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Clearing the Smoke on Cannabis

Maternal Cannabis Use during Pregnancy – An Update

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Key Points

- Cannabis is the illicit drug most commonly used during pregnancy.
- Constituents of cannabis can pass into breast milk during lactation and are absorbed and metabolized by the infant.
- Frequent cannabis use during pregnancy is associated with low birth weight and is part of a cluster of risk-factors correlated with other adverse birth outcomes.
- Prenatal and early exposure to cannabis can alter neurodevelopment leading to adverse effects on cognition and academic achievement.
- There are also effects on behaviour in children and young adults, including attention deficits, increased hyperactivity and impulsivity, and increased likelihood of substance use.
- Information on the effects of cannabis use during pregnancy is essential to help healthcare providers advise patients about the impact of cannabis use and improve the health and well-being of patients and their children.

This is the second 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 maternal cannabis use during pregnancy on children and young adults 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 chronic cannabis use on cognitive functioning and mental health, cannabis use and driving, and respiratory effects of cannabis use. This series is intended for a broad audience, including health professionals, policy makers and researchers.

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Background

After alcohol, cannabis (also referred to as marijuana) is the most widely used psychoactive substance in Canada. According to the 2015 Canadian Tobacco, Alcohol and Drugs Survey (CTADS), 12.3% of Canadians aged 15 years and older reported using cannabis at least once in 2015 (Statistics Canada, 2016a), an increase from 10.6% in 2013. The use of cannabis is generally more prevalent among young people, with 20.6% of youth aged 15 to 19 and 29.7% of young adults aged 20 to 24 reporting past-year use in 2015. Approximately 24% of Canadians aged 15 and older who used cannabis in the past three months reported that they used this drug every day or almost every day. In April 2017, the Government of Canada introduced Bill C-45 to regulate the legal production,

distribution and sale of cannabis. The main objectives of Bill C-45 are to protect public health and safety through product safety and quality requirements, to prevent youth from accessing cannabis, to deter criminal activity and to reduce burdens on the criminal justice system.

A growing body of evidence suggests that cannabis use can negatively impact several aspects of people's lives, including mental and physical health, cognitive functioning, ability to drive a motor vehicle, and pre- and post-natal development among children. In this report—one in a series reviewing the effects of cannabis use on various aspects of human functioning and development (see Beirness & Porath, 2017; McInnis & Plecas, 2016; Kalant & Porath, 2016; McInnis & Porath, 2016)—the effects of prenatal cannabis exposure on offspring, including the birth outcomes, neurocognitive development, behaviour and mental health of children are explored. Following a review of the evidence, this report discusses implications for policy and practice.

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. While possession of cannabis for medical purposes is currently legal, the Canadian government introduced legislation in April 2017 to implement a national framework for controlling the production, distribution, selling and possession of cannabis.

Much of the available evidence on this topic is derived from three prospective longitudinal cohort studies that describe the impact of cannabis use during pregnancy on child development and behaviour, the details for which are summarized in Table 1. The prospective longitudinal nature of these three studies is preferred over retrospective research designs because it follows the same group of mothers and children over a long period of time. This allows for reliable measurement of the extent and timing of cannabis exposure, as well as numerous lifestyle variables (e.g., maternal health, socioeconomic status, maternal use of drugs other than cannabis, etc.) during pregnancy and assesses developmental differences in children's behaviour and functioning over time. On the other hand, retrospective research designs compare groups of participants who differ on some developmental characteristic and draw inferences based on an examination of exposure to potential risk factors (including cannabis use) at some previous point in time.

Smoking is the only route of consumption for which the effects of cannabis exposure during pregnancy were assessed. While consuming cannabis in edible or vaporized forms eliminates the risks from smoking, the baby will still be exposed to the psychoactive components of cannabis (Colorado Department of Public Health and Environment, 2017). No studies to date have assessed risks associated with the consumption of cannabis through other means than smoking.

