





### Matternal Mental Health Matters for Two Generations:

Impact of Perinatal Mood and Anxiety Disorders on Fetal and Child Development

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Diana Vegelos Chair of Women's Mental Health, Dept of Ob/Gyn
Professor of Medical Psychology, Dept of Psychiatry
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Research Scientist VI, New York State Psychiatric Institute







### Speaker:

### Catherine Monk, Ph D

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### Disclosures

**Grant with Curio, start up app company** 

Sit on the board of Zero to Three

**NIH** funding

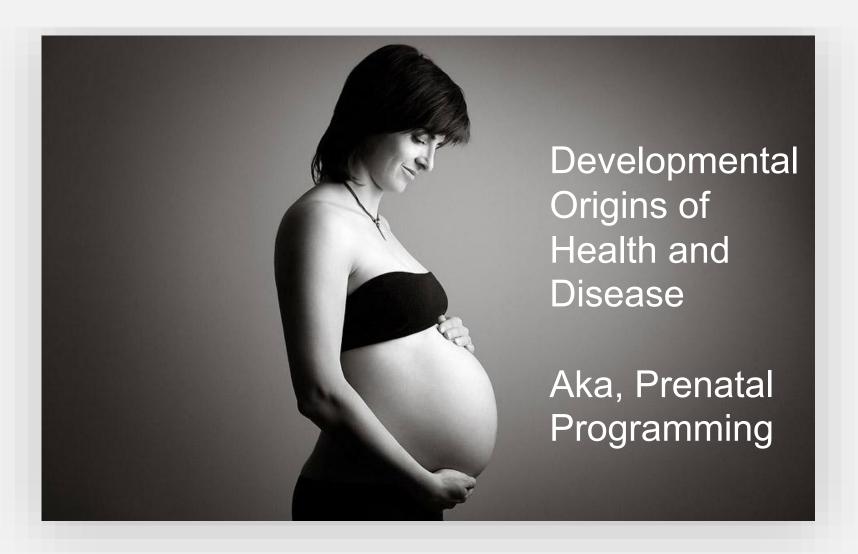


### **OVERVIEW**

- I. DOHaD & adaptation
- II. DOHaD & maternal mental health
- III. Mechanisms of transmission
- IV. Inter-Generational & health disparities lenses: An *In-Utero* frame is too narrow
- V. Pandemic Effects?
- VI. Implications for the perinatal care ecosystem



### I. DOHaD





### COMMENT

HISTORY How James Watt moved from steam engines to sculpture p.134

on the social roots of disasters p.135



LAB LIFE Ethics codes could protect field workers from harassment p.136



rom folk medicine to popular culture, there is an abiding fascination with how the experiences of pregnant women imprint on their descendants. The latest wave in this discussion flows from studies of epigenetics — analyses of heritable changes to DNA that affect gene activity but not nucleotide sequence. Such DNA modification has been implicated in a child's future risk of obesity, diseases such as diabetes, and poor response to stress.

Headlines in the press reveal how these findings are often simplified to focus on the maternal impact: 'Mother's diet during pregnancy alters baby's DNA' (BBC), 'Grandma's Experiences Leave a Mark on Your Genes' (Discover), and 'Pregnant 9/11 survivors transmitted trauma to their children' (The Guardian). Factors such as the paternal contribution, family life and social environment receive less attention.

Questions about the long shadow of the uterine environment are part of a burgeoning field known as developmental origins of health and disease (DOHaD)<sup>1</sup>. For example, one study revealed<sup>2</sup> that 45% of children born to women with type 2 diabetes develop diabetes by their mid-twenties, compared with 9% of children whose mothers developed diabetes after pregnancy.

DOHaD would ideally guide policies that support parents and children, but exaggerations and over-simplifications are making scapegoats of mothers, and could even increase surveillance and regulation of pregnant women. As a cademics working in DOHaD and cultural studies of science, we are concerned. We urge researchers, press officers and journalists to consider the ramifications of irresponsible discussion.

#### ALARMING PRECEDENTS

There is a long history of society blaming mothers for the ill health of their children. Preliminary evidence of fetal harm has led to regulatory over-reach. First recognized in the 1970s, fetal alcohol syndrome (FAS) is a collection of physical and mental problems in children of women who drink heavily during pregnancy. In 1981, the US Surgeon General advised that no level of alcohol consumption was safe for pregnant women. Drinking during pregnancy was stigmatized and even criminalized. Bars and restaurants were required to display wamings that drinking

2 | NATURE | VOL 512 | 14 AUGUST 2014

### Don't blame the mothers

Careless discussion of epigenetic research on how early life affects health across generations could harm women, warn **Sarah S. Richardson** and colleagues.

8

- Most women and children are unaffected (fathers/partner have influence too)
- These maternal experience factors are a few of thousands of points of variability and not randomly distributed (look to society for change)

The level of exposure is typically high\*

Effects are modifiable throughout development







## The Wellcome Foundation Lecture, 1994. The fetal origins of adult disease

#### D. J. P. BARKER

MRC Environmental Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, SO16 6YD, U.K.

SUMMARY



Recent findings suggest that many human fetuses have to adapt to a limited supply of nutrients and in doing so they permanently change their physiology and metabolism. These 'programmed' changes may be the origins of a number of diseases in later life, including coronary heart disease and the related disorders: stroke, diabetes and hypertension.

Proceedings of the Royal Society (1995)

### **Prenatal Programming**

- Evolutionary perspective (Glover, 2011, Pike, 2005)
- Prenatal exposures 'forecast' the postnatal environment
- Fetus responds with adaptations
   Improve fitness to a later stage in development
- Health outcomes may result, in part, from the match between the prenatal and postnatal environments

# Maternal Prenatal Experience & Adaptations in Development

# Density Triggers Maternal Hormones That Increase Adaptive Offspring Growth in a Wild Mammal

Ben Dantzer, 1\*† Amy E. M. Newman, 2 Rudy Boonstra, 3 Rupert Palme, 4 Stan Boutin, 5 Murray M. Humphries, 6 Andrew G. McAdam 1, 2

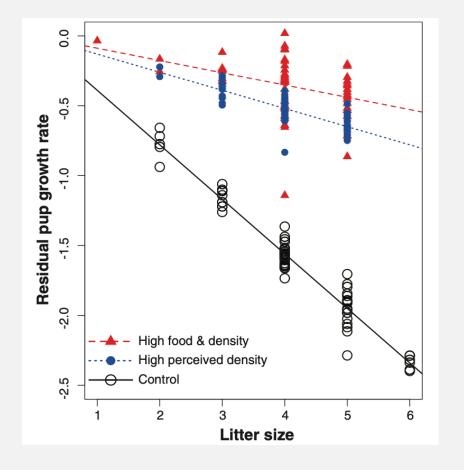
www.sciencemag.org SCIENCE VOL 340 7 JUNE 2013



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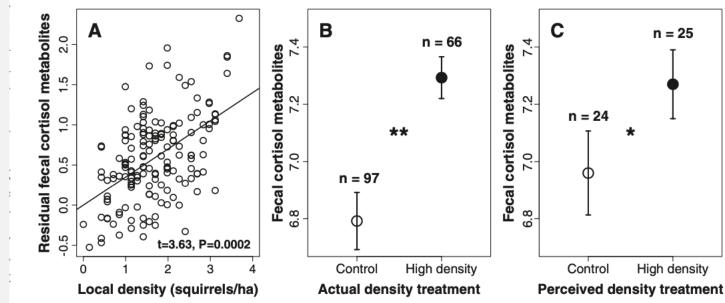


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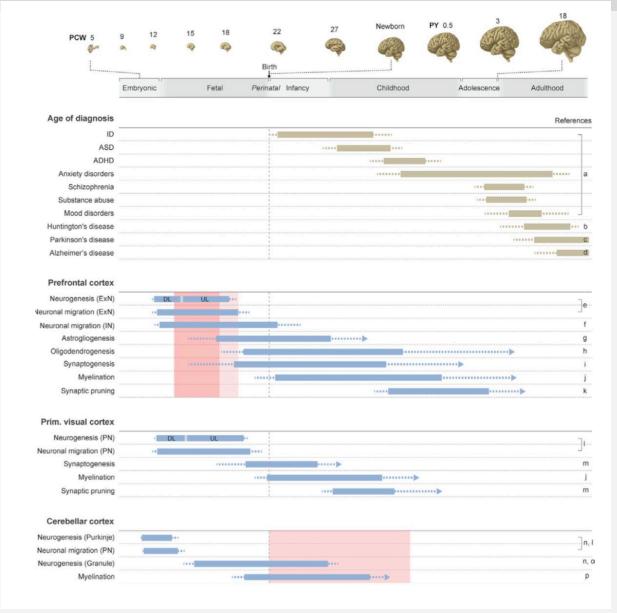
Ben Dantzer, 1\*† Amy E. M. Newman, 2 Rudy Boonstra, 3 Rupert Palme, 4 Stan Boutin, 5 Murray M. Humphries, 6 Andrew G. McAdam 1, 2

Mediated "communicated" to fetus via cortisol?



