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5HT2a Receptors – a New Target for Depression?

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Cortical 5HT2A receptors are largely expressed in layer 5 pyramidal neurons and appear to play a pivotal role in brain function in that they gate top-down descending inputs to local cortical microcircuits. There is evidence that they may play a role in depression in that the number of these receptors is increased in some people with depression and the augmenting action of atypical antipsychotics in depression is thought to be – at least in part – due to blockade of these receptors. We have explored this possibility by studying the effects of agonists at these receptors – the psychedelic druds psilocybin and LSD. We found they had profound effects to **reduce** brain activity particularly in regions that higly express the 5HT2A receptor such as the default mode network [DMN]. As this region is **overactive** in depression this may explain the improvements in mood that users of psychedelic often report. Based on these findings a study of psilocybin in resistant depression has been funded by the UK MRC and will start in early 2015.

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