Title: The Effects of Prenatal Marijuana Exposure on Child Development: A Review of the Literature
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When retail marijuana was legalized in Oregon and the Public Health Division explored the effects of marijuana, we found little evidence about the effect of marijuana use during pregnancy on either mothers or children.

The Effects of Prenatal Marijuana on Child Development

I was particularly interested in the effects of prenatal marijuana on child development. There were studies on the short-term effects of prenatal marijuana (through the first few months of life) but these changes are not particularly significant if they are not associated with long-term child development. There have been some studies of the effects of perinatal marijuana on laboratory animals but it is difficult to generalize from animal to human effects – which is why these studies are generally used to generate hypotheses rather than to impute cause. There seemed to be a lot of studies but many of them had the same authors.

48 Articles From 7 Studies

I found 48 articles published in peer reviewed literature about the effects of prenatal marijuana exposure on child development. It turned out that they all came from only 7 studies. This included 2 studies with follow-up for more than 20 years (and many publications each) -- and 5 studies with shorter follow-up and one publication each. Understanding the underlying scientific literature in this way made it easier to explore the strengths and weaknesses of the literature. Six of the studies began before 1995 and all 7 relied exclusively on self-report of women who had smoked marijuana. Table 1 summarizes the 7 human studies on the effects of prenatal marijuana exposure on child development. The rest of this presentation is about these 7 studies and the 48 articles.

Potential sources of bias in the publications from these 7 studies

There are 4 potential sources of bias in the publications from these 7 studies:

(1) Selection of controls: The controls in these 7 studies vary; some used population controls (in either high-risk or low-risk populations); and one used matched pairs. Selection of controls is important because child development is strongly influenced by factors like race/ethnicity, family income and household education. Comparing children whose mothers used marijuana during pregnancy with a high-education, high-income group of controls could be very misleading. It seems likely that children of non-MJ using controls from a high-risk, low-SES clinic population might be more comparable to the children of MJ-using children. The best controls would be matched pairs: the Jamaica study matched each marijuana-using woman with a non-user according to age, parity and SES. Another interesting feature of the Jamaica study that would be hard to replicate in North America is

that use of marijuana by women in Jamaica in the late 1980s was not stigmatized. Therefore, users and non-users may have been more similar than in North American studies.

(2) The use of multiple comparisons: it is difficult to assess statistical significance if many outcomes have been assessed. Some of these studies tested many child development outcomes including multiple psychologic tests and each of their subtest scores. The publications do not always describe what outcomes were explored and which ones were found to be not associated with prenatal marijuana use. The publications mostly focus on the outcomes that WERE associated with prenatal marijuana use. None of the publications comment on statistical corrections for multiple comparisons.

(3) Publication bias: publication bias under-reports negative findings. Publication bias is most likely where there is only one publication on marijuana from a larger study that generated many other publications on other topics. These publications are particularly susceptible to publication bias since positive associations are much more likely to be pursued and submitted for publication than those with no statistically significant associations. Interestingly, 3 of the 5 single-publication studies that I found published results with no statistically significant associations. There were certainly additional no-association analyses that were never published.

(4) The mental health of the marijuana-using pregnant women is a difficult confounder for research that seeks to assess whether maternal prenatal marijuana has adverse effects on child development. At this point, we do not even have exploratory psychologic methods to see the extent to which women who use marijuana are treating themselves for depression or other mental health problems. If our goal is to explore the effect of marijuana (rather than the effect of the MJ-using mother), it is important to find a way to control for maternal mental health.

Other Limitations of These Studies:

There are 6 other limitations of these studies:

(5) Subgroup analysis: One publication (from the Netherlands study) had a subgroup analysis as their main finding: that girls had attention problems when they were 18 months old but boys did not. Subgroup analysis doesn't mean that the conclusion is not true but it makes the conclusion less robust and begs for confirmation in independent studies.

(6) Limited follow-up: 3 of the studies followed the children only for 5 or less years. Studies that followed children longer were more likely to provide insight into important lifelong developmental outcomes.

(7) maternal use of multiple substances: Statistically, most of these studies included women who used multiple substances. It's not clear what problems are introduced into analysis by using cocaine-exposed children (or alcohol-exposed children) as controls for marijuana-exposed children. And most of these studies were not designed to explore the effects of prenatal marijuana exposure.