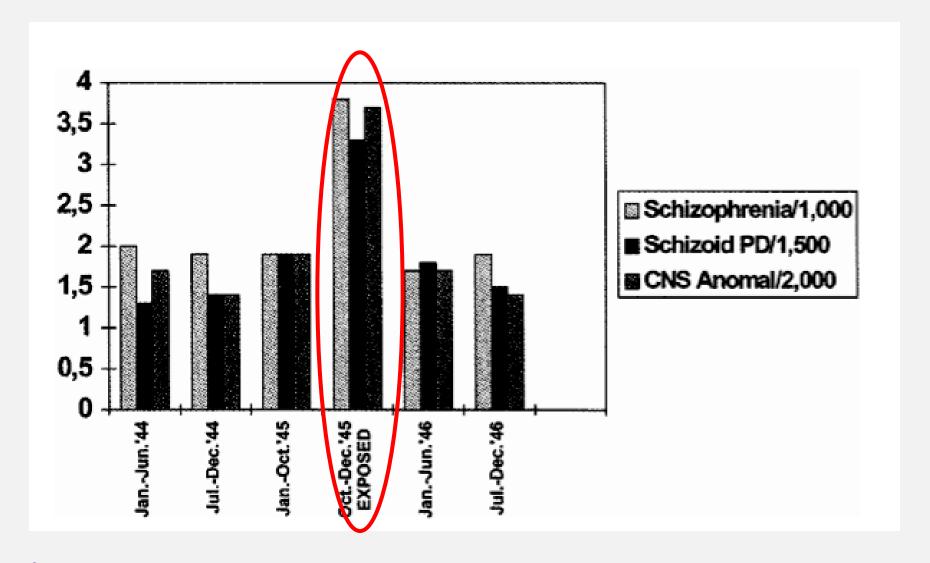
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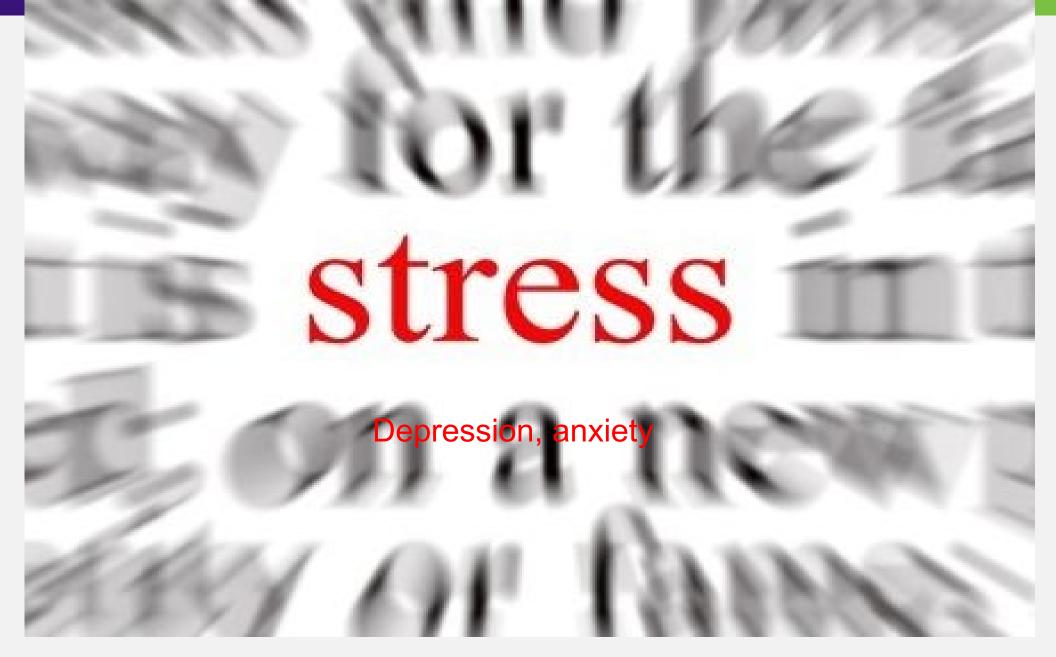
### When the brain is developing...



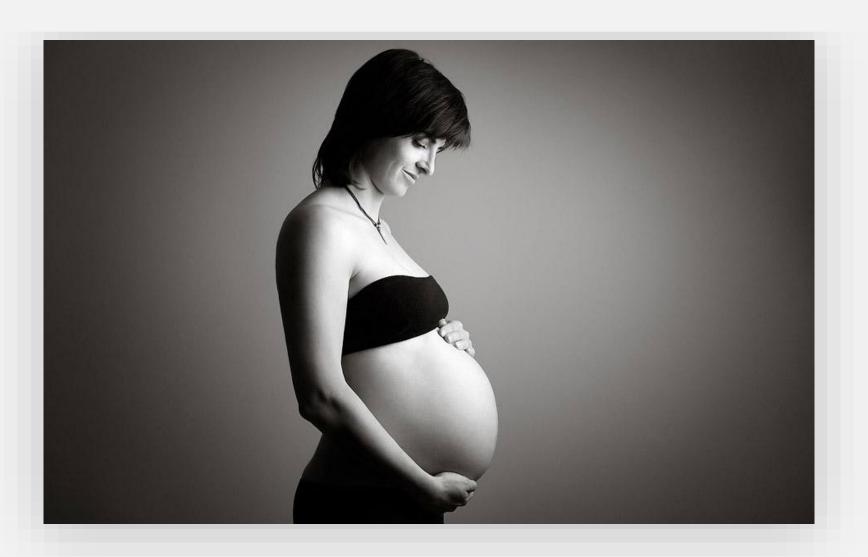
Sestan & State, 2018

### Dutch Famine Increases Risk for Schizophrenia Spectrum Disorders in Men





### **II. DOHaD & Maternal Mental Health**



#### The persisting effect of maternal mood in pregnancy on childhood psychopathology

KIERAN J. O'DONNELL, a VIVETTE GLOVER, b EDWARD D. BARKER, AND THOMAS G. O'CONNOR a McGill University; b Imperial College London; birkbeck University; and d University of Rochester Medical Center

#### Abstract

Developmental or fetal programming has emerged as a major model for understanding the early and persisting effects of prenatal exposures on the health and development of the child and adult. We leverage the power of a 14-year prospective study to examine the persisting effects of prenatal anxiety, a key candidate in the developmental programming model, on symptoms of behavioral and emotional problems across five occasions of measurement from age 4 to 13 years. The study is based on the Avon Longitudinal Study of Parents and Children cohort, a prospective, longitudinal study of a large community sample in the west of England (n = 7,944). Potential confounders included psychosocial and obstetric risk, postnatal maternal mood, paternal pre- and postnatal mood, and parenting. Results indicated that maternal prenatal anxiety top 15% was associated with a twofold increase in risk of a probable child mental disorder, 12.31% compared with 6.83%, after allowing for confounders. Results were similar with prenatal depression. These analyses provide some of the strongest evidence to date that prenatal maternal mood has a direct and persisting effect on her child's psychiatric symptoms and support an in utero programming hypothesis.

Developmental or adaptive programming, including in the fetal period, has emerged as a major model for understanding the developmental origins of health outcomes. The model proposes that in utero exposures instigate an adaptive response in the organism that is carried forward in development with persisting effects on behavior and biology. Much of this work focuses on poor nutrition or an index of poor growth (e.g., low birth weight) as the causal factor, although other and additional sources of stress with causal effects may be operating (Barker, 1999; Gluckman & Hanson, 2004; Painter, Roseboom, & Bleker, 2005; Wadhwa, Buss, Entringer, & Swanson, 2009). Evidence for the model as applied to cardiovascular and metabolic outcomes is substantial, derives from numerous large-scale investigations in diverse settings, and has spawned an influential line of study because of its potential to influence health and development of populations in developed and developing countries (Gillman et al., 2007).

We are extremely grateful to all of the families who took part in this study; the midwives for their help in recruiting them; and the whole Avon Longitudinal Study of Parents and Children team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists, and nurses. The UK Medical Research Council, the Wellcome Trust, and the University of Bristol currently provide core support for the Avon Longitudinal Study of Parents and Children. This particular project was funded in part by NIH Grant Roll MH073842.

Address correspondence and reprint requests to: Thomas G. O'Connor, Department of Psychiatry, Wynne Center for Family Research, University of Rochester Medical Center, 300 Crittenden Boulevard, Rochester, NY 14642; E-mail: Tom\_OConnor@URMC.Rochester.edu.

Building on the fetal programming model for somatic health, several research groups are seeking to translate the model for psychological and neuroscience outcomes. These studies focus on maternal prenatal anxiety or stress as a putative causal agent initiating a developmental programming response. The focus on prenatal anxiety or stress follows from decades of experimental animal studies linking prenatal stress to sizable and lasting effects on offspring fear, neurogenesis, immunity, and stress physiology, among other outcomes (Coe et al., 2003; Maccari et al., 2003). A number of observational studies in humans show that prenatal anxiety or stress in the mother is associated with behavioral outcomes in children (Bergman, Sarkar, O'Connor, Modi, & Glover, 2007; Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003; Davis, Glynn, Waffarn, & Sandman, 2011; O'Connor, Heron, Golding, & Glover, 2003; Robinson et al., 2011; van den Bergh et al., 2006). These results raise important conceptual challenges for studies of developmental models of psychopathology that, with a few exceptions (Fisher et al., 2011; Liu, Portnoy, & Raine, 2012), tend to consider neither prenatal exposures nor programming effects. Furthermore, the hypothesis that there are prenatal programming effects for psychopathology has sizable implications for intervention, and particularly the timing of early interventions. Interventions starting in early infancy to promote the mother-infant relationship and the quality of parenting (Allen, 2011; Melhuish, Belsky, Leyland, & Barnes, 2008) are grounded in research linking the quality of the early postnatal rearing environment and the behavioral, emotional, and cognitive development of the child (Murray et al., 2011; Nelson et al., 2007; Ramchandani

## Maternal Anxiety & a 2-Fold Increase in Child Mental Health Disorder

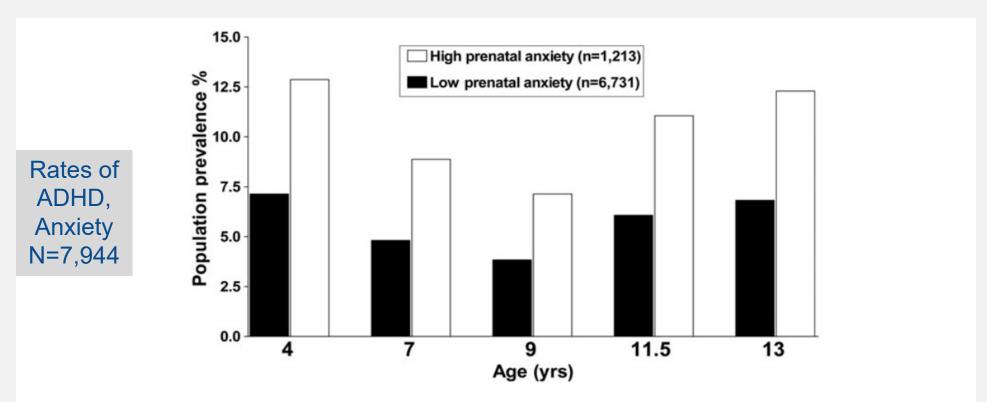


Figure 3. The predicted population prevalence of a probable mental health disorder in children born to high (open bars represent the top 15%) and low (filled bars) anxiety mothers. Estimates are based on total Strengths and Difficulties Questionnaire scores generated using growth curve analysis controlling for birth weight, gestational age, substance use in pregnancy, maternal age, education, crowding as index of socioeconomic status, parenting style (see Methods), maternal depression at 8 weeks postnatal, maternal postnatal anxiety at 33 months, paternal prenatal anxiety, paternal postnatal depression at 8 weeks, and paternal postnatal anxiety at 33 months.



