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Investigating the Effects of Psilocybin on Neural Tissue Repair and Neural Network Reconstruction in Comatose Patients

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ABSTRACT

Objective: The human body functions as an intelligent system, constantly striving to maintain its internal balance and stability while preventing disorder (entropy). The brain, as the command this system, is responsible coordinating the body's organs to maintain stability and equilibrium. However, continuous changes in environmental or physiological conditions can challenges to the brain. If the brain cannot quickly adapt to these changes, it may lead to increased entropy and, in severe cases, the collapse of the body's systems and even death. Coma is a complex condition resulting from severe brain injuries such as stroke, traumatic brain injury, infections, or oxygen deprivation. This condition not only profoundly impacts patients' quality of life but It also imposes significant costs.

Method: Current treatments for coma are largely limited to life support and rehabilitation, highlighting a need for innovative therapeutic approaches.

Results: psychedelic compounds such as psilocybin have garnered attention due to their potential to promote neural repair and brain network reconstruction. Psilocybin, an active compound found in "magic mushrooms," works by activating serotonin receptors (particularly HT2A) and upregulating neurotrophic factors such as BDNF. These mechanisms enable psilocybin to reduce neural inflammation and enhance neurogenesis and synaptogenesis.

Conclusions: Psilocybin offer new hope for the development of effective treatments.

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Introduction

The human body functions as an intelligent system, constantly striving to maintain its stability and internal balance while avoiding disorder (entropy) (Aoki, 1989; McFarland et al, 2016). The brain, as the command center of this system, is responsible for controlling and coordinating the body's organs to ensure stability and equilibrium. As a highly sensitive organ, the brain is influenced by various internal and external factors, such as environmental conditions, and adjusts its commands to optimize the body's performance. When disorder arises within the system, the brain selects the best strategy to restore stability and prevent further damage (McEwen, 2017; Sennesh et al., 2022).

However, continuous changes in environmental or physiological conditions can pose significant challenges to the brain. If the brain cannot quickly adapt to new conditions, it may lead to a lack of coordination in the body's regulatory functions, increasing the system's entropy. In severe cases, this rise in entropy can result in the collapse of the body's systems and even death, as the time required for system recalibration is often too prolonged (McEwen, 2007; Kleckner et al, 2017).

Since the body operates as an intelligent system, the brain's ability to swiftly choose the optimal path to regulate bodily functions ensures the system's stability (McEwen, 2007; Kleckner et al, 2017).

Coma is a complex and debilitating condition resulting from severe brain injuries such as stroke, traumatic brain injury, infections, or oxygen deprivation. if this condition is left untreated or slow to improve, it can cause disruption to other systems and death (Laureys & Schiff, 2012; Edlow et al, 2021**).**

In recent years, psychedelic compounds such as psilocybin have garnered attention due to their potential to promote neural repair and brain network reconstruction. Psilocybin, an active compound found in "magic mushrooms," acts by activating serotonin receptors (particularly Hydroxytryptamine Receptor 2A (HT2A)) and upregulating neurotrophic factors such as BDNF. These mechanisms enable psilocybin to reduce neural inflammation, enhance neurogenesis and synaptogenesis, and improve functional connectivity patterns in the brain—factors that are critically important for patients in a coma (Carhart-Harris & Goodwin, 2017; Ly et al., 2018; Zhao et al., 2024).

Given the central role of integrated brain networks in maintaining consciousness, along with emerging evidence of psilocybin's ability to induce neuroplasticity, investigating the effects of this compound as a novel therapeutic strategy for coma patients appears both imperative and

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promising. This review could open new avenues for restoring neuro-somatic homeostasis in such individuals.

Mechanisms of Action of Psilocybin

Psilocybin, a naturally occurring psychedelic compound found in certain species of mushrooms, primarily exerts its effects through the activation of serotonin receptors, particularly the HT2A subtype. These receptors are widely distributed in the cerebral cortex and play a key role in regulating neural activity. The activation of these receptors by psilocybin leads to increased activity of glutamatergic neurons in the cortex, resulting in the release of glutamate and the enhancement of synaptic signaling (Carhart-Harris et al., 2012; Smausz et al., 2022).

In addition, psilocybin upregulates the expression of neurotrophic factors such as BDNF (brain-derived neurotrophic factor), which plays a critical role in neuronal repair and regeneration. BDNF, as a key molecule in neuroplasticity, promotes dendritic growth, the formation of new synapses, and neuronal survival. Furthermore, psilocybin reduces levels of inflammatory cytokines such as TNF-α and IL-1β, thereby mitigating neuroinflammation and preventing secondary damage to brain tissue (Flanagan & Nichols, 2018; Zanikov et al., 2023).

