Introduction

Cannabis is probably the drug most commonly used globally since ancient times, with an annual prevalence of 3.8% of the adult population, or an estimated 183 million people (range 128 million to 238 million) having used cannabis in 2016 [1]. Following the trend of legalization of access to cannabis in several Western countries, its use has increased in North America over the past few years. In spite of warnings of the potential hazards associated with in-utero exposure to cannabis, approximately 10% of pregnant women in an American study reported using cannabis in recent years, and most of them on a daily basis. Significant effects of prenatal cannabis exposure have been found on children’s sleep, cognitive functions (memory and scholastic skills), as well as on executive (frontal lobe) functions (reasoning, attention, impulsivity, and motivation), and affective (depression) and anxiety symptoms throughout the stages of development. Following the presentation of two case vignettes, we integrate the published information on outcomes of maternal use of cannabis during pregnancy on the developing fetus and the “soft” neurological deficits and neuro-behavioral disturbances manifested by them from early childhood and evolving to peaks in adolescence. Taken together, these data serve to define what we call a heretofore unspecified “fetal cannabis spectrum disorder”.

Abstract

Cannabis is probably the drug most commonly used globally since ancient times. Following the trend of legalization of access to cannabis in several Western countries, its use has increased in North America over the past few years. In spite of warnings of the potential hazards associated with in-utero exposure to cannabis, approximately 10% of pregnant women in an American study reported using cannabis in recent years, and most of them on a daily basis. Significant effects of prenatal cannabis exposure have been found on children’s sleep, cognitive functions (memory and scholastic skills), as well as on executive (frontal lobe) functions (reasoning, attention, impulsivity, and motivation), and affective (depression) and anxiety symptoms throughout the stages of development. Following the presentation of two case vignettes, we integrate the published information on outcomes of maternal use of cannabis during pregnancy on the developing fetus and the “soft” neurological deficits and neuro-behavioral disturbances manifested by them from early childhood and evolving to peaks in adolescence. Taken together, these data serve to define what we call a heretofore unspecified “fetal cannabis spectrum disorder”.

Keywords:
Cannabis
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Psychiatric manifestations
Fetal cannabis spectrum disorder

Cannabis use during pregnancy: Are we at the verge of defining a “fetal cannabis spectrum disorder”?

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the physical and behavioral development of the child [15], as documented in a Maternal Health Practices and Child Development publication [16]. Significant effects of prenatal cannabis exposure were found on children’s sleep, cognitive functions (memory, scholastic skills), as well as on executive (frontal lobe) functions (reasoning, attention, impulsivity, motivation) and affective (depression) and anxiety symptoms throughout the stages of development [15]. Furthermore, the lower attention span and the higher number of depressive symptoms during middle childhood have been associated with delinquency in early adolescence of these children [16,17]. Even though there are theoretical reasons to expect possible gender differences following prenatal exposure to cannabis [18], only few studies reported on higher rates of behavior problems for cannabis-exposed girls [19].

**Hypothesis**

The increasing rate of admissions to the psychiatric day hospital of young people affected since early childhood by a combination of neurodevelopmental disorders and severe anxiety, the ever increasing numbers of children (and adults) diagnosed with ADHD, and the ‘epidemic-like’ expansion of autistic spectrum disorder during the last decade, call for a search for possible direct hazards, especially during pregnancy.

We propose to integrate the growing published information (both basic- and clinical-studies) on the outcomes of maternal use of cannabis during pregnancy on the developing fetus and the “soft” neurological deficits and neurobehavioral disturbances manifested since early childhood and evolving to peak in adolescence to define a “fetal cannabis spectrum disorder”. The following two vignettes (out of many seen in the clinic over the years) will illustrate the gradual emergence of this disorder by early adulthood as monitored in the clinical setting.

