



Psilocybin-Based Breakthroughs in Natural Medicine

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Abstract

Nature created a mushroom-based compound known as psilocybin that can biochemically alter perception and affect mental anguish. Medical research shows that psilocybin activates the brain, engendering new cognition and awareness. Although psilocybin usage dates to ancient times, its contemporary medical usefulness is still in its infancy. This review discusses a potential breakthrough in natural medicine; psilocybin-based therapy may be a life-changing experience bringing hope to many suffering from mental anguish based on emotional and physical pain.

Introduction

Kosentka et al. [1] teach that ancient civilizations relied upon natural remedies to overcome physical ailments and attain spiritual enlightenment through the naturally-occurring pharmacopeia found in fungi. Conventional medicine continues the herculean effort to evaluate fungi (i.e., psilocybin-based mushrooms) to improve mental health and well-being. Research shows that psilocybin activates the brain, engendering new cognition and awareness. Rediscovering the benefit of psilocybin is both enlightening and fascinating. The catalytic effect of psilocybin micro dosing can induce acceptance and cooperation with others to provide a greater sense of well-being. Studies indicate that psilocybin-assisted therapy often has an ego-dissolution impact that can support a feeling of universal connection and intimacy. Furthermore, a medical breakthrough for psilocybin may be its use for those suffering traumatic brain injuries from concussions. Research efforts continue to explore the potential of psilocybin to change the mind and its processing pathways beneficially.

Discussion

Depression

Depression, or major depressive disorder, is a common and serious medical illness that negatively affects how one feels, thinks, and acts. Depression causes sadness and a loss of interest in formerly enjoyable activities. It can lead to various emotional and physical

problems and decrease one's ability to function at work and at home. Depression affects an estimated one in 15 adults (6.7%), and one in six people (16.6%) will experience depression at some time in their life [2].

Clinical trials demonstrate remarkable immediate and relatively long-lasting effects in mitigating depression's debilitating effects when patients combine psilocybin with "talk therapy."

Yasemin Saplakoglu [3] reports that the U.S. Food and Drug Administration (FDA) has designated psilocybin therapy — currently being tested in clinical trials — as "breakthrough therapy," an action to accelerate the typically slow process of drug development and review. It is frequently requested by a drug company and granted only when preliminary evidence suggests the drug may be an enormous improvement over already available therapy, according to the FDA. The FDA has given "breakthrough therapy" status to psilocybin therapy. For example, in the still-ongoing clinical trials run by Compass Pathways, which are looking into psilocybin's potential to treat severe treatment-resistant depression, i.e., patients who have not improved after undergoing two different antidepressant treatments. Now, the FDA has granted another "breakthrough therapy" status to the psychedelic treatment, this time for a U.S.-based clinical trial conducted by the nonprofit Usona Institute, according to a statement from the company. This clinical trial, which includes 80 participants at seven different sites across the U.S., focuses on the efficacy of treating

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patients with major depressive disorder (MDD) with a single dose of psilocybin. There are more than 17 million people in the U.S. who have MDD, or severe depression that lasts more than two weeks, according to the statement. Psilocybin, with a single dose, could profoundly impact the brain and have long-lasting impacts after wiping away depressive symptoms, according to the report.

Goldberg et al. [4] describe the experimental effects of psilocybin on symptoms of anxiety and depression. The meta-analysis examined the effects of psilocybin in combination with behavioral interventions on anxiety and depression in samples with elevated symptoms. Across three placebo-controlled studies, pre-post placebo-controlled results were also large and statistically significant; no serious adverse events occurred. Limitations include the small number of studies and the risk of bias within studies. Nevertheless, results support future research on psilocybin for treating anxiety and depression. Compared with traditional cognitive-behavioral psychotherapy and selective serotonin uptake inhibitor drugs, depressive patients respond relatively quickly to psilocybin treatments. Furthermore, their clinical response is relatively long-lasting; psilocybin-based mushrooms may provide sufferers with faster and more effective means of relief.

Suicidal ideation

Harmer et al. [5] teach that suicidal ideation, often called suicidal thoughts or ideas, is a broad term used to describe a range of contemplations, wishes, and preoccupations with death and suicide. While such ideations are often symptoms of patients with major depressive disorders, including bipolar disorder, suicidal ideation may occur in those with other mental illnesses and those with no diagnosed condition. Unfortunately, there is no universally accepted, consistent definition of suicidal ideation, leading to ongoing challenges for clinicians, researchers, and educators.

Jones & Nock [6] disclose that MDMA/ecstasy and psilocybin use are associated with lowered odds of psychological distress and suicidal thoughts in a sample of United States of America adults. They call for further study on the effects of psilocybin on patients tormented by suicidal ideation: Suicide is one of the leading causes of death worldwide, and rates within the United States have risen over the past two decades. This study aimed to assess non-causal associations between MDMA/ecstasy and classic psychedelic use and psychological distress and suicide risk. The researchers examined the associations among 484,732 adult participants in a National Survey on Drug Use and Health. The researchers concluded that MDMA/ecstasy and psilocybin use are associated with reduced odds of suicidal thinking. However, studies are needed to determine whether these associations are causal.

Considering its ability to reduce psychological distress, psilocybin-assisted therapy, replete with integration strategies, holds tremendous potential in emotion-focused coping—that is, actively changing one’s relationship with negative emotions and their sources.

Post traumatic stress disorder (PTSD)

PTSD is a psychiatric disorder that may occur in people who have experienced or witnessed a traumatic event such as a natural disaster, severe accident, terrorist act, war/combat, or rape. Also, those threatened with death, sexual violence,

or severe injury. PTSD has been known by many names, such as “shell shock” during World War I and “combat fatigue” after World War II, but PTSD does not just happen to plague combat veterans. PTSD can occur in all people of any ethnicity, nationality, culture, and age. PTSD affects approximately 3.5 percent of U.S. adults annually, and an estimated one in 11 people will be diagnosed with PTSD in their lifetime. Women are twice as likely as men to have PTSD. Three ethnic groups – U.S. Latinos, African Americans, and American Indians – are disproportionately affected and have higher rates of PTSD than non-Latino whites. People with PTSD have intense, disturbing thoughts and feelings related to their experience that last long after the traumatic event. PTSD victims may relive the event through flashbacks or nightmares; they may feel sadness, fear, or anger and may feel detached or estranged from other people. People with PTSD may avoid situations or people that remind them of the traumatic event, and they may have strong adverse reactions to something as ordinary as a loud noise or an accidental touch [7].

Although patients can benefit from specialized therapy, including trauma-focused behavioral therapies, PTSD is not curable. The potential for symptoms to recur is often likely. Conventional exposure-based treatments and synthetic drugs have not relieved the fear-based, traumatic memories that dysregulate PTSD patients. An urgent need exists to explore new therapies for this debilitating disorder. The targeted use of psilocybin and other psychotherapeutic treatments may hold immense value in addressing neurotransmitter trajectories and brain circuits in recovery from this chronic illness. In the service of synaptic plasticity and identifying and extinguishing loci of fear, psilocybin-assisted therapy offers new hope for patients suffering from recurrent traumatic memory.

Krediet et al. [8] reviewed the potential of psychedelics for the treatment of PTSD. The researchers teach that classical psychedelics such as psilocybin and LSD have shown promising results for treating a variety of psychiatric indications. However, clinical trials focusing on the treatment of PTSD are still lacking. Nevertheless, observations from clinical use in the previous century suggest a significant potential for treating PTSD. Their potential may benefit from stringent patient selection, lower doses, and specifically structured settings. In addition, clinical observations suggest that classical psychedelics are advantageous after patients have previously experienced MDMA.

