Calcium-Dependent Protein Kinase C is not Required for Post-Tetanic Potentiation at the Hippocampal CA3 to CA1 Synapse

Chih-Chieh Wang[1], Christopher Weyrer[1,2], Mounica Paturu[1], Diasynou Fioravante[1,3], and Wade G. Regehr[1].

1. Department of Neurobiology, Harvard Medical School, Boston MA 02115.

2. Department of Physiology, Development & Neuroscience, University of Cambridge, Cambridge, CB2 3EG, United Kingdom

3. Present address: Center for Neuroscience, University of California at Davis, Davis CA 95618.

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Post-tetanic potentiation (PTP) is a widespread form of short-term synaptic plasticity in which a period of elevated presynaptic activation leads to synaptic enhancement that lasts tens of seconds to minutes. A leading hypothesis for the mechanism of PTP is that tetanic stimulation elevates presynaptic calcium that in turn activates calcium-dependent Protein Kinase C (PKC) isoforms to phosphorylate targets and enhance neurotransmitter release. Previous pharmacological studies have implicated this mechanism in PTP at hippocampal synapses, but the results are controversial. Here we combine genetic and pharmacological approaches to determine the role of classic PKC isoforms in PTP. We find that PTP is unchanged in PKC triple knockout (TKO) mice in which all calcium-dependent PKC isoforms have been eliminated (PKCα, PKCβ, and PKCγ). We confirm previous studies and find that in wildtype mice 10 μM of the PKC inhibitor GF109203 eliminates PTP and the PKC activator PDBu enhances neurotransmitter release and occludes PTP. However, we find that the same concentrations of GF109203 and PDBu have similar effects in TKO animals. We also show that 2 μM GF109203 does not abolish PTP even though it inhibits the PDBu-dependent phosphorylation of PKC substrates. We conclude that at the CA3 to CA1 synapse Ca^{2+}-dependent PKC isoforms do not serve as calcium sensors to mediate PTP.

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