Psilocybin Can Diminish Depression

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Depressive disorders were the third leading cause of disability in the world according to findings from the Global Burden of Disease Study.[1] Therapeutic options for depression with psychedelic substances such as psilocybin and lysergic acid diethylamide are undergoing research.[2] Treatment-resistant depression investigations with psilocybin have shown it to be effective with no serious adverse effects.[2] In terminally ill depressed cancer patients, treatment benefits lasted 6 months.[3] Long-term studies of psilocybin efficacy are not available, but there is support for the medication as pharmacotherapy for mental illnesses.[2]

Psilocybin is an indolealkylamine (4-phosphoryloxy-*N*,*N*-dimethyltryptamine), which acts on serotonergic receptor subtypes 5-HT_{1A}, 5-HT_{2A}, and 5-HT_{2C}.[4] The actions of psilocybin are correlated to 5-HT_{2A} activation and downstream release of dopamine in the striatum.[4] The emotional effects include depersonalization, euphoria, and mystical experiences.[2,4] These mystical feelings reportedly prompt a reduction in anxiety and depression.[2] Described as psychospiritual events, they may activate inner mechanisms for healing.[5] This phenomenon is part of neurotheology and is a biological basis of spiritual experiences.[5]

Patients with major depressive disorder have persistent amygdala dysregulations.[6] Psilocybin decreases the connectivity of the amygdala during stress.[6] Imaging reveals increased blood flow and metabolism in the amygdala of depressed patients; following psilocybin administration, there is a decrease in blood flow to the left amygdala and improved mood.[7] There are decreased amygdala responses (and less emotional response) after prescribing selective serotonin reuptake inhibitors (SSRIs), while treatment with interventions applying psilocybin increase emotional responses.[8] Psilocybin and SSRI administration induce different therapeutic actions in the amygdala.[8]

Brain functionality is divided into large-scale bioelectric networks.[9] In a resting state network, the functional connectivity evidences how such networks interact in patterns with psychological phenomena.[9] In the prefrontal cortex, 5-HT_{2A} increased expression or binding is linked to depression, suicidality, and negative affect.[6] Psilocybin decreases activity in the medial prefrontal cortex and decreases connectivity within smaller networks such as the default mode network of the prefrontal cortex, while increasing other brain connections.[9] This disintegration of connections may be the cause of mystical or transcendent experiences.[9] Once interrupted, unhealthy pathways are replaced with healthier ones.[9] Resting state networks in patients with neurologic or psychiatric disorders deviate from optimal connectivity patterns, such that reintegration to optimal networking can reportedly restore the brain to a predisease state.[9]

Psilocybin has been used historically for spiritual purposes. Evidence is mounting that psilocybin can successfully improve mood. The long-standing effects are currently under evaluation.

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