Reviewer's report

Title: Antinociceptive tolerance effects of NSAIDs microinjected into dorsal hippocampus

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Reviewer: Robert Pechick

Reviewer's report:

This is an interesting manuscript examining whether the microinjection of three different nonsteroidal anti-inflammatory drugs into the dorsal hippocampus produces analgesia that can be reduced by naloxone, and whether tolerance develops to these effects after repeated drug administration. The results are intriguing; however, the lack of experimental details and the problems with experimental design and how the data were analyzed raise serious concerns.

1. Some experimental details are not provided. For example, what was done with subjects wherein the microinjections sites were found to be outside of the target area? Did microinjections out of the target areas produce the same effects? What was the pH of the solutions that were microinjected? In addition, it is not clear whether different animals were used for experiments 1, 2 and 3. These details should be provided in the manuscript.

2. The data showing the time course of the effects of the drug treatments should be analyzed by two-way, repeated measure ANOVAS, with time the repeated measure. The data should be reinterpreted based upon the results of the new analysis.

3. The time course of the effects of each drug needs to be shown in order to justify the decision to measure the analgesic response at a single time point.

4. F values should be provided for the first set of experiments (i.e., Figure 2).

5. Experiment 2 is missing a critical control group. The response to saline injections on days 2 and 3 should be shown to demonstrate that the response in controls is not affected by repeated testing. Similarly, Experiments 2 and 3 also are missing an important set of control groups. These experiments inject naloxone before or after the test drugs, but there are no data showing if naloxone by itself produces any effects after single or repeated administration.

6. The Discussion section is much too long for the amount of data shown in the manuscript.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interest