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Clearing the Smoke on Cannabis

Regular Use and Cognitive Functioning

Robert Gabrys, Ph.D., Research and Policy Analyst, CCSA
Amy Porath, Ph.D., Director, Research, CCSA

Key Points

- Regular use refers to weekly or more frequent cannabis use over a period of months to years. Regular cannabis use is associated with mild cognitive difficulties, which are typically not apparent following about one month of abstinence. Heavy (daily) and long-term cannabis use is related to more noticeable cognitive impairment.
- Cannabis use beginning prior to the age of 16 or 17 is one of the strongest predictors of cognitive impairment. However, it is unclear which comes first — whether cognitive impairment leads to early onset cannabis use or whether beginning cannabis use early in life causes a progressive decline in cognitive abilities.
- Regular cannabis use is associated with altered brain structure and function. Once again, it is currently unclear whether chronic cannabis exposure directly leads to brain changes or whether differences in brain structure precede the onset of chronic cannabis use.
- Individuals with reduced executive function and maladaptive (risky and impulsive) decision making are more likely to develop problematic cannabis use and cannabis use disorder.
- Regular cannabis use is related to alterations in the brain's natural reward pathways. Among individuals with pre-existing vulnerabilities (e.g., genetic, early life experiences), these alterations might be associated with disrupted motivational processes and increase the risk for cannabis dependence.
- To better understand the effects of chronic cannabis use on cognitive functioning, standardized measurement of cannabis use is greatly needed. It is also important to consider individual characteristics, including polysubstance use, sex and gender differences, and genetic background.
- It is important to inform individuals about the health effects associated with chronic and heavy cannabis use. Indeed, public awareness and education is needed now more than ever given the recent shift in Canada in the legal status of cannabis for non-medical purposes.

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 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 link between chronic cannabis use and mental health, the effects of maternal cannabis use during pregnancy, cannabis use and driving, the respiratory effects of cannabis use 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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Background

Cannabis, also referred to as marijuana, is the second most widely used psychoactive substance in Canada, led only by alcohol. According to the 2018 National Cannabis Survey (second quarter), 16% of Canadians aged 15 years and older reported using cannabis in the past three months. The use of cannabis is generally more prevalent among young people, with 33% of individuals between the age of 15 to 24 reporting use in the past three months compared to 13% of those aged 25 or older (Statistics Canada, 2018). Given the proportion of Canadians using cannabis and in light of the recent legalization of non-medical cannabis use, it is important that individuals be well informed of the health effects of cannabis use.

A growing body of research suggests that chronic cannabis use can have a negative impact on several aspects of a person's life, including their mental and physical health, ability to drive a motor vehicle, and pre- and post-natal development of offspring among mothers who have used cannabis during pregnancy (World Health Organization, 2016). This report — part of a series reviewing the effects of cannabis use on various aspects of human health and development (see McInnis & Porath-Waller, 2016; McInnis & Plecas, 2016; Porath, Kent & Konefal, 2018; Beirness & Porath-Waller, 2017; Kalant & Porath-Waller, 2016) — provides an update on the effects of chronic cannabis use on cognitive functioning.

Regular and Heavy Cannabis Use

Although there is no single definition in the scientific literature as to what constitutes regular 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 regular use include frequent use, chronic use and long-term use. Heavy use, by contrast, typically refers to daily or more frequent use, and can be a sign of dependence and cannabis use disorder.

Effects on Cognitive Functioning

The available evidence suggests that, for most individuals, chronic cannabis use does not produce severe or grossly debilitating impairment of cognitive functioning. Instead, the effects appear to be more subtle and no longer measurable after a few days to weeks of abstinence (Scott et al., 2018). However, initiating regular cannabis use in early adolescence and continuing through young adulthood can lead to more pronounced and long-term cognitive deficits (Meier et al., 2012; Morin et al., 2018). There is ongoing debate about whether heavy cannabis use (e.g., daily use) results in permanent changes in cognition or whether cognitive deficits are reversible after extended abstinence from the substance (Jackson et al., 2016; Meier et al., 2012; 2018; Morin et al., 2018; Volkow, Baler, Compton, & Weiss, 2014).

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. Cannabis can be consumed by smoking, vaporization, ingestion (edibles), oral application of tinctures, and by topical application of creams, oils and lotions. Cannabis consists of more than 100 cannabinoids, but delta-9-tetrahydrocannabinol (THC) is the main psychoactive ingredient responsible for the "high" feeling. Cannabidiol (CBD), another important cannabinoid, does not have psychoactive properties, but may interact with THC. The acute effects of cannabis include euphoria and relaxation, changes in perception, time distortion, deficits in attention span and memory, body tremors, increased heart rate and blood pressure, and impaired motor functioning. Over the past few decades, there has been an increase in the concentrations of THC (and decrease in CBD levels) in illicit cannabis, increasing from 4% in 1995 to 12% in 2014 (ElSohly et al., 2016). Canada legalized the use of cannabis for non-medical purposes for individuals over 18 years of age (19 in some provinces) on October 17, 2018. A review of Canadian online cannabis retail outlets (e.g., ocs.ca, bccannabisstores.com, albertacannabis.org) revealed that dried cannabis products have up to 30% THC, and products in the 15% to 20% THC range are common.

Learning and Memory

Learning and memory deficits have been one of the more commonly studied aspects of cognitive functioning among individuals engaging in regular cannabis use (Scott et al., 2018, Schoeler & Bhattacharyya, 2013; Solowij & Battisti, 2008). Overall, the available evidence is inconsistent, in part due to the many sources of variability across studies, including sample characteristics and study methodology. On the one hand, the link between frequent cannabis use and learning and memory deficits has been observed in adolescents, young and older adults (Battisti et al., 2010; Becker Collins, & Luciana, 2014; Cuttler, McLaughlin, & Graf, 2012; Dougherty et al., 2013; Medina et al., 2007; Solowij et al., 2011). Long-term cannabis use has also been shown to contribute to a progressive decline in learning and memory capacity over time (Becker et al., 2018; Meier et al., 2012). On the other hand, a large Australian longitudinal study failed to find an association between frequent cannabis use and accelerated memory decline (McKetin, Parasu, Cherbuin, Eramudugolla, & Anstey, 2016). Similarly, an almost equal number of cross-sectional studies found no meaningful differences in these cognitive abilities between individuals who frequently used cannabis and those who did not (e.g., Ashtari et al., 2011; Hooper, Woolley, & De Bellis, 2014; Lisdahl & Price, 2012).

