Reviewer’s report

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

Version: 1 Date: 10 Oct 2017

Reviewer: Jun-Xu Li

Reviewer’s report:

Tsiklauri and colleagues studied the development of antinociceptive tolerance to NSAIDs after they were repeatedly microinjected into the ACC. All NSAIDs studied developed profound antinociceptive tolerance after 4 days of daily treatment. The antinociceptive effects of these NSAIDs were blocked by the opioid antagonist naloxone. The authors concluded that antinociceptive tolerance was mediated by endogenous opioid system.

Overall, this is a well developed small study, the hypothesis was clear, the design was fine and the results were clear. This is an extension to previous studies from the same lab and adds to the growing literature that NSAIDs act on opioid system and develop antinociceptive tolerance. I have no major concerns.

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

Yes

Does the work include the necessary controls?
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Yes

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

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I am able to assess the statistics

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