Prenatal cannabis exposure and cognitive function: a critical review

CIARA A. TORRES[1,4], CARL L. HART[2,3,4]

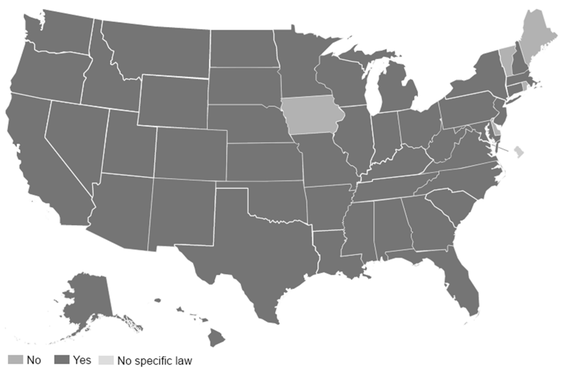
[1]School of Social Work, [2]Division on Substance Abuse, N.Y. State Psychiatric Institute, [3]Departments of Psychology and Psychiatry, [4]Columbia University, New York, N.Y. 10032

T32 HIV, Substance Abuse and Criminal Justice Fellowship Program

ABSTRACT

Despite limited data demonstrating catastrophic effects of prenatal cannabis exposure, popular opinion and public policies still reflect the belief that cannabis is a uniquely dangerous teratogen. This article provides a critical review of results from longitudinal studies examining the impact of prenatal cannabis exposure on multiple domains of cognitive functioning. In addition, neuroimaging data on cannabis-exposed offspring are reviewed in order to better understand possible mechanisms of action. Statistically significant differences between prenatally exposed individuals and control participants have been observed on a minority of measures (8.2 percent). More importantly, however, the clinical significance of these findings is limited because cognitive functioning overwhelmingly falls within the normal range when compared against normative data. In short, there is no convincing evidence that prenatal cannabis exposure is associated with unique deleterious effects on cognitive functioning.

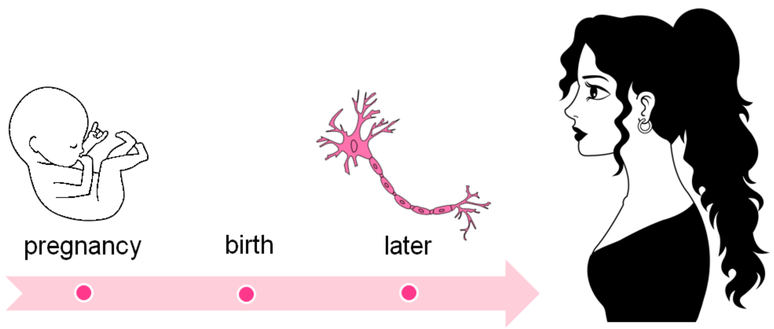
STATES THAT SOUGHT TO PROSECUTE WOMEN FOR DRUG USE DURING PREGNANCY



Propublica, 2015

•Tennessee amended its fetal assault law to include newborns that are "born *addicted* to or *harmed* by the narcotic drug" (TN SB1391, 2014). The law does not describe what constitutes an addicted newborn nor what should be considered to determine whether the baby has been harmed.

THE ASSUMPTION OF HARM



•Cannabis is the most frequently used illicit substance by women of reproductive age in the U.S. (NPHS, 1996; Van Gelder et al., 2010).

•The dominant popular view is that prenatal cannabis exposure causes a broad range of deleterious outcomes, especially on cognitive functioning (for a review, see Huizink and Mulder 2006; Jutras-Aswad et al. 2009).

WHAT WE DID: A CRITICAL REVIEW

•Included studies on prenatal cannabis exposure and cognition

PubMed Google Scholar

•Defined as processes of knowing, including attending, perceiving, imagining, remembering, reasoning and problem solving (APA, 2015)

•Identify cohorts
-Ottawa Prospective Prenatal Study (Fried at Ottawa, Canada)
-Mental Health Practices & Child Development Project (Day at Pittsburg, PA)
-Prenatal Cocaine Exposure Studies (Singer at Cleveland, OH & Frank at Boston, MA)
-Jamaican Study (Dreher at Saint Thomas, Jamaica)

WHAT WAS OUR GOAL?

