Abstract

Psilocybin was recently declared a breakthrough therapy by the FDA due to its therapeutic effects for psychiatric disorders like major depression disorder, anxiety, and addiction. One brain region that is implicated in these psychiatric disorders is the central amygdala (CeA) which serves as the main output nucleus of the amygdala. The CeA plays an essential role in emotion processing and affective behavior. Psilocin, the active metabolite of psilocybin, is thought to exert its hallucinogenic and therapeutic actions via the 5-HT2A receptor. This receptor is robustly expressed in the PFC; however, currently, there is no quantification of the number of 5HT2A receptors in the CeA, as well as no quantification of the expression of these receptors in the CeA when activated by psilocin. We studied psilocin-induced cFOS expression of 5-HT2A neurons in the CeA using a novel 5-HT2AR-eGFP-CreERT2xAi9 transgenic mouse line as well using ex vivo electrophysiology to look at the inhibitory or excitatory effects of psilocin. We found that neuronal activity in the CeA is significantly altered by psilocin and that psilocin selectively and differentially modulates activity in the different sub-compartments of the central amygdala which holds further importances to possible microcircuits within the amygdala complex that might be playing a role in these differences. These findings further our understanding of how psilocin acts and can help future research on its implications on psychiatric disorders like depression and addiction.

keywords: psilocybin, central amygdala, microcircuits, 5-HT2AR