# Kainic acid-induced neurotrophic activities in developing cortical neurons

李怡萱

Lee YH;Fang KM;Yang CM;Hwang HM;Chiu CT;Tsai WH

摘要

## Abstract

Using primary cultured cortical neurons from embryonic rat brains, we elucidated an α-amino-3-hydroxy-5-methyl-4-isoxazole propionate (AMPA)/kainic acid (KA) receptor-mediated neuroprotective mechanism through actions of nerve growth factor (NGF) in developing neurons. Neurotoxicity of KA in early days in vitro neurons was quite low compared with the mature neurons. However, pretreatment with anti-NGF antibody or TrkA inhibitor AG-879 profoundly raised KA toxicity. Furthermore, KA stimulation resulted in an increase of Trk A expression and phosphorylation, which was blocked not only by the AMPA/KA receptor antagonist 6-cyano-7-nitroquinoxaline-2,3-dione and AG-879, but also by the phospholipase C inhibitor U73122 and the intracellular calcium chelator BAPTA. A study of polyphosphoinositide turnover showed that KA-stimulated phospholipase C (PLC) activity was directly triggered by the AMPA/KA receptor activity, but not by the activity of TrkA or other excitatory amino acid receptor subtypes. Sources of KA-increased intracellular calcium levels were contributed by both extracellular calcium influx and intracellular calcium release and were partially sensitive to guanosine 5'-O-(2-thiodiphosphate). These results indicate that in developing cortical neurons, activation of AMPA/KA receptors by KA may induce expression, followed by activation of TrkA via PLC signaling and intracellular calcium elevation and hence increase reception of NGF on KA-challenged neurons. A G protein-coupled AMPA/KA receptor may be involved in these metabotropic events for neuronal protection.