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Clearing the Smoke on Cannabis

Chronic Use and Cognitive Functioning and Mental Health – An Update

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This is the first in a series of reports that reviews the effects of cannabis use on various aspects of human functioning and development. This report on the effects of chronic cannabis use on cognitive functioning and mental health provides an update of a previous report with new research findings that validate and extend our current understanding of this issue. Other reports in this series address the effects of maternal cannabis use during pregnancy, cannabis use and driving, the respiratory effects of cannabis and the medical use of cannabis and cannabinoids. This series is intended for a broad audience, including health professionals, policy makers and researchers.

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Key Points

- Chronic cannabis use is related to mild cognitive impairments and an increased risk for poor mental health. These relationships raise the possibility that its use can also interfere with academic, workplace and social functioning, particularly in young people. There is a need for efforts that focus on preventing, delaying and reducing the use of cannabis by adolescents and young adults.
- Chronic cannabis use has been associated with mild impairments of memory, attention and other cognitive functions. The degree to which these impairments are reversible following cessation of cannabis use is uncertain.
- There is emerging evidence that chronic cannabis use can affect brain development and functioning in areas that are important for cognitive and emotional processes.
- Longitudinal studies indicate that chronic cannabis use and an earlier onset of use is associated with an increased risk of developing psychotic symptoms or schizophrenia, particularly among those who might have a pre-existing genetic risk. Preliminary research suggests that the risk might be greater for individuals who use cannabis that is high in (–)-trans-Δ^{9}-tetrahydrocannabinol (THC) and low in cannabidiol (CBD).
- Emerging research indicates a relationship between chronic cannabis use and risk of adverse mental health outcomes, such as depressive disorders, anxiety and suicidal behaviours. However, more robust longitudinal research is required to understand the nature of the relationships and ascertain whether they can be explained by other factors.

Background

After alcohol, cannabis, also referred to as marijuana, is the most widely used psychoactive substance in Canada. According to the 2013 Canadian Tobacco, Alcohol and Drugs Survey (CTADS), 10.6% of Canadians aged 15 years and older reported using cannabis at least once in the past year (Statistics Canada, 2015), virtually

unchanged from 10.2% in 2012. The use of cannabis is generally more prevalent among young people, with 22.4% of youth aged 15 to 19 and 26.2% of young adults aged 20 to 24 reporting past-year use. Approximately 28% of Canadians aged 15 and older who used cannabis in the past three months reported that they used this drug every day or almost daily.

A growing body of evidence suggests that cannabis use might have a negative impact on several aspects of people's lives, including their mental and physical health, cognitive functioning, ability to drive a motor vehicle, and pre- and post-natal development among offspring whose mothers smoked during pregnancy. This report—part of a series reviewing the effects of cannabis use on various aspects of human functioning and development (see Beirness & Porath-Waller, 2015; Kalant & Porath-Waller, 2016; McInnis & Plecas, 2016; Porath-Waller, 2015)—provides an update on the topic of the cognitive functioning and mental health effects of chronic cannabis use. Although there is no single definition in the 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, dependence, and cannabis use disorder. Following a review of the evidence, this report discusses implications for policy and practice.

The research outlined in this report is the most up-to-date evidence on the link between chronic cannabis use and cognitive functioning and mental health conditions. It should be noted, however, that a causal link between chronic cannabis use and deficits in cognitive functioning has not been fully demonstrated, particularly as younger individuals with poorer cognitive functioning are also more likely to use cannabis regularly (World Health Organization, 2016). It remains a possibility that there are differences among individuals that precede chronic cannabis use, and these pre-existing differences could be accounting for the results outlined in this report. As well, there are several gaps in the research outlined; for example, gender and sex have largely not been attended to in the studies described.

Effects on Cognitive Functioning

Evidence suggests that continued chronic cannabis use does not produce severe or grossly debilitating impairment of memory, attention, psychomotor[1] and other cognitive functioning; the effects on these cognitive abilities are generally more subtle. These effects are particularly evident when cannabis use begins in adolescence and continues throughout young adulthood (Meier et al., 2012; Volkow, Baler, Compton, & Weiss, 2014).

