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The Role of Cannabis in Cognitive Functioning of Patients with Schizophrenia: A Review

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ABSTRACT

Schizophrenia is a long-standing psychiatric disease with a diverse genetic and neurobiological prominent that holds early brain development and is convey as a fusion of psychotic symptoms such as hallucinations, disappointments and disorganization and motivational and cognitive dysfunctions. The commonality of schizophrenia is close to 1% internationally, the prevailing opinion that the pathology is best treated with drugs that act on monoamine receptors. Cannabis use is very common amongst people with schizophrenia and, together with impaired cognition, it is believed to increase the hazard of developing the disease. However, the overuse of cannabis has been linked with cognitive deficits in long-term consumers but the studies on schizophrenia patients have been contradictory. A detailed review of the literature indicates that the rationale use of phytocannabinoids can be a trustworthy and effectual therapy option for schizophrenia as primary or adjuvant therapy.

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INTRODUCTION

Schizophrenia is a long-standing psychiatric disease with a diverse genetic and neurobiological history that influence on early brain development and is conveyed as a combination of psychotic symptoms such as hallucinations, disappointments and disorganization and motivational and cognitive dysfunctions. Schizophrenia is a word used to describe a mental disorder that presents a spectrum of symptoms that include alterations in perception, thinking and in the sense of a reduction in violation, psychomotor deceleration and symptoms of illegality behavior[1]. The main characteristics of schizophrenia include "positive", "negative", "cognitive" and "effective" symptoms[2].

CLINICAL FEATURES

Schizophrenia has various symptoms that bascially start in early adulthood and generally proceed throughout life. Majority of patients have a history of behavioral dysfunction, mainly social and learning obstacles. The characteristics appearance of schizophrenia include auditory hallucinations (an incident involving the apparent perception of something not present) and disappointments (the act of deception or the condition of deception). Patients may have undergone through these symptoms, but this event may or may not be true and is now in a problematic condition. Schizophrenia has several main symptoms which can be divided into several stages; Positive, negative and cognitive symptoms. Positive symptoms are those that can be easily identified and not seen in well people. Such symptoms include hallucinations, delirium and atypical motor behavior with fluctuating degrees of severity. Negative symptoms cannot be easily identified and are linked with a high morbidity rate. The most common negative symptoms included avoidance, alogia, anhedonia and decreased emotional expression. Cognitive symptoms, being the most recent classification. Ultimately, this alters the individual's communication skills by disturbing his language and attention[3,4].

ETIOLOGY

Researchers has recognized different factors that commit to the hazard of establishing schizophrenia. Scientists have long acknowledged that schizophrenia occasionally runs in families. The disease appears in less than 1 percent of the typical population, but this range turns into the 10 percent that have first degree relatives with the disorder, such as parents, siblings. Several environmental influencer may be associated, such as disclosure to viruses or malnutrition before birth, problems during childbirth and other unknown psychosocial

factors. Researchers conjointly consider that the brain structure of human with schizophrenia is somewhat distinct from that of healthy human. For example, the fluid-filled cavities of the brain called the ventricles are bigger in certain number of human with schizophrenia. In addition, the common source of schizophrenia has revealed that most people recognize with schizophrenia have increased level of dopamine, but it is not yet known how all people diagnosed with schizophrenia have considerable amount of dopamine[5,6].

EPIDEMIOLOGY

Schizophrenia occurs worldwide. The commonality of schizophrenia is close to 1% globally. The proportion is around 1.5 per 10,000 people. The count of male are diagnosed with schizophrenia is more than women at an early age, but women are more prevailing in old age. The usual age of outbreak ranges from 18 to 25 for men and 25 to 35 for women. In the more recent review, which combined data from 33 countries, concluded that the frequency of schizophrenia varied by geographical location[7,8].

DIAGNOSIS

The American Psychiatric Association's criteria for a schizophrenic diagnosis include only mental and behavioral symptoms: delusions, hallucinations, disorganized speeches, confused behavior and the presence of negative symptoms, which may include anhedonia, loneliness, apathy and alogia. Two or more than the symptoms must have continued for at least a month, along with some other considerable diagnosis, such impairment of functioning for a compelling period of time, signs of the disorder lasting an extended period of at least six months and excluding schizoaffective, bipolar or depressive disorder along with psychotic characteristics.

