Cannabidiol attenuates seizures and EEG abnormality in Angelman syndrome model mice

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Angelman syndrome (AS) is a neurodevelopmental disorder characterized by intellectual disability, lack of speech, motor dysfunction, EEG abnormalities, and epilepsy. Seizures in AS individuals are often resistant to existing antiepileptic medications. Therefore, there is an unmet need for better seizure control, which could potentially also improve other symptomatic domains. Cannabidiol (CBD), a major phytocannabinoid constituent of cannabis, has been shown to have antiseizure activity and behavioral benefits in several preclinical and clinical studies for other disorders, suggesting that CBD may also provide a viable treatment opportunity for seizures and other core pathologies of AS. Here we show that acute treatment of CBD (100 mg/kg) exhibited anticonvulsant effects by attenuating acoustic and hyperthermia induced seizure in a mouse model of AS. While CBD administration could effectively prevent or attenuate the subsequent induction of seizures, it failed to prevent the emergence of a pro-epileptogenic AS phenotype when administered after repeated seizure inductions. CBD administration caused a mild sedative effect, as measured by reduced open field activity, but did not have a major impact on motor performance, as measured in a rotarod test. CBD also partially normalized the abnormal EEG activity observed in AS model mice, suggesting that in addition to attenuating seizures, CBD administration could also help normalize the EEG deficits observed in AS individuals. Our results provide critical preclinical evidence supporting CBD treatment of epilepsy and alleviation of EEG abnormality linked to AS, and will thus help guide the rational development of CBD as an AS treatment.