

Induction of kir6.2 and KCNQ4 potassium channels in NAGM of chronic MS patients

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Research question and background

Although grey matter demyelination and atrophy correlates with the progression of multiple sclerosis (MS), the question remains how does GM pathology arise? Several pathological mechanisms have been proposed, like meningeal inflammation and glutamate excitotoxicity. In addition, many genes involved in synaptic plasticity and glutamate neurotransmission are regulated in MS. However, the precise signaling pathways involved in these pathological processes are still relatively unclear. Here, we investigate underlying signaling pathways of GM pathology, including abnormalities in ion channels and transporters, neurotrophins and receptors, and synaptic plasticity, in normal appearing grey matter (NAGM).

Methods and tissues used

Frozen NAGM cingulate cortex from 5 chronic MS and 5 control cases were selected for real time quantitative PCR arrays. Three RT² profiler PCR arrays (Qiagen) were used to examine mRNA levels of genes involved in ion channels & transporters, neurotrophins & receptors and synaptic plasticity. Data was normalized with housekeeping genes and a student t-test was used to analyze differences in gene expression. Additionally, the cellular source of two genes, kir6.2 and KCNQ4 were investigated using immunohistochemistry. Finally, an in-vitro model was used to investigate the regulation of kir6.2 and KNCQ4 after treatment with glutamate or IFN γ & TNF α

Results and conclusion

qPCR array results revealed a significant regulation of genes, particularly with the ion channels and transporter array. Two genes, kir6.2 and KCNQ4, which are both potassium channels, survived the correction for multiple comparisons. Immunohistochemical analysis revealed that kir6.2 and KNCQ4 channels are expressed by neurons in NAGM. So far, our in vitro experiments demonstrate that the expression of kir6.2 channels are possibly involved in glutamate excitotoxic conditions. Currently, we are still investigating the expression of KNCQ4 in our in vitro model.