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Mushroom-Based Restoration of Psychological and Neurobiochemical Alterations in Suicidal Brain

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Abstract

Nowadays, suicidal ideation, suicidal attempts and suicidal cases have gone skyrocketing. Psychological and neurobiochemical underpinnings of these issues have not received serious attention. Interventional approaches including edible and medicinal mushrooms against suicide seem beaconing. Thus, this present article pinpoints the psychological and neurobiochemical underpinnings of suicide and therapeutic approaches against suicide for the betterment of the researchers, healthcare professionals, those suffering from suicidal issues and their caregivers as well as to the policy makers and public health concerns.

Keywords: Suicidal Attempts, Suicidal Ideation, Mushrooms, Psilocybin, Psychedelics

Introductions

According to the world health organization (WHO), suicide (killing oneself) is the third leading cause of death globally [1]. Every year, more than 8 million people take their own lives and the rate of "attempt to commit suicide" is much higher than this [1]. Though people of both the developing and developed countries commit suicide, the rate is higher in the developing countries and people at the age range of 15-29 years have been found to fall victim to this heinous act much [1-5]. Though attempts had been taken from multiple sectors involving social, religious, academic and health institutional approaches, suicidal trend cases still remain escalating. Psychological and neurobiochemical underpinnings of suicide entice attention to impede the augmenting suicide cases both at national and international levels.

Neurobiochemical Underpinnings of Suicide

Serotonergic Systm

Serotonin [5-hydroxytryptamine (5-HT)] is synthesized from tryptophan via tryptophan hydroxylase (TH) in serotonergic nerve endings [6]. Its activity in the synapse is terminated by its reuptake into serotonergic terminals and through enzymatic degradation and diffusion. 5-hydroxyindoleacetic acid (5-HIAA) is the degradation product of 5-HT [6]. 5-HT plays a role in mood, anxiety, sleep, cognition, memory, and aggression. Blood and cerebrospinal fluid (CSF) levels of 5-HT and 5-HIAA are potent hallmarks of mood disorder, anxiety, depression as well as suicidal ideation, suicidal thoughts and suicide. In most of the suicidal cases, serotonin levels have been found plummeted in both blood and CSF [6]. Molecular biological studies associate overexpression of serotonin receptors with suicidal cases. Reasons might be, excessive re-uptake and lowered level of serotonin for neurotransmission at the synapse level that ultimately govern towards suicidal cases [6].

Dopaminergic System / DOPA

Dopamine plays an important role in aggression, attention, motivation, reward and mood maintenance. Dopamine is produced from its precursor, levo-dopa (L-DOPA). Dopamine is meta-bolized into 3,4-dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) whose levels have been found higher in the hippocampi of the suicidal brains [7].

Adrenergic System

Adrenaline (epinephrine) plays pivotal role in mood and cognitive functions. Adrenaline is synthesized from the amino acid phenylalanine and tyrosine in the adrenal glands and in brains while the locus coeruleus (LC) neurons synthesize noradrenaline. Levels of adrenaline and locus coeruleus (LC) neurons have been found lowered in the left hemisphere of the suicidal brains. mRNA expression levels of the adrenaline receptors have been found higher in the suicidal brains that correlate with excessive uptake of the adrenalines leaving little amount to overcome suicidal mood [8].

GABAergic System

The inhibitory neurotransmitter gamma-aminobutyric acid (GABA) acts through two types of receptors: GABA-A and GABA-B. Role of GABA in suicidal cases could not be conclusively stated [9].

Hypothalamic-Pituitary-Adrenal (HPA) Axis

The hypothalamic-pituitary-adrenal (HPA) axis remains as one of the mostly concerned suicide-related neurobiochemical underpinnings [10-11]. HPA abnormalities are associated with various sorts of mood disorder, suicidal ideation, suicidal attempt and suicide conduction [10-11].

Acetylcholine (Ach)

Acetylcholine is an excitatory neurotransmitter of the central nervous system (CNS). Acetylcholine plays pivotal role in learning and memory, cognitive and psychological performances. Increased uptake of acetylcholine or breakdown or reduced production leads towards depression, memory loss and diseases like Alzheimer's disease, Myasthenia Gravis, etc [12].

