

**Psychiatric effects of cannabis use: A critical analysis of scientific results and research methods \***

Databank van de Federale Onderzoeksacties (FEDRA) (Project DR/06)

Promotor: Prof. Dr. J. Peuskens

Kristof Vansteelandt, Phd.

Universitair Psychiatrisch Centrum, St. Jozef, Kortenberg

Katholieke Universiteit Leuven

Nowadays, cannabis is widely used by young people and, as a consequence, many questions have risen about the effects of cannabis use on the etiology and course of psychiatric disorders such as psychotic or mood disorders. The goal of this project is to review the available research literature (Medline en PsycINFO, 1985-2003) with respect to the effects of cannabis use and its impact on psychotic and mood disorders. We first discuss the psychotic disorders; subsequently, we deal with the mood disorders.

Research indicates that the acute effects of cannabis use bear a close resemblance with psychiatric symptoms in general and psychotic symptoms in particular (Thomas, 1993, 1996). Cannabis users experience euphoria and changes in thought processes with thoughts being experienced as fragmented or more accurate. In addition, changes occur in visual and auditive perception and in the perception of time as well as changes in short term memory and attention. The use of high doses of cannabis may even result in psychotic symptoms like delusions and hallucinations; the latter phenomena are sometimes described as a cannabis psychosis (Basu et al., 1999; Chaudry et al., 1991; Imade & Ebie, 1991; Núñez & Gurpegui, 2002; Onyango, 1986). Factors that contribute to the latter adverse reactions include high dose, oral intake, first use and the use of other drugs. However, the incidence and prevalence of such a cannabis psychosis are not well-known because the concept of cannabis psychosis is poorly defined and the specificity and existence of such a nosological entity remains controversial (Cantwell & Harrison, 1996; Poole & Brabbins, 1996). Recently, however, it was shown (Verdoux et al., 2003) that the acute effects of cannabis are modified by the subject's level of vulnerability for schizophrenia. Finally, the acute psychotic effects of cannabis may be more severe these days because the concentration of delta 9 tetrahydrocannabinol (THC), the active psychoactive ingredient of cannabis sativa, is higher in selected plant cultures and extracts nowadays (Hall & Swift, 2000; Iversen, 2000; Rigter & van Laar, 2002). THC activates the endogenous cannabis receptors resulting in changes in cerebral neurotransmission which offer a biological explanation for the occurrence of psychotic phenomena in control subjects, and especially in vulnerable persons. Moreover, this also explains why symptoms may increase in schizophrenic patients using cannabis.

---

\* This is the English summary of a more comprehensive (Dutch) project text; to obtain this text, please contact Kristof Vansteelandt, U.C. St. Jozef, Leuvensesteenweg 517, 3070 Kortenberg (e-mail: [Kristof.Vansteelandt@uc-kortenberg.be](mailto:Kristof.Vansteelandt@uc-kortenberg.be); telephone: 02/7580814)

In addition to the research on the acute effects of cannabis use, a vast amount of research examined the relation between cannabis use and psychotic disorders like schizophrenia, schizophreniform disorder and schizoaffective disorder. The results of this research indicate that cannabis use and psychotic symptoms, schizophrenia or schizophreniform disorder co-occur more often than what can be expected by chance (Degenhardt, Hall & Lynskey, 2001; Fergusson, Horwood & Swain-Campbell, 2003; Tien & Anthony, 1990). Then, the question becomes how this significant association can be explained; in this context, several hypotheses are formulated and tested.

A first and important conclusion is that several longitudinal, prospective studies indicate that cannabis use is an independent risk factor for the emergence of psychotic disorders like schizophrenia or schizophreniform disorder. Moreover, the relation between cannabis use and the emergence of these disorders is dose dependent (Andréasson et al., 1987; Arseneault et al., 2002; Johnstone et al., 2000; Miller et al., 2001; Tien & Anthony, 1990; van Os et al., 2002; Zammit et al., 2002). Thus, although most people use cannabis without harm, cannabis use does result in an increased dose dependent risk in the development of a psychotic syndrome like schizophrenia or schizophreniform disorder.

