Reviewer's report

Title: (R)-[11C]Verapamil PET studies to assess changes in P-glycoprotein expression and functionality in rat blood-brain barrier after exposure to kainate-induced status epilepticus

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Reviewer: David Reutens

Reviewer's report:

This is a study aiming to examine the function of P-gp at the blood-brain barrier with PET and the tracer [C11]verapamil. Animals were studied a week after treatment with kainate or saline and with and without co-administration of the P-gp inhibitor tariquidar. A range of analytic methods were used and reported. P-gp expression was also studied in the brain post-mortem using immunohistochemistry.

The histological studies showed a non-significant trend in P-gp area. PET showed significant differences between kainate and saline treated animals only with tariquidar administration. In both groups tariquidar increased the brain-blood concentration ratio. Both K1 and k2 were reduced and Vbr1 increased in the kainate group.

MINOR ESSENTIAL REVISIONS

The authors indicate that the kainate model is one of pharmacoresistance, but the development of chronic epilepsy was not able to be examined in the animals used in this study. Outcome in this epilepsy model is not invariable in terms of development of spontaneous seizures or pharmacoresistance. This should be reflected in the introduction / discussion.

The overall conclusion is that P-gp expression and functionality ‘do not seem to change’ at the time studied in this model. The conclusion does not take into account the positive findings in this study. What do the authors conclude from the differential effects of tariquidar on K1 and k2 in the kainate-treated animals using several of the analytic methods? What does the differential response indicate about differences in P-gp function in the kainate-treated group?

Analyses are carried out at whole brain level. While I understand the limitations in terms of resolution of the tomograph, some comment should be made in relation to the impact of this on the results. Could this have obscured significant regional changes?

DISCRETIONARY REVISIONS

In general the paper is well written. However, it is a complex paper with many analyses and results. It would be easier to read if the key findings are summarized at the end of the results section.
**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interest