EMERGING PERSPECTIVE

Right away, genetic and epigenetic susceptibility models endure the predominant dogma, therefore schizophrenic symptoms are believed to demonstrate themselves from an underlying aberrant or sensitive genotype, independent or coinciding with disclosure to an environmental risk factor (biological or social) at some mark in the early development[9].

Antipsychotic drugs frequently prescribed for the therapy of schizophrenia are generally create around a hypothesis of the monoamine neurotransmitter, usually, the dopamine

hypothesis, which accomplice the disorder with a dysfunction in the dopaminergic pathways, committing to positive and negative symptoms and cognitive disease[10-12]. First-generation (typical) antipsychotics distribute the primary pharmacological estate of the D2 antagonism. The postulate is that an excitable mesolimbic pathway can become the source of positive psychotic manifestation. The required effectiveness of typical antipsychotics is accomplish by blocking 60-65% of the D2 receptors in the mesolimbic pathway. While the D2 receptors simultaneously block throughout the brain in other pathways, such as the mesocortical, nigrostriatal and tuberoinfundibular pathways. The mesocortical pathway is thought to be linked with negative symptoms. Hence, blocking this pathway can cause negative side symptoms and cognitive effects. Therefore, holding around 77% or more of the D2 receptors at nigrostriatal pathway may increase the hazard of extrapyramidal symptoms, such as dystonia (involuntary muscle contractions), akathisia (restlessness), bradykinesia (slow movements) and tardive dyskinesia. Chronic treatment with typical antipsychotics can occupy 70-90% of the D2 receptors[13].

The second-generation (atypical) antipsychotics have a decreased affinity towards dopamine D2 receptors and an increased affinity towards other different neuroreceptors, such as norepinephrine and serotonin receptors, mainly with 5-HT2A. The vulnerability of neurological symptoms may be decreased with atypical antipsychotics, but the vulnerability of metabolic problems such as weight gain, dyslipidemia, hypertension and diabetes, has been seen to be higher, especially with the people treated with Clozapine or Olanzapine[13,14,15]. Antipsychotic drugs, both typical and atypical, can be harmful and may cause long list of neurological, metabolic and cardiovascular hazards that can conclusively contribute to a significantly decreased quality of life and decreased life expectancy[12,16-20]. In general, typical antipsychotics often reduce the severity of positive symptoms but are generally less effective in dealing with negative symptoms[21-23]. Atypical antipsychotics are usually assumed to be more effective in treating negative symptoms. However, intolerable side effects still lead to discontinuation of treatment[24-26]. Commonly seen hazards of antipsychotics (e.g. constipation, weight gain, tardive dyskinesia, cardiovascular disorders and metabolic glucose deregulation) may add the polypharmacy to treat these side effects, which results in polypharmaceutical risks additional for patients[27-29].

One therapeutic choice that emerge to have the potential to regulate essential psychophysiological functioning is the cannabis plant. Recently, the medical community has

slowly started to accept the idea that historically such increased proportions of cannabis use with schizophrenia people may reflect the self-medication instead of recreational utilization of the plant[30,31]. While cannabis was once prevalent and sometimes still explained as a ingredient to cause schizophrenia[32,33], different studies now indicate that the use of medical cannabis can be effective therapy for schizophrenia[34,35]. According to the theory of endocannabinoid deficiency, many alterations of mental and physical health are the result of deregulation of the innate system of endocannabinoids (ECS), generally expressed as an important network of chemical signals that boost somatic and psychological homeostasis or efficiency of the psychobiological state[9]. ECS made of natural ligands (eg; Anandamide and 2-AG) and receptors (CB1 and CB2) which seems to act as an important role in the efficient regulation of systems that include sleep, nutrition (eg; intestinal permeability and adipogenesis), libido and fertility, perception of pain, motivation, happiness, anxiety, learning and memory, social functioning and pathophysiology of cancer[36,37-43]. Different studies have conducted to linked cannabis use with an increase in psychotic symptoms. It has been said that cannabis can influence N-methyl-D-aspartate receptors (NMDAR) and decrease the functioning of NMDAR[44]. A study on conducted by the University of Melbourne in Australia also showed that difference in the brain's cannabinoid system may be involved in the pathology of schizophrenia, including changes in CB1 receptors in the dorsolateral prefrontal cortex[45]. Also from the case study of London Health Sciences Center reveals that a 38-year-old schizophrenic patient shown a 20% reduction in striatal dopamine D2 receptor activity, which means there was an increase in synaptic dopamine activity[46]. Presently there are several studies that indicate, CBD (cannabidiol) could block the temporary symptoms of psychosis aggravate by THC. In the study conducted by Murat Yu Cell suggest that the acute administration of striatal and amygdala activation modulated by THC and its effects were related to psychotic symptoms and anxiety, but CBD had an opposite action on neural activation in these regions, which adds a series already solid evidence to support the hypothesis that the together use of CBD and THC results in a reduction in paranoia[47].