Inconsistent findings seem to be partly related to differences in length of abstinence prior to learning and memory testing (Schoeler & Bhattacharyya, 2013). Generally, the relationship between cannabis use and learning and memory deficits is progressively weaker with longer periods of abstinence (Scott et al., 2018). The link between frequent cannabis use and difficulties in learning and memory, if present, is strongest among individuals who engage in heavy cannabis use and in those who initiate use early in life (prior to the age of 16 or 17) (Gruber, Sagar, Dahlgren, Racine, & Lukas, 2012; Solowij et al., 2011). As a whole, the available evidence suggests that chronic and heavy cannabis use is related to learning and memory difficulties that might not be entirely reversible, especially among individuals who initiated regular use early in life and have been using cannabis for a significant part of their life (Schoeler & Bhattacharyya, 2013).

Attention

Chronic cannabis use has also been associated with difficulties in attention and concentration, although these difficulties have been much less consistently observed than those associated with learning and memory deficits (Scott et al., 2018). On the one hand, young adults and adolescents who regularly used cannabis exhibited poor performance across several tasks measuring attention, after relatively brief (12 hours) and long (23 days) abstinence periods, and after controlling for alcohol use and symptoms of depression (Dougherty et al., 2013; Lisdahl & Price, 2012; Medina et al., 2007; Solowij et al., 2011). On the other hand, adolescents and adults who frequently engaged in cannabis use were also shown not to differ in attention and concentration from those who rarely or never used cannabis (Fried, Watkinson, & Gray, 2005; Hooper et al., 2014), even after less than 24 hours of abstinence (Becker et al., 2014; Grant, Chamberlain, Schreiber, & Odlaug, 2012). Methodological differences, such as inclusion criteria for the "chronic cannabis group" and tasks used to assess attention and concentration might be partly responsible for discrepancies across studies (Scott et al., 2018).

Individuals who initiate regular cannabis use early in life or have heavy cannabis use patterns, or those with long lifetime exposure to cannabis might be most likely to display attention deficits (Ehrenreich et al, 1999; Scott et al., 2017; Solowij et al., 2011). Among studies examining the relationship between chronic cannabis use and attention, impairments were more commonly reported among adolescents (Dougherty et al., 2013; Harvey, Sellman, Porter, & Frampton, 2007; Hanson et al., 2010; Medina et al., 2007; Scott et al., 2017; Solowij et al., 2011) relative to adults (Ehrenreich et al, 1999; Lisdahl & Price, 2012; Messinis, Kyprianidou, Malefaki, & Papathanasopoulos, 2006). However, more research is needed to determine whether adolescents are more susceptible to attention deficits following regular cannabis use.

Executive Functions

Executive functions refers to a set of cognitive processes that play an important role in the ability to adapt to continuously changing environments and in the control of behaviour. These cognitive processes include working memory, inhibition and cognitive flexibility (also known as mental "set-shifting"). Executive functions underlie "high-order" cognitive abilities, such as problem solving, reasoning, planning and multi-tasking, and have increasingly been implicated in self- and emotion-regulation (Hofmann, Schmeichel, & Baddeley, 2012; Koster, De Lissnyder, Derakshan, & De Raedt 2011). The available evidence indicates that chronic cannabis use is associated with mild to moderate deficits in executive functions, similar to that observed for attention, learning and memory. Relative to working memory, there have been few studies looking at chronic cannabis use in relation to inhibition and cognitive flexibility. Thus, it is not possible to suggest that certain aspects of executive functions are more or less affected by frequent cannabis use (Scott et al., 2018). Finally, while a number of correlational studies have shown a link between frequent cannabis use and deficits in executive functioning, there have been few prospective or longitudinal studies establishing causality in this respect (but see Meier et al., 2012; Morin et al., 2018).

Working Memory

Working memory refers to a form of short-term memory that allows an individual to store and manipulate information in their mind for a short period of time (seconds to minutes), long enough to carry out or accomplish a particular task (e.g., solve a problem). Although cannabis use has consistently been shown to acutely impair this aspect of executive functioning, whether difficulties of working memory persist beyond the intoxication period is unclear (Schoeler & Bhattacharyya, 2013). A recent meta-analysis indicated that chronic cannabis use was associated with a small to medium effect size (average effect across studies) on working memory (Scott et al., 2018). Yet a relatively large number of studies reported that individuals who regularly used cannabis perform equally well on working memory tests compared to individuals who rarely or never use cannabis (e.g., Dougherty et al., 2013; Hanson, Thayer, & Tapert, 2014; Hooper et al., 2014; Winward, Hanson, Tapert, & Brown, 2014).

The effects of regular cannabis use on working memory appear to be relatively short term, rather than a persistent cognitive disturbance (Owens et al., 2018). For example, deficits in working memory among individuals who regularly used cannabis were only observed in studies employing shorter abstinence periods (i.e., 36 hours or less) (Becker et al., 2014; Gruber et al., 2012; Herzig, Nutt, & Mohr, 2014; Scott et al., 2017; Smith et al., 2014; Tamm et al., 2013). Following longer periods of abstinence, these cognitive difficulties were not readily apparent (Hanson et al., 2014; Hooper et al., 2014; Price et al., 2015; Schweinsburg et al., 2005, 2010; Winward et al., 2014). Impaired working memory might, however, be particularly apparent among individuals who initiated regular cannabis use at an early age and those who use cannabis heavily (i.e., at least once per day) (Gruber et al., 2012; Tamm et al., 2013). Otherwise, the effects of regular cannabis use on working memory might only be detectible on tasks that are more complex or those with greater cognitive load (Solowij & Battisti, 2008).

Inhibition

Inhibition, also referred to as inhibitory control, plays an important role in the regulation of thoughts and behaviour, including those that might be impulsive, reactive or inappropriate in a particular situation. There are generally two types of inhibition: cognitive inhibition and response inhibition. Cognitive inhibition refers to the ability to prevent irrelevant or intrusive information from entering one's mind and can be viewed as a type of mental filter. Difficulties in cognitive inhibition can make it difficult to ignore distracting information (e.g., thoughts) and concentrate on a particular task. Response inhibition is the ability to suppress actions or behaviours that are no longer appropriate in a situation. Response inhibition can be seen as the brakes on a car, where a functional break system gives you control over your driving. A deteriorating brake system makes it increasingly difficult to stop in situations that require it. Reduced response inhibition, as measured through behavioural tasks, is considered to be one aspect of impulsivity (MacKillop et al., 2011). Chronic cannabis use among adolescents and adults has been associated with difficulties in both forms of inhibition (Behan et al., 2014; Cousijn, Watson et al., 2013; Dahlgren, Sagar, Racine, Dreman, & Gruber, 2016; Dougherty et al., 2013; Gruber et al., 2012; Moreno et al., 2012).