Discrepancies in birth and developmental outcomes among studies might be due to the increasing potency of cannabis in the past few decades (ElSohly et al., 2016; European Monitoring Centre for Drugs and Drug Addiction, 2017; Mehmedic et al., 2010; University of Mississippi, National Center for Natural Products Research, 2013). This possibility is especially relevant for comparisons between the Ottawa Prenatal Prospective Study (OPPS) and the Maternal Health Practices and Child Development (MHPCD) studies and the more recent Generation R study, as it is possible that the children enrolled in the later study were exposed to higher levels of Δ9-tetrahydrocannabinol (THC). Conclusions about the effects of prenatal cannabis exposure can also be confounded by other maternal risk factors that tend to occur more frequently in women who use cannabis. These factors include poor nutrition, poor physical and mental health, lower socioeconomic status, and the use of other illicit drugs, as well as alcohol and tobacco. Prospective longitudinal studies in particular are better able to adjust for these factors to parse out direct associations with prenatal cannabis exposure.

Prevalence of Cannabis Use during Pregnancy

Cannabis is the most frequently used illicit drug during pregnancy. Based on data from the 2016 National Survey on Drug Use and Health in the United States, 4.9% of pregnant women aged 15-44 years reported past-month cannabis use, a rate that is slightly higher than that reported in 2015 (3.4%) (Substance Abuse and Mental Health Services Administration, 2017). In 2016, the use of cannabis was reportedly highest during the first trimester (10.4%) as compared to the second (2.5%) and third (2.3%) trimesters (Substance Abuse and Mental Health Services Administration, 2017). The annual National Survey

on Drug Use and Health reported a 62% increase in the prevalence of past-month cannabis use among pregnant women between 2002 and 2014 (2.37% to 3.85%) (Brown et al., 2017). Drug screening data from women admitted for delivery at a community hospital in Oregon found an increased proportion of positive urine screens for THC (11.8% to 18%) following legalization of recreational cannabis (Merritt, Wilkinson, & Chervenak, 2016).

In Canada, approximately 16.9% of women of childbearing age (i.e., 15–44 years) reported past-year use of cannabis in 2015 (Statistics Canada, 2016a), a statistically significant increase from 12.6% in 2013 (Statistics Canada, 2015). The 2008 Canadian Perinatal Health Report noted that 5% of pregnant women reported illicit drug use during pregnancy; however, it did not specify the actual percentage that had used cannabis (Ordean & Kahan, 2011). A report from the Reproductive Health Working Group (2006) in Alberta indicated that 2.3% of women who gave birth in 2006 reported using street drugs while pregnant, with cannabis being the most commonly used substance. Similarly, in Southwestern Ontario, the prevalence of women who reported using cannabis during pregnancy at the London Health Science Centre was 2.2% for births between February 2009 and February 2014 (576 out of 26,654 live births) (Campbell et al., 2018). Prevalence of cannabis use during pregnancy in several studies ranges from 2 to 5% (El Marroun, Tiemeier et al., 2011; van Gelder et al., 2010), but can be as high as 15 to 28% in disadvantaged or urban, low-income women (Beatty, Svikis, & Ondersma, 2012; Passey, Sanson-Fisher, D'Este, & Stirling, 2014; Schempf & Strobino, 2008). Prevalence measures rely largely on self reporting and are likely underestimated due to stigma or legal consequences. As evidence, a study conducted in Pittsburgh found that only 36% of pregnant patients who tested positive for THC actually disclosed their cannabis use (Chang et al., 2017).

Table 1. Summary of details from three longitudinal, prospective cohort studies evaluating outcomes of maternal cannabis use during pregnancy.

	Ottawa Prenatal Prospective Study (OPPS)	The Maternal Health Practices and Child Development (MHPCD)	Generation R
Start year	1978	1982	2001
Location	Ottawa, Canada	Pittsburgh, USA	Rotterdam, Netherlands
Sample demographic	Caucasian, predominantly middle class families	Mostly African-American women from low socioeconomic backgrounds	Multi-ethnic cohort with predominantly higher socioeconomic status
Total sample size	583	763	7,452
Initial sample size (cannabis exposed[1] during pregnancy)	78	307	214
Categorization of cannabis exposure	Irregular user (no more than one "marijuana cigarette" per week or 2nd hand smoke), moderate user (average 2–5 per week), or heavy user (average use greater than 5 per week)	Light use (between 0 and 0.4 average daily joints or ADJ), moderate use (between 0.4 and 1 ADJ) or heavy use (1 or more ADJ)	Occasional (monthly), moderate (weekly), heavy (daily) or nonuse
Times at which maternal cannabis use measured	Rate of use calculated at each trimester	Rate of use calculated at each trimester, and at 8 months, 18 months and 36 months	Rate of use calculated before pregnancy, in early pregnancy and in late pregnancy
Reference	Fried, Watkinson, & Willan, 1984	Day et al., 1992	El Marroun et al., 2009

[1] Including women who also smoked tobacco and who may have only used cannabis during the first trimester.

