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Oral Presentation

Pharmacological Modulation of Thalamic KCNQ-Potassium Channels: Insight from Knock-out Mice

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Abstract

The channels belonging to the KCNQ gene family consist of 5 different subtypes, which assemble as pentameric channels. The KCNQ2-5 subunits are highly expressed in the ventrobasal thalamus (VB) where they function primarily as KCNQ2/3 heteromers. They underlie an outward potassium (K⁺)-current, called M-current (IM), which provides a hyperpolarizing drive, thus regulating neuronal excitability. In order to understand the contribution of the KCNQ3 channel subunits to the regulation of the firing patterns and the generation of IM in VB neurons, we performed electrophysiological recordings using a mouse line lacking this subunit (KCNQ3 KO). Application of the specific channel activator Retigabine (Ret) induced hyperpolarization of the resting membrane potential, and significantly reduced the number of action potentials elicited in response to a given current step in control animals. In a similar manner, voltage-clamp experiments showed an increased IM following Ret application, while administration of the specific channel inhibitor XE991 reversed this effect. Preliminary recordings performed in KCNQ3 KO mice indicated a smaller IM amplitude in the same experimental conditions. However, increasing the group size and using other specific modulators will help us understanding better the role of KCNQ3 in VB and identify potential compensatory mechanisms exerted by other subunits.

Keywords: Mice, Potassium Channels, Thalamus

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