The association between cannabis use and psychotic symptoms and/or disorders can also be explained by the hypothesis that patients use cannabis as a form of self-medication (Dixon et al., 1991; Frances, 1997; Khantzian, 1997). Within the framework of the self-mediation hypothesis, several subhypotheses can be considered. A first subhypothesis reads that schizophrenics use cannabis in particular to relieve the specific symptoms of their disorder (Frances, 1997; Khantzian, 1997). However, the majority of studies in this line of research indicate that cannabis use has rather an unfavorable effect on the symptomatology and the course of schizophrenia and related disorders. On the basis of the reviewed literature (Bersani et al., 2002; Brunette et al., 1997; Caspari, 1999; Hambrecht & Häfner, 1996, 2000; Hamera et al., 1995; Linszen, Dingemans & Lenior, 1994; Mathers & Ghodse, 1992; McGuire et al., 1994; Negrete et al., 1986; Peralta en Cuesta, 1992; Sembhi & Lee, 1999; Van Ammers et al., 1997; Verdoux et al., 2003) it can be concluded that schizophrenics who use cannabis have the same amount of negative and/or affective symptoms and the same amount or even more positive symptoms in comparison to schizophrenics who do not use cannabis. Moreover, patients who use cannabis appear to be younger most of the time (which is associated with poorer prognosis), and the course is characterized by more hospitalizations and more frequent and earlier relapses (Linszen, Dingemans & Lenior, 1994). It should be mentioned that some authors formulate the hypothesis, which should be further examined, that cannabis use can have a different effect on different subtypes of patients (Bersani et al., 2002; Hambrecht & Häfner, 1996, 2000). A second, related subhypothesis is that cannabis is used to cope with prodromes; prodromes are limited dysfunctions (for example, somewhat poor social functioning) which appear years before the first psychotic breakdown and before the diagnosis of schizophrenia is finally made. Until now, this hypothesis is only examined to a limited extent (Arseneault et al., 2002; Zammit et al., 2002). Finally, a third subhypothesis within the framework of the self-medication hypothesis is that the reasons and motives why schizophrenics use cannabis are very much the same as the reasons and motives why people from a general population use cannabis; patients do not use cannabis to relieve the specific symptoms of their disorder but because they have the subjective experience of feeling better when using cannabis (Baigent, Holme & Hafner,

1995; Spencer, Castle & Michie, 2002). Also this hypothesis still has to be examined more thoroughly in future research.

Inspection of the literature on the relation between cannabis use and mood disorders quickly reveals that this relation has not received as much attention as the links between cannabis use and psychotic disorders. Given the fact that there is almost no literature concerning cannabis use and bipolar disorders, we limit this review to the relation with uni-polar depressive disorders like major depressive or dysthymic disorder. In analogy with the psychotic disorders, almost all studies indicate that there exist a significant association between cannabis use and depressive disorders (Degenhardt, Hall & Lynskey, 2001; Chen, Wagner & Anthony, 2002; Rey et al., 2002; Kelder et al., 2000; Troisi et al., 1998; Angst, 1996; Alpert et al., 1994; Miller et al., 1996; Winokur et al., 1998); however, this association is not as strong as it is the case between cannabis use and psychotic disorders. Until now, it is not clear how this significant association can be explained. There is no clear-cut evidence that cannabis use is a risk factor for the development of depressive symptoms, major depressive or dysthymic disorder; the results from different studies are inconsistent (Arseneault et al., 2002; Bovasso, 2001; Brook, Cohen & Brook, 1998; Patton et al., 2002). However, it is clear from a limited number of prospective studies that there is not much support for a relation between depressive symptoms, major depressive or dysthymic disorder and subsequent cannabis use (Arseneault et al., 2002; Bardone et al., 1998; Henry et al., 1993; McGee et al., 2000; Kandel & Davies, 1986; Patton et al., 2002; Bovasso, 2001; Brook, Cohen en Brook, 1998); persons who suffer from depressive symptoms, major depressive or dysthymic disorder do not tend to use more cannabis later on in their life in comparison to persons without these symptoms or disorders. From this finding, it may be concluded that it is not very plausible that depressive persons use cannabis to alleviate the specific symptoms of their disorder. Furthermore, research with respect to the impact of cannabis use on the course of depressive disorders or with respect to the subjective reasons or motives of cannabis use among depressive persons is completely lacking. A recurrent finding in all studies is, however, that contaminating variables play an important role in the explanation of the association between cannabis use, depressive symptoms, major depressive or dysthymic disorder (Chen, Wagner & Anthony, 2002; Degenhardt, Hall & Lynskey, 2001; Green en Ritter, 2000; Fergusson, Horwood en Swain-Campbell, 2002; Field et al., 2001; Kelder et al., 2000; Rey et al., 2002; Way et al., 1994); contaminating variables are variables –like, for example, emotional deprivation, leaving school without formal qualifications, leaving home early, unemployment, use of other licit and illicit drugs, affiliations with delinquent peers– that are associated both with cannabis use and depressive disorders. At this point, it is not clear how these variables relate to cannabis use, depressive symptomatology, major depressive or dysthymic disorder. On the basis of the literature reviewed, no conclusions can be given (a) whether cannabis use, after correction for contaminating variables, is a direct risk factor for the development of depressive symptoms, major depressive or dysthymic disorders, (b) whether contaminating variables that are prior in time to cannabis use as well as to depressive disorders (for example, emotional deprivation as a child) can explain the association between both or (c) whether cannabis use leads to a number of negative consequences (like, for example, not finishing school, unemployment, use of other licit and illicit drugs), which, in turn, result in an increased likelihood of developing a depressive disorder (Fergusson & Horwood, 1997; Fergusson, Horwood en Swain-Campbell, 2002). Future research still has to resolve the latter issue.

