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Review Paper

The Maternal Adversity, Vulnerability and Neurodevelopment Project: Theory and Methodology

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Objective: To describe the theory and methodology of the multi-wave, prospective Maternal Adversity, Vulnerability and Neurodevelopment (MAVAN) study. The goal of MAVAN is to examine the pre- and postnatal influences, and their interaction, in determining individual differences in mental health.

Method: MAVAN is a community-based, birth cohort study of pregnant Canadian mothers and their offspring. Dyads are assessed longitudinally, with multiple assessments of both mother and child in home and laboratory across the child's development. Study measures, including assessments of cognitive and emotional function, are described. The study uses a candidate gene approach to examine gene–environment interdependence in specific developmental outcomes. Finally, the study includes measures of both brain-based phenotypes and metabolism to explore comorbidities associated with child obesity. One of the unique features of the MAVAN protocol is the extensive measures of the mother–child interaction. The relation between these measures will be discussed.

Results: Evidence from the MAVAN project shows interesting results about maternal care, families, and child outcomes. In our review, preliminary analyses showing the correlations between measures of maternal care are reported. As predicted, early evidence suggests that maternal care measures are positively correlated, over time.

Conclusions: This review provides evidence for the feasibility and value of laboratory-based measures embedded within a longitudinal birth cohort study. Though retention of the samples has been a challenge of MAVAN, they are within a comparable range to other studies of this nature. Indeed, the trade-off of somewhat greater participant burden has allowed for a rich database. The results yielded from the MAVAN project will not only

describe typical development but also possible targets for intervention. Understanding certain endophenotypes will shed light on the pathogenesis of various mental and physical disorders, as well as their interrelation.

Le projet sur l'adversité maternelle, la vulnérabilité et le neuro-développement : théorie et méthodologie

Objectif : Décrire la théorie et la méthodologie de l'étude prospective en plusieurs cycles Adversité maternelle, vulnérabilité et neuro-développement (MAVAN), dont le but est d'examiner les influences prénatales et postnatales, et leur interaction pour déterminer les différences individuelles de santé mentale.

Méthode : MAVAN est une étude en communauté de cohorte de naissance de mères canadiennes enceintes et de leurs enfants. Les dyades sont évaluées longitudinalement, avec de multiples évaluations de la mère et de l'enfant à la maison et en laboratoire durant le développement de l'enfant. Les mesures de l'étude, y compris les évaluations de la fonction cognitive et émotionnelle, sont décrites. L'étude utilise une approche de gène candidat pour examiner l'interdépendance gène–environnement dans des résultats spécifiques du développement. Enfin, l'étude comporte des mesures des phénotypes du cerveau et du métabolisme pour explorer les comorbidités associées à l'obésité des enfants. L'une des caractéristiques du protocole de MAVAN consiste dans les mesures répétées de l'interaction mère–enfant. La relation entre ces mesures sera discutée.

Résultats : Les données probantes du projet MAVAN indiquent des résultats intéressants sur les soins maternels, les familles, et les résultats chez les enfants. Dans notre revue, les analyses préliminaires révélant les corrélations entre les mesures des soins maternels sont décrites. Comme prévu, les premières données probantes suggèrent que les mesures des soins maternels sont positivement corrélées, avec le temps.

Conclusions : Cette revue offre des preuves de la faisabilité et de la valeur des mesures en laboratoire intégrées dans une étude de cohorte de naissance longitudinale. Bien que la conservation des échantillons ait été une difficulté pour MAVAN, ils sont dans un intervalle comparable à d'autres études de cette nature. En fait, le choix d'une charge plus grande pour les participants a donné une base de données riche. Les résultats issus du projet MAVAN décriront le développement typique mais aussi des cibles d'intervention possibles. Comprendre certains endophénotypes éclairera la pathogenèse de divers troubles mentaux et physiques, et leur interrelation.

Individual differences in child development are associated with diverse, interrelated proximal influences that include genomic variation, materno–fetal interactions, and familial context. Distal forces, such as socioeconomic context, shape this developmental matrix.[1–3] These influences operate interdependently over time. Thus the influence of genomic variation on any developmental outcome is a function of both context and developmental stage. The interdependence of gene and environment[4–6] reflects the biological reality of genomic structure and function; transcription is an environmentally regulated event.[7] Likewise, environmental influences operate through neural processes to influence psychological function, and the activity of relevant brain mechanisms is influenced by genomic function that reflects both heritable sequence-based variation and epigenetic modifications.

