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Clearing the Smoke on Cannabis

Chronic Use and Cognitive Functioning and Mental Health

Amy J. Porath-Waller, Ph.D.,
Senior Research & Policy Analyst, CCSA

CCSA - CCLAT

Canadian Centre on Substance Abuse

This is the first in a series of reports that reviews the effects of cannabis use on various aspects of human functioning and development. In this report, the effects of chronic cannabis use on cognitive functioning and mental health are presented. Subsequent reports address the effects of maternal cannabis use during pregnancy, cannabis use and driving, and respiratory effects of cannabis use.

Background

Cannabis is the most widely used illicit drug in Canada. According to the 2004 Canadian Addiction Survey (CAS), nearly 45% of Canadians aged 15 years and older reported using cannabis at least once and 14% reported use in the past year (Adlaf, Begin & Sawka, 2005). The use of cannabis is generally more prevalent among youth, with 39.3% of 15- to 17-year-olds and 69.9% of 18- to 19-year-olds reporting lifetime use. Rates of past-year use increase from 15–17 years of age (29.2%) to 18–19 years of age (47.2%). Approximately 46% of past-year cannabis users in Canada aged 15 and older reported using cannabis two or fewer times during the three months prior to the survey. A sizable percentage of past-year users indicated that they use cannabis more regularly on either a weekly (20.1%) or daily (18.1%) basis.

A growing body of evidence suggests that cannabis use may negatively impact several aspects of people's lives, including mental and physical health, cognitive functioning, ability to drive a motor vehicle, and pre- and postnatal development among offspring. In this paper, the effects of chronic cannabis use on facets of cognitive functioning are

described. Although there is no single definition in scientific literature as to what constitutes *chronic cannabis use*, the phrase generally refers to a pattern that entails weekly or more frequent use over periods of months or years and poses a risk for adverse health effects. Terms that are often used interchangeably with *chronic use* include *heavy use, frequent use, regular use, long-term use, abuse, and dependence.* This report also addresses the recent surge of worldwide interest in understanding the link between chronic cannabis use and mental health problems such as psychosis, depression and anxiety. The paper's conclusion discusses implications for policy and practice based on the reviewed evidence.

> Cannabis is a tobacco-like greenish or brownish material consisting of the dried flowering, fruiting tops and leaves of the cannabis plant, *Cannabis sativa.* Hashish or cannabis resin is the dried brown or black resinous secretion of the flowering tops of the cannabis plant. Cannabis produces euphoria and relaxation, changes in perception, time distortion, deficits in attention span and memory, body tremors, and impaired motor functioning. It is a controlled substance under the *Controlled Drugs and Substances Act*—meaning that the acts of growing, possessing, distributing and/or selling cannabis are illegal.

Effects on Cognitive Functioning

Evidence suggests that chronic cannabis use does not produce severe or grossly debilitating impairment of memory, attention and other cognitive functioning; the effects on these cognitive abilities are generally more subtle. After about a month of discontinued use, chronic cannabis users have demonstrated performance deficits in psychomotor speed, attention, memory, and executive functioning as compared to non-using controls (Grant, Gonzalez, Carey, Natarajan & Wolfson, 2003; Medina et al., 2007). Dose-related alterations in brain activity have been noted in the frontal areas, hippocampus and cerebellum, which are regions of the brain responsible for decision-making, executive functioning, and memory (Bolla, Eldreth, Matochik & Cadet, 2005; Schweinsburg et al., 2008). Recent evidence also indicates that chronic cannabis use is associated with reductions in the hippocampal and amygdala brain structures (Yucel et al., 2008). In contrast, studies that have examined the effects of chronic cannabis use following more than a month of abstinence have failed to find evidence indicating any significant cognitive impairment (Fried et al., 2005; Lyketsos, Garrett, Liang & Anthony, 1999; Pope et al., 2002), suggesting that cognitive deficits may be reversible after about a month of discontinued use and that impairment is related to recent but not cumulative use.

