

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Self Reported Feelings Of Anger And Aggression Towards Others In Patients On Levetiracetam: Data from the UK Anti Epileptic Drug Register
<b>AUTHORS</b>	Wiesmann, Udo; Baker, Gus

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Hugh Rickards Hon. Reader in Neuropsychiatry Birmingham University UK  No competing interests
<b>REVIEW RETURNED</b>	31-Jan-2013

<b>GENERAL COMMENTS</b>	<p>Excellent paper with just a couple of comments</p> <p>This is a good study addressing a clinically relevant point. The design is simple but effective and it confirms clinical observations. There are potential biases in the study in that patients on LEV may be more poorly and taking higher doses of other medications. However, the types of comparisons made in this study (in the context of other studies in the field) make it most likely that LEV has a direct effect of anger/irritability. I would definitely recommend publication.</p> <p>There are just minor errors or clarifications as follows.</p> <p>P7 line 25. When the authors refer to "this study" I don't know if they mean their own study or reference number 9</p> <p>P7 Line 48 refers to the "anti-contraceptive pill".. I'm not sure this is what the authors really meant to say</p>
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<b>REVIEWER</b>	Marco Mula MD PhD A. Avogadro University Italy
<b>REVIEW RETURNED</b>	05-Feb-2013

<b>GENERAL COMMENTS</b>	<p>This study retrospectively investigates self-reported feelings of anger and aggression in patients with epilepsy taking LEV, using the LAEP.</p> <p>In general terms the paper is well written and clearly organized. References are adequate.</p> <p>The major limitation is the retrospective nature but there are some elements of novelty such as the patient's perspective. As correctly stated by the authors, it can be difficult for the treating neurologist to identify subtle mood changes, if not adequately trained. In this paper, it is clearly demonstrated that a high proportion of patients taking LEV may subjectively experience feelings of anger even if not severe enough to gain medical attention.</p> <p>A couple of points need to be further expanded just to improve the quality of the paper:</p> <ul style="list-style-type: none"> <li>- More clinical data regarding the investigated sample: how many symptomatic (e.g. HS)? Any correlation between clinical variables and LEV-related anger/aggression?</li> <li>- More data on "others" AEDs: Any difference comparing LEV with mood stabilizers (i.e. CBZ, OXC, VPA, LTG) or with depressogenic AEDs (i.e. PB, TPM, ZNS).</li> </ul>
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### VERSION 1 – AUTHOR RESPONSE

In response to Hugh Rickards we made the following changes:

We are grateful for the positive feedback.

We clarified on P7 line 25 that we referred to the current study.

On page P7 we improved the paragraph on the advantages of Levetiracetam including low toxicity and lack of pill interactions.

In response to Marco Mula we made the following changes:

We entirely agree that it would be desirable to have more information on neuroimaging including the presence or absence of hippocampal sclerosis (HS). Unfortunately, this information was not available. We also agree that more data on "other" AEDs would have been very interesting. An analysis comparing patients on LEV and mood stabilizers (i.e. CBZ, OXC, VPA, LTG) with patients on LEV with depression causing AEDs (i.e. PB, TPM, ZNS) would have been most interesting. Unfortunately, the numbers of patients on these combinations were too small to draw any firm conclusions (tab 1.). In the discussion we added a paragraph on unanswered questions for future studies.