Effects on Pregnancy, Fetal Development and Birth Outcomes

After controlling for maternal tobacco, alcohol and other illicit drug use and various demographic covariates, there is little evidence to suggest an association of cannabis use during pregnancy with an increased risk of pregnancy complications, premature birth, small head circumference, small length, still birth or major congenital abnormalities (Gunn et al., 2016; Metz & Stickrath, 2015; National Academies of Sciences, Engineering, and Medicine, 2017). However, substantial evidence highlights an elevated risk for low birthweight in infants from mothers who used cannabis during pregnancy (National Academies of Sciences, Engineering, and Medicine, 2017). Further, while reports on the effects of prenatal cannabis exposure are mixed, heavy cannabis use in particular is more strongly associated with certain adverse outcomes of pregnancy.

In the Generation R study, maternal cannabis use during pregnancy was associated with reduced fetal growth in mid and late pregnancy as well as a lower birth weight, and these associations were independent of various lifestyle and socio-economic factors (El Marroun et al., 2009). The results from this study also suggested a dose–response relationship such that heavier cannabis use during pregnancy was particularly associated with lower birth weight. Findings from the MHPCD study noted a small but significant negative relationship between cannabis use during the first trimester and length of the child at birth (Day et al. 1991). In a study of a large cohort of Australian women presenting for public prenatal care at a large hospital between 2000 and 2006, Hayatbakhsh and colleagues (2011) reported that use of cannabis during pregnancy significantly predicted negative birth outcomes, including low birth weight, preterm birth, small size for gestational age and admission to the neonatal intensive care unit. These effects were independent of the mother's socio-demographic characteristics, cigarette smoking, alcohol consumption and use of other illicit drugs. In contrast, the OPPS did not observe any differences in growth measures at birth between newborns born to women using cannabis and those not using cannabis (Fried & O'Connell, 1987). Fried, Watkinson and Willan (1984) have noted a statistically significant reduction of approximately one week in the gestational age of infants born to mothers in the OPPS who used cannabis six or more times per week.

Two recent meta-analyses assessed neonatal health outcomes following maternal cannabis exposure. The first meta-analysis included results from 24 studies that did not control for polysubstance use and found that exposure to cannabis *in utero* was associated with decreased birth weight and an increased likelihood of admission to the neonatal intensive care unit (Gunn et al., 2016). The second meta-analysis included results from 31 observational cohort or case-control studies where cannabis use in addition to other substance use had been recorded (Conner et al., 2016). The authors noted a significantly elevated risk of low birth weight and premature birth in women who used cannabis, a risk that doubled when the frequency of cannabis use was at least once per week. These associations, however, disappeared after adjusting for tobacco use.

Three recent retrospective cohort studies not included in these meta-analyses adjust for concurrent tobacco use and report mixed results on risks associated with prenatal cannabis exposure (Chabarria et al., 2016; Ko et al., 2018; Warshak et al., 2015). One study reported an increased risk for admission to the neonatal intensive care unit and small size for gestational age, but no effect on birth weight (Warshak et al., 2015). Ko and colleagues (2018) only looked at mean infant birth weight and gestational age, and, after controlling for relevant covariates such as cigarette smoking, found no significant differences in infants from women who used cannabis during pregnancy. The other study found that while smoking only cannabis had no significant effect on any of the birth outcomes assessed, co-use of both cannabis and tobacco was associated with an increased risk for low birth weight, as well as preterm birth and decreased head circumference (Chabarria et al., 2016). Smoking cannabis during pregnancy in a recent large-scale study in Southwestern Ontario was also found to increase the odds of having an infant with low birth weight by almost three times, although these authors did not adjust their analysis for tobacco or alcohol use (Campbell et al., 2018).

