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Clinical perspective to inform development of large cohorts & public outreach

APrON Alberta Pregnancy Outcomes and Nutrition

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N. Letourneau RN PhD FCAHS

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APrON cohort: community influences and impacts

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APrON
Alberta Pregnancy
Outcomes and Nutrition

APrON Team

Management Team	Legacy Members	Staff & Trainees
N. Letourneau (PI), *University of Calgary* R. Bell, *University of Alberta* D. Dewey, *University of Calgary* C. Field, *University of Alberta* G. Giesbrecht, *University of Calgary* C. Lebel, *University of Calgary* B. Leung, *University of Lethbridge* C. McMorris, *University of Calgary*	B. J. Kaplan F. Bernier M. Cantell L. Casey M. Eliasziw A. Farmer L. Gagnon L. Goonewardene D. Johnston L. Kooistra D. Manca L. McCargar J. Martin M. O'Beirne V. Pop, N. Singhal	A. Deane H. Ntanda J. Novick E. Ali M. Grisbrook & many others

THANK YOU to

- **Our participants: mothers, fathers (& co-parents) and children**
- **APrON Scientific Advisors**
- **All study staff and trainees in Calgary & Edmonton**
- **Funders**

Funders
$19 million since 2009

APrON is a longitudinal pregnancy cohort study

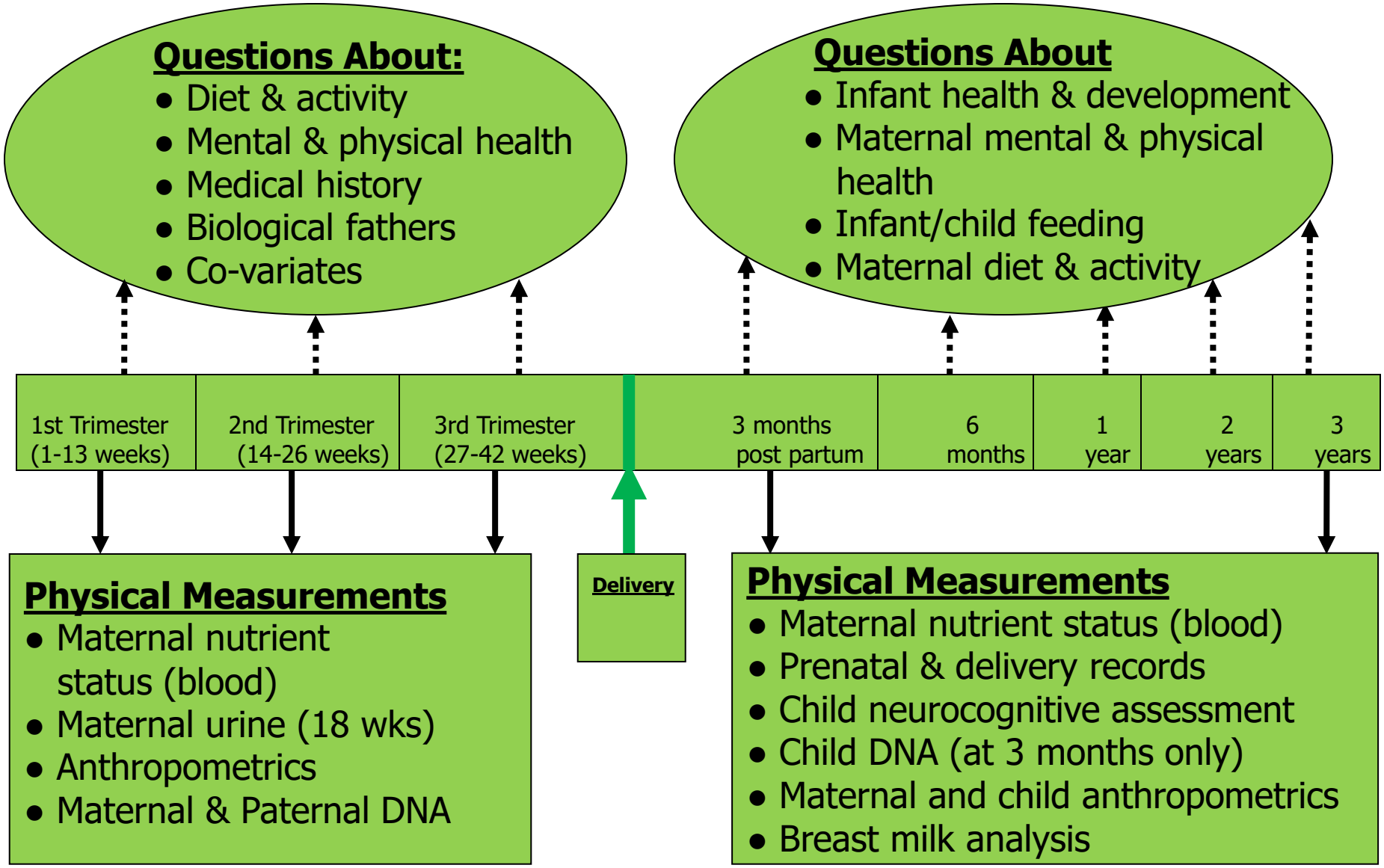
It evolved from 3 health concerns:

- Increasing burden of **mental disorders, especially maternal depression**
- Increasing burden of **neurodevelopmental disorders**
- **Concerns about nutritional impacts** on maternal and child mental health and child neurodevelopment

Target population

- Pregnant women ≥16 years old
- <27 weeks gestation
- Able to complete questionnaires in English
- Not planning to move out of the city within 6 months of recruitment

Measurements



Measures of Development

Birth-2 years

- Infant Behavior Questionnaire-revised (IBQ-R)
- Scales of Independent Behaviour-Revised (SIB-R)
- Brief Rating Inventory of Executive Function (BRIEF)
- Child Behavior Checklist (CBCL)

3-5 years

- BRIEF-Preschool
- CBCL
- Behavior Assess-ment System for Children (BASC) II

Neurocognitive

(2, 3 and/or 5 years, n=600)

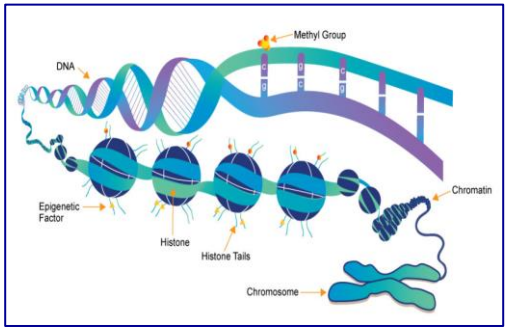
- Bayley II/III
- Weschler Preschool Primary Scale of Intelligence (WPPSI) IV
- NEPSY (Neuropsych Assessment)
- Movement Assessment Battery for Children (MABC) II

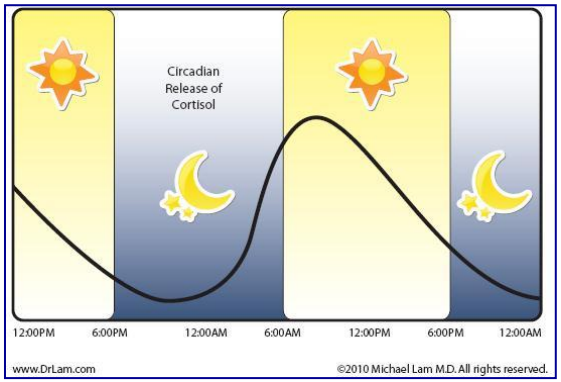
Parenting & Attachment

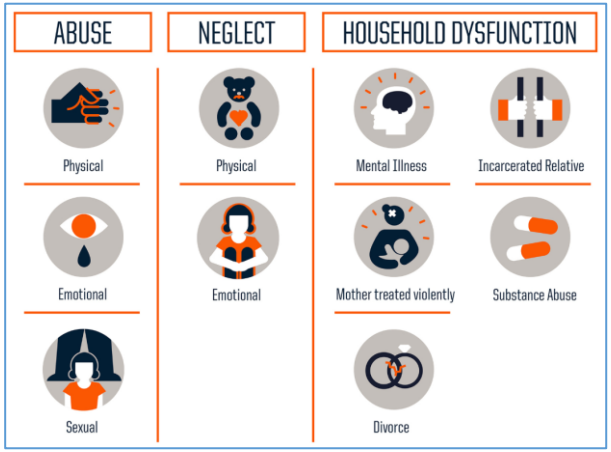
(6 & 18 months and 3-5 years, n=275)

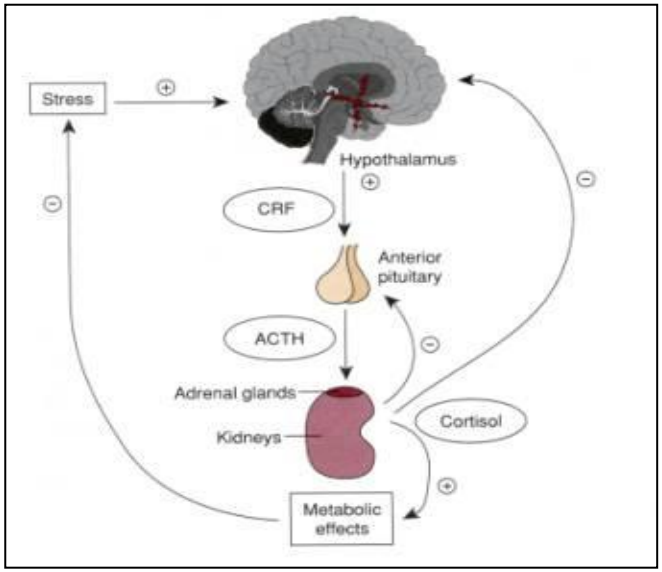
- Parent-child interaction teaching scale
- Infant and Toddler CARE-Index
- Strange Situation Procedure (ABCD, DMM & MAC)
- Parent Development interview and Adult Attachment Interview (n=150)

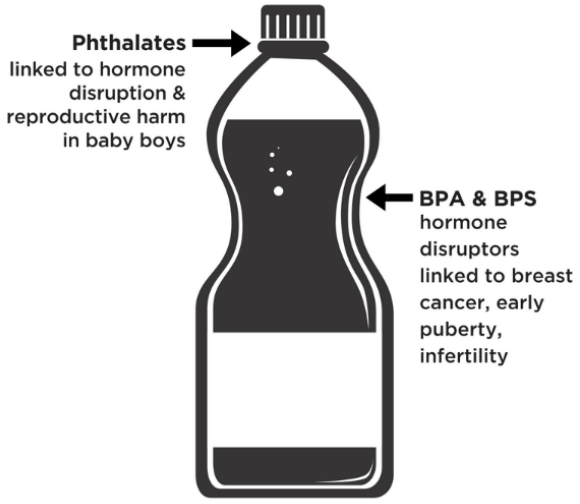
Other Measures











APrON Participants

We have ~2200 mothers, ~1300 fathers and 2225 children enrolled

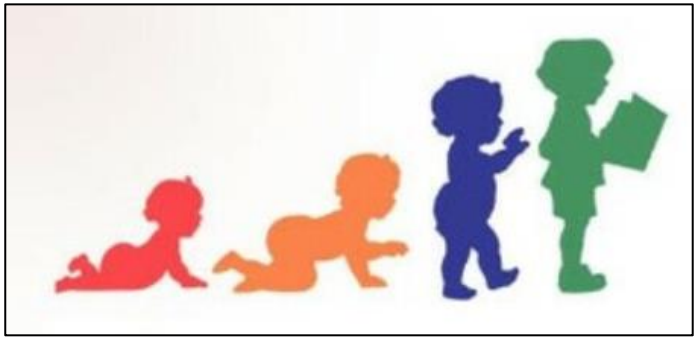
Time point	# sent questionnaires	# received questionnaires	Response Rate
A or B – 1st or 2nd trimester	2189	2124	97.03%
B – 2nd trimester	539	479	88.87%
C – 3rd trimester	2030	1843	90.79%
E – 3 months postnatal	1960	1831	93.42%
F – 6 months postnatal	1930	1538	79.69%

