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Oral Presentation

Functional Characterization of Human $GABA_A$ Autoantibodies in the Context of Limbic Encephalitis

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Abstract

Limbic encephalitis is an adaptive autoimmune disease, induced by different autoantibodies, which target extracellular neuronal epitopes, such as NMDA or GABAB receptors1GABA(B,2consequences of autoimmune inflammation of the amygdala are largely unknown. The amygdala is central for the generation of adequate homoeostatic behavioral responses to emotionally significant external stimuli following processing in a variety of parallel neuronal circuits. Here, we hypothesize that adaptive cellular and humoral autoimmunity may target and modulate distinct inhibitory or excitatory neuronal networks within the amygdala, and thereby strongly impact processing of emotional stimuli and corresponding behavioral responses. This may explain some of the rather poorly understood neuropsychiatric symptoms in limbic encephalitis.", "author" : [{ "dropping-particle" : "", "family" : "Melzer", "given" : "Nico", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Budde", "given" : "Thomas", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Stork", "given" : "Oliver", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Meuth", "given" : "Sven G", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }], "container-title" : "Frontiers in neurology", "id" : "ITEM-1", "issued" : { "date-parts" : [["2015"]] }, "page" : "171", "publisher" : "Frontiers Media SA", "title" : "Limbic Encephalitis: Potential Impact of Adaptive Autoimmune Inflammation on Neuronal Circuits of the Amygdala.", "type" : "article-journal", "volume" : "6" }, "uris" : ["http://www.mendeley.com/documents/?uuid=ddaf6fd2-c5de-3d66-9314-327e706fb8dd"] }], "mendeley" : { "formattedCitation" : "²", "plainTextFormattedCitation" : "2", "previouslyFormattedCitation" : "²" }, "properties" : { }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }. Recently our group found another human antibody, which binds to the α1 subunit of the GABAA receptor. Since the GABAA receptor is responsible for the majority of fast inhibitory neurotransmission, we inves tigated changes in GABAergic activity and the excitability in brain regions containing the α1 subunit. Therefore, we performed a functional in-vitro characterization by incubating acute brain slices with the antibody and performing electrophysiological recordings in the somatosensory cortex (S1). The single-cell analysis of pyramidal neurons in S1 showed a significantly reduced frequency of GABAergic events. In contrast examining the excitability by counting the number of action potentials generated in response to a current step, showed no effect of the antibody. By using transgenic GFP-GAD-65 mice we separately explored the antibody's effects in interneurons only. There, we found a non-significant difference in the amplitude of GABAergic events, but no changes in the frequency. Fluorescence s taining confirmed the specificity of the antibody binding in S1 and hippocampal regions. In conclusion, the antibody seems to cause an increased excitability especially in pyramidal cortical neurons mediated by a reduced GABAergic activity.

Keywords: Limbic, Autoimmune Disease, Especially

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