Neuroimaging studies (fMRI) have also demonstrated that psilocybin can improve functional connectivity patterns in the brain, particularly within the default mode network (DMN). This network plays a crucial role in coordinating brain activity and maintaining neural balance, and its dysfunction is associated with numerous neuropsychiatric disorders (Carhart-Harris et al., 2014; Tagliazucchi et al., 2016**;** Doss et al., 2021).

Psilocybin, due to its unique molecular structure, exhibits significant antioxidant properties . This compound, with its active functional groups such as hydroxyl (OH) and amine (NH2), demonstrates a high capacity for scavenging and neutralizing free radicals. Free radicals are recognized as primary contributors to oxidative stress and neuronal cell damage. By reducing the levels of these radicals, psilocybin prevents cellular degradation and contributes to neuroprotection and inflammation reduction. These properties position psilocybin as a promising compound in the treatment of neurological disorders (Carhart-Harris & Goodwin, 2017; Ly et al., 2018).

The Impact of Psilocybin on Neurogenesis and Synaptogenesis

Psilocybin stimulates the proliferation and differentiation of neural stem cells through signaling pathways associated with the mTOR protein (mechanistic target of rapamycin in mammals). mTOR is a key regulator of cellular growth, protein synthesis, and neuroplasticity. The activation of this pathway by psilocybin leads to the increased expression of neurotrophic factors such as BDNF (brain-derived neurotrophic factor), which plays a vital role in

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neurogenesis (the generation of new neurons) and synaptogenesis (the formation of new synapses) (Ly et al., 2018; de Vos et al., 2021).

Molecular Mechanisms of Synaptogenesis by Psilocybin

1. Activation of HT2A Serotonin Receptors:

Psilocybin binds to HT2A serotonin receptors in cortical neurons, triggering intracellular signaling pathways. This activation increases the levels of glutamate, an excitatory neurotransmitter, at synapses. Glutamate, by binding to AMPA and NMDA receptors, induces neuronal membrane depolarization and activates calcium-dependent pathways (Carhart-Harris et al., 2012; Szpręgiel & Bysiek, 2024).

2. Upregulation of BDNF Expression:

Psilocybin enhances the expression of BDNF, which plays a central role in promoting synaptogenesis. BDNF binds to TrkB receptors (tyrosine kinase B receptors), activating intracellular signaling pathways such as PI3K/Akt and MAPK/ERK. These pathways, in turn, increase the synthesis of proteins essential for the formation of new synapses, including synapsin and PSD-95 (postsynaptic density protein 95) (Nagahara & Tuszynski, 2011; Shafiee et al., 2024, retracted 2025).

3. Enhancement of Dendritic Growth and Synapse Formation:

BDNF also promotes dendritic growth and increases the number of dendritic spines, which are the sites of new synapse formation. This process occurs through the activation of calcium-dependent pathways and the regulation of genes associated with synaptic structure (Park & Poo, 2013; Shao et al., 2021).

4. Reduction of Neuroinflammation:

Psilocybin reduces levels of inflammatory cytokines such as TNF-α and IL-1β, creating a favorable environment for synaptogenesis. Neuroinflammation is a major inhibitor of new synapse formation, and its suppression by psilocybin enhances neuroplasticity processes (Flanagan & Nichols, 2018).

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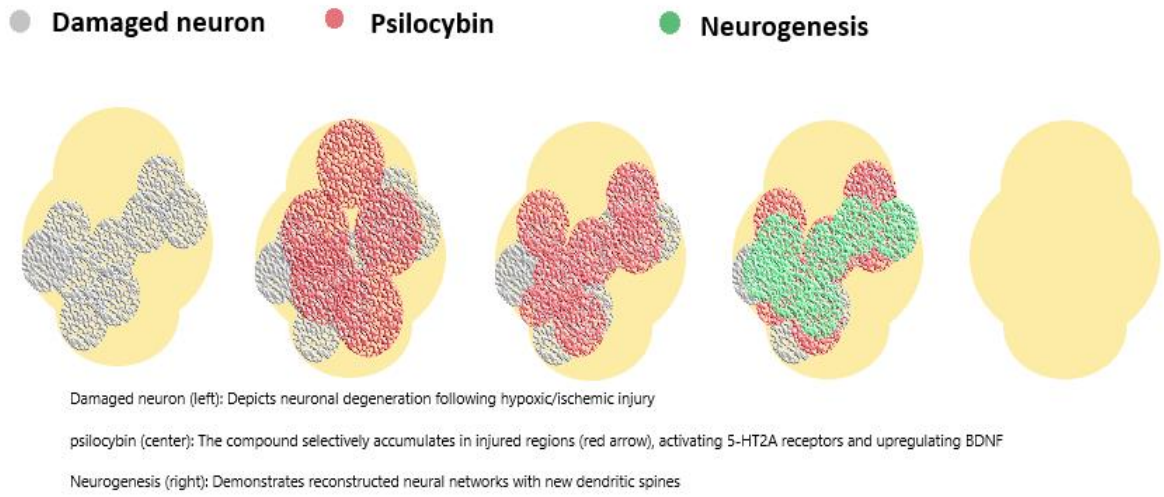