APrON Mothers

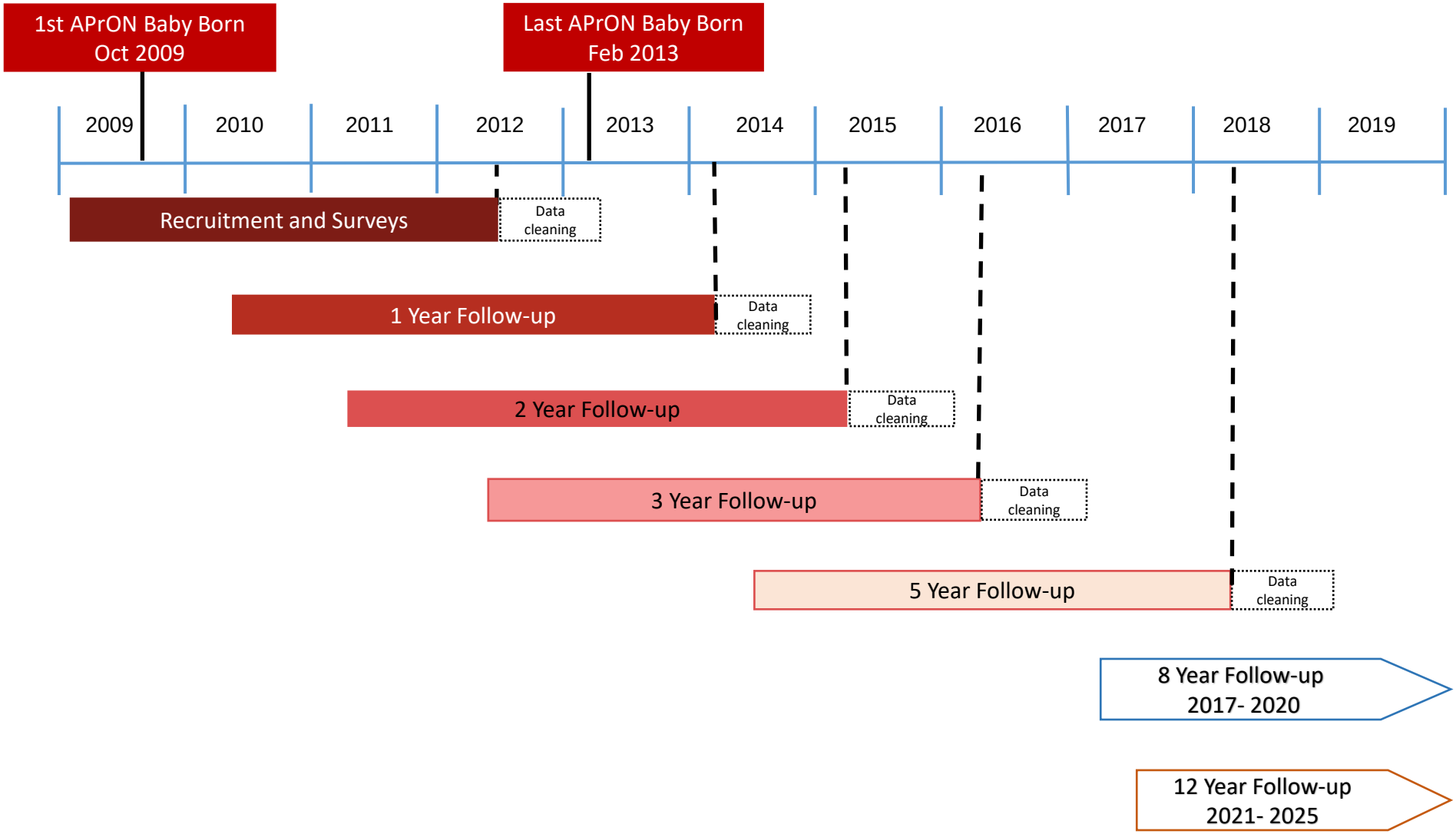
Maternal Characteristics (n)	n (%)
Maternal Age (2143)	Mean (SD) 31.1±4.5
Parity (2103)	Nulliparous 1185 (56.3%) Primiparous 714 (33.9%) Multiparous 204 (9.7%)
Marital Status (2104)	Married 1780 (84.6%) Common-law 240 (11.4%) Single 69 (3.3%) Divorced 8 (0.4%) Separated 7 (0.3%)
Maternal Education (2084)	Less than high school diploma 58 (2.8%) Completed high school diploma 200(9.6%) Completed trade, technical 406(19.5%) Completed University 948 (45.5%) Completed post-grad 472(22.6%)
Ethnicity (2098)	Caucasian 1684 (80.3%) Other 414 (19.7 %)
Family Income (2081)	Less than $20,000 66 (3.2%) $20,000-$39,999 121 (5.8%) $40,000-$69,999 279 (13.4%) $70,000-$99,999 467 (22.4%) $100,000 or more 1148 (55.2%)

APrON Children

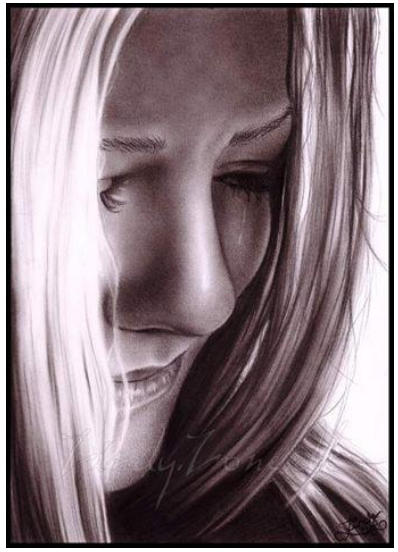
Child Characteristics (n)	Mean (SD) or n (%)
Gestational Age (wk) (2089)	38.8 ± 2.15
Birth weight (kg) (2079)	3.33 ± 0.54
Biological Sex (2090)	Female 980 (46.9%) Male 1110 (53.1%)

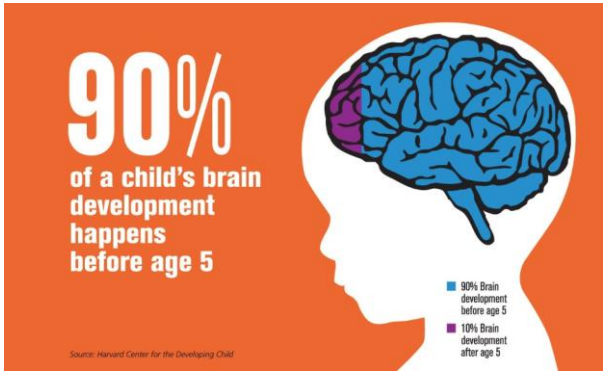


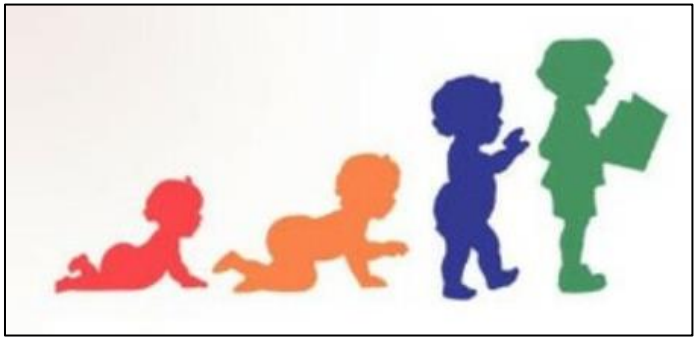
APrON Timeline

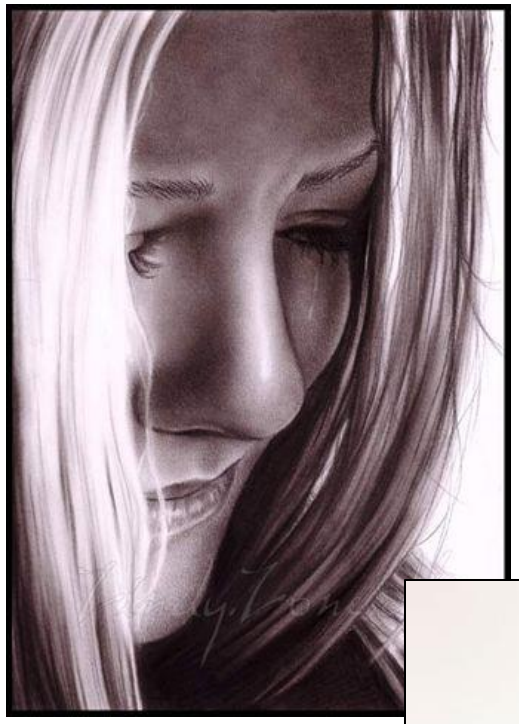


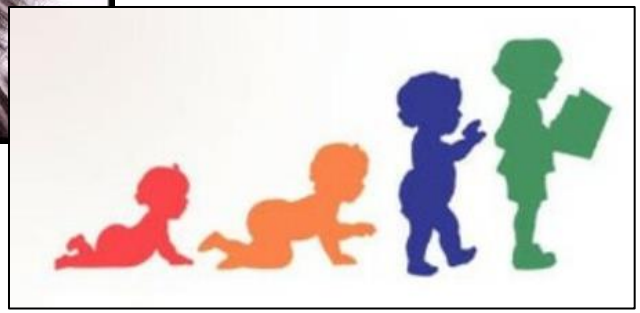
Exemplar APrON Published Findings and Impacts











Letourneau et al. BMC Pediatrics _####################_
https://doi.org/10.1186/s12887-019-1775-1

BMC Pediatrics

RESEARCH ARTICLE Open Access

Maternal and paternal perinatal depressive symptoms associate with 2- and 3-year-old Children's behaviour: findings from the APrON longitudinal study

Nicole Letourneau[1,2*], Brenda Leung[3], Henry Ntanda[4], Deborah Dewey[5], Andrea J. Deane[4], Gerald F. Giesbrecht[6] and The APrON Team

Abstract

Background: Prenatal and postnatal depressive symptoms are common in expectant and new mothers and fathers. This study examined the association between four patterns of probable perinatal depressive symptoms (mother depressed, father depressed, both depressed, neither depressed) in co-parenting mothers and fathers and their children's internalizing and externalizing behaviours at 24 and 36 months of age. The influence of sociodemographic, risk and protective factors was also examined.

Methods: Probable depressive symptoms were measured during pregnancy and at 3 months postpartum and children's behaviour was assessed at 24 and 36 months of age. Families ($n = 634$) provided data on their children's internalizing (i.e. emotionally reactive, anxious/depressed, somatic complaints, withdrawn and total) and externalizing (i.e. attention problems, aggression and total) behaviour. Marginal models were employed to determine the relationship between children's behaviour over the two time points and the four patterns of probable parental depression. Sociodemographic variables as well as risk (stress) and protective (social support) factors were included in these models.

