Genetic ablation of tau improves mitochondrial function and cognitive abilities in the hippocampus

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Tau is a key protein for microtubule stability; however, post-translationally modified tau contributes to neurodegenerative diseases by forming tau aggregates in the neurons. Previous reports from our group and others have shown that pathological forms of tau are toxic and impair mitochondrial function, whereas tau deletion is neuroprotective. However, the effects of tau ablation on brain structure and function in young mice have not been fully elucidated. Therefore, the aim of this study was to investigate the implications of tau ablation on the mitochondrial function and cognitive abilities of a litter of young mice (3 months old). Our results showed that tau deletion had positive effects on hippocampal cells by decreasing oxidative damage, favoring a mitochondrial pro-fusion state, and inhibiting mitochondrial permeability transition pore (mPTP) formation by reducing cyclophilin D (Cyp-D) protein. More importantly, tau deletion increased ATP production and improved the recognition memory and attentive capacity of juvenile mice. Therefore, the absence of tau enhanced brain function by improving mitochondrial health, which supplied more energy to the synapses. Thus, our work opens the possibility that preventing negative tau modifications could enhance brain function through the improvement of mitochondrial health.

Hippocampus

Learning

Memory

Mitochondria

Tau

adenosine triphosphate

complementary DNA

cyclophilin D

mitochondrial permeability transition pore

reduced nicotinamide adenine dinucleotide dehydrogenase (ubiquinone)

RNA

tau protein

ubiquinol cytochrome c reductase

carrier protein

cyclophilin

cyclophilin D

Mapt protein, mouse

mitochondrial permeability transition pore

tau protein

animal cell

animal experiment

animal tissue

Article

behavior assessment

brain cell

cell isolation

cognition

controlled study

enzyme activity

genetic ablation

genetic procedures

hippocampal slice

hippocampus

male

mitochondrion

Morris water maze test

mouse

nonhuman

novel object recognition test

open field test

oxidative stress

priority journal

real time polymerase chain reaction

recognition

reverse transcription

RNA extraction

social behavior

social interaction

synapse

animal

gene deletion

genetics

hippocampus

knockout mouse

learning

maze test

memory

metabolism

mitochondrion

physiology

Animals

Cognition

Cyclophilins

Gene Deletion

Hippocampus

Learning

Male

Maze Learning

Memory

Mice

Mice, Knockout

Mitochondria

Mitochondrial Membrane Transport Proteins

Oxidative Stress

tau Proteins