DEPARTMENT OF HEALTH

# Lysergic Acid Diethylamide (LSD) Literature Overview

## Introduction

The health conditions in which LSD-assisted therapy may be efficacious identified in the initial search included anxiety (either with or without a life-threatening illness), alcohol use disorder, opioid use disorder, cluster headache, pain, and schizophrenia. Of these, only anxiety disorders and alcohol use disorders had a sufficient number of published randomized controlled trials (RCTs) to be able to evaluate the efficacy of LSD treatment as compared with standard treatments.

There was one RCT for opioid use disorder, a trial occurring in the 1960s and carried out in a prison population. There have been no trials since, and no meta-analyses that would allow us to compare the efficacy of this as a treatment against current treatments. There were no RCTs for cluster headache. There were a number of survey studies, but most were anonymous, retroactive, and include polydrug use, so the true extent of LSD as a treatment is unclear. There were no RCTs investigating LSD as a treatment for pain. There were non-RCTs carried out in the 1960s, which found that the analgesic effects of LSD were not long-lasting, presumably leading to this not being an avenue of further study. Finally, there were no RCTs for schizophrenia. This health condition was investigated in two non-RCTs in the 1960s. In fact, schizophrenia may be a contraindication for LSD; in some instances LSD-induced psychosis may be a drug-induced form of schizophrenia, and there may be a greater risk of a psychosis response to LSD in those with a genetic disposition for schizophrenia[1].

## Anxiety Disorders

In the search, two RCTs were identified[2,3]. Both explored the efficacy and safety of LSD-assisted psychotherapy in patients experiencing anxiety with life-threatening illnesses. One of these studies[3] also included participants with anxiety disorders, but without a life-threatening condition. Both studies were double-blind, placebo-controlled, phase II clinical trials. Each study consisted of two visits in which the drug was administered accompanied with psychotherapy, and a further five to six therapy visits without the drug. Anxiety was measured using the State-Trait Anxiety Inventory (STAI) in both studies, including the STAI-State (S) and STAI-T (Trait) subdivisions. Follow-ups were conducted regularly up to 12 months after treatment.

Between the two studies, a total of 49 participants completed treatment. Doses of LSD ranged from 20 micrograms (µg) (an active control dose) to 200 µg (the treatment dose). While there were methodological differences between the studies, ultimately both showed statistically significant reductions in anxiety following LSD-assisted psychotherapy. These results last as long as 16 weeks post-treatment[3], and may last at least 12 months after the conclusion of therapy[2]. Both studies also investigated secondary outcomes, including measures of depression, and both found concomitant decreases in depressive symptomology. Measures of quality of life increased.

While not included in the formal literature review, 10 additional non-RCTs from the 1960s and 1970s report data supporting the beneficial outcome of LSD-assisted therapy in the treatment of anxiety, particularly in those with life-threatening illnesses[4-13].

## Unpublished Data

Mind Medicine, Inc. (MindMed) is a biopharmaceutical company developing new treatments for brain health, researching both LSD and MDMA for a variety of health conditions. The company recently announced positive results of a completed phase IIb trial investigating LSD as a treatment for generalized anxiety disorder (GAD)[14]. They also announced that they have received Breakthrough Therapy Designation from the FDA to continue the research (through use of their proprietary compound MM120 (lysergide d-tartrate)). The results of this trial are not published in peer-review literature yet, but will be summarized here.

The trial was a randomized, double-blind, placebo-controlled 12 week trial. A total of 198 participants with GAD were enrolled into one of five groups: placebo, 200 µg, 100 µg, 50 µg, or 25 µg dose of MM120. Each participant received a single administration of MM120 or placebo, with no psychotherapy intervention. No concurrent use of medication for anxiety allowed by participants. This study did not use the same anxiety measurement tool as the above-mentioned RCTs[2,3], rather they used the Hamilton Anxiety Scale (HAM-A). One single dose of LSD (based on 100 µg results) resulted in statistically and clinically significant reductions in anxiety measurements out to week 12. This was true for comorbid depression scores as well. At the end of the study, 65% of participants showed a reduction in anxiety, and nearly 50% of the participants showed remission from the condition. A phase III trial is expected to begin at the end of 2024.

