Functional uncoupling between Ca\textsuperscript{2+} release and afterhyperpolarization in mutant hippocampal neurons lacking junctophilins

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Abstract

Junctional membrane complexes (JMCs), composed of the electrically active (active) and nonactive (inactive) portions of the membrane and endoplasmic reticulum (ER), are thought to be a structural platform for channel clustering. Junc- tophilins (JPNs) contribute to JMC formation by interacting with the ER passive membrane to maintain active channels. In this article, we report that mutant JPN double-knockout (JPN\textsuperscript{-/-}) mice lacking both JPN subtypes exhibit an irregular baseline spike and impaired memory. Electrophysiological experiments indicated that the channels responsible for afterhyperpolarization in hippocampal neurons were small conductance Ca\textsuperscript{2+} release (SKCa) channels. These results show that JPN double-knockout mice exhibit characteristic electrophysiological and behavioral defects, similar to those of a knockdown of JPNs. Thus, JPNs are essential for maintaining the normal electrophysiology of hippocampal neurons and for memory formation.

Introduction

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