Reno [9] describes how psychedelic drugs are helping veterans and others with PTSD and depression. Reno teaches that despite what some see as growing evidence that psychedelics can positively treat people with PTSD and other psychological conditions, Veterans Health Administration (VA) officials haven’t given them much attention. Gary J. Kunich communicated that the use of psychedelic treatments such as MDMA-assisted psychotherapy and psilocybin-assisted psychotherapy is “not part of the standard of care for treatment of mental health conditions at the VA and is not an approved clinical treatment.” He added that the use of psychedelics as part of a research protocol might be permissible, “but this would require Institutional Review Board and Research and Development Committee approval at the local facility.” He continued, “The Veterans Health Administration Office (VHA) of Mental Health and Suicide Prevention is closely monitoring the developing scientific literature in this area.” When

considering evolving scientific literature around innovative mental health treatments, Kunich said, the VA looks for outcomes from “rigorous and well-designed clinical trials” and things such as FDA approval or recommendations in clinical practice guidelines. “When implementing a new, evidence-based mental health treatment, VA puts the safety of veterans first and foremost,” he said. While the VA hasn’t endorsed any psychedelics or funded any trials at the federal level, several individual VA hospitals have begun looking at psychedelics as a possible treatment alternative. “The VA is lagging way behind concerning psychedelics,” said Rick Doblin, Ph.D., the founder, and executive director of the Multidisciplinary Association for Psychedelic Studies (MAPS). “Most veterans believe that the VA should be the active voice for veterans. If some treatment can help the veteran, they should be first to study it,” Doblin told Healthline. “But that is not the case. Much of the funding has been from private donors.” Doblin, who received his doctorate in public policy from Harvard’s Kennedy School of Government, wrote his dissertation on the regulation of psychedelics and cannabis for medical use. His professional goal is to change the public’s perception of psychedelics. He supports the development of psychedelics as prescription medications and for personal growth for otherwise healthy people.

Loneliness

Loneliness is a state of disconnectedness from companionship and other forms of social networking. Loneliness is more a function of meaningful relationships in that an individual surrounded by people may still suffer from loneliness. While loneliness is often related to a lack of significant people in one’s life, more commonly, loneliness happens to those with many social connections.

Sparks [10] teaches that while different forms of loneliness exist—emotional, social, situational—chronic loneliness occurs over time, i.e., it becomes a way of life that often requires intervention. When the mind is locked alone inside, we feel vulnerable and unable to forge deeper connections. In this state, we feel as if we are facing the world’s trials alone.

Studies point to the effect of loneliness as a serious public health issue. For example, in 2019, a national survey conducted by Cigna Health showed that 61 percent of all Americans report feeling lonely [11]. In addition, the Covid-19 pandemic, whose protocols include protracted periods of quarantine and social isolation, has had disastrous social implications for humankind globally.

Panchal et al. [12] conducted a 2020 study observing people aged 50 and over across 26 European countries. Among them, 64 percent of those experiencing depressed moods and 73 percent experiencing anxiety symptoms said their symptoms worsened during the pandemic.

Yet, the most brutal hit appears to be young adults. For example, Vahratian et al. [13] showed that some 63 percent of American teenagers surveyed reported experiencing substantial symptoms of anxiety and depression.

Psilocybin dramatically increases explicit and implicit empathy; it forges powerful feelings of social connection. Main [14] teaches that psilocybin can decrease the pain of social exclusion. The author notes that psilocybin increases subjective feelings of interconnection with the environment and others, which may lead to more substantial and more empathetic connections between people.

Memory Effect

Zlotnik & Vansintjan [15] teach that memory is simply the repository capacity for storing and retrieving information. In the collective sense, “memories” tend to allude to past events perceived as symbolic and subjective. By contrast, “memory” refers to general information storage, including DNA, digital information storage, and neurochemical processes.

The active ingredients in psilocybin catalyze a dynamic response in associative ideations and memory retrieval. It is these qualities that harness tremendous potential when visited in therapeutic settings. With contemporary emphasis placed on the power of neuroplasticity and resetting brain functions, researchers are poised to apply hallucinogens in clinical settings with great verve. Could psilocybin commensurately accelerate experts’ collective drive toward greater well-being? With caveats, preliminary evidence strongly suggests so.

Barrett et al. [16] teach that psilocybin acutely alters the functional connectivity of the claustrum with brain networks that support perception, memory, and attention. The study used a pharmacological intervention to provide the first empirical evidence in any species for a significant role of 5-HT_{2A} receptor signaling in claustrum functioning and supports a possible role of the claustrum in the subjective and therapeutic effects of psilocybin.

Healy [17] shows a significant correlation between memory recall, memory, and vividness with psilocybin ingestion.

Well-being

Sinclair [18] teaches that well-being is comfort, good health, and happiness. It also includes how satisfied one is with life, how one perceives the ability to exert control in one’s daily affairs, and whether an individual feels a sense of purpose. Thus, well-being encompasses calmness, contentment, excitement, happiness, good physical health, joy, meaningful social relationships, and wonder.

It should come as no surprise that, in 2022, on a global basis, well-being is a trait that is increasingly difficult to find. Patrick [19] teaches that magic mushrooms and nature heal you and the planet. The author posits a solution to global malaise and writes that we live in a time of tremendous environmental challenges. Envisioning solutions to these issues are essential to our collective well-being and survival. Yet, for many people, we also live in a time of collective frustration as we become disenchanted with the lack of action to address this impending crisis. But there’s more here. Both magic mushrooms and nature decrease anxiety, offer enhanced meaning in life and general well-being, create mystical experiences, and inspire awe. As legendary psychedelic psychotherapist Stanislav Grof theorized, psychedelics are “non-specific amplifiers,” meaning they work by expanding whatever state one’s psyche is already experiencing. So, a powerful synergy and connection become apparent when we understand the power of nature and psychedelics on our well-being.

Findings show a strong correlation between psilocybin ingestion and heightened well-being. Mason et al. [20] report that creative thinking and empathy are crucial for everyday interactions and subjective well-being. Anecdotal reports and recent studies suggest that a single administration of psilocybin can enhance such processes and be a potential treatment. Results indicated that psilocybin enhanced divergent thinking and emotional empathy the morning after use. Enhancements in convergent thinking, valence-specific emotional heart, and

well-being persisted seven days after use. Sub-acute changes in empathy correlated with changes in well-being. The study demonstrates that a single administration of psilocybin in a social setting may be associated with sub-acute enhancement of creative thinking, empathy, and subjective well-being.

Even bad trips on mushrooms may also impart silver linings for psychic well-being. Dolan [21] writes that 'bad trips' from magic mushrooms often result in an improved sense of personal well-being. The author discloses that new research suggests a bad trip isn't always bad. About 84 percent of drug users who have experienced a "bad trip" from hallucinogenic mushrooms say they benefited from the psychologically tricky situation. The study, led by Roland Griffiths of Johns Hopkins University, surveyed 1,993 adults regarding their worst "bad trip" after ingesting psilocybin mushrooms. More than 9 out of 10 participants had used psilocybin more than two times. The average dose that produced the bad trip was about 4 grams.

Most participants — 62 percent — said their lousy trip was among their lives' top 10 most psychologically tricky situations. Eleven percent said it was their number one most challenging experience. But 34 percent of participants said the bad trip was among the top five personally meaningful life experiences, and 31 percent said it was among the top five most spiritually significant. And 76 percent said the bad trip had resulted in an improved sense of personal well-being or life satisfaction. Forty-six percent said they would be willing to experience the lousy trip again.

Interestingly, the degree of psychological difficulty was statistically associated with beneficial outcomes. More complicated or challenging experiences are more valuable or meaningful. However, longer bad trips were associated with less beneficial results. The study also demonstrated that bad trips could have severe consequences. Eleven percent of the participants said they put themselves or others at risk of physical harm, while 2.6 percent reported behaving physically aggressively or violently; this related to longer, more challenging experiences in which the participant had little physical comfort or social support. About 3 percent reported seeking medical help. "Three cases appeared associated with the onset of enduring and impairing psychotic symptoms and three cases with attempted suicide," the researchers noted. The researchers said, "It is important to note that risks of dangerous behavior or enduring psychological problems are extremely low in laboratory studies of psilocybin with carefully screened, well-prepared participants who are supported during and after psilocybin administration.

Mood

A mood is a disposition to respond emotionally in a particular way that may last for hours, days, or even weeks, perhaps at a low level and without knowing what prompted the state. Moods differ from emotions in lacking an object; for example, anger can come from an insult, but an angry mood may arise when one does not know what one is mad about or what elicits anger [22].