## Comparison of Efficacy, Anxiety Disorders

Anxiety disorders, with or without a life-threatening illness, are typically treated with psychotherapy, pharmacotherapy, or a combination of the two[15]. Because there have been only two RCTs, meta-analyses have not been published, and so we cannot directly compare the efficacy of LSD as a treatment for anxiety against current treatments. Imperfect comparisons using effect sizes from meta-analyses of psychotherapy and/or pharmacotherapy can be used in the meantime. Effect sizes are a statistical measure of the magnitude of differences between two populations. Effect sizes are typically considered small if they are 0.2 or less, medium if they are around 0.5, large if they are 0.8, very large if they are 1.2, and huge if they are 2.0 and above. Values can be negative, with the magnitude ranges being the same (i.e., the further away from 0, the greater the effect).

A meta-analysis investigating the effects of a range of psychotherapeutic interventions for generalized anxiety disorder found that the effect size of psychotherapy versus control groups was large (0.84)[16]. The effects on depression were also large (0.71). In this particular meta-analysis, the authors provided information on the outcomes of the anxiety on the same scales as used by Gasser et al.[2] and Holze et al.[3]. The effect of psychotherapy on STAI-State measurements was 0.73, and the effect on STAI-Trait measurements was 0.6416. Both of these

are considered medium or moderate effect sizes. In the above-mentioned RCTs, the first study found that the effect size of LSD on the State measure of anxiety was 1.2 and the effect size was 1.1 for the Trait measurement2. The second study found that the effect sizes were -0.75 and -0.87, respectively[3]. (The scores were negative due to the order of comparison.)

A separate meta-analysis compared psychotherapy and pharmacotherapies, and the combination of the two[17]. Note though that these results are not specific to the scale used by the two published studies on LSD. This meta-analysis found that the effect size for individual cognitive behavioral therapy (CBT), comparing the change between pre- and post-treatment against a control was 1.30. When statistically combined, all of the different types of evaluated psychotherapies (which included mindfulness, psychodynamic therapy, etc.) resulted in an effect size of 1.22. In investigating pharmacotherapies, the study found that the effect size of selective serotonin reuptake inhibitors (SSRIs) was 2.09, and benzodiazepines had an effect size of 2.15. The effect size for the combination of psychotherapies and pharmacotherapies was 2.12.

Another meta-analysis investigating both psychological and pharmacological outcomes in the treatment of generalized anxiety disorder was also evaluated[18]. This study focused on a different anxiety scale than reported by Gasser et al.[2] and Holze et al.[3]. Comparing psychotherapy against a control condition, the authors found a medium effect size of 0.76 immediately following treatment, which dropped to a low effect size of 0.27 at follow-up time periods. Medication alone was found to have an effect size of 0.39 post-treatment, with no follow-up measurements.

Overall, the effect sizes at the conclusion of the trials reported by Gasser et al. (1.2, 1.1)[2] , Holze et al. (-0.75, -0.87)[3], and MindMed (0.81)[14] appear to fall within the range of reported effect size measurements for psychotherapy alone, pharmacotherapy alone, or a combination of the two, suggesting that the efficacy of LSD as a treatment for anxiety may be comparable to current standard treatments. However, this can only be used as an approximation, since presently we are comparing three individual studies, with effect sizes measured at different time points, against the composite of many studies.

## Alcohol Use Disorder

Five RCTs investigating the efficacy of LSD in the treatment of alcohol use disorder (AUD) were analyzed, all of which were conducted in the late 1960s into the early 1970s[19-23]. In total, these studies included a total of 550 participants, 327 of whom were exposed to an experimental dose of LSD. The doses of LSD employed in these studies ranged anywhere from 300 µg to 800 µg, with one study dosing instead 3 µg of the drug per kilogram of body weight.

The methodology varied widely between the studies. Most, but not all, of these studies attempted some sort of blinding. Most included a therapeutic component in at least one group that received LSD, but a corresponding therapeutic component was not always employed equally in the no-drug condition. Most, but not all, employed a type of control group. These control groups were not always treated the same as the LSD groups, however. Each study

followed-up with patients after treatment, ranging from one month to twelve months post-treatment.

Most of these studies found that all groups, regardless of if they received LSD or not, showed at least acute improvements when comparing between pre-treatment and post-treatment time points. However, in the majority of studies, LSD groups did not tend to show substantial or significant differences when compared directly against control groups. Ultimately, the conclusions drawn by each of these studies indicated that treatment with LSD provided no meaningful benefit over other therapeutic modalities in the treatment of alcohol use disorder.