The linking of neurocognitive impairment in memory, attention, and executive functioning with chronic cannabis use is biologically plausible. The regions of the brain primarily involved with these forms of cognitive functioning include the hippocampus, prefrontal cortex, and cerebellum. Delta-9-tetrahydrocannabinol (THC), the main psychoactive ingredient in cannabis, has been shown to cause deleterious effects on these areas of the brain, which are dense with cannabinoid receptors (Herkenham et al., 1990).

Evidence indicates that individuals who initiate cannabis use at an early age—when the brain is still developing—may be more vulnerable to lasting neuropsychological deficits than those who begin use later in life. Visual scanning is a cognitive function that undergoes a major maturational process around 12–15 years of age, and Ehrenreich et al. (1999) found that early-onset regular cannabis users (onset before age 16), but not late-onset regular users (onset at 16 years or later), exhibited significantly longer reaction times than controls on a visual scanning task[1]. Another study reported that long-term cannabis users who had initiated use before age 17 had smaller brains, with a lower percentage of gray matter and a higher percentage of white matter, as compared to long-term users who had initiated use at age 17 or later (Wilson et al., 2000). Cannabis use before age 17 has also been associated with poor neurocognitive performance on tasks involving verbal ability (Pope et al., 2003); however, it is not clear from Pope and colleagues' study whether these associated verbal decrements are directly related to cannabis use or if they may be accounted for by lower overall premorbid cognitive ability.

Effects on Mental Health

Psychosis

Findings from a recent meta-analysis revealed that cannabis users—particularly frequent users—are at increased risk of experiencing a psychotic outcome as compared to non-users, even after adjusting for a variety of confounding factors (Moore et al., 2007). A biological mechanism is thought to underlie this relationship; psychotic disorders involve disturbances in the dopamine neurotransmitter systems, and cannabinoids such as THC are associated with increased release of dopamine (Stahl, 2000).

The relationship between cannabis use and psychosis appears to be stronger in people who show a predisposition to psychosis, such as those with a family history of psychotic outcomes (Degenhardt et al., 2007; Henquet et al., 2005; van Os et al., 2002). Some researchers have suggested that this may be the result of an interaction between cannabis use and a genetic vulnerability to psychosis (Henquet et al., 2005; van Os et al., 2002). Others suspect that repeated exposure to cannabis sensitizes the mesolimbic dopamine system in the brain, which makes those individuals with a predisposition to psychosis particularly vulnerable (Stefanis et al., 2004).

Reports are mixed as to whether cannabis has differential effects on psychosis according to the age of first use. Some studies have observed a stronger effect of cannabis on psychotic outcomes among individuals who first used cannabis before the age of 16 compared to those who used after this age (Arseneault et al., 2002; Stefanis et al., 2004), while other research has failed to find any age-related difference (Zammit, 2004). The effects of cannabis may be greater in those who initiate use early in adolescence because their developing brains are vulnerable to persistent alterations that affect behaviour (Viveros, Liorente, Moreno & Marco, 2005). Adolescent cannabis users may also be at greater risk because their pattern of cannabis use is generally more frequent.

[1] The mean period of abstinence among this sample of users was about 30 hours. Thus, these results may reflect residual or withdrawal effects.

Some reports found that cannabis use may occur as a form of self-medication among people suffering from psychotic symptoms (for a review, see Degenhardt & Hall, 2007). However, epidemiological studies exploring whether individuals with a vulnerability to psychosis are more likely to start using cannabis to ameliorate their symptoms have generally failed to find evidence to support this hypothesis (Fergusson, Horwood & Ridder, 2005; Henquet et al., 2005; Stefanis et al., 2004; van Os et al., 2002). A report by Ferdinand et al. (2005) revealed that cannabis use was not only a risk factor for psychotic symptoms but was also a consequence of such symptoms, suggesting that an underlying common vulnerability (e.g., biological, social, environmental) may exist between cannabis use and psychosis.