#### ARTICLE IN PRESS

#### **NEW RESEARCH**

# Associations of Maternal Prenatal Stress and Depressive Symptoms With Childhood Neurobehavioral Outcomes in the ECHO Cohort of the NICHD Fetal Growth Studies: Fetal Growth Velocity as a Potential Mediator

Vanessa Babineau, PhD®, Yaneve N. Fonge, MD®, Emily S. Miller, MD, MPH, William A. Grobman, MD, MBA, Pamela L. Ferguson, PhD®, Kelly J. Hunt, PhD®, John E. Vena, PhD, Roger B. Newman, MD, Constance Guille, MD, MSCR, Alan T.N. Tita, MD, PhD, Paula C. Chandler-Laney, PhD®, Seonjoo Lee, PhD®, Tianshu Feng, MS, Pamela Scorza, ScD, MPH®, Lea Takács, PhD®, Ronald J. Wapner, MD, Kristy T. Palomares, MD, PhD, Daniel W. Skupski, MD, Michael P. Nageotte, MD, Anthony C. Sciscione, DO, Stephen Gilman, ScD®, Catherine Monk, PhD®



# Maternal Depression and Stress Are Associated with Children's Neurodevelopmental Outcomes

	Prenatal Stress	Prenatal Stress ≥85 <sup>th</sup> (n=108)	Prenatal Depression	Prenatal Depression ≥10 (n=50)
Executive functions	ns	ns	ns	<ul> <li>Cognitive flexibility deficits</li> <li>Inhibitory control/sustained attention deficits in males†</li> </ul>
Motor skills	ns	ns	- Strength deficits	- Strength deficits in males <sup>†</sup>
Psychiatric problems	<ul> <li>Attention problems</li> <li>Oppositional defiant†</li> <li>Conduct problems</li> <li>Depression</li> </ul>	<ul><li>Attention problems</li><li>Oppositional defiant</li><li>Conduct problems</li><li>Depression</li></ul>	<ul><li>Attention problems</li><li>Depression</li></ul>	<ul><li>Attention problems</li><li>Oppositional defiant</li></ul>

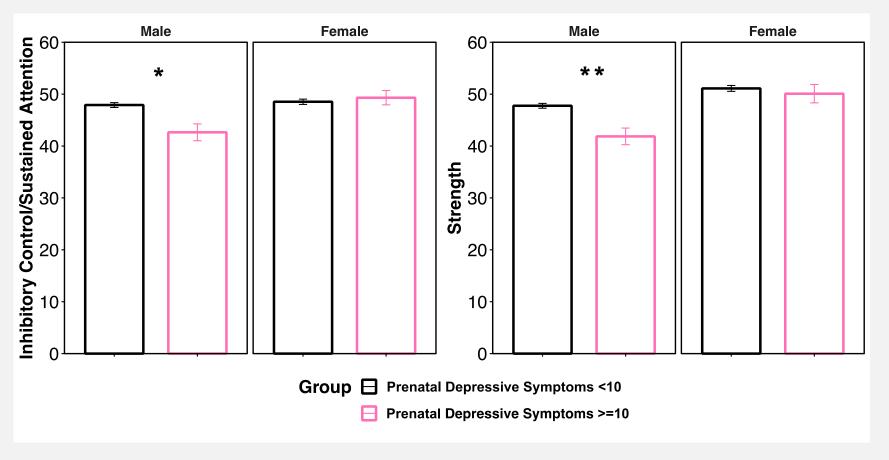
**Notes:** Models adjusted with covariates maternal age, pre-gravid body mass index, education background, income adjusted for household family size, prenatal social support, maternal stress and depressive symptoms at time of child neurobehavioral assessment, fetal exposure to secondhand smoke, biological sex, maternal self-reported race/ethnicity, mode of delivery, and gestational age at birth.

†Remained significant after multiple comparison correction





# Maternal Depression and Stress Are Associated with Children's Neurodevelopmental Outcomes: Sexually Dimorphic Findings



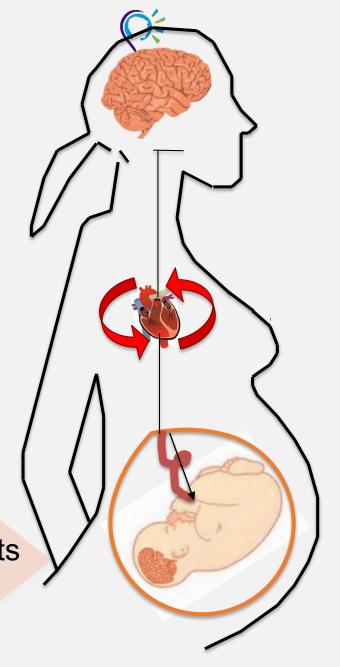
*Note*: Maternal prenatal depressive symptoms measured on *EPDS*. \*\*p<0.01, \*p<0.05





### Maternal Prenatal Distress

Prenatal distress predicts
Postnatal environment



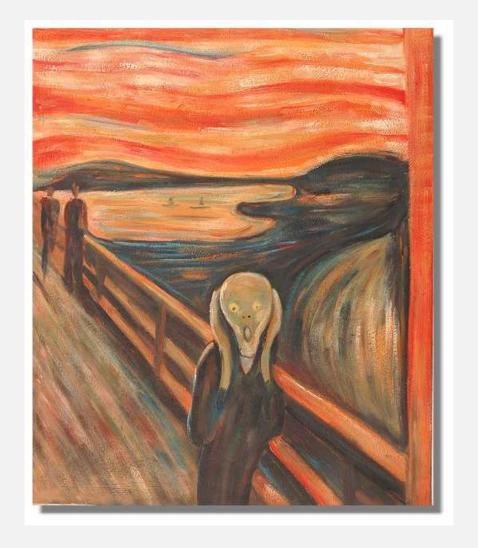
Child Risk for Psychopathology

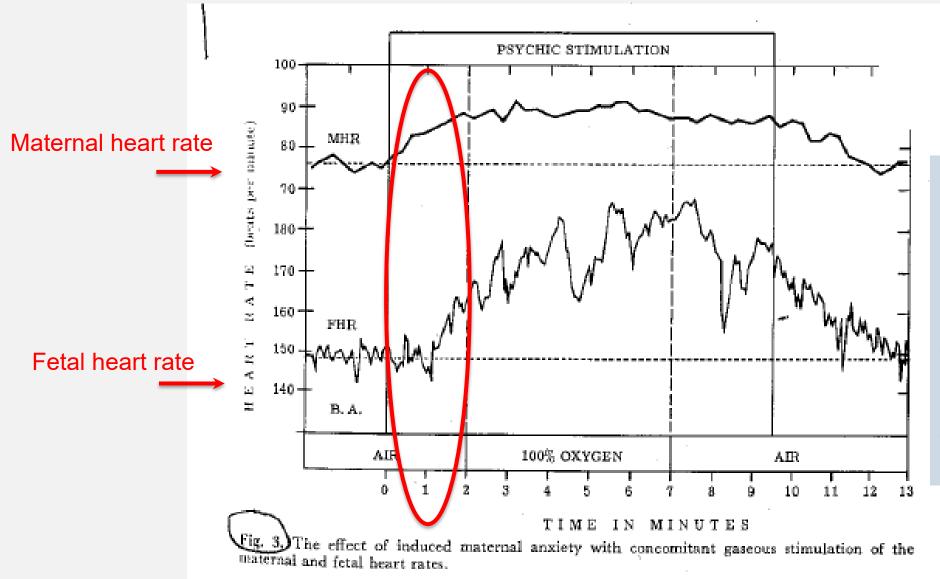
### How to ask the fetus questions...



### In one study from 1967....

"the patient was told that she was breathing a gas which contained only half the amount of oxygen necessary to support fetal life, but that her normal body mechanisms would probably compensate for this altered environmental condition" (Copher & Huber, 1967)



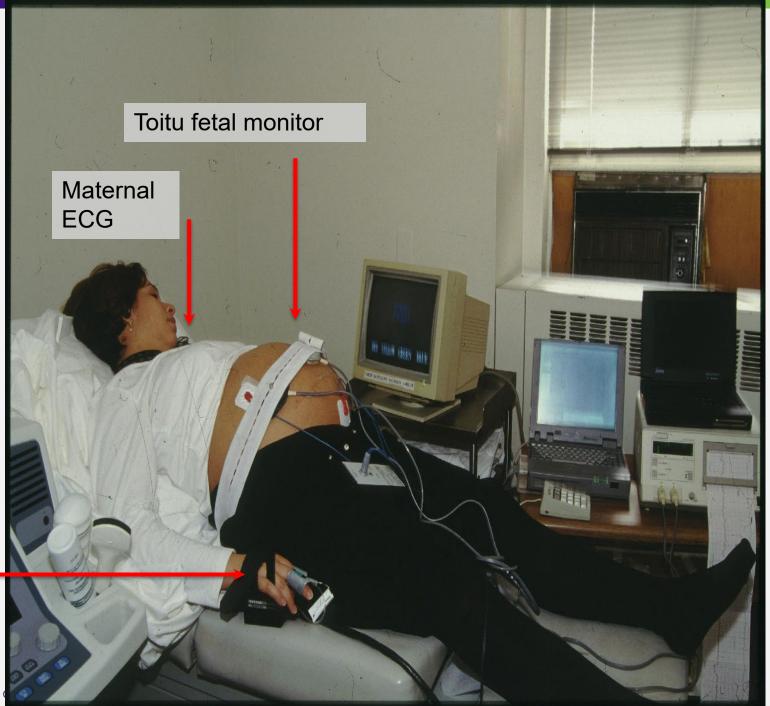


Fetus registers mother's *acute* emotional experience

Implication: fetus may be shaped over gestation based on exposure to *chronic* maternal affect dysregulation

NEW YORK STATE Mental Health

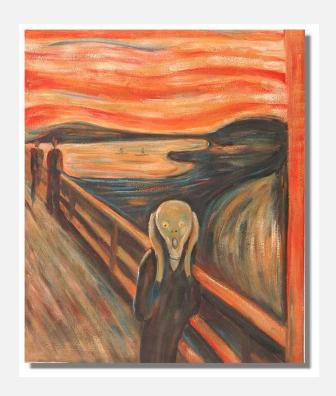
3<sup>rd</sup> trimester fetus



**Blood** pressure

### IRB Sanctioned Approach to Eliciting Stress in the Lab

- Elicit maternal stress in the laboratory
- Observe transmission to the fetus via fetus registering experience and showing a change in fetal heart rate
- Stressor
- Stroop color word matching task
- NADA

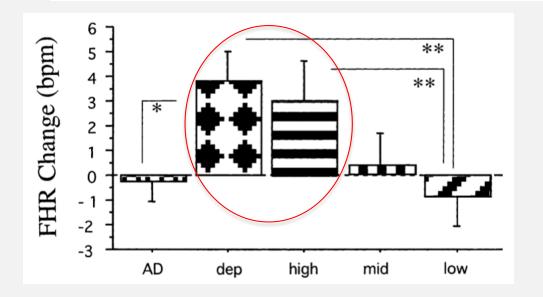




### Fetal Heart Rate Reactivity Differs by Women's Psychiatric Status: An Early Marker for Developmental Risk?

CATHERINE MONK, Ph.D., RICHARD P. SLOAN, Ph.D., MICHAEL M. MYERS, Ph.D., LAUREN ELLMAN, B.A., ELIZABETH WERNER, B.A., JIYEON JEON, B.A., FELICE TAGER, Ph.D., AND WILLIAM P. FIFER, Ph.D.