Few adverse effects were reported in these RCTs, but whether that was through lack of collection or true lack of occurrence is unclear. Those that were reported included occasional moderate agitation, vomiting, and mild confusion. In one study, patients were given an antipsychotic medication "as needed," but neither what necessitated that use nor the number of patients who needed it were reported. One serious adverse event was reported, wherein a participant experienced a grand mal seizure without injury (this participant had a history of seizures)[20]. It should be noted that the overwhelming majority of participants in these studies were male.

## Comparison of Efficacy, Alcohol Use Disorder

Alcohol use disorder is typically treated through the use of pharmacotherapy and/or psychotherapy. Three commonly-prescribed standard medications include naltrexone, acamprosate, and disulfiram; psychotherapy is typically CBT[24]. One meta-analysis discussing these same RCTs as above was analyzed and found that, when combined, the data indicated that LSD treatment resulted in a statistically significant beneficial effect on symptoms of alcohol use disorder[25]. This paper also provided a direct comparison of LSD against current treatments by calculating the pooled benefit difference between each treatment and its control groups (instead of through effect sizes). The benefit difference is defined as the percentage of improved patients in the treatment group (in this case the drug) minus the percentage of improved patients in the control group. A larger number indicates a greater difference between drug and control outcomes. When investigating the improvement on alcohol misuse, the benefit difference of LSD was 16%, naltrexone was 11%, and acamprosate was 1%. They were unable to calculate this number for disulfiram. The authors also investigated each treatment on maintained abstinence from alcohol and found the benefit difference of LSD was 15%, naltrexone was 3%, acamprosate was 11%, and disulfiram was 11%. The meta-analysis thus concluded that LSD treatment was comparable to the effectiveness of daily naltrexone, acamprosate, or disulfiram in the treatment of AUD. The authors of this meta-analysis did not compare LSD against psychotherapeutic treatments.

Overall, while the original RCTs concluded that the treatment was not any more beneficial than any other treatment, these studies were small, and each alone did not hold great statistical power. When combined in a meta-analysis, it appears as though LSD treatment, with or without a therapeutic component, may be both efficacious in treating alcohol use disorder and comparable to current standard pharmacotherapeutic treatments.

# Overall Risks of LSD as a Treatment

## Risks in Clinical Trials

In general, the clinically-reported adverse effects of LSD were mild-to-moderate and transient. From the studies investigating anxiety, common reports were fatigue, headache, nausea, transient anxiety, illusions, feeling abnormal, and feeling cold[2,3,14]. Most of these effects resolved when the drug treatment wore off. One patient was treated for anxiety with delusions, and another patient with a comorbid diagnosis of major depressive disorder reported transient feelings of depression, including suicidal thoughts (but no increase in suicidality) 8 weeks after the last LSD treatment[3]. From the trials investigating alcohol use disorder, one individual experienced a seizure[20]. However, this patient had a history of seizures which may have been associated with alcohol withdrawal.

Physiologically, LSD was shown to significantly increase blood pressure and heart rate during treatment as compared to the control group[3]. This is consistent with clinical trials investigating LSD in healthy individuals[26,27], and special consideration regarding the action of these types of psychedelic drugs on the heart is included in the guidance document for clinical investigation of psychedelics developed by the Food and Drug Administration[28]. Other adverse effects reported in these trials involving healthy individuals have included headaches (including migraine), low mood, restlessness, vivid dreams, and involuntary movement of the lower extremities. These effects appear to be dose-dependent, with increased doses increasing subjective, physiological, and adverse effects[29].

Some participants in the anxiety-focused RCTs, and investigations of healthy participants, reported flashbacks lasting anywhere between a day to a week after treatment[30]. "Flashback" is a colloquial term related to hallucinogen-persisting perception disorder. However, a diagnosis of this disorder requires the flashbacks to cause significant distress or impairment. No participant in any trial reported flashbacks to be distressing. This diagnosis is reported much more commonly after LSD use outside of the clinic.

## Abuse Potential and Toxicity

Though listed as a Schedule I drug by the Drug Enforcement Agency, research indicates that the abuse potential of LSD is low. Exposure to the drug does not typically lead to compulsive drug-seeking behavior, nor does use result in dependence, though there may be instances of tolerance[31].

