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Changes in Protein kinase D activity during neurotoxic treatments

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Protein kinase D (PKD) is a serine-threonine kinase, activated through a number of signal transducing cascades. The enzyme is widely expressed in neuronal cells, playing a role in several important processes ranging from dendritic development and maintenance to the regulation of plasma membrane directed protein trafficking. Previous studies on non–neuronal cells have provided evidence on increased PKD activation during hypoxic conditions. Upon hydrogen-peroxide treatment, PKD activation at the mitochondria has been shown to induce specific protective signaling pathways responsible for the elimination of reactive oxygen radicals. During our studies, we aimed at examining the possibility of a similar protective role of PKD in neurodegenerative processes, such as ischemic stress. Different stages of the ischemic process were modeled in primary hippocampal cultures by treatment with excessive glutamate, potassium-cyanide and hydrogen-peroxide to resemble excitotoxic, hypoxic and oxidative stress, respectively. In all cases, active PKD levels increased transiently in response to the individual treatments. Elucidating PKD-mediated downstream signaling mechanisms will help to determine whether PKD can be a potential target in the treatment of neurodegenerative diseases.