BMC Neuroscience

Poster presentation

Intrinsic hippocampal network activity is altered in MeCP2-deficient mice

Liang Zhang*, Jiwei He, Denis GM Jugloff and James H Eubanks

Address: Toronto Western Research Institute, University Health Network, Departments of Medicine and Surgery, University of Toronto Epilepsy Research Program, University of Toronto, Toronto, Ontario, Canada M5S 1A8

Email: Liang Zhang* - liangz@uhnres.utoronto.ca

* Corresponding author

from Sixteenth Annual Computational Neuroscience Meeting: CNS*2007
Toronto, Canada. 7–12 July 2007

Published: 6 July 2007

BMC Neuroscience 2007, **8**(Suppl 2):P186 doi:10.1186/1471-2202-8-S2-P186

The mammalian medial temporal lobe is capable of generating synchronous rhythmic activities in isolation. For example, brain slices prepared from patients with temporal lobe epilepsy, as well as slices prepared from normal monkey hippocampus, exhibit spontaneous, IPSP-based rhythmic field potentials that have frequencies of between 0.5–3 Hz. These inhibitory rhythmic activities are mediated by GABA-A receptors, and culminate from the network activity of local GABAergic inhibitory interneurons. Analogous spontaneous population rhythmic activities of 0.5–4 Hz are also evident in the isolated rodent hippocampus. These IPSP-based population activities are referred to as spontaneous rhythmic field potentials (SRFPs), as they are readily detected with conventional extracellular recordings. Several lines of evidence suggest that the SRFPs are of physiological significance. The SRFPs spread from the hippocampus to subicular and entorhinal cortical areas, and their frequencies and regional spread are similar to hippocampal electroencephalographic irregular activities that occur in behaving animals during slow wave sleep and wake immobility. In addition, the SRFPs appear during the 2nd postnatal week and then persist in adulthood. Such development profile is in keeping with activity-dependent modifications of hippocampal networks. Moreover, field rhythms similar to SRFPs have been shown to regulate memory-related synaptic plasticity such as long-term potentiation. It remains to be explored whether SRFPs can be used as a neurophysiological marker for detecting disease-related alterations in hippocampal networks.

Rett syndrome is a neurodevelopmental condition caused by loss of function mutations within the gene encoding methyl-CpG-binding protein 2 (*MeCP2*). While a subtle decrease in synaptic activity has been found in *Mecp2*-deficient mouse cortical and hippocampal neurons, it remains to be determined whether or how these changes affect the network activity of the *Mecp2*-deficient brain. To address this issue, we examined the SRFPs in conventional hippocampal slices via extracellular and whole-cell patch recordings. We found that although SRFPs were present in *Mecp2*-deficient slices, their frequency was significantly reduced. This reduction was not associated with significant alterations in the intracellular correlates of SRFPs, but was associated with diminished glutamate receptor-mediated excitatory activities in individual hippocampal CA3 neurons. The diminished excitatory drive appears to contribute to the slow SRFPs in the *Mecp2*-deficient hippocampus, as pharmacological attenuation of glutamate receptor activity was sufficient to induce similar slow SRFP activity in wild type slices. However, high frequency electrical stimulation of CA3 circuit in *Mecp2*-deficient slices did not reverse the slow SRFP phenotype, but rather induced excitatory, sharp wave like population events that were not observed in wild type slices. Taken together, our data indicate that the *Mecp2*-deficient hippocampus displays a reduction in basal glutamatergic activity in the CA3 recurrent network, that this reduced activity provides insufficient drive to the GABAergic inhibitory interneuronal network that establishes the normal SRFP frequency, but that there is a narrow window of tolerance for the

Mecp2-deficient hippocampal network to excitatory stimulation.