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Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex *in vivo*

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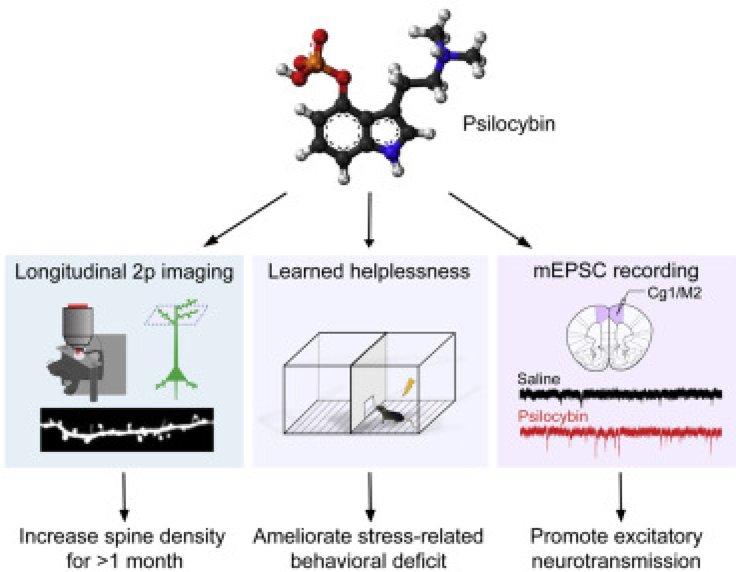
Highlights

- Psilocybin ameliorates stress-related behavioral deficit in mice
- Psilocybin increases spine density and spine size in frontal cortical pyramidal cells
- Psilocybin-evoked structural remodeling is persistent for at least 1 month

Summary

Psilocybin is a serotonergic psychedelic with untapped therapeutic potential. There are hints that the use of psychedelics can produce neural adaptations, although the extent and timescale of the impact in a mammalian brain are unknown. In this study, we used chronic two-photon microscopy to image longitudinally the apical dendritic spines of layer 5 pyramidal neurons in the mouse medial frontal cortex. We found that a single dose of psilocybin led to ~10% increases in spine size and density, driven by an elevated spine formation rate. The structural remodeling occurred quickly within 24 h and was persistent 1 month later. Psilocybin also ameliorated stress-related behavioral deficit and elevated excitatory neurotransmission. Overall, the results demonstrate that psilocybin-‍ᅟ‍d synaptic rewiring in the cortex is fast and enduring, potentially providing a structural trace for ‍rm integration of experiences and lasting beneficial actions.

Graphical abstract



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dendrites • neural plasticity • structural remodeling • serotonergic psychedelic • hallucinogen • antidepressant • psilocybin • synapse • pyramidal neuron • medial prefrontal cortex

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