Importantly, negative perinatal outcomes appear more pronounced in infants when mothers smoke both cannabis and tobacco compared to use of either substance alone, suggesting an additive effect of using cannabis with tobacco (Chabarria et al., 2016; El Marroun et al., 2009). Smoking both tobacco and cannabis synergistically increases the risk of respiratory symptoms and Chronic Obstructive Pulmonary Disease (COPD) in older adults (Tan et al., 2009), and could play a role in increasing the harms associated with using both substances during pregnancy. These are important results considering that pregnant women who use cannabis often use additional drugs, including tobacco, alcohol and illicit substances (Day et al., 1992; El Marroun et al., 2016; Goldschmidt, Richardson, Willford, & Day, 2008; Hill & Reed, 2013; Noland et al., 2005; Passey, Sanson-Fisher, D'Este, & Stirling, 2014). In

the Generation R longitudinal study, only 14.8% of pregnant women used only cannabis without also smoking tobacco. (El Marroun et al., 2016). Therefore polysubstance use and smoking may increase the risks associated with using cannabis during pregnancy. While not yet corroborated by evidence in humans, animal studies suggest that cannabis and alcohol during pregnancy can also have synergistic effects (Hansen et al., 2008; Seleverstov et al., 2017; Subbanna et al., 2018).

Despite difficulties ascertaining the unique effects of cannabis exposure on pregnancy and fetal development, the National Academies of Sciences, Engineering, and Medicine (2017) report concludes overall that there is substantial evidence for a statistically significant association between maternal cannabis smoking and low birth weight of exposed infants *in utero*. Low birth weights are subsequently associated with poor long-term outcomes throughout childhood and adulthood, including increased risk for Type 2 diabetes, hypertension, cardiovascular disease and respiratory problems (Gluckman, Hanson, Cooper, & Thornburg 2008; Statistics Canada, 2016b).

Effects on Neurocognitive Functioning

Findings from the OPPS and MHPCD longitudinal studies suggest that maternal cannabis use during pregnancy has effects on children's neurocognitive development. Beginning at age three to four, children of mothers who used cannabis heavily while pregnant in the OPPS and MHPCD studies have demonstrated deficits in memory, verbal and perceptual skills, and verbal and visual reasoning after adjusting for potentially confounding variables[2] (Day et al., 1994; Fried & Watkinson, 1990). In contrast, the results from the Generation R study did not find evidence of such cannabis-related deficits when children were assessed at about age three (El Marroun, 2010). Impaired performance in verbal and quantitative reasoning and short-term memory has also been found in the MHPCD among six-year-old children whose mothers reported smoking one or more cannabis cigarettes per day while pregnant (Goldschmidt, Richardson, Willford, & Day, 2008). Both the OPPS and MHPCD studies reported that in children around the age of nine, prenatal cannabis exposure has been linked with impaired abstract and visual reasoning, poor performance on tasks reflecting executive functioning (i.e., visual-motor integration, nonverbal concept formation and problem solving), and deficits in reading, spelling and academic achievement (Fried, Watkinson, & Gray, 1998; Fried & Watkinson, 2000; Goldschmidt, Richardson, Cornelius, & Day, 2004; Richardson, Ryan, Willford, Day, & Goldschmidt, 2002). Vulnerability in visual-cognitive functioning has been shown to persist into early adolescence among those children heavily exposed to cannabis (Fried, Watkinson, & Gray, 2003).

Neurocognitive and Behavioural Effects

18 months	3–6 years	9–10 years	14–16 years	17-22 years
Increased aggressive behaviour[c] Attention deficits (females)[c]	Deficits in: • Verbal and perceptual skills[ab] • Verbal reasoning[ab] • Visual reasoning[ab] • Verbal and quantitative reasoning[b] • Short-term memory[ab] Hyperactivity[ab] Attention deficits[ab] Impulsivity[ab] Impaired vigilance[b]	Deficits in: • Abstract and visual reasoning[ab] • Executive functioning[ab] • Reading[ab] • Spelling[ab] Hyperactivity[ab] Attention deficits[b] Impulsivity[b] Depressive and anxious symptoms[b]	Deficits in: • Visual-cognitive functioning[a] • Academic achievement[b] • Information processing speed[b] • Visual motor coordination[b] Delinquency[b]	Deficits in: • Executive functioning[a] • Response inhibition[a] • Visuospatial working memory[a] Smoking[ab] Substance use[ab] Early initiation of substance use[ab]