Barrett et al. [23] teach that one of the most significant attributes of psilocybin use appears to be the positive effects of neuroplasticity, which are surprisingly long-lasting. The research indicates that acute psilocybin effects include reduced negative mood, increased positive mindset, and reduced amygdala response to negative affective stimuli. However, no study has investigated the long-term, enduring impact of

psilocybin on negative affect and associated brain function. Twelve healthy volunteers (7F/5M) completed an open-label pilot study, including assessments 1-day before, 1-week after, and 1-month after receiving a 25 mg/70 kg dose of psilocybin to test the hypothesis psilocybin administration leads to enduring changes in effect and neural correlates of effect. One-week post-psilocybin, negative affect and amygdala response to facial affect stimuli showed a reduction. In contrast, positive affect and dorsal lateral prefrontal and medial orbitofrontal cortex responses to emotionally conflicting stimuli increased. Furthermore, one-month post-psilocybin, negative affective and amygdala response to facial affect stimuli returned to baseline levels while positive affect remained elevated and reduced trait anxiety. Finally, the number of significant resting-state functional connections across the brain increased from baseline to 1-week and 1-month post-psilocybin. These preliminary findings suggest that psilocybin may increase emotional and brain plasticity, and the reported results support the hypothesis that negative affect may be a therapeutic target for psilocybin.

Valentino [24] discusses using the antidepressant escitalopram before receiving psilocybin-involved treatments. The author reports that MindMed has published the results of a study it sponsored to examine the interaction of the selective serotonin uptake inhibitor (SSRI) escitalopram with the acute response to psilocybin in humans. The study was a randomized, double-blind, placebo-controlled, crossover pharmacology study in healthy volunteers that the University Hospital Basel Liechti Lab conducted. Escitalopram was found pre-treatment to have no relevant impact on psilocybin's positive mood effects but significantly reduced negative consequences, such as anxiety and adverse cardiovascular reactions, compared with a placebo.

Inner Trust

Ikonn [25] describes inner trust as being connected to your inner self, knowing your values, vision, motivation, and beliefs in life on a profound level. Self-knowledge takes a great deal of continuous self-awareness and introspection.

The efficacy of psilocybin-assisted inner trust relies on a process of releasing and thereby providing relief from strong or repressed emotions. Because childhood trauma and repressed emotion are at the epicenter of chronic depression, anxiety, and drug addiction, psychedelics such as psilocybin offer more significant outcomes than conventional treatments after just one or two sessions. It is highly plausible that psychedelics may become the standard treatment for mental illness and addiction within the next few years.

In an interview published in Maclean's (2021) titled "Mark Messier on leadership, trust, and magic mushrooms," author Marie-Danielle Smith records her Q & A with a six-time Stanley Cup winner:

Q: You describe taking magic mushrooms at 19 as a transformative experience. Tell me more about how your perspective expanded.

Well, that's what it did for me. I had no idea the mind was that powerful. And how could eating a natural mushroom that was organically grown create that kind of stimulus? It turned out to be a fantastic experience, but more important was the question afterward: wow, how can I use my mind to empower myself to be a better player, to be a better person, to have more energy, to create a better aura? [26]

Mindfulness

Mindfulness is the ability to be fully present, aware of where you are and what you're doing, and not overly reactive or overwhelmed by what's happening around you. To achieve heightened consciousness and maximize one's psilocybin experience, pragmatics such as dosage, frequency, and setting are essential variables—and more so for the first-time user. In addition, a sense of physical and emotional security and safety is paramount for a positive or healing experience.

Madsen [27] disclosed a robust positive correlation between psilocybin, mood, and heightened states of mindfulness. The research shows that a single dose of the serotonin 2A receptor (5-HT_{2A}R) agonist psilocybin can have long-lasting beneficial effects on mood, personality, and potentially on mindfulness, but underlying mechanisms are unknown. The cerebral 5-HT_{2A}R binding did not change across individuals. Still, the negative association between changes in 5-HT_{2A}R binding and mindfulness suggests that individual change in 5-HT_{2A}R levels after psilocybin is variable and represents a potential mechanism influencing the long-term effects of psilocybin on mindfulness.

While the psilocybin experience, grounded in conscious intention, can release the effects of past trauma lodged in repressed memory, after-care therapy, known as the “integration phase,” brings much to bear on long-term relief from depressive or anxious states.

Psychedelic therapy helps reduce the likelihood of relapsing into a state of poor mental health and helps to maintain positive outcomes. Finighan [28] writes that many images, memories, and often cryptic messages surface during a psychedelic trip. It can be hard to make sense of them, but it is essential to consolidate these feelings and experiences through integration. Integration aims to implement lessons learned during a trip into our daily lives. In trials of psychedelic therapy, a follow-up talk therapy session is an integration tool to help patients achieve long-lasting transformations in lifestyle and mindset. Integration has a less rigid definition for those who take psychedelics in pursuit of enjoyment or self-understanding. Some will journal or write poetry about their experience. Others will seek guidance from friends or a counselor. Mindfulness is not just helpful during a trip, but it may hold promise as an integration tool. Bringing attention to the mind and body during mindfulness is a grounding experience. After an eventful psychedelic journey, this could help us re-center our thoughts and confront emotions from the psychedelic experience without judgment. Mindfulness can improve emotional resilience with sustained practice, making us more equipped to deal with negative emotions.

Psilocybin-Assisted Therapies

A therapy-assisted psilocybin experience adds validity to mental health interventions because a caring and thought-provoking perspective can increase self-awareness and healing.

Robertson [29] teaches that psychedelic-assisted psychotherapy is a type of psychiatric practice involving ingesting a psychedelic substance and talk therapy. Psilocybin, the main compound in magic mushrooms, has shown positive results in treating depression and anxiety in people with terminal illnesses. The first step is usually an initial consultation to discuss your background and any goals or concerns about psychedelic therapy and ensure that you don't have any contraindications to the treatment. The second phase involves ingesting, either orally or via injection,

the psychedelic substance under the supervision of a trained therapist. Psilocybin therapy typically involves at least two sessions. The final phase is the integration process when the therapist and client work together to integrate meaning from the psychedelic experiences. There's still a lot to learn about the potential of psychedelic therapy, but the existing research is promising, particularly for those with severe PTSD. Because of this, advocates and lobbyists are working to decriminalize some psychedelic substances to improve access and research opportunities.

Tullis [30] reports on the rapidly-changing status of psilocybin-assisted therapies in treating the most recalcitrant of mental disorders: Once dismissed as the dangerous dalliances of the counterculture, these drugs are gaining mainstream acceptance. Several states and cities in the United States are legalizing or decriminalizing psilocybin for therapeutic or recreational purposes. And respected institutions such as Imperial; Johns Hopkins University in Baltimore, Maryland; the University of California, Berkeley; and the Icahn School of Medicine at Mount Sinai in New York City have opened centers devoted to studying psychedelics. Regulators will soon grapple with how to safely administer powerful psychedelics for treating depression and post-traumatic stress disorder. Psychedelic-assisted psychotherapy could provide needed options for debilitating mental health disorders, including PTSD, major depressive disorder, alcohol use disorder, anorexia nervosa, and more. These disorders kill thousands yearly in the United States and cost billions worldwide in lost productivity. In scarce instances, psychedelics such as psilocybin and LSD can evoke a lasting psychotic reaction, more often in people with a family history of psychosis. Those with schizophrenia, for example, are excluded from trials involving psychedelics as a result.

Music Therapy

Music therapy aims to enhance the experience of using psilocybin and has been found to influence psychedelic therapy significantly. The premise behind the method is that music is a profound emotional catalyst that may promote memory enhancement, improved communication, and the expression of feelings. While music rivets our attention positively, it diverts the mind from compulsivity, distress, and anguish. Music also activates cognition, primarily through the renaissance of associative memory.

Musical experiences are encoded, stored, and retrieved in the brain's auditory cortex. The therapeutic process aims to capitalize on this ability to free up more emotional, relationship-centered ways to communicate. In therapy, clients select musical pieces to sing, move, or listen to; they may create their compositions, play instrumental accompaniment, or discuss the semantics of lyrics. In tandem with psychedelic therapy, music may shape the trip experience by supporting the period leading up to the peak experience.