One outstanding concept in the evaluation of risks of psychedelic drugs, and particularly LSD, is the notion of the "bad trip," which is a mentally or physically horrifying drug-taking experience. No such instances were reported in the clinical literature evaluated here. It has been reported that these sorts of extremely negative experiences tend to happen more frequently in response to the recreational consumption of drugs, in settings that are uncontrolled, and/or by those who are inexperienced with psychedelics[32].

Most serious adverse reactions to LSD occur when the drug is taken outside of a clinical setting, and in doses that are much larger than those used in a clinical setting. Overdose by LSD is rare, but can occur following consumption outside of a controlled environment. The estimated lethal oral dose for a human may sit somewhere around 100 milligrams, which is significantly higher than clinical doses. Presently there are only two documented cases where LSD presumably directly led to a fatality. In both of these cases, the post-mortem analyses indicated that each individual had ingested incredibly large quantities of LSD[31]. Some users of LSD outside of a clinical environment have reported impairment in color vision[33], and there is at least one report of an individual with co-morbid migraine who experienced transient cortical blindness following LSD exposure[34].

Finally, there have been only a few observational reports exploring the reproductive consequences of LSD. It is important to note that the RCTs evaluated in this report each explicitly excluded individuals who were pregnant. Case reports indicate birth defects in infants born to mothers who have taken LSD, particularly during the first trimester. This includes ocular malformations, limb defects, and an elevated rate of spontaneous abortions[35,36].

### Drug-Drug Interactions

Due to the current legal standing of the LSD, formal tests of drug interactions are scarce. Most understanding about drug-drug interactions comes from case reports, and as such are anecdotal in nature, though some systematic reviews exist[37]. LSD binds to certain serotonin and dopamine receptors[38], and is metabolized by a number of cytochrome P450 (CYP) enzymes[39]; therefore any drugs that interact with these will likely result in an interaction with LSD. Antipsychotics, certain antidepressants (e.g., SSRIs, MAOIs), and other agonists of serotonin receptors, including those that inhibit CYP activity, typically result in a dampening or lessening of LSD effects—this includes subjective and physiological effects[29,40-45].

On the other hand, tricyclic antidepressants increase the effects of LSD. This enhancement also may occur following chronic lithium use[42]. Furthermore, there have been reports of seizures in response to chronic lithium and concurrent LSD use[46]. Finally, reserpine has been shown to increase and prolong the (negative) effects of LSD, including hallucinations, as well as the development of tremors[47,48].

## Overall Risks of Current Treatments

While generally safe, CBT can result in negative reactions, or side effects, as well as some adverse or unwanted events. Additionally, inadequate treatment may result in unintended consequences. A systematic survey of therapists reported at least one side effect from treatment. Of these, 27% of patients reported negative well-being or distress. In total, 21% of patients suffered from severe side effects of the treatment (e.g., suicidality, breakups, feeling of shame/guilt, intensive crying, etc.). These effects were considered persistent in 5% of the individuals[50].

Pharmacotherapy, while frequently used in the treatment of anxiety disorders, also can result in a number of adverse or side effects. Particularly with SSRIs and SNRIs, there may be an

increase in anxiety symptoms or jitteriness within the first two weeks of treatment--the latency for onset of anxiolytic effects is often two to four weeks. Further adverse effects reported include headache, fatigue, insomnia, nausea, dizziness, changes in appetite, sexual dysfunction, gastrointestinal effects, and others[51]. While approved and often prescribed for anxiety disorders, benzodiazepines should not be used for long-term treatment. Though the onset of anxiolytic action is rapid and typically does not result in the same sorts of adverse effects (e.g., jitteriness, insomnia), use of the drug may be associated with central nervous system depression, fatigue, dizziness, increased reaction time, and impaired cognitive functions (particularly in elderly patients). Long-term treatment may also result in dependency[51].

Pharmacotherapy in the treatment of alcohol use disorder also carries some risk of adverse effects. Dizziness and headaches are commonly-reported adverse effects in response to naltrexone[52-54]. Gastrointestinal distress, including diarrhea, nausea, vomiting, can occur in response to both naltrexone and acamprosate[52-56]. Nausea and vomiting tend to be more common with naltrexone, while diarrhea appears to be more common with acamprosate[54-56]. Acamprosate may also result in anxiety[53]. Adverse effects of disulfiram include headache, fatigue, sleepiness, and anxiety[57]. Furthermore, disulfiram is typically not suggested for use in individuals with liver or heart diseases, or in those with certain psychiatric disorders[58].

