MIND FOUNDATION

Hot topics in psychedelic research

DATE PUBLISHED

25 September 2020



> When combing through new research on psychedelics, one trend sticks out immediately: *expansion.* More researchers are studying psychedelics than ever before.1 Not only are there more scientists, but they're in more places, studying more substances, and testing psychedelic treatments on more disorders. This is the bleeding edge of psychedelic science, and it's growing every day.

Testing The Boundaries Of Psychedelic Medicine

Psychedelics are winning scientists and clinicians over because of their potential for improving mental health.2 Most research these days is done with psilocybin, with some centers also focusing on LSD and other psychedelics, as well as MDMA for the treatment of PTSD. Psilocybin in particular is exciting because of its favorable safety profile and capacity to improve symptoms in *multiple disorders.*3 Not that this property is unique to psychedelics: SSRIs, for example, are used to treat both depression and anxiety.4 But psychedelics seem to have an unusually broad range of uses. Scientists want to know just how broad it really is.

So far, initial evidence from clinical trials supports psychedelic-assisted therapy for mood disorders, PTSD, and alcohol and nicotine dependence.5,6 Scientists are continuously building on this research, their sights set on getting the regulatory green light for psychedelic therapy in the next five years – if further trials confirm its efficacy. Worldwide, eighteen Phase 2 and 3 clinical trials for these diagnoses are currently ongoing, with several more in the works. The MIND Foundation, in collaboration with Charité Universitätsmedizin Berlin and the Central Institute for Mental Health Mannheim, will also conduct a large study on psilocybin therapy for depression beginning next year.

Meanwhile, research is expanding to other mental health conditions. At its Center for Psychedelic & Consciousness Research, Johns Hopkins University has expanded its studies with psilocybin to include eating disorders. Imperial College London, also boasting a Centre for Psychedelic Research, plans to do the same.

Beyond that, research teams at Yale and the University of Arizona are testing whether psilocybin is effective against obsessive-compulsive disorder.

Scientists also hope that psychedelics might help people overpower addictions beyond alcohol and nicotine. The University of Alabama is finishing up a study investigating psilocybin for cocaine addiction, and the University of Wisconsin will soon do the same for opioid use disorder.

Clinical research is also taking some more surprising turns. One notable avenue is the treatment of cluster headaches and migraines, with clinical trials running at Yale, in Basel, and in Copenhagen. The Beckley Foundation has also sponsored a recent trial in which a low dose of LSD decreased pain perception.29 And researchers at Imperial College London have proposed using psilocybin as a last resort for chronic coma patients, although their theory has yet to be tested.7

How To Change Your Ability To Change

Beyond knowing that psychedelics may treat certain disorders, it's also important to know *why.*

Researchers have recently examined whether specific aspects of a trip make psychedelic therapy more likely to work. One crucial phenomenon appears to be the *mystical experience* (now an official scientific term!). Mystical experiences are characterized by feelings of ecstasy, oneness and unity, and transcendence of time and space. They are also known for being both saturated with meaning and difficult to put into words.8 Recent studies suggest that these kinds of experiences are important – perhaps even essential – for fruitful psychedelic therapy.9

At the physical level, psychedelics may promote *neuroplasticity* – that is, the brain's ability to form new connections and restructure itself.10 In rats, most psychedelics promote several components of neuroplasticity in the pre-frontal cortex, and they're more potent and quicker potent at it than nearly any other substance.11 In humans, scientists think augmented neuroplasticity may explain psychedelics' long-term effects, and they're busy trying to verify it.12,13 (If this sounds interesting, check out our blog post on neuroplasticity.)

Psychedelics may also work by counteracting inflammation in the brain, which is out of control in certain psychiatric disorders.14 According to Dr. Stephen Ross at NYU, reducing inflammation could also have uses beyond improving mental health. Drugs which enhance neuroplasticity and dampen neuroinflammation could be uniquely suited to treat Alzheimer's disease and other neurodegenerative disorders. There is no evidence for this right now, but since Alzheimer's can't yet be cured or slowed down, it may be worth a try. Scientists at Johns Hopkins are conducting a study on psilocybin treatment for depression in Alzheimer's disease, with plans to also measure changes in cognitive ability. And researchers at Yale have recently shown that LSD microdoses of up to 20µg are safe for older adults, opening the door for further clinical trials.14

Less Is More?