Depression and Anxiety

Research is mixed as to whether chronic cannabis use influences subsequent depression and anxiety. Some recent longitudinal evidence suggests that such use increases the risk for developing depressive, anxious and manic symptoms, and major depression and bipolar disorder, and that this risk appears greater for frequent users who start using cannabis before age 15 (Hayatbakhsh et al., 2007; Henquet, Krabbendam, de Graaf, ten Have & van Os, 2006; van Laar, Dorsselaer, Monshouwer & de Graaf, 2007). In other investigations, however, statistical adjustment for confounding factors explained all of the observed associations between chronic cannabis use and affective symptomatology and disorders (Harder, Morral & Arkes, 2006; Moore et al., 2007). Such results appear to suggest that common factors (e.g., biological, personality, social, environmental, or a combination of these) predispose people to both affective problems and cannabis use. Pre-existing affective symptoms might raise the likelihood of cannabis use through a mechanism of self-medication. However, several longitudinal studies investigating this possibility have reported that depression and anxiety do not appear to increase the risk of later cannabis use (Bovasso, 2001; Brook, Cohen & Brook, 1998; Hayatbakhsh et al., 2007; Henquet et al., 2006; Patton et al., 2002).

Conclusions and Implications

Studies examining the effects of chronic cannabis use on cognition have generally failed to yield evidence of severe abnormalities. There are reports of mild impairments, however, in memory, attention, psychomotor speed and executive functioning, particularly among those who started using cannabis during early compared to late adolescence. The nature of these cognitive deficits suggests that chronic cannabis users would perform reasonably well on routine, everyday life tasks but are likely to encounter difficulties when performing complex tasks that are novel or cannot be solved by automatic application of previous knowledge. Tasks that rely heavily on a memory component or require strategic planning and multitasking would also be difficult for chronic cannabis users, and such cognitive impairment has the potential to impact academic achievements and occupational proficiency. With approximately 20% of past-year Canadian cannabis users reporting frequent, regular use of cannabis, there is a need for educational campaigns to inform the public of the effects of chronic cannabis use. Recent increases in the use of cannabis for medicinal purposes also

highlight the importance for physicians to discuss the cognitive consequences of such use with their patients when this form of therapy is considered; advice on daily activities to avoid (e.g., driving) while using this substance should also be provided.

A growing body of evidence also indicates that chronic cannabis use may increase the risk of mental health outcomes, including psychosis, depression and anxiety. Adolescent cannabis users may be at greatest risk, perhaps because their use becomes longstanding or due to the effects such exposure has on their developing brains. A biological mechanism may underlie the cannabis-psychosis relationship, but further research is needed to develop a clearer understanding of this possibility. Little research attention has been directed towards possible links between cannabis use and depression and anxiety. Assuming that chronic use increases the risk for affective impairment, two potential mechanisms may underlie this association. First, it is possible that chronic exposure to cannabis may cause changes in neurotransmitter systems, which contribute to the development of depression and anxiety. Alternatively, the effects of chronic cannabis use may be socially mediated, with frequent use leading to various adverse social and psychological consequences that are associated with poor mental health. At this point, it is not clear which mechanism is involved or whether a combination of these mechanisms accounts for this relationship.

Based on the evidence at hand, young people need to be informed about the mental health risks associated with using cannabis. Efforts aimed at preventing, reducing, or delaying the use of this substance among youth may be accompanied by corresponding decreases in subsequent mental health disorders and the associated suffering and health-service costs of such conditions. From a treatment perspective, early detection of cannabis use may be facilitated if clinicians, physicians and other treatment providers are aware that such use may increase an individual's risk of developing psychotic and affective symptoms and disorders. Screening for chronic cannabis use may also be a clinically useful assessment tool relevant to decreasing the risk of mental health problems.

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Canadian Centre on Substance Abuse

75 Albert Street, Suite 500
Ottawa, ON K1P 5E7
Canada
Phone: (613) 235-4048
Fax: (613) 235-8101
info@ccsa.ca
Website: www.ccsa.ca

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