Despite a large number of studies examining the impact of cannabis on various aspects of cognitive functioning, it is uncertain whether the effects of cannabis on cognition are reversible following cessation of the drug. Studies that have examined the long-term consequences of cannabis use following cessation report mixed findings (Solowij et al., 2002). For example, after about a month of discontinued use, some studies of those who used cannabis chronically demonstrated performance deficits in psychomotor speed, attention, memory and executive functioning when compared to individuals who did not use cannabis (also referred to as controls) (Grant, Gonzalez, Carey, Natarajan, & Wolfson, 2003; Medina et al., 2007). A longitudinal cohort study of more than 1,000 individuals assessed at age 13 and 38 reported an association between early onset chronic cannabis use and lower IQ scores (an average decline of eight points) compared to individuals who did not use cannabis chronically over the course of the study. Among individuals who began using cannabis during adolescence and who subsequently were abstinent from the drug, IQ scores did not return to pre-use levels (Meier et al.,

Cannabis is a 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. The acute effects of cannabis include 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 selling cannabis are illegal. The Canadian government elected in 2015 has indicated its intention to introduce legislation in spring 2017 to legalize and regulate cannabis for non-medical use. There is also currently an exemption for those possessing cannabis for medical purposes as supported by a physician.

[1] Research describing the effects of cannabis use on psychomotor functioning is reviewed in Beirness & Porath-Waller (2015).

2012). Although this study was criticized for not controlling for socioeconomic status (Rogeberg, 2013), a subsequent analysis of the data suggested that socioeconomic status did not account for the effects of chronic cannabis use on IQ score decline (Moffitt, Meier, Caspi, & Poulton, 2013). In contrast, other studies that have examined the effects of chronic cannabis use after abstinence have failed to find any persistent cognitive impairment (Fried, Watkinson, & Gray, 2005; Hooper, Woolley, & De Bellis, 2014; Lyketsos, Garrett, Liang, & Anthony, 1999; Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd, 2002). These studies have suggested that cognitive deficits might be reversible after about a month of discontinued use and that cognitive impairment is related to recent rather than cumulative use. The reason for these discrepancies in results could be due to differences in the questions asked related to cannabis use across these studies. For example, some studies did not provide information on the age of onset of cannabis use (Fried et al., 2005; Lyketsos et al., 1999; Pope et al., 2002), and others involved relatively short-term heavy use of cannabis (Hooper et al., 2014). In sum, these results are not necessarily in disagreement with one another, and the data linking chronic cannabis use to lower IQ should be considered when assessing the potential harms of cannabis.

Memory

Many studies have observed associations between acute cannabis use and deficits in short-term memory (Ranganathan & D'Souza, 2006). However, fewer studies have established consistent links between chronic cannabis use and memory deficits (Solowij & Battisti, 2008), even though impaired memory is a frequent complaint in those seeking treatment for cannabis use (Hall, 2015). A three-year longitudinal study of 49 individuals using functional magnetic resonance imaging (fMRI)[2] observed no changes in working memory[3] functionality between individuals who used cannabis chronically and controls, even though there were increases in substance use among those who used cannabis across the study period (Cousijn et al., 2014a). Similarly, another study did not observe differences in working memory between 32 individuals who used cannabis chronically and 41 controls. There were also no differences in brain functioning in areas associated with working memory (Cousijn et al., 2014b). Among adolescents who used cannabis chronically, performance on a spatial working memory task was similar to controls. However, during the task, the brain responses of 15 adolescents who used cannabis chronically were lower in the right dorsolateral prefrontal and occipital cortex (an area of the brain that is important for visual processing). There was also greater activity in the right parietal cortex (an area of the brain that is important for integrating sensory information) among individuals who used cannabis heavily (n=15) compared to controls (n=17), an effect which persisted after one month's abstinence. The clinical meaningfulness of these brain alterations is not clear (Schweinsburg et al., 2008).