Difficulties in inhibition are not present in all individuals who engage in chronic cannabis use (Grant et al., 2012; Hooper et al., 2014; Price et al., 2015). Once again, some of the variation across studies seems to be related to differences in the length of abstinence (Scott et al., 2018). In essence, for most individuals who regularly use cannabis, inhibition difficulties might be noticeable within a few days to weeks following cessation, after which they are typically no longer evident (Hooper et al., 2014; Gruber et al., 2012). However, there is evidence showing that, among adolescents, chronic cannabis use can lead to persistent inhibition difficulties (Morin et al., 2018).

Individuals who engage in heavy cannabis use, as well as those seeking treatment for a cannabis use disorder, tend to show the most pronounced deficits in inhibition (Cousijn, Watson et al., 2013; Dougherty et al., 2013; Gruber et al., 2012). The association between frequent cannabis use and inhibition difficulties is more likely to be present among individuals who initiated regular cannabis use early in life (e.g., prior to the age of 16) (Dahlgren et al., 2016; Gruber et al., 2012). Although there is research in humans and animals supporting a causal effect of chronic cannabis use on inhibition deficits (Irimia, Polis, Stouffer, & Parsons, 2015; Morin et al., 2018), it is also possible that difficulties in inhibition lead to excessive or problematic cannabis use. In fact, disturbances of inhibitory control and alterations of brain regions supporting this cognitive ability have been implicated in the development and maintenance of substance use disorders, including those related to cannabis (Ivanov, Schulz, London, & Newcorn 2008; Koob & Volkow, 2016). Consistent with this view, poorer baseline performance on tests assessing inhibition in early adolescence predicted greater use of cannabis (and alcohol) in late adolescence (Morin et al., 2018; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Thus, chronic cannabis use can lead to inhibition difficulties and be the consequence of reduced inhibition.

Cognitive Flexibility

Cognitive flexibility refers to being able to adjust cognitive processes (e.g., attention, thoughts) and behaviour in response to novel, unexpected and continuously changing environments. This flexibility can be expressed as being able to quickly come up with a new solution to a problem when the first approach was not effective. Another common expression of cognitive flexibility is multi-tasking, such as when a person shifts their attention between responding to emails, writing a report and answering phone calls. Cognitive flexibility plays a fundamental role in creative problem solving, fluid intelligence[1] and abstract reasoning, and has most commonly measured by the Wisconsin Card Sorting Task (WCST)[2] (Grant & Berg, 1948).

Individuals with difficulties in cognitive flexibility tend to persist in a behaviour in spite of the response no longer being effective in dealing with a situation. Although limited, the available data suggest that chronic cannabis use might be associated with reduced cognitive flexibility (Dougherty et al., 2013; Gruber et al., 2012), lasting at least a few weeks after cessation of use (Hanson et al., 2014). Individuals who initiated regular cannabis use early in life (i.e., before the age of 16 or 17) and those with heavy cannabis use patterns (Dougherty et al., 2013; Gruber et al., 2012; Pope et al., 2003; Tamm et al., 2013) showed the most noticeable impairment in cognitive flexibility.

As with other executive functions, chronic cannabis use has not always been associated with reduced cognitive flexibility (Harvey et al., 2007), even after relatively brief abstinence periods (Solowij et al., 2002). Since there have been limited studies, it is currently not clear why, for some individuals but not others, chronic cannabis use might be accompanied by difficulties in this cognitive ability. However, variability across studies might be partly related to the neuropsychological task used to assess this cognitive flexibility. Among studies reporting no performance differences between individuals who use cannabis and those who do not, many (but not all) used the Trail Making Test (TMT)[3] (Herzig et al.,

The brain produces its own natural compounds, called endocannabinoids, that act like THC. Endocannabinoids, which include anandamide (AEA) and 2-arachidonoylglycerol (2-AG), exert their effects by binding to cannabinoid (CB1 and CB2) receptors. Cannabinoid receptors are present throughout the brain and body, meaning that cannabinoids can influence a broad range of psychological and biological processes, such as cognition, emotional processing and regulation, stress response, appetite, immune functioning, the endocrine (hormone) system, sleep and pain signalling (Zou & Kumar, 2018). THC mimics the activity of AEA and binds at the CB1 receptors. It binds, however, at much higher levels than AEA itself, flooding the endocannabinoid system leading to altered functioning of each process. This flooding means that chronic use of cannabis (i.e., repeated brain exposure to THC) can alter the functioning of the endocannabinoid system, which can include changes in AEA and 2-AG activity, and the distribution of cannabinoid receptors (Jacobson, Watts, Boileau, Tong, & Mizrahi, in press).

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[1] Fluid intelligence refers to the capacity to quickly learn and adapt new information across different situations. Aspects of this type of intelligence include the ability to identify patterns and relationships in novel situations, using logic and reasoning to solve problems, and being flexible in problem solving across new and different situations. Fluid intelligence is in contrast to crystalized intelligence, which is the type of intelligence that has been learned or acquired over time through experience.

[2] On the WCST, participants are asked to sort cards, through trial and error, according to one of three stimulus dimensions (colour, shape, number of shapes). After a predetermined number of correctly sorted cards, a new sorting rule is introduced without the participant being made aware of this change. The challenge, then, is to figure out the new sorting rule (e.g., colour) while ignoring information related to the previously, but no longer, relevant rule (e.g., shape). Impaired cognitive flexibility, as assessed by the WCST, is reflected by the frequency of "perseverative errors" — the number of trials in which the individual continues to sort cards according to a previously, but no longer, correct sorting rule.

[3] The TMT is a two-part task that involves connecting a set of 25 dots as quickly as possible while still maintaining accuracy. In the first part, the participant must connect numbers in sequential order (1 to 25). Part two involves alternating between numbers and letters (1, A, 2, B, etc.). Part one of the TMT has been used to assess visual attention and processing speed, whereas part two of this task has been used to measure cognitive flexibility.

2014; Jacobus, Squeglia, Sorg, Nguyen-Louie, & Tapert, 2014; Winward et al., 2014), a task that is considerably different and arguably easier than the WCST. Based on the current research, chronic cannabis use initiated early in life might be associated with difficulties in complex forms of cognitive flexibility.

Brain Regions Supporting Cognitive Functioning

From a biological perspective, chronic and early exposure to cannabis might influence brain structure and function. In studies using animals, repeated administration of THC produced changes in several brain regions important for learning, memory and executive functions (Bilkei-Gorzo et al., 2017; Kolb, Li, Robinson, & Parker 2018). Similar findings have come from growing neuroimaging evidence indicating that multiple brain structures differ in size, density and shape in individuals who engage in chronic cannabis use relative to those who do not use cannabis or do so less frequently (Lorenzetti, Solowij, Fornito, Lubman, & Yücel, 2014).

