

Publication

A Single Dose of LSD Does Not Alter Gene Expression of the Serotonin 2A Receptor Gene (HTR2A) or Early Growth Response Genes (EGR1-3) in Healthy Subjects

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Rationale: Renewed interest has been seen in the use of lysergic acid diethylamide (LSD) in psychiatric research and practice. The repeated use of LSD leads to tolerance that is believed to result from serotonin (5-HT) 5-HT_{2A} receptor downregulation. In rats, daily LSD administration for 4 days decreased frontal cortex 5-HT_{2A} receptor binding. Additionally, a single dose of LSD acutely increased expression of the early growth response genes EGR1 and EGR2 in rat and mouse brains through 5-HT_{2A} receptor stimulation. No human data on the effects of LSD on gene expression has been reported. Therefore, we investigated the effects of single-dose LSD administration on the expression of the 5-HT_{2A} receptor gene (HTR2A) and EGR1-3 genes. Methods: mRNA expression levels were analyzed in whole blood as a peripheral biomarker in 15 healthy subjects before and 1.5 and 24 h after the administration of LSD (100 µg) and placebo in a randomized, double-blind, placebo-controlled, cross-over study. Results: LSD did not alter the expression of the HTR2A or EGR1-3 genes 1.5 and 24 h after administration compared with placebo. Conclusion: No changes were observed in the gene expression of LSD's primary target receptor gene or genes that are implicated in its downstream effects. Remaining unclear is whether chronic LSD administration alters gene expression in humans.

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