Some other studies have reported links between chronic cannabis use and deficits in working memory. One study comparing individuals with chronic cannabis use to those who did not use found greater deficits in a verbal working memory task among those who use and these deficits were tied to altered neural activity. The differences were greatest among individuals who reported the longest histories of cannabis use and had the earliest age of onset (Battisti et al., 2010). An fMRI study of 45 adolescent boys found no performance differences between individuals who used cannabis chronically and controls on a verbal working memory task and a pictorial associative memory task (a task that tests the ability of an individual to learn the relationship between two images). However, during the verbal working memory task, adolescent boys who used cannabis chronically displayed while learning the task increased activity in prefrontal regions (areas of the brain that are thought to be important in complex cognitive behaviour such as planning, decision making, goal setting and expectancies, among others) (Jager, Block, Luijten, & Ramsey, 2010). The authors suggested that increased frontal activity could reflect a compensatory mechanism among individuals who use cannabis chronically (i.e., that those who use cannabis require more activation in order to perform as well as controls). In line with this possibility, several other studies have observed no differences in cognitive task performance between individuals who use cannabis chronically and controls, but heightened activity in brain regions involved in cognitive tasks (Behan et al., 2014; Kanayama, Rogowska, Pope, Gruber, & Yurgelun-Todd, 2004; Smith, Longo, Fried, Hogan, & Cameron, 2010). In general, when examining performance on memory tasks, the results are somewhat mixed, although the data indicate a potential for memory deficits among those who use cannabis chronically. The findings were relatively consistent across studies showing that brain activity differed between those who use cannabis and those who do not during memory tasks, suggesting a potential compensatory effect.

[2] fMRI is a form of imaging that can measure regional brain activity by detecting blood flow.

[3] Working memory is a memory process that involves transient retention of information, as well as the processing and manipulation of information.

Attention

Studies of attentional deficits among individuals who use cannabis chronically have also yielded mixed results. Specifically, an fMRI study that compared those who use cannabis chronically to controls during a visual-attention task showed no differences in task performance. However, individuals who were currently abstinent from cannabis use displayed decreased activation in several brain regions during the task. The association between chronic cannabis use and decreased regional brain activity during an attention task was more pronounced among individuals who reported greater lifetime exposure to cannabis and an earlier onset of use. These differences in brain activity were diminished among individuals who reported longer periods of abstinence from cannabis (Chang, Yakupov, Cloak, & Ernst, 2006). Another brain imaging study of 28 adolescents found more errors and a longer reaction time during attentional tasks among individuals who used heavily as compared to controls and these behaviours were accompanied by greater activation in the right prefrontal cortex and parietal cortices (Abdullaev, Posner, Nunnally, & Dishion , 2010). Individuals with long-term heavy cannabis use displayed increased functional connectivity[4] between several brain areas during an attentional task than controls in the absence of any differences in the performance of the task. The authors suggested that the increased activity between the brain regions reflected a compensatory response to the possible effect of chronic cannabis use on visual and attentional processes (Harding et al., 2012). Together, the data examining the link between chronic cannabis use and attentional deficits is similar to what was observed in memory. Specifically, results are mixed but brain activation appears to differ between those who use cannabis and those who do not. More research is needed to determine whether these brain differences are related to functional impairments in attention.

Attentional biases have also been observed among those who use cannabis chronically when they are presented with cannabis-related cues. Attentional biases towards drug cues is related to problematic substance use (Stacy & Wiers, 2010). A sample of individuals who reported heavy cannabis use (n=27) showed greater attentional bias to cannabis words than did controls (n=26), and the bias was strongest among individuals with a cannabis use disorder (Cousijn et al., 2013). This finding is in line with other reports that individuals who use cannabis chronically show increased activity in brain areas that have been associated with habit-based learning when presented with positive cannabis-related cues (Ames et al., 2013).