(8) Dosing: Another limitation of these studies is that they studied marijuana use 14-38 years ago (and the 2 multi-publication studies began around 1980). There is more variety in currently available marijuana including hi-CBD strains and higher levels of THC. And little is known about other dosage formats including ingested and vaped THC.

(9) These are all observational studies. None are randomized control trials. Randomized control trials are valuable in summarizing a literature because they contain less bias than observational studies. It would be possible but difficult for researchers to create a randomized control study that focused on the effects of prenatal marijuana use on child development.

(10) studying the effects of the mothers vs studying the effects of marijuana. We are trying to understand the effect of marijuana on child development. All of these are studies of the women who smoked marijuana during their pregnancy. We are hoping that studying the mothers is a good proxy for studying the effects of marijuana but that may not be true.

Conclusions

All of these studies contained one or more serious methodologic flaws. The main strength of this literature is that similar methods have been used in several research studies. The conclusions that seem the most robust would come from the Pittsburgh study because children were followed for 22 years and because low-income mothers were used as controls. Many psychologic tests were administered to the children over that time. They reported that children were more likely to be depressed, have lower IQ and executive function deficits after prenatal marijuana exposure (PME). My main conclusion is that the literature is shaky but there are some indications that prenatal marijuana exposure may cause depression and decreased executive function. Because of the difficulty in creating a randomized control trial, it seems likely that the best methods for future study would use a prospective, double-blinded, matched pairs method (including some way to control for maternal mental health issues) with long-term follow-up.

References

The publications cited for each study are listed here. See Table 1 (below).

Ottawa (25 publications)

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Pittsburgh (18 publications)

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Denver (1 publication)

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Jamaica (1 publication)

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Netherlands (1 publication)

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Avon (1 publication)

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Table 1. Seven Studies of the Effects of Prenatal Marijuana Exposure (PME) on Child Development

Site	Study Type	Substances studied	Outcomes Studied	Controls	Findings: PME associated with	Year study began	Number of publications about PME	Limitations
Ottawa (Canada)	Longitudinal (22 year follow-up)	Marijuana, cigarettes, alcohol	Language development, memory, visual/perceptual functioning, sustained attention, intelligence, impulse control, and executive function	High-SES women in obstetrics practices	Deficits on executive function tasks	1978	25 (1980-2010)	High-SES controls; Multiple comparisons; Publication bias; Mothers' mental health.
Pittsburgh	Longitudinal (22 year follow-up)	alcohol, marijuana, tobacco	Many outcomes (including school achievement at age 14)	Low-SES Medicaid women in prenatal clinic	Increased depressive symptoms among 10 year olds; decreased executive function; decreased IQ	1982	18 (1994-2015)	Low-SES controls; Multiple comparisons; Publication bias; Mothers' mental health.
Denver	Longitudinal (one year follow-up)	marijuana	Child's development (motor, mental and growth) and behavior	Low-SES women in 2 prenatal clinics	No effect on child development or breastfeeding duration	1981	1 (1985)	Low-SES controls; Multiple comparisons; Publication bias; Mothers' mental health; Limited follow-up.
Jamaica (West Indies)	Longitudinal (5 year follow-up)	marijuana	Brazelton Neonatal Behavioral Assessment Scales; McCarthy Scales of Children's Abilities (age 4-5 years)	Matched controls: Marijuana-using women were matched with non-users according to age, parity, SES	No significant differences in development	Late 1980s	1 (1991)	Publication bias; Mothers' mental health; Limited follow-up.
Netherlands	Longitudinal (2 year follow-up)	Marijuana, tobacco	Child's development (motor, mental and growth)	Population-based birth cohort	Increased aggressive behavior and attention problems at 18 months in girls (but not boys)	2002	1 (2011)	Medium-SES controls; Multiple comparisons; Limited follow-up; Publication bias; Mothers' mental health Subgroup analysis;
Avon (England)	Longitudinal (12 year follow-up)	Alcohol, marijuana, tobacco	Psychosis among 12 year olds	Population-based birth cohort	Not associated with psychosis among 12 year olds	1991	1 (2009)	Medium-SES controls; Multiple comparisons Publication bias; Mothers' mental health.

Cleveland	Longitudinal study (12 year follow-up)	cocaine, tobacco, alcohol and marijuana	Wechsler Preschool and Primary Scales of Intelligence-Revised (age 4 years)	Low-SES women with overlapping substance use	Not significantly associated with omission errors	1994	1 (2005)	Low-SES controls; Multiple comparisons; Publication bias; Mothers' mental health.