Knowledge Notes

Cannabis Use and Psychosis

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Objectives

To provide a review of current research on cannabis use and its association with psychosis.

Introduction

Cannabis is clearly a problem for those who have a psychotic illness and is known to exacerbate existing symptoms. In individuals who have been diagnosed with a first episode of psychosis it has been reported that more than 30% of these young people present with an existing cannabis use disorder. Those with a cannabis use disorder tend to be younger, male and have had an earlier age of onset of psychosis (Addington & Addington, 2007). Furthermore, these young people tend to have increased positive symptoms. However, it was observed that in a comprehensive early psychosis program, these rates could be reduced with a concomitant reduction in positive symptoms (Addington & Addington, 2007). This has been supported in other studies (Baeza et al., 2009).

It has been suggested that cannabis use could be a contributory cause of schizophrenia and other psychotic illnesses. It has been demonstrated that cannabis use in the general population is associated with increased levels of psychotic symptoms or psychotic like experiences. In addition, many studies have confirmed that patients with psychosis are more likely to use cannabis than someone without psychosis. Furthermore, individuals with psychosis who use are more likely to relapse. Thus, it has been suggested that cannabis use might be secondary to psychosis or liability to psychosis. The current review engages the debate on the association between cannabis use and causation of psychosis.

The Debate

The question that is always being debated is whether cannabis use may cause psychosis or whether abuse of cannabis is a result of having a psychotic illness. There are several meta-analyses that review whether cannabis use is a cause or consequence of psychosis (Arseneault et al., 2004; Henquet et al., 2005b). These reviews present a range of evidence that the use of cannabis does increase the risk of later developing a psychotic illness. Even when the authors of these reviews adjust for variables such as age, sex, social class, ethnicity, other drug use and urbanicity, the effect of cannabis on the later development of a psychotic illness remains significant.

What is most important to note is that only a small proportion of cannabis users actually develop psychosis. There are several possible explanations for this. First, this may be a dose response effect; that is it can be partially explained by the amount and duration of use. This has been supported by several studies (Henquet et al., 2005a).

Another possibility is the age at which an individual uses cannabis. Adolescence seems to be a particularly risky time. For example, results of the Dunedin Birth Cohort Study in New Zealand suggested that the use of cannabis before age 15 was associated with a greater risk of developing schizophreniform disorder by age 26 (Arseneault, 2002). This has been supported by other quality studies in Greece and Trinidad. Thirdly, it is possible that only a minority of cannabis users develop psychosis because they are genetically vulnerable.

The issue of gene-environment interplay has been reviewed in detail in a recent comprehensive review (Henquet et al., 2008). These authors suggest that genetic vulnerability to cannabis abuse seems to be polygenic and possibly mediated by an early response to cannabis use. Thus cannabis use does not seem to be influenced by genes. The research reviewed did not support the notion that genetic influences on cannabis use are associated with being vulnerable or prone to psychosis.

However, there is much support for a genetic-environment interplay underlying what can be considered to be a complex interaction between cannabis use and psychosis. In their comprehensive review, Henquet and colleagues (2008) present evidence that those who developed psychosis after cannabis use are more likely to have a positive family history of schizophrenia. Secondly, they reviewed in detail the work of Caspi and colleagues (2005) who were the first to demonstrate direct evidence of a gene-environment interplay in the cannabis-psychosis relationship by studying a functional polymorphism in the catecho-O-methyltransferase (COMT) gene. COMT is critical in the breakdown of dopamine and the COMT gene contains a functional polymorphism which involves a *Met* to *Val* substitution at codon 158 which results in two common allelic variants. Previously, research investigating the COMTval158Met genotype in relation to psychosis had shown no associations. What was exciting about Caspi's finding was that COMT moderated the risk of developing adult schizophreniform disorder following cannabis use during adolescence. However, Henquet et al., point out that further studies suggest that it is unlikely that variation in a single gene accounts for the differential sensitivity to cannabis in individuals at risk for psychosis. What is more likely is that there is a three way interaction. Henquet demonstrated that indeed carriers of the *Val* allele were more sensitive to psychotogenic effects of cannabis but that this was conditional on there being evidence of a proneness to psychosis. Although exciting and promising, this work does need replication.

Another potential interaction is between stress and cannabis use. There has been evidence suggesting that childhood abuse and trauma may be a risk factor for psychosis. Henquet et al. (2008) in their review present evidence that the additive effects of early childhood trauma and cannabis use on the later development of psychosis may result from a cross-sensitization process between repeated exposures to various stressful events plus the use of cannabis.

Conclusions

In summary there appears to be sound evidence that cannabis may contribute to the development of psychosis. This is, however, only the case for a very small proportion of those who use cannabis. The actual mechanisms are unclear. However, the comprehensive review by Henquet et al (2008) suggests that gene-environment interplays possibly underlie the complex interactions between cannabis and psychosis. They suggest that multiple variations within multiple genes and not one single polymorphism

determine at birth an individual's risk of developing psychosis. Several environmental factors including cannabis and stress often in combination may then impact on these vulnerabilities.

References

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