# References


1. Vardy, M. M., & Kay, S. R. (1983). LSD psychosis or LSD-induced schizophrenia?: A multimethod inquiry. Archives of General Psychiatry, 40(8), 877-883.
2. Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., & Brenneisen, R. (2014). Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. The Journal of Nervous and Mental Disease, 202(7), 513.
3. Holze, F., Gasser, P., Müller, F., Dolder, P. C., & Liechti, M. E. (2023). Lysergic acid diethylamide–assisted therapy in patients with anxiety with and without a life-threatening illness: a randomized, double-blind, placebo-controlled phase II study. Biological Psychiatry, 93(3), 215-223.
4. Kast, E. C., & Collins, V. J. (1964). Study of lysergic acid diethylamide as an analgesic agent. Anesthesia & Analgesia, 43(3), 285-291.
5. Kast E. LSD and the dying patient. (1966) Chic Med Sch Q. 1966 Summer;26(2):80-7. PMID: 4163076.
6. Kast, E. (1967). Attenuation of anticipation: a therapeutic use of lysergic acid diethylamide. Psychiatric Quarterly, 41(4), 646-657.
7. Pahnke, W. N. (1969). The psychedelic mystical experience in the human encounter with death. Harvard Theological Review, 62(1), 1-21.
8. Pahnke, W. N., Kurland, A. A., Goodman, L. E., & Richards, W. A. (1969). LSD-assisted psychotherapy with terminal cancer patients. Current psychiatric therapies, 9, 144-152.

9. Pahnke, W. N., Kurland, A. A., Unger, S., Savage, C., Wolf, S., & Goodman, L. E. (1970). Psychedelic therapy (utilizing LSD) with cancer patients. Journal of Psychedelic Drugs, 3(1), 63-75.
10. Kurland, A. A., Grof, S., Pahnke, W. N., & Goodman, L. E. (1972). Psychedelic drug assisted psychotherapy in patients with terminal cancer. Journal of Thanatology.
11. Richards, W., Grof, S., Goodman, L., & Kurland, A. (1972). LSD-assisted psychotherapy and the human encounter with death. The Journal of Transpersonal Psychology, 4(2), 121.
12. Grof, S., Goodman, L. E., Richards, W. A., & Kurland, A. A. (1973). LSD-assisted psychotherapy in patients with terminal cancer. International pharmacopsychiatry, 8(3), 129-144.
13. Kurland, A. A. (1985). LSD in the supportive care of the terminally ill cancer patient. Journal of psychoactive drugs, 17(4), 279-290.
14. MindMed receives FDA breakthrough therapy designation and announces positive 12-week durability data from phase 2b study of MM120 for generalized anxiety disorder. (2024, March 7). Mind Medicine (MindMed) Inc. https://ir.mindmed.co/news-events/press-releases/detail/137/mindmed-receives-fda-breakthrough-therapy-designation-and-announces-positive-12-week-durability-data-from-phase-2b-study-of-mm120-for-generalized-anxiety-disorder
15. National Institute of Mental Health (NIMH). (2023). Anxiety Disorders. Retrieved March 7, 2024, from https://www.nimh.nih.gov/health/topics/anxiety-disorders#part_2225.
16. Cuijpers, P., Sijbrandij, M., Koole, S., Huibers, M., Berking, M., & Andersson, G. (2014). Psychological treatment of generalized anxiety disorder: a meta-analysis. Clinical psychology review, 34(2), 130-140.
17. Bandelow, B., Reitt, M., Röver, C., Michaelis, S., Görlich, Y., & Wedekind, D. (2015). Efficacy of treatments for anxiety disorders: a meta-analysis. International clinical psychopharmacology, 30(4), 183-192.
18. Hidalgo, R. B., Tupler, L. A., & Davidson, J. R. (2007). An effect-size analysis of pharmacologic treatments for generalized anxiety disorder. Journal of Psychopharmacology, 21(8), 864-872.
19. Smart, R. G., Storm, T., Baker, E. F., & Solursh, L. (1966). A controlled study of lysergide in the treatment of alcoholism. I. The effects on drinking behavior. Quarterly journal of studies on alcohol, 27(3), 469-482.
20. Hollister, L. E., Shelton, J., & Krieger, G. (1969). A controlled comparison of lysergic acid diethylamide (LSD) and dextroamphetamine in alcoholics. American Journal of Psychiatry, 125(10), 1352-1357.
21. Ludwig, A., Levine, J., Stark, L., & Lazar, R. (1969). A clinical study of LSD treatment in alcoholism. American Journal of Psychiatry, 126(1), 59-69.