O'Callaghan et al. [31] discuss the potential place of music in therapeutic settings: Further understanding of participants' idiosyncratic and shared responses to music during drug therapy phases will inform the optimal development of flexible music protocols which enhance psychedelic therapy. Music therapists could be involved in the psychedelic therapy research renaissance by assisting with research to optimize music-based protocols used. If psychedelics become approved medicines, music therapists may be interested in offering psychedelic therapy as part of therapeutic teams.

Shapiro [32] outlines the organizational schemata in which music correlates with the patient's therapeutic drug session: The playlist is in segments: background music that plays as the participant arrives for their session, music that plays when the drug is starting to take effect, at which point they are lying down and wearing eyeshades and headphones; the ascent; the peak; the post-peak; and the "welcome back" music. There are usually two researchers in the room, referred to as guides, who simultaneously listen to the playlist through speakers.

Music therapy and music psychology are multi-disciplinary sciences that draw from musicology, psychology, acoustics, sociology, anthropology, and neurology. These epistemologies converge in treating those afflicted with depression, anxiety, and cognitive disorders. In tandem with verbal and pharmacological therapies, music therapy's unique blueprint caters to personalized wellness whereby the client co-creates their auditory template by narrowing attention, heightening concentration, and forging cerebral pathways toward transcendence.

In short, music accentuates emotions that surface during therapeutic psilocybin sessions. Haghorn [33] writes that pairing psilocybin with music may be a helpful depression treatment. Psilocybin enhanced the emotional response to music compared to the reaction before taking the drugs. This multi-sensorial approach has yielded relief for people of all ages who suffer from developmental and learning disabilities, Alzheimer's patients, substance abuse problems, brain injury, and chronic pain.

Couple Therapy

In couple therapy, the same therapist treats both partners simultaneously. Couple therapy communicates problems within and between individuals that affect the relationship. For example, one partner may have undiagnosed depression affecting the relationship, or both partners may have trouble communicating effectively [34].

Even in the best circumstances, relationships present challenges, as human nature consists of egoic desiderata that can clash and conflict with those of significant others. Over time, individual vested interests can easily dig entrenched defense posts deeply grounded in resentment, alienation, and, at worst, violent exchange. When differences become dangerous to the continuance of matrimony, couples seek therapy. Strategies include behavioral modifications to defray experiential wounds, mistrust, boredom, and deep-seated pain. As individuals draw on defense mechanisms such as silence and manifestations of frustration and anger to protect themselves, couple therapy is a daunting project. If divorce rates are a litmus test to success, it follows that marriage counseling is a 50-50 crapshoot. A prolonged healing effort occurs as minds become entrenched in egoic perceptions and limits. Brain circuitry becomes hard-wired in the service of ego gratification. Stalemate inscribes stalemate. Where to turn when conscious behavioral modifications fail to reimagine copacetic compromise?

To complement conventional couple therapy techniques, the regulated use of psilocybin may proffer solutions by blazing empathic neuron pathways that would liberate negative perseveration. Opening the heart and mind to compassion and empathy is one of the most laudable hallmarks of psilocybin protocols.

In an article published in GQ (2021) titled "The Case for Psychedelic Couples Counseling," author Gabriella Paiella writes: Gumpel is a licensed clinical social worker with over 25 years of experience as a couple's therapist. She also works for

Fluence, an organization that trains therapists to incorporate psychedelic integration in their practices. She doesn't (and can't legally) recommend or administer MDMA or psilocybin to her clients, but if they approach her saying they're planning on trying it, she'll help them prepare for the journey. Then, after they've tripped, they'll come back and incorporate their findings—which, she says, are "very profound very often"—into their ongoing work [35].

Psilocybin can be life-altering once it changes immutable mindsets. The shared intentions of "magic mushroom" ingestion in pursuit of empathic enhancement, the forging of neuro-epigenetic pathways, the potential for euphoria, ensuing therapeutic debriefing sessions, and the intensification of renewed couple's commitment may be special tools in the hands of progressive counselors.

Sex Therapy

Holland [36] teaches that sex therapy is talk therapy designed to help individuals and couples address medical, psychological, personal, or interpersonal factors impacting sexual satisfaction. The goal of sex therapy is to help people move past physical and emotional challenges to have a satisfying relationship and pleasurable sex life. Sexual dysfunctions are common. For example, 43 percent of women and 31 percent of men report experiencing some sexual dysfunction during their lifetimes.

Aaron [37] writes that the current research on psilocybin is promising for sex therapy. While no studies look directly at the possible impact psilocybin might have on sexuality, research suggests that there might be several applications in sex therapy. Psilocybin reduces or eliminates existential anxiety and distress and increases openness (increased capacity for fantasy, appreciation of aesthetics and feelings, and increased tolerance). Aaron says, "My friend and colleague Dr. Katherine Maclean, a research scientist who has studied psilocybin extensively, was able to show that even a single session with psilocybin that occasioned a mystical experience in the user could change personality traits instantly and more profoundly than occurs over a decade in an average adult. Given my knowledge of this research and my sex therapy work, I believe psilocybin can assist with body image issues, sexual performance-related anxiety, and feelings of shame. Clients may experience a sense of entitlement to pleasure and experience an increased ability to be present with pleasure."

Magolin [38] reports that psilocybin can confer intimacy and intensity that can promote sexual healing: "Sex, like everything else on psychedelics, is amplified," says Neal Goldsmith, a New York-based psychologist and author of *Psychedelic Healing*. "Psychedelics enhance what is already there; they put you in touch with reality with greater clarity and intensity than you generally experience." Because, he says, "sex is so different from everyday walking life, such as going to the grocery store," or making sandcastles for that matter, sex on psychedelics could also be exceptionally "emotional, visceral, hormonal, or psychological." But that is not to say there is no risk involved; the intention is as vital to your safety as the setting is, whether you are aiming to heal from sexual trauma or to connect with a loved one.

Parenting Therapy

Parenting practices worldwide share three primary desires: to ensure children's health and safety, prepare offspring for productive adulthood, and transmit cultural values. Therefore, a high-quality parent-child relationship is critical for healthy development [39].

Azoulay [40] discusses the unique role of psilocybin in treating early childhood trauma in the service of healthy parenting: The Brooklyn Psychedelic Society hosted a “Plant Parenthood” event to educate moms and dads on how psychedelics can make a person a better — and more present — parent. Psychedelics help people battling depression and anxiety by disrupting ruminative thought patterns and enabling people to connect more deeply to the world around them. Several parents at the “Plant Parenthood” event said that psychedelics had helped them overcome childhood trauma and keep it from interfering with how they now relate to their children.

Psilocybin-assisted parenting encompasses learning to communicate better with others to make it a life-affirming experience. Pleger [41] discusses how psychedelics can help to be a parent. Jonathon Thompson says, “The good is that being open about my use of these substances has introduced me to some of the highest caliber people that I have the opportunity to know and allowed me to rather quickly build an intense connection with many people. Coming out — really being open — has allowed me to have amazing conversations with people in the broader psychedelic community”.

Pregnancy

Pregnancy, when a fetus develops inside a woman's womb or uterus, usually lasts about 40 weeks or just over nine months, measured from the last menstrual period to delivery. Although psilocybin ingestion is not adequately studied, current advice unequivocally warns against its usage in pregnancy. Because the chemical can pass through the blood barrier via the placenta, the fetus's natural development may increase the chances of stillbirth or physical defects [42].

Schaefer et al. [43] discuss drugs during pregnancy and lactation. The authors caution that pregnant women should avoid hallucinogens under all circumstances.

Childhood Trauma Therapy

Studies indicate strong correlations between adverse childhood experiences (ACEs), which comprise traumatic childhood events, and lasting effects on subjects' long-term health and well-being. Childhood trauma, including physical and emotional abuse and neglect, and childhood sexual abuse, can lead to emotional dysregulation and the adult onset of chronic diseases. These include heart disease, depression, PTSD, drug abuse, violence, and victimization [44].

