Role of c-jun N-terminal kinases (JNKs) in epilepsy and metabolic cognitive impairment

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Previous studies have reported that the regulatory function of the different c-Jun N-terminal kinases isoforms (JNK1, JNK2, and JNK3) play an essential role in neurological disorders, such as epilepsy and metabolic-cognitive alterations. Accordingly, JNKs have emerged as suitable therapeutic strategies. In fact, it has been demonstrated that some unspecific JNK inhibitors exert antidiabetic and neuroprotective effects, albeit they usually show high toxicity or lack therapeutic value. In this sense, natural specific JNK inhibitors, such as Licochalcone A, are promising candidates. Nonetheless, research on the understanding of the role of each of the JNKs remains mandatory in order to progress on the identification of new selective JNK isoform inhibitors. In the present review, a summary on the current gathered data on the role of JNKs in pathology is presented, as well as a discussion on their potential role in pathologies like epilepsy and metabolic-cognitive injury.

Moreover, data on the effects of synthetic small molecule inhibitors that modulate JNK-dependent pathways in the brain and peripheral tissues is reviewed.

Brain

C-Jun-N-terminal kinase

Cognitive impairment

Epilepsy

JNK inhibitor

Metabolism

Type 2 diabetes

activating transcription factor 6

BIM protein

cytochrome c

cytochrome P450

glucose regulated protein 78

glutathione peroxidase

growth arrest and DNA damage inducible protein 153

immunoglobulin enhancer binding protein

insulin

interleukin 1beta

isoenzyme

licochalcone A

mitogen activated protein kinase

mitogen activated protein kinase 1

mitogen activated protein kinase 3

mitogen activated protein kinase 7

mitogen activated protein kinase p38

peroxiredoxin

protein Bax

protein bcl 2

protein bcl xl

protein c jun

protein tyrosine phosphatase 1B

proton transporting adenosine triphosphate synthase

reactive oxygen metabolite

second mitochondrial activator of caspase

stress activated protein kinase

stress activated protein kinase inhibitor

tumor necrosis factor receptor associated factor 2

unindexed drug

antidiabetic agent

isoprotein

mitogen activated protein kinase

neuroprotective agent

stress activated protein kinase

apoptosis

autophagy (cellular)

cell cycle progression

cell death

cell proliferation

cell respiration

citric acid cycle

cognitive defect

dementia

dentate gyrus

disease course

dyslipidemia

endoplasmic reticulum stress

epilepsy

epileptogenesis

human

hyperinsulinemia

in situ hybridization

insulin resistance

metabolic syndrome X

nerve degeneration

neuroprotection

non insulin dependent diabetes mellitus

nonhuman

obesity

oxidative phosphorylation

oxidative stress

protein degradation

protein phosphorylation

Review

seizure

temporal lobe epilepsy

unfolded protein response

upregulation

animal

brain

cognitive defect

drug effect

epilepsy

MAPK signaling

metabolism

mitochondrion

pathology

physiology

Animals

Brain

Cognitive Dysfunction

Diabetes Mellitus, Type 2

Endoplasmic Reticulum Stress

Epilepsy

Humans

Hypoglycemic Agents

JNK Mitogen-Activated Protein Kinases

MAP Kinase Signaling System

Mitochondria

Mitogen-Activated Protein Kinases

Neuroprotective Agents

Protein Isoforms