Inhibition, Impulsivity and Decision Making

The ability to suppress inappropriate behaviours is a part of normal brain development (Luna & Sweeney, 2004). Disturbances in inhibitory control have been tied to the initiation and continuation of problematic substance use (Whelan et al., 2012). Among adults who use cannabis chronically, deficits in performance have been demonstrated during various tasks that assess inhibitory control (Bolla, Eldreth, Matochik, & Cadet, 2005; Gruber & Yurgelun-Todd, 2005; Hester, Nestor, & Garavan, 2009). For example, in two studies using an inhibitory control task, those who used cannabis chronically failed to appropriately inhibit their responses more often than those who did not, and showed more altered brain activation than the non-using control group (Eldreth, Matochik, Cadet, & Bolla, 2004; Gruber & Yurgelun-Todd, 2004). However, it could be argued that the observed differences in inhibitory control led to differences in cannabis use. A positron emission tomography (PET)[5] study during a task to assess inhibitory control found that those who used cannabis chronically (n = 16) performed as well as controls (n = 16), but those who did use chronically were less aware of the errors that they made and showed decreased activity in several brain regions (Hestor, Nestor, & Garavan, 2009). Adolescents who were being treated for a cannabis use disorder displayed poorer performance on an inhibitory task than controls, but showed differences in resting levels of brain activity (i.e., while not performing a task) between parietal and cerebellar regions while undergoing an fMRI. This finding suggests that the lower inhibitory control observed among adolescents who use cannabis regularly could be related to altered connectivity between brain regions important in response inhibition (Behan et al., 2014).

Measures of decision making and impulsivity have also been examined in those who report chronic cannabis use. For example, in a decision-making task called the Iowa Gambling Task, participants must learn to choose from “good” versus “bad” decks of cards in order to maximize their monetary gains. Individuals who use cannabis perform more poorly on this task than controls (Bolla et al., 2005; Fridberg et al., 2010; Wesley, Hanlon, & Porrino, 2011). Poorer performance on the task has also correlated with the number of weekly joints smoked, as well as altered brain activation (Bolla et al., 2005). Deficits in decision-making tasks have not been observed between those who use cannabis chronically and controls in a standard version of the Iowa Gambling Task, although when a variant version was used deficits were observed (Vaidya et al., 2012). However, in a different reward-related decision-making

[4] Functional connectivity refers to the level to which brain regions interacts.

[3] PET is a form of imaging that can assess brain functioning via introducing a radioactive tracer into the body; it can also be used to assess the functioning of specific brain cells depending on the type of tracer used.

task, differences were not observed between those who used cannabis chronically and controls (Johnson et al., 2010). In sum, these findings indicate that chronic cannabis use is related to differences in decision making compared to those who do not use cannabis, but these differences might be dependent on the context in which individuals are tested.

Affective Processing

Individuals who use cannabis often report increased perceptions of interpersonal closeness and empathy as an acute effect of cannabis use (Galanter et al., 1974). There is some emerging research to suggest that those who use cannabis chronically process emotional stimuli differently from those who do not. For example, an fMRI study that compared 15 controls and 15 individuals who reported chronic cannabis use found lower cingulate and amygdala activity (areas of the brain that are important for detecting and experiencing emotions) when presented with pictures of masked angry and happy faces (Gruber, Rogowska, & Yurgelun-Todd, 2009). Individuals who used cannabis chronically also took longer to identify emerging happy, sad and angry emotions when presented with faces than did controls (Platt, Kamboj, Morgan, & Curran, 2010).

Age of Onset

Individuals who initiate cannabis use at an early age—when the brain is still developing—might be more vulnerable to lasting neuropsychological deficits than those who begin to use it later in life (see George & Vaccarino, 2015 for a comprehensive review on the effects of cannabis use during adolescence). Visual scanning is a cognitive function that undergoes a major maturational process around 12–15 years of age. Ehrenreich et al. (1999) found that early-onset regular cannabis use (onset before age 16; n = 48), but not late-onset regular use (onset at 16 years or later; n = 51) was associated with significantly longer reaction times than no use (n = 49) on a visual scanning task. Another study reported that long-term cannabis use among those who had initiated use before age 17 was associated with smaller brains, a lower percentage of gray matter and a higher percentage of white matter than for those who also used cannabis long-term, but 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). It is not clear from Pope and colleagues' study, however, whether these verbal decrements were directly related to cannabis use or if they reflected poorer premorbid cognitive ability that might be associated with cannabis use. Another study that assessed executive functioning found that individuals who began chronic cannabis use before the age of 15 demonstrated poorer performance than those who began use after the age of 15 and controls who did not use cannabis (Fontes et al., 2011). Overall, there is a growing body of research that indicates that cannabis use at a younger age (i.e., up to mid-20s) is associated with a greater risk of harms than those who begin later in adulthood.