22. Bowen, W. T., Soskin, R. A., & Chotlos, J. W. (1970). Lysergic acid diethylamide as a variable in the hospital treatment of alcoholism: a follow-up study. The Journal of nervous and mental disease, 150(2), 111-118.

23. Johnson, F. G. (1970). A comparison of short-term treatment effects of intravenous sodium amytal-methedrine and LSD in the alcoholic. Canadian Psychiatric Association Journal, 15(5), 493-497.

24. National Institute on Alcohol Abuse and Alcoholism (NIAAA). (2023). Treatment for Alcohol Problems: Finding and Getting Help. NIH Publication No: 21-AA-7974. Retrieved March 7, 2024, from https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/treatment-alcohol-problems-finding-and-getting-help#pub-toc1.

25. Krebs, T. S., & Johansen, P. Ø. (2012). Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. Journal of Psychopharmacology, 26(7), 994-1002.

26. Schmid, Y., Enzler, F., Gasser, P., Grouzmann, E., Preller, K. H., Vollenweider, F. X., ... & Liechti, M. E. (2015). Acute effects of lysergic acid diethylamide in healthy subjects. Biological psychiatry, 78(8), 544-553.

27. Holze, F., Caluori, T. V., Vizeli, P., & Liechti, M. E. (2021a). Safety pharmacology of acute LSD administration in healthy subjects. Psychopharmacology, 1-13.

28. Food and Drug Administration. (2023). Psychedelic drugs: Considerations for clinical investigations guidance for industry (Draft guidance). Docket: FDA-2023.

29. Holze, F., Vizeli, P., Ley, L., Müller, F., Dolder, P., Stocker, M., ... & Liechti, M. E. (2021b). Acute dose-dependent effects of lysergic acid diethylamide in a double-blind placebo-controlled study in healthy subjects. Neuropsychopharmacology, 46(3), 537-544.

30. Holze, F., Ley, L., Müller, F., Becker, A. M., Straumann, I., Vizeli, P., ... & Liechti, M. E. (2022). Direct comparison of the acute effects of lysergic acid diethylamide and psilocybin in a double-blind placebo-controlled study in healthy subjects. Neuropsychopharmacology, 47(6), 1180-1187.

31. Nichols, D. E., & Grob, C. S. (2018). Is LSD toxic?. Forensic science international, 284, 141-145.

32. Ona, G. (2018). Inside bad trips: Exploring extra-pharmacological factors. Journal of psychedelic studies, 2(1), 53-60.

33. Abraham, H. D. (1982). A chronic impairment of colour vision in users of LSD. The British Journal of Psychiatry, 140(5), 518-520.

34. Bernhard, M. K., & Ulrich, K. (2009). Recurrent cortical blindness after LSD-intake. Fortschritte der Neurologie-psychiatrie, 77(2), 102-104.

35. Dishotsky, N. I., Loughman, W. D., Mogar, R. E., & Lipscomb, W. R. (1971). LSD and genetic damage: Is LSD chromosome damaging, carcinogenic, mutagenic, or teratogenic?. Science, 172(3982), 431-440.

36. Chan, C. C., Fishman, M., & Egbert, P. R. (1978). Multiple ocular anomalies associated with maternal LSD ingestion. Archives of Ophthalmology, 96(2), 282-284.

37. Halman, A., Kong, G., Sarris, J., & Perkins, D. (2024). Drug–drug interactions involving classic psychedelics: A systematic review. Journal of psychopharmacology, 38(1), 3-18.

38. Halberstadt AL & Geyer MA (2011) Multiple receptors contribute to the behavioral effects of indoleamine hallucinogens. Neuropharmacology 61(3): 364–381

39. Wagmann L, Richter LHJ, Kehl T, et al. (2019) In vitro metabolic fate of nine LSD-based new psychoactive substances and their analytical detectability in different urinary screening procedures. Anal Bioanal Chem 411: 4751–4763.

