PSYCHEDELIC-ASSISTED NEUROREHABILITATION

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Introduction

Psychedelic-assisted neurorehabilitation is a novel approach aimed at enhancing recovery from neurological conditions such as stroke, concussion, and brain injury.

This ebook delves into the fascinating world of psychedelic-assisted neurorehabilitation, exploring the concepts of neuroplasticity, metaplasticity, and anti-inflammatory effects.

We will also examine the groundbreaking research conducted in this field.

What
is Neurorehabilitation?

Neurorehabilitation is a specialized form of rehabilitation aimed at restoring function and reducing disability in individuals with neurological conditions. It involves a range of interventions and therapies, but the introduction of psychedelics as an assistive tool represents a significant paradigm shift.

In this section, we will explore the traditional methods of neurorehabilitation and how psychedelics can complement these approaches.

Read More

Understanding Neurorehabilitation | World Health Organization

https://www.who.int/news-room/fact-sheets/detail/rehabilitation

The Role of Psychedelics

Psychedelics have been shown to alter perception, mood, and cognitive processes.
More importantly, they have been found to induce neuroplasticity - the brain's ability to adapt and change.

According to various studies, psychedelics have three principal effects that can benefit neurorehabilitation:

Psychedelics have been demonstrated to increase neuroplasticity / metaplasticity
Psychedelics have been demonstrated to re-open critical periods (CP) of development
This may include motor, sensory, and other types of critical periods
It may be possible to leverage this re-opening of CP paired with adjunctive interventions to elicit context-dependent re-learning experience akin to acute periods of neurological responsiveness/repair

1

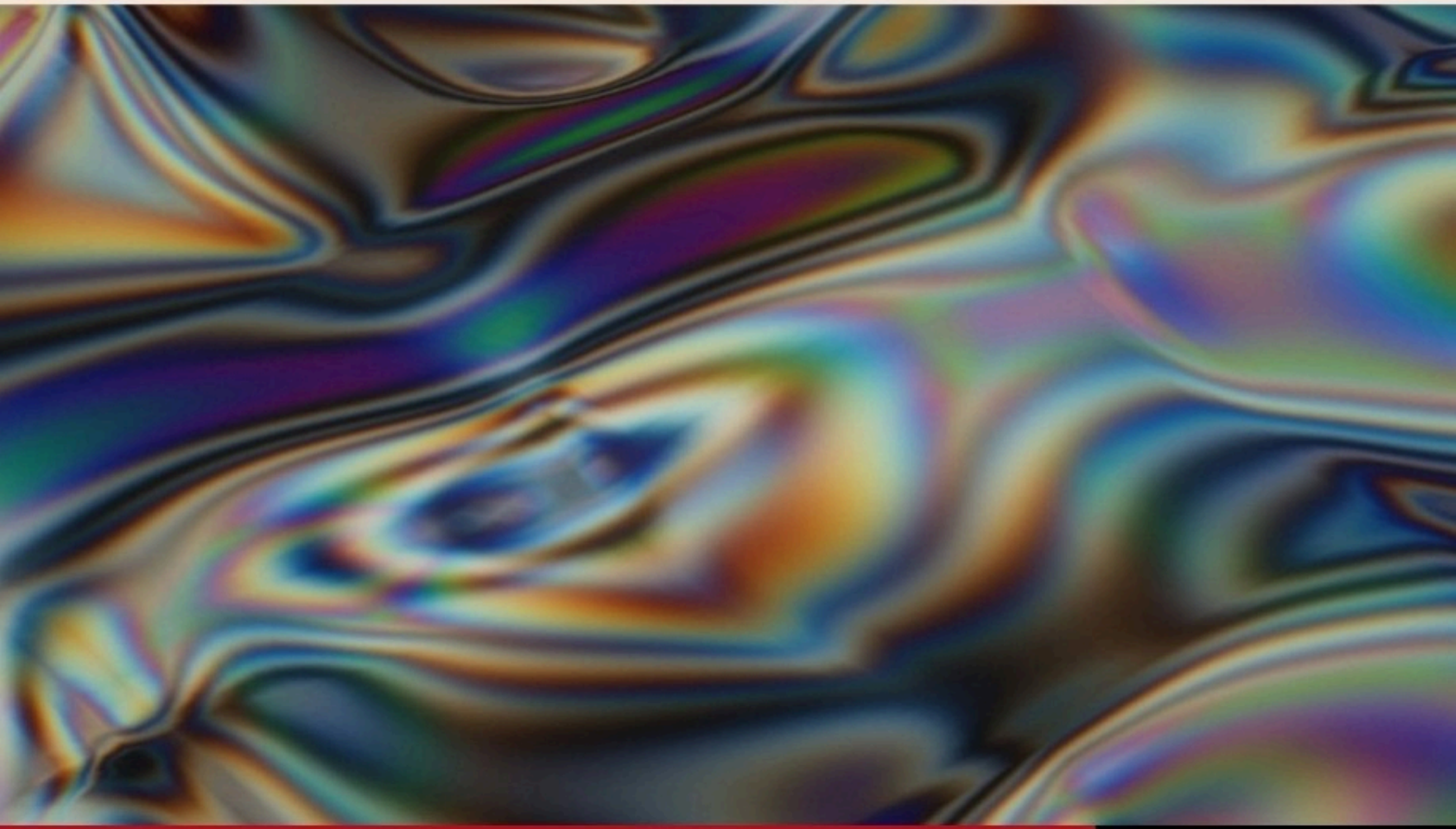
Induction of neuroplasticity /metaplasticity can lead to functional recovery