**Patients and methods**

**Vignette 1**

YC was a 20-year-old single male referred by an outpatient clinic in the community to the psychiatric daycare hospital following the exacerbation of his abnormal mental condition and behavior. He had been diagnosed in early childhood as having mixed specific neurodevelopmental disorders (speech articulation, mixed scholastic skills, fine motor function, conduct, and emotions), depressive conduct disorder (DSM-5 Disruptive Mood Dysregulation Disorder [DMDD]), attention deficit and hyperactivity disorder (ADHD) and post-traumatic stress disorder. He had been treated in various psychiatric ambulatory settings throughout most of his life. Upon the index admission, his mother reported that his was not a premature birth and that there had been no complications during delivery. However, he was considered as being a “not OK” newborn and was put in an incubator for several days (she did not know why). She mentioned that he had undergone repeated diagnostic procedures since early childhood, and there have never been any clear-cut diagnoses for the many difficulties he manifested, such as failure to identify facial expressions, restlessness and hyperactivity, impaired scholastic skills, inadequate social skills, and mood swings accompanied by death ideation (no suicide attempt ever), low arousal threshold and repeated, life-long episodes of temper tantrums. Prolonged treatment with neuroleptics and SSRIs was only partially effective, and at the age of 14 years he was transferred to a boarding school for adolescents with special needs, where he stayed for 5 years. Both the patient and his mother insisted that he never used either alcohol or drugs of any kind (he did smoke tobacco for several years), however, his mother was concerned that he might start smoking weed, since both she and the children’s father, as well as some relatives and various friends and guests at home often do (“It is always on the table in the living room”). When questioned explicitly, she admitted that smoking weed is a regular habit of hers since she was a teenager, that both she and her children’s father (and some of their relatives and many of their friends) do it as a life-long habit, and that she definitely did not quit during her pregnancy or lactation period after having given birth to the patient and to his younger sister. The patient’s mother adamantly denied the possibility that there might be any association between her use of cannabis during pregnancy and lactation (and thereafter) and her son’s neurodevelopmental disorders, as well as her daughter’s (relatively minor) difficulties.

**Vignette 2**

AS was a 19-year-old single female who had been referred to the psychiatric daycare hospital for evaluation, diagnosis and treatment recommendations. Her past history revealed repeated psychiatric diagnostic procedures since the age of 3 years, as a result of which she was first diagnosed with severe prolonged diffuse anxiety and separation anxiety, restlessness and hyperactivity accompanied by repeated episodes of temper tantrum, and later (in addition) with oppositional defiant disorder. At the age of 6 years, she began having auditory hallucinations with full insight, and they have continued to date. She was later diagnosed with depressive conduct disorder (DSM-5, DMDD) accompanied by social skills impairment and mood swings (the diagnosis was changed to bipolar II affective disorder when she was 10 years of age), and she has been treated in various psychiatric ambulatory settings throughout most of her life. When asked about her family’s medical and mental history, she disclosed that her mother has been habitually smoking cannabis since she was a teenager (including throughout her 3 pregnancies). When AS was 13 years old, her mother was additionally heavy on cocaine and LSD for around two years at which point she quit using them and continued on with cannabis alone. AS reported having sporadically smoked cannabis since she was 13 years of age, and using cocaine for one year when she was 17 years of age. A battery of psycho-diagnostic tests revealed a significant gap between her intellectual potential and actual abilities, with impaired learning capacity mainly due to low scholastic skills (dyscalculia, dysgraphia) accompanied by prominent difficulties in executive functions.

**Results and discussion**

A growing body of evidence supports the notion that substances, such as alcohol and cannabis that are generally considered only moderately harmful when consumed at low doses by adults, may pose severe threats to the developing fetus when consumed at the same low doses by the pregnant mother-to-be [20]. The effects of alcohol on the developing fetal brain during pregnancy may manifest since early childhood as an evolving cascade of neurodevelopmental impairments, and they have already been studied in depth and were well-described (fetal alcohol spectrum disorders, for review see [21]). The teratological and perinatal toxicological effects of cannabis on the developing fetal brain during pregnancy in rats have been studied and described by Abel in a series of pioneer and seminal studies during the 1970s [22] (for review of findings in rat, mouse, rabbit and hamster, see [23]). The possible effects of cannabis use by pregnant women on their fetuses have been described as well (for review see [24]), however, integration of all the available knowledge and support for a potential “fetal cannabis spectrum disorder” by basic laboratory studies on animal models are still lacking.

The last 20–30 years have been characterized by a persistent increase in the frequency of diagnosing ADHD and autistic spectrum disorder among children and adolescents, reaching 2–3 folds higher than before the 1980’s [25–29]. Based on the accumulated published data and the clinical experience with many young adult psychiatric patients who were exposed to cannabis in-utero, we hypothesize the existence of a “fetal cannabis spectrum disorder”. Moreover, in the face of the trend in some Western countries to legalize cannabis use, we stress an urgent need for targeted studies, both basic science (animal...
models) and clinical, to investigate this hypothesis. If “fetal cannabis spectrum disorder” emerges as a valid diagnosis, flags must be raised about the liberal use of that drug worldwide.

**Conflict of interest statement**

Both Shaull Schreiber (M.D.) and Chaim G. Pick (Ph.D.) declare no conflict of interest of any kind.

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Both authors contributed equally to the development of the concept, data (PubMed) search and integration, conclusions reached and manuscript writing and reviewing. Both have read and approved the submitted version.

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**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.mejhy.2019.02.017.

**References**