40. Resnick O, Krus DM & Raskin M (1964) LSD-25 action in normal subjects treated with a monoamine oxidase inhibitor. Life Sci 3: 1207–1214.

41. Grof S & Dytrych Z (1965) Blocking of LSD reaction by premedication with Niamid. Act Nerv Super 7: 306.

42. Bonson KR & Murphy DL (1996) Alterations in responses to LSD in humans associated with chronic administration of tricyclic antidepressants, monoamine oxidase inhibitors or lithium. Behav Brain Res 73: 229–233.

43. Bonson KR, Buckholtz JW and Murphy DL (1996) Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans. Neuropsychopharmacol: Off Publ Am Coll Neuropsychopharmacol 14: 425–436.

44. Vizeli P, Straumann I, Holze F, et al. (2021) Genetic influence of CYP2D6 on pharmacokinetics and acute subjective effects of LSD in a pooled analysis. Sci Rep 11: 10851.

45. Straumann I, Ley L, Holze F, et al. (2023) Acute effects of MDMA and LSD co-administration in a double-blind placebo-controlled study in healthy participants. Neuropsychopharmacol: Off Publ Am Coll Neuropsychopharmacol 48: 1840–1840.

46. Nayak SM, Gukasyan N, Barrett FS, et al. (2021) Classic psychedelic coadministration with lithium, but not lamotrigine, is associated with seizures: An analysis of online psychedelic experience reports. Pharmacopsychiatry 54: 240–245.

47. Isbell H & Logan CR (1957) Studies on the diethylamide of lysergic acid (LSD-25). II. Effects of chlorpromazine, azacyclonol, and reserpine on the intensity of the LSD-reaction. A.M.A. Arch Neurol Psychiatry 77: 350–35

48. Freedman DX (1963) Psychotomimetic drugs and brain biogenic amines. Am J Psychiatry 119: 843–850

49. Resnick O, Krus DM & Raskin M (1965) Accentuation of the psychological effects of LSD-25 in normal subjects treated with reserpine. Life Sci 4: 1433–1437.

50. Schermuly-Haupt, M. L., Linden, M., & Rush, A. J. (2018). Unwanted events and side effects in cognitive behavior therapy. Cognitive Therapy and Research, 42, 219-229.

51. Bandelow, B., Michaelis, S., & Wedekind, D. (2017). Treatment of anxiety disorders. Dialogues in clinical neuroscience, 19(2), 93-107.

52. Carmen, B., Angeles, M., Ana, M., & María, A. J. (2004). Efficacy and safety of naltrexone and acamprosate in the treatment of alcohol dependence: a systematic review. Addiction, 99(7), 811-828.

53. Jonas, D. E., Amick, H. R., Feltner, C., Bobashev, G., Thomas, K., Wines, R., ... & Garbutt, J. C. (2014). Pharmacotherapy for adults with alcohol use disorders in outpatient settings: a systematic review and meta-analysis. Jama, 311(18), 1889-1900.

54. McPheeters, M., O'Connor, E. A., Riley, S., Kennedy, S. M., Voisin, C., Kuznacic, K., ... & Jonas, D. E. (2023). Pharmacotherapy for Alcohol Use Disorder: A Systematic Review and Meta-Analysis. JAMA, 330(17), 1653-1665.

55. Rösner S, Hackl-Herrwerth A, Leucht S, et al. (2010b) Opioid antagonists for alcohol dependence. Cochrane Database Syst Rev 12: CD001867.

56. Rösner S, Hackl-Herrwerth A, Leucht S, et al. (2010a) Acamprosate for alcohol dependence. Cochrane Database Syst Rev 9: CD004332.

57. Malcolm, R., Olive, M. F., & Lechner, W. (2008). The safety of disulfiram for the treatment of alcohol and cocaine dependence in randomized clinical trials: guidance for clinical practice. Expert opinion on drug safety, 7(4), 459-472.

58. Skinner, M. D., Lahmek, P., Pham, H., & Aubin, H. J. (2014). Disulfiram efficacy in the treatment of alcohol dependence: a meta-analysis. PloS one, 9(2), e87366.