c-Jun N-terminal Kinase 1 ablation protects against metabolic-induced hippocampal cognitive impairments

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Abstract: The development of metabolic alterations like insulin resistance has been associated with dysfunctions in mitochondrial oxidative capacity, induction of neuroinflammatory responses, and the appearance of cognitive impairments in the brain. The c-Jun N-terminal Kinase 1 (JNK1) is a potential key modulator of these mechanisms. The current study identifies a protective effect of whole-body JNK1 knockout in the presence of a high-fat diet (HFD). Specifically, the data suggest that mice missing JNK1 show increased insulin sensitivity and mitochondrial activity, as well as reduced body weight, and astrocyte and microglial reactivity. Finally, these animals are also protected against HFD-induced cognitive impairments as assessed through novel object recognition test, the observation of dendritic spines, and the levels of BDNF or other proteins like spinophilin and ARC. Thus, modulation of JNK1 activity seems like a promising approach for the design of therapies aimed at treating metabolic-induced cognitive impairments. Key messages: JNK1 is a link

between obesity/type 2 diabetes and cognitive lossInhibition of JNK1 is neuroprotectiveJNK1 constitutes a therapeutic strategy for cognitive loss.

c-Jun N-terminal Kinase 1

Cognitive impairments

High-fat diet

brain derived neurotrophic factor

citrate synthase

spinophilin

stress activated protein kinase 1

actin binding protein

brain derived neurotrophic factor

nerve protein

neurabin

stress activated protein kinase 1

animal experiment

animal model

antioxidant activity

Article

astrocyte

body weight

cognitive defect

comparative study

controlled study

dendritic spine

disease association

enzyme activity

fat content

glucose tolerance test

Golgi stain

immunofluorescence

insulin resistance

insulin sensitivity

insulin tolerance test

lipid diet

long term care

long term exposure

male

metabolic disorder

motor activity

mouse

neuromodulation

non insulin dependent diabetes mellitus

nonhuman

novel object recognition test

observation

oxidative phosphorylation

real time polymerase chain reaction

Western blotting

adverse event

animal

C57BL mouse

cognition assessment

cognitive defect

complication

enzymology

genetics

hippocampus

metabolism

microglia

mitochondrion

physiology

transgenic mouse

Animals

Astrocytes

Body Weight

Brain-Derived Neurotrophic Factor

Cognitive Dysfunction

Dendritic Spines

Diabetes Mellitus, Type 2

Diet, High-Fat

Hippocampus

Insulin Resistance

Male

Memory and Learning Tests

Mice

Mice, Inbred C57BL

Mice, Transgenic

Microfilament Proteins

Microglia

Mitochondria

Mitogen-Activated Protein Kinase 8

Nerve Tissue Proteins