2

Modification of anti-inflammatory responses which can reduce neuroinflammation

3

Enhancement of mood and cognition which can improve patient engagement



Critical Periods and Windows of Neuroplasticuty

"there are developmental "critical" periods with exquisite sensitivity to environmental input… psychedelics may remove the brakes on adult neuroplasticity, inducing a state similar to that of neurodevelopment."

- Dr. Lauren Lepow

"It might be that if what it feels like to be in that altered state of consciousness or that mystical experience that we think of with psychedelics is just what it feels like to reopen critical periods"

- Dr. Gül Dölen, MD, PhD

"Really what psychedelics are are this master key for unlocking critical periods….
There are lots of different critical periods... we are beginning to get a sense that many of the critical periods close using the same sort of governing principle, the same kind of molecules, if not the exact same molecules, & will or have been implicated in the closure of, say, the visual critical period or the touch critical period or the motor critical period."

- Dr. Gül Dölen, MD, PhD

Lepow L, Morishita H, Yehuda R. Critical Period Plasticity as a Framework for Psychedelic-Assisted Psychotherapy. Front Neurosci. 2021 Sep 20;15:710004. doi: 10.3389/fnins.2021.710004. PMID: 34616272; PMCID: PMC8488335.

Research and Findings

With Neurological Trauma such as concussion, stroke, and brain injury there is a short period, a critical period, of neuroplasticity in which the brain heals itself and creates new neural connections. Like all critical periods, this window closes, in this case within a few months after an injury

Combining psychedelics with physical therapy in digitally enriched environments may restore the ability to recover functionality after stroke, concussion, or brain injury, even in cases where the injury occurred months to years prior."

https://secure.jhu.edu/form/phathom-study
Nardou, R., Sawyer, E., Song, Y.J. et al. Psychedelics reopen the social reward learning critical period. Nature 618, 790–798 (2023). https://doi.org/10.1038/s41586-023-06204-3

Impact of Psychedelic on Neuroplasticity

Psychedelics play a crucial role in enhancing neuroplasticity, the brain's ability to form and reorganize connections in response to learning and experience.

They induce the release of various neurotrophic factors which promote the growth and differentiation of neurons.

Additionally, psychedelics have been shown to alter gene expression patterns associated with synaptic plasticity and memory formation.

Calder, A.E., Hasler, G. Towards an understanding of psychedelic-induced neuroplasticity. Neuropsychopharmacol. 48, 104–112 (2023). https://doi.org/10.1038/s41386-022-01389-z

Other Benefits of Psychedelics in Neurorehabilitation

REDUCES OXIDATIVE STRESS, MITOCHONDRIAL DYSFUNCTION, & EXCITOTOXICITY

Psilocybin mushrooms have potent antioxidant effects. Serotonergic psychedelics like psilocybin are able to buffer from stress on the brain by increasing the oxidative capacity of neurons.

PROMOTES NEUROPROTECTION & BLOOD FLOW

Psychedelics can reduce cell death and increase brain-derived neurotrophic factor (BDNF) that is important in healing and neuroprotection. Serotonergic psychedelics directly bind to TrkB, a protein that binds to BDNF, at a rate 1000x greater than anti-depressants and inhibits factors of cognitive decline and neurodegeneration.

REDUCES NEUROINFLAMMATION

Psilocybin can influence the body's immune response markers and lower pro-inflammatory cytokines such as TNF-α, IL-1β, & IL-6

NETWORK-WIDE BRAIN CHANGES

Psychedelics increase global functional connectivity and synchronized timing of neural activity between distinct brain regions and functional brain networks. This has been shown to allow for lasting changes in brain areas, bolstering cognitive processes & positive shifts in mood

Allen, J., Dames, S.S., Foldi, C.J. et al. Psychedelics for acquired brain injury: a review of molecular mechanisms and therapeutic potential. Mol Psychiatry 29, 671–685 (2024). https://doi.org/10.1038/s41380-023-02360-0

Impacts of Psychedelics on Psychomotor Performance

A study of subperceptual doses (microdoses) of psilocybin that included over 900 people showed improvements in psychomotor performance that were specific to older adults.

Improvements were shown with a finger tap test, often used to evaluate frontal brain function and tends to slow in neurodegenerative conditions such as Parkinson's and Alzheimer's Disease.