Figure ١. Emerging evidence suggests that psilocybin, through a mechanism involving its preferential accumulation in damaged neural regions and activation of serotonergic 5-HT2A receptors, induces the expression of Brain-Derived Neurotrophic Factor (BDNF). This process, in turn, holds the potential to reverse the course of neurodegeneration and induce both neurogenesis and synaptogenesis, ultimately leading to the reconstruction and repair of neural networks (Vargas et al., 2023).

Method

Clinical and preclinical studies

Preclinical and clinical studies have demonstrated thatpsilocybin can reduce neuroinflammation and oxidative stress. In animal models, the administration of psilocybin has been shown to upregulate the expression of neurotrophic factors and promote neuronal network regeneration, leading to improved neural plasticity. Furthermore, psilocybin has been found to induce significant changes in cognitive and emotional functioning (De Gregorio et al., 2021).

Research has also highlighted that 5-HT2A receptors (5-HT2AR), which are located within neural cells, play a pivotal role in mediating neuroplasticity. These receptors are critically involved in the antidepressant effects of psilocybin, underscoring their importance in modulating mood and cognitive processes (Carhart-Harris & Nutt, 2017).

Given that 5-HT2AR functions as an intracellular receptor, ligands must effectively cross the cell membrane to access and activate these receptors. Psilocybin, a lipophilic molecule, is capable of efficiently penetrating the cell membrane due to its chemical properties. To experimentally validate this mechanism, Maxemiliano V. Vargas et al., a study in which they systematically modified the membrane permeability of specific ligands. They transformed membrane-permeable compounds, including DMT, psilocin (PSI), and ketanserin (KTSN), into their membrane-impermeable analogs: TMT, psilocybin (PSY), and methylated ketanserin (MKTSN). Remarkably, these modified ligands maintained a high binding affinity for 5-

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HT2ARs, demonstrating that the intracellular localization of these receptors is essential for their functional activity.

In the subsequent phase of the experiment, embryonic rat cortical neurons were treated with 1 µM of DMT and PSI, as well as their membrane-impermeable counterparts, under conditions both with and without electroporation. The results demonstrated that membrane-permeable 5-HT2AR agonists effectively promoted dendritogenesis irrespective of whether electroporation was applied. In contrast, the membrane-impermeable compounds only induced neuronal growth when electroporation was employed to facilitate their intracellular delivery (Vargas et al., 2023).

The serotonergic system plays a critical role in hippocampal (HPC)-dependent learning processes. Studies have shown that the administration of SSRIs (selective serotonin reuptake inhibitors) can alter performance in learning tasks that rely on the hippocampus (Flood & Cherkin, 1987; Popova et al., 2017). For instance, in a knockout (KO) mouse model, mice with central 5-HT deficiency exhibited enhanced contextual fear conditioning, which was reversed by intracerebroventricular microinjection of 5-HT (Dai et al., 2008; Fonseca et al., 2015) .Similarly, 5-HT1A receptor KO mice displayed impaired learning in the Morris water maze, along with functional abnormalities in the hippocampus (Sarnyai et al., 2000). Activation of 5-HT1A receptors in the medial septum has also been shown to modulate encoding and consolidation in HPC-dependent memory tasks (Koenig et al., 2008). Additionally, LSD (lysergic acid diethylamide) has been found to facilitate learning in brightness discrimination reversal tasks (King et al., 1972; King et al., 1974; Torrado Pacheco et al., 2023).

