GABA\textsubscript{B} Receptor Subtypes Differentially Modulate Chemoconvulsant-induced Seizure

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Epilepsy is a neurological disorder caused by synchronous neuronal discharge under hyperexcitable conditions. GABA\textsubscript{B} receptors, the G-protein-coupled receptors for the inhibitory neurotransmitter GABA, are strongly implicated in the genesis and spread of seizures, but the precise roles of the receptors located at different synaptic localisation and neuronal networks are yet to be defined. In mice lacking either the GABA\textsubscript{B1a} or GABA\textsubscript{B1b} isoforms, we examined the roles of the two main subtypes, GABA\textsubscript{B(1a,2)} and GABA\textsubscript{B(1b,2)} receptors, in the genesis and spread of seizure. The chemoconvulsant, pentylenetetrazol, triggered more severe forms of convulsion in GABA\textsubscript{B1a}\textsuperscript{-/-} than GABA\textsubscript{B1b}\textsuperscript{-/-} or wild-type mice, showing an increased seizure susceptibility in GABA\textsubscript{B1a}\textsuperscript{-/-} mice. In addition, in these mice the excitability of hippocampal CA1 neuronal circuit measured by the input-output relationship was not inhibited by the activation of GABA\textsubscript{B} receptors, due to the loss of presynaptic GABA\textsubscript{B(1a,2)} receptors. Immunolabelling of both GABA\textsubscript{B1} and GABA\textsubscript{B2} subunits showed that GABA\textsubscript{B(1a,2)} receptors are widely and uniformly expressed across the brain, and they are the predominant subtypes in the caudate putamen, globus pallidus, amygdala and CA3 stratum lucidum, which are brain areas involved in the genesis and spread of seizure activities. The GABA\textsubscript{B(1a,2)} receptors, by way of modulating the excitability of neural networks and the spread of seizure activity, are, therefore, shown to be essential for the control of seizure threshold. Deficits in the transcriptional and posttranslational mechanisms for GABA\textsubscript{B1a} isoforms may, thereby, lead to increased seizure susceptibility.