Alzheimer’s disease (AD) is a severe neurodegenerative disorder. Progressive loss of mitochondrial function or defects in mitochondrial metabolism in the disease can lead to the generation of reactive oxygen species resulting in oxidation of membrane lipids and accumulation of toxic aldehydes in the brain and blood.

A mechanism for rapid clearance of these highly diffusable and harmful aldehydes is crucial to protect cells / tissues from damage. ADLH2 is located in the mitochondrial matrix and is a major enzyme involved in the clearance of reactive aldehydes. AD-9308 is a produg of a potent and selective activator (AD-5591) of ADLH2. The parent compound and active metabolite, AD-5591, has been found to promote ADLH2 activity in the oxidation of acetaldehyde, 4-hydroxy-2-nonenal (4-HNE), malondialdehyde (MDA) and propionaldehyde to the corresponding acid.

The MWM test revealed a significant improvement of spatial learning in ADLH2 activator-treated animals compared to vehicle treated animals. AD-9308 did not reduce neuroinflammation in the brain but Aβ-40 and MDA levels were significantly decreased. Additionally, acetate levels were increased in AD-9308 treated animals compared to the control group. Further analysis has to be performed to better understand the pharmacological effect of the compound.

Our results demonstrate that increasing the detoxification activity of ADLH2 is a promising approach to target AD.

For more information about the model please visit: www.qpsneuro.com or send us an e-mail: office-austria@qps.com

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