One of the most notable and consistently reported findings is that individuals who regularly use cannabis have a smaller hippocampus than individuals who do not or who rarely use cannabis (Batalla et al., 2013; Lorenzetti et al., 2014; but see Block et al., 2000; Tzilos et al., 2005). The hippocampus is a brain region critical in the formation and consolidation of long-term memories. Hippocampus volume has been shown to be negatively correlated with higher doses of regular cannabis use (Ashtari et al., 2011; Demirakca et al., 2011), even after accounting for alcohol and tobacco use (Battistella et al., 2014; Schacht, Hutchison, & Filbey, 2012). Several studies have also observed reduced volume of the orbital frontal cortex — a brain region involved in decision making and emotional regulation — among individuals who used cannabis chronically (Filbey et al., 2014; Battistella et al., 2014) and those who initiated regular cannabis use early in life (Churchwell, Lopez-Larson, & Yurgelun-Todd, 2010). Although less consistently, chronic cannabis use has also been related to alterations of the brain structures involved in motivation, emotion and motor responses, including the amygdala, striatum and cerebellum (Lorenzetti et al., 2014). Additionally, there is evidence that chronic cannabis use might alter the structural integrity of brain white matter, which is involved in the communication of neural signals in the brain (Arnone et al., 2008; Gruber, Silveri, Dahlgren, & Yurgelun-Todd, 2011). In light of these findings, it has been suggested that chronic cannabis use might be associated with structural changes in brain regions that are dense in cannabinoid receptors (Lorenzetti, Solowij, & Yücel, 2016).

A noteworthy proportion of studies did not find brain structure (size, volume, density or shape) differences between individuals who chronically use cannabis and those who do not (Batalla et al., 2013; Ganzer, Bröning, Kraft, Sack, & Thomasius, 2016). Variability across studies is partly attributable to i) the type and potency of cannabis used, ii) the usual dosage and frequency of use, iii) the age of onset of regular use and iv) the presence (or risk) of cannabis use disorder (Batalla et al., 2013; Lorenzetti et al., 2016). The influence of cannabis exposure on brain development might also depend on the individual's genetic makeup. For example, heavy cannabis use was associated with smaller volumes of the hippocampus and amygdala, but only among individuals carrying a specific genetic variant that codes for a cannabinoid (CB1) receptor (Schacht et al., 2012). There is also preliminary evidence suggesting that the relation between chronic cannabis use and structural brain changes might differ for males and females (Medina et al., 2009; McQueeny et al., 2011). It should also be underscored that most of the current research is correlational. Therefore, while it is possible that chronic cannabis exposure leads to changes in brain size, volume and shape, it is also possible that pre-existing differences in brain structure favour regular cannabis use (Lorenzetti et al., 2014; 2016). Consistent with the latter possibility, a smaller orbitofrontal cortex among 12-year olds predicted initiation of cannabis use at 16 years of age (Cheetham et al., 2012)

In addition to brain structure, individuals who frequently use cannabis have been shown to differ in brain activation patterns while performing cognitive tasks (Blest-Hopley, Giampietro, & Bhattacharyya, 2018; Yanes et al., 2018). For instance, studies have shown that individuals who frequently use cannabis generally display reduced activation of brain regions supporting executive functions, particularly the anterior cingulate and prefrontal cortex (Eldreth, Matochik, Cadet, & Bolla, 2004; Gruber & Yurgelun-Todd, 2005; Hester, Nestor, & Garavan, 2009; Kober, DeVito, DeLeone, Carroll, & Potenza, 2014; Owens et al., 2018). Instead, while performing cognitive tasks, cannabis-using individuals display activity in a collection of brain regions referred to as the default mode network (DMN), which are involved in consciousness and thinking about one's self. It appears that this pattern of cannabis-related brain activity (i.e., reduced task-related activity and increased DMN activity) is a relatively short-term effect, rather than a long-term and persistent brain disturbance (Owens et al., 2018).

Several studies have also reported greater brain activation during cognitive performance, especially on tasks measuring working memory (Blest-Hopley et al., 2018). For example, although performance was often comparable, individuals who frequently used cannabis displayed greater activation in the frontal brain regions necessary for task performance (Jager, Block, Luijten, & Ramsey, 2010; Kanayama, Rogowska, Pope, Gruber, & Yurgelun-Todd, 2004). As well, individuals who used cannabis frequently were more likely to recruit supporting brain regions and those not typically involved in working memory in order to match their performance to that of non-using controls (Padula, Schweinsburg, & Tapert, 2007; Schweinsburg et al., 2008; Smith, Longo, Fried, Hogan, & Cameron, 2010). The effects of regular cannabis use and altered brain activity were reported after relatively short (six to 36 hours) and long (28 days) abstinence periods, suggesting that brain alterations might persist beyond the intoxication period (Kanayama et al., 2004; Padula et al., 2007). This neuroimaging data has been interpreted as evidence of a compensatory mechanism, whereby individuals who frequently use cannabis need to engage more neural resources to cognitively function at the level of those who do not regularly use cannabis. Once again, it is unclear whether differences in brain activation are the result of chronic cannabis use or precede it. However, in support of the latter possibility, among individuals who engaged in heavy cannabis use inefficient brain activity (greater cognitive resources needed to complete a task) predicted escalations in cannabis use over a six-month period (Cousijn, Wiers, et al., 2014).

Decision Making

Decision making is a complex process that involves several cognitive abilities operating at the same time. Research has only recently begun to examine aspects of decision making among individuals who frequently use cannabis to see whether they differ from individuals who do not use cannabis. The available data, even though it is limited, suggests that heavy cannabis use and cannabis use disorder is associated with maladaptive decision making and with altered brain activity in regions that govern decision-making processes. However, it appears that not all aspects of decision making are affected equally, and it is currently unclear whether heavy cannabis use leads to changes in decision making or whether maladaptive decisions result in heavy cannabis use and cannabis use disorder.

Risk-taking

Risk-taking among individuals who regularly use cannabis has been assessed through various laboratory-based tasks, following periods of short (e.g., 12 to 18 hours) and extended abstinence (e.g., more than 25 days). The most commonly used task in this respect has been the Iowa Gambling Task, which is designed to assess real-life decisions involving uncertainty, reward and punishment. On this task, participants try to earn as much hypothetical money as possible by choosing cards from four decks, each of which leads to varying amounts of monetary gain or loss as determined by set probabilistic schedules. Two of the decks provide large monetary gains, but occasionally even larger losses (the “risky” decks), whereas the other two decks provide smaller monetary gains but also smaller losses (the “safe” decks).