Endocannabinoids

Endocannaboids of various sorts have been involved in maintaining mood and behavior. Their altered production and distribution disrupt neuorbiochemical harmony leading towards psychological deranged mainfestations. Tetrahydrocannabinol and its structural analogue "anadamide" have been reported controlling psychological normalcy and their alteration tend to initiate suicidal attempts [13].

Lipid Metabolism

Lipid profile is an important biochemical hallmark of sound health. Usually, hypercholesterolemia has been implicated in numerous physiological complications. On the contrary, hypocholesterolemia has been implicated in lowered serotonergic neurotransmitter production and tempting towards mood disorder and suicidal ideation [14,15].

Brain Derived Neurotrophic Factor (BDNF)

Reduced level of the brain derived neurotrophic factor (BDNF) has been reported in those brains who committed suicide and those suffering from mood disorder. Along with BDNF, its receptor, TrkB, has also been found less expressed in the suicidal brains [16].

Neuroimmunobioechemical Underpinning

Compared with the healthy individuals, brains and CSF of the people who committed suicide, exhibit excessive microgliosis, IL-1β, IL-3 and IL-6 and TNF-α levels [2-5].

Mushrooms for Treating Suicidal Incidences

Mushrooms, the edible and medicinal macrofungi, have long been included in culinary and elixir items in the history of mankind [17,18]. Though, human physiological intervention of mushrooms have gained noteworthy attention in this era, their integration into psychopathological implications, especially towards suicidal attenuation, has not received considerable focus [19]. In the recent past, several researchers from distinct laboratories, universities and medical centers have highlighted the involvement of some edible and medicinal mushrooms in ameliorating neurobiochemical and psychological maladies including suicidal ideation, suicidal attempts and suicide [20]. Among the mushroom species, the magic mushrooms, also called ase the "psilocybin mushrooms" or the "shrooms", have received epoch-making attention [21,22].

Magic Mushrooms for Treating Suicidal Instances

The magic mushrooms belong to the genus Psilocybe, of which the most potent are *P. azurescens, P. semilanceata,* and *P. cyanescens* [21-22]. Almost all of these produce the pro-drug "psilocybin (O-phosphoryl-4-hydroxy-N,N-dimethyltryptamine)" that is converted into the active drug "psilocin(4-hydroxy-N,N-dimethyltryptamine)" and acts as mood enhancer [21-22]. This is the "magic" of this mushroom that has enabled its usage in impeding suicide and associated phenomena. In the gastrointestinal tract, psilocybin is de-phosphorylated into psilocin and can cross the blood-brain barrier [23-25]. Psilocin acts as a selective agonist of the 5-HT receptors [23-25]. Psilocin also bonds to the dopamine D3 receptors and can engage in mood enhancing events (23-25). It also affects circadian rhythm, learning and cognitive processing occurring in the amygdala, hippocampus and hypothalamus that potentiates its involvement in suicide treatment [23-25].

People attempting suicide suffer from suicidal ideation that very often predates depression. Treatment-resistant depression (TRD) is the most severe form of depression from where few can return towards normalcy. Magic mushroom supplementation to the TRD patients have come out with fruitful results [26-30]. Compared with the traditional anti-depression agents (such as ketamine, uridine), the magic mushrooms provided long-lasting anti-depression effects to the TRD patients [26-30]. Functional magnetic resonance imaging (fMRI) of the magic mushroom-treated people show ameliorated default mode network (DMN) in their brains that is another indication of thwarting suicidal ideation [29,30]. In this connection, anti-oxidant and anti-inflammatory effects of almost all the magic mushrooms have been reported from different laboratories of the world [29,30]. These prioritizes prospect of the magic mushrooms in treating suicidal ideation, suicidal attempts and suicide incidences. Now, FDA has approved the usage of the magic mushrooms as therapeutics against TRD and suicidal ideation [31]. Similar observations have been reported for the Reishi mushroom, *Ganoderma lucidum* [32-34]. However, determination of appropriate dosage regimen is an important aspect that warrants attention.

Conclusion

Suicide and associated psychological and neurobiochemical underpinnings have been impeding normal physique and psyche heavily. Time is up to take appropriate measures against these nuisances. Edible and medicinal mushroom-based therapeutic approaches seem promising in attenuating suicidal approaches. Thus, proper attention in this aspect is called for.

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