## References

- Alpert, J.E., Maddocks, A., Rosenbaum, J.F., & Fava, M. (1994). Childhood psychopathology retrospectively assessed among adults with early onset major depression. *Journal of Affective Disorders, 31*, 165–171.
- Andréasson, S., Allebeck, P., Engström, A., & Rydberg, U. (1987). Cannabis and schizophrenia. A longitudinal study of Swedish conscripts. *Lancet:ii: 1483–1486*.
- Angst, J. (1996). Comorbidity of mood disorders: A longitudinal prospective study. *British Journal of Psychiatry, 168*, 31–37.
- Arseneault, L., Cannon, M., Poulton, R., Murray, R., Caspi, A., & Moffitt, T.E. (2002). Cannabis use in adolescence and risk for adult psychosis : Longitudinal prospective study. *British Medical Journal, 325*, 1212–1213.
- Baigent, M., Holme, G., & Hafner, R.J. (1995). Self reports of the interaction between substance abuse and schizophrenia. *Australian and New Zealand Journal of Psychiatry, 29*, 69–74.
- Bardone, A.M., Moffitt, T.E., Caspi, A., Dickson, N., Stanton, W.R., & Silva, P.A. (1998). Adult physical health outcomes of adolescent girls with conduct disorder, depression, and anxiety. *Journal of Academic Child Adolescent Psychiatry, 37*, 594–601.
- Basu, D., Malhotra, A., Bhagat, A., Varma, V.K. (1999). Cannabispsychosis and acute schizophrenia. A case Control study from India. *Addiction and Mental Health, 5*, 71–73.
- Bersani, G., Orlandi, V., Kotzalidis, G.D., & Pancheri, P. (2002). Cannabis and schizophrenia : Impact on onset, course, psychopathology and outcomes. *European Archives of Psychiatry and Clinical Neurosci, 252*, 86–92.
- Bovasso, G.B. (2001). Cannabis abuse as a risk factor for depressive symptoms. *American Journal of Psychiatry, 1058*, 2033–2037.
- Brook, J.S., Cohen, P., & Brook, D.W. (1998). Longitudinal study of co-occurring psychiatric disorders and substance use. *Journal of American Academic Child Psychiatry, 37*, 322–331.
- Brunette, M.F., Mueser, K.T., Xie, H., Drake, R.E. (1997). Relationships between symptoms of schizophrenia and substance abuse. *Journal of nervous and mental disease, 185*, 13–20.
- Cantwell, R., & Harrison G. (1996). Substance misuse in the severely mentally ill. *Advances in Psychiatric Treatment, 2*, 117-124.

Caspari, D. (1999). Cannabis and schizophrenia: Results of a follow-up study. *Eur Arch Clin Neurosci*, 249, 46–49.

Chaudry, H.R., Moss, H.B., d& Bashir, A., & Suliman, T. (1991). Cannabis psychosis following bhang ingestion. *Britisch Journal ofAddiction*, 86, 1075–1081.

Chen, C., Wagner, F.A., & Anthony, J.C. (2002). Marijuana use and the risk of major depressive episode. Epidemiologic evidence from the United States National Comorbidity Survey. *Social Psychiatry and Psychiatric Epidemiology*, 37, 199–206.

