ABSTRACT

Cannabis is the most commonly used illicit drug in the world, and numbers are even higher among adolescents as compared to the general population. Cannabinoids have been shown to modulate immune responses, including microglial activation, and oxidative stress pathways; however, the effects of cannabis use on brain immune cells (i.e. microglial activation) and redox status have never been investigated in vivo in human brain. In this study, for the first time, we investigated microglial activation and glutathione (GSH) levels, a major redox regulator, in regular cannabis users. Twenty regular cannabis users and 27 healthy controls were scanned using positron emission tomography with $^{[18}\text{F}]$FEPPA, a radioligand specific for translocator protein 18kDa (TSPO), a marker of microglial activation. Given previous evidence of the effects of cannabis on the prefrontal cortex, our two main regions of interest were the dorsolateral prefrontal cortex (DLPFC) and medial prefrontal cortex (mPFC). We also explored other brain regions including anterior cingulate cortex, temporal cortex, hippocampus and gray matter. All of the cannabis users and the majority of healthy controls (n=14) also underwent a proton magnetic resonance spectroscopy scan to quantify glutathione levels in the mPFC. There was a significant difference in $^{[18}\text{F}]$FEPPA $V_T$ in the DLPFC ($F_{(1,44)}= 5.614, p= 0.022$) and mPFC ($F_{(1,44)}= 5.733, p= 0.021$) between groups, such that regular cannabis users had higher microglial activation compared to healthy controls. In contrast, no group differences were observed in GSH levels in the mPFC. Our findings suggest a link between regular cannabis use and microglial activation, but not redox status.