Table 3 Predictors of Children's internalizing behaviours[a]

	Emotionally reactive	Anxious/depressed	Somatic complaints	Withdrawn	Total internalizing
Effect	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate (SE)	Estimate (SE)
Intercept	1.69 (0.15)	0.88 (0.08) $P = < 0.000$	2.28 (0.39) $P = < 0.000$	1.56 (0.31) $P = < 0.000$	4.71 (0.18) ($p < 0.001$)
Groups (ref: Non- Depressed Mothers and Fathers)					
• Depressed Fathers	−0.14 (0.18) $P = 0.378$	−0.10 (0.15) $P = 0.494$	− 0.26 (0.17) $P = 0.134$	−0.21 (0.12) $P = 0.090$	− 0.74 (0.46) ($p = 0.111$)
• Depressed Mothers	0.64 (0.14) $P = < 0.000$	0.28 (0.11) $P = 0.019$	0.30 (0.14) $P = 0.028$	0.09 (0.10) $P = 0.334$	1.47 (0.36) ($p < 0.001$)
• Depressed Mothers and Fathers	0.50 (0.23) $P = 0.031$	0.31 (0.19) $P = 0.108$	0.37 (0.22) $P = 0.088$	0.44 (0.16) $P = 0.005$	1.65 (0.59) ($p = 0.005$)

Table 3 Predictors of Children's internalizing behaviours[a]

	Emotionally reactive	Anxious/depressed	Somatic complaints	Withdrawn	Total internalizing
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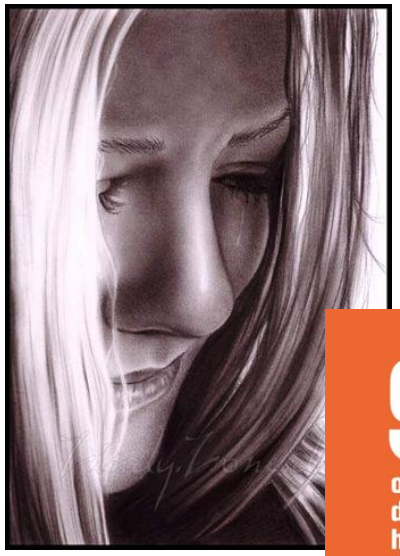
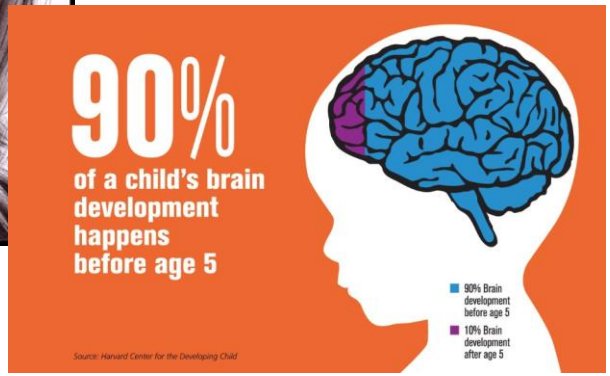
Table 4 Predictors of Children's externalizing behaviours[a]

	Attention problems	Aggressive behaviour	Total externalizing
Effect	Estimate (SE)	Estimate (SE)	Estimate (SE)
Intercept	5.45 (0.81) P = < 0.000	6.62 (0.63) P = < 0.000	8.19 (0.33) P = < 0.000
Groups (ref: Non- Depressed Mothers & Fathers)			
• Depressed Fathers	0.17 (0.21) *P* = 0.413	− 0.34 (0.62) *P* = 0.580	−0.26 (0.76) *P* = 0.736
• Depressed Mothers	0.51 (0.18) P = 0.005	1.52 (0.49) *P* = 0.002	2.20 (0.60) *P* = 0.000
• Depressed Mothers and Fathers	0.13 (0.29) *P* = 0.659	1.13 (0.79) *P* = 0.156	1.41 (0.97) *P* = 0.145




90%
of a child's brain development happens before age 5
90% Brain development before age 5
10% Brain development after age 5
Source: Harvard Center for the Developing Child

Archival Report

Biological Psychiatry

Prepartum and Postpartum Maternal Depressive Symptoms Are Related to Children's Brain Structure in Preschool

Catherine Lebel, Matthew Walton, Nicole Letourneau, Gerald F. Giesbrecht, Bonnie J. Kaplan, and Deborah Dewey

ABSTRACT

BACKGROUND: Perinatal maternal depression is a serious health concern with potential lasting negative consequences for children. Prenatal depression is associated with altered brain gray matter in children, though relations between postpartum depression and children's brains and the role of white matter are unclear.

METHODS: We studied 52 women who provided Edinburgh Postnatal Depression Scale (EPDS) scores during each trimester of pregnancy and at 3 months postpartum and their children who underwent magnetic resonance imaging at age 2.6 to 5.1 years. Associations between maternal depressive symptoms and magnetic resonance imaging measures of cortical thickness and white matter structure in the children were investigated.

RESULTS: Women's second trimester EPDS scores negatively correlated with children's cortical thickness in right inferior frontal and middle temporal regions and with radial and mean diffusivity in white matter emanating from the inferior frontal area. Cortical thickness, but not diffusivity, correlations survived correction for postpartum EPDS. Postpartum EPDS scores negatively correlated with children's right superior frontal cortical thickness and with diffusivity in white matter originating from that region, even after correcting for prenatal EPDS.

CONCLUSIONS: Higher maternal depressive symptoms prenatally and postpartum are associated with altered gray matter structure in children; the observed white matter correlations appear to be uniquely related to the postpartum period. The reduced thickness and diffusivity suggest premature brain development in children exposed to higher maternal perinatal depressive symptoms. These results highlight the importance of ensuring optimal women's mental health throughout the perinatal period, because maternal depressive symptoms appear to increase children's

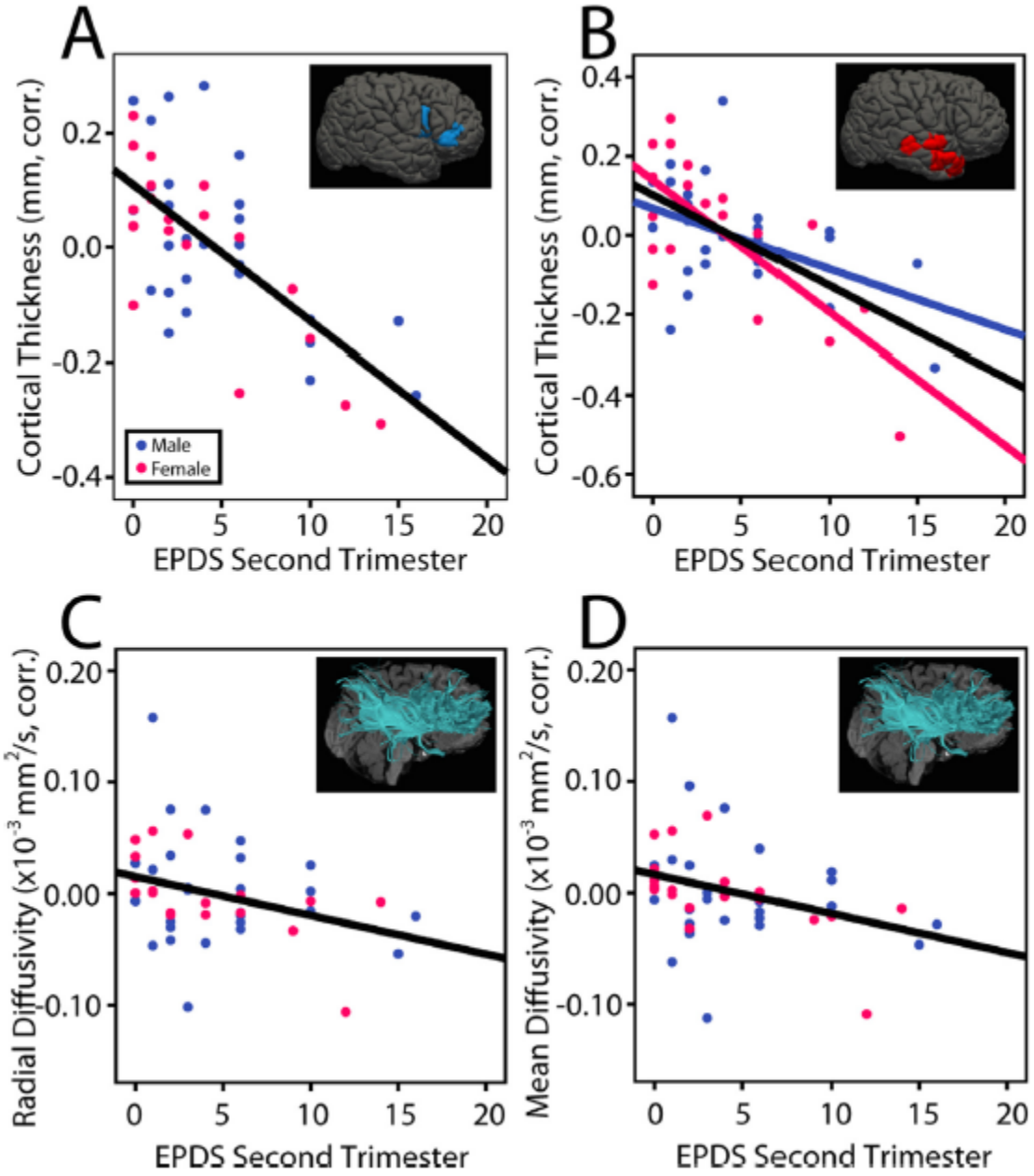


Figure 2. Correlations between brain structure and maternal prenatal depressive symptoms. Maternal depressive symptoms in the second trimester were significantly correlated with cortical thickness in two regions, as well as with radial and mean diffusivity in the white matter emanating from one region. Scatter plots show second trimester maternal Edinburgh Postnatal Depression Scale (EPDS) scores versus cortical thickness in each region **(A, B)** and radial **(C)** and mean diffusivity **(D)** of the white matter fibers passing through the inferior frontal region; all imaging parameters are corrected for maternal postsecondary education and child's age, sex, gestational age at birth, and birth weight. Cortical thickness in the right middle temporal area showed a significant EPDS-sex interaction, with girls showing a stronger and more negative association between EPDS scores and cortical thickness than boys. EPDS correlations with cortical thickness remained significant after controlling for postpartum depressive symptoms, but the diffusivity correlations did not. corr., corrected.

Findings more pronounced for boys

ACEs are

ADVERSE CHILDHOOD EXPERIENCES

Journal of Developmental Origins of Health and Disease

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Intergenerational transmission of adverse childhood experiences via maternal depression and anxiety and moderation by child sex

N. Letourneau, D. Dewey, B. J. Kaplan, H. Ntanda, J. Novick, J. C. Thomas, A. J. Deane, B. Leung, K. Pon, G. F. Giesbrecht and the APrON Study Team

Department of Pediatrics, University of Calgary, Child Development Center, Calgary, AB, Canada

Original Article

Cite this article: Letourneau N, Dewey D, Kaplan BJ, Ntanda H, Novick J, Thomas JC, Deane AJ, Leung B, Pon K, Giesbrecht GF and the APrON Study Team. (2018) Intergenerational transmission of adverse childhood experiences via maternal depression and anxiety and moderation by child sex. *Journal of Developmental Origins of Health and Disease* page 1 of 12. doi: 10.1017/S2040174418000648

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Key words:
adverse; child behaviour; internalizing and externalizing behaviour; maternal anxiety; maternal depression

Abstract

Adverse childhood experiences (ACEs) of parents are associated with a variety of negative health outcomes in offspring. Little is known about the mechanisms by which ACEs are transmitted to the next generation. Given that maternal depression and anxiety are related to ACEs and negatively affect children's behaviour, these exposures may be pathways between maternal ACEs and child psychopathology. Child sex may modify these associations. Our objectives were to determine: (1) the association between ACEs and children's behaviour, (2) whether maternal symptoms of prenatal and postnatal depression and anxiety mediate the relationship between maternal ACEs and children's behaviour, and (3) whether these relationships are moderated by child sex. Pearson correlations and latent path analyses were undertaken using data from 907 children and their mothers enrolled the Alberta Pregnancy Outcomes and Nutrition study. Overall, maternal ACEs were associated with symptoms of anxiety and depression during the perinatal period, and externalizing problems in children.