Evidence further suggests that neurogenesis in the dentate gyrus (DG) of the hippocampus significantly influences performance in HPC-dependent learning tasks(van Praag et al., 2002; van Praag et al., 1999; Nilsson et al., 1999; Shors et al., 2001; Shors et al., 2002). This was elegantly demonstrated by Shors et al. (2001, 2002), who used methylazoxymethanol acetate (MAM), an antimitotic agent, to eliminate progenitor cells in the DG before testing mice on both HPC-dependent and HPC-independent learning tasks. MAM-treated animals exhibited significantly fewer BrdU+ cells in the subgranular zone (SGZ) but showed no impairment in spatial navigation (an HPC-dependent task) or delay eyeblink conditioning (an HPC-independent task). This indicates that the hippocampal progenitor cell population is not essential for these specific tasks. However, MAM treatment severely impaired performance in trace fear conditioning and trace eyeblink conditioning, providing strong evidence for the involvement of DG progenitor cells in trace classical conditioning. These findings highlight the importance of hippocampal neurogenesis in specific forms of learning and memory, particularly those involving trace conditioning, while also underscoring the role of the serotonergic system in modulating these processes(Catlow et al., 2013; Fölsz, Trouche, & Croset, 2023).

In this study, the effects of psilocybin on hippocampal neurogenesis (the production of new neurons) and the extinction of trace fear conditioning in mice were investigated. The main objective was to determine whether psilocybin, by acting on serotonin receptors (particularly

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5-HT2A), could influence the generation of new neurons and the process of fear extinction. Mice were subjected to fear conditioning, and then fear extinction and the number of new cells in the hippocampus were measured. The results showed that low doses of psilocybin accelerated fear extinction (Catlow et al., 2013; Alenina & Klempin, 2015).

In a study conducted at Yale University, Ling-Xiao Shao and colleagues investigated the effects of psilocybin on neural structure and function in the mouse medial prefrontal cortex (mPFC). To assess the compound's impact on neural plasticity, the researchers first evaluated the head-twitch response - a behavioral proxy for psychedelic activity - across multiple psilocybin doses (0.25, 0.5, 1, and 2 mg/kg, i.p.)Results showed that the 1 mg/kg dose elicited the most pronounced head-twitch response, so this dose was selected for subsequent experiments.The experiment used Thy1-GFP transgenic mice, in which a subset of layer 5 and 6 pyramidal neurons in the medial frontal cortex express GFP.Mice were subjected to a prolonged stress protocol involving inescapable foot shocks.mice were injected with psilocybin (1 mg/kg), ketamine (10 mg/kg, as a positive control), or saline (as a negative control).Dendritic spines of these neurons were imaged before and after psilocybin or saline administration over 7 days, with an additional imaging session one month later.Results revealed that psilocybin induced a significant increase in dendritic spine density and size, and these changes persisted for at least one month.Electrophysiological recordings showed that psilocybin increased the frequency of miniature excitatory postsynaptic currents (mEPSCs), indicating enhanced excitatory neurotransmission.psilocybin's effects on increasing spine density were observed across different cortical regions and in both dendritic types (Shao et al., 2021).

Recent clinical studies, such as those conducted at Johns Hopkins University and New York University, have demonstrated that psychedelics like psilocybin can significantly reduce symptoms of anxiety and depression in cancer patients, with positive effects lasting up to six months after a single dose. Additionally, research suggests that psychedelics may help restore healthy brain connectivity patterns by altering connections within the brain's Default Mode Network (DMN). Inflammation plays a critical role in the pathophysiology of psychiatric disorders such as depression and addiction. Animal studies have shown that pro-inflammatory cytokines like TNF-α and IL-1β can induce depression-like behaviors and social withdrawal. Furthermore, elevated levels of inflammation are associated with treatment resistance in depression. Psychedelics, through the activation of 5-HT2A receptors, not only produce rapid antidepressant effects but also reduce neuroinflammation, potentially preventing the brain from reverting to a pathological inflammatory state.

Thomas W. Flanagan and Charles D. Nichols designed an experimental study to investigate the anti-inflammatory effects of 5-HT2A receptor agonists, particularly the compound (R)-DOI. Their research aimed to explore how activation of the 5-HT2A receptor by psychedelics could modulate inflammatory pathways, both in cellular and animal models. Aortic smooth muscle cells from mice were exposed to TNF-α, a potent pro-inflammatory cytokine, to induce inflammation. The effects of (R)-DOI, a selective 5-HT2A receptor agonist, on this

