Role of low-threshold Ca^{2+} currents in absence seizures

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Spontaneous mutations of the α_{1A} gene, the pore-forming subunit of the P/Q-type high-voltage-gated Ca^{2+} channels, have been associated with genesis of 6-9 Hz spike-and-wave discharges (SWDs) on the electroencephalography (EEG), a sign of absence seizures. We show that the null mutants of α_{1A} develop severe absence seizures with 3-Hz SWDs on EEG, and showed enhanced T-type Ca^{2+} currents in the thalamic relay neurons in addition to decreased high-voltage-activated Ca^{2+} currents. Furthermore, when the α_{1G} locus, the predominant gene for T-type calcium channel in thalamic relay neurons, was disrupted additionally, SWDs of the α_{1A} mutants disappeared. These results may suggest a possibility that the increase of the T-type Ca^{2+} currents is a primarycomponent in the genesis of SWDs in the α_{1A} null mice. To test this possibility directly we have examined the phenotypes of the mice that are α_{1A} (-/-), α_{1G} (+/-). These mice contain T-type Ca^{2+} currents below the wildtype level, and thus give an opportunity to examine whether the enhancement of T-type Ca^{2+} currents has a role in the generation of SWDs in α_{1A} (-/-) mice. Results indicate that a basal level of T-type Ca^{2+} currents is sufficient to support SWDs in the mouse, and the enhancement of T-type Ca^{2+} currents is not an essential factor in this process.