APrON Alberta Pregnancy Outcomes and Nutrition

Journal of Developmental Origins of Health and Disease

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Intergenerational transmission of adverse childhood experiences via maternal depression and anxiety and moderation by child sex

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APrON Alberta Pregnancy Outcomes and Nutrition

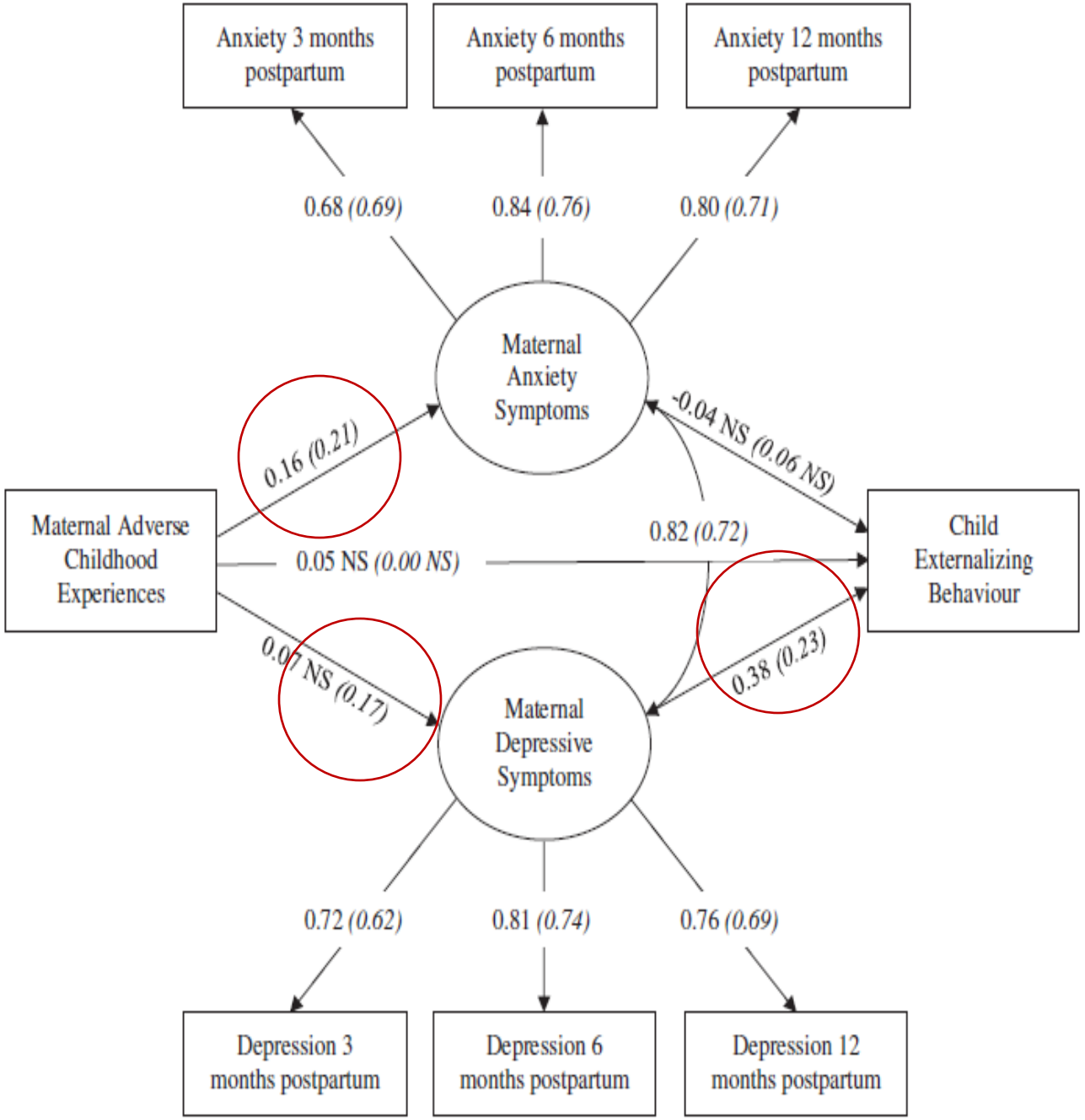


Fig. 3. Standardized parameter estimates for the moderated mediator model for child externalizing behaviour. Parameter estimates are for girls and boys (*in brackets*). Non-significant associations are designated as NS, otherwise all associations were significant at $P < 0.05$

Development and Psychopathology **30** (2018), 921–939

doi:10.1017/S0954579418000512

Social buffering of the maternal and infant HPA axes: Mediation and moderation in the intergenerational transmission of adverse childhood experiences

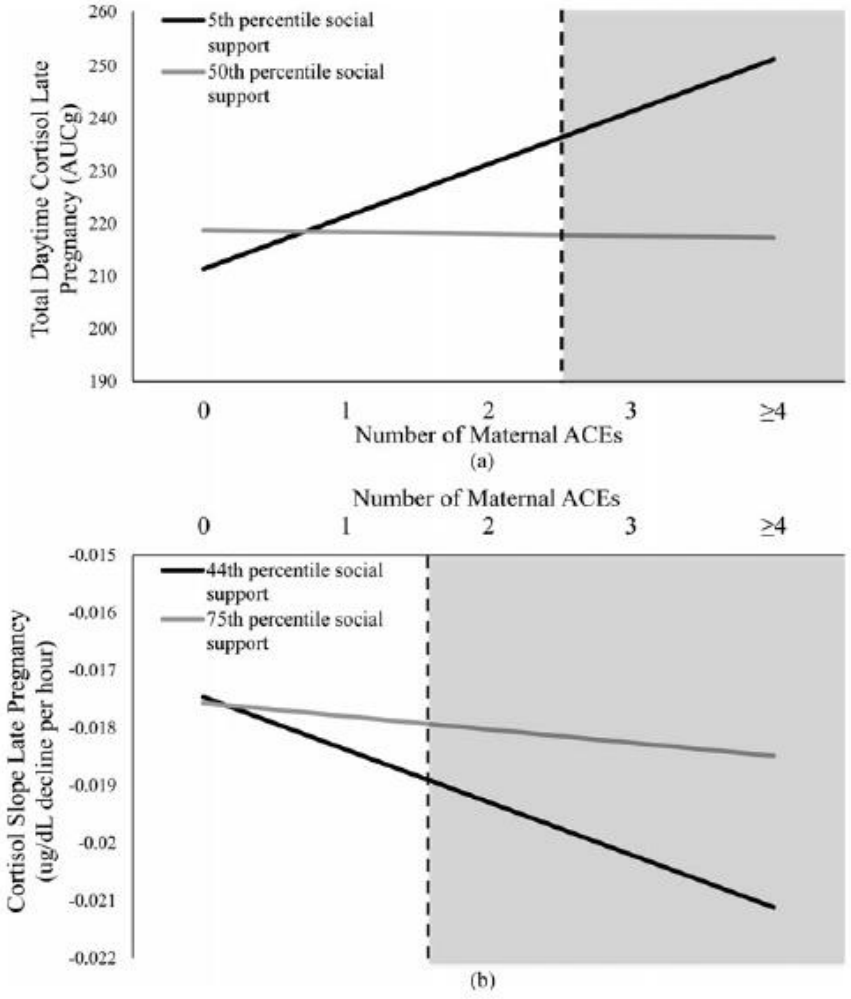
JENNA C. THOMAS, NICOLE LETOURNEAU, TAVIS S. CAMPBELL, GERALD F. GIESBRECHT, AND APRON STUDY TEAM
University of Calgary

Abstract

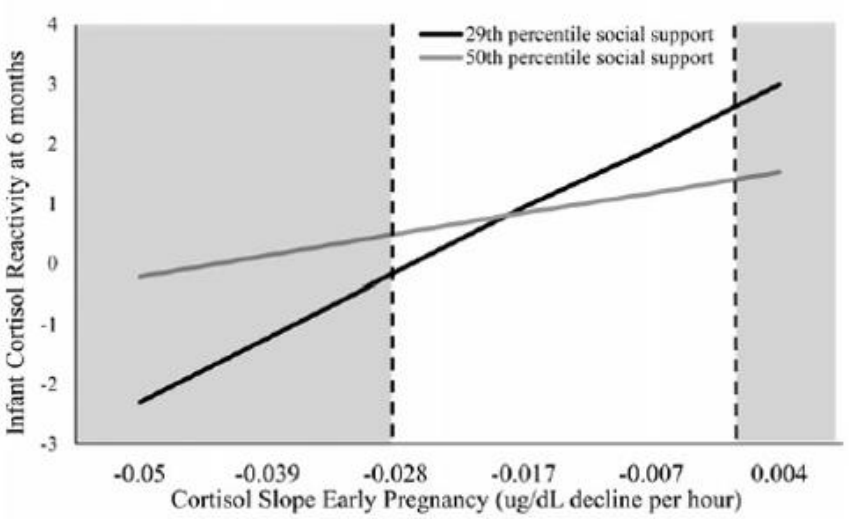
Supportive social relationships can reduce both psychological and physiological responses to stressful experiences. Recently, studies have also assessed the potential for social relationships to buffer the intergenerational transmission of stress. The majority of these studies, however, have focussed on social learning as a mechanism responsible for the intergenerational transmission of stress. Evidence of biological mechanisms is lacking. The objective of the current study was, therefore, to determine whether the association between maternal adverse childhood experiences (ACEs) and infant hypothalamic–pituitary–adrenal (HPA) axis function is mediated by maternal HPA axis function during pregnancy and moderated by social support. Data were from 243 mother–infant dyads enrolled in a prospective longitudinal cohort (the Alberta Pregnancy Outcomes and Nutrition Study). Maternal history of ACEs was retrospectively assessed while maternal perceived social support and salivary cortisol were assessed prospectively at 6–22 weeks gestation (Time 1) and 27–37 weeks gestation (Time 2), and infant cortisol reactivity to a laboratory stressor and maternal perceived social support were assessed at 5–10 months postnatal (Time 3). Results revealed that maternal HPA axis function during pregnancy mediated the effects of maternal ACEs on infant HPA axis reactivity, suggesting that the maternal HPA axis is a mechanism by which maternal early life stress is transmitted to offspring. Furthermore, social support in the prenatal and postnatal periods moderated the cascade from maternal ACEs to infant HPA axis reactivity. Specifically, prenatal social support moderated the association between ACEs and maternal HPA axis function during pregnancy, and postnatal social support moderated the association between maternal HPA axis function and infant cortisol reactivity. These findings highlight the social sensitivity of the HPA axis and suggest the utility of social relationships as an intervention target to reduce the effects of maternal early life stress on infant outcomes.

APrON Alberta Pregnancy Outcomes and Nutrition

ACES, Maternal Cortisol & Social Support



Maternal Cortisol, Infant Cortisol & Social Support



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DOI 10.1002/dev.21505

RESEARCH ARTICLE

WILEY Developmental Psychobiology

Biological embedding of perinatal social relationships in infant stress reactivity

Jenna C. Thomas[1,2] | Nicole Letourneau[2,3,4] | Crystal I. Bryce[5] | Tavis S. Campbell[1] | Gerald F. Giesbrecht[2,3] | The APrON Study Team

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Email: ggiesbre@ucalgary.ca

Funding information
Alberta Innovates–Health Solutions; Canadian Child Health Clinician Scientist Program; Canadian Institutes of Health Research; Alberta

Abstract

Whereas significant advances have been made in understanding how exposure to early adversity "gets under the skin" of children to result in long term changes in developmental outcomes, the processes by which positive social relationships become biologically embedded remain poorly understood. The aim of this study was to understand the pathways by which maternal and infant social environments become biologically embedded in infant cortisol reactivity. Two hundred seventy-two pregnant women and their infants were prospectively assessed during pregnancy and at 6 months postpartum. In serial mediation analyses, higher perceived social support from partners during pregnancy was associated with lower infant cortisol reactivity or larger decreases in cortisol in response to a stressor at 6 months of age via lower self-reported prenatal maternal depression and higher mother–infant interaction quality. The findings add to our understanding of how perinatal social relationships become biologically embedded in child development.