Shame is an adverse childhood experience. Shame, or negative self-judgment, instills worthlessness, emptiness, and alienation. Shame becomes a catalyst for self-destructive behaviors, such as persevering, self-recrimination, self-neglect, narcissism, and suicidal ideation or attempts in worst-case scenarios. Because toxic shaming occurs during early childhood, it is as deep-seated as one's sense of identity frequently fraught with anxiety, anger, and self-loathing. Untreated adult victims of ACEs develop dysfunctional coping methods, often hurting themselves and others.

The therapeutic use of psychedelics in regulating the effects of ACEs shows promise and hope for adult victims. Dolan [45] describes early childhood shame's debilitating and cyclical role as it inflicts on parenting: Researchers found that child maltreatment was associated with higher levels of both posttraumatic stress symptoms and internalized shame. Notably, the researchers found that reporting more than five occasions of intentional therapeutic psychedelic use weakened the relationship between emotional abuse/neglect and disturbances in self-organization. The findings suggest

that using psychedelics with therapeutic intentions, even in non-clinical settings, may help reduce internalized shame and complex trauma symptoms in people with childhood trauma histories.

Healy et al. [46] teach that using psychedelics with therapeutic intent is associated with lower shame and complex trauma symptoms in adults with histories of child maltreatment. Moreover, the research shows positive results with difficult trauma symptoms in relatively short order: A history of more than five occasions of intentional therapeutic psychedelic use significantly moderated the relationship between emotional abuse and neglect and complex trauma symptoms.

Cancer Therapy

Cancer is a disease in which some of the body's cells divide, grow uncontrollably, and spread to other body parts. The human body has trillions of cells, and cancer can start anywhere. Human cells grow and multiply through cell division to form new cells as the body needs them. When cells grow old or become damaged, they die, and new cells take their place. Sometimes this orderly process breaks down, and abnormal or damaged cells grow and multiply when they shouldn't. These cells may form tumors, which are lumps of tissue. Tumors can be cancerous or benign. Via the process known as metastasis, cancerous tumors spread into or invade nearby tissues and can travel to distant places in the body to form new tumors by metastasis [47].

Ross et al. [48] show acute and sustained reductions in loss of meaning and suicidal ideation following psilocybin-assisted psychotherapy for psychiatric and existential distress in life-threatening cancer. The researchers concluded that people with advanced cancer are at heightened risk of desire for hastened death, suicidal ideation, and completed suicide. We conducted a randomized controlled trial in which psilocybin-assisted psychotherapy (PAP) produced rapid and sustained improvements in depression, demoralization, and hopelessness in cancer patients. Exploratory analyses support our hypothesis and suggest that PAP may be an effective anti-suicidal intervention following a cancer diagnosis due to its positive impact on hopelessness and demoralization and its effects on meaning-making. These preliminary results implicate psilocybin treatment as a potentially effective alternative to existing antidepressant medications in patients with cancer with elevated levels of depression and suicidality.

Sharping [49] teaches that psilocybin brings much-needed relief. However, the author highlights advanced treatment challenges: Research Hindered by Ban. These powerful, surreal experiences of psilocybin and other drugs like it were banned in the late 1960s after a rash of largely unfounded reports emerged, painting the drugs as highly dangerous (i.e., schedule-I drugs, the same class as heroin) and halting research. Before the ban, hundreds of studies showed the potential medical benefits of psychedelic drugs, including their use in treating alcoholism, depression, and obsessive-compulsive disorder, among other things. For researchers to conduct similar studies now, it requires wading through reams of paperwork and jungles of red tape. As a result, studies are small because obtaining these drugs is difficult.

Hospice-Care Therapy

Hospice is a special kind of care that focuses on the quality of life for patients and their caregivers experiencing an advanced, life-limiting illness. Hospice care provides compassionate care for people in the last phases of incurable disease so they can live as fully and comfortably as possible [50].

Gordon [51] reviews psilocybin therapy for emotional suffering caused by terminal illness. The author advocates for the integration of Psilocybin as part of end-of-life palliative care: The medical community has made significant progress in developing treatments to extend life. It has also created new medical fields devoted to treating the pain and suffering associated with debilitating or terminal diseases. End of Life Washington recognizes the evolution of palliative care as an essential contributor to the quality of life at its end. Therefore, we support efforts to legalize psilocybin therapy for depression and anxiety experienced by terminally ill individuals. Studies show that psilocybin therapy effectively relieves emotional and existential distress at the end of life for 65-85% of terminally ill people in clinical trials when administered properly. Furthermore, there are no lasting adverse effects and many significant and enduring positive benefits. These findings fit in with the goals of palliative care, which integrates the psychological and spiritual aspects of patient care; enhances the quality of life.

The National Institute of Health (2021) published a feasibility study that examines the effect of integrated psilocybin treatments within the hospice setting. This research study involves a combined drug/talk therapy intervention. This research study is a feasibility study; investigators examine psilocybin-assisted therapy in the context of hospice care. Psilocybin is an "Investigational" drug not approved by the FDA as a treatment for any disease. However, the FDA has granted Psilocybin the status of "breakthrough therapy" in treating depression, and the investigators have permission from the FDA to use this drug in this research study [52].

Alzheimer's Disease Therapy

Alzheimer's Disease is a brain disorder that slowly destroys memory and thinking skills and, eventually, the ability to carry out the simplest tasks. In most people with the Disease — those with the late-onset type symptoms first appear in their mid-60s. Early-onset Alzheimer's occurs between a person's 30s and mid-60s and is very rare. Alzheimer's Disease is the most common cause of dementia among older adults [53].

Vann Jones et al. [54] discuss psychedelics as a treatment for Alzheimer's Disease (AD). The authors write that research underscores the intractability of Alzheimer's treatments concerning symptom attenuation and the potential that psilocybin presents: After decades of repeated failure of treatments for dementia, there is an urgent need to develop new therapies for AD. The potential for psychedelic compounds to enhance cognition provides a new therapeutic target and a compelling argument for further investigation of the potential for psychedelics as a disease-modifying compound in conditions where currently none exists. Studies looking at both micro-dosing and psychedelic doses, longer-term, in cognitively impaired individuals are lacking and urgently needed.

George [55] asks, "Could Psychedelics Help Treat Dementia?" The author writes that in the absence of data, the promise of psychedelics is, at present, primarily speculative or theoretical. Much must be learned about proper dosages, safety and supervision protocols, ethics around consent, addressing adverse reactions, staff training, and other questions surrounding modern treatment regimens for these ancient compounds. We must also be cautious of market forces—companies, entrepreneurs, and bad actors with vested interests who excite treatments as quick-fix commodities. Thankfully, rigorous studies are happening internationally, and what we learn in the next decade should help light the path forward (or

not). In the meantime, we can still, as citizens, bring the arts into long-term care environments—and to our elder relatives in general—and help provide the "altered states" that we know are protective, enjoyable, and supportive of QOL for all of us.

Coma

Severe injury or illness can cause a person to go into a coma, a state of deep unconsciousness for a prolonged or indefinite period. For example, a comatose patient is unconscious and will not respond to voices, sounds, or contact. The patient is alive, but the brain is at its lowest alert stage. Typically, a coma can last a few days or weeks. However, a patient can be in a coma for several weeks, months, or even years in rare cases. In coma resurrection therapy, the goal is to safely bring the patient back to consciousness.

Lewis-Healy [56] asks, "Can psychedelic mushrooms jumpstart a comatose mind?" The author writes that Dr. Hyder Khoja hopes to treat coma patients with psychedelics to "jumpstart" them back into consciousness. Dr. Khoja highlights an issue with the connections in the brains of coma patients. Traumatic brain injuries that often underlie comas may have damaged the neural circuits that allow consciousness to arise. Those damaged circuits keep these patients locked in this state. But Dr. Khoja argues that psychedelics may be able to reignite these connections. He says this could be the secret to "jumpstarting" awareness and consciousness. While Dr. Khoja's idea is in its embryonic stages, other researchers theoretically support it. Neuroscientists from the Division of Brain Sciences at Imperial College London recently published a paper arguing that psychedelics can help treat these "disorders of consciousness." Individuals in a coma, under anesthesia, or in other reduced states of consciousness have brain signals lower in complexity than ordinary waking consciousness. But recent neuroscientific studies find that psychedelics reliably increase the "complexity" of brain signals. Within the paper, the researchers argue that this may allow patients to jump from a non-conscious to a conscious state. However, while theoretical research is there, it's hard to turn theory into practice, especially when working with coma patients. Furthermore, being comatose prevents people from providing informed consent, creating unethical terrain. The first step may be to use animal models with anesthetic, and then psychedelics can be administered to see if they're roused back into awareness.