Neurobiological Alterations

It is biologically plausible that neurocognitive impairment in memory, attention and executive functioning could be linked to chronic cannabis use. The regions of the brain primarily involved in these forms of cognitive functioning include the hippocampus, prefrontal cortex, and cerebellum. (–)-trans-Δ9-tetrahydrocannabinol (THC), the main psychoactive ingredient in cannabis, has been shown in animal studies to adversely affect these areas of the brain, which are dense with cannabinoid receptors (Herkenham et al., 1990). Indeed, it has been suggested that differences in cognitive performance between those who use cannabis chronically and those that do not could arise because chronic THC exposure reduces the number of cannabinoid receptors in brain areas that play an important role in cognition (Hirvonen et al., 2012).

Dose-related alterations in brain activity have been noted in the frontal areas, hippocampus and cerebellum, regions of the brain responsible for decision making, executive functioning and memory (Bolla et al., 2005; Schweinsburg et al., 2008). A systematic review found a consistent reduction in hippocampal volume across studies, particularly when studies included participants who reported heavier cannabis use (Lorenzetti et al., 2014). However, another systematic review reported mixed findings from structural brain studies of those who use cannabis (Martin-Santos et al., 2010). For instance, three studies did not find significant differences in grey matter volume between controls and individuals who use cannabis (Block et al., 2000; Tzilos et al., 2005; Jager et al., 2007). However, another comparison study found differences in grey matter volume in several brain regions (Matochik, Eldreth, Cadet, & Bolla, 2005). Similarly, other studies have reported volume reductions in the hippocampus and amygdala (see Batalla et al., 2013). Further, reductions in hippocampus and amygdala volumes were associated with a specific genetic variant that codes for a cannabinoid receptor (CNR1) (Schacht, Hutchison, & Filbey, 2012). Recently, Battistella and colleagues reported decreases in grey matter in several brain regions in individuals who used cannabis chronically compared to controls (i.e., medial temporal cortex, temporal pole, parahippocampal gyrus, left insula and orbitofrontal cortex) (Battistella et al., 2014).

Finally, there is evidence that chronic cannabis use can alter the structural integrity of brain white matter (involved in the communication between neural signals in the brain) (Arnone et al., 2008; Gruber, Silveri, Dahlgren, & Yurgelun-Todd, 2011). Together, these data suggest a possible link between chronic cannabis use and structural alterations, but we cannot exclude the possibility that brain differences preceded cannabis use.

There is preliminary evidence that structural differences related to cannabis use could be more common among females than males who used cannabis (Batalla et al., 2013). Specifically, a study of 35 adolescent females who used cannabis showed larger right amygdala volumes compared to controls (n=47), and higher volumes were associated with greater depression and anxiety symptoms (McQueeny et al., 2011). Adolescent females who used cannabis had greater prefrontal cortex volumes than female controls and greater prefrontal cortex volumes were associated with poorer executive functioning. By contrast, males who used cannabis had smaller prefrontal cortex volumes than controls (Medina et al., 2009). Greater cannabis use was more strongly associated with poorer performance on an episodic memory task in females and with poorer performance on a decision-making task in males. The latter relationship was not apparent in females (Crane, Schuster, Fusar-Poli, & Gonzalez, 2013). Together, these emerging data suggest that there might be sex differences in the neurological, cognitive and mental health effects of cannabis.

