Neuroprotective Effects of the Absence of JNK1 or JNK3 Isoforms on Kainic Acid-Induced Temporal Lobe Epilepsy-Like Symptoms

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The activation of c-Jun-N-terminal kinases (JNK) pathway has been largely associated with the pathogenesis and the neuronal death that occur in neurodegenerative diseases. Altogether, this justifies why JNKs have become a focus of screens for new therapeutic strategies. The aim of the present study was to identify the role of the different JNK isoforms (JNK1, JNK2, and JNK3) in apoptosis and inflammation after induction of brain damage. To address this aim, we induced excitotoxicity in wild-type and JNK knockout mice (jnk1?/?, jnk2?/?, and jnk3?/?) via an intraperitoneal injection of kainic acid, an agonist of glutamic-kainate-receptors, that induce status epilepticus. Each group of animals was divided into two treatments: a single intraperitoneal dose of saline solution, used as a control, and a single intraperitoneal dose (30 mg/kg) of kainic acid. Our results reported a significant decrease in neuronal degeneration in the hippocampus of jnk1?/? and jnk3?/? mice after kainic acid treatment, together with reduced or unaltered expression of several apoptotic genes compared to WT treated mice. In addition, both jnk1?/? and jnk3?/? mice exhibited a reduction in glial reactivity, as shown by the lower expression of inflammatory genes and a reduction of JNK phosphorylation. In addition, in jnk3?/?mice, the c-Jun phosphorylation was also diminished. Collectively, these findings provide compelling evidence that the absence of JNK1 or

JNK3 isoforms confers neuroprotection against neuronal damage induced by KA and evidence, for the first time, the implication of JNK1 in excitotoxicity. Accordingly, JNK1 and/or JNK3 are promising targets for the prevention of cell death and inflammation during epileptogenesis.

c-Jun N-terminal kinase

Excitotoxicity

Hippocampus

Inflammation

Kainic acid

Knockout mice

Neurodegeneration

Neuroprotection

isoprotein

JNK1 protein

JNK3 protein

kainic acid

unclassified drug

isoenzyme

kainic acid

mitogen activated protein kinase 10

neuroprotective agent

stress activated protein kinase 1

animal cell

animal experiment

animal tissue

apoptosis

Article

brain damage

cell death

controlled study

epileptic state

epileptogenesis

excitotoxicity

gene expression

inflammation

knockout mouse

mouse

nerve cell degeneration

neuroprotection

nonhuman

protein function

protein phosphorylation

single drug dose

temporal lobe epilepsy

treatment response

wild type mouse

animal

C57BL mouse

deficiency

enzyme activation

enzymology

genetics

hippocampus

inflammation

metabolism

pathology

phosphorylation

temporal lobe epilepsy

Animals

Apoptosis

Enzyme Activation

Epilepsy, Temporal Lobe

Hippocampus

Inflammation

Isoenzymes

Kainic Acid

Mice, Inbred C57BL

Mice, Knockout

Mitogen-Activated Protein Kinase 10

Mitogen-Activated Protein Kinase 8

Neuroprotective Agents

Phosphorylation