KYOTO UNIVERSITY GRADUATE SCHOOL OF MEDICINE
DEPARTMENT OF PHARMACOLOGY

Intracellular signaling by NE drives AMPAR surface expression and synaptic plasticity

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Norepinephrine (NE) mediates arousal and attention and augments learning. However, the molecular mechanisms beyond adrenergic receptor (AR) stimulation are largely unknown. The β2AR and its effector proteins Gs, adenylyl cyclase, and PKA, are associated with AMPA receptors (AMPARs) to drive their phosphorylation and thereby surface expression (Joiner et al., 2010: EMBO J. 29, 482-495). Here we provide multiple lines of evidence that intracellular signaling by the β2AR is required for NE to stimulate AMPAR surface insertion and drive different forms of long-term potentiation (LTP) via phosphorylation of the AMPAR GluA1 subunit on S845. The organic cation transporter 3 (OCT3) and the plasma membrane monoamine transporter (PMAT) are members of the high-capacity uptake 2 system and mediate NE transport into various cell types. Blocking those impairs phosphorylation of GluA1 on S845 by PKA, GluA1 surface insertion, two forms of LTP, and upregulation of miniature excitatory postsynaptic currents induced by injection of NE into neurons. NE-driven upregulation of postsynaptic responses is not affected by sotalol, a membrane-impermeant blocker of the β2AR, arguing against involvement of signaling from β2AR at the cell surface. These results provide strong evidence for intracellular signaling by NE in neurons in general and specifically in synaptic plasticity.

No registration is required.

Host: Yasunori Hayashi x84393