The challenge is to identify the relevant gene–environment interactions regarding specific developmental outcomes. Emotional and cognitive function emerge as the result of activity within a hierarchically organized brain, reflecting top-down and bottom-up processes, that occur as a function of activity in cortical, limbic, and midbrain systems, as well as signals from peripheral systems, such as endocrine, immune, and gastrointestinal tissues. This is a moving target. For example, emotional function at 8 years of age will reflect a greater influence of the PFC than at 2 years. Genomic variants that are largely expressed in the PFC (for example, the *COMT* gene that encodes for catechol-*O*-methyltransferase) may have a greater impact on emotional function at 8, compared with 2, years of age, as variation in emotional function comes under increasingly greater influence of the PFC. Thus we expect a dynamic relation between a specific gene–environment interaction and a

Abbreviations

EAS	Etch A Sketch
IQ	intelligence quotient
MAVAN	Maternal Adversity, Vulnerability and Neurodevelopment
PFC	prefrontal cortex

specific developmental outcome that can be examined only within a longitudinal study.

There is also evidence for the interdependency between environmental influences over time.[8] Thus the relation between the quality of parenting and child development is substantially greater for children with a history of adversity, than for those who experience normal development. Any phenotypic outcome is a function of a cascade of influences operating over time and with the potential to influence sensitivity to subsequent conditions. Variation occurs as a function of phenotype by environment interactions, where phenotype at any point in time is defined by gene–environment interactions during the developmental history of the person.

Maternal Adversity, Vulnerability and Neurodevelopment Project

The MAVAN project was established in 2003 and designed to examine the consequences of fetal adversity as a function of the quality of the postnatal environment, focusing on mother–infant interactions (the focus exclusively on the mother rather than on both parents reflects funding constraints). The MAVAN study is a prospective, cohort study of mother–child dyads followed from mid-pregnancy.

The design of the MAVAN project reflects a series of critical decisions. First, MAVAN protocols reflect a commitment to laboratory-based testing based on the consideration of statistical power as a function not only of sample size but also of measurement error.[9] Our assumption was that direct measures of the child would entail less measurement error than indirect measures, such as parental reports. We employed standard laboratory-based tests (for example, measures of attachment and computer-based cognitive tests) across the entire sample. Second, MAVAN emphasizes the study of comorbid conditions, which demands testing across multiple domains at the same developmental time points. This approach increases subject burden, but MAVAN is not a representative sample. Rather, it is an attempt to develop databases from the analysis of genotype and precise measures of phenotype to provide unique opportunities for testing specific hypotheses, especially those involving gene–environment interdependency. Therefore, we are less concerned with the issue of subject attrition than would be true for an epidemiologic cohort study. The third consideration was based on our focus on developmental trajectories, and thus we interact with mothers and children extensively during the first 24 months of life, and annually thereafter.

Clinical Implications

- The findings of the MAVAN study may lead to the further identification, characterization, and validation of high-risk phenotypes.
- The longitudinal design may shed light on the etiological pathways of certain mental health problems, thus identifying areas to target for prevention and interventions.

Limitations

- Extensive phenotyping and resulting participant burden is associated with a smaller sample size, as well as difficulties with sample retention for the MAVAN project.
- Additionally, the MAVAN sample is largely based on a Caucasian sample, from the provinces of Ontario and Quebec. Thus the generalizability of these results to other samples should be approached with caution.

Theory

Prenatal

The organism begins a dynamic, interactive relationship with the environment at conception. Indeed, development influences include those acting on the mother and grandparents through transgenerational effects that include the germline as well as the maternal phenotype. A life history perspective posits that the context of fetal development informs the developing organism about the nature of the postnatal environment.[10] Critical environmental signals, including maternal nutrition and stress, both of which impair fetal growth, are thought to produce anticipatory responses that may prove adaptive, assuming the environmental conditions of postnatal life resemble those prevailing during fetal development. Exposure to poor maternal nutrition may signal the fetus about potential food scarcity, prompting a developmental strategy that favours insulin resistance, which then dampens satiety signals, permitting the increased consumption of available foods, as well as the increased capacity to retain and store fats. This physiological profile may be adaptive if nutrient supplies remain low. However, this same metabolic imprint set within conditions of nutritional abundance enhances the risk for obesity and associated states of metabolic dysregulation. This pathway is thought to mediate the well-established relation between birth weight and the risk for adult type 2 diabetes and cardiovascular disease.[11]

Fetal programming is also apparent in mental health outcomes. Birth weight, corrected for gestational age, predicts the risk for attentional-deficit hyperactivity disorder as well as internalizing and externalizing problems[12–14] and associated endophenotypes. Children at 2 years of age who experienced intrauterine growth restriction are impaired in divided, focused, and sustained attention and are more impulsive.[14] Nonhuman animal research report effects of both maternal nutrition and stress during pregnancy on endophenotypes, such as stress reactivity, that predict the risk for psychopathology in humans.[15,16] Birth weight in humans is inversely correlated with negative emotionality[17] and adrenocortical responses to acute stress.[18,19] Thus the uterine environment that defines fetal development associates with important influences on mental health.