Disorders of consciousness include coma (wherein a patient cannot be aroused, eyes remain closed), vegetative state (in which a patient can appear to be awake but unable to interact purposefully), and minimally conscious state (at which point a patient possesses minimal but definite awareness) [57].

Love [58] discusses that scientists want to try using shrooms to revive people in vegetative states. The author writes that one ethical concern is the self-awareness paradox. While the end goal is to restore consciousness, what if you make someone more aware of their situation by doing so? Awareness of their injury may inflict emotional or physical pain.

Traumatic Brain injury

Traumatic brain injury (TBI) is a sudden injury--a blow, bump or jolt to the head---that causes damage to the brain. This form of injury is known as a closed head injury. When an object penetrates or fractures the skull, the damage is known as a penetrating injury. TBI symptoms run the gamut from mild to moderate to severe. Concussions, for example, are a type of mild TBI. The effects of a concussion can sometimes be serious, but in time, most people completely recover. More

severe TBI can lead to severe physical and psychological symptoms, coma, and even death. Increasing focus on critical, high-profile cases from the sports world and the tragic effects of constant head battering suffered by football players, boxers, and mixed martial artists. The most alarming examples of TBI fall-out include incidents of such profound, unabated rage that have culminated in victims committing homicide and suicide. Degeneration of cells can lead to Alzheimer's, Parkinson's, and chronic traumatic encephalopathy. Survivors of severe TBIs are likely to suffer long-term affliction affecting their physical, cognitive, and behavioral ability to live independently. Compared to those who have not sustained brain trauma, victims of TBI life expectancy averages nine years shorter [59].

Recent medical research examines psychedelics' potential to alleviate TBIs' symptoms. Khan et al. [60] review psychedelics for brain injury. The authors write that scientists report that recent *in vitro*, *in vivo*, and case report studies suggest psychedelics may influence the future of brain injury treatment.

De Vos et al. [61] review the systemic unraveling of psychedelics and neuroplasticity. Research indicates that psychedelics induce molecular and cellular adaptations related to neuroplasticity and suggest those run parallel to the clinical effects of psychedelics, potentially underlying them. Future (pre)clinical research might focus on deciphering the specific cellular mechanism activated by different psychedelics. In addition, long-term clinical and biological effects may increase our understanding of the therapeutic potential of these compounds.

Gormally [62] discusses traumatic brain injury (TBI) and psilocybin. The author writes that The Center for Psychedelic Research at Imperial College London is partnering with the UK- and USA- based branches of the nonprofit Heroic Hearts Project (HHP); to explore the psychological and physiological effects of psilocybin (magic mushrooms) on veterans with a history of TBI. According to an article on Canex, the observational study will take place at retreats run by HHP starting in Fall 2021. The UK branch will run retreats in the Netherlands, and the US will run retreats in Jamaica. HHP prioritizes veterans who sustain head trauma during their service and veterans experiencing psychological difficulties. Therefore, this study aims to produce measurable outcomes regarding the psychological and physiological effects of psilocybin in TBI treatment.

Although still in their infancy, such studies on TBI disorders will focus on the protective properties of activating 5-HT_{2A} serotonin receptors catalyzed by psychedelics. These receptors are well-known regulators of inflammation within the central nervous system and peripherally. From a psychological standpoint, researchers are encouraged by the well-documented success of a psychogenic in the service of PTSD and depression rehabilitation. Future studies are promising as researchers explore how psilocybin and its metabolites manifest in the brain.

Migraines

Tucker [63] teaches that there are many disorders for which no known cures exist, and among the most common—and painful—are migraines. Excruciating, unbearable pain (like that of passing kidney stones or childbearing) results in as many as 25% of migraine sufferers contemplating suicide to relieve their agony.

A migraine headache can cause severe throbbing pain or a pulsing sensation on one side of the head, usually accompanied by nausea, vomiting, and extreme sensitivity to light and sound.

Migraine attacks can last for hours to days, and the pain can be so severe that it interferes with your daily activities. In addition, a warning symptom known as an aura can cause headaches for some people. An aura can include visual disturbances, such as flashes of light or blind spots, or other irritations, such as tingling on one side of the face or in an arm or leg and difficulty speaking [64].

Schindler et al. [65] discuss the migraine-suppressing effects of psilocybin. The research shows that psilocybin was well-tolerated; there were no unexpected or severe adverse events or withdrawals due to adverse events. This exploratory study suggests an enduring therapeutic effect in migraine headaches after a single administration of psilocybin. The separation of acute psychotropic and lasting therapeutic effects is an important finding, urging further investigation into the mechanism underlying the clinical effects of select 5-HT_{2A} receptor compounds in migraine and other neuropsychiatric conditions.

In an article from Neurosciencenews.com (2020) titled "Psilocybin Shows Potential as Migraine Treatment," it is written that a small-scale study conducted by researchers at Yale University reveals psilocybin appears to be effective in the treatment of migraine disorders. Previous studies have shown psilocybin's promise to treat migraines and cluster headaches. Still, most of the results have been anecdotal—the first study to compare the effects of psilocybin and placebo for treating chronic migraine. Ten participants were involved in this study. All subjects were required to monitor their headaches for two weeks and complete a "migraine diary" before starting the survey. During the double-blind study, participants received either a placebo or a low dose of psilocybin during two sessions, two weeks apart. Compared to the participants in the placebo group, those administered psilocybin treatments reported a significant decrease in migraine days one week after the first session [66].

Cluster Headaches

Cluster headaches, which occur in cyclical patterns or cluster periods, are one of the most painful headaches. Distinct from migraines, cluster headaches afflict approximately 1 out of 1,000 people. A cluster headache commonly awakens you in the middle of the night with intense pain in or around one eye on one side of your head. Bouts of frequent attacks, known as cluster periods, can last from weeks to months, usually followed by remission periods when the headaches stop. No headaches occur for months and sometimes even years [67].

Sewell et al. [68] show the response of cluster headaches to psilocybin and LSD. The research shows that eighty-five percent (85%) of psilocybin users had relief from attacks; fifty-two percent (52%) of psilocybin users and eighty-eight percent (88%) of LSD users reported cluster period termination. Ninety-five percent (95%) of psilocybin users and eight percent (80%) of LSD users said there was a remission period extension.

Yan [69] discusses that a team of Harvard University researchers conducted preliminary trials deploying psilocybin in cluster headache patients. Of the 19 patients surveyed, 17 found its use effective in arresting attacks altogether.

Concussions

A concussion is a traumatic brain injury caused by a bump, blow, or jolt to the head or by a hit to the body that causes the head and brain to move back and forth rapidly. This sudden movement can cause the brain to bounce around or twist in the skull, creating chemical changes in the brain and sometimes

stretching and damaging brain cells [70].

Post-concussion syndrome occurs when concussion symptoms last beyond the expected recovery period after the initial injury. Some experts believe persistent post-concussive symptoms are from structural damage to the brain or disruption of the messaging system within the nerves caused by impact. Others believe persistent post-concussive symptoms are related to psychological factors. The most common symptoms — headache, dizziness, and sleep problems — are like those often experienced by people diagnosed with depression, anxiety, or post-traumatic stress disorder.

In many cases, both physical damage from brain trauma and emotional reactions to these effects play a role in developing symptoms. However, some research shows that certain factors are more common in people who develop persistent post-concussive symptoms than in those who don't. These factors include a history of depression, anxiety, post-traumatic stress disorder, significant life stressors, a poor social support system, and a lack of coping skills [71].