Some researchers wonder whether microdosing, or the use of sub-hallucinogenic doses of psychedelic substances, could have benefits too. Anecdotal reports on its effects abound, and science can help separate truth from hype. The newly minted Canadian Centre for Psychedelic Science studies microdoses of psilocybin, and other teams across three continents are researching microdosing in both patients and healthy subjects.

Due to regulatory limitations, much of this work has been done by surveying people who microdose privately. Although this study design has the advantage of taking place in a natural setting, its drawbacks loom large: True control groups and blinding are rare, many reports are retrospective and of questionable accuracy, and the study samples are likely skewed toward those with pro-psychedelic views. Nevertheless, researchers are

doing their best. Several recent publications have explored self-reported effects of microdosing, finding both positive and unwanted outcomes.15–17 Another of these studies is taking place at Imperial College London right now.

Placebo-controlled trials with microdosing have also sprung up in the literature. A research team in Chicago administered microdoses of LSD to healthy volunteers, and like the survey studies, they found both positive and negative effects (as well as a big dollop of the placebo effect).18 Low doses of psilocybin are also being investigated for their ability to treat depression and migraines, since high doses may not always be feasible or desirable for patients. And a study on microdosing LSD with healthy subjects has just finished data collection , with another beginning in New Zealand. Some researchers hope microdosing will be an alternative to antidepressantsfor patients who experience unwanted side effects, or no effects at all. Others even hope for a safe way to enhance mood and cognitive performance in healthy subjects. But only time – and data – will tell.

The Dmt Entourage

DMT (N, N-dimethyltryptamine) has not been forgotten in the psychedelic renaissance, and its unique properties may earn it a niche in psychedelic therapy. DMT has a short duration of action which can be controlled intravenously, and unlike LSD and psilocybin, it doesn't induce tolerance.19 Researchers in London have been studying DMT's effects on brain activity using EEG,20 while scientists in Basel are conducting a clinical safety trial. DMT also has the distinction of being the only psychedelic substance found to be present naturally in a mammalian brain, and we are closer than ever to figuring out what it's doing there.4,5

Research has also picked up on ayahuasca, the traditional Amazonian brew containing DMT. Much of ayahuasca research comes from Brazil, where researchers are testing its effects on mental health and brain functioning.21 Meanwhile, researchers in Switzerland are developing an ayahuasca pill. A synthetic pill would standardize the doses used in studies and could also temper some of ayahuasca's unpleasant side effects, as well as protect Amazonian plants from over-harvesting.

DMT's close cousin 5-MeO-DMT, traditionally obtained by milking live toads, has also appeared in the literature. Researchers from Maastricht University recently characterized 5-MeO-DMT's effects on various measures of well-being,22 while a team at Johns Hopkins found that it might reduce symptoms of depression and anxiety.23 Similar to what is happening with ayahuasca, scientists are beginning to prefer synthetic sources of 5-MeO-DMT, in this case to avoid bothering any innocent toads.

Windows On The Mind

Participants in psychedelic studies these days often end up in an MRI machine or wearing an EEG cap, allowing researchers to measure their brain activity while they trip. Using fMRI, one fascinating study from Maastricht University managed to capture which areas of the brain may cause the experience of ego dissolution.24 They're currently using neuroimaging and behavioral methods to examine how psilocybin affects creative thinking, social cognition, and emotion.

Over in Switzerland, researchers have made enormous progress in identifying the receptors necessary for psychedelic effects.25 They are investigating how psychedelics affect brain activity, and recently characterized psilocybin's effects on specific brain regions.26 In another line of research, scientists in Zürich and elsewhere are interested in the synergy between psychedelics and mindfulness meditation.27

These types of studies have allowed neuroscientists to develop theories to explain psychedelics' peculiar effects. One of these is the entropic brain theory, developed by Dr. Carhart-Harris and his team in London.28

According to entropic brain theory, consciousness exists on a continuum between highly ordered and highly chaotic brain activity. While the brain's activity is relatively orderly during normal consciousness, psychedelics push it into a more chaotic state. Carhart-Harris and his fellow scientists continue to test this theory with MRI and EEG experiments (Read more on the entropic brain theory in this blog post).