Individuals who regularly use cannabis and have so for a long time have often been shown to make risky decisions on the Iowa Gambling Task. Specifically, these individuals tend to repeatedly select cards that have the potential (although statistically less likely) for large immediate rewards, but are typically associated with long-term negative consequences (e.g., less overall monetary gain) (Moreno et al., 2012; Bolla, Eldreth, Matochik, & Cadet, 2005; Grant et al., 2012; Whitlow et al., 2004; Verdejo-Garcia et al., 2007; Wesley, Hanlon, & Porrino, 2011). Greater frequency of cannabis use has been associated with increasingly more risky responses, a relationship that was evident even after 25 days of abstinence (Bolla et al., 2005; Verdejo-Garcia et al., 2007).

Computational models of Iowa Gambling Task performance indicate that individuals who use cannabis chronically tend to be under-influenced by the magnitude of loss, treating each loss as a constant and minor negative outcome regardless of the size of the loss. Instead, they are more influenced by gains (rewards), and make decisions that are inconsistent with their expectancies (Fridberg et al., 2010). Consistent with these models, individuals who use cannabis frequently display altered activity of brain regions involved in decision making, including the anterior cingulate and orbital frontal cortices, during performance on the Iowa Gambling Task (Bolla et al., 2005; Cousijn, Wiers, Ridderinkhof, van den Brink, Veltman, Porrino et al., 2013; De Bellis et al., 2013; Vaidya et al., 2012; Wesley et al., 2011). It is important to make clear that this pattern of risk-taking and brain activity is mostly seen in individuals with heavy cannabis use and those seeking treatment for a cannabis use disorder (Bolla et al., 2005; Cousijn, Wiers, Ridderinkhof, van den Brink, Veltman, Porrino et al., 2013; De Bellis et al., 2013). Furthermore, as with the findings presented for learning, memory and executive functions, it is currently not clear whether persistent exposure to cannabis results in increased risk taking, whether risky decisions lead to heavy and problematic cannabis use, or both.

There is evidence suggesting that risky decision making might predate heavy cannabis use or serve as a predictor of problematic use patterns. Specifically, greater frequency of cannabis use (lifetime, 12-month and 30-day) was associated with more cannabis-related problems, but only among individuals with poor decision making (Gonzalez, Schuster, Mermelstein, & Diviak, 2015). Moreover, among individuals who engaged in heavy cannabis use, altered frontal and temporal brain activity during performance on the Iowa Gambling Task predicted increased weekly cannabis use six months later (Cousijn, Wiers, Ridderinkhof, van den Brink, Veltman, Porrino et al., 2013).

Delayed Reward Discounting

Another dimension of decision making that has received increased empirical attention as a factor among individuals who use cannabis is termed delayed reward discounting. Delayed reward discounting is a specific type of impulsive decision making that represents how fast a reward loses its value based on the delay in time in which the reward is received (MacKillop et al., 2011). This aspect of decision making can be viewed as the opposite of delayed gratification and is reflected by choosing a smaller, more immediate reward (e.g., $100 now) over a larger, but delayed reward (e.g., $500 a year from now) (Green, Fry & Myerson, 1994). Steep delayed reward discounting (i.e., a preference for smaller immediate rewards instead of larger delayed rewards) has frequently be observed among individuals with alcohol use disorders, nicotine dependence, cocaine dependence, opiate dependence and gambling disorder (Amlung, Vedelago, Acker, Baladis, & MacKillop, 2017). Interestingly, this aspect of decision making appears to be mostly unaffected in individuals who use cannabis heavily and those who have cannabis use disorder (Amlung et al., 2017; MacKillop et al., 2011). Therefore, when considering the evidence as a whole, while individuals who use cannabis heavily tend to make risky decisions and exhibit difficulties in self-control (e.g., response inhibition), their decision making is not entirely impulsive, in that they are capable of delaying the receipt of reward.

Motivation and Reward Processing

Acute cannabis intoxication is known to transiently reduce motivation (Lawn et al., 2016), but whether this effect persists beyond the intoxication period, particularly among individuals who regularly use cannabis, is not clear. Several studies reported reduced motivation among individuals who frequently used cannabis across several self-report and performance-based measures (Lane, Cherek, Pietras, & Steinberg, 2005; Looby & Earleywine, 2007). In a recent prospective study, after controlling for personality, alcohol and tobacco consumption, regular cannabis use still predicted several indices of reduced motivation (e.g., self-efficacy) one month later (Lac & Luk, 2018), supporting a causal role of cannabis use in reduced motivation. Motivational disturbances have not always been observed among individuals who engage in frequent cannabis use (Pacheco-Colón, Limia, & Gonzalez, 2018), especially after considering the presence of depressive symptoms (Pacheco-Colón et al., 2018). Among adolescents, the relationship between cannabis use and several indices of motivation was no longer present after controlling for symptoms of depression in addition to several other covariates (Pacheco-Colón et al., 2018). This finding is particularly important given that motivational difficulties, potentially stemming from anhedonia (i.e., reduced ability to experience pleasure or a diminished interest in engaging in pleasurable activities), are a hallmark characteristic of depressive illness, which has been associated with cannabis use (see *Clearing the Smoke: Chronic Use and Cognitive Functioning and Mental Health*).

A blunted neurobiological response and insensitivity to rewarding information might contribute to the motivational difficulties observed among individuals who engage in heavy cannabis use. Individuals who frequently used cannabis showed reduced activation in several key brain regions involved in the processing of reward, including the ventral striatum and medial prefrontal cortex, during the anticipation of monetary rewards (van Hell et al., 2010). In a longitudinal study, greater cannabis use at the beginning of the study was associated with blunted activation of a central region of the ventral striatum, referred to as the nucleus accumbens, approximately two years later (Martz et al., 2016). Consistent with these findings, individuals who regularly used cannabis displayed reduced connectivity between the striatum and prefrontal regions. However, these connections were strengthened following one month of abstinence, suggesting that alterations in brain regions responsible for reward processing might normalize following extended cessation of cannabis use (Blanco-Hinojo et al., 2017).

In a positron emission tomography (PET) study, higher levels of apathy in individuals who chronically used cannabis were associated with reduced production of dopamine — a neurotransmitter involved in motivation and reward — in the striatum (Bloomfield, Morgan, Kapur, Curran, & Howes, 2014). In another PET study, dopamine reactivity in response to methylphenidate (Ritalin®), a stimulant drug that typically produces elevations of dopamine in reward areas of the brain, was compared between individuals with problematic cannabis use and those who did not use (Volkow, Wang et al., 2014). Relative to the control group, individuals with problematic cannabis use showed a blunted dopamine response and reported lower positive emotionality when administered methylphenidate. These studies suggest that chronic cannabis use might be associated with blunted dopamine activity in brain regions involved the processing of reward and motivated behaviour.