KEYWORDS
biological embedding, cortisol reactivity, mother-infant interaction quality, social support

APrON Alberta Pregnancy Outcomes and Nutrition

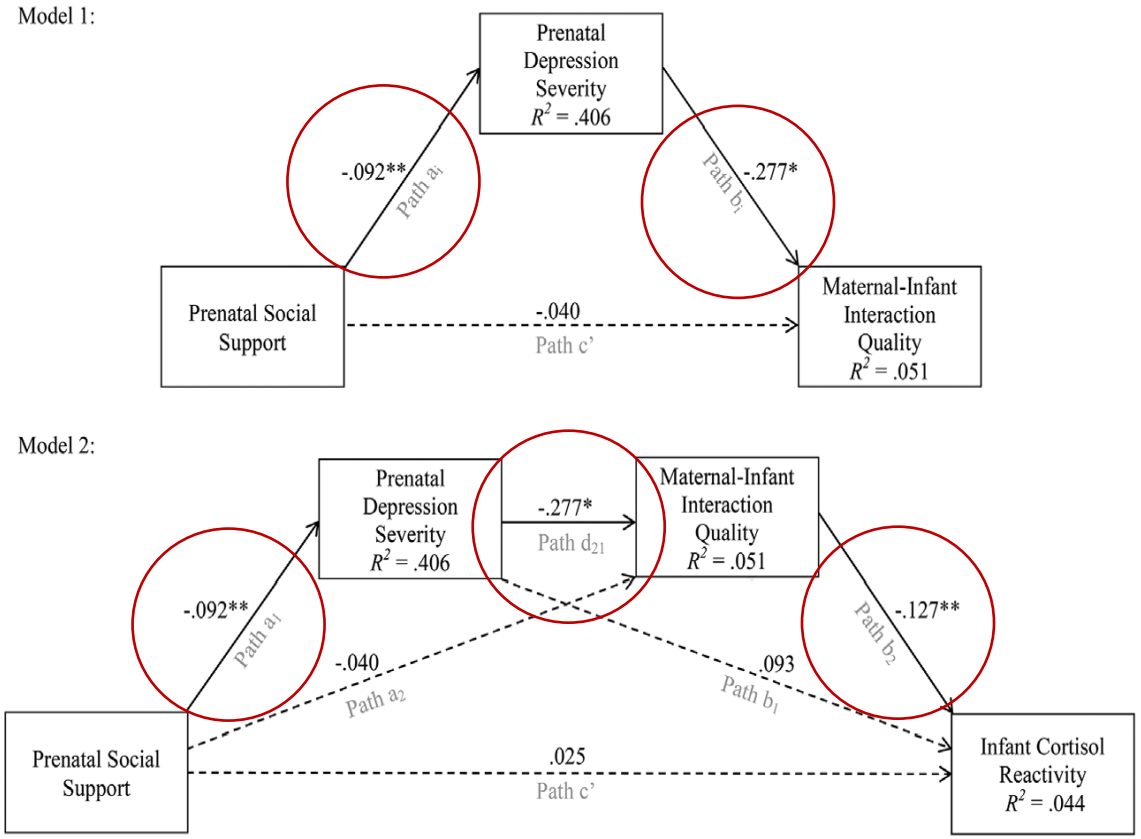

FIGURE 1 Longitudinal path models examining the relations between prenatal social support, prenatal depression severity, maternal–infant interaction quality, and infant cortisol reactivity. Unstandardized estimates are displayed. Significant paths are represented by solid lines, non-significant paths are represented by dashed lines

Summary

- Women's depressive symptoms impact children's behavioural and brain development
- Social support attenuated impacts of maternal depressive symptoms on children
- Women's exposure to ACES predict children's behavioural problems, mediated by depression (postnatally)
- Mothers with exposure to a higher number of ACES had altered prenatal cortisol output with lower levels of social support; mothers with altered prenatal cortisol predicted infant cortisol alterations, especially with lower social support
- Mothers who reported higher perceived social support reported less depressive symptoms
- Perceived maternal social support had a positive indirect association with maternal-infant interaction quality via its association with lower maternal depressive symptoms
- Higher maternal-infant interaction quality was associated with lower infant cortisol reactivity or larger decreases in infant cortisol
- These findings underpin 2 trials:

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VID-KIDS: Video interaction guidance for mothers with depression and their infants

Alberta Health Services

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

- **Dr. Nicole Letourneau** RN PhD, Alberta Children's Hospital Foundation Research Chair in Parent-Infant Mental Health, University of Calgary
- **Dr. Penny Tryphonopoulos** RN PhD, Assistant Professor, Brandon University
- **Dr. Monica Oxford** PhD, University of Washington, Executive Director of Parent-Child Relationships Programs
- **Denise Findlay** RN, BSN, University of Washington, Director of Education and Outreach, Parent-Child Relationships Programs
- **Dr. Cindy-Lee Dennis** RN PhD, Canada Research Chair in Perinatal Community Health, University of Toronto
- **Dr. Deb McNeil** RN PhD, Director Research, Alberta Health Services
- **Dr. Linda Duffett-Leger** RN PhD, University of Calgary
- **Dr. Gillian Currie** PhD, University of Calgary

Baseline Measures

- Maternal Depression (EPDS[1])
- Maternal – Infant Interaction Quality (PCITS[2])
- Maternal & Infant Stress (Diurnal Cortisol; AUC_G & AUC_I)

Intervention

VID-KIDS

- Session 1 — 3 weeks post-randomization
- Session 2 — 6 weeks post-randomization
- Session 3 — 9 weeks post-randomization

Hypothesized Outcomes

N.B. Arrows indicate direction of effect

- ↑ Maternal – Infant Interaction Quality
- ↓ Infant Stress
- ↓ Maternal Depression/Anxiety
- ↑ Infant Developmental Outcomes

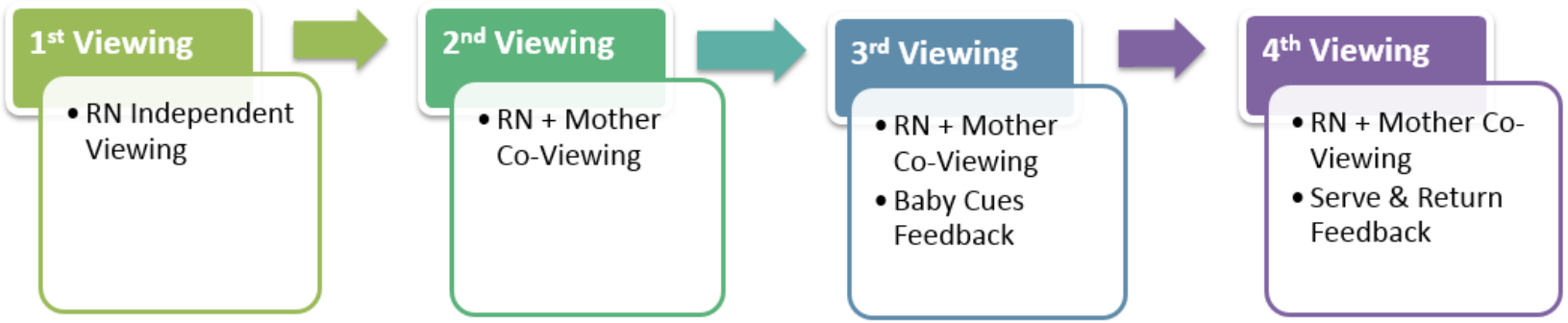
Pre-test → Randomization → 3 VID-KIDS Sessions → Post-test

1. Edinburgh Postnatal Depression Scale: α=.87; sensitivity 79% & specificity 85%
2. Parent-Child Interaction Teaching Scale: α=.87; test-retest r=.55 - .85

Delivered by RN's trained in Keys to Caregiving & Parent-Child Interaction Assessment

3 home visits, lasting 1-1.5 hours

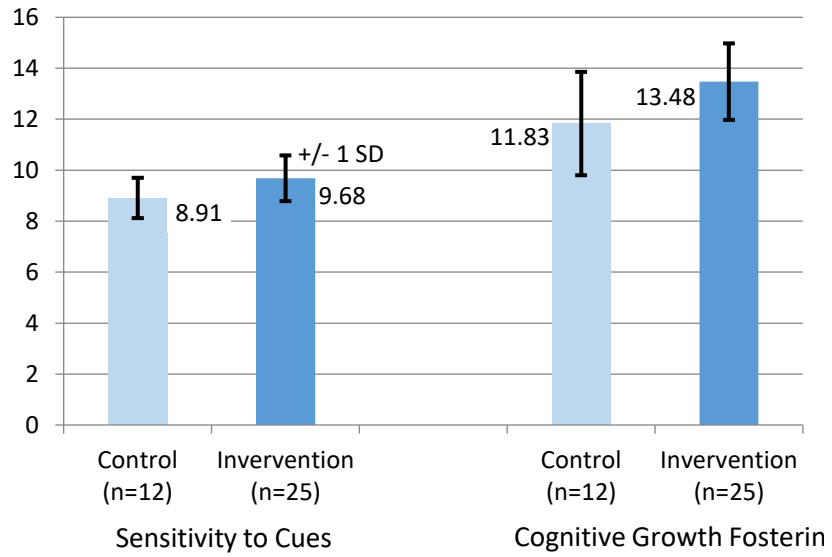
- **Videotaping mother-child interaction**
- **Teaching baby cues**
- **Reviewing video**



Pilot RCT completed (n=12):

- Did not affect s/s of depression
- Improved parent-child interaction scores
- Reduced infant cortisol levels

Measure	Tx Mean (SD)	Control Mean (SD)	P	d
Depression (EPDS) Total				
Pre-test	17.17 (2.99)	13.67 (3.88)		
Post-test	14.00 (2.83)	12.33 (2.66)	0.456	0.42
Parent-Child Interaction (NCATS Total)				
Pre-test	50.17 (4.26)	52.83 (5.85)		
Post-test	61.00 (4.52)	53.50(4.04)	0.007	1.43
Daily Decline of Infant Salivary Cortisol				
Pre-test	650.2(0.29)	1208 (464.5)		
Post-test	1667(449.14)	856.1 (459.6)	0.027	0.939



FULL TRIAL IN TESTING WITH CALGARY PUBLIC HEALTH, current n=100; target 200 recruiting until 2021

ATTACH™

ATTACH™: Attachment and Child Health

Discovery House
domestic violence ends here.

