## Multidrug resistance associated protein 1

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Sun et al. conducted a metaanalysis of studies on expression and cellular distribution of multidrug resistance-associated protein 1 (MRP1) in intractable epilepsy (IE) patients to evaluate the contribution of this protein to antiepileptic drug (AED) resistance. In addition, they summarize experiments examining MRP1 expression and substrates in animal models of IE.

The literature search based on pre-established inclusion and exclusion criteria, as well as quality assessment, data extraction and statistical analyses were conducted concurrently by two independent researchers.

They identified nine high-quality studies (Jadad score  $\geq$ 3) published between 2000 and 2014 on the expression and cellular distribution of MRP1 in IE patients. A fixed effect model was used to calculate pooled odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs). Forest and funnel plots were constructed to assess study heterogeneity and publication bias, respectively.

MRP1 expression was significantly higher in both astrocytes (OR = 17.04, 95% CI: 7.69-37.76, P < 0.00001) and neurons (OR = 22.13, 95% CI: 8.52-57.46, P < 0.00001) of IE patients compared to controls, while there was no significant difference in endothelial cell MRP1 expression (OR: 1.47, 95% CI: 0.09-1.79, P = 0.48). Funnel plot symmetry indicated no substantial publication bias. Most relevant preclinical studies from 2000 to 2014 found higher MRP1 expression in IE model rodents. Furthermore, MRP1 overexpression reduced the extracellular concentration of AEDs in brain, while MRP1 inhibitors enhanced brain AED concentrations.

Pooled results strongly suggest that MRP1 is overexpressed in both neurons and astrocytes of IE patients. Inhibition of MRP1 may enhance AED efficacy by increasing local drug availability <sup>1)</sup>.

## 1)

Sun Y, Luo X, Yang K, Sun X, Li X, Zhang C, Ma S, Liu Y, Yin J. Neural overexpression of multidrug resistance-associated protein 1 and refractory epilepsy: a meta-analysis of nine studies. Int J Neurosci. 2016 Apr;126(4):308-17. doi: 10.3109/00207454.2015.1015724. Epub 2015 Sep 29. PubMed PMID: 26000815.

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