J. AM. ACAD. CHILD ADOLESC. PSYCHIATRY, 43:3, MARCH 2004



No baseline differences fetal heart rate

No differences in maternal responses to lab stressor

As if a door suddenly opens...











www.nature.com/tp

#### **ORIGINAL ARTICLE**

### Alterations in amygdala-prefrontal circuits in infants exposed to prenatal maternal depression

J Posner<sup>1,2,5</sup>, J Cha<sup>1,2,5</sup>, AK Roy<sup>3</sup>, BS Peterson<sup>4</sup>, R Bansal<sup>4</sup>, HC Gustafsson<sup>1</sup>, E Raffanello<sup>2</sup>, J Gingrich<sup>1,2</sup> and C Monk<sup>1,2</sup>







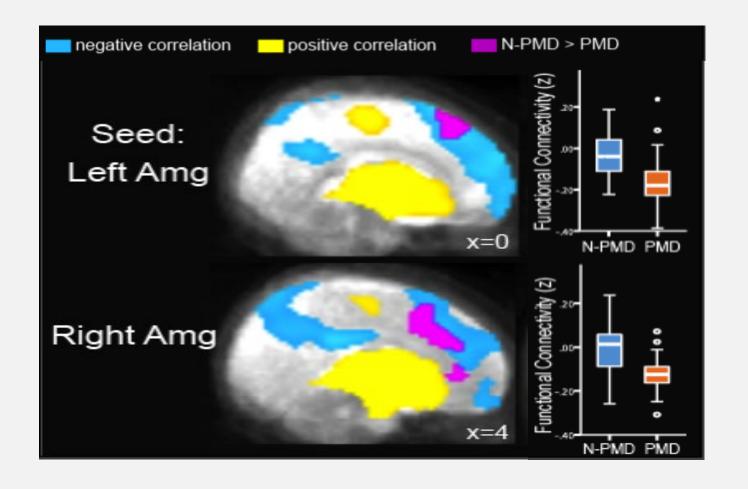




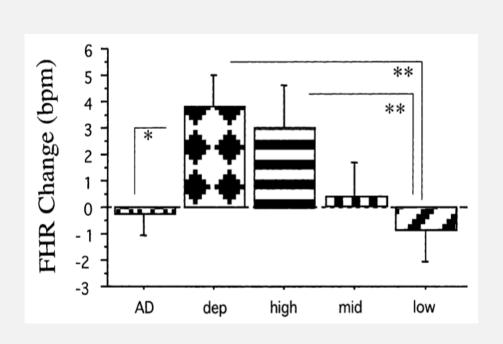


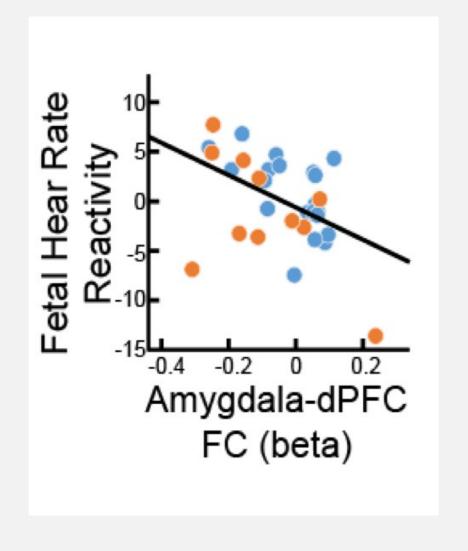
Jiook Cha, Jonathan Posner, Jay Gingrich

# fMRI Results: Newborns Exposed to Untreated Maternal Depression versus No Depression Have Less Connectivity between the Prefrontal Cortex and the Amygdala – a More Reactive Brain



# Fetal Heart Rate Reactivity is Associated with Infants' Brain Connectivity





# Fetal Heart Rate Reactivity is Associated with Infant Behavior

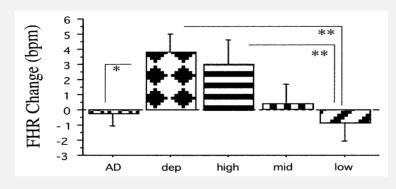


# Elizabeth A. Werner Michael M. Myers William P. Fifer Bin Cheng Yixin Fang Rhiannon Allen Catherine Monk

Department of Psychiatry Behavioral Medicine Program Columbia University Medical Center 1150 St Nicholas Avenue Suite 1–121 New York, NY 10032 E-mail: cem31@columbia.edu

### Prenatal Predictors of Infant Temperament

ABSTRACT: Emerging data suggest that prenatal factors influence children's temperament. In 50 dyads, we examined fetal heart rate (FHR) activity and women's antenatal psychiatric illness as predictors of infant temperament at 4 months (response to novelty and the Infant Behavior Checklist). FHR change during maternal challenge was positively associated with observed infant motor reactivity to novelty (p = .02). The odds of being classified as high versus low motor among fetuses who had an increase in FHR during maternal stress was 11 times those who had a decrease in FHR (p = .0006). Antenatal psychiatric diagnosis was





Elizabeth Werner

#### Early Childhood Predictors of Adult Anxiety Disorders

Jerome Kagan and Nancy Snidman

From Harvard University, Cambridge, Massachusetts.

Address reprint requests to: Jerome Kagan, Department of Psychology, Harvard University, 33 Kirkland Street, Cambridge, MA 02138.

Received February 5, 1999; revised May 3, 1999; accepted May 4, 1999.

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REPORTS

### Inhibited and Uninhibited Infants "Grown Up": Adult Amygdalar Response to Novelty

Carl E. Schwartz, 1,2,3\* Christopher I. Wright, 2,3,4 Lisa M. Shin, 2,5

Jerome Kagan, 6 Scott L. Rauch 2,3

20 JUNE 2003 VOL 300 SCIENCE www.sciencemag.org





#### **ARTICLES**

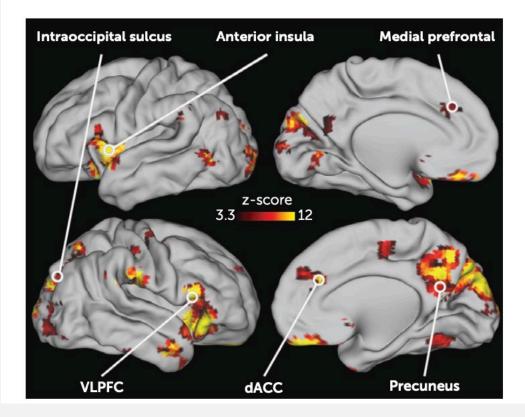
### Neonatal Brain Response to Deviant Auditory Stimuli and Relation to Maternal Trait Anxiety

Chad M. Sylvester, M.D., Ph.D., Michael J. Myers, B.A., Michael T. Perino, Ph.D., Sydney Kaplan, B.S., Jeanette K. Kenley, B.S., Tara A. Smyser, M.S., Barbara B. Warner, M.D., Deanna M. Barch, Ph.D., Daniel S. Pine, M.D., Joan L. Luby, M.D., Cynthia E. Rogers, M.D., Christopher D. Smyser, M.D.

AJP, August '21



FIGURE 3. Brain areas in which neonatal neural activity following onset of deviant sounds varied depending on maternal trait anxiety<sup>a</sup>



**Results:** Neonates manifested a robust and widespread neural response to deviant stimuli that resembles patterns found previously in adults. Higher maternal trait anxiety was related to higher responses within multiple brain regions, including the left and right anterior insula, the ventrolateral prefrontal cortex, and multiple areas within the anterior cingulate cortex. These areas overlap with brain regions previously linked to anxiety disorders and other psychiatric illnesses in adults.

**Conclusions:** The neural architecture sensitive to deviant stimuli robustly functions in newborns. Excessive responsiveness of some circuitry components at birth may signal risk for anxiety and other psychiatric disorders.

### **Maternal Mental Health & Prenatal Programming**

- Prenatal maternal distress associated with greater reactivity to environment
- Evolutionary perspective
- Prenatal distress exposure 'forecasts' an adverse (dangerous) environment
- Heightened reactivity
- Adaptive: prepared for (challenging) postnatal environment to come
- Consequences for the child:
   Match or mismatch with environment
   ADHD, anxiety

### **III. Mechanisms**







#### Annual Review of Clinical Psychology

Prenatal Developmental Origins of Future Psychopathology: Mechanisms and Pathways

Catherine Monk, 1,2,3 Claudia Lugo-Candelas, 1,3 and Caroline Trumpff<sup>1,3</sup>

Department of Psychiatry, Columbia University, New York, NY 10032, USA; email: cem31@cumc.columbia.edu

<sup>2</sup>Department of Obstetrics and Gynecology, Columbia University, New York, NY 10032,

3 New York State Psychiatric Institute, New York, NY 10032, USA; email: Claudia.Lugo@nyspi.columbia.edu, Caroline.Trumpff@nyspi.columbia.edu

Annu. Rev. Clin. Psychol. 2019. 15:16.1-16.28

The Annual Review of Clinical Psychology is online at clinpsy.annualreviews.org

https://doi.org/10.1146/annurev-clinpsy-050718-

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#### Keywords

prenatal stress, DOHaD, brain development, depression, placenta

The developmental origins of health and disease hypothesis applied to neurodevelopmental outcomes asserts that the fetal origins of future development are relevant to mental health. There is a third pathway for the familial inheritance of risk for psychiatric illness beyond shared genes and the quality of parental care: the impact of pregnant women's distress-defined broadly to include perceived stress, life events, depression, and anxiety-on fetal and infant brain-behavior development. We discuss epidemiological and observational clinical data demonstrating that maternal distress is associated with children's increased risk for psychopathology: For example, high maternal anxiety is associated with a twofold increase in the risk of probable mental disorder in children. We review several biological systems hypothesized to be mechanisms by which maternal distress affects fetal and child brain and behavior development, as well as the clinical implications of studies of the developmental origins of health and disease that focus on maternal distress. Development and parenting begin before birth.



