

**BIOLOGICAL ASPECTS OF CANNABIS CONSUMPTION IN
SCHIZOPHRENIA**

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Abstract - Schizophrenia and psychotic disorders are major health issues with particular implications for both the individual and the medical system. Epidemiological data show a more frequent consumption of drugs in schizophrenic patients when compared to the general population. Studies have shown that the abuse of substances is the most common comorbidity associated with schizophrenia. Among illicit substances, cannabis is the most commonly encountered among patients with schizophrenia. Similar clinical features of schizophrenia and cannabis consumption could be explained by some common neurobiological implications. N-methyl-D-aspartate (NMDA) receptor stimulation is associated with psychotic-type phenomena

and schizophrenia and NMDA receptors are involved in the clinical effects of cannabis consumption. Thus, the CB1 receptors that are spread mainly at the level of the NMDA secretary neurons are activated by tetrahydrocannabinol, the psychoactive component of cannabis. Moreover, cannabis abuse in association with other factors may contribute in triggering schizophrenia. Therefore, patients diagnosed with schizophrenia that abuse substances such as cannabis could represent a special category of patients that require a complex therapeutic approach, especially considering the multiple problems implicated, such as reduced compliance with treatment, unfavorable evolution and prognosis with multiple relapses and frequent hospitalizations.

Key words: schizophrenia; cannabis consumption; biological psychiatry.

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INTRODUCTION

Schizophrenia is a chronic, debilitating condition with an unfavorable general prognosis that requires a permanent pharmacological treatment. The presence of comorbidities in this category of patients is very frequent and accelerates the progress of the disease (Padurariu et al., 2010, Ciobica et al., 2011). Therefore, strict control of the comorbidities associated with schizophrenia is a medical priority. An important comorbidity in schizophrenia could be represented also by an increased rate of cannabis consumption. In fact, there are several authors that drawn the attention lately on the problem of higher rate of drug consumption on schizophrenic patients, with special focus on cannabis (Wobrock

et al., 2005). However, the subject is still undertreated in the current literature. In a reference study conducted in 2008 by Mayfrank it was shown that with regard to age, adolescents and young people represent the most affected category (Gouzoulis-Mayfrank, 2008). Considering the high incidence of drug abuse and drug dependence in this category of patients and the negative impact on the development of the disease, early identification and appropriate management have priority. Another important study conducted on 325 subjects with mental disorders, of which 53% were diagnosed with schizophrenia or with other schizoaffective type disorders, has reported the consumption of cannabis as being 2nd place after alcohol consumption (Mueser et al., 2000).

THE BIOLOGICAL PSYCHIATRY OF CANNABIS CONSUMPTION IN SCHIZOPHRENIA

Clinical trials and studies indicate a very complex relationship between psychotic pathology and the abuse of substances. Regarding the explanations and the mechanisms that could sustain the connections between cannabis consumption and schizophrenia, we could mention for example the organic-induced psychotic episode associated with remission or the fact that consumption of cannabis may be associated with a schizophreniform disorder or a functional psychosis. Other possible explanations could be represented by the fact that chronic consumption of cannabis can induce chronic psychosis that will persist during the period of abstinence or the fact that the consumption of cannabis could represent a risk factor for development of schizophrenia (Iversen, 2003).

Most commonly, acute drug consumption generates several psychotic-like symptoms such as hallucinations, delusions, delusional ideas or psychomotor agitation. The abuse of cannabis in particular can generate phenomena of derealization and depersonalization, paranoid ideas of persecution and hallucinations (Thomas et al., 1993). The acute response after the consumption of cannabis also includes euphoria, detachment and relaxation. In the context of the chronic consumption of cannabis, several authors described the occurrence of 'amotivational' syndrome dominated by negative symptoms such as apathy, social withdrawal, hypobulia, restriction of interests, lethargy, disturbances of the cognitive function or of functional and aptitudinal potential (Castle et al., 2004). When consumption of cannabis is associated with schizophrenia, it aggravates the disorder by exacerbation of psychotic symptoms with negative valences over the course of the condition.

Importantly, the similar clinical features of schizophrenia and cannabis consumption could be explained by common neurobiological implications. It is known that stimulation of NMDA receptors is associated with psychotic-type phenomena and schizophrenia. The NMDA receptor is also involved in the clinical effects of cannabis consumption (Webster, 2005). CB1-type receptors that are spread mainly at the level of NMDA secretory neurons are activated by the basic psychoactive component of cannabis, which is tetrahydrocannabinol (THC) (Iversen, 2003). The connection between the two entities is supported on a clinical level. Thus, the people who are likely to develop psychosis could manifest psychotic symptoms at lower drug doses.

