UNCOVERING THE UNTAPPED POTENTIAL OF PSILOCYBIN THERAPY IN ALLEVIATING CANCER-RELATED DEPRESSION: AN URGENT CALL TO RE-EVALUATE TREATMENT STRATEGIES

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Schedule I controlled substances, as categorized by the US Department of Justice – Drug Enforcement Administration, are highly addictive compounds with no experimentally proven medical benefit, whose production, sale, and use are punishable by law (Drug Scheduling, 2023). This characterization, albeit necessary, often limits researchers from exploring the therapeutic potential of these drugs while simultaneously creating a stigma around them among the general population. In recent years the use of the Schedule I substance, psilocybin, as a treatment for cancer-related mood disorders, namely depression and anxiety, has faced controversy despite strong clinical evidence of its benefits (Lowe et al. 2022). Interestingly, the debate surrounding the use of psilocybin therapy shows stark similarities to that of the use and legalization of medicinal marijuana for Parkinson's disease.

Psilocybin is a natural tryptamine that affects the biochemical and metabolic pathways of the neurotransmitter serotonin. Its use falls under psychedelic drug-assisted psychotherapy, which, during the 1960-1970s (prior to schedule I classification) was under exploration as an intervention for the abovementioned mood disorders (Hristova & Perez-Jover 2023). It is reported that 40% of cancer patients suffer from a mood disorder for which currently recommended treatments (antidepressants, benzodiazepines, and psycho-therapy) show limited improvement and increased contraindications. This highlights the importance of developing psilocybin therapy as mood disorders amongst cancer patients have been linked to suicide ideation and lower treatment adherence (Griffiths et al. 2016).

Recent clinical trials have brought psilocybin back into the limelight as a potential form of psycho-therapy for mood disorders. In 2016, a randomized double-blind trial of 46 participants showed high efficacy of psilocybin for symptoms of depression and anxiety with an overall 65% and 57% remission at a 6-month follow-up after high dose administration for 5 weeks. Self-reporting showed that 80% of study participants experienced more satisfaction from life (Griffiths et al. 2016). Another 2016 trial by Ross et al., demonstrated similar results, with an 83% remission of depression symptoms 7 weeks after psilocybin dosage compared to only 14% with niacin as a comparator. An immediate and long-lasting improvement was also seen in anxiety and 87% of participants reported increased well-being (Ross 2016). Both studies reported no serious contraindications to low and high doses of psilocybin. Only transient and easily manageable mild adverse events were reported (Griffiths et al. 2016, Ross 2016). This high safety indicates low physiological toxicity, addictiveness, lack of withdrawal effects, and minimal link to neurological dysfunction. As a result of these promising findings, psilocybin-based therapy has received FDA approval as a 'breakthrough therapy' for treatment-resistant depression and major depressive disorder (Lowe 2022).

However, its clinical use and FDA approval remain controversial. This controversy stems mainly from the high rates of psilocybin abuse in recreational settings and the fact that being a psychoactive substance it can elicit episodes of panic, depersonalization, and delusion. Clinical administration of psilocybin also requires the active involvement of a medical professional and a strong doctor-patient relationship to assist the patient through the effects of the drug. Extensive infrastructure is also required as a quiet, dark environment in conjunction with therapeutic music is recommended for optimal effects (Hristova, Perez-Jover 2023).

For the effective implementation of psilocybin psychotherapy, there is a need to address the stigmatization and criminalization of its use in medical settings. A cross-sectional survey conducted in 2020 showed that 92.4% of psychologists would discourage the use of psilocybin among their patients suffering from depression caused by a life-threatening illness (Kruger et al. 2022). This is indicative of a lack of awareness amongst medical practitioners regarding the benefits of psilocybin as mentioned above. It also highlights a lack of substantial research that may change clinical guidelines and clinicians' views of psilocybin. Further research into its therapeutic potential may require reclassification of psilocybin to non-schedule I, to reduce the financial and legal burden on researchers (Dos Santos 2021).

Nevertheless, psilocybin therapy presents a new frontier for the management of depression and anxiety in cancer patients. Its use still requires more large-scale trials and an extensive media campaign effort to overcome its stigmatization.

Comments for reviewers: None
Ethical Considerations: Does this study include human subjects? NO
Conflict of interest: No conflict of interest
Funding sources: The authors received no funding from an external source

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RESTLESS LEG SYNDROME: DISEASES BETWEEN PSYCHIATRY AND NEUROLOGY

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Dear Editor-in-Chief,

I am writing to you regarding restless leg syndrome, a disease from the spectrum of movement disorders that has significant repercussions in other areas of medicine, primarily in the area of psychiatry, which has recently shifted this syndrome from its focus of interest. Throughout the history of study, this syndrome has evolved from a predominantly psychiatric disorder (Coccagna et al. 2004), when considered a form of hysteria, to a predominantly neurological disorder from the group of movement disorders with manifest symptoms of pain in the extremities, burning or stabbing sensations, which decrease or disappear with limb movement. The feelings generally happen when at rest and therefore can make it hard to sleep. Due to the disturbance in sleep, people with RLS may have daytime sleepiness, low energy, irritability and a depressed mood (Saletu et al. 2013; Gossard et al. 2021).

Large community studies in Europe and North America show RLS prevalence rates from 7% to 10% in the general adult population. Prevalence increases with age with some studies estimating prevalence to be as high as 18-23% in the elderly, and increases in the presence of coexisting morbidities, and it is higher in women, twice as often as men (Ohayon et al. 2012).

Interestingly, studies have also indicated that RLS is relatively common in children and adolescents, affecting 1–4% of this population (Picchietti et al. 2007).

The frequency of this syndrome during pregnancy triples (Ohayon et al. 2012; Lepuzanović et al. in press). In addition to the above, an increased frequency has been observed in people suffering from anemia caused by iron deficiency, chronic renal insufficiency, diabetes mellitus, hypertension, and Parkinson's disease (Šabić et al. 2016).

The latest diagnostic criteria for RLS were updated in 2014 by the IRLSSG and consist of five key features that must be met for a diagnosis of RLS (Allen et al. 2014): 1) Increasing discomfort in the legs, accompanied by an overwhelming need and urge to move legs or other body parts; 2) Symptoms appear and worsen during periods of rest, such as lying down or sitting; 3) After moving the limbs affected by the discomfort, there is a partial or complete relief of the symptoms; 4) Appearance or worsening of symptoms in the evening or at night, and; 5) Exclusion of another primary cause of symptoms (eg, myalgia, venous stasis, leg edema, arthritis, leg cramps, discomfort in position, habitual foot tapping).

According to the etiology, RLS can be divided into: Primary (idiopathic) form, which is characterized by an earlier onset of symptoms, a slower course of the disease, but also a better prognosis. It usually appears before the age of 40, sometimes already in early childhood when it is often misinterpreted as