Degenhardt, L., Hall, W., & Lynskey, M. (2001). The relationship between cannabis use, depression and anxiety among Australian adults: Findings from the National Survey of Mental Health and Well-being. *Social Psychiatry and Psychiatric Epidemiology*, 36, 219–227.

Dixon, L., Haas, Haas, G., Weiden, P.J., Sweeney, J., & Frances, A.J. (1991). Drug abuse in schizophrenic patients: Clinical correlates and reasons for use. *American Journal of Psychiatry*, 148, 224–230.

Fergusson, D.M., & Horwood, L.J. (1997). Early onset cannabis use and psychosocial adjustment in young adults. *Addiction*, 92, 279–296.

Fergusson, D.M., Horwood, L.J., & Swain-Campbell, N. (2002). Cannabis use and psychosocial adjustment in adolescence and young adulthood. *Addiction*, 97, 1123–1135.

Field, T., Diego, M., & Sanders, C.E. (2001). Adolescent depression and risk factors. *Adolescence*, 36, 491–498.

Frances, R.J. (1997). The wrath of grapes versus the self-medication hypothesis. *Harvard Review of Psychiatry*, 4, 287–289.

Green, B.E., & Ritter, C. (2000). Marijuana use and depression. *Journal of Health and Social Behavior*, 41, 40–49.

Hall, W., & Swift, W. (2000). The THC content of cannabis in Australia: Evidence and implications. *Australian and New Zealand Journal of Public Health*, 5, 503–508.

Hambrecht, M. & Häfner, H. (1996). Substance abuse and the onset of schizophrenia. *Biological Psychiatry*, 40, 1155–1163.

Hambrecht, M. & Häfner, H. (2000). Cannabis, vulnerability, and the onset of schizophrenia: An epidemiological perspective. *Australian and New Zealand of Psychiatry*, 34, 468–475.

Hamera, E., Schneider, J.K., Deviney, S. (1995). Alcohol, cannabis, nicotine, and caffeine use and symptom distress in schizophrenia. *Journal of Nervous and Mental Disease*, 183, 559–565.

Henry, B., Feehan, M., McGee, R., Stanton, W., Moffitt, T.E., & Silva, P. (1993). The importance of conduct problems and depressive symptoms in predicting adolescent substance use. *Journal of Abnormal Child Psychology*, *21*, 469–480.

Imade, A.G.T., & Ebie, J.C. (1991). A retrospective study of symptom patterns of cannabis-induced psychosis. *Acta Psychiatr Scand*, *83*, 134–136.

Iversen, L.L. (2000). *The science of marijuana*. Oxford University Press.

Johnstone, E.C., Abukmeil, S.S., Byrne, M., Clafferty, R., Grant, E., Hodges, A., Lawrie, S.M. & Owens, D.G.C. (2000). Edinburgh high risk study – findings after four years: Demographic, attainment and psychopathological issues. *Schizophrenia Research*, *45*, 1–15.

Kandel, D.B., & Davies, M. (1986). Adult sequelae of adolescent depressive symptoms. *Archives of General Psychiatry*, *43*, 255–262.

Kelder, S.H., Murray, N.G., Orpinas, P., Prokhorov, A., McReynolds, L., Zhang, Q., & Roberts, R. (2000). Depression and substance use in minority middle-school students. *American Journal of Public Health*, *91*, 761–766.

Keshaven, M.S., & Lishman, W.A. (1986). Prolonged depersonalization following cannabis abuse. *British Journal of Addiction*, *81*, 140–142.

Khantzian, E.J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry*, *4*, 231–244.

Linszen, D.H., Dingemans, P.M., & Lenior, M.E. (1994). Cannabis abuse and the course of recent-onset schizophrenic disorders. *Archives of General Psychiatry*, *51*, 273–279.

Mathers, D.C. & Ghodse, A.H. (1992). Cannabis and psychotic illness. *British Journal of Psychiatry*, *161*, 648–653.

McGee, R., Williams, S., Poulton, R., & Moffitt, T. (2000). A longitudinal study of cannabis use and mental health from adolescence to early adulthood. *Addiction*, *95*, 491–503.

McGuire, P.K., Jones, P. Harvey, I., Bebbington, P., Toone, B., Lewis, S., Murray, R.M. (1994). Cannabis and acute psychosis. *Schizophrenia Research*, *13*, 161–168.

