results. It is designed to investigate the development of tolerance to the analgesic effects of NSAIDs microinjected into the anterior cingulate cortex, and contribution of endogenous opioid system in this effect. It describes new and carefully confirms findings, and experimental procedures are given in sufficient detail. Introduction provides a clear statement of the problem, the relevant literature, and the proposed approach. Methodology, Results and Discussion are clear and substantiated.

The subject is important since development of tolerance during treatment of pain is a major problem. The authors showed microinjection of NSAIDs into the anterior cingulate cortex for 4 days resulted in a progressive decrease in their analgesic effects. Moreover, naloxone prevented the analgesic action of NSAIDs. As a result, the authors suggested that endogenous opioids are involved in the development of tolerance to NSAID antinociception.

This effort of the authors is worth to be published. This manuscript can be accepted without revision.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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