Effects on Mental Health

Psychosis and Schizophrenia

A meta-analysis found that those who used cannabis—particularly those who use frequently—had a higher risk of experiencing a psychotic outcome compared to those who did not use, even after adjusting for a variety of confounding factors such as other substance use, sociodemographic factors, personality and other mental health conditions (Moore et al., 2007). There is a plausible biological mechanism for this relationship: psychotic disorders involve disturbances in the dopamine neurotransmitter systems, and cannabinoids such as THC increase dopamine release (Stahl, 2000). Double-blind studies indicate that THC induces increases in psychotic symptoms among participants in a dose-dependent way (D'Souza et al., 2004; Morrison et al., 2009; Murray et al., 2013). As well, there is emerging evidence that chronic use of cannabis products that have a higher THC content and a lower cannabidiol content might increase the risk of schizophrenia and that it will occur at an earlier age of onset (Di Forti et al., 2009; 2014; 2015).

The relationship between cannabis use and psychosis appears to be stronger in people with a predisposition to psychosis, such as those with a family history of psychosis (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). Studies that have examined the degree to which cannabis use and psychoses are caused by a shared genetic risk factor have suggested that genetic risk factors account for some, but not all of the relationship between cannabis use and psychosis (Giordano, Ohlsson, Sundquist, Sundquist, & Kendler, 2015; McGrath et al., 2010; Power et al., 2014). Others suspect that repeated exposure to cannabis sensitizes the mesolimbic dopamine system in the brain, which makes individuals with a predisposition to psychosis particularly vulnerable to its effects (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 first used it after this age (Arseneault et al., 2002; Stefanis et al., 2004). Other research has failed to find any age- related differences (Zammit, 2004). The effects of cannabis might be greater in those who initiate use early in adolescence because developing brains are more vulnerable to persistent alterations that affect behaviour (Viveros, Llorente, Moreno, & Marco, 2005). Adolescents who use cannabis might also be at greater risk if they use more frequently (George & Vaccarino, 2015).

There remains debate about whether there is a causal link between cannabis use and psychosis. Reports that have examined whether population increases in cannabis use coincide with increased incidence rates of schizophrenia are mixed (Ajdacic-Gross et al., 2007; Boydell et al., 2006; Degenhardt, Hall, & Lynskey, 2003; Hickman, Vickerman, Macleod, Kirkbride, & Jones, 2006). As well, some authors have suggested that cannabis use may be a form of self-medication in 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). Ferdinand et al. (2005) suggested that cannabis use was not only a risk factor

for psychotic symptoms, but was also a consequence of these symptoms, suggesting that a shared vulnerability (e.g., biological, social, environmental) might exist between cannabis use and psychosis. To date, there has been a substantial amount of research on the link between chronic cannabis use and psychosis, and together the findings suggest that cannabis use is a risk factor for the development of psychosis. The degree to which chronic cannabis use serves a causal factor in the onset of psychosis has not been fully established.

Depression, Anxiety, and Post-Traumatic Stress Disorder

Fewer studies have been conducted on the link between chronic cannabis use and other mental health disorders. Research is mixed as to whether chronic cannabis use influences subsequent depressive disorders and anxiety. Meta-analyses of longitudinal studies of the relationship between chronic cannabis use and depressive disorders have reported modest associations (Moore et al., 2007; Lev-Ran et al., 2014). Confounding factors that might play an important role in explaining this relationship have often not been adequately controlled for in these studies and in some studies the association has disappeared after controlling for confounders (Feingold, Weiser, Rehm, & Lev-Ran, 2015; Green & Ritter, 2000). Animal studies have demonstrated that the serotonin receptor levels are altered by long-term cannabinoid administration (Hill et al., 2006), and changes in serotonin are thought to play an important role in depressive disorders (Mahar, Bambico, Mechawar, & Nobrega, 2014). The link between chronic cannabis use and depressive disorders might also be explained by cannabis use contributing to poorer psychosocial adjustment, which could increase the risk of negative mental health outcomes (Degenhardt et al., 2003).