[a] OPPS [b] MHPCD [c] Generation R

[2] In all three longitudinal studies, the analyses controlled for various covariates such as the children's gender and ethnicity, home environment, maternal socioeconomic status, prenatal exposure to tobacco and alcohol, and current maternal substance use.

Prenatal exposure to heavy maternal cannabis use during the first trimester also predicted significantly poorer scores on a test of academic achievement (particularly in reading) at the age of 14 in the MHPCD (Goldschmidt, Richardson, Willford, Severtson, & Day, 2012). Interestingly, these latter effects were found to be related to the effects of prenatal cannabis exposure on intelligence test performance at age six, attention problems and depression symptoms at age 10, and early initiation of cannabis use. At the age of 16, deficits in information processing speed, interhemispheric transfer of information and visual-motor coordination have been linked with prenatal exposure to cannabis, and these effects were found at light to moderate levels of prenatal cannabis exposure in the MHPCD (Willford, Chandler, Goldschmidt, & Day, 2010). General intelligence, however, does not appear to be impacted by prenatal cannabis exposure (Fried, Watkinson, & Gray, 1998, 2003).

Findings from brain imaging studies of young adults aged 18–22 enrolled in the OPPS indicate that *in utero* cannabis exposure negatively impacts the neural circuitry involved in aspects of executive functioning, including response inhibition, attention and visuospatial working memory (Smith, Fried, Hogan, & Cameron, 2004, 2006; Smith et al., 2016). Consistent with these findings, results from a neuroimaging study with the Generation R cohort showed altered brain morphology, specifically in the frontal cortex, in children aged 6–8 who were exposed prenatally to cannabis (El Marroun et al, 2016). These findings are consistent with a report of altered functional connectivity in neonates with prenatal cannabis exposure (Grewen, Salzwedel, & Gao, 2015) and are particularly noteworthy as they indicate that smoking cannabis during pregnancy can lead to long-term changes in children's neurocognitive development.

Behavioural Effects

The behavioural effects of prenatal cannabis exposure have also been documented, although it is unclear as to how early such effects first present themselves. The Generation R study has reported that prenatal exposure to cannabis is associated with an increased risk of aggressive behaviour and attention problems as early as 18 months of age in girls, but not boys (El Marroun, Hudziak et al., 2011). At the age of four, the OPPS failed to find evidence of a negative relationship between cannabis exposure and attention (Fried & Watkinson, 1990), whereas the MHPCD has reported impaired vigilance among exposed children at this age (Noland et al., 2005). When children reach age six, the effects of maternal cannabis use during pregnancy become much more evident. Compared to children of non-users, children born to cannabis users— particularly those who are using heavily —have been found to be more hyperactive, inattentive and impulsive (Fried, Watkinson, & Gray, 1992; Leech, Richardson, Goldschmidt, & Day, 1999). At age 10, prenatally exposed children display increased hyperactivity, inattention and impulsivity, and show increased rates of delinquency and externalizing problems as reported by their mothers and teachers, compared to those children who were not exposed prenatally to cannabis (Fried et al., 1998; Goldschmidt, Day, & Richardson, 2000). More recently, the MHPCD reported that the children of heavier cannabis users during the first trimester (i.e., one or more joints per day) were almost twice as likely to display delinquent behaviour at the age of 14 as the children who were not exposed to cannabis or those who were exposed to lesser amounts (Day, Leech, & Goldschmidt, 2011). The study authors also noted that the relationship between prenatal exposure to cannabis and delinquent behaviour also appears to be mediated by the effects of cannabis on depressive symptoms and by attention deficits in the cannabis-exposed children. In children aged 13–16, however, the effects of prenatal cannabis exposure on some aspects of attention (i.e., flexibility, encoding and focusing) appear to wane (Fried et al., 2003).

