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Evaluating Psychedelic Therapies for Neurodegenerative Disorders: Research Gaps, Risks, and Future Directions

Company Description

Tidal Care Inc. is an Alberta-based psychedelics therapeutics research company, working to bring the nascent psychedelics to the forefront of healthcare and mental health industries. The primary research focus of Tidal is on psilocybin and other nutraceutical mushrooms, but it has board members who have worked with other potentially therapeutic substances like methylenedioxymethamphetamine (MDMA). In addition to that, Tidal is also open to researching the benefits of other psychedelic substances.

Tidal frequently partners up its research efforts with the University of Guelph and the University of Toronto and companies like Canna Stream Solutions. Tidal is committed to the scaling and manufacturing of the highest quality psychedelics at compliant laboratory facilities to ensure highest safety standards first and foremost.

Building on its strong academic collaborations, Tidal focuses on the therapeutic potential of psychedelics to improve human health by enhancing neuroplasticity, regulating inflammation, and supporting emotional and cognitive resilience. These mechanisms are increasingly recognized as crucial for addressing complex conditions such as depression, anxiety, neurodegenerative disorders like Alzheimer's and Parkinson's disease, and chronic pain.

What makes Tidal Care Inc. unique is its integrated approach: it not only invests in preclinical and clinical research but also emphasizes pharmaceutical-grade manufacturing capabilities to ensure scalability and compliance with regulatory standards. Its multidisciplinary leadership team, with experience in developing other psychoactive therapeutics such as MDMA, positions Tidal at the intersection of scientific innovation and real-world medical application.

Project Description

Background

Recent years have seen a resurgence of interest in the therapeutic potential of psychedelics. Initially researched for their capacity to alleviate mental disorders, these substances are now being examined for a wide range of medical applications, including improving mood and social connectivity in patients with Alzheimer’s Disease and related dementias (McManus et al., 2022; Sinha et al., 2024; Vann Jones & O’Kelly, 2020; Zheng et al., 2024), offering potential disease-modifying effects in neurodegenerative disorders like Parkinson’s Disease (Ordovich-Clarkson et al., 2024; Katchborian-Neto et al., 2020), modulating eating behaviors and metabolism in obesity (Fadahunsi et al., 2022; Huang et al., 2022), and influencing chronic pain, cancer, and autoimmune conditions through complex psychosocial and spiritual processes (Schmid, n.d.). However, the current evidence base remains fragmented and

preliminary, often relying on small, non-representative samples or studies conducted in non-patient populations. Ethical, regulatory, and methodological challenges further complicate efforts to safely and effectively integrate psychedelics into clinical practice.

Goals

The primary objectives of this project are to synthesize and critically evaluate the current evidence on the therapeutic potential of psychedelics in various health contexts, with a particular focus on neurodegenerative disorders like Alzheimer's and Parkinson's Disease. Specifically, this project aims to identify proposed mechanisms of action like serotonergic modulation, enhancement of brain-derived neurotrophic factor (BDNF), regulation of the mTOR pathway, and reductions in neuroinflammation that may underpin the observed or hypothesized clinical benefits.

Beyond mechanistic insights, the project seeks to assess the range of clinical benefits suggested by early studies, including improvements in mood, cognition, neuroplasticity, emotional resilience, and social connectivity. At the same time, the project emphasizes identifying outstanding risks, including perceptual abnormalities, ethical concerns around informed consent, and limitations arising from the translation of findings from non-patient samples or animal models.

By illuminating critical evidence gaps, inconsistencies across studies, limitations in current research designs, and the pressing need for standardized dosing regimens, validated outcome measures, and longer-term follow-up, this project intends to serve as a guide for designing future clinical trials. In addition, it explores potential market or industrial applications, evaluating how psychedelic treatments could be safely and ethically scaled for therapeutic use in emerging healthcare landscapes.

Methodology

This project employs a structured literature review approach, drawing on multiple scientific databases (like PubMed, JSTOR) to synthesize peer-reviewed studies published over the past 15 years. Emphasis is placed on examining a diverse range of conditions—Alzheimer's Disease and other dementias, Parkinson's Disease, obesity, and beyond—to understand how psychedelic interventions have been studied in controlled trials, observational studies, preclinical models, and qualitative research. Throughout this process, the methodology includes critical appraisal of study design, examination of ethical and regulatory contexts, and careful consideration of confounding variables and biases. Ultimately, this approach enables an integrative understanding of where the field stands, what remains uncertain, and how future research might produce more robust and clinically applicable findings.

