Acute Effects of Lysergic Acid Diethylamide on Circulating Steroid Levels in Healthy Subjects

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Lysergic acid diethylamide (LSD) is a serotonin 5-hydroxytryptamine-2A (5-HT2A) receptor agonist that is used recreationally worldwide. Interest in LSD research in humans waned after the 1970s, although the use of LSD in psychiatric research and practice has recently gained increasing attention. LSD produces pronounced acute psychedelic effects, although its influence on plasma steroid levels over time has not yet been characterised in humans. The effects of LSD (200 μg) or placebo on plasma steroid levels were investigated in 16 healthy subjects using a randomised, double-blind, placebo-controlled, cross-over study design. Plasma concentration-time profiles were determined for 15 steroids using liquid-chromatography tandem mass-spectrometry. LSD increased plasma concentrations of the glucocorticoids cortisol, cortisone, corticosterone and 11-dehydrocorticosterone compared to placebo. The mean maximum concentration of LSD was reached at 1.7 h. Mean peak psychedelic effects were reached at 2.4 h, with significant alterations in mental state from 0.5 h to >10 h. Mean maximal concentrations of cortisol and corticosterone were reached at 2.5 h and 1.9 h, and significant elevations were observed 1.5-6 h and 1-3 h after drug administration, respectively. LSD also significantly increased plasma concentrations of the androgen dehydroepiandrosterone but not other androgens, progestogens or mineralocorticoids compared to placebo. A close relationship was found between plasma LSD concentrations and changes in plasma cortisol and corticosterone and the psychotropic response to LSD, and no clockwise hysteresis was observed. In conclusion, LSD produces significant acute effects on circulating steroids, especially glucocorticoids. LSD-induced changes in circulating glucocorticoids were associated with plasma LSD concentrations over time and showed no acute pharmacological tolerance.

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