There is accumulating evidence that indicates prenatal cannabis exposure may contribute to the initiation and frequency of subsequent substance use during adolescence. Animal studies indicate that repeated exposure to THC in early development may enhance responses to other addictive substances later in life (Cadoni, Pisanu, Solinas, Acquas, & Chiara, 2001; Panlilio, Zanettini, Barnes, Solinas, & Goldberg, 2013). Porath and Fried (2005) reported that 16- to 21-year-old children (particularly males) of women who used cannabis during pregnancy were at increased risk, in a dose-related manner, for the initiation and daily use of tobacco and cannabis, compared to children of non-using mothers. Similar results were noted by Day, Goldschmidt and Thomas (2006). At age 14, children of mothers who used cannabis heavily while pregnant not only reported using this substance more frequently than children of women not using, but they also initiated use at an earlier age. These findings were also evident when the offspring were 22 years of age and the likelihood of cannabis use was related to the extent of prenatal exposure (Sonon, Richardson, Cornelius, Kim, & Day, 2015). The long-term behavioural effects of maternal cannabis exposure may be particularly relevant in populations where other socioeconomic risk factors are also present. The continued use of cannabis by one or both parents in addition to parental attitudes towards cannabis can contribute to transgenerational trends in substance use.

Effects on Children's Mental Health

There is emerging evidence linking *in utero* cannabis exposure to depressive and anxious symptomatology. After controlling for prenatal exposure to other drugs and risk factors for childhood depression, children of women using cannabis during pregnancy expressed significantly more depressive and anxious symptoms at age 10 compared to children of women not using cannabis during pregnancy (Gray, Day, Leech, & Richardson, 2005; Leech, Larkby, Day, & Day, 2006). There is also some evidence that prenatal cannabis exposure is associated with psychotic symptomology. Young adults from the MHPCD study who were exposed prenatally to cannabis were 1.3 times more likely to display psychotic symptoms compared to unexposed young adults, after controlling for other significant covariates (Day, Goldschmidt, Day, Larkby, & Richardson, 2015). The potential impact of prenatal cannabis exposure on the mental health of children is critical to their long-term health and well-being and needs to be examined more carefully in longitudinal studies.

Mechanisms of Action

The mechanisms responsible for the effects of prenatal cannabis exposure are becoming better understood with the discovery and investigation into the endocannabinoid system (our own endogenous cannabinoid receptors and THC-like neurotransmitters). This research has shown that the endocannabinoid system plays a significant role in a broad array of developmental processes in the prenatal brain, including growth and maturation, and contributes to brain functioning later in childhood (Galve-Roperh, Palazuelos, Aguado, & Guzmán, 2009). These normal processes can be altered with exposure to external cannabinoids. Cannabinoids are lipophilic and able to cross both the placental and blood-brain barrier where they can activate endogenous cannabinoid receptors (Park, Gibbons, Mitchell, & Glass, 2003). In the brain, this activation could affect the expression of key genes for neural development, leading to neurotransmitter and behavioural alterations (Gomez et al., 2003; Jaques et al., 2014). Studies in humans have demonstrated that prenatal cannabinoid exposure may lead to alterations in neurotransmitter (i.e., GABAergic,[3] glutamatergic, serotonergic and opioidergic) systems in children (Fernández-Ruiz, Berrendero, Hernández, & Ramos, 2000; Jutras-Aswad, Dinieri, Harkany, & Hurd, 2009; Trezza, Cuomo, & Vanderschuren, 2008).

In animal studies, exogenous cannabinoids can also lead to changes in brain circuits regulating motivation and the response to stress (Panlilio, Zanettini, Barnes, Solinas, & Goldberg, 2013; Pistis et al., 2004; Spano, Ellgren, Wang, & Hurd, 2007), which may affect mood and other behavioural outcomes in children. Alterations to these systems may explain the effects that cannabis has on children exposed early on to this drug. Therefore, cannabinoids from maternal cannabis exposure can directly affect the prenatal brain and significantly disrupt the well-orchestrated processes of neural development, leading to adverse effects on child development and brain function, including cognition and memory (Fride, 2008). It is not yet known whether cannabinoids can directly alter gene expression in humans during prenatal and early development or if there are genetic factors underlying lifestyle habits of the pregnant mother (including cannabis use) and her child's neurodevelopment and behaviour.

