Research and Reviews: Drug Delivery

Heritability of Substance use Disorders and Twin Studies

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Commentary

Received: 01-Jun-2022, Manuscript No. DD-22-56257;
Editor assigned: 02-Jun-2022, PreQC No. DD-22-56257(PQ);
Reviewed: 16-Jun-2022, QC No. DD-22-56257;
Revised: 23-Jun-2022, Manuscript No. DD-22-56257(R);
Published: 30-Jun-2022, DOI : 10.4172/resrevdrugdeliv.6.S1.001
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DESCRIPTION

Psychedelics are part of a larger category of drugs known as hallucinogens. These drugs alter normal brain activity and create shifts in consciousness and perception. These effects put users at risk for injuring themselves while under the drug's influence.

The Harvard Twin Study revealed that genetic influences accounted for only 26% of the risk for abuse of psychedelics. Not only is this a particularly low heritability estimate, but the data also indicated that 100% of the genetic risk of psychedelic abuse is attributed to the first category of genetic vulnerability the common genetic vulnerability for SUDs. Thus, psychedelic abuse appears to involve no drug-specific genetic risk factors. However, it is unclear how much can be concluded from these findings, because few studies have addressed the heritability of psychedelic use. Additional research is needed to confirm these findings.

Psychedelics are a collection of psychoactive compounds that act as agonists or partial agonists at the serotonin 2A receptor (5-HT2AR). Interest in psychedelics has grown in recent years given their marked potential as clinical therapeutics, a utility that was first speculated during the 1950s and 1960s and was freshly renewed in focus over the past decade following a period of relative research dormancy.

During mid-20th century, the scientific evaluation of psychedelics and the treatment of tens of thousands of patients with psychedelics was described in some of the leading medical and scientific journals. The basic science

of psychedelics drugs, including the remarkable potency of Lysergic Acid Diethylamide (LSD), added to the emerging biobehavioral model of brain function supplanting the existing dominance of psychodynamic models. At the same time, clinical applications were evaluated to include the treatment of addictive behaviors by psychedelics. However, human laboratory and clinical research on psychedelics largely came to a halt in the early 1970s. This was due to a combination of factors to include increasing marginalization owing to use of psychedelics outside clinical research settings, regulatory changes surrounding FDA scheduling, halted production of LSD and termination of access to the LSD drug master file by the pharmaceutical company Sandoz, and psychedelic's association with ongoing counter-culture movements. Although ethical and responsible human research occurred during this time by scientific pioneers like Abram Hoffer, Humphry Osmond, and Sidney Cohen, others who eventually abandoned the scientific approach were highlighted as rationales for wider restrictions and scientific prohibitions.

It was not until the 1990s that human subjects research began anew, first by a small number of investigators in the United States and Europe and now within an increasingly widescale network of laboratory science and clinical trials. In these decades since, researchers have established and closely followed safety guidelines for administering psychedelics that involve careful screening and preparation before drug administration sessions, close monitoring during these sessions, and follow-up care involving both clinically supportive discussion of session experiences and assessment for any adverse effects resulting from drug administration. Compared to the earlier era, modern psychedelic science has increasingly used novel methods and technological approaches including double-blind designs and neuroscience techniques (e.g., brain imaging). With these advances have come newly identified challenges in isolating the behavioral and therapeutic contributions of psychedelics and identifying the mechanisms of action in clinical practice.

The human behavioral pharmacology of psychedelics. We focus on three prototypic or “classic” (5-HT2AR agonist) psychedelics including psilocybin (a compound present in many species of mushrooms), LSD, and Dimethyltryptamine (DMT). First, we provide a brief overview of classic psychedelics, including naming conventions and drug classification. Second, we describe some of the special considerations and current challenges when conducting human behavioral pharmacology research with psychedelics. Human behavioral pharmacology research that has evaluated the subjective, physiological, and clinical effects of each compound. Finally, we provide a summative state of the field and key future directions.