Hippocampal epileptogenesis in LGI1, CASPR2 and $GABA_BR$ encephalitis: a preliminary study (O3009)

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ABSTRACT

Objective

Autoantibody-mediated forms of encephalitis (AE) include neurological disorders characterized by subacute memory loss, movement disorders and, often, frequent, focal epileptic seizures. Yet, the electrophysiological effects of these autoantibodies on neuronal function have received little attention. In this study, we assessed the effects of CSF-containing autoantibodies on intrinsic and extrinsic properties of hippocampal neurons, to define their epileptogenic potential.

Methods

We compared the effects of CSF containing leucine-rich glioma inactivated 1 (LGI1), contactin associated protein-like 2 (CASPR2) or γ-aminobutyric acid receptor B ($GABA_BR$)-antibodies on *ex vivo* electrophysiological parameters after stereotactic hippocampal inoculation into mice. Whole-cell patch-clamp and extracellular recordings from CA1 pyramidal neurons and CA3-CA1 field recordings in *ex vivo* murine brain slices were used to study neuronal function.

Results

By comparison to control CSF, AE CSFs increased the probability of glutamate release from CA3 neurons. In addition, LGI1- and CASPR2-antibody containing CSFs induced epileptiform activity at a population level following Schaffer collateral stimulation. CASPR2-antibody containing CSF was also associated with higher spontaneous firing of CA1 pyramidal neurons. On the contrary, $GABA_BR$-antibody containing CSF did not elicit changes in intrinsic neuronal activity and field potentials.

Interpretation

Using patient CSF, we have demonstrated that the AE-associated antibodies against LGI1 and CASPR2 are able to increase hippocampal CA1 neuron excitability, facilitating epileptiform activity. These findings provide *in vivo* pathogenic insights into neuronal dysfunction in these conditions.