Sports players—notably boxers and NFL football players—are particularly vulnerable to devastating, repeated brain trauma, often leading to brain degeneration. Cerebral damage from repeat injury results in the emission of tau proteins which accumulate in the brain as waste and aggregate as "tau tangles." Furthermore, cells continue to die years and sometimes even decades after the original injuries occur. Tau tangles are distinctive features in Alzheimer's disease and other forms of degenerative dementia. The evolving story of Daniel Carcillo, a two-time Stanley Cup winner turned mushroom entrepreneur, is inspirational and cutting-edge. Spiegel [72] writes about ex-NHL enforcer Daniel Carcillo who forges a new path using psychedelics to treat TBI and post-concussion syndrome. At age 30, the NHL enforcer was forced into early retirement in 2015 after his seventh diagnosed concussion. After 429 games spread over 11 seasons, capped off by his second Stanley Cup, his career was over. He spent the next four years trying to pull himself out of a debilitating battle with post-concussion syndrome that eventually drove him to be suicidal. "Everyday anxiety and depression lessened in intensity," he recalled about his symptoms after a psilocybin "ceremony," which is a guided and monitored psychedelic experience. "The third day I remember going out on the farm without glasses, which wasn't normal because my light sensitivity was extreme. And then I found myself FaceTiming my wife and my kids more often because I wanted to, I just couldn't wait to race back to hug them. I just felt more connected. I felt like my brain fog was lifting and just really remarkable, remarkable things in a very short amount of time." It was a life-changing moment for Carcillo. He started feeling better. His symptoms began to subside as he stayed on a specific protocol of loading doses (3-5 mg) and maintenance doses of psilocybin and other adaptogens. He underwent a qEEG (brain mapping) and re-did bloodwork — something he did after every new thing he tried over the years to see whether it was truly working — and this time it showed no abnormalities and that his bloodwork was clear. "That was a really big aha moment," he told Sporting News during a recent phone interview. "So, I dove into the science and realized that this could be the first novel care option for TBI survivors. Waited about a year till I got that second clear test and then I said, OK, this is enough data for me to start going public with this. And then I just started to put the pieces of the puzzle in place to make this a reality and build a championship team around me that I know how to play in." That championship team is part of a company Carcillo co-founded called Wesana

Health Inc., "an emerging life sciences company committed to patient empowerment and the advancement of psilocybin-based medicine to improve health and wellness." It closed on \$4 million in financing back in January and announced on March 31, the last day of Brain Injury Awareness Month, the successful closing of \$16.1 CAD million oversubscribed private placement ahead of completing its go-public transaction. Proceeds from the financing will be used primarily to fund the company's preclinical and clinical development of psychedelic-assisted therapy to treat TBI. They also announced Wednesday the addition of George Steinbrenner IV as a new investor who is joining the board of directors. "Tremendous advancements in science have finally given us the tools to recognize and better understand the consequences of traumatic brain injuries, especially those that occur often in professional sports," Steinbrenner said in the company's news release, citing how he's seen athletes in his sport (motorsports) deal with TBI. "It's critical that we continue to push forward in this field to deliver innovative treatment options that can help people recover from the neurological and psychological damage associated with that trauma." As things move forward with Wesana Health, the ultimate goal for the ex-NHL enforcer nicknamed "Car Bomb," who amassed more than 1,200 penalty minutes during his career, is to help people, to protect people, just like he did on the ice. He's spoken to TBI survivors for the past six years and understands what they're going through better than anyone. He understands how scary it is to face the unknown and the uncertainty. He's asked the same questions: Will I get better? Will I get back to who I was before the injury? How much longer will my symptoms last? When will it happen? How much longer do I have to suffer? Carcillo knows all about it because of his experiences playing professional hockey, and while he is focused on his new company and the work it's doing, he pointedly states that he is still going to hold the NHL accountable regarding its attitude toward concussions and brain injuries. "I'm not going anywhere," he said. "The reason that I know so much about concussions is because of them. So, like, honestly, I can say this, I can rest my head on the pillow, I am not upset at them. I am so thankful that they've acted and continue to act the way they do because it just continues to fuel me. And here we are on the cusp of bringing novel care options for TBI survivors. It's f— amazing." That option is for TBI survivors across the spectrum: athletes, veterans, domestic violence survivors. And Carcillo wants to show them that they too can get better, and that there's hope. He speaks passionately about psilocybin, because after years of suffering, after thousands and thousands of dollars spent, after reaching his breaking point, it changed his life for the better. But he is quick to stress that psilocybin is not a miracle drug — it just "shakes the snow globe" — and that a lot of work needs to be done in addition to its usage. And, he adds, that people need to wait for the science — yes, the research — to back-up everything he is saying. "They shouldn't listen to me. They really shouldn't," he said when asked why someone should follow his lead. "They should just wait till I do the work. I'm just telling my story. I don't need people to listen to me to validate it. This is why I'm raising hundreds of millions of dollars to go through the FDA process to validate what's happened to me. That's why we're here. That's why we're talking. This is just what I'm doing and I'm going to continue to do it because I know this is the way for TBI survivors. "And I will help people. My goal is to help a million people, and I will get that done before the end of my life" [71]. Carcillo's miraculous recovery included alternating psilocybin macro-and microdosing over 18 months. At that

point, a qEEG showed no brain abnormalities whatsoever. Along with Wesna Health Inc., Carcillo works on psilocybin decriminalization and furthering its therapeutic applications.

Chronic Pain

Pain starts in receptor nerve cells found beneath the skin and in organs throughout the body. When sick, injured, or having other problems, these receptor cells send messages along nerve pathways to the spinal cord, transmitting the message to the brain. Pain medicine reduces or blocks these messages before they reach the brain. Chronic pain persists for months or even years. As a result, chronic pain is one of the costliest health problems in the United States. Increased medical expenses, lost income, productivity, compensation payments, and legal charges are some of the economic consequences of chronic pain [73].

A longitudinal study, eagerly anticipated, may suggest that psilocybin's impact on neurochemical activity is the key to alleviating chronic pain by disrupting dysfunctional pathways as it reorganizes new ones.

Jones story: The pain in my feet was frequently very severe, debilitating, and chronic. I saw many specialists and used many prescription drugs and experienced little or no pain relief. I have consistently had pain-free evenings for the first time in many years; once I decided to try mushroom therapy, I felt this could be an option for patients with treatment-resistant chronic pain. I decided to try psilocybin mushrooms after I read about the use of psychedelics to treat psychological disorders. I learned that there was often great success compared to prescription drugs and interventional treatments [74].

Castellanos et al. [75] teach that the development of chronic pain is a complex mechanism that is still not fully understood. Multiple somatic and visceral afferent pain signals, when experienced over time, cause a strengthening of neural circuitry through peripheral and central sensitization, resulting in the physical and emotional perceptual chronic pain experience. The mind-altering qualities of psychedelics have been attributed, through serotonin 2A (5-HT_{2A}) receptor agonism, to "reset" areas of functional connectivity (FC) in the brain that play prominent roles in many central neuropathic states. Psychedelic substances have a generally favorable safety profile, especially opioids analgesics. Clinical evidence for their use for chronic pain is limited; however, over the past 50 years, several studies and reports have shown potential analgesic benefits in cancer pain, phantom limb pain, and cluster headaches. While the mechanisms by which the classic psychedelics may provide analgesia are unclear, several possibilities exist given the similarity between the 5-HT_{2A} activation pathways of psychedelics and the nociceptive modulation pathways in humans. Additionally, the alterations in FC seen with psychedelic use suggest that these agents could help reverse the changes in neural connections seen in chronic pain states. Given the current state of the opioid epidemic and the limited efficacy of non-opioid analgesics, it is time to consider further research on psychedelics as analgesics to improve the lives of patients with chronic pain conditions.

Bornemann et al. [76] discuss self-medication for chronic pain using classic psychedelics. The researchers concluded that pain scores improved substantially during and after psychedelic experiences across a range of psychedelic substances and doses. In addition, two processes, "positive reframing" and "somatic presence," play a role in improvements in mental well-being, relationship with pain, and physical (dis)comfort. The

inclusion of other strategies, such as mindfulness, breathwork, and movement, was also widely reported. Conclusion: This pre-trial PI work guarantees the confidence to test psychedelic therapy for chronic pain in a forthcoming controlled trial.