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inflammation were then examined. (R)-DOI significantly inhibited the expression of inflammatory genes such as ICAM-1, VCAM-1, and IL-6. It also blocked the activation and nuclear translocation of the transcription factor NF-κB and the activity of nitric oxide synthase (NOS). Notably, these anti-inflammatory effects were observed even at very low doses (in the picomolar range). Mice were sensitized with allergens such as ovalbumin (OVA) to simulate symptoms of allergic asthma, including lung inflammation, airway hyperresponsiveness (AHR), and eosinophilia. (R)-DOI was then administered intranasally or intraperitoneally to the mice. (R)-DOI significantly reduced lung inflammation, AHR, and eosinophil accumulation. It also inhibited the expression of certain pro-inflammatory cytokines such as IL-5 and GM-CSF. Interestingly, these anti-inflammatory effects were observed at doses that did not induce psychedelic behaviors. This study demonstrates that 5-HT2A receptor agonists, particularly (R)-DOI, exhibit potent anti-inflammatory effects in both models. These compounds may act through novel mechanisms such as functional selectivity and epigenetic modulation, highlighting their potential for treating various inflammatory disorders (Flanagan & Nichols, 2018; Koseli et al., 2025).

Conclusions

Psilocybin, as a naturally occurring psychedelic compound, demonstrates significant potential in enhancing brain function and promoting neuroregeneration in comatose patients. Preclinical and clinical studies have indicated that this compound can reduce neuroinflammation and enhance neurogenesis and synaptogenesis. However, further research is required to confirm the efficacy and safety of psilocybin in the treatment of comatose patients. This review highlights that psilocybin could be explored as a novel therapeutic option for severe brain disorders.

Reference

Aoki I. Entropy flow and entropy production in the human body in basal conditions. J Theor Biol. 1989 Nov 8;141(1):11-21. doi: 10.1016/s0022-5193(89)80004-9. PMID: 2634157.

Alenina N, Klempin F. The role of serotonin in adult hippocampal neurogenesis. Behav Brain Res. 2015 Jan 15;277:49-57. doi: 10.1016/j.bbr.2014.07.038. Epub 2014 Aug 11. PMID: 25125239.

Carhart-Harris RL, Erritzoe D, Williams T, Stone JM, Reed LJ, Colasanti A, Tyacke RJ, Leech R, Malizia AL, Murphy K, Hobden P, Evans J, Feilding A, Wise RG, Nutt DJ. Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. Proc Natl Acad Sci U S A. 2012 Feb 7;109(6):2138-43. doi: 10.1073/pnas.1119598109. Epub 2012 Jan 23. PMID: 22308440; PMCID: PMC3277566.

[DOI: 10.22034/NBR.12.2.6]

Carhart-Harris RL, Goodwin GM. The Therapeutic Potential of Psychedelic Drugs: Past, Present, and Future. Neuropsychopharmacology. 2017 Oct;42(11):2105-2113. doi: 10.1038/npp.2017.84. Epub 2017 Apr 26. PMID: 28443617; PMCID: PMC5603818.

Carhart-Harris RL, Leech R, Hellyer PJ, Shanahan M, Feilding A, Tagliazucchi E, Chialvo DR, Nutt D. The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. Front Hum Neurosci. 2014 Feb 3;8:20. doi: 10.3389/fnhum.2014.00020. PMID: 24550805; PMCID: PMC3909994.

Carhart-Harris RL, Nutt DJ. Serotonin and brain function: a tale of two receptors. J Psychopharmacol. 2017 Sep;31(9):1091-1120. doi: 10.1177/0269881117725915. Epub 2017 Aug 31. PMID: 28858536; PMCID: PMC5606297.

Catlow BJ, Song S, Paredes DA, Kirstein CL, Sanchez-Ramos J. Effects of psilocybin on hippocampal neurogenesis and extinction of trace fear conditioning. Exp Brain Res. 2013 Aug;228(4):481-91. doi: 10.1007/s00221-013-3579-0. Epub 2013 Jun 2. PMID: 23727882.

Dai JX, Han HL, Tian M, Cao J, Xiu JB, Song NN, Huang Y, Xu TL, Ding YQ, Xu L. Enhanced contextual fear memory in central serotonin-deficient mice. Proc Natl Acad Sci U S A. 2008 Aug 19;105(33):11981-6. doi: 10.1073/pnas.0801329105. Epub 2008 Aug 11. PMID: 18695238; PMCID: PMC2575315.

de Vos CMH, Mason NL, Kuypers KPC. Psychedelics and Neuroplasticity: A Systematic Review Unraveling the Biological Underpinnings of Psychedelics. Front Psychiatry. 2021 Sep 10;12:724606. doi: 10.3389/fpsyt.2021.724606. PMID: 34566723; PMCID: PMC8461007.

