NMDA preconditioning protects against Quinolinic Acid-induced seizures through PKA and ERK signaling pathways

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This study aimed to evaluate the participation of the Protein Kinase C (PKC), cAMP-dependent Protein Kinase (PKA), extracellular signal regulated Kinase (ERK), Ca^{2+} /calmodulin II-dependent Protein Kinase (CaMKII) and PKB/Akt signaling pathways in the neuroprotection attained through NMDA preconditioning.

Adult Swiss Male mice were preconditioned with NMDA (75 mg/kg, i.p) 24 h prior to the infusion of QA (4 µl, 36.8 nmol i.c.v.) and received specific inhibitors of the aforementioned signaling pathways either 15 minutes before the preconditioning, or 15 minutes before the infusion of QA. Inhibition of the PKA and Akt pathways by i.c.v. infusion of H-89 (5 µg/site) and wortmanin (0.43 µg/site), abolished the protection evoked by NMDA. Inhibition of ERK pathway by i.c.v. infusion of PD98059 (1 µg/site), reduced the NMDA protection rate from 50 % to 12.5%. Treatment with PKC and CaMKII inhibitors (chelerytrine and KN-62) did not alter the protection rate. Inhibition of the PKC pathway resulted in a high mortality rate when carried out before NMDA preconditioning followed by QA infusion, and when carried out before the QA infusion. Inhibition of the ERK pathway resulted in a high mortality rate when followed by the infusion of QA. Inhibition of signaling pathways in this model did not alter latency or duration of QA-induced seizures.

The results herein presented suggest that the PKA, Akt and ERK pathways have a crucial role in the achievement of a neuroprotective state induced by the NMDA preconditioning.

Keywords: preconditioning, NMDA, Quinolinic Acid, signaling pathways