Rhodes [77] writes that psilocybin, MDMA, and other psychedelic drugs are growing in therapeutic interest and use – could they be game-changers in the pain management space, either for chronic conditions or their psychiatric comorbidities? "Given the current state of the opioid epidemic and limited efficacy of non-opioid analgesics," says Dr. Castellanos, "it is time to consider further research on psychedelics as analgesics to improve the lives of patients with chronic pain conditions."

Obesity

Obesity, a weight disorder, is defined as abnormal or excessive fat accumulation that presents a health risk. A body mass index over 25 is considered overweight, and a BMI over 30 is obese. The prevalence of obesity has grown to epidemic proportions: in 2017, over 4 million people died due to obesity. Rates of the deadly disorder continue to grow in both adults and children. From 1975 to 2016, the prevalence of overweight or obese children and adolescents aged 5–19 increased more than four-fold, from 4% to 18% globally [78].

Naftulin [79] writes about the correlation between weight loss, self-esteem, and self-actualization through psilocybin therapy. That's because psychedelics like psilocybin can change how information moves through the brain, decreasing negative thoughts, self-criticisms, and overwhelming feelings. A mindset change can positively affect a person's overall outlook and how they move about the world daily. Dr. C. Laird Birmingham, an eating disorder specialist and epidemiologist, is working with psychedelics research startup NeonMind to design a study that examines whether the trippy drug could be effective for weight-loss purposes. Psilocybin has the potential to serve as a new and different tool to help people lose weight and maintain their weight loss by changing neural pathways. Those neural changes could teach the brain to stop linking "life stress and trauma to eating behavior."

In a Press Release from NeonMind (2021) titled "NeonMind Files Four Additional Provisional Patents on Psilocybin Preclinical Data," it is written that the provisional patent applications include data derived from NeonMind's initial preclinical trial in November 2020, which examined the potential use of psilocybin as a treatment for weight loss. NeonMind's proprietary preclinical data shows that both low and high-dose psilocybin may reduce weight gain and that the reduction in weight gain can occur quickly. "We are encouraged with the preliminary results obtained from our preclinical trial," says NeonMind President & CEO Robert Tessarolo. "Through an expanded portfolio of patent applications, NeonMind is uniquely positioned to pursue exciting drug development opportunities in the underserved weight management market. So many solutions have been developed in the past that have disappointed; a new approach is desperately needed. We are actively building our capabilities to execute the critical phases of drug development needed to support new drug applications to the FDA" [80].

Anorexia Nervosa

Anorexia nervosa — often called anorexia — is a psychologically-based eating disorder characterized by abnormally low body weight, intense fear of gaining weight, and distorted weight perception. Anorexic individuals place a high value on controlling their weight and shape, using

extreme efforts that tend to interfere significantly, often drastically, with their lives. To prevent weight gain or continue losing weight, people with anorexia usually severely restrict the amount of food they consume. They may control calorie intake by vomiting after eating or by misusing laxatives, diet aids, diuretics, or enemas. They may also try to lose weight by exercising excessively. No matter how much weight is lost, the anorexic fears weight gain.

Anorexia isn't really about food. Instead, it's a highly unhealthy and sometimes life-threatening way to cope with emotional problems. When diagnosed with anorexia, they often equate thinness with self-worth.

Anorexia, like other eating disorders, can take over one's life and be exceedingly difficult to overcome.

Successful outcomes include:

- Gaining a better sense of self-worth.
- Returning to healthier eating habits.
- Reversing some of anorexia's deadly complications.

Because, to date, no pharmacological protocols exist for anorexia, the medical industry is desperately seeking ways to heal this devastating psychiatric disorder [81].

Spriggs et al. [82] study psilocybin as a treatment for anorexia nervosa. The researchers teach that anorexia nervosa (AN) is a severe and life-threatening psychiatric condition. With a lack of approved therapies, there is a desperate need for novel treatment avenues to be explored. Here, we present (1) an overview of the ways through which Public Patient Involvement (PPI) has informed a trial of psilocybin-assisted therapy for AN and (2) a protocol for a pilot study of psilocybin-assisted therapy in AN currently underway at Imperial College London. The study aims to assess the feasibility, brain mechanisms, and preliminary outcomes of treating anorexia nervosa with psilocybin.

In a clinical trial published by the NIH (2020) titled "Psilocybin as a treatment for anorexia nervosa: a pilot study," the authors state unequivocally that anorexia nervosa is the most fatal of all psychiatric conditions. With the current lack of effective pharmacological and psychological treatments, and fewer than half of those diagnosed making a full recovery, there is a great need for new treatment avenues to be explored [83].

Obsessive-compulsive disorder

Obsessive-Compulsive Disorder, or OCD, is a common, chronic, and long-lasting disorder in which a person has uncontrollable, reoccurring thoughts—obsessions--- and behaviors—compulsions---that they feel the urge to repeat over and over. Because people with OCD may have obsessions, compulsions, or both, these symptoms can interfere with all aspects of life, including work, school, and personal relationships. Habits are repeated thoughts, urges, or mental images that produce anxiety.

Common symptoms include:

- Fear of germs or contamination.
- Unwanted, forbidden, or taboo thoughts involving sex, religion, or harm.
- Aggressive thoughts towards others or self.
- Arranging items symmetrically or in patterned, perfect order.

Compulsions are repetitive behaviors in response to obsessive thoughts. For example, common compulsions include excessive cleaning and handwashing, ordering and arranging things with utmost precision, constantly checking on things,

repeatedly checking if the door is locked or the oven is off, and repetitive counting [84].

Lugo-Radillo et al. [85] describe the long-term amelioration of OCD symptoms in patients who chronically consume psilocybin-containing Mushrooms. The research showed a clinically meaningful reduction of OCD symptomatology after consuming psilocybin-containing mushrooms. Future research will determine if psilocybin and other psychoactive compounds of psilocybin-containing mushrooms are effective and safe for treating OCD.

In a communication published in BrainWays titled "Psychedelics and OCD," the authors suggest that traditional pharmacological drugs such as SSRIs are not effective as they might be: Yet, with popular solutions such as SSRIs achieving a modest remission rate and many patients with OCD considered treatment-resistant, experts are turning to less conventional options, discovering how the interplay between psychedelics and OCD may yield more significant relief for patients. For OCD, a critical advantage that psychedelic treatment offers is letting go. On a theoretical level, since OCD seems to revolve around the inability to relinquish control over one's mind in the face of adverse thought content, it makes sense to circumvent the mental structures placed in one's mind, via defense mechanisms and automatic thinking, with a drug that reaches deep within one's unconscious. That said, psychedelic mental health research—and particularly psychedelic OCD research—is still in its infancy, and much more needs to be verified before it can be considered a broad alternative to current, first-line OCD treatments such as SSRIs and CBT. All psychedelic drug treatment options should be carried out in a safe environment and administered by a licensed mental health professional with experience in this form of therapy. Studies have cited that psilocybin can cause immediate improvement in OCD severity instead of the weeks it usually takes for SSRI medication to take effect. In addition, psychedelics alleviate OCD symptoms of doubt and rumination. Such results can, for example, allow patients with OCD to go about their day without an unending concern over whether they locked their front door or over the chance of catching an infection from using a public toilet. Psilocybin is safe and well-tolerated, somewhat contradicting its more concerning reputation as a psychedelic. That said, it can cause specific side effects. These include panic, paranoia, drowsiness, anxiety, and psychosis—also known as a "bad trip." Due to these and other possible side effects, patients with a history of bipolar disorder, mania, or psychosis are discouraged from treating their OCD with psilocybin [86].

Conclusion

Psilocybin may provide effective treatment for mental anguish and is safe when administered by trained medical professionals. Foremost, when mental anguish severely diminishes one's quality of life and the lives of those within proximity, one may consider psilocybin-assisted therapy.

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Conflicts of interest

The authors declare no conflict of interest..

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