A number of studies reported no differences in brain activation in anticipation, or following the receipt, of reward among individuals who frequently use cannabis compared to those who have never used or use infrequently (Enzi et al., 2015; Filbey et al., 2016; Karoly et al., 2015). Yet, other studies have found the opposite effect — hypersensitivity to rewarding information among individuals engaging in chronic cannabis use (reviewed in Pacheco-Colón, Limia, & Gonzalez, 2018). For instance, individuals who engaged in chronic cannabis use displayed heightened activity of the ventral striatum during the anticipation of monetary rewards, and this brain activation was related to the amount and duration of lifetime cannabis use (Nestor, Hester, & Garavan, 2010). Likewise, adolescents who used cannabis chronically showed hyper-activation of the striatum during the anticipation of both rewards and non-rewards, which was suggested to reflect an overly sensitive motivational system (Jager, Block, Luijten, & Ramsey 2013). Furthermore, individuals who frequently used cannabis displayed greater activation of the orbitofrontal cortex (involved in decision making, inhibition and attributing emotional value to a particular item or event) when winning versus losing (fictitious) money on a computer task, whereas those who did not use cannabis had greater activation of the brain region during losses compared to wins (Filbey, Dunlop, & Myers 2013). These findings suggest that chronic cannabis use might be associated with a general hypersensitivity to the anticipation of rewards, but a blunted response to anticipated losses.

There is also research suggesting that chronic, and especially problematic, cannabis use might be accompanied by a hypersensitivity specifically for cannabis-related information, rather than a generalized sensitivity to all rewarding material. For example, individuals who frequently engaged in cannabis use exhibited increased activation of a part of the brain's reward circuit (ventral tegmental area) in response to cannabis images, but not neutral images. Among a subset of individuals with problematic cannabis use, the neuronal response to cannabis images extended to prefrontal areas and striatum (Cousijn, Goudriaan et al., 2013). In line with these findings, compared to a non-using control group, individuals who used cannabis daily for a long period of time displayed greater responses during cannabis cues (e.g., images of cannabis paraphernalia) relative to natural reward cues (i.e., images of fruit) in the orbitofrontal cortex, striatum, anterior cingulate and the ventral tegmental area (Filbey et al., 2016). These findings support the incentive sensitization theory of addiction, which proposes that repeated exposure to a potentially addictive drug (e.g., cannabis) can alter the brain's natural reward and motivation pathways so that they become increasingly sensitive (responsive) to that particular drug or cues associated with the drug (e.g., a cannabis pipe), in turn promoting a 'wanting' of the drug (Berridge & Robinson, 2016). These neuroimaging studies also point to the possibility that, through changes in the brain's natural reward pathways, problematic cannabis use might be associated with enhanced motivation to seek out cannabis at the expense of pursuing personally meaningful goals (e.g., academic achievement). However, it is not clear if altered brain functioning is a cause or consequence of chronic cannabis use.

Social Cognition

Social cognition refers to a collection of cognitive and emotional processes that play an important role in an individual's ability to communicate and interact with others. One of the more important aspects of social cognition is the ability to read social signals, including being able to identify another individual's emotional state through their facial expressions. Although limited, there is evidence suggesting that individuals who frequently use cannabis might have difficulties in processing facial expressions. For example, compared to a control group, individuals who frequently used cannabis took longer to identify emerging happy, sad and angry emotions presented on a computer screen, and were less accurate in doing so (Hindocha et al., 2014; Platt, Kamboj, Morgan, & Curran, 2010). Difficulties in recognizing facial expressions were more noticeable among cannabis dependent individuals, especially when presented with negative emotions, and these difficulties persisted after more than one month of abstinence (Bayrakçı et al., 2015). On the other hand, individuals who engaged in occasional cannabis use were shown to be better at social cognition, reflected through the ability to identify and differentiate individuals' emotions and age when looking at pictures of their face (Scott et al., 2017).

The presence of social cognition deficits might be related to how the brain processes emotional information. When presented with images of masked[4] angry and happy faces, individuals who chronically used cannabis displayed less

[4] Masking refers to the presentation of a stimulus (e.g., an image of a person's face) for very brief periods of time (30 milliseconds), which is said to be below the level of conscious processing.

activity of the anterior cingulate cortex and amygdala (areas of the brain that are important for detecting and experiencing emotions) (Gruber, Rogowska, & Yurgelun-Todd, 2009). In a more recent study, individuals who used cannabis heavily displayed less activity of the medial prefrontal cortex (an area involved in the processing, representing and integrating of social and affective information) during positive and negative evaluation (Wesley, Lile, Hanlon, & Porrino, 2016).

In addition to difficulties in processing emotions, individuals who regularly use cannabis might be less sensitive to social exclusion. The cyberball task is a commonly used paradigm of social rejection, which consists of a computerized game of catch. Unknown to the study participant, the other "players" in the game are computers and are programmed to exclude the participant for a portion of the game. Ordinarily, being excluded from the game leads to activation of the anterior insula, a region associated with negative emotion and social rejection. However, cannabis-using individuals failed to show activation of this brain region (Gilman, Curran, Calderon, Schuster, & Evins, 2016), a finding that is consistent with the general blunted emotional response (e.g., apathy) that is exhibited by individuals who frequently use cannabis. Together, these neuroimaging studies suggest that individuals who frequently use cannabis might have difficulties in processing and responding to social and emotional situations. However, it remains unclear whether these difficulties might be a common, pre-existing trait of cannabis-using individuals or a byproduct of the cannabis use itself.

Intelligence

The potential impact of chronic cannabis use on intelligence has received a great deal of attention and has been a highly contentious topic of recent discussion. In one longitudinal cohort study, early onset cannabis use was associated with a decline in intelligence (an average IQ decline of eight points) over the course of a 25 year period (age 13 to 38), and this relationship was independent of years of education. Among individuals who began using cannabis prior to the age of 18 and who subsequently were abstinent from the drug, IQ scores remained significantly lower compared to those who did not engage in chronic use (Meier et al., 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 sum, earlier longitudinal studies suggested that chronic cannabis use that begins early in life and is continued for many years might lead to a sustained decline in intelligence over the course of the individual's life.