Longitudinal evidence from 4,815 individuals indicated that cannabis use increased the risk of developing bipolar disorder (specifically the presence of manic symptoms) (Henquet, Krabbendam, de Graaf, ten Have, & van Os, 2006). There is fairly consistent data that cannabis use can worsen bipolar symptoms among those who already have bipolar disorder. For example, a systematic review indicated that cannabis use worsened clinical outcomes, such as symptom severity and duration of manic phases, in those with a bipolar disorder (van Rossum, Boomsma, Tenback, Reed, & van Os, 2009; Strakowski, DelBello, Fleck, & Arndt, 2000; Baethge et al., 2008).

The potential link between cannabis and anxiety disorders was investigated in a birth cohort study of 3,239 young adults. It found that individuals who began to use cannabis before the age of 15 years and who used it chronically at age 21, were more likely to report symptoms of an anxiety disorder in early adulthood (Hayatbaksh et al., 2007). As well, in a longitudinal study conducted among 1,709 individuals, cannabis use and cannabis dependence were associated with panic attacks and panic disorder, but these relationships were no longer significant when daily cigarette smoking was controlled for (Zvolensky et al., 2008). Some prospective studies have found that anxiety disorders in adolescence might be associated with regular cannabis use (Wittchen et al., 2007). Together, the possibility remains that common factors (e.g., biological, personality, social and environmental or a combination of these) predispose people to develop affective disorders and cannabis use. Pre-existing affective symptoms might increase the likelihood of using cannabis as a form of self-medication. However, several longitudinal studies investigating this possibility have reported that depression and anxiety do not 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). Together, the research suggests a clear association between cannabis use and depressive disorders, bipolar disorders and anxiety disorders; however, the directionality between these links is not well understood. Research does suggest that chronic cannabis use can been associated with worse clinical outcomes, particularly among those with bipolar disorder.

The link between cannabis use and the alleviation or exacerbation of symptoms of post-traumatic stress disorder (PTSD) has been debated (see Haney & Evins, 2016). On the one hand, there are high levels of co-morbidity between PTSD and cannabis use disorders (Agosti, Nunes, & Levin, 2002). A longitudinal study of 2,276 veterans reported that cannabis use was associated with greater PTSD symptom severity and violent behaviour (Wilkinson, Stefanovics, & Rosenheck, 2015). On the other hand, many individuals with PTSD report using cannabis to cope with their symptoms (Cougle, Bonn-Miller, Vujanovic, Zvolensky, & Hawkins, 2011; Bonn-Miller, Vujanovic, Boden, & Gross, 2011). There is some preliminary human research supporting a possible role for cannabinoids in extinguishing the fear response associated with the trauma (a common therapeutic method for PTSD) (Rabinak et al., 2013). As well, there is emerging evidence for the biological plausibility of cannabinoids in modulating fear responses (Dincheva et al., 2015; Hariri et al., 2009). To date, there are limited data from controlled trials on the impact of smoking cannabis on PTSD outcomes. More research is required before conclusions can be drawn about either the potential benefits or adverse effects of chronic cannabis use among those with PTSD (Haney & Evins, 2016).

Suicidal Behaviours

Some preliminary research has shown associations between cannabis use and suicidal behaviours (i.e., completed suicide, suicide attempts and ideation) (Borges, Bagge, & Orozco, 2016). A longitudinal study (n = 1,265) of the relationship between cannabis use and suicidal behaviours found that chronic cannabis use at the age of 15 increased the risk of suicidal ideation or attempt at age 16–17 years. However, when confounding factors were controlled for (e.g., social disadvantage, childhood adversity, substance using peers, educational attainment, etc.), this relationship was no longer significant (Fergusson & Horwood, 1997). When this same cohort was assessed 30 years later there was a significantly increased risk of suicidal ideation in males who used cannabis chronically, but not in females (van Ours, Williams, Fergusson, & Horwood, 2013). A combined analysis of two longitudinal studies observed a dose-response relationship between the frequency of cannabis use prior to 17 years and suicide attempts between the ages of 17 and 25 (Silins et al., 2014). Death by suicide has been infrequently assessed in relation to cannabis use. In those longitudinal studies that have found an association, the association has not persisted after controlling for confounding factors (Andréasson & Allebeck, 1990; Price, Hemmingsson, Lewis, Zammit, & Allebeck, 2009). However, some case control studies have reported an increased risk of suicide among individuals with cannabis use disorders after controlling for a subset of potential confounding factors (Kung, Pearson, & Liu, 2003; Kung, Pearson, & Wei, 2005). Research exploring the link between cannabis use and suicidal behaviours is still emerging, and determining the robustness of this relationship should be a key consideration for future research on the mental health effects of cannabis.