#### **Cortisol/HPA Axis**

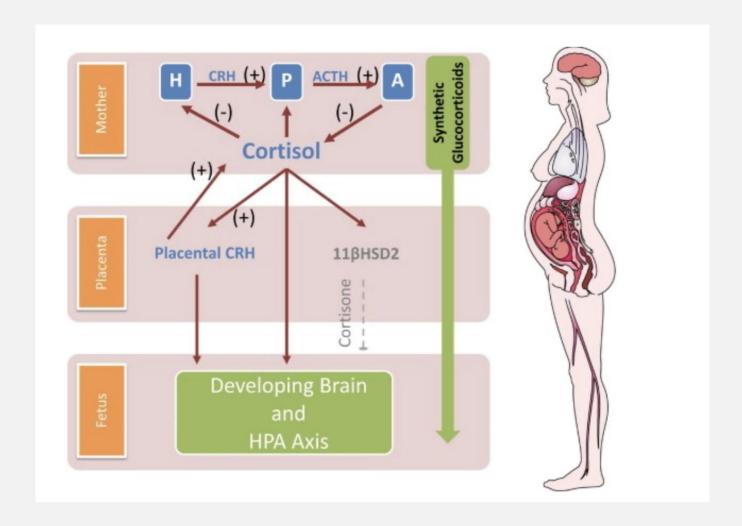
Major effector of stress response system

Prenatal cortisol exposure influences development

- Hyperactivity in the amygdala
- Neuronal migration, neurotransmitter activity, synaptic plasticity
- Alters set point of stress hormone regulation
- Heightened anxiety behaviors in the offspring (Seckl & Holmes, 2007)

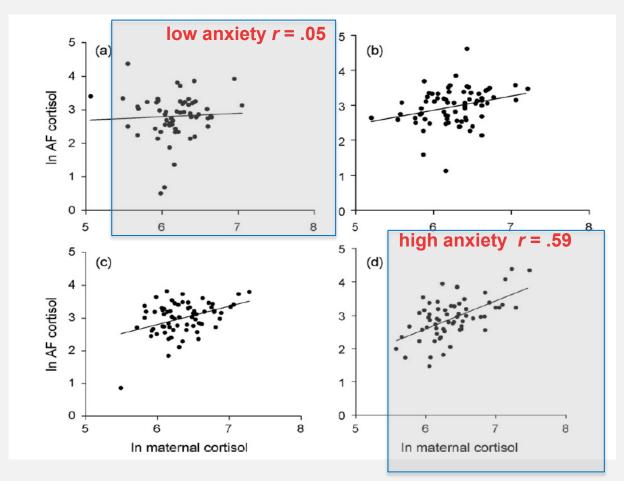
### **Cortisol during Pregnancy**

 Placenta enzyme 11BHSD2 inactivates cortisol to cortisone



### Maternal Anxiety Moderates the Association between Maternal Plasma & Amniotic Fluid Cortisol

Glover, V. et al., 2009, Psychoneuroendocrinology



# Distress During Pregnancy: Epigenetic Regulation of Placenta Glucocorticoid-Related Genes and Fetal Neurobehavior

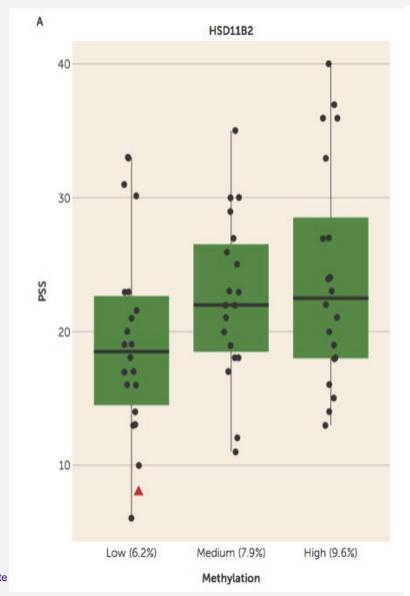
Catherine Monk, Ph.D., Tianshu Feng, M.S., Seonjoo Lee, Ph.D., Izabela Krupska, M.A., Frances A. Champagne, Ph.D., Benjamin Tycko, M.D., Ph.D.

Am J Psychiatry 00:0, ■ 2016



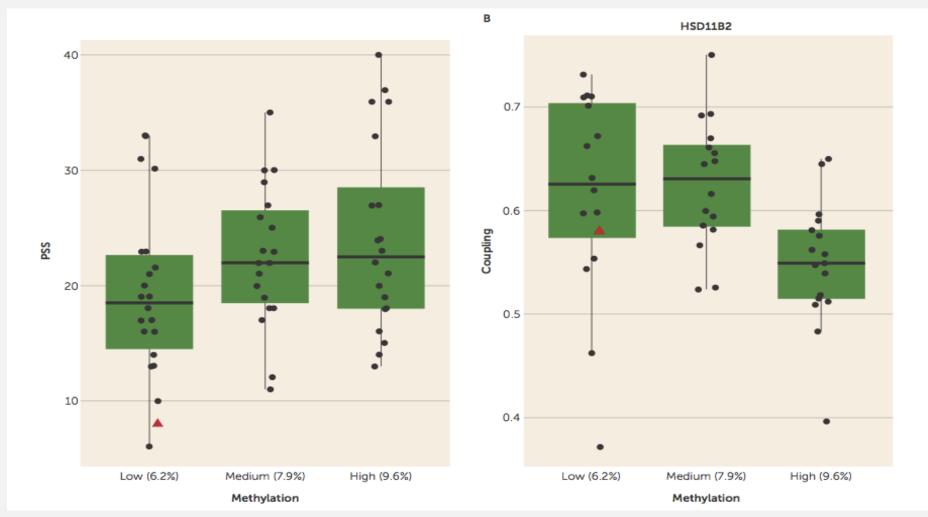


## Maternal Prenatal Stress is Associated with Greater Placenta HSD11B2 Gene Methylation





# **Greater HSD11B2 Gene Methylation** is Associated with Less Fetal Coupling

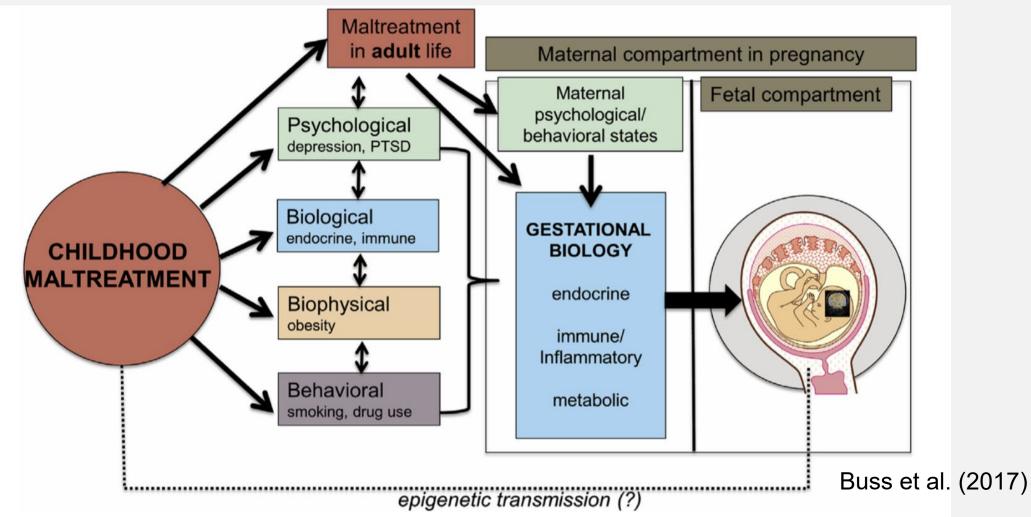


Fetal coupling: **CNS** development, Integration of ANS + somatic systems; associated with more rapid brainstem auditory evoked responses at birth

### IV. Inter-Generational & Health Disparities Lenses: An In-Utero Frame is Too Narrow



# Inter-Generational Transmission of Risk – Gestational Biology Transmission





#### ORIGINAL ARTICLE

BIPOLAR DISORDERS WILEY

Pregnant women with bipolar disorder who have a history of childhood maltreatment: Intergenerational effects of trauma on fetal neurodevelopment and birth outcomes

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Vanessa Babineau<sup>1</sup> | Clare A. McCormack<sup>2</sup> | Tianshu Feng<sup>3</sup> | Seonjoo Lee<sup>4,5</sup> |
Obianuju Berry<sup>6</sup> | Bettina T. Knight<sup>7</sup> | Jeffrey D. Newport<sup>8</sup> | Zachary N. Stowe<sup>9</sup> |
Catherine Monk<sup>10</sup>
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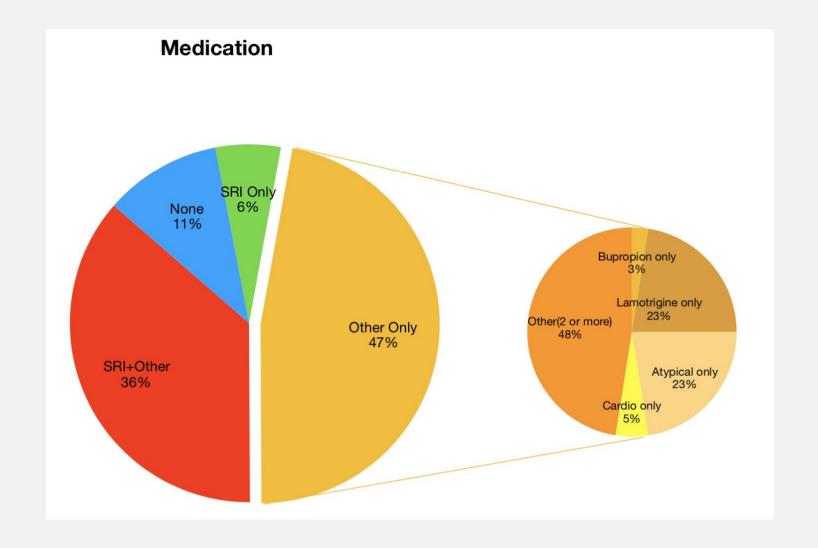


Vanessa Babineau, Zach Stowe, Jeff Newport

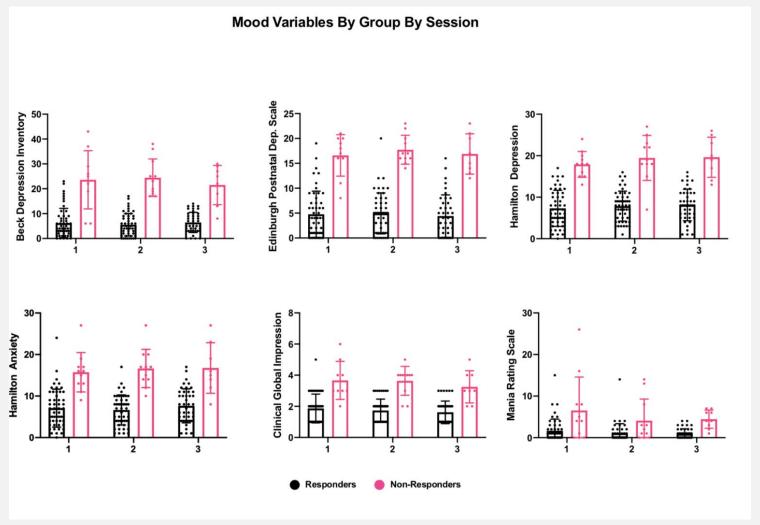
#### **Methods**

- Diagnosed Bipolar Disorder, ages 18-45
   2% prevalence rate
- Psychiatric care; psychopharm and support
- Mood depression, anxiety, mania clinician and patient ratings
   x3 pregnancy