Breastfeeding

Maternal cannabis use after pregnancy can also pose risks to the infant. Breastfeeding provides many health benefits to the development of an infant, but these benefits must be weighed against any potential risks resulting from exposure to cannabis during lactation. Concerns about the use of cannabis during lactation stem from observations in humans indicating that THC is secreted in breastmilk (de Oliveira Silveira et al., 2017; Garry et al., 2009; Marchei et al., 2011; Merritt, Wilkinson, & Chervenak, 2016; Metz & Stickrath, 2015) and is also absorbed, metabolized and excreted by the infant (Djulus, Moretti, & Koren, 2005; Garry et al., 2009; Liston, 1998; Perez-Reyes & Wall, 1982). There are no sizeable studies in humans measuring the actual amount of THC transferred to an infant via breastmilk from the mother. A recent study estimated that within four hours after a single quantity of inhaled cannabis, breastfeeding infants ingest 2.5% of the maternal dose of THC (Baker et al., 2018). Another analysis that has been widely cited calculated an infant's exposure to THC through ingestion in one feeding to be 0.8% of the mother's consumption (Bennett, 1997). Given that THC is lipophilic and that the brain is largely made up of fat, small amounts of THC transferred to the infant during breastfeeding could potentially have long-lasting effects on brain development.

The short- and long-term effects of cannabis exposure on infant development that are uniquely associated with breastfeeding have not been examined thoroughly to date and any conclusions are generally confounded by *in utero* cannabis exposure. Several reports suggest that the use of cannabis during breastfeeding contributes to negative short-term effects on infants including sedation, lethargy and poor feeding habits (Djulus, Moretti, & Koren, 2005; Liston, 1998; Miller, 2012). Two limited studies to date with very small sample sizes have attempted to examine the isolated

[3] GABA (gamma aminobutyric acid) is an inhibitory neurotransmitter.

effects of cannabis exposure via breastmilk on longer-term infant health and development. While the first study reports that occasional use of cannabis during lactation has no effect on motor and mental development after one year (Tennes et al., 1985), the second study suggests that THC exposure via breastmilk in the first month after birth could be associated with decreased motor development at age one (Astley & Little, 1990). Neither study adequately controlled for prenatal exposure to THC. In the absence of sufficient evidence for an association between cannabis use during lactation and health outcomes for the infant, using cannabis during lactation is discouraged due to potential risks (Reece-Stremtan & Marinelli, 2015; Committee on Obstetric Practice, 2017; Society of Obstetricians and Gynaecologists of Canada, 2017a).

Finally, breastfeeding is important for encouraging maternal behaviour and bonding between the mother and infant. Maternal consumption of cannabis can compromise mother-infant bonding, which may contribute to children's neurodevelopmental alterations later in life (Best Start Resource Centre, 2017; Shieh & Kravitz, 2006). Cannabis affects alertness, understanding and judgment and so could compromise the mother's ability to recognize cues for hunger, comfort. playing and learning (Best Start Resource Centre, 2017; Centre of Excellence for Women's Health, 2017; Sachs, 2013). Breastfeeding mothers should also consider harms associated with second hand cannabis smoke, which is especially harmful for infants and young children (Best Start Resource Centre, 2017; Centre of Excellence for Women's Health, 2017; Colorado Department of Public Health and Environment, 2017; Wilson et al., 2016). Further research is required to fully evaluate the influence of cannabis on maternal behaviour and the impact of this influence on child development and outcomes.

