Reviewer's report

Title: Significance of MDR1 and Multiple Drug Resistance in Refractory Human Epileptic Brain

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Reviewer: Eleonora Aronica

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General
The failure to respond to anticonvulsant drug treatment is a crucial clinical problem in human epilepsy. This well written and very interesting paper sheds new light on the still enigmatic functions of MDR1/P-glycoprotein (Pgp), which would better enable us to understand the molecular phenomena underlying drug delivery to the brain under physiological and pathological conditions. The data presented indicate that in addition to the known role of Pgp in drug efflux at the BBB, this protein may critically regulate neuroglia survival in the epileptic brain. The authors suggest that upregulation of multi drug resistant proteins could be associated with prevention of apoptosis. A better understanding of the functional consequences of Pgp upregulation is important in view of the possible use of Pgp inhibitors as adjunctive treatment in patients with intractable epilepsy. Therefore, this study is interesting, the experiments overall seem to be competently conducted. Nevertheless, some concerns remain which detract from the impact and clearness of the manuscript.

Discretionary Revisions (which the author can choose to ignore)

There should be more clinical information about the patients included in the study and about the histopathological features of the material used.
- Type and frequency of seizures, age at seizure onset, duration of epilepsy, antiepileptic drugs used and postoperative outcome should be included in table 1 or the material and methods section (human tissue).
- The information regarding the pathology shown in table 1 should be reorganized. It is important to show clearly the type of tissue used for each patient (i.e. hippocampus, frontal or temporal cortex; right or left) and separately the histopathological diagnosis (i.e. cortical dysplasia, hippocampal sclerosis, tumor etc.) and the extent or type of resection (i.e. hemishperectomy, hippocampal or mesial-structures resection).
- For the cortical dysplasia (CD) cases they should indicate the type according to the most recent proposed classification criteria of CD (Palmini et al., Neurology, 62, 2004; Type IA or B; Type II A, or B).
- Table I should also include information about the control material used. In the result section it would appear that normal brain distal from the dysplastic tissue was used as control. However, it is not clear whether this material was available only for the CD cases or was used in all cases.

Since different types of pathologies associated with pharmaco-resistance and upregulation of Pgp were studied, it should be important to know whether immunocytochemical or functional differences were detected comparing different pathologies (i.e. CD versus temporal lobe epilepsy (TLE) with hippocampal sclerosis (HS) or TLE without HS).
Which journal?: Appropriate or potentially appropriate for BMC Medicine: an article of importance in its field

What next?: Accept for publication in BMC Medicine after discretionary revisions

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests: None