Frontiers of INNOVATION

PolicyWise for Children & Families

Alberta Children's Hospital Foundation

Sonshine community services

Center on the Developing Child HARVARD UNIVERSITY

Palix Foundation

CUPS resilience for life

CALGARY FOUNDATION FOR COMMUNITY, FOREVER

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- Psychoeducational intervention designed to help parents enhance and develop their capacity for better parent-child relationships to promote child development
- Intended for at-risk parents suffering from toxic stress (e.g. (e.g. depression) current or past (e.g. ACES)
- 10 weekly face-to-face sessions
- Dyadic and triadic sessions with co-parent to build up social support

Primary caregivers affected by toxic stress may be traumatized, depressed or distressed which reduces their regulation of the infant's stress (e.g. are withdrawn, emotionally unavailable, or frightening). (Lyons-Ruth, 1999)

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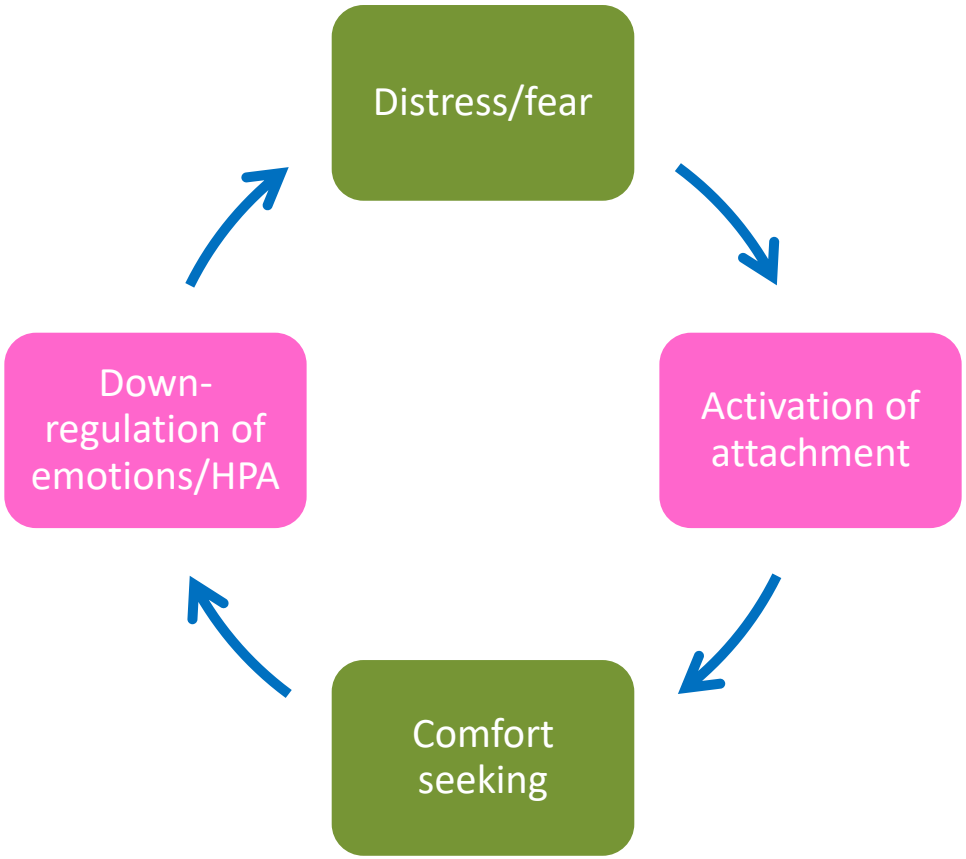

(Mayes 2012)

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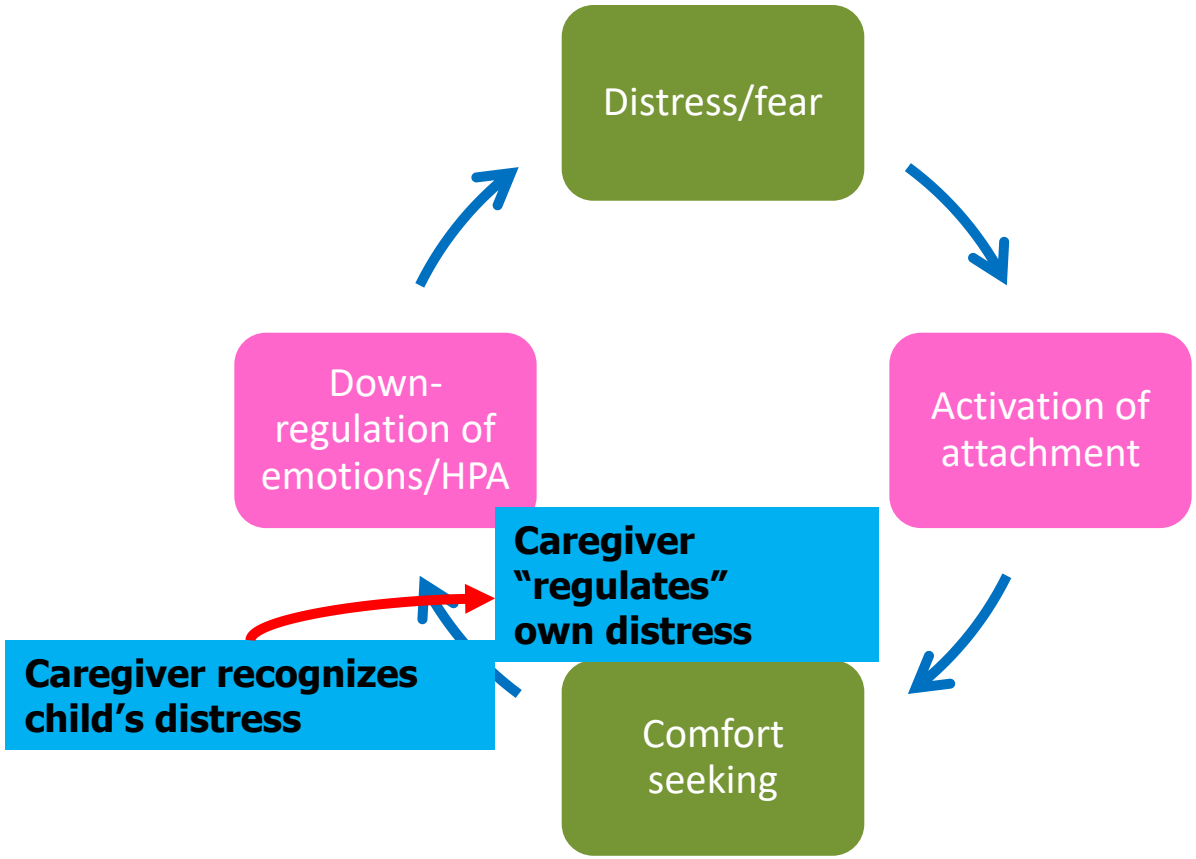

(Mayes 2012)

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- RF is defined as the parents' **capacity** to understand their own and their child's mental states, feelings and thoughts (Steele 1996)
- RF contributes to a parent's ability to regulate their own feelings and behavior toward their child, which may buffer the negative effects of toxic stress on attachment and development (Steele 1996)

Arietta Slade described reflective function—

"A mother's capacity to reflect upon and understand her child's internal experience is what accounts for the relation between attachment status and her child's sense of security and safety."

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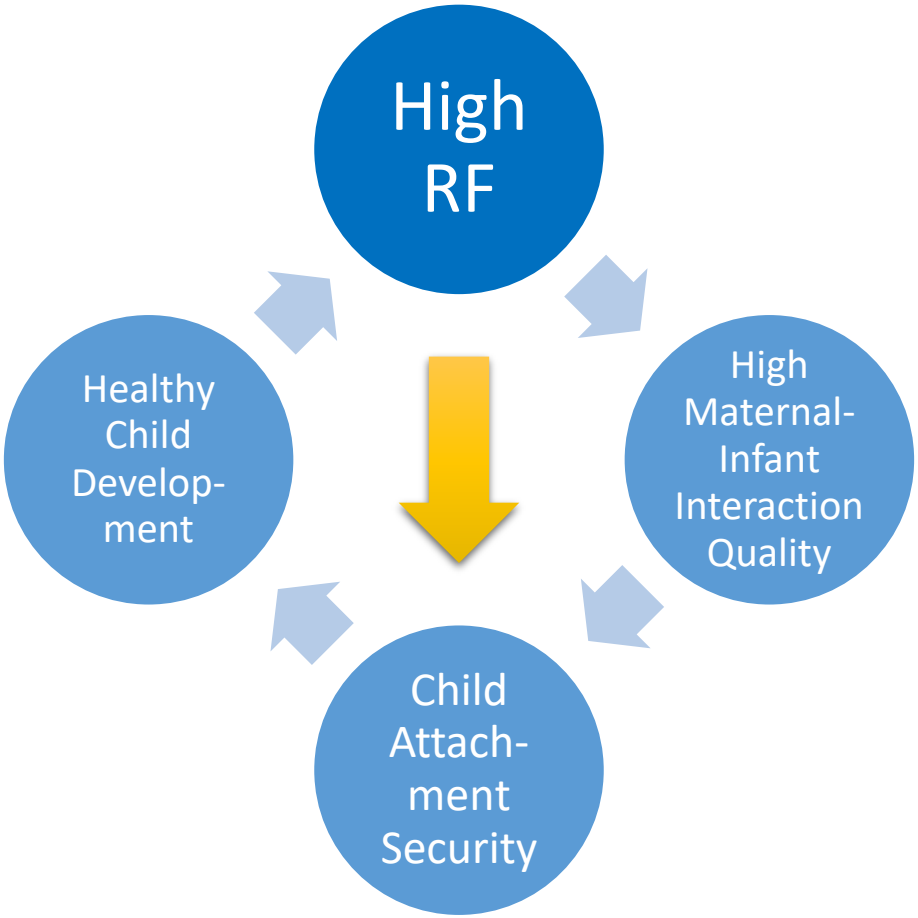

Parental Reflective Function is associated with infant attachment security
(Fonagy 1991, Meins 2002, Sadler 2013)

Attachment security is associated with healthy child development
(Cyr 2010, Fearon 2010, Groh 2012)

ATTACH™

- Focuses on teaching parents reflective function skills (to improve parent-child interaction, attachment and development) via practicing hypothetical and real life situations
- Promotes RF skill building by practicing RF via three processes:
  - Video feedback of free play mother-child interactions
  - Hypothetical situations
  - Real life situations

ATTACH™

Table 1. Design, sample sizes and results of researcher-led ATTACH™ pilot studies to date

		Design		Reflective Function		
	Pilot	RCT (N)	QE[a] (N)	RFQ	PRFQ	PDI
Phase 1	1	20		Not asked	Not asked	SIG (*d*=.8-1.1)
	2		10	Not asked	Not asked	SIG (*d*=.51-.61)
	3	10		Not asked	Not asked	SIG (*d*=1.5-2.0)
Phase 2	4	14		NS (+ trend)	SIG (*d*=1.4)	Not asked
	5		7	NS	SIG (*d*=1.2)	Not asked
	6	20		NS (+ trend)	NS (+ trend)	Not asked
	7		10	NS (+ trend)	NS (+ trend)	Not asked
	Totals	64	27			
	Grand Total	101 Comparisons				

Note:
ASQ3=Ages and Stages Questionnaire 3rd Edition;
ASQ:SE2=Ages and Stages Questionnaire: Social Emotional 2nd Edition;
DAA=data awaiting analysis;
NS=No significant difference;
QE=quasi-experimental design;
PCITS: Parent-Child Interaction Teaching Scale;
PDI=Parent Development Interview, coded with Fonagy's 11-point scale;
PRFQ=Parental Reflective Function Questionnaire;
RCT=randomized controlled trial;
RFQ=Reflective Function Questionnaire;
SIG=Significant differences
Cohen's d interpretation: small= .2, medium=.5, large≥.8
Eta^2 interpretation: small=.-2, medium=.13, large=.2

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Table 1. Design, sample sizes and results of researcher-led ATTACH™ pilot stud

		Design		Outcome			
		RCT	QE[a]	Parent-Child Relationships		Child Development	
	Pilot	(N)	(N)	PCITS	Attachment[b]	ASQ-3	ASQ-SE2
Phase 1	1	20		SIG (*d*=.34-.41)	NS (+ trend)	SIG (*d*=.98)	NS
	2		10	SIG (*d*=.66-.95)	NS (+ trend)	NS	NS
	3	10		SIG (*d*=.36-1.2	NS (+ trend)	SIG (*d*=2.3)	NS
Phase 2	4	14		SIG (*d*=.75-1.1	SIG (eta^2=.30-.47)	SIG (*d*=1.4)	NS
	5		7	SIG *d*=.41-.88)	DAA	SIG (*d*=1.4)	NS
	6	20		SIG (*d*=.62-.79)	DAA	NS	NS
	7		10	SIG (*d*=1.5)	DAA	SIG (*d*=.47-.61)	NS
	Totals	64	27				
	Grand Total	101 Comparisons					

Note:
ASQ3=Ages and Stages Questionnaire 3rd Edition;
ASQ:SE2=Ages and Stages Questionnaire: Social Emotional 2nd Edition;
DAA=data awaiting analysis;
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SIG=Significant differences
Cohen's d interpretation: small= .2, medium=.5, large≥.8
Eta^2 interpretation: small=.-2, medium=.13, large=.2

ATTACH™

(1) Examining differences in **child attachment security** for children in the intervention group and wait-list control group for Pilot Studies 1, 2, 3 and 4.

Table 1a. Frequency table of post-intervention attachment security in intervention verses control group children (N = 45). Note that more children in the intervention group were securely attached post-intervention (46%) compared to children in the control group (18%).