Conclusions and Implications

Brain development involves a complex cascade of events influenced by prenatal, physical, social and emotional factors early in life, which can have long-lasting impacts on behaviour (for reviews, see Finnegan, 2013; Leyton & Stewart, 2014). The scientific evidence indicates that prenatal exposure to cannabis via smoking (particularly heavy exposure) has adverse effects, beginning as early as age three, on subsequent cognitive functioning, behaviour, mental health and substance use during adolescence. Therefore it is prudent to advise pregnant women and women thinking of becoming pregnant of the risks associated with cannabis use during pregnancy. Little is known about the effects of cannabis exposure through other routes of administration. However, there is no determined amount of cannabis exposure that is safe and until the effects of prenatal cannabis exposure are well understood, the safest option available to pregnant women is to avoid using cannabis (Best Start Resource Centre, 2017; Canada FASD Research Network, 2017). Medical cannabis use for therapeutic purposes during pregnancy or lactation is also contraindicated (Health Canada, 2016, College of Family Physicians of Canada, 2013). Moreover, experts recommend against using any type of cannabis during pregnancy or breastfeeding (Committee on Obstetric Practice, 2017; Society of Obstetricians and Gynaecologists of Canada, 2017a). Appropriate counselling services, however, should be offered to nursing mothers who are not able to stop using cannabis as the benefits of breastfeeding can still outweigh the possible harms of exposure from occasional cannabis use (Djulus, Moretti, & Koren, 2005; Garry et al., 2009). Prevention and intervention efforts directed towards reducing maternal cannabis use during pregnancy could have a significant impact on improving the health and development of infants and could also help reduce the percentage of youth who experience mental health conditions and other comorbid problem behaviours, such as substance use and delinquency.

In 2016, the Society of Obstetricians and Gynaecologists of Canada conducted a national online survey of over 3,200 Canadian women and estimated that 61% of pregnancies are unintended (Society of Obstetricians and Gynaecologists of Canada, 2017b). That finding, combined with the fact that close to 17% of Canadian women of childbearing age (15–44 years) reported past-year cannabis use in 2015 (Statistics Canada, 2016a), indicates the potential risk for children to be prenatally exposed to cannabis. With the upcoming legalization and regulation of non-medical cannabis use in Canada, an investment in public education efforts to increase awareness of the effects of cannabis use during pregnancy is warranted. This investment would be useful considering that online media frequently report benefits of cannabis use that are not consistent with scientific evidence. Such reports include the portrayal of cannabis use as beneficial for morning sickness (Jarlenski et al., 2018).

Despite the high prevalence of cannabis use among women of childbearing age, the potential impact of cannabis on the developing brain and the long-term influence on cognition, behaviour and mental health are still not well-appreciated by society. To this end, it is vitally important that professionals who provide health care to pregnant women are well informed of the latest clinical evidence and research, and that pregnant women and those of childbearing age are advised of the potential risks. Healthcare professionals need to explore these issues with patients and provide unbiased, compassionate information to women of childbearing age and their partners.

There is currently, however, a concern expressed in the literature that the medical community does not have sufficient guidance for addressing maternal cannabis use during pregnancy, and there is a strong need for training in the management of cannabis use during pregnancy. A survey of gynecologists, obstetricians, midwives and general practitioners practicing in France revealed that only 51% of healthcare professionals asked their pregnant patients about drug use. In addition, approximately 68% did not feel sufficiently informed about the risks of cannabis use during pregnancy to provide advice to their patients and lacked the means to inform and take care of their patients who used cannabis (Gérardin, Victorri-Vigneau, Louvigné, Rivoal, & Jolliet, 2011). Prevention efforts aimed at reducing prenatal cannabis exposure could be aided by clinical guidelines developed for healthcare practitioners about discussing the health effects of cannabis use during pregnancy and breastfeeding such as those available in Colorado (Colorado Department of Public Health and Environment, 2017).

More research on maternal cannabis use during pregnancy is needed. Knowledge gaps exist around quantity and quality of cannabis used, issues pertaining to breastfeeding, and the impact of different types of cannabis exposure apart from smoking. Increased efforts to understand the effects of prenatal cannabis exposure are especially important in the face of several factors that can increase risk for adverse outcomes. These factors include increasing accessibility to cannabis, decreased perceptions of risk, increased THC concentrations in cannabis and the advent of potent synthetic cannabinoid products. Finally, an important consideration for research and prevention efforts is that women who use substances during pregnancy are more likely to experience social and economic risk factors such as low education and financial insecurity (Brown et al., 2016; Havens, Simmons, Shannon, & Hansen, 2009; Passey et al., 2014). Addressing these comorbid conditions needs to be part of a holistic approach to reducing risks associated with cannabis use during pregnancy.

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