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, most evident among those who started using cannabis during early adolescence and who persisted in using throughout young adulthood. The nature of these cognitive deficits suggests that individuals who use cannabis chronically would perform reasonably well on routine, everyday life tasks, but might encounter difficulties when performing complex tasks that are novel or cannot be solved by the automatic application of previous knowledge. Tasks that rely heavily on a memory component or require strategic planning and multitasking might also be difficult for those who use cannabis chronically. These cognitive impairments have the potential to reduce academic achievements and occupational proficiency. With 28% of Canadians reporting to have used cannabis regularly in the past three months in 2012 (Health Canada, 2013), there is a need to educate the public about the adverse cognitive effects of chronic cannabis use, particularly given pending changes to cannabis policy in Canada. Recent increases in the use of cannabis for medical purposes also highlight the need for physicians to discuss the cognitive consequences of regular use with their patients especially when regular use of this form of therapy is being considered. The discussion should include advice on daily activities to avoid (e.g., driving) while using the substance. Finally, finding effective approaches to reduce the frequency of use and delay initiation of use among youth is needed to reduce the potential for cannabis-related harms (Canadian Centre on Substance Abuse, 2010). Similarly, there is a need to increase the capacity of those who work with youth by providing them evidence-informed tools and resources (Canadian Centre on Substance Abuse, 2016).

A growing body of evidence also indicates that chronic cannabis use might increase the risk of mental health conditions, particularly psychosis. Adolescents who use cannabis might be at greatest risk, perhaps because their use more likely becomes chronic and because such exposure might adversely affect their developing brains. A biological mechanism might underlie the cannabis–psychosis relationship, but further research is needed to evaluate this possibility. Although research has consistently reported high co-occurring rates of cannabis use and several mental health outcomes, more research is needed on the links between cannabis use and depression, anxiety and suicidal behaviours. It is possible that chronic exposure to cannabis might change neurotransmitter systems in ways that contribute to the development of these disorders. Alternatively, the effects of chronic cannabis use might be socially mediated in that frequent use leads to various adverse social and psychological consequences that are associated with poor mental health. As well, individuals with poor mental health might use cannabis as a means to cope with their symptoms or a third factor (e.g., genetics) could underlie this relation. At this point, it is not clear which mechanisms are involved.

There are several lines of research that would further our understanding of the link between chronic cannabis use and cognitive and mental health outcomes. Given the recent increases in THC concentrations (European Monitoring Centre for Drugs and Drug Addiction, 2014), more information is needed on the effects of high potency THC cannabis and other cannabinoids on cognitive functioning and mental health. We also need to understand whether

the method of administration (i.e., ingesting, smoking or vaporizing) differentially affects cognitive and mental health outcomes.

When cannabis products become legally available in Canada, understanding these issues will inform the ways in which the THC, CBD and other cannabinoid composition of cannabis products is regulated to minimize mental health and cognitive harms. These regulatory considerations are complex and will have to be balanced against other factors, such as limiting the unregulated distribution of high potency products in the black market. We also need better designed longitudinal studies that combine multiple types of evidence (including neurobiological and genetic) to establish whether causal links exist between chronic cannabis use and cognitive functioning and poor mental health.

Young people need to be informed about the possible mental health risks of using cannabis. Our success in preventing, reducing or delaying the use of this substance by youth might be accompanied by decreases in the harms associated with cannabis. From a treatment perspective, early detection of cannabis use could be facilitated if clinicians, physicians and other treatment providers are aware that its use could increase an individual's risk of developing psychotic and affective symptoms and disorders. Screening for chronic cannabis use could also be a clinically useful assessment tool in decreasing the risk of mental health problems among those who use cannabis (Bernstein et al., 2009).

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