

# Molecular and structural insights into the serotonin 5-HT<sub>2C</sub> receptor as a therapeutic target for substance use disorders

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## Abstract

Substance use disorder (SUD) is a chronic condition with maintained abuse of a substance leading to physiological and psychological alterations and often changes in cognitive and social behaviours. Current therapies mainly consist of psychotherapy coupled with medication; however, alarmingly high relapse rates reveal the shortcomings of the current standard of care. The signalling and expression profile, and neurological function of the serotonin 2C receptor (5-HT<sub>2C</sub> receptor) make it an ideal candidate of interest for the treatment of SUD. This is further corroborated by pre-clinical and clinical evidence of therapeutically relevant compounds acting at the 5-HT<sub>2C</sub> receptor. Notwithstanding, drug binding at closely related serotonin receptor subtypes has impeded drug development. More recently, psychedelics, which broadly act at 5-HT<sub>2</sub> receptors, have indicated promising potential for the treatment of SUD, implicating in part, the 5-HT<sub>2C</sub> receptor. The modern psychedelic movement has rekindled therapeutic interest in the 5-HT<sub>2C</sub> receptor, resulting in an influx of new studies, especially structural analyses. This review delves into the structural, molecular and cellular mechanisms governing the 5-HT<sub>2C</sub> receptor function, in the context of SUD. This provides the basis of the preclinical and clinical evidence for their role in SUD and highlights the potential for future exploration.

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