# Possible role of mitochondrial permeability transition pore in the pathogenesis of Huntington disease

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Huntington disease (HD) is a devastating neurological disorder that affects the striatum and cortex of patients. HD patients develop progressive motor dysfunction and psychiatric disturbances with gradual dementia. HD is caused by a pathological expansion of CAG repeats in the huntingtin gene that codifies for a protein called huntingtin (Htt), which principal function is not completely understood. Accumulative evidence shows that this pathological expansion modifies Htt function affecting different neuronal targets, including mitochondrial function which is an important factor that contributes to HD. Interestingly, several groups have shown mitochondrial disturbances including calcium handling defects, depolarization, decrease of mitochondrial transport, ATP reduction, and increase of reactive oxygen species (ROS) in cellular and murine HD models. Systematic analysis of this evidence indicates that a mitochondrial structure, the mitochondrial permeability transition pore (mPTP), could be responsible for these changes that affect mitochondria. The mPTP plays an important role in apoptosis and neurodegeneration. It has also been reported to have some physiological functions in heart development and synaptic communication. In HD, the presence of mutant huntingtin (mHtt) activates this mechanism producing a significant compromise of mitochondrial metabolism and bioenergetics. Considering these findings this review explores the evidence that suggests the important role of mPTP in the mitochondrial impairment induced by mHtt, which leads to calcium derangement and contributes to neuronal dysfunction in HD. 

Calcium

Huntington disease

Mitochondria

Mitochondrial permeability pore

Oxidative stress

calcium

huntingtin

lead

mitochondrial permeability transition pore

carrier protein

HTT protein, human

huntingtin

mitochondrial permeability transition pore

bioenergy

brain dysfunction

brain function

clinical feature

human

Huntington chorea

mitochondrial respiration

neuropathology

neurotoxicity

nonhuman

priority journal

Review

genetics

Huntington chorea

pathology

pathophysiology

physiology

Humans

Huntingtin Protein

Huntington Disease

Mitochondrial Membrane Transport Proteins