### **Medications**



# Responders & Non-Responders By Mood (no differences on medications)





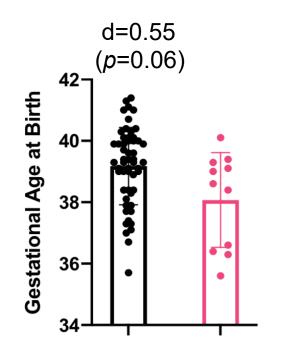
### Responders & Non-Responders **Well-Resourced Sample**

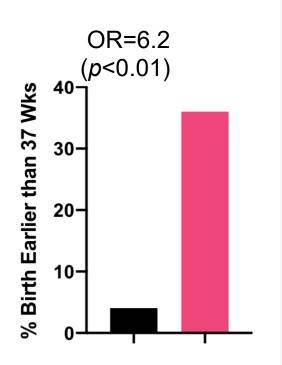
		Total Sample (n=82)		Responders (n=67)		Ion-Responders (n=15)	Group Differences		
	n	Mean (SD) or %	n	Mean (SD) or %	n	Mean (SD) or %	p -value <sup>a</sup>		
Race							0.014		
White	66	80.5%	58	86.6%	8	53.3%			
Black	8	9.8%	5	7.5%	3	20%			
Othe	r 8	9.8%	4	6%	4	26.7%			
Ethinicity Hispanic	2	2.4%	2	3%	0	0%	1		
Mother's age	86	32.4 (4.6)	67	32.6 (4.6)	15	31.8 (5.2)	0.64		
Mother's years of education	n 86	15.4 (2.2)	67	15.7 (2.2)	15	14.5 (2)	0.059		
Marital Status Married	60	73.2%	51	76.1%	9	60.00%	0.213		
Gravidity	86	2.7 (1.7)	67	2.5 (1.5)	15	3.3 (2.1)	0.194		
Parity	86	0.8 (1.2)	67	0.8 (1.1)	15	0.9 (0.8)	0.373		
Hollingshead	86	45.1 (11.8)	67	46.2 (10.6)	15	40.9 (15.7)	0.287		
Baby Sex Male	45	55.6%	37	56.1%	8	53.3%	1		
Planned Pregnancy Yes	54	67%	48	73%	6	40%	0.031		
Desired Pregnancy							0.001		
N	0 2	2.5%	1	1.5%	1	6.7%			
Ye	s 60	75%	54	83.1%	6	40%			
office of Mental Health Ambivaler	nt 18	22.5%	10	15.4%	8	53.3%	55		



### Fetuses of Non-Responder Women are Born Earlier







Red: Depressed, Non

Responder

Black: Euthymic, Responder

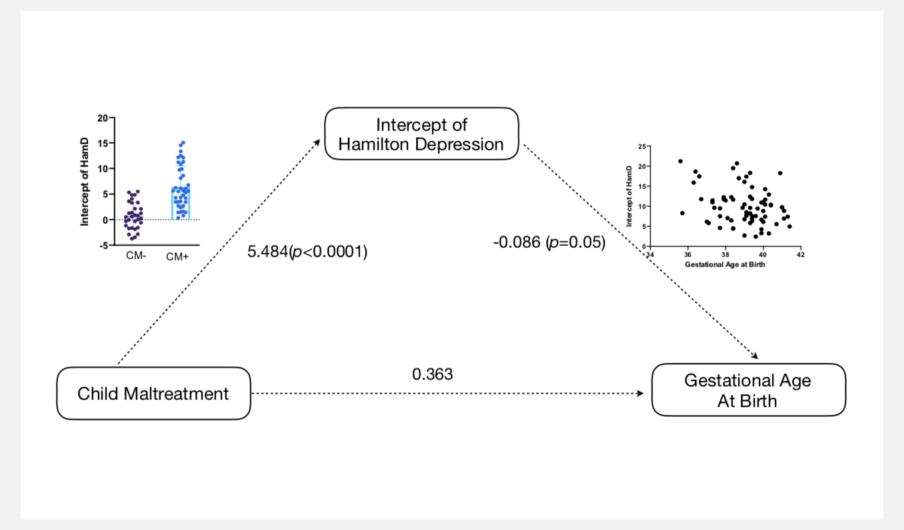


### Responders & Non-Responders Differ by Maternal Childhood Maltreatment

(n=82)         (n=67)         (n=15)         Difference           n         Mean (SD) or %         n         Mean (SD) or %         n         Mean (SD) or %         p-value <sup>a</sup> CTQ Physical Abuse         86         7.2 (3.4)         67         6.8 (2.9)         15         9.3 (4.7)         0.006           CTQ Physical Neglect         86         7.1 (3.1)         67         6.6 (2.5)         15         8.6 (4.2)         0.003           CTQ Sexual Abuse         86         7.0 (4.2)         67         6.3 (3)         15         9.5 (6.5)         0.015           CTQ Emotional Abuse         86         10.7 (4.8)         67         10.1 (4.8)         15         13.3 (4)         0.009           CTQ Emotional Neglect         86         10.8 (5.0)         67         10.2 (4.7)         15         13 (5.3)         0.066           CTQ Denial         86         0.4 (0.8)         67         0.4 (0.9)         15         0.1 (0.4)         0.3									/	
n Mean (SD) or% n Mean (SD) or% n Mean (SD) or% p-value CTQ Physical Abuse 86 7.2 (3.4) 67 6.8 (2.9) 15 9.3 (4.7) 0.006 CTQ Physical Neglect 86 7.1 (3.1) 67 6.6 (2.5) 15 8.6 (4.2) 0.003 CTQ Sexual Abuse 86 7.0 (4.2) 67 6.3 (3) 15 9.5 (6.5) 0.015 CTQ Emotional Abuse 86 10.7 (4.8) 67 10.1 (4.8) 15 13.3 (4) 0.009 CTQ Emotional Neglect 86 10.8 (5.0) 67 10.2 (4.7) 15 13 (5.3) 0.066 CTQ Denial 86 0.4 (0.8) 67 0.4 (0.9) 15 0.1 (0.4) 0.3			Total Sample		Responders	N	Non-Responders	/	Group	\
CTQ Physical Abuse         86         7.2 (3.4)         67         6.8 (2.9)         15         9.3 (4.7)         0.006           CTQ Physical Neglect         86         7.1 (3.1)         67         6.6 (2.5)         15         8.6 (4.2)         0.003           CTQ Sexual Abuse         86         7.0 (4.2)         67         6.3 (3)         15         9.5 (6.5)         0.015           CTQ Emotional Abuse         86         10.7 (4.8)         67         10.1 (4.8)         15         13.3 (4)         0.009           CTQ Emotional Neglect         86         10.8 (5.0)         67         10.2 (4.7)         15         13 (5.3)         0.066           CTQ Denial         86         0.4 (0.8)         67         0.4 (0.9)         15         0.1 (0.4)         0.3			(n=82)		(n=67)		(n=15)	þ	ifferenc	es
CTQ Physical Neglect       86       7.1 (3.1)       67       6.6 (2.5)       15       8.6 (4.2)       0.003         CTQ Sexual Abuse       86       7.0 (4.2)       67       6.3 (3)       15       9.5 (6.5)       0.015         CTQ Emotional Abuse       86       10.7 (4.8)       67       10.1 (4.8)       15       13.3 (4)       0.009         CTQ Emotional Neglect       86       10.8 (5.0)       67       10.2 (4.7)       15       13 (5.3)       0.066         CTQ Denial       86       0.4 (0.8)       67       0.4 (0.9)       15       0.1 (0.4)       0.3		n	Mean (SD) or %	n	Mean (SD) or %	n	Mean (SD) or %	p-v	alue <sup>a</sup>	
CTQ Sexual Abuse       86       7.0 (4.2)       67       6.3 (3)       15       9.5 (6.5)       0.015         CTQ Emotional Abuse       86       10.7 (4.8)       67       10.1 (4.8)       15       13.3 (4)       0.009         CTQ Emotional Neglect       86       10.8 (5.0)       67       10.2 (4.7)       15       13 (5.3)       0.066         CTQ Denial       86       0.4 (0.8)       67       0.4 (0.9)       15       0.1 (0.4)       0.3	CTQ Physical Abuse	86	7.2 (3.4)	67	6.8 (2.9)	15	9.3 (4.7)		0.006	
CTQ Emotional Abuse       86       10.7 (4.8)       67       10.1 (4.8)       15       13.3 (4)       0.009         CTQ Emotional Neglect       86       10.8 (5.0)       67       10.2 (4.7)       15       13 (5.3)       0.066         CTQ Denial       86       0.4 (0.8)       67       0.4 (0.9)       15       0.1 (0.4)       0.3	CTQ Physical Neglect	86	7.1 (3.1)	67	6.6 (2.5)	15	8.6 (4.2)		0.003	
CTQ Emotional Neglect 86 10.8 (5.0) 67 10.2 (4.7) 15 13 (5.3) 0.066 CTQ Denial 86 0.4 (0.8) 67 0.4 (0.9) 15 0.1 (0.4) 0.3	CTQ Sexual Abuse	86	7.0 (4.2)	67	6.3 (3)	15	9.5 (6.5)		0.015	
CTQ Denial 86 0.4 (0.8) 67 0.4 (0.9) 15 0.1 (0.4) <b>0.3</b>	CTQ Emotional Abuse	86	10.7 (4.8)	67	10.1 (4.8)	15	13.3 (4)		0.009	
	CTQ Emotional Neglect	86	10.8 (5.0)	67	10.2 (4.7)	15	13 (5.3)		0.066	
Total CTQ score 86 42.9 (15.0) 67 40 (13.8) 15 53.7 (16.3) <.001	CTQ Denial	86	0.4 (0.8)	67	0.4 (0.9)	15	0.1 (0.4)		0.3	
	Total CTQ score	86	42.9 (15.0)	67	40 (13.8)	15	53.7 (16.3)		<.001	
Childhood Maltreatment         41         50%         28         41.8%         13         86.7%         0.003	Childhood Maltreatment	41	50%	28	41.8%	13	86.7%		0.003	

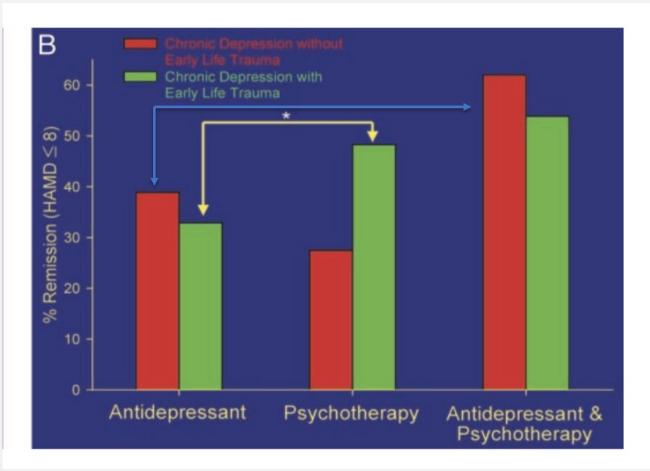
CTQ total score range 5-125, each question rated 1-5.