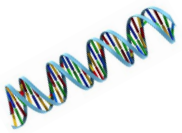
Child attachment	Treatment Group		
	Intervention Group	Control Group	Total
Insecure Attachment	15	14	29
Secure Attachment	**13**	**3**	16
Totals	28	17	45

Table 1b. Summary of chi-square tests examining differences in post-intervention child attachment by treatment group (intervention verses wait-list controls) (N = 45). Note that chi-square results indicate that the differences in child attachment security by treatment group is statistically significant.

Statistic	Value	Df	Asymptotic significance (2-sided)	Exact Significance (2-sided)	Exact Significance (1-sided)
Pearson Chi-square	3.824	1	.051		
Fisher's Exact Test				.062	**.049**

Next Steps

- Publication of APrON data on association between RF, attachment and child development, to further support theory underpinning ATTACH™
- Test online delivery of ATTACH™
- Examining genes/allelic variants that connote differential susceptibility and ePRS scores in APrON and potentially both trials



- Examine epigenetic changes associated with exposure to intervention

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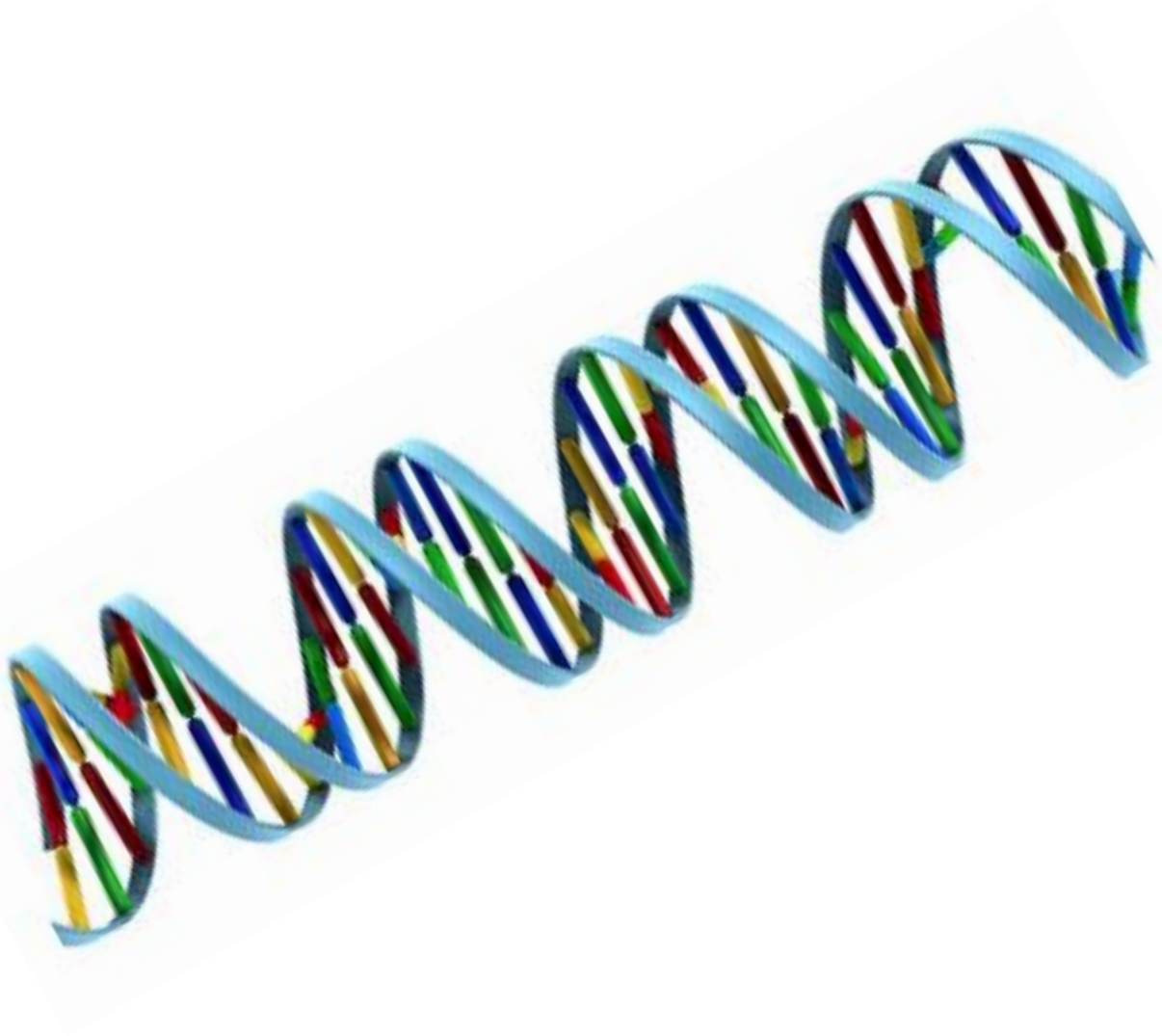

Original Quantitative Research Report

Parenting Interacts With Plasticity Genes in Predicting Behavioral Outcomes in Preschoolers

Canadian Journal of Nursing Research
0(0) 1–18

DOI: 10.1177/0844562119863612
journals.sagepub.com/home/cjn
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Nicole L. Letourneau[1,2,3], A. P. Jason de Koning[4], Bikram Sekhon[1], Henry N. Ntanda[2], Michael Kobor[5], Andrea J. Deane[2], Alexander M. Morin[5], Deborah Dewey[2], Tavis S. Campbell[6], Gerald F. Giesbrecht[2], and the APrON Study Team

Abstract

Background: Public health and pediatric nurses typically focus on supporting parenting to reduce the likelihood of children's behavioral problems. Studies have identified interactions between early exposures to stress in caregiving and child genotype in predicting children's behavioral problems, such that certain genotypes connote greater differential susceptibility or plasticity to environmental stressors. We sought to uncover the interaction between observational measures of parent–child relationship quality and genotype in predicting early-onset behavioral problems in 24-month-olds, using prospective methods.

Methods: We conducted a secondary analysis of data collected on a subsample of 176 women and their infants enrolled during pregnancy in the ongoing Alberta Pregnancy Outcomes and Nutrition (APrON) cohort study. Inclusion criteria required mothers to be ≥18 years of age, English speaking and ≤22 weeks gestational age at enrollment. Genetic data were obtained from blood leukocytes and buccal epithelial cell samples, collected from infants at three months of age. For each child, the presence of plasticity alleles was determined for *BDNF, CNR1, DRD2/ANKK1, DRD4, DAT1, 5-HTTLPR*, and *MAOA*

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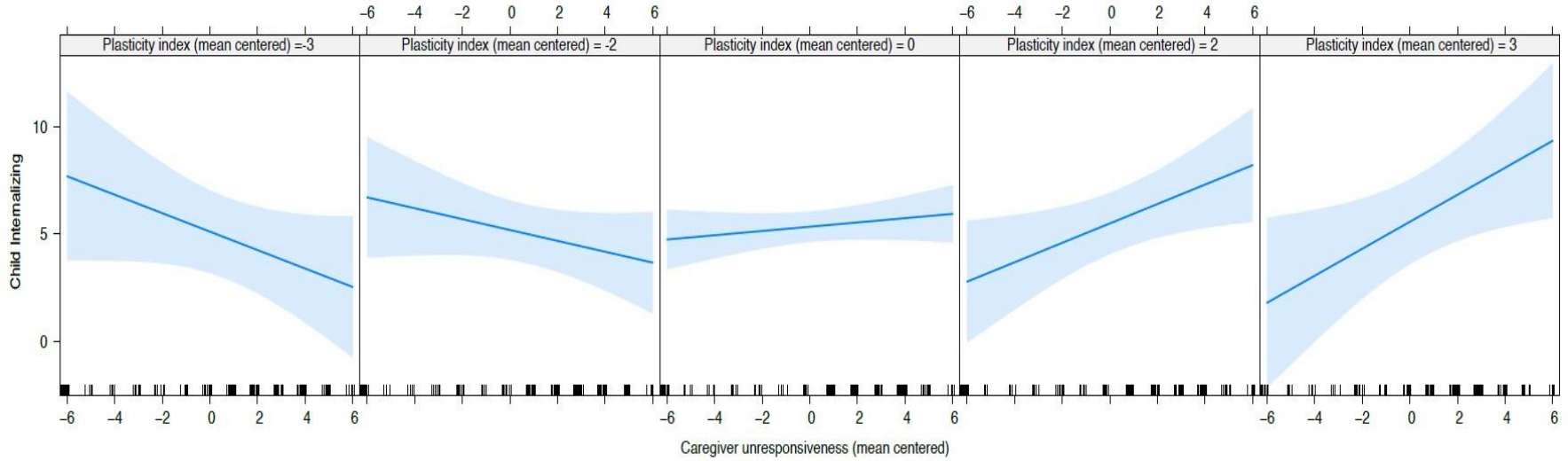
Effect of Interactive Terms in the AIC-Best Model Explaining Internalizing Behaviours

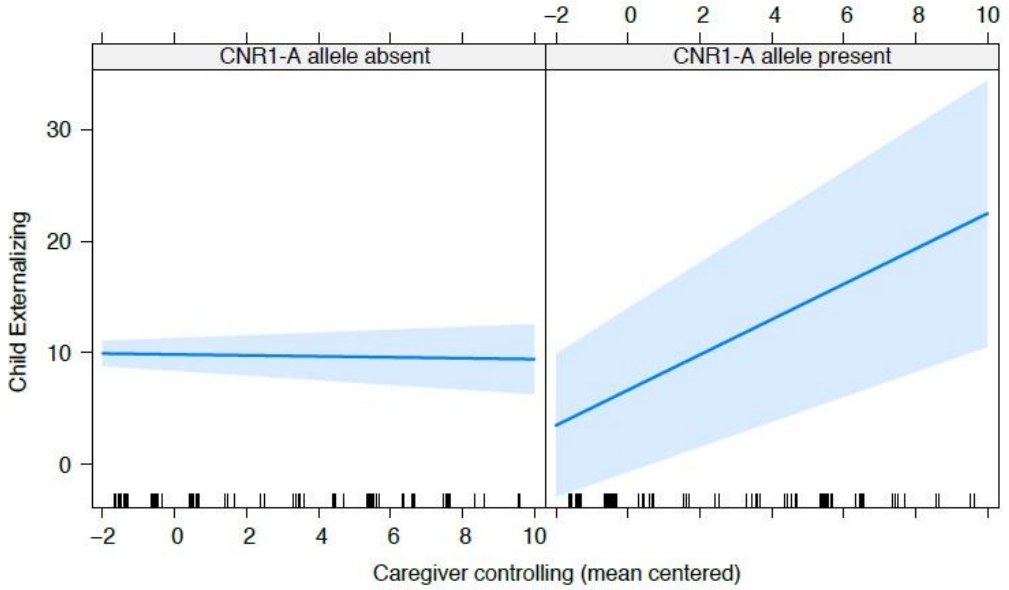


The **higher** the plasticity index (indicating genetic susceptibility to the environment) and the **more unresponsive** were caregivers, the **more children displayed internalizing problems**

Effect Display for Interactions in the AIC-Best Model Explaining Child Externalizing Behaviour

