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The role of membrane-delimited AKT in regulation of LTP expression and basic synaptic activity

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Background: Serine/threonine kinase AKT/PKB plays a fundamental role in a wide variety of neuronal functions, including neuronal cell development, axonal growth and synaptic plasticity. Recently, a further downstream mechanism of AKT involvement in long-term depression (LTD) prevention and late phase long-term potentiation (LTP) has been revealed. However, no solid knowledge has been accumulated regarding the downstream effectors mediating AKT's effects on early phase LTP (eLTP).

Aim: Elucidating the role of AKT in eLTP regulation.

Results: Using different regimes for application of the AKT inhibitor A6730 (30 min drug exposure before high frequency stimulation (HFS), drug for 30 min before and 20 min after HFS, drug for 20 min 30 min after HFS), to acute hippocampal slices trained with the HFS paradigm, we observed that AKT regulates LTP induction and expression without affecting its maintenance. Further, we delivered an AKT activator to combine with inhibitors of various signaling pathways to prevent AKT activation-induced effect on LTP and to characterize a potential downstream mechanism of LTP regulation. Unexpectedly, SC79 (activator of AKT), which also prevents AKT translocation to the plasma membrane, induced a significant decrease in basal synaptic activity and in expression of LTP.

Conclusions: 1) Translocation of AKT towards the plasma membrane is necessary for regulation of synaptic activity and LTP. 2) AKT related LTP expression is not dependent on downstream cytosolic factors, but is mediated via direct effects of AKT on post-synaptic density components and glutamate receptors.

Biography

Borovok N has completed her PhD from Institute of Chemical Physics, Russian Academy of Sciences, Moscow, Russia and Post-doctoral studies from Tel-Aviv University, Department of Biochemistry, Israel. She is the Senior Researcher of the Department of Biochemistry and Molecular Biology, Tel-Aviv University. She has published more than 30 papers in reputed scientific journals.

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