Miller, P., Lawrie, S.M., Hodges, A., Clafferty, T., Cosway, R. & Johnstone, E.C. (2001). Genetic liability, illicit drug use, life stress and psychotic symptoms: Preliminary findings from the Edinburgh study of people at high risk for schizophrenia. *Social Psychiatry and Psychiatric Epidemiology*, *36*, 338–342.

Negrete, J.C., Knapp, W.P., Douglas, D. E., & Smith, W.B. (1986). Cannabis affects the severity of schizophrenic symptoms: Results of a clinical survey. *Psychological Medicine*, *16*, 515–520.

Núñez, L.A., & Gurpegui, M. (2002). Cannabis-induced psychosis: A cross-sectional comparison with acute schizophrenia. *Acta Psychiatr Scand*, *105*, 173–178.

Onyango, R.S. (1986). Cannabis psychosis in young psychiatric inpatients. *British Journal of Addiction*, *81*, 419–423.

Patton, G.C., Goffey, C., Carlin, J.B., Degenhardt, L., Lynskey, M., & Hall, W. (2002). Cannabis use and mental health in young people: Cohort study. *British Medical Journal*, *325*, 1195–1198.

Peralta, V. & Cuesta, M.J. (1992). Influence of cannabis use on schizophrenic psychopathology. *Acta Psychiatri Scand*, *85*, 127–130.

Poole, R. & Brabbins, C. (1996). Drug induced psychosis. *British Journal of Psychiatry*, *168*, 135-138.

Rey, J.M., Sawyer, M.G., B. Raphael, Patton, G.C., & Lynskey, M. (2002). Mental health of teenagers who use cannabis. *Journal of Psychiatry*, *180*, 216-221.

Rigter, H., & van Laar, M. (2002, februari). *Epidemiological aspects of cannabis use*. International Scientific Conference on Cannabis, Brussels, Belgium.

Sembhi, S. & Lee, J.W.Y. (1999). Cannabis use in psychotic patients. *Australian and New Zealand Journal of Psychiatry*, *33*, 529–532.

Spencer, C.R., Castle, D., & Michie, P.T. (2002). Motivations that maintain substance use among individuals with psychotic disorders. *Schizophrenia Bulletin*, *28*, 233-247.

Thomas, H. (1993). Psychiatric symptoms in cannabis users. *British Journal of Psychiatry*, *163*, 141–149.

Thomas, H. (1996). A community survey of adverse effects of cannabis use. *Drug and Alcohol Dependence*, *47*, 201–207.

Tien, A.Y., & Anthony, J.C. (1990). Epidemiological analysis of alcohol and drug use as risk factors for psychotic experiences. *Journal of Nervous and Mental Disease*, *1990*, 473–480.

Troisi, A., Pasini, A., Saracco, M., & Spalletta, G. (1998). Psychiatric symptoms in male cannabis users not using other illicit drugs. *Addiction*, *93*, 487–492.

Van Ammers, E.C., Sellman, J.D. & Mulders, R.T. (1997). Temperament and substance abuse in schizophrenia: Is there a relationship? *Journal of Nervous and Mental Disease*, *185*, 283–287.

Van Os, J., Bak, M., Hanssen, M., Bijl, R.V., de Graaf, R., & Verdoux, H. (2002). Cannabis use and psychosis: A longitudinal population-based study. *American Journal of Epidemiology*, *156*, 31–327.

Verdoux, H., Gindre, C., Sorbara, F., Tournier, M., & Swendsen, J.D. (2003). Effects of cannabis and psychosis vulnerability in daily life: An experience sampling test study. *Psychological Medicine*, *33*, 23–32.

Way, N., Stauber, H.Y., Nakkula, M.J., & London, P. (1994). Depression and substance use in two divergent high school cultures: A quantitative and qualitative analysis. *Journal of Youth and Adolescence*, *23*, 331–357

Winokur, G., Turvey, C., Akiskal, H., Coryell, W., Solomon, D., Leon, A., Mueller, T., Endicott, J., Maser, J., & Keller, M. (1998). Alcoholism and drug abuse in three groups – bipolar I, unipolars and their acquaintances. *Journal of Affective Disorders*, *50*, 81–89.

Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I., & Lewis, G. (2002). Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: Historical cohort study. *British Medical Journal*, *325*, 1195–1212.