De Gregorio D, Aguilar-Valles A, Preller KH, Heifets BD, Hibicke M, Mitchell J, Gobbi G. Hallucinogens in Mental Health: Preclinical and Clinical Studies on LSD, Psilocybin, MDMA, and Ketamine. J Neurosci. 2021 Feb 3;41(5):891-900. doi: 10.1523/JNEUROSCI.1659-20.2020. Epub 2020 Nov 30. PMID: 33257322; PMCID: PMC7880300.

Doss MK, Považan M, Rosenberg MD, Sepeda ND, Davis AK, Finan PH, Smith GS, Pekar JJ, Barker PB, Griffiths RR, Barrett FS. Psilocybin therapy increases cognitive and neural flexibility in patients with major depressive disorder. Transl Psychiatry. 2021 Nov 8;11(1):574. doi: 10.1038/s41398-021-01706-y. PMID: 34750350; PMCID: PMC8575795.

Edlow BL, Claassen J, Schiff ND, Greer DM. Recovery from disorders of consciousness: mechanisms, prognosis and emerging therapies. Nat Rev Neurol. 2021 Mar;17(3):135-156. doi: 10.1038/s41582-020-00428-x. Epub 2020 Dec 14. PMID: 33318675; PMCID: PMC7734616.

Flanagan TW, Nichols CD. Psychedelics as anti-inflammatory agents. Int Rev Psychiatry. 2018 Aug;30(4):363-375. doi: 10.1080/09540261.2018.1481827. Epub 2018 Aug 13. PMID: 30102081.

[DOI: 10.22034/NBR.12.2.6]

Flood JF, Cherkin A. Fluoxetine enhances memory processing in mice. Psychopharmacology (Berl). 1987;93(1):36-43. doi: 10.1007/BF02439584. PMID: 3114813.

Fölsz O, Trouche S, Croset V. Adult-born neurons add flexibility to hippocampal memories. Front Neurosci. 2023 Feb 15;17:1128623. doi: 10.3389/fnins.2023.1128623. PMID: 36875670; PMCID: PMC9975346.

Fonseca MS, Murakami M, Mainen ZF. Activation of dorsal raphe serotonergic neurons promotes waiting but is not reinforcing. Curr Biol. 2015 Feb 2;25(3):306-315. doi: 10.1016/j.cub.2014.12.002. Epub 2015 Jan 15. PMID: 25601545.

King AR, Martin IL, Melville KA. Reversal learning enhanced by lysergic acid diethylamide (LSD): concomitant rise in brain 5-hydroxytryptamine levels. Br J Pharmacol. 1974 Nov;52(3):419-26. doi: 10.1111/j.1476-5381.1974.tb08611.x. PMID: 4458849; PMCID: PMC1777004.

King AR, Martin IL, Seymour KA. Reversal learning facilitated by a single injection of lysergic acid diethylamide (LSD 25) in the rat. Br J Pharmacol. 1972 May;45(1):161P-162P. PMID: 5041478; PMCID: PMC1666253.

Kleckner IR, Zhang J, Touroutoglou A, Chanes L, Xia C, Simmons WK, Quigley KS, Dickerson BC, Barrett LF. Evidence for a Large-Scale Brain System Supporting Allostasis and Interoception in Humans. Nat Hum Behav. 2017;1:0069. doi: 10.1038/s41562-017-0069. Epub 2017 Apr 24. PMID: 28983518; PMCID: PMC5624222.

Koenig J, Cosquer B, Cassel JC. Activation of septal 5-HT1A receptors alters spatial memory encoding, interferes with consolidation, but does not affect retrieval in rats subjected to a water-maze task. Hippocampus. 2008;18(1):99-118. doi: 10.1002/hipo.20368. PMID: 17924524.

Koseli E, Buzzi B, Honaker T, Rakholia Y, Lewis M, Gaines-Smith M, Jaster AM, Gonzalez-Maeso J, Damaj MI. IUPHAR Article: Psilocybin induces long-lasting effects via 5-HT$_{2A}$ receptors in mouse models of chronic pain. Pharmacol Res. 2025 May;215:107699. doi: 10.1016/j.phrs.2025.107699. Epub 2025 Mar 17. PMID: 40107634; PMCID: PMC12107474.

Ly C, Greb AC, Cameron LP, Wong JM, Barragan EV, Wilson PC, Burbach lF, Soltanzadeh Zarandi S, Sood A, Paddy MR, Duim WC, Dennis MY, McAllister AK, Ori-McKenney KM, Gray JA, Olson DE. Psychedelics Promote Structural and Functional Neural Plasticity. Cell Rep. 2018 Jun 12;23(11):3170-3182. doi: 10.1016/j.celrep.2018.05.022. PMID: 29898390; PMCID: PMC6082376.