IMPACT OF CANNABIS

The counts of disorder in substance use with schizophrenic patients are more than in the general population, with cannabis being the most frequent illicit drug. While the therapy with cannabis use has been associated with poorer therapy result, the exacerbation of symptoms

that it is also linked with cognitive deficits arguable. The use of cannabis among healthy consumers has been accomplice with cognitive deficits, such as memory and attention deficits, even several days after withdrawal[48]. In the studies of people without a medical or psychiatric background have revealed that the longer time use of cannabis is linked with structural brain abnormalities and psychotic symptoms below the threshold in a dose-dependent manner. However, among patients with schizophrenia, the association is less clear. While the acute therapy of tetrahydrocannabinol (THC) to people with schizophrenia may worsen the symptoms and cognitive deficiencies and may have lasting effects[49], it is also found that the use of cannabis has some beneficial action on cognition, at least in some patients - patient groups[50]. Recently the meta-analysis continued by Potvin and his colleagues supports this notion, his analysis does not include studies conducted after 2006 and does not focus specifically on cannabis, but does include patients with multiple substance abuse. In their study, they aim to clarify the nature of the relationship among cannabis use and cognitive disorders observed in schizophrenia. First study includes an empirical study on the action of cannabis on cognition in patients with established schizophrenia. In second study, they correlate the neuropsychological functioning of people with first episode psychosis (FEP) with and without having a background history of cannabis use. The cannabis use is very common with schizophrenia people and, along with impaired cognition, it is believed to increase the vulnerability of developing the disease. Though, while overuse of cannabis has been linked with cognitive deficits in people who were consuming for longer period of time, the studies of schizophrenia patients have been contradictory. In Study, I, a meta-analysis of 10 studies was performed on 572 people with confirmed schizophrenia (with and without the use of comorbid cannabis). The people with a background history of cannabis use have increased neuropsychological functioning. Their finding were largely driven by studies that included people with background history of lifelong cannabis use rather than current or recent use. In second study, they studied the neuropsychological performance of 85 people with first episode psychosis (FEP) and 43 healthy controls without use. In relation to controls, FEP people with a background history of cannabis use (FEP+CANN; n=59) showed only selective neuropsychological deficits and those without a history (FEP - CANN; n=26) revealed generalized deficits. In direct comparison, patients with FEP + CANN performed better on visual memory, working memory and executive functioning tests. Patients with early-onset cannabis use had less neuropsychological hazards than people with late-onset use. Together, these results revealed that people with schizophrenia or FEP with a background history of cannabis use have improved neuropsychological functioning compared to people who were

not using. This association between improved cognitive performance and cannabis use in schizophrenia can be led by a subset of "less cognitive neuroscientific" patients who developed psychosis only after a relatively early start to cannabis use[49,50].

CONCLUSIONS

Cognitive deficits represent a central symptom of schizophrenia and are strongly related not only to the disease itself, but also to the possible recovery. People with schizophrenia show significant cognitive deficits and verbal memory deficits are consistently reported as one of the most compromised cognitive Domains. Although a different triggers can leads to psychosis, inflammation and activation of the CNS immune system are almost always present. A literature review suggests that CBD (cannabidiol) in optimized patients may be a safe and effective therapy option for schizophrenia as primary or adjuvant therapy, supporting both the inflammatory causes of schizophrenia and the potential importance of targeting to ECS (endocannabinoid system) in the therapy of this little-known disease instead of poorly tolerated antipsychotics with debilitating side effects. Meta-analysis and experimental data converge to indicate that cannabis use in both FEP (first-episode psychosis) and confirmed schizophrenia is linked with greater cognitive performance than non-use and less cognitive impairment in relation to healthy controls. In this review, we found that a subclass of psychotic patients may show better results (i.e. partial recovery of cognitive functioning and less disability) if their cannabis use can be controlled.

CONFLICTS OF INTREST

All authors have declared that there are no conflicts of interest in relation to the subject of this study.

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