Role of RNA Editing of Cav1.3 Channels in Learning and Memory

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Abstract

Posttranscriptional mechanism such as RNA editing isan exquisite means to fine-tune Ca^{2+}-dependent regulation of voltage-gated (Ca_V) calcium channels. The generation of edited channels not only diversify function but it also influences the pharmacology of the channels. Post-transcriptional modifications of the IQ-domain, encoded by exon 41, of the $Ca_v1.3$ L-type channels regulate Ca^{2+}-dependent inhibition (CDI). The lack of CDI in the $Ca_v1.3$ channels may play an important role in cochlear amplification, neurotransmitter release and activity-dependent transcription in the hair cells or in the pacemaker activity of the suprachiasmatic neurons. We have recently discovered RNA editing at the IQ-domain resulting in the reduction of CDI. This pin-point modification is mediated by adenosine deaminases acting on RNA 2 (ADAR2) enzyme. $ECS^{-/-}$ mice genetically targeted to produce unedited $Ca_V1.3$ channels exhibited lower action potential spike frequencies in electrophysiological slice recordings of spontaneous oscillations in the suprachiasmatic neurons. These mice have better ability in spatial learning and have altered sleep patterns. Overall, RNA editing contributes significantly to Ca^{2+} homeostasis via regulating Ca^{2+}-dependent inhibition (CDI), a negative feedback mechanism on $Ca_V1.3$ channel function.

Keywords: *Ca_V calcium channel, RNA, Adenosine deaminases, Suprachiasmatic neurons, $ECS^{-/-}$ mice, CDI*

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