More To Explore

Psychedelic research is exploding in new and exciting directions – we are now at a point where fresh studies are published every single week. And every day, scientists all over the world are exploring different psychedelic substances, their effects on the brain, and how they might help improve mental health.

Summarizing the recent wave of science is a bit like trying to fit the ocean in a teacup. You can also check out the projects the MIND Foundation is working on right now.

References:

1. Doblin RE, Christiansen M, Jerome L, Burge B. The Past and Future of Psychedelic Science: An Introduction to This Issue. Journal of Psychoactive Drugs [Internet]. 2019;51(2):93–7. Available from:- https://doi.org/10.1080/02791072.2019.1606472
2. Johnson MW, Richards WA, Griffiths RR. Human hallucinogen research: Guidelines for safety. Journal of Psychopharmacology. 2008;22(6):603–20.
3. Nichols DE, Johnson MW, Nichols CD. Psychedelics as Medicines: An Emerging New Paradigm. Clinical Pharmacology and Therapeutics. 2017;101(2):209–19.
4. Lochmann D, Richardson T. Selective Serotonin Reuptake Inhibitors. In: Handbook of Experimental Pharmacology. Springer New York LLC; 2019. p. 135–44.
5. dos Santos RG, Hallak JEC. Therapeutic use of serotoninergic hallucinogens: A review of the evidence and of the biological and psychological mechanisms. Neuroscience and Biobehavioral Reviews [Internet]. 2020;108(October 2019):423–34. Available from:https://doi.org/10.1016/j.neubiorev.2019.12.001
6. Mithoefer MC, Feduccia AA, Jerome L, Mithoefer A, Wagner M, Walsh Z, et al. MDMA-assisted psychotherapy for treatment of PTSD: study design and rationale for phase 3 trials based on pooled analysis of six phase 2 randomized controlled trials. Psychopharmacology. 2019;236(9):2735–45.
7. Scott G, Carhart-Harris RL. Psychedelics as a treatment for disorders of consciousness. Neuroscience of Consciousness. 2019;
8. Johnson MW, Hendricks PS, Barrett FS, Griffiths RR. Classic psychedelics: An integrative review of epidemiology, therapeutics, mystical experience, and brain network function. Vol. 197, Pharmacology and Therapeutics. Elsevier Inc.; 2019. p. 83–102.
9. Roseman L, Nutt DJ, Carhart-Harris RL. Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. Frontiers in Pharmacology. 2018;8(JAN).
10. Kraus C, Castrén E, Kasper S, Lanzenberger R. Serotonin and neuroplasticity – Links between molecular, functional and structural pathophysiology in depression. Neuroscience and Biobehavioral Reviews [Internet]. 2017;77:317–26. Available from:http://dx.doi.org/10.1016/j.neubiorev.2017.03.007
11. Ly C, Greb AC, Cameron LP, Wong JM, Barragan E v., Wilson PC, et al. Psychedelics Promote Structural and Functional Neural Plasticity. Cell Reports [Internet]. 2018;23(11):3170–82. Available from:- https://doi.org/10.1016/j.celrep.2018.05.022
12. Hasler G. Toward specific ways to combine ketamine and psychotherapy in treating depression. CNS Spectrums. 2020;25(3):445–7.