•To examine the assumption that prenatal cannabis exposure is harmful to cognitive functioning.

summarize	evaluate
• # of studies • # of groups • from where • methods	• findings • limitations • interpretation • clinical relevance

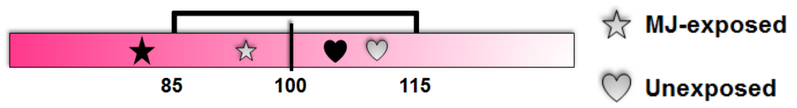
DETERMINING CLINICAL RELEVANCE

•Of every day, real-world, practical or functional import.

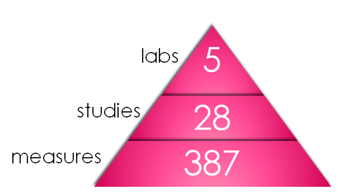
•Clinical relevance can be determined by comparing individual scores or measurements with normative data obtained from a large, randomly selected representative sample of the wider population. It should also incorporate important variables such as age, education, and gender.

•Normative data establish a baseline distribution for a score or measurement, and against which the score or measurement in experimental studies can be compared.

•Such comparisons allow researchers to determine whether statistically significant findings are clinically of functionally meaningful.



WHAT WE FOUND: THE PRIMARY DATA



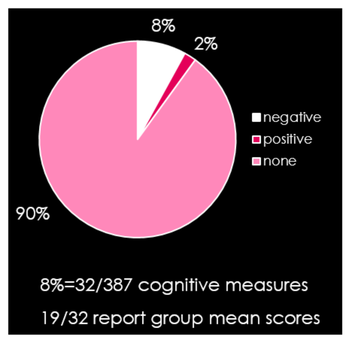
infants & toddlers (up to 24mo)	young children (3-9y)	older children (9-12y)	adolescents & young adults (13-22y)
• Fried & Watkinson, 1988 • Richardson et al., 1995 • Noland et al., 2003 • Singer et al., 2005	• Fried & Watkinson, 1990 • Hayes et al., 1991 • O'Connell & Fried, 1991 • Fried et al., 1992 • Day et al., 1994 • Leech et al., 1999 • Noland et al., 2003 • Frank et al., 2005 • Noland et al., 2005 • Beeghly et al., 2006 • Goldschmidt et al., 2008	• Fried et al., 1997 • Fried et al., 1998 • Fried & Watkinson, 2000 • Richardson et al., 2002 • Goldschmidt et al., 2004 • Rose-Jacobs et al., 2011 • Rose-Jacobs et al., 2012	• Fried & Watkinson, 2001 • Fried et al., 2003 • Smith et al., 2004 • Day et al., 2006 • Smith et al., 2006 • Goldschmidt et al., 2012

ANALYSIS: AN EXAMPLE OF NON-REPRESENTATIVE FINDINGS

Investigators	Domain Tested	Participants	Time of Exposure	Findings	Caveats
Goldschmidt et al., 2008 Funding Source: NIDA and NIAAA	*General intelligence* [SBIS-IV, (Composite score composed of verbal reasoning, quantitative reasoning, abstract/visual reasoning and short-term memory subtests)] **Total no. of outcome measures** = 15	Six year old children of women who reported MJ use during: 1st trimester (heavy MJ: N=93; light-moderate MJ: N=175; CTL: N=380), 2nd trimester (heavy MJ: N=30; light-moderate MJ: N=103; CTL N=455); 3rd trimester (heavy MJ: N=32; light-moderate MJ: N=88; CTL N=528)	MJ use self-reported at 4th & 7th pregnancy months and at 24-28h post-delivery **Categories:** Light-moderate = 0<ADJ<1 Heavy = ADJ≥1	**1st and 2nd trimester:** Heavy prenatal MJ exposure group performed more poorly on measures of short-term memory, verbal and quantitative reasoning, and the composite score **3rd trimester:** Heavy prenatal MJ exposure group performed more poorly on measure of quantitative reasoning and the composite score	Participants performed in the normal range on the majority of the cognitive tests. There were three exceptions: 1) 2nd trimester exposure - composite score (1 point below the norm); 2) quantitative reasoning score (2 points below); and 3) 3rd trimester exposure - quantitative reasoning score (1 point below) Only one cognitive measure used to assess a specific domain Mothers who used MJ during pregnancy were more likely to be poor, single, and provide a poorer home environment, as measured by the HSQ. They were also more likely to report using alcohol, tobacco, and cocaine Relatively small number of participants studied in heavy MJ-exposed group

