Neuroplastic Pathways to Recovery: Psilocybin's Emerging Role in Treating Alcohol Use Disorder

University of Wisconsin – Madison
Audrey Tharp
atharp@wisc.edu

Abstract

Alcohol Use Disorder (AUD) is a chronic, relapsing condition with high rates of recurrence despite available treatments. **Psilocybin-assisted therapy (PAT)** is emerging as a promising alternative for individuals unresponsive to standard interventions[1]. This poster synthesizes recent findings to explore how psilocybin's neurobiological effects may support recovery from AUD. Psilocybin is metabolized into psilocin, a potent 5-HT2A receptor agonist. This activation increases cortical glutamate release and promotes neuroplasticity, enabling the formation of new neural connections[2,3]. Neuroimaging studies show psilocybin disrupts hyperactivity in the **default mode network (DMN)** and enhances connectivity between segregated brain regions[4], changes linked to improved emotional processing, cognitive flexibility, and openness[5].

These mechanisms align with clinical outcomes. In randomized and open-label studies, PAT led to a **58% reduction in heavy drinking days** over 32 weeks[6], along with **increased abstinence, emotional stability, and self-compassion**[7,8]. Treatment was well tolerated, with no serious adverse events and high adherence; mild, transient anxiety was the most common side effect[8]. Psilocybin's impact on brain networks and plasticity may facilitate meaningful psychological and behavioral change. Further research is needed to assess long-term effects, optimize protocols, and evaluate efficacy across diverse populations[9].

Alcohol Use Disorder

Alcohol Use Disorder (AUD) affects over 280 million people globally and is associated with increased morbidity and mortality. Since 2019, AUD diagnoses have been increasing, attributed to situations like COVID 19[1].

According to DSM-5 criteria, AUD is diagnosed when individuals meet at least two out of eleven symptoms, including tolerance, withdrawal, and persistent use despite harm, within a 12-month period.

Standard therapies, such as cognitive-behavioral interventions and medications like naltrexone or acamprosate, have modest success in achieving sustained abstinence[1].

Novel interventions are needed to address this growing diagnosis rate and provide options for individuals who have not found success in the traditional methods.

Psilocybin's Mechanism of Action

Mechanistic Domain	Description	Functional Implication
Metabolism & Receptor Activation	Psilocybin → psilocin, a 5-HT$_2$A agonist	Triggers serotonergic signaling
Neuroplasticity Enhancement	↑ glutamate, synaptogenesis, and dendritic growth[2,3]	Promotes neural rewiring that supports long term behavioral change
DMN Disruption	↓ DMN activity[4]	↓ Maladaptive self-focus, supports cognitive flexibility and psychological insight
Increased Global Connectivity	↑ communication between brain regions typically segregated[4,5]	Supports more flexible cognition and emotional openness
Emotional Processing & Fear Modulation	Alters amygdala activity[2,5]	Lowers fear; heightens emotional insight
Therapeutic Window of Plasticity	Temporary boost in neuroplasticity[3]	Increases receptivity to therapy, Optimal window

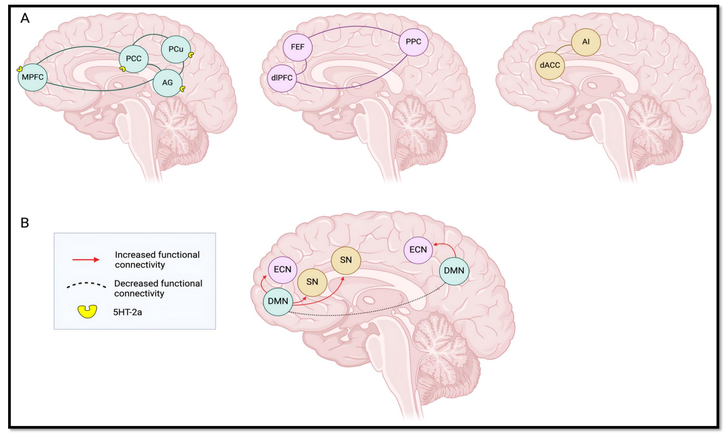

Figure 1.[10] The psychedelic effect on the connectivity between the default mode network, executive control network, and salience network.
(**A**) Key areas involved in DMN, ECN and SN networks.
(**B**) Psychedelics' assumption increases connectivity between DMN and SN and between DMN and ECN, together with a decreased connectivity within the hubs of the DMN.
DMN: default mode network; ECN: executive control network; SN: salience network; AG: angular gyrus; AI: anterior insula; dACC: dorsal anterior cingulate cortex; dlPFC: dorsolateral prefrontal cortex; FEF: frontal eye field; MPFC: medial prefrontal cortex; PCu: precuneus; PCC: posterior cingulate cortex; PPC: posterior parietal cortex.