However, two more recent longitudinal twin studies challenge these initial findings and provide an alternative explanation for the relationship between chronic cannabis use and intellectual functioning (Jackson et al., 2016). Similar to previous findings (Meier et al., 2012), cannabis-using adolescents scored lower on tests of intelligence between pre-adolescence and late adolescence relative to those who did not use cannabis. However, in these latter longitudinal studies, cannabis-using twins did not show a significant IQ decline relative to their abstinent siblings. These findings were interpreted to suggest that the observed decline in measured IQ might not be a direct result of cannabis exposure but rather attributable to familial factors that underlie both cannabis initiation and low intellectual attainment (Jackson et al., 2016). A similar finding was recently reported from the Environmental Risk Longitudinal Twin Study (Meier et al., 2018), which showed that adolescents who used cannabis had lower IQs in childhood prior to cannabis initiation and lower IQs at age 18. However, there was little evidence showing that cannabis use was associated with a decline in IQ from ages 12 to 18 since twins who used cannabis more frequently than their co-twin performed similarly to their siblings on tests of intelligence. These findings suggest that short-term (i.e., up to, but no more than, a few years) cannabis use in adolescence does not appear to cause IQ decline (or impair executive functions), even when cannabis use reaches the level of dependence. Instead, family background factors may explain why adolescents who use cannabis perform worse on IQ and executive function tests (Meier et al., 2018).

It was recently proposed that the seemingly conflicting findings across longitudinal studies might not be as incompatible as previously thought (Meier et al., 2018). Generally, studies with the longest follow-up and greatest cannabis exposure (i.e., from adolescence to adulthood) showed the strongest evidence of cannabis-related neuropsychological and intelligence decline (Auer et al., 2016; Fried et al., 2005; Meier et al., 2012). In contrast, studies with shorter follow-up periods and less cannabis exposure (i.e., studies of adolescent cannabis use) tended to show weaker evidence (Boccio & Beaver, 2017; Jackson et al., 2016; Mokrysz et al., 2016). From this perspective, it is possible that neuropsychological deficits, including lower intelligence, will only emerge after a significant number of years of regular cannabis use (Meier et al., 2018). That said, it is important to note that regular cannabis use among adolescents has been associated with a progressive decline in intelligence and neuropsychological functioning even after a relatively short period of time (e.g., four years) (Castellanos-Ryan et al., 2017; Morin et al., 2018). Yet, once again, the extent to which early onset regular cannabis exposure directly contributes to compromised intellectual functioning, beyond that which is attributable to related factors (e.g., lower socioeconomic status and academic achievement, as well as psychiatric and substance use disorders) remains to be determined.

Individual Differences

With the exception of several longitudinal investigations, most studies examining chronic cannabis use in relation to cognitive functioning have consisted of small samples. Because of the small samples, it has been difficult to explore the contribution of individual differences, including sex and gender, genetics and life experiences, to this association. Indeed, little is known about whether and how the effects of frequent cannabis use on cognitive functioning might vary across individuals. Nevertheless, there is preliminary evidence suggesting the importance of considering these characteristics.

Individuals who frequently use cannabis also often use other substances, such as tobacco and alcohol (Hindocha, Freeman, Ferris, Lynskey, & Winstock 2016; Subbaraman & Kerr, 2015). Although many studies have controlled for polysubstance use, few studies have considered the potential additive or interactive effects of cannabis in combination with other substances on cognitive functioning. Still, it is becoming increasingly evident that the impact of chronic cannabis use on certain aspects of cognition might be exacerbated by the co-use of other substances. For instance, individuals who used cannabis and alcohol frequently displayed deficits across several aspects of cognition, including attention and memory (Jacobus et al., 2015), and the combination of cannabis and alcohol use was associated with worse working memory performance than cannabis use alone (Winward et al., 2014). There is also evidence suggesting that smoking tobacco might mask the adverse effects of cannabis use on learning and memory (Schuster, Crane, Mermelstein, & Gonzalez, 2015) and that the co-use of cannabis and tobacco might be accompanied by structural and functional differences in brain regions supporting learning and memory (Filbey, McQueeny, Kadamangudi, Bice, & Ketcherside, 2015).

Males and females differ in their cannabis use patterns and experiences (Cuttler, Mischley, & Sexton, 2016), and there is evidence indicating steroid hormones (e.g., estrogens and testosterone) can modulate endocannabinoid system functioning (Struik, Sanna, & Fattore, 2018). However, there has been less attention devoted to examining whether the effects of chronic cannabis use on cognition vary for women and men. Heavy cannabis use was associated with impaired memory among women (Crane, Schuster, Fusar-Poli, & Gonzalez, 2013), but reduced psychomotor speed (Lisdahl & Price, 2012) and poor decision making among males (Crane et al., 2013). Although preliminary, these data suggest possible sex-specific effects of chronic cannabis use on cognitive function. More research is required to confirm these findings and determine the extent to which potential sex differences in cannabis-related cognitive functioning are attributed to biological (e.g., sex hormones) versus psychosocial (e.g., social development) factors.

There is also evidence suggesting that the effects of cannabis use on cognitive functioning might depend on the individual's genetic makeup. For instance, cannabis-using individuals who carried two copies of the Val allele for a gene coding for the enzyme that regulates dopamine activity (catechol-O-methyltransferase) displayed deficits in sustained attention compared to individuals with the same genotype but who did not use cannabis. Furthermore, among individuals who used cannabis, having at least one copy of the Val allele was related to difficulties in monitoring and shifting attention (Verdejo-García et al., 2013). In the same study, frequent cannabis use was related to poor decision making on the Iowa Gambling Task, but only among individuals who carried a common mutation in a gene coding for a serotonin protein (5-HTTLPR) (Verdejo-García et al., 2013).

The available evidence suggests that the relationship between regular cannabis use and cognitive functioning substantially varies from one individual to another. A more limited number of studies point to specific factors that explain the variability. Therefore, to better understand the effects of cannabis use on cognitive functioning, it is important to consider individual characteristics, including polysubstance use, sex and gender differences, and genetic background.

Conclusions and Implications

A significant proportion of Canadians aged 15 or older (almost 16% or about 4.6 million individuals) report using cannabis at least once in the past three months (Statistics Canada, 2018), and there are still many misconceptions about the effects of cannabis on health, particularly among youth (e.g., McKiernan & Fleming, 2017). It is, therefore, important to inform individuals about the health and safety impacts of regular and heavy cannabis use. Indeed, public awareness and education is needed now more than ever given the recent legalization of non-medical cannabis use in Canada. The present report objectively synthesizes the currently available research to assist decision makers and health practitioners in developing health policy and public education resources.