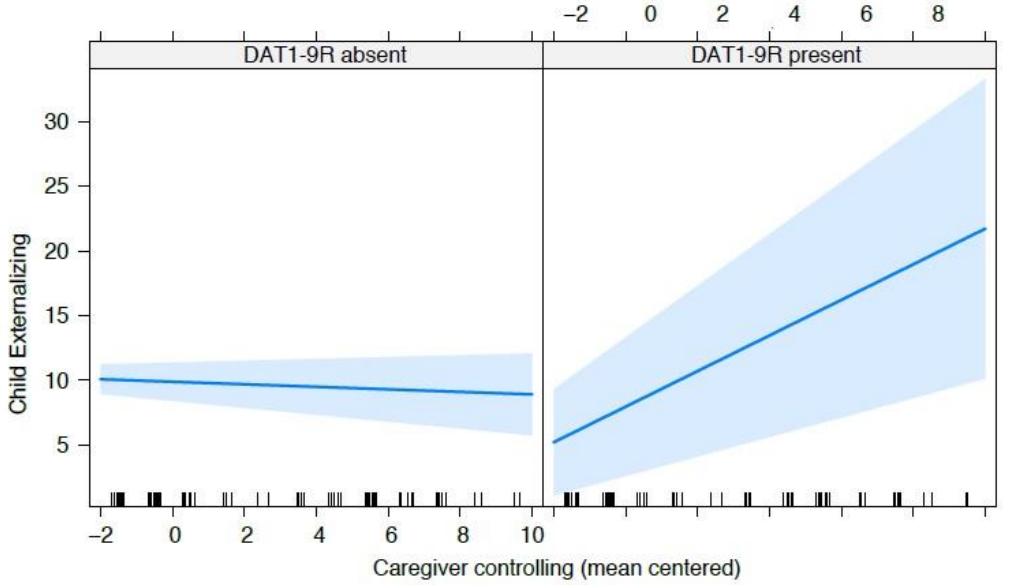
In presence of CNR1, the **more** controlling parents, the **more** externalizing behaviours

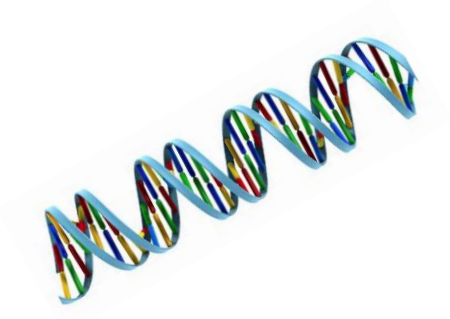
a.



In presence of DAT1-9R, the **more** controlling parents, the **more** externalizing behaviours

b.





Summary

- INTERNALIZING BEHAVIOUR:
  - Higher scores on plasticity index interacted with *higher* parental unresponsiveness in predicting *more* problem behaviours
  - Higher scores on plasticity index interacted with *lower* parental unresponsiveness in predicting *fewer* problem behaviours
- EXTERNALIZING BEHAVIOUR:
  - *CNR1-A* and DAT1-9r plasticity alleles interacted with *higher* parental controlling behaviours in predicting *more* problem behaviours
  - *CNR1-A* and DAT1-9r interacted with *lower* parental controlling behaviours in predicting *fewer* problem behaviours

Now examining plasticity alleles in

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ATTACH

The PedBE clock accurately estimates DNA methylation age in pediatric buccal cells

Lisa M. McEwen[a], Kieran J. O'Donnell[b,c], Megan G. McGill[b], Rachel D. Edgar[a], Meaghan J. Jones[a], Julia L. MacIsaac[a], David Tse Shen Lin[a], Katia Ramadori[a], Alexander Morin[a], Nicole Gladish[a], Elika Garg[b], Eva Unternaehrer[b], Irina Pokhvisneva[b], Neerja Karnani[d,e], Michelle Z. L. Kee[d], Torsten Klengel[f], Nancy E. Adler[c,g,h], Ronald G. Barr[c,i], Nicole Letourneau[j,k], Gerald F. Giesbrecht[j,l], James N. Reynolds[m], Darina Czamara[n], Jeffrey M. Armstrong[o], Marilyn J. Essex[o], Carolina de Weerth[p], Roseriet Beijers[q], Marieke S. Tollenaar[r], Bekh Bradley[s], Tanja Jovanovic[s], Kerry J. Ressler[f], Meir Steiner[t], Sonja Entringer[u,v], Pathik D. Wadhwa[v,w,x,y], Claudia Buss[u], Nicole R. Bush[g], Elisabeth B. Binder[c,n,s], W. Thomas Boyce[c,g,h], Michael J. Meaney[b,c,d,z], Steve Horvath[aa,bb,1,2], and Michael S. Kobor[a,c,1,2]

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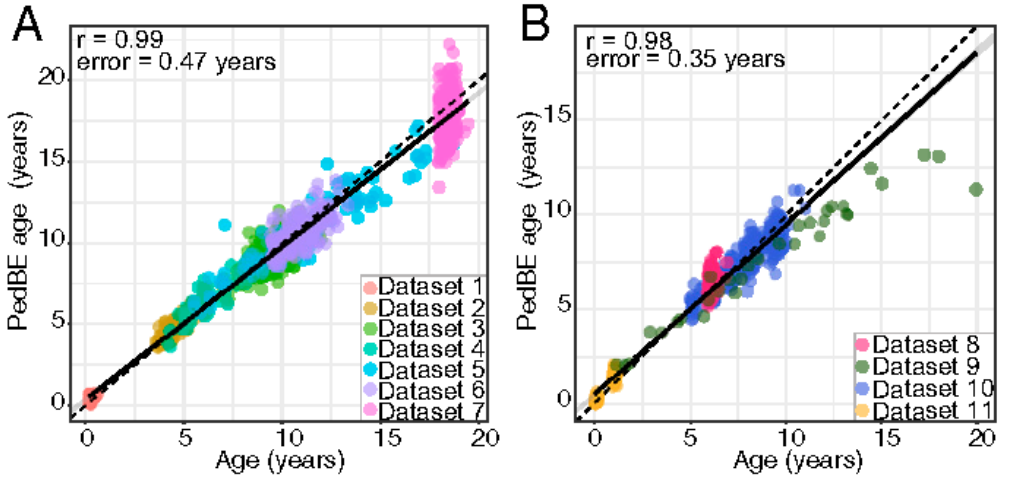
Edited by Marla B. Sokolowski, University of Toronto, Toronto, ON, Canada, and accepted by Editorial Board Member Gene E. Robinson August 23, 2019 (received for review February 19, 2019)

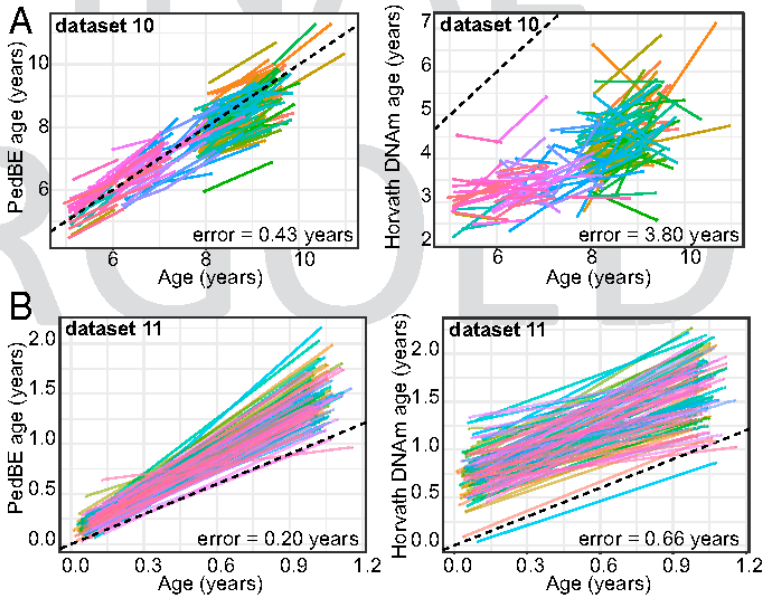
The development of biological markers of aging has primarily focused on adult samples. Epigenetic clocks are a promising tool for measuring biological age that shows impressive accuracy across most tissues and age ranges. In adults, deviations from the DNA methylation (DNAm) age prediction are correlated with several age-related phenotypes, such as mortality and frailty. In children, however, fewer such associations have been made, possibly because DNAm changes are more dynamic in pediatric populations as

clock has been applied to many independent datasets, each showing strong correlations with chronological age. Deviations between DNAm age and chronological age, referred to as DNAm age acceleration, are associated with several age-related health variables, with higher epigenetic age associated with an increase in mortality, cognitive decline, and a decrease in time until death (2).

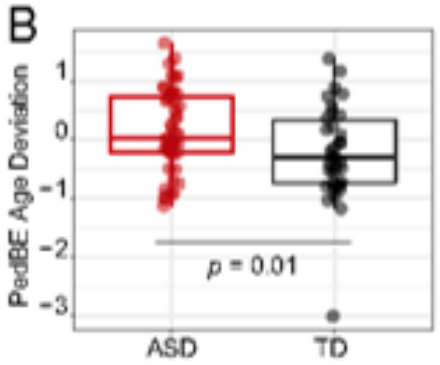
Pediatric buccal DNA methylation age accurately predicted chronological age.

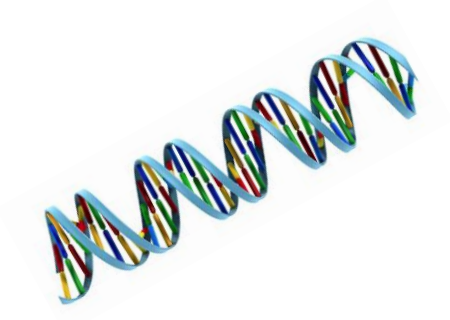


Longitudinal data demonstrated higher accuracy of the PedBE clock as compared to the pan-tissue Horvath DNAm clock.



PedBE deviation was associated with ASD in independent cohorts.





Summary

- Pediatric-Buccal-Epigenetic (PedBE) clock of DNAm age accurately predicted chronological age

- The clock was characterized in multiple cohorts, showcasing the accuracy in longitudinal data, the performance in nonbuccal tissues and adult age ranges, and the association with obstetric outcomes

- PedBE age in children with a neurodevelopmental disorder, ASD, which showed a higher PedBE age than those considered to be typically developing

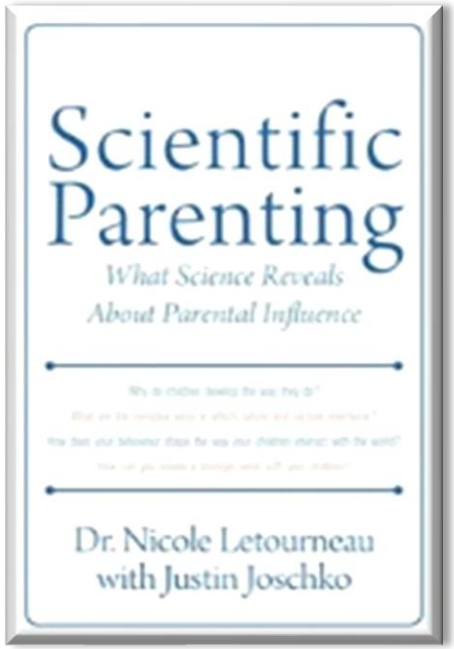
- We will use this in

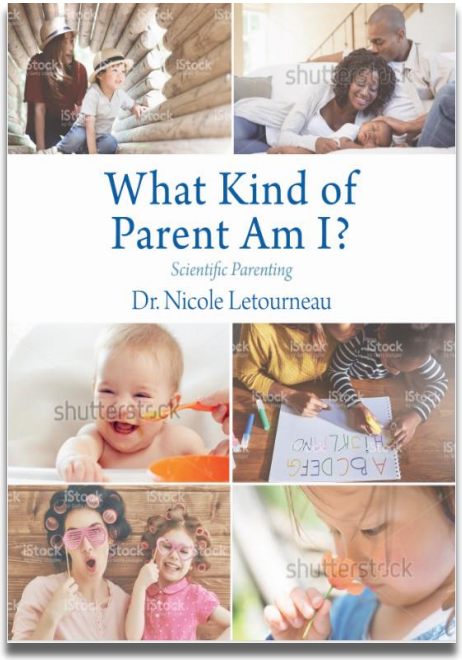
Want to know more?

APrONstudy.ca

Nicole.Letourneau@UCalgary.ca

@DrNLetourneau





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