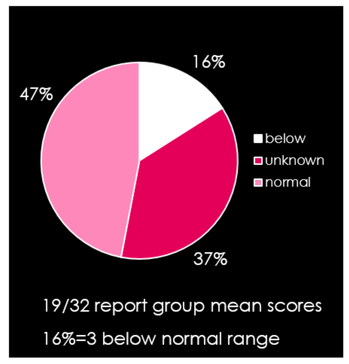
THE QUESTION: WHAT IS REPRESENTATIVE?

RESULTS SUMMARY



Any association between prenatal cannabis exposure and cognitive scores? Only a minority (10%) do.

Is clinical relevance determined? No individual scores reported.



Move on with group mean scores…

1. Only one study compares scores with normative data (Richardson et al., 1995).
2. Compare rest if possible (never normed, out of circulation or inaccessible)

TOTAL FOR ENTIRE LITERATURE <1%

OTHER IMPORTANT FINDINGS

•Overinterpretations in some (9/28) studies
-language (such as deficit and impairment) when referring to findings
-even though none compared against normative data

•Positive relationships minimized
-example (Leech et al., 1999): "Although finding fewer errors of omission may, at first, appear to be a positive effect of prenatal exposure… children may do less well over the long-term, particularly in time limited situations."

•All funded by same institution (NIDA)

TAKE-HOME MESSAGE

•There is no convincing evidence that prenatal cannabis exposure produces clinically relevant effects in term of cognition

•Might change in future

-cognitive scores are compared against normative data

-address impact of disproportionate contribution of research groups & funders

ACKNOWLEDGEMENTS

Support contributed by NIDA's T32 in HIV and Substance Abuse in the Criminal Justice System (Dr. Nabila El-Bassel, primary investigator). We thank Drs. Jennifer Manly and Anthony Ahmed for providing access to normative data for cognitive tests.

We certify that there is no conflict of interests with any financial organization regarding the material discussed in this study.

REFERENCES

TN SB1391, 2013–2014, 108th General Assembly. (2014). LegiScan. Retrieved September 08, 2015, from http://legiscan.com/TN/bill/SB1391/2013

National Pregnancy and Health Survey: Drug Use Among Women Delivering Live Births, 1992 (ICPSR 2835):http://www.icpsr.umich.edu/icpsrweb/NACJD/studies/2835 Accessed on September 9, 2015.

Van Gelder, M. M., Reefhuis, J., Caton, A. R., Werler, M. M., Druschel, C. M., Roeleveld, N., & National Birth Defects Prevention, S. (2010). Characteristics of pregnant illicit drug users and associations between cannabis use and perinatal outcome in a population-based study. Drug Alcohol Depend, 109(1-3), 243-247.

Huizink, A. C., & Mulder, E. J. (2006). Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring. Neurosci Biobehav Rev, 30(1), 24-41.

Jutras-Aswad, D., DiNieri, J. A., Harkany, T., & Hurd, Y. L. (2009). Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. Eur Arch Psychiatry Clin Neurosci, 259(7), 395-412.

Richardson, G. A., Day, N. L., & Goldschmidt, L. (1995). Prenatal alcohol, marijuana, and tobacco use: infant mental and motor development. Neurotoxicol Teratol, 17(4), 479-487.

Leech, S. L., Richardson, G. A., Goldschmidt, L., & Day, N. L. (1999). Prenatal substance exposure: effects on attention and impulsivity of 6-year-olds. Neurotoxicol Teratol, 21(2), 109-118.