For most individuals, chronic cannabis use does not appear to lead to significant impairment in cognitive functioning, including major deficits in learning, memory and executive functions. Instead, it seems that chronic use can result in mild, but measureable, cognitive difficulties. Based on these findings, individuals who regularly use cannabis 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 automatic application of previous knowledge. Tasks that rely heavily on a memory component, or require strategic planning or multitasking might also be difficult for individuals who chronically use cannabis. It is certainly credible that individuals in safety-sensitive jobs (e.g., police officers, air traffic controllers) or positions with high cognitive demands could experience meaningful decrements in performance.

Individuals who have been using cannabis heavily for long periods might be more prone to cognitive difficulties that might be sustained over time (Meier et al., 2012). Individuals with pre-existing cognitive vulnerabilities, especially those related to executive functions, decision making and motivational (reward) processes, are more likely to display heavy and problematic cannabis use patterns, and are at an increased risk for developing dependence and a cannabis use disorder. From this research, individuals should be aware of their potential pre-existing cognitive vulnerabilities prior to the initiation of cannabis use.

An important question that does not have a definitive answer is whether chronic cannabis use leads to irreversible changes in cognitive functioning. For most individuals, it appears that cognitive difficulties associated with chronic cannabis use typically resolve after sufficient abstinence (several weeks to a month). However, for some individuals, including those who have been using cannabis heavily for many years, cognitive deficits might not be entirely reversible. The extent to which cognitive deficits are directly attributable to chronic cannabis exposure (i.e., brain changes resulting from repeated exposure to cannabinoids that are present in cannabis) and not to common factors linking chronic cannabis use and cognitive functioning (e.g., familial genetics and upbringing) is currently not known. Nevertheless, current research emphasizes the importance of limiting the frequency and quantity of cannabis use, especially among vulnerable populations.

A commonly held view is that, since the brain continues to mature into early adulthood (about the age of 25), adolescents are more susceptible to the adverse cognitive effects of regular cannabis use than adults. However, several lines of evidence suggest that this might not be the case (Scott et al., 2018; Meier et al., 2018; Mokrysz & Freeman, 2018). Instead, it appears that brief periods of regular cannabis use impacts both populations equally. Specifically, frequent cannabis use has been associated with similar (mild) cognitive deficits in both adolescents and adults, which are no longer visible after extended abstinence (e.g., one month). It is extremely important to distinguish these observations from those related to early onset cannabis use — regular cannabis use beginning at or prior to the age of 16 or 17. In fact, early onset cannabis use, which is typically associated with heavier use patterns, has been accompanied by more pronounced and potentially irreversible cognitive impairment (Castellanos-Ryan et al., 2017; Meier et al., 2012, 2018; Morin et al., 2018). In this respect, it has been suggested that longer durations of regular cannabis use, beginning in adolescence, are more likely to result in long-lasting cognitive impairment (Meier et al., 2012), rather than frequent cannabis use for short periods of time during adolescence (Meier et al., 2018). That being said, a progressive decline in cognitive functioning has been observed among adolescents who used cannabis frequently over a four-year period (Morin et al., 2018). More research is needed to determine what factors predict blunted cognitive development among adolescents who regularly use cannabis. It is also very important to not mistake these findings on cognitive functioning with those pertaining to mental health and, in particular, psychosis and schizophrenia. There is strong evidence suggesting that cannabis use, particularly heavy use, is associated with increased risk for psychosis and schizophrenia, especially among individuals with a family history of these conditions, and the risk is even greater among individuals who began using cannabis during early adolescence (see *Clearing the Smoke on Cannabis: Chronic Use and Cognitive Functioning and Mental Health*).

It is important to keep in mind that the link between early onset chronic cannabis use and cognitive difficulties might be manifested through several distinct, but not mutually exclusive, pathways. For some individuals, initiating chronic cannabis use early in adolescence might directly lead to cognitive deficits over time, although the extent to which repeated exposure to THC (and other cannabinoids) affect brain functioning in humans is not yet known. For other individuals, cognitive difficulties, especially those related to executive functions and decision-making, might increase the risk for early onset, and pathological, cannabis use. Yet, for others, the link between early onset chronic cannabis use and reduced cognitive functioning might be accounted for by a common factor, such as familial background. Certainly, there are multiple pathways through which early onset chronic cannabis use might be linked to cognitive impairment. Yet, all pathways lead to the same conclusion - that initiation of cannabis use should be delayed as much as possible, especially among vulnerable youth. From this perspective, there is a need to increase the capacity of those who work with youth by providing them with evidence-informed tools and resources (Canadian Centre on Substance Abuse, 2016), such as the *Cannabis Communication Guide* and the "Blunt Truth" that stemmed from the Lower-Risk Cannabis Use Guidelines developed by CAMH (Fischer et al., 2017)

It is important to keep in mind several limitations of current research when interpreting the evidence presented in this report. Since most of the available research is correlational, it has been difficult to establish causal conclusions concerning the effects of chronic cannabis use on cognitive functioning. Moreover, while some longitudinal studies have shown that chronic cannabis use predicted a decline in cognitive functioning and intelligence over time, it has not always been possible to rule out contributing factors. Additionally, there is a large amount of variability across studies, as some studies reported impaired cognitive functioning among individuals who used cannabis chronically, while an equal number of studies have failed to find such associations. These mixed findings are partly attributed to differences in the measurement of cannabis use and, ultimately, the most accurate and informative definition of "chronic cannabis use." It is also not clear whether regular use of different types of cannabis products (e.g., edibles, oils and concentrates) and strains, which vary in their cannabinoid profiles (e.g., THC to CBD ratio), can differentially impact cognition. There are also different methods of use, including smoking dried cannabis plants, vaping oils and concentrates, and eating cannabis-infused edibles (e.g., brownies). Different methods of use again vary in the cannabinoid levels they deliver and their pharmacokinetics (e.g., absorption and metabolism by the body), which might also contribute to different effects on cognitive functioning. To provide answers to these questions and to compare findings across studies more effectively, standardized and detailed information about frequency and quantity of cannabis used as well as methods of use is greatly needed (Lorenzetti et al., 2016).

An equally important direction for future cannabis research will be the increased emphasis on personal characteristics, including differences in sex and gender, genetic makeup, and life experiences. We currently know very little about how individual differences modify the effects of regular cannabis use on cognitive functioning. We also do not know how cannabis use might interact with other substances, such as alcohol and tobacco, and how long-term polysubstance use can affect cognition and mental health. Although researchers have made impressive progress in understanding the effects of chronic cannabis use on cognitive functioning, there are still many unresolved questions. The recent legalization of cannabis for non-medical purposes in Canada could facilitate research into these inquiries and enhance our understanding of the impact of cannabis use on health, including cognitive functioning.

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