13. de Almeida RN, Galvão AC de M, da Silva FS, Silva EA dos S, Palhano-Fontes F, Maia-de-Oliveira JP, et al. Modulation of serum brain-derived neurotrophic factor by a single dose of ayahuasca: Observation from a randomized controlled trial. Frontiers in Psychology. 2019;10(JUN).
14. Flanagan TW, Nichols CD. Psychedelics as anti-inflammatory agents. International Review of Psychiatry [Internet]. 2018;30(4):363–75. Available from:https://doi.org/10.1080/09540261.2018.1481827
15. Lea T, Amada N, Jungaberle H. Psychedelic Microdosing: A Subreddit Analysis. Journal of Psychoactive Drugs [Internet]. 2020;52(2):101–12. Available from:https://doi.org/10.1080/02791072.2019.1683260
16. Polito V, Stevenson RJ. A systematic study of microdosing psychedelics. PLoS ONE [Internet]. 2019;14(2):1–26. Available from:http://dx.doi.org/10.1371/journal.pone.0211023
17. Anderson T, Petranker R, Rosenbaum D, Weissman CR, Dinh-Williams LA, Hui K, et al. Microdosing psychedelics: personality, mental health, and creativity differences in microdosers. Psychopharmacology. 2019;236(2):731–40.
18. Bershad AK, Schepers ST, Bremmer MP, Lee R, de Wit H. Acute Subjective and Behavioral Effects of Microdoses of Lysergic Acid Diethylamide in Healthy Human Volunteers. Biological Psychiatry [Internet]. 2019;86(10):792–800. Available from:https://doi.org/10.1016/j.biopsych.2019.05.019
19. Strassman RJ, Qualls CR, Berg LM. Differential tolerance to biological and subjective effects of four closely spaced doses of N,N-Dimethyltryptamine in humans. Biological Psychiatry. 1996;39(9):784–95.
20. Timmermann C, Roseman L, Schartner M, Milliere R, Williams LTJ, Erritzoe D, et al. Neural correlates of the DMT experience assessed with multivariate EEG. Scientific Reports [Internet]. 2019;9(1):1–13. Available from:http://dx.doi.org/10.1038/s41598-019-51974-4
21. Jiménez-Garrido DF, Gómez-Sousa M, Ona G, dos Santos RG, Hallak JEC, Alcázar-Córcoles MÁ, et al. Effects of ayahuasca on mental health and quality of life in naïve users: A longitudinal and cross-sectional study combination. Scientific Reports. 2020 Dec 1;10(1).
22. Uthaug M v, Lancelotta R, Oorsouw K van, Kuypers KPC, Mason N, Rak J, et al. (200) A single inhalation of vapor from dried toad secretion containing 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) in a naturalistic setting is related to sustained enhancement of satisfact.pdf. 2019;
23. Alan K. Davis, PhDa, Sara So, MSb, Rafael Lancelotta, MSc, Joseph P. Barsuglia, PhDd, and Roland R. Griffiths, PhDa E. 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) used in a naturalistic group setting is associated with unintended improvements in depression and anxiety. Physiology & behavior. 2016;176(1):100–106.
24. Mason NL, Kuypers KPC, Müller F, Reckweg J, Tse DHY, Toennes SW, et al. Me, myself, bye: regional alterations in glutamate and the experience of ego dissolution with psilocybin. Neuropsychopharmacology [Internet]. 2020;(March). Available from:http://dx.doi.org/10.1038/s41386-020-0718-8
25. Preller KH, Burt JB, Ji JL, Schleifer CH, Adkinson BD, Stämpfli P, et al. Changes in global and thalamic brain connectivity in LSD-induced altered states of consciousness are attributable to the 5-HT2A receptor. eLife. 2018;7:1–31.
26. Preller KH, Duerler P, Burt JB, Ji JL, Adkinson B, Stämpfli P, et al. Psilocybin Induces Time-Dependent Changes in Global Functional Connectivity. Biological Psychiatry. 2020;
27. Smigielski L, Kometer M, Scheidegger M, Krähenmann R, Huber T, Vollenweider FX. Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat. Scientific Reports. 2019;
28.

Carhart-Harris RL, Leech R, Hellyer PJ, Shanahan M, Feilding A, Tagliazucchi E, et al. The entropic brain: A theory of conscious states informed by neuroimaging research with psychedelic drugs. Frontiers in Human Neuroscience. 2014;8(1 FEB):1–22.

29. Ramaekers JG, Hutten N, Mason NL, Dolder P, Theunissen EL, Holze F, Liechti ME, Feilding A, Kuypers KP. A low dose of lysergic acid diethylamide decreases pain perception in healthy volunteers. Journal of Psychopharmacology. 2020 Aug 25:0269881120940937.