Reviewer's report

Title: Pretreatment with Intrathecal Amitriptyline Potentiates Anti-Hyperalgesic effects of Post-Surgical Systemic Amitriptyline following Spinal Nerve Ligation

Version: 2 Date: 10 November 2011

Reviewer: jana sawynok

Reviewer's report:

This manuscript describes effects of adding i.t. amitriptyline (200 ug) to a regimen of systemic amitriptyline (12.5 mg/kg twice daily for 3 days) on behavioural (allodynia, hyperalgesia) and neurochemical changes resulting from L5 spinal nerve ligation. The i.t. ami augments the effects of systemic ami on several measures. The data are novel and interesting.

This manuscript is a resubmission. It is improved from before, but still needs quite a bit of attention.

1. This study uses “intra-abdominal” to refer to systemic administration of amitriptyline, yet the more common expression for such delivery is “intraperitoneal” administration. Please use this expression.

2. At the start of the Introduction, there needs to be a clear distinction made between clinical and preclinical references.

3. References. Throughout, there were several references cited that did not seem appropriate for the point being made. Please check the accuracy of all citations.

4. p.19, line 16. This should refer to a review of amitriptyline actions. A detailed consideration of this was included in the response to the referees, but it really belongs in the manuscript.

5. Why was 90ul used for the i.t. injections? This is a large volume compared to the overall CSF volume. Rostral spread of the drug is inevitable with this volume, and this must be considered directly.

6. Need to quote the Gebhart and Eisenach 1994 study which showed analgesia by i.t. amitriptyline. 200 ug is a very large dose in comparison with that dose. Why was such a high dose chosen?

Minor editorial corrections

There are many minor editorial corrections that need to be made. These are too numerous to list here, so I have attached a pdf version of the marked 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: No, the manuscript does not need to be seen by a statistician.

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