PubMed

Format: Abstract

Full text links

IOS Press Full Text

J Alzheimers Dis. 2013;35(3):525-39. doi: 10.3233/JAD-130050.

Natural cannabinoids improve dopamine neurotransmission and tau and amyloid pathology in a mouse model of tauopathy.

Casarejos MJ[1], Perucho J, Gomez A, Muñoz MP, Fernandez-Estevez M, Sagredo O, Fernandez Ruiz J, Guzman M, de Yebenes JG, Mena MA.

Author information

Abstract

Cannabinoids are neuroprotective in models of neurodegenerative dementias. Their effects are mostly mediated through CB1 and CB2 receptor-dependent modulation of excitotoxicity, inflammation, oxidative stress, and other processes. We tested the effects of Sativex®, a mixture of Δ9-tetrahydrocannabinol and cannabidiol, acting on both CB1 and CB2 receptors, in parkin-null, human tau overexpressing (PK-/-/TauVLW) mice, a model of complex frontotemporal dementia, parkinsonism, and lower motor neuron disease. The animals received Sativex®, 4.63 mg/kg, ip, daily, for one month, at six months of age, at the onset of the clinical symptoms. We evaluated the effects of Sativex® on behavior, dopamine neurotransmission, glial activation, redox state, mitochondrial activity, and deposition of abnormal proteins. PK-/-/TauVLW mice developed the neurological deficits, but those treated with Sativex® showed less abnormal behaviors related to stress, less auto and hetero-aggression, and less stereotypy. Sativex® significantly reduced the intraneuronal, MAO-related free radicals produced during dopamine metabolism in the limbic system. Sativex® also decreased gliosis in cortex and hippocampus, increased the ratio reduced/oxidized glutathione in the limbic system, reduced the levels of iNOS, and increased those of complex IV in the cerebral cortex. With regard to tau and amyloid pathology, Sativex® reduced the deposition of both in the hippocampus and cerebral cortex of PK-/-/TauVLW mice and increased autophagy. Sativex®, even after a short administration in animals with present behavioral and pathological abnormalities, improves the phenotype, the oxidative stress, and the deposition of proteins in PK-/-/TauVLW mice, a model of complex neurodegenerative disorders.

PMID: 23478312 DOI: 10.3233/JAD-130050

[Indexed for MEDLINE]

Publication type, MeSH terms, Substances

LinkOut - more resources