Laureys S, Schiff ND. Coma and consciousness: paradigms (re)framed by neuroimaging. Neuroimage. 2012 Jun;61(2):478-91. doi: 10.1016/j.neuroimage.2011.12.041. Epub 2011 Dec 27. PMID: 22227888.

[DOI: 10.22034/NBR.12.2.6]

Ly C, Greb AC, Cameron LP, Wong JM, Barragan EV, Wilson PC, Burbach KF, Soltanzadeh Zarandi S, Sood A, Paddy MR, Duim WC, Dennis MY, McAllister AK, Ori-McKenney KM, Gray JA, Olson DE. Psychedelics Promote Structural and Functional Neural Plasticity. Cell Rep. 2018 Jun 12;23(11):3170-3182. doi: 10.1016/j.celrep.2018.05.022. PMID: 29898390; PMCID: PMC6082376.

McEwen BS. Neurobiological and Systemic Effects of Chronic Stress. Chronic Stress (Thousand Oaks). 2017 Jan-Dec;1:2470547017692328. doi: 10.1177/2470547017692328. Epub 2017 Apr 10. PMID: 28856337; PMCID: PMC5573220.

McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol Rev. 2007 Jul;87(3):873-904. doi: 10.1152/physrev.00041.2006. PMID: 17615391.

McFarland J, Wenderoth MP, Michael J, Cliff W, Wright A, Modell H. A conceptual framework for homeostasis: development and validation. Adv Physiol Educ. 2016 Jun;40(2):213-22. doi: 10.1152/advan.00103.2015. PMID: 27105740; PMCID: PMC5002438.

Nagahara AH, Tuszynski MH. Potential therapeutic uses of BDNF in neurological and psychiatric disorders. Nat Rev Drug Discov. 2011 Mar;10(3):209-19. doi: 10.1038/nrd3366. PMID: 21358740.

Nilsson M, Perfilieva E, Johansson U, Orwar O, Eriksson PS. Enriched environment increases neurogenesis in the adult rat dentate gyrus and improves spatial memory. J Neurobiol. 1999 Jun 15;39(4):569-78. doi: 10.1002/(sici)1097-4695(19990615)39:4<569::aid-neu10>3.0.co;2-f. PMID: 10380078.

Park H, Poo MM. Neurotrophin regulation of neural circuit development and function. Nat Rev Neurosci. 2013 Jan;14(1):7-23. doi: 10.1038/nrn3379. PMID: 23254191.

Popova D, Castrén E, Taira T. Chronic fluoxetine administration enhances synaptic plasticity and increases functional dynamics in hippocampal CA3-CA1 synapses. Neuropharmacology. 2017 Nov;126:250-256. doi: 10.1016/j.neuropharm.2017.09.003. Epub 2017 Sep 6. PMID: 28887184.

Sarnyai Z, Sibille EL, Pavlides C, Fenster RJ, McEwen BS, Toth M. Impaired hippocampal-dependent learning and functional abnormalities in the hippocampus in mice lacking serotonin(1A) receptors. Proc Natl Acad Sci U S A. 2000 Dec 19;97(26):14731-6. doi: 10.1073/pnas.97.26.14731. PMID: 11121072; PMCID: PMC18987.

Sennesh E, Theriault J, Brooks D, van de Meent JW, Barrett LF, Quigley KS. Interoception as modeling, allostasis as control. Biol Psychol. 2022 Jan;167:108242. doi: 10.1016/j.biopsycho.2021.108242. Epub 2021 Dec 20. PMID: 34942287; PMCID: PMC9270659.

[DOI: 10.22034/NBR.12.2.6]

Shao LX, Liao C, Gregg I, Davoudian PA, Savalia NK, Delagarza K, Kwan AC. Psilocybin induces rapid and persistent growth of dendritic spines in frontal cortex in vivo. Neuron. 2021 Aug 18;109(16):2535-2544.e4. doi: 10.1016/j.neuron.2021.06.008. Epub 2021 Jul 5. PMID: 34228959; PMCID: PMC8376772.

Shafiee A, Arabzadeh Bahri R, Rafiei MA, Esmaeilpur Abianeh F, Razmara P, Jafarabady K, Amini MJ. The effect of psychedelics on the level of brain-derived neurotrophic factor: A systematic review and meta-analysis. J Psychopharmacol. 2024 May;38(5):425-431. doi: 10.1177/02698811241234247. Epub 2024 Feb 22. Retraction in: J Psychopharmacol. 2025 May 15:2698811251341228. doi: 10.1177/02698811251341228. PMID: 38385351.