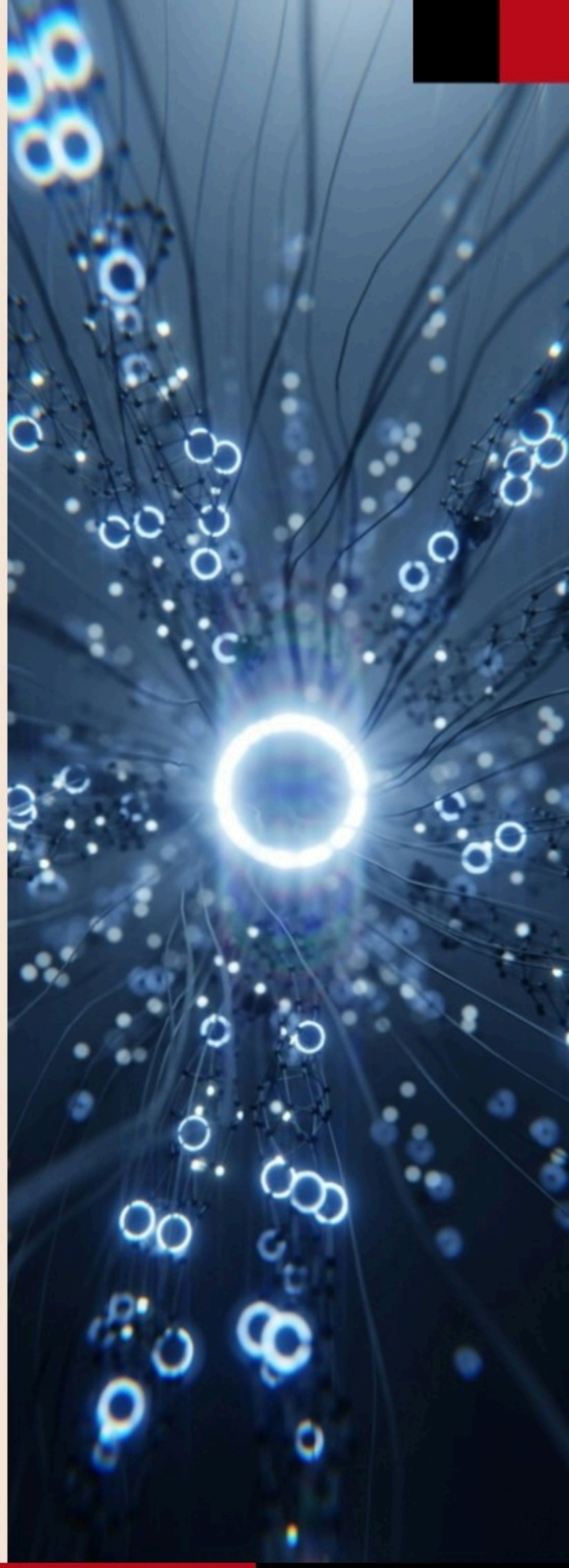
Further analyses showed combining psilocybin, lion's mane mushroom, and a vasoldilator (Vitamin B3) was associated with psychomotor greater improvements than psilocybin alone.

Rootman, J.M., Kiraga, M., Kryskow, P. et al. Psilocybin microdosers demonstrate greater observed improvements in mood and mental health at one month relative to non-microdosing controls. Sci Rep 12, 11091 (2022). https://doi.org/10.1038/s41598-022-14512-3

Exploring Psychedelics in Neurodegenerative Disorders

Because psychedelics stimulate neurogenesis and gliogenesis, reduce inflammation, and ameliorate oxidative stress; they are being explored as promising candidates for future therapeutics for psychiatric, neurodegenerative, and movement disorders including Alzheimer's and Parkinson's Disease

"Importantly, psychedelics hold the promise of being disease-modifying therapeutics, and not simply just providing symptomatic relief."



Kozlowska U, Nichols C, Wiatr K, Figiel M. From psychiatry to neurology: Psychedelics as prospective therapeutics for neurodegenerative disorders. J Neurochem. 2022 Jul;162(1):89-108. doi: 10.1111/jnc.15509. Epub 2021 Oct 22.

Combined Benefits of Microdosing Psilocybin with Neuromodulation

Research looking at psilocybin's ability to promote neural flexibility found combining six microdoses of psilocybin with frontal-midline theta neurofeedback, a well-established technique for enhancing executive functions, increased frontal-midline theta activity, indicative of enhanced learning and engagement

Executive functions—skills like working memory updating, cognitive flexibility, and inhibition—are critical for navigating daily life.
When these are impaired, they can limit one's capacity for adaptation and learning. Traditional interventions for executive function deficits can be slow and limited in their impact, potentially constrained by the brain's baseline plasticity.

Participants reported "notable gains in their daily lives, including enhanced working memory, cognitive shifting, monitoring, and inhibition."

This supports the idea that psilocybin may create a more fertile neural environment, allowing neurofeedback and neuromodulation interventions to work more effectively.

Enriquez-Geppert S, Krc J, O'Higgins FJ, Lietz M. 2024 Psilocybin-assisted neurofeedback for the improvement of executive functions: a randomized semi-naturalistic-lab feasibility study. Phil. Trans. R. Soc. B 379: 20230095.