I-4

Attenuation of NMDA and free radical toxicity in cortical neurons maintained in high glucose via enhanced mitochondrial function

So Young Seo1, Eun Young Kim1, Harriet Kim2, Ilo Jou and Byoung J. Gwag1.
1 Department of Pharmacology, Ajou University School of Medicine, Suwon, Kyungkido and 2.Department of Neutritional Biochemistry, Seoul National University, Seoul, Korea

Maintaining appropriate levels of glucose is essential for maintenance and survival of brain cells. Accumulating evidence has supported that hyperglycemia as well as hypoglycemia aggravates brain injuries following ischemia or epilepsy. However, several studies raise the possibility that increasing glucose entry to neurons may be beneficial against excitotoxicity and hypoxic-ischemia. To understand exact role of glucose in neurodegeneration, we first examined if cultured cortical neurons grown in high glucose (HG neurons) would show different vulnerability to NMDA, AMPA, or kainate. Among these, NMDA toxicity was substantially reduced in HG neurons. The protective effect of HG was associated with counteracting [Ca2+]i accumulation following exposure to NMDA. The neuroprotective action of HG extended to damages induced by deprivation of oxygen or glucose. The present study provides direct evidence that HG increases threshold for NMDA neurotoxicity and oxygen/glucose deprivation in part via regulation of [Ca2+]i accumulated following injuries.