Shors TJ, Miesegaes G, Beylin A, Zhao M, Rydel T, Gould E. Neurogenesis in the adult is involved in the formation of trace memories. Nature. 2001 Mar 15;410(6826):372-6. doi: 10.1038/35066584. Erratum in: Nature 2001 Dec 20-27;414(6866):938. PMID: 11268214.

Shors TJ, Townsend DA, Zhao M, Kozorovitskiy Y, Gould E. Neurogenesis may relate to some but not all types of hippocampal-dependent learning. Hippocampus. 2002;12(5):578-84. doi: 10.1002/hipo.10103. PMID: 12440573; PMCID: PMC3289536.

Smausz R, Neill J, Gigg J. Neural mechanisms underlying psilocybin's therapeutic potential - the need for preclinical in vivo electrophysiology. J Psychopharmacol. 2022 Jul;36(7):781-793. doi: 10.1177/02698811221092508. Epub 2022 May 30. PMID: 35638159; PMCID: PMC9247433.

Szpręgiel I, Bysiek A. Psilocybin and the glutamatergic pathway: implications for the treatment of neuropsychiatric diseases. Pharmacol Rep. 2024 Dec;76(6):1297-1304. doi: 10.1007/s43440-024-00660-y. Epub 2024 Oct 16. PMID: 39412581; PMCID: PMC11582295.

Tagliazucchi E, Roseman L, Kaelen M, Orban C, Muthukumaraswamy SD, Murphy K, Laufs H, Leech R, McGonigle J, Crossley N, Bullmore E, Williams T, Bolstridge M, Feilding A, Nutt DJ, Carhart-Harris R. Increased Global Functional Connectivity Correlates with LSD-Induced Ego Dissolution. Curr Biol. 2016 Apr 25;26(8):1043-50. doi: 10.1016/j.cub.2016.02.010. Epub 2016 Apr 13. PMID: 27085214.

Torrado Pacheco A, Olson RJ, Garza G, Moghaddam B. Acute psilocybin enhances cognitive flexibility in rats. bioRxiv [Preprint]. 2023 Jan 9:2023.01.09.523291. doi: 10.1101/2023.01.09.523291. Update in: Neuropsychopharmacology. 2023 Jun;48(7):1011-1020. doi: 10.1038/s41386-023-01545-z. PMID: 36712091; PMCID: PMC9881983.

van Praag H, Schinder AF, Christie BR, Toni N, Palmer TD, Gage FH. Functional neurogenesis in the adult hippocampus. Nature. 2002 Feb 28;415(6875):1030-4. doi: 10.1038/4151030a. PMID: 11875571; PMCID: PMC9284568.

[DOI: 10.22034/NBR.12.2.6]

van Praag H, Schinder AF, Christie BR, Toni N, Palmer TD, Gage FH. Functional neurogenesis in the adult hippocampus. Nature. 2002 Feb 28;415(6875):1030-4. doi: 10.1038/4151030a. PMID: 11875571; PMCID: PMC9284568.

Vargas MV, Dunlap LE, Dong C, Carter SJ, Tombari RJ, Jami SA, Cameron LP, Patel SD, Hennessey JJ, Saeger HN, McCorvy JD, Gray JA, Tian L, Olson DE. Psychedelics promote neuroplasticity through the activation of intracellular 5-HT2A receptors. Science. 2023 Feb 17;379(6633):700-706. doi: 10.1126/science.adf0435. Epub 2023 Feb 16. PMID: 36795823; PMCID: PMC10108900.

Zanikov T, Gerasymchuk M, Ghasemi Gojani E, Robinson GI, Asghari S, Groves A, Haselhorst L, Nandakumar S, Stahl C, Cameron M, Li D, Rodriguez-Juarez R, Snelling A, Hudson D, Fiselier A, Kovalchuk O, Kovalchuk I. The Effect of Combined Treatment of Psilocybin and Eugenol on Lipopolysaccharide-Induced Brain Inflammation in Mice. Molecules. 2023 Mar 14;28(6):2624. doi: 10.3390/molecules28062624. PMID: 36985596; PMCID: PMC10056123.

Zhao X, Du Y, Yao Y, Dai W, Yin Y, Wang G, Li Y, Zhang L. Psilocybin promotes neuroplasticity and induces rapid and sustained antidepressant-like effects in mice. J Psychopharmacol. 2024 May;38(5):489-499. doi: 10.1177/02698811241249436. Epub 2024 Apr 28. PMID: 38680011.

[DOI: 10.22034/NBR.12.2.6]