# Maternal Childhood Maltreatment Affects Next Generation via Maternal Depression (non responders)



# Differential responses to psychotherapy versus pharmacotherapy in patients with chronic forms of major depression and childhood trauma

Charles B. Nemeroff\*<sup>†‡</sup>, Christine M. Heim\*<sup>†</sup>, Michael E. Thase<sup>†‡</sup>, Daniel N. Klein<sup>§</sup>, A. John Rush<sup>†¶</sup>, Alan F. Schatzberg<sup>†</sup>, Philip T. Ninan\*<sup>†</sup>, James P. McCullough, Jr.\*\*, Paul M. Weiss<sup>††</sup>, David L. Dunner<sup>†‡‡</sup>, Barbara O. Rothbaum\*<sup>†</sup>, Susan Kornstein<sup>†§§</sup>, Gabor Keitner<sup>†¶¶</sup>, and Martin B. Keller<sup>†¶¶</sup>





Check for updates

### Maternal prenatal stress phenotypes associate with fetal neurodevelopment and birth outcomes

Kate Walsh<sup>a,b</sup>, Clare A. McCormack<sup>c</sup>, Rachel Webster<sup>d</sup>, Anita Pinto<sup>e</sup>, Seonjoo Lee<sup>f,g</sup>, Tianshu Feng<sup>g</sup>, H. Sloan Krakovsky<sup>d</sup>, Sinclaire M. O'Grady<sup>d</sup>, Benjamin Tycko<sup>h</sup>, Frances A. Champagne<sup>i,j</sup>, Elizabeth A. Werner<sup>d,i</sup>, Grace Liu<sup>i</sup>, and Catherine Monk<sup>d,f,i,1</sup>

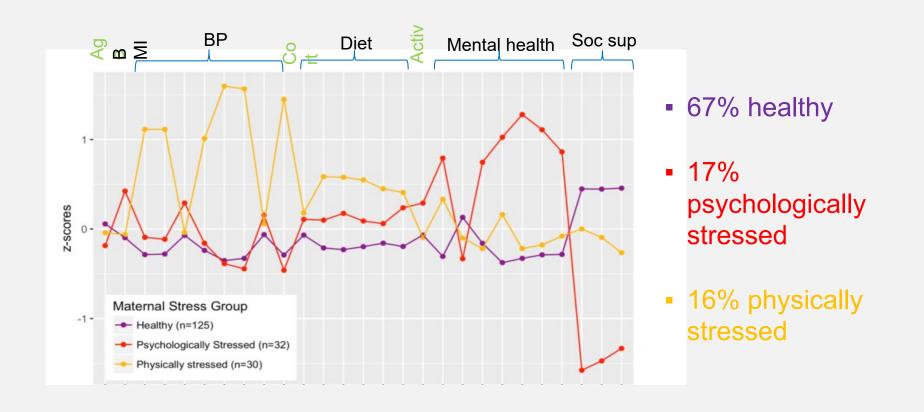
<sup>a</sup>Ferkauf Graduate School of Psychology, Yeshiva University, The Bronx, NY 10461; <sup>b</sup>Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY 10032; Center for Science and Society, Columbia University, New York, NY 10027; Department of Obstetrics and Gynecology, Columbia University Medical Center, New York, NY 10032; Data Science, Columbia University, New York, NY 10027; Division of Behavioral Medicine, New York State Psychiatric Institute, New York, NY 10032; 9Department of Biostatistics (in Psychiatry), Mailman School of Public Health, Columbia University, New York, NY 10032; hackensack-Meridian Health Center for Discovery and Innovation, Nutley, NJ 07110; Department of Psychiatry, Columbia University, New York, NY 10032; and <sup>j</sup>Department of Psychology, University of Texas at Austin, Austin, TX 78712

Edited by Bruce S. McEwen, Rockefeller University, New York, NY, and approved September 18, 2019 (received for review April 16, 2019)



PNAS

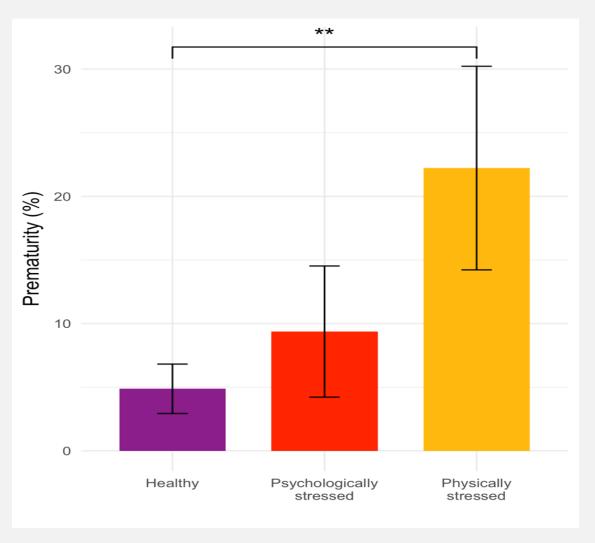
# LPA: Three Different Stress Groups in a Sample of Healthy Pregnant Women



### Health Disparities: Social Demographics & Childhood Maltreatment

- Compared to the healthy group:
  - psychologically stressed group had
    - Higher % Latinas
    - Lower education
    - Lower income
    - Higher % health insurance covered by Medicaid
    - Greater use of WIC
    - Higher % of prior pregnancies and adverse outcomes
  - Psychologically and physically stressed groups had
    - Higher rates of childhood trauma (abuse & neglect)

# Baby Outcomes Prematurity (<= to 37 weeks) by Stress Groups





# Maternal Childhood Maltreatment & Prenatal Programming

- Earlier birth in stress groups with higher rates of maternal childhood trauma
- Pregnancy outcomes responsive to environmental cues related to woman's life and childhood
- Evolutionary perspective, less time in a non-optimal environment
- Yet earlier birth is a significant risk factor for ADHD and other neurodevelopmental problems

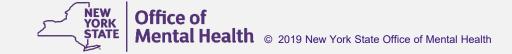
### Many Factors Shape Maternal Mental Health and a Child's Life before Birth

- Maternal childhood trauma
- Maternal untreated depression, anxiety
- Race/ethnicity Including systemic racism in medical care

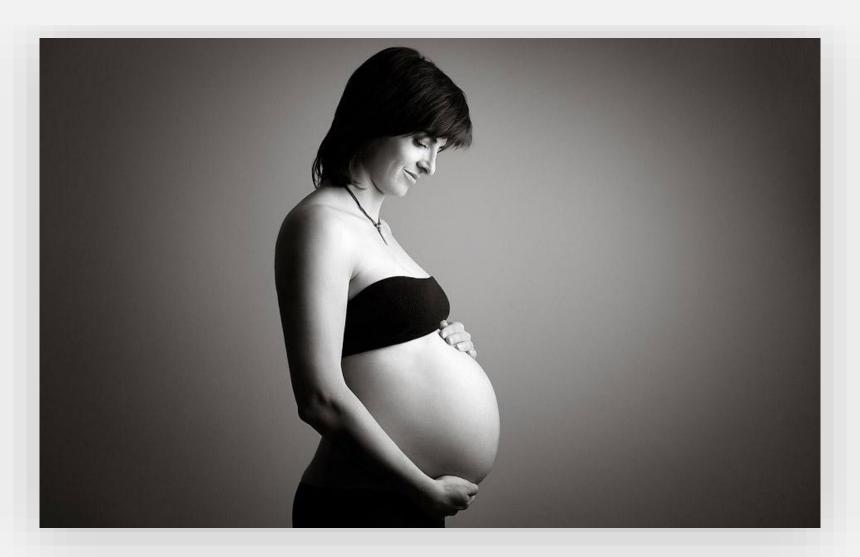
#### BRIEF: MATERNAL AND CHILD HEALTH INEQUITIES EMERGE BEFORE BIRTH

https://stateofbabies.org/MaternalandChildHealthInequitiesBrief

This companion brief to the *State of Babies Yearbook: 2020* addresses serious inequities in maternal health and birth outcomes, when health data are disaggregated and examined by race and ethnicity.



### V. Possible Pandemic Effects



# Birth during the COVID©19 Pandemic, but Not Maternal SARS-CoV-2 Infection in Pregnancy, is Associated with Lower Neurodevelopmental Scores at 6-Months

### @COMBOstudy www.ps.columbia.edu/COMBO









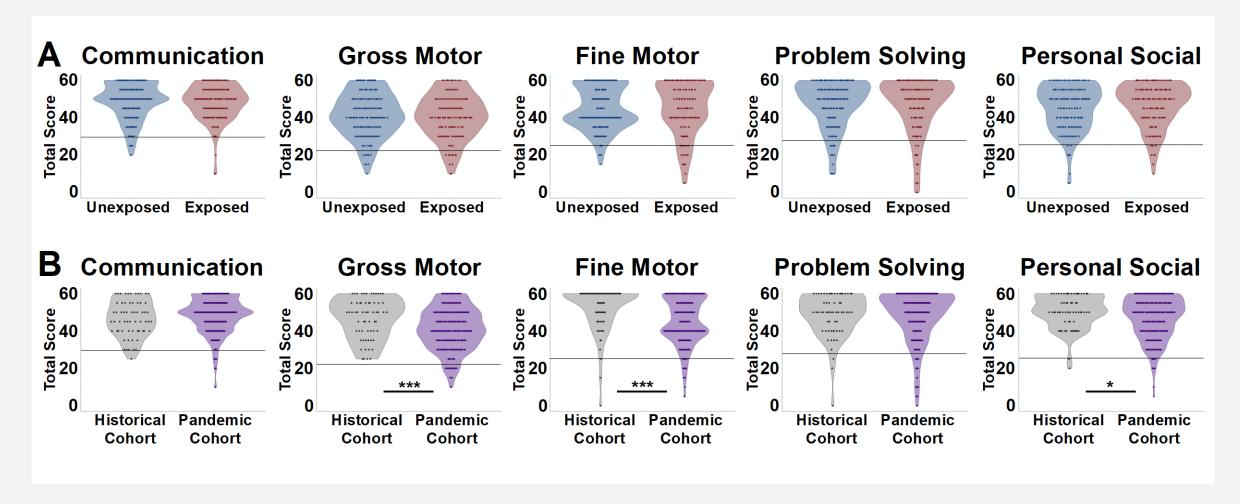
#### JAMA Pediatrics | Original Investigation

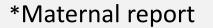
#### Association of Birth During the COVID-19 Pandemic With Neurodevelopmental Status at 6 Months in Infants With and Without In Utero Exposure to Maternal SARS-CoV-2 Infection