Clinical Outcomes of PAT in AUD

📉 **Reduction in Alcohol Use**
- ↓ 58% in heavy drinking days[6] **(Figure 2)**
- 48% extended abstinence
- Sustained across follow-up[6]

🧠 **Personality & Psychological Change**
- ↑ Openness
- ↑ Emotional stability
- ↑ Self-compassion
- Observed 3+ months post treatment[7] **(Figure 3)**

💊 **Safety & Tolerability**
- No serious adverse effects[8]
- Most common: mild anxiety[8]
- High adherence to protocols

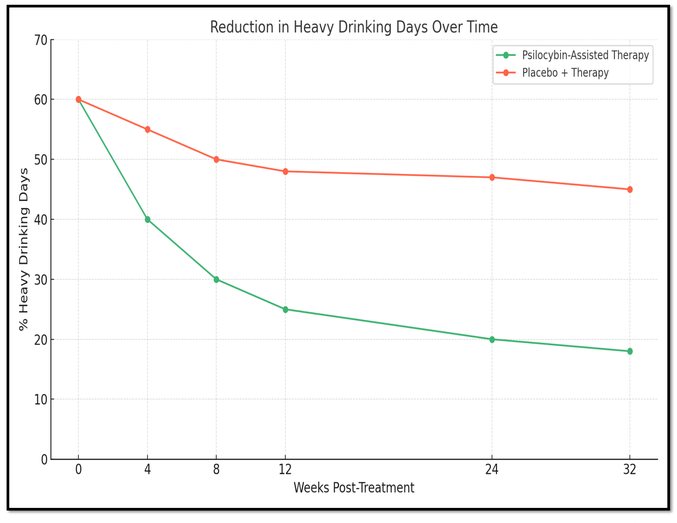

Figure 2. Comparison of PAT vs Placebo in reducing heavy drinking days[6]

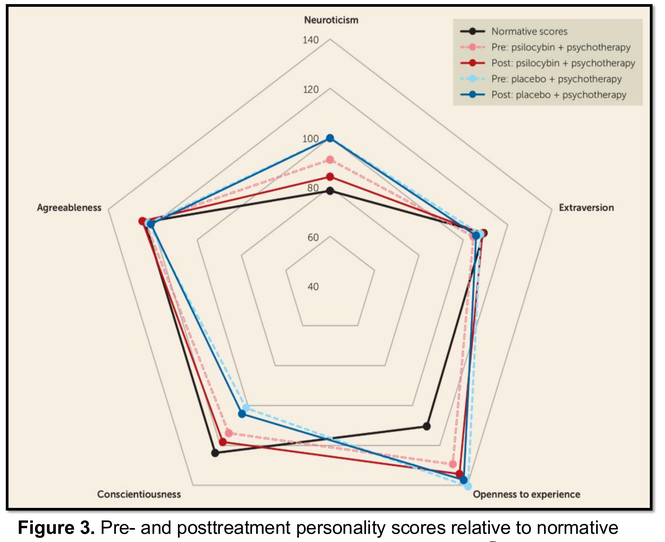

Figure 3. Pre- and posttreatment personality scores relative to normative scores, assessed with revised NEO Personality Inventory[7]

Conclusions

PAT significantly reduced heavy drinking days with effects sustained over time[6]. Patients reported increase openness, emotional stability, and self compassion[7]. There was a high adherence to the protocols and no serious adverse effects reported make it a safe option in controlled settings[8]. However, participants were predominantly white, male and middle aged. Across studies, there was variability in dosing, psychotherapy approaches and the duration of the follow up periods. More research is needed to look at differences in dosing options (single vs multi)[9], diverse populations and severity of AUD, standardization of protocols[4], larger sample sizes, and longer follow up durations[1].

SCAN ME

References