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Progress to Date

The literature review has led to the identification and initial appraisal of key studies examining the potential therapeutic roles of psychedelics in various conditions. This includes research on Alzheimer's Disease and related dementias, Parkinson's Disease, obesity, and a range of other conditions where psychological, metabolic, and neurobiological dimensions intersect.

Preliminary analysis suggests that while promising mechanisms like enhanced neuroplasticity, potential anti-inflammatory effects, improved mood and social connectivity, and neuroprotective properties are frequently cited, substantial gaps remain in terms of robust clinical evidence, standardization of dosing, and long-term safety data.

A provisional categorization of the literature has been achieved, with sources separated into: (1) preclinical and animal studies, (2) human clinical studies, and (3) qualitative and ethnographic research. Across these categories, serotonin 5-HT2A receptor modulation has repeatedly emerged as a central mechanistic pathway potentially underlying therapeutic effects, suggesting a shared target for diverse applications.

One particularly important finding from the final phase of this review was the identification of research on non-hallucinogenic 5-HT2A receptor agonists. A landmark study (Cameron et al., 2020) demonstrated that through careful chemical engineering, it is possible to create analogues such as Tabernanthalog (TBG)—a non-hallucinogenic, non-toxic derivative of the psychedelic alkaloid ibogaine—that retains therapeutic properties such as promoting neuroplasticity and reducing addiction-like behaviors in animal models. This discovery highlights a critical future direction for psychedelic research: the development of compounds that can separate therapeutic benefits from hallucinogenic side effects, thereby improving the safety profile for vulnerable populations like those with neurodegenerative diseases.

Although no definitive conclusions can be drawn from existing clinical studies, the preliminary work completed through this review underlines the urgent need for more targeted, well-controlled, and ethically guided trials. Additionally, comparisons between conditions hint at the possibility of shared therapeutic pathways, particularly through serotonin receptor modulation, that may be of utmost importance for designing future interventions and translational research in neurodegenerative and psychiatric disorders

Further Steps

Building on the findings of this project, several future research directions are recommended. First, there is a need for the development and clinical testing of non-hallucinogenic 5-HT2A receptor agonists, such as Tabernanthalog, to evaluate their safety

and efficacy in treating neurodegenerative disorders like Alzheimer's and Parkinson's Disease. Future trials should prioritize standardized dosing protocols, longitudinal study designs, and validated outcome measures to assess both short- and long-term therapeutic impacts.

Additionally, greater emphasis should be placed on mechanistic studies that link psychedelic-induced neuroplasticity with functional clinical outcomes, using tools such as PET and fMRI imaging. Research should also investigate population-specific risk profiles, particularly among elderly patients with cognitive impairments, to ensure ethical and safe implementation. Finally, interdisciplinary collaboration between pharmacologists, neuroscientists, and clinical trialists will be essential to translate emerging findings into scalable, ethically sound therapeutic applications.

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Self-reflection

One of the primary challenges I faced during this internship was the lack of a well-defined project scope, which initially made it difficult to chart a clear research direction and avoid drifting into obscure, less relevant areas. To address this, I narrowed down a handful of focused topics and committed to exploring those, despite the company's evolving and sometimes uncertain research priorities.

The unstructured nature of the project also helped cultivate important soft skills, such as self-direction, critical thinking, and project management under uncertain conditions. Defining a clear and coherent scope independently, refining research questions iteratively, and maintaining consistent progress despite initial ambiguities were major personal milestones during this experience. Throughout the project, I developed several key hard skills, including the ability to critically appraise interdisciplinary scientific literature across pharmacology, neuroscience, and psychiatry.

The internship significantly contributed to my academic and professional development. I expanded my understanding of psychedelic applications beyond commonly explored areas like depression, uncovering their potential relevance to neurodegenerative and metabolic disorders. I am also pivoting myself to a research-oriented career in computational neuroscience and neuromodulation to study the pathology and etiology of neurological disorders. I am starting a PhD in Biomedical Engineering at the University of Toronto at the Translational Neurophysiology and Brain Stimulation Lab. This internship was a huge part of my decision to do so. For that, I am very grateful!