P1101 / #1444

Topic: AS08 Diseases of The Nervous System (including, infective and psychiatric)

α-SYNUCLEIN ALTERS THE MORPHOLOGY OF SYNAPTIC MITOCHONDRIA IN GIANT AXONS OF SEA LAMPREY

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Parkinson's disease (PD) is a neurodegenerative disease characterized by the aggregation of α-synuclein throughout neurons, including at synapses. Prior studies from the Morgan Lab indicate that excess α-synuclein disrupts synaptic vesicle trafficking. However, the impact of excess α-synuclein on synaptic mitochondria is unknown, which is important because mitochondrial dysfunction leads to neurodegeneration. Therefore, my goal is to determine whether α-synuclein alters the morphology of synaptic mitochondria. To address this, we used the sea lamprey (Petromyzon marinus) as a model. The lamprey spinal cord has giant reticulospinal axons (30-60 microns) making it ideal for microinjecting human α-synuclein into the axon. Electron micrographs were obtained at three regions from the injection site, representing control synapses and synapses with a low or high concentration of monomeric, multimeric (80 kDa), and phosphorylated versions of α-synuclein. These variants were chosen because they are drastically increased in PD brains. I analyzed the number of mitochondria at synapses, as well as their perimeters and distance from the active zone using Fiji ImageJ software. After phosphoserine 129 α-synuclein injection, the perimeter of presynaptic mitochondria significantly increased by 24.4%, compared to controls, indicating mitochondrial swelling. After multimeric α-synuclein injection, the number of mitochondria around the synapses decreased by 55.2%, as compared to controls. In addition, multimeric α-synuclein caused mitochondrial swelling and decreased the distance to the active zone by 308 nm on average. After monomeric α-synuclein injection, the number of synaptic mitochondria decreased and swelling occurred. Together, these results indicate that α-synuclein decreases the number of synaptic mitochondria, and other variant-specific phenotypes. Additional experiments are underway to determine how α-synuclein interacts with mitochondria to cause such effects using live imaging and immunofluorescent staining. Understanding how α-synuclein affects presynaptic mitochondria will reveal cellular or metabolic pathways that can be targeted to slow the progression of PD.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.1107

P1102 / #1325

Topic: AS08 Diseases of The Nervous System (including, infective and psychiatric)

EFFECTS OF CANNABIDIOL ON THE LOCOMOTOR SENSITIZATION AND NEUROINFLAMMATION INDUCED BY A COMBINATION OF COCAINE AND CAFFEINE IN MICE

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Cannabidiol (CBD), a non-psychotomimetic cannabinoid from the plant *Cannabis sativa*, has been reported as a potential candidate for the treatment of cocaine use disorders in humans. However, the underlying mechanisms mediating these effects remain largely unknown. Prior work from our laboratory has shown that in Uruguay, street-seized cocaine samples were frequently adulterated with caffeine. We have shown that the presence of caffeine acts as an enhancing agent in the induction of cocaine-induced locomotor sensitization. Administration of CBD completely blocked this behavioral effect. Expression of this behavior was associated with neuroinflammatory processes. We thus hypothesized that the anti-inflammatory properties of CBD could prevent the drug-induced neuroinflammatory process, halting the neural-glial adaptation thought to be responsible for the locomotor sensitization. Male adult mice were treated with CBD and CocCaf or its respective vehicles, for 5 days. Locomotor activity was automatically recorded and quantified in an open field by the video-tracking software EthoVision XT 17.0. In the current work we report that administration of cocaine and caffeine combined resulted in locomotor sensitization and that this behavioral effect was attenuated by the presence of CBD. Histological analysis of reward related structure Nucleus Accumbens revealed that animals exposed to the drugs combination had developed neuroinflammatory processes in this area, as measured by increased microglial activation (Iba-1 immunoreactivity). Modulation by CBD of the drug-induced neuroinflammatory processes might be involved in the attenuation of the behavioral response to repeated exposure to cocaine and caffeine combination that we report here.

Declaration of Interest Statement: None

https://doi.org/10.1016/j.ibneur.2023.08.1108