

Titre du résumé : Reduction of alcohol consumption by psilocybin: role of serotonin type 2A receptors in the nucleus accumbens and identification of genetic regulations by PCR array

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Description précise des objectifs

After falling out of favour in the 1960s, psychedelics are making a comeback in the treatment of psychiatric and addictive disorders. A proof of concept was published in 2015 showing that psilocybin sustainably (36 weeks) reduces alcohol consumption in patients with alcohol use disorders (AUD). In the present work we measured the effects of psilocybin on alcohol consumption and relapse after abstinence in rats as well as the mechanism of action (brain structure and serotonin receptor involved).

Matériel et méthodes

Two operant self-administration procedures were used in rats to study the "post-dependent state" induced by inhalation of ethanol vapour and the second one of binge drinking behaviour. Rats were given a reward of ethanol (0.1ml at 20%) after pressing a lever. Psilocybin was injected either intraperitoneally or directly into the brain (nucleus accumbens or ventral tegmental area) and after, or without, injection of ketanserin directly into the brain. A screening of gene expression changes of neurotransmission systems (glutamatergic, serotonergic, dopaminergic and gabaergic) was performed in the nucleus accumbens using a PCR array technique.

Résultats et conclusions

Our unpublished results show that acute psilocybin administration reduces not only relapse after abstinence but also alcohol consumption prior to withdrawal. Interestingly, we show that this effect of psilocybin is mediated by serotonin type 2A

receptors in the nucleus accumbens in an experiment where psilocybin and/or the 5-HT2A antagonist ketanserin are injected intraperitoneally, or in the nucleus accumbens or ventral tegmental area. Our genetic screening allowed us to identify, among others, an involvement of the mGluR2 glutamatergic receptor which is known to create heterodimers with the 5-HT2A receptor. Our project provides major results in the understanding of the neurobiological mechanisms underlying the beneficial effects of psilocybin in the treatment of AUD and reinforces the interest in conducting further clinical trials.

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