Postnatal Environment

There is compelling evidence for the importance of parenting for child development and health. First, parental style relates to emotional and cognitive development.[3,8,20] Second, parenting predicts vulnerability or resilience for psychopathology. Child abuse greatly increases the risk for mental illness[21–26]; children need not be overtly abused for development to be compromised. Persistent emotional neglect, family conflict, and conditions of harsh, inconsistent discipline all serve to constrain growth[27] and intellectual development, increase the risk for adult obesity,[24,28] depression, and anxiety disorders.[29] More subtle relationships exist. Cold, distant parent–child relationships are associated with a significantly increased risk of chronic illness (for examples, see Parker et al,[30] Mäntymaa et al,[31] Russak and Schwartz,[32] Canetti et al,[33] and Parker[34]).

Third, parenting is a critical mediator for the effects of socioeconomic conditions on child development. Poverty undermines parental emotional well-being and thus promotes family dysfunction and forms of parenting that endanger the health and development of the offspring.[1,3,35,36] Indeed, the effects of poverty on child development, especially those related to behavioural problems, are directly mediated by parenting.[37–39] Fourth, programs that target parenting practices improve behavioural and cognitive outcomes.[40–42] Such effects are observed in randomized clinical trials and persist over time. Family life is also a source of resilience.[43] Warm, nurturing families promote resistance to stress and diminish vulnerability to stress-induced illness.[44] Finally, individual differences in parenting appear to be transmitted across generations,[45–47] and thus contribute to estimates of the heritability of multiple complex traits.

Differential Effects of Parenting

The impact of the postnatal environment, including that of parenting, on any specific developmental outcome varies across people and is, in part, determined by the quality of fetal life.[8,42,48–50] In rodents, the effects of postnatal handling, a form of infantile environmental stimulation, are greater in the offspring of stressed mothers.[51] In rhesus monkeys,[52] anxious newborn infants cross-fostered onto highly nurturing mothers show dramatic decreases in timidity and behavioural inhibition. Less anxious infants are unaffected. This same point emerges from studies of environmental enrichment. In rodents, postweaning enrichment of the offspring of mothers who show a consistently reduced frequency of pup licking (an important maternal care behaviour) produces an increase in hippocampal synaptogenesis and cognitive performance, with little or no effect on the offspring of high licking mothers.[53]

Similarly, in humans, parental style accounted for only 4% of the variance in behavioural inhibition among children initially evaluated as low on negative emotionality, but for almost 30% of the variance in behavioural inhibition among those high in negative emotionality.[54] Likewise, among children with a negative temperament in infancy, there are significant effects of parental care or daycare on emotional problems, while no such effects emerge among children exhibiting a positive temperament.[55] The National Institute of Child Health and Human Development (commonly referred to as the NICHD) Early Child Care Research Network[56] revealed a significant relationship between parental sensitivity and emotional and (or) behavioural disorders in childhood, but only among children with a negative infant temperament. Moreover, hostile and (or) harsh maternal care predicts behavioural problems in children, but again, only in children scoring high on irritability distress in infancy.[57] More phlegmatic infants are less affected by parental style.

These findings suggest that high-risk infants are more susceptible to the influence of postnatal family life than are less vulnerable children. Hence the proverbial 0.3 correlation that so routinely emerges between parenting styles and developmental outcomes in children may likely be the result of a null association in the nonsusceptible child, with stronger associations in more susceptible (that is, highly vulnerable) children.[8] These findings dovetail with the notion of variation in biological sensitivity to context,[58] and suggest that prenatal conditions may contribute to differential susceptibility (also see Belsky and Pluess[59]). Thus while the exact origins of such variations in susceptibility are unknown, the quality of fetal development may define variations in plasticity to postnatal environmental conditions.

The moderate correlations between maternal care and infant attachment[60] contrast with clinical data. van den Boom[61] randomly assigned low socioeconomic status mothers with highly irritable infants to an experimental group that received an intervention structured to promote maternal sensitivity or to control conditions. The intervention significantly increased maternal sensitivity and secure infant attachment. Among control subjects, 22% of the infants showed secure attachment, compared with 66% of those in the treatment group. These findings suggest impressive treatment effects, with interventions focused on more vulnerable populations. Finally, among low birth weight babies from economically disadvantaged homes, an enriched form of education daycare, which included home visiting and parental support, significantly reduced the risk for emotional and (or) behavioural disorders, but only among children who exhibited highly