Lauren C. Shuffrey, PhD; Morgan R. Firestein, PhD; Margaret H. Kyle, BA; Andrea Fields, MA; Carmela Alcántara, PhD; Dima Amso, PhD; Judy Austin, PhD; Jennifer M. Bain, MD, PhD; Jennifer Barbosa, MA; Mary Bence, BA; Catherine Bianco, BA; Cristina R. Fernández, MD, MPH; Sylvie Goldman, PhD; Cynthia Gyamfi-Bannerman, MD, MS; Violet Hott, BA; Yunzhe Hu, BA; Maha Hussain, MS; Pam Factor-Litvak, PhD; Maristella Lucchini, PhD; Arthur Mandel, MD, PhD; Rachel Marsh, PhD; Danielle McBrian, MD; Mirella Mourad, MD; Rebecca Muhle, MD, PhD; Kimberly G. Noble, MD, PhD; Anna A. Penn, MD, PhD; Cynthia Rodriguez, BA; Ayesha Sania, ScD; Wendy G. Silver, MD, MA; Kally C. O'Reilly, PhD; Melissa Stockwell, MD; Nim Tottenham, PhD; Martha G. Welch, MD; Noelia Zork, MD; William P. Fifer, PhD; Catherine Monk, PhD; Dani Dumitriu, MD, PhD

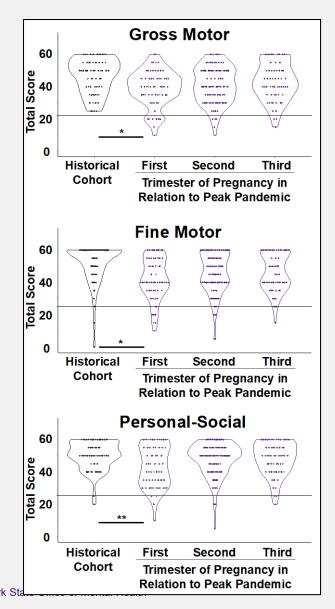


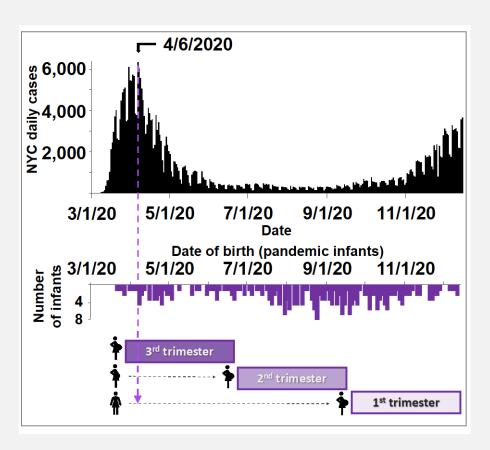
# No Effect of SARS-CoV2, Effects of Perinatal Period during the Pandemic



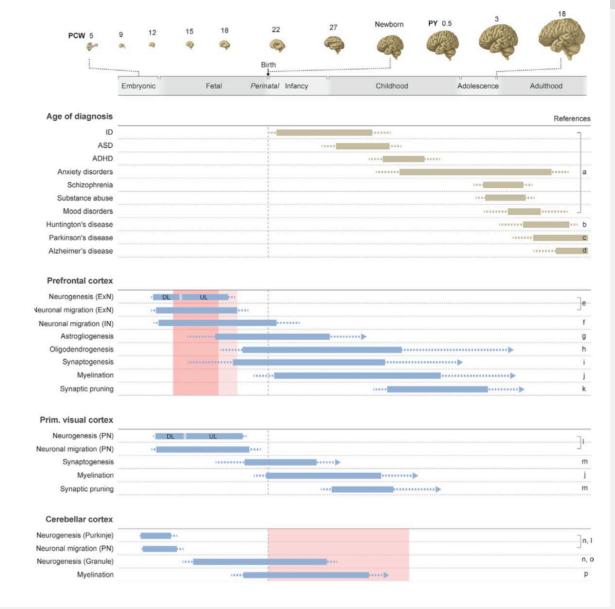


### Pandemic Effects during 1st Trimester?





### When the brain is developing...

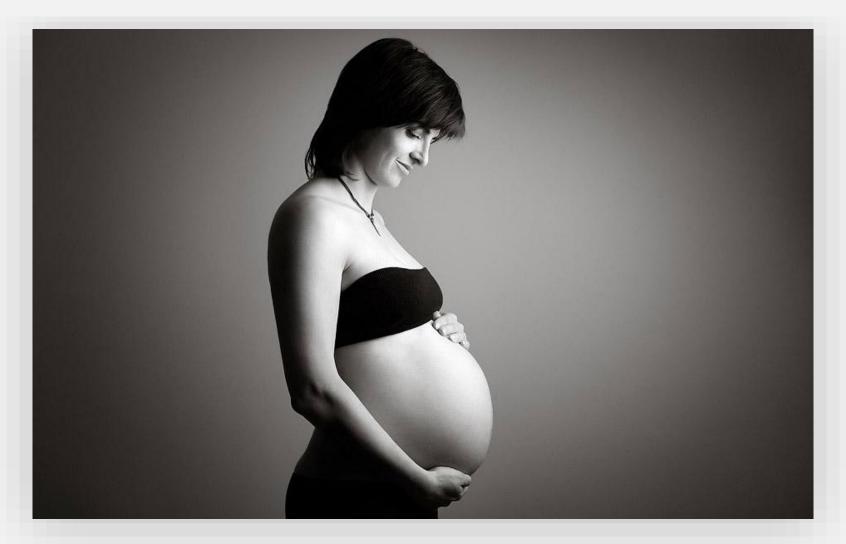




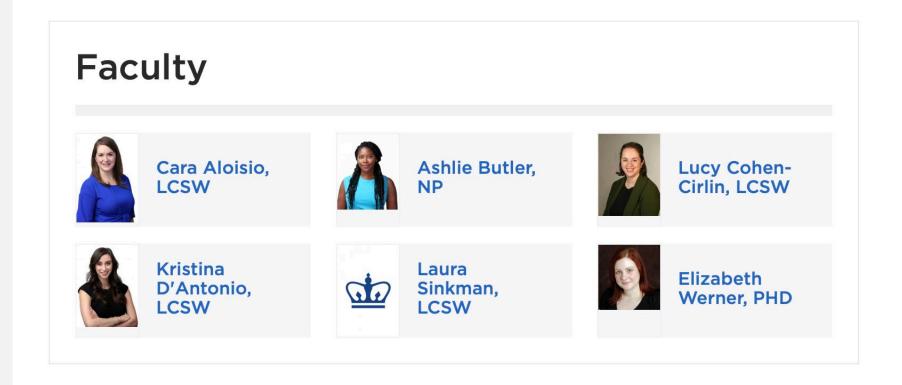
#### **Pandemic Effects**

- Maternal report versus observer based assessment
- Stress during pregnancy?
- Aspects of postnatal environment?
- · Likely can be modified

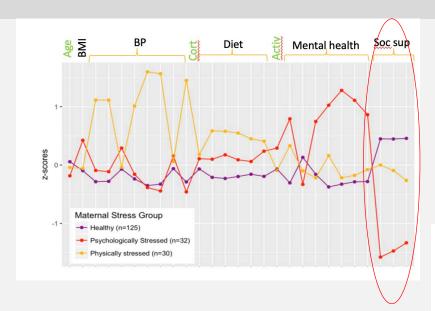
### VI. Implications for Prenatal Care Ecosystem



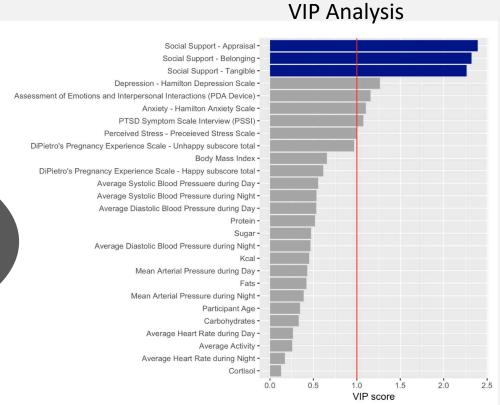
# Women's Mental Health @Ob/Gyn



### Social Support



Target social support in day to day interactions and interventions





### **Transforming Perinatal Care Ecosystem**

#### Planning for daily life

- Doula
- Family support (or no?)
- Sleep
- Physical activity
- Time to decompress

#### Managing expectations

- Loss
- Identity shifts
- Marital relationship decline
- Expecting the unexpected
- Time not one's own

- Intentional reflection on parent want to be
  - How parented affects how you parent

- Co-located mental health care
  - Accessible, affordable

### **Last Thoughts & Future Directions**



- A life course perspective is essential for researching and treating maternal mental health conditions
- A woman's mental health during pregnancy and the postpartum period reflect the life she is living and has lived and the socialeconomic context of her life
- When we treat women's mental health issues and overall wellbeing, we also are helping the next generation



less therapy than the generation before."



### 1<sup>st</sup> MMH Intensive Training

- Monday, May 16, 2022
   4:00pm 7:00pm
- Epidemiology of Perinatal Mood and Anxiety Disorders (PMADs) & Psychiatric Assessment and Diagnosis
- Screening for PMADs and Assessing Suicide Risk
- Non-pharmacologic and Antidepressant Treatments for PMADs (pregnancy and lactation)
- Interactive Case Vignettes

#### Intensive Training includes three, 1-hour follow-up sessions, held on Mondays from 12 pm – 1 pm.

- Unipolar depression: Special dosing considerations during the perinatal period and what to do with antidepressant partial/non-response.
- Advanced Suicide Risk Assessment and Management in Obstetric and Family Medicine Practices
- Role of OBGYNs and PCPs in the assessment and management of bipolar disorder during the perinatal period





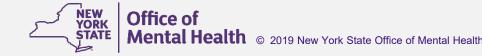


Webinars will be offered live and recorded for posting on the website.

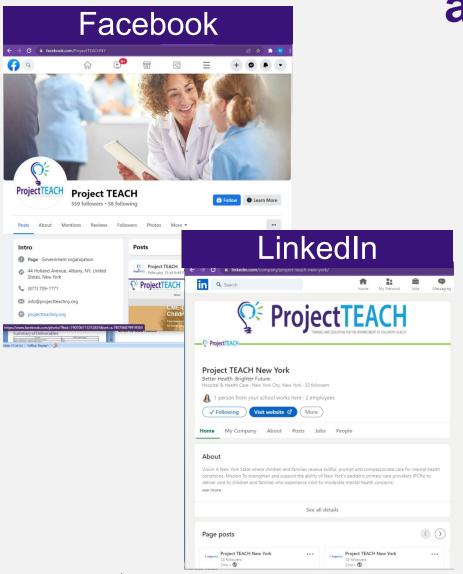
#### Planned webinar topics

- Substance use disorders during the perinatal period
- Perinatal anxiety disorders
- Treatment of ADHD in perinatal patients

- Understanding sleep and treatment of insomnia in perinatal patients
- Transition to parenthood: Transforming obstetrical care to enhance family health
- Intimate partner violence and mental health in the perinatal period



### Stay in touch with us, access resources and register for no-cost CME







### Thank you!

