JNK Isoforms Are Involved in the Control of Adult Hippocampal Neurogenesis in Mice, Both in Physiological Conditions and in an Experimental Model of Temporal Lobe Epilepsy

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Neurogenesis in the adult dentate gyrus (DG) of the hippocampus allows the continuous generation of new neurons. This cellular process can be disturbed under specific environmental conditions, such as epileptic seizures; however, the underlying mechanisms responsible for their control remain largely unknown. Although different studies have linked the JNK (c-Jun-N-terminal-kinase) activity with the regulation of cell proliferation and differentiation, the specific function of JNK in controlling adult hippocampal neurogenesis is not well known. The purpose of this study was to analyze the role of JNK isoforms (JNK1/JNK2/JNK3) in adult-hippocampal neurogenesis. To achieve this goal, we used JNK-knockout mice (Jnk1?/?, Jnk2?/?, and Jnk3?/?), untreated and treated with intraperitoneal injections of kainic acid (KA), as an experimental model of epilepsy. In each condition, we identified cell subpopulations at different stages of neuronal maturation by immunohistochemical specific markers. In physiological conditions, we evidenced that JNK1 and JNK3 control the levels of one subtype of early progenitor cells (GFAP+/Sox2+) but not the

GFAP+/Nestin+ cell subtype. Moreover, the absence of JNK1 induces an increase of immature neurons (Doublecortin+; PSA-NCAM+ cells) compared with wild-type (WT). On the other hand, Jnk1?/? and Jnk3?/? mice showed an increased capacity to maintain hippocampal homeostasis, since calbindin immunoreactivity is higher than in WT. An important fact is that, after KA injection, Jnk1?/? and Jnk3?/? mice show no increase in the different neurogenic cell subpopulation analyzed, in contrast to what occurs in WT and Jnk2?/? mice. All these data support that JNK isoforms are involved in the adult neurogenesis control.

Adult hippocampal neurogenesis

JNK isoforms

Kainic acid

Knockout mice

calbindin

doublecortin

kainic acid

mitogen activated protein kinase 12

mitogen activated protein kinase p38

nestin

stress activated protein kinase

stress activated protein kinase 1

transcription factor Sox2

calbindin

glial fibrillary acidic protein

isoenzyme

kainic acid

nerve cell adhesion molecule L1

nestin

polysialyl neural cell adhesion molecule

sialic acid derivative

stress activated protein kinase

transcription factor Sox

adult

animal experiment

animal model

Article

cell maturation

cell subpopulation

controlled study

homeostasis

immunocompetent cell

immunohistochemistry

immunoreactivity

knockout mouse

mouse

nerve cell

nervous system development

nonhuman

temporal lobe epilepsy

aging

animal

C57BL mouse

cell count

dentate gyrus

disease model

enzymology

hippocampus

metabolism

neural stem cell

pathology

temporal lobe epilepsy

Aging

Animals

Calbindins

Cell Count

Dentate Gyrus

Disease Models, Animal

Epilepsy, Temporal Lobe

Glial Fibrillary Acidic Protein

Hippocampus

Isoenzymes

JNK Mitogen-Activated Protein Kinases

Kainic Acid

Mice, Inbred C57BL

Nestin

Neural Cell Adhesion Molecule L1

Neural Stem Cells

Neurogenesis

Neurons

Sialic Acids

SOXB1 Transcription Factors