There are recent evidences supporting a possible causal relationship between schizophrenia and cannabis consumption. Cannabis abuse in association with other

factors may contribute to triggering schizophrenia in more susceptible individuals (Gouzoulis-Mayfrank, 2008). Recent research has shown the presence of a temporal relationship between the consumption of cannabis and the onset of schizophrenia. A study from 2010 performed on 112 patients examined the relationship between age of antipsychotic treatment onset and the history of cannabis consumption in patients with a first psychotic episode. These results showed the existence of a direct correlation between the age of antipsychotic treatment onset and the consumption of cannabis, regardless of gender or other toxic consumption as cocaine, alcohol or smoking. The study also identified a dose-response connection between cannabis and psychosis onset, speculating the idea of a catalytic role of cannabis in psychosis (Barrigón et al., 2010). Similar studies of schizophrenia onset were also published by other research groups (Compton et al., 2009).

The causal relationship between cannabis and schizophrenia also seems to be confirmed by other surveys. In a more recent study performed by Galvez-Buccollini et al. (2012), the temporal relationship between psychosis onset and the initiation of cannabis consumption was analyzed. The study was comprised of 57 people who had consumed cannabis before developing psychosis. The results of the study showed a direct connection between the initiation moment of cannabis consumption and the age of psychosis onset/manifestation. The authors suggested a possible causal link between cannabis and schizophrenia. However, only a small number of people who consume cannabis develop schizophrenia. For this reason, it is important to consider this idea with a dose of skepticism, especially since the hypothesis of cannabis involvement in the etiology of schizophrenia has its supporters.

Nonetheless, the consumption of cannabis as a comorbidity represents a serious problem for patients with schizophrenia, and early identification and treatment is a priority. An important step in identifying subjects prone to substance abuse could be done by analysis of several demographic factors. A study published by Dervaux et al. (2003) examined the differences between sociodemographic factors in patients with schizophrenia and the abuse or dependence on cannabis versus patients with schizophrenia who never succumbed to abuse or addiction. The results of their research revealed important aspects such as a statistical connection between male gender and young age and history of cannabis consumption, as well as the fact that cannabis abuse precedes psychotropic treatment initiation. Dervaux stated that the duration of hospitalization is higher in patients with substance abuse and that there is a significant correlation between autolytic attempts and the abuse of cannabis in schizophrenic patients.

It is important to increase clinical vigilance in identifying persons with substance abuse problems. In this context, it is necessary to take into account the risk factors that may assist diagnosis. Thus, the most relevant risk factors could be represented by young age, legal antecedents, antisocial personality disorder or male gender (Mueser et al., 2000).

The identification of risk factors for substance abuse is important in creating the possibility of setting up a plan of action for the prevention of addiction in vulnerable patients. This is very important, as it is known that substance abuse in this category of patients aggravates the disease evolution, subjecting them to risks as relapse, re-hospitalization and hetero-aggressive behavior.

In the long term, the coexistence with the abusive consumption of cannabis darkens the prognosis of the disease. Thus, the high incidence of cannabis consumption in patients with schizophrenia can be explained, at least in part by the hypothesis of 'self-medication', which refers to the tendency of patients to reduce the symptoms associated with the disease. However, the consumption of cannabis aims only at the negative-type symptoms. This aspect is also supported by a study published by the Henquett et al. (2010), which assayed the effect of cannabis consumption on positive and negative phenomena of schizophrenia in comparison with the general population control. The authors identified an enhancing of the positive symptoms in psychotic patients, as well as a reduction in the negative symptoms.

Thus, patients diagnosed with schizophrenia and abuse of substances constitute a special category of patients requiring a complex therapeutic approach, especially considering the multiple problems posed, such as reduced compliance with treatment, unfavorable evolution and prognosis with multiple relapses and frequent hospitalizations. We think that a first step in the management of these patients is to increase vigilance of the therapeutic aspects in order to identify and diagnose the patients.

In conclusion, the management of patients who exhibit schizophrenia and cannabis abuse/dependence must integrate both schizophrenia treatment and addiction therapy, and it must be adapted to the needs of each individual patient. Integrated treatments would include both pharmacological methods and various forms of psychotherapy, such as cognitive-behavioral therapy, group therapy, counseling, motivational interview or family-centered psychotherapy (Gouzoulis-Mayfrank et al., 2008). There is enough evidence to say that integrated therapeutic programs can lead to

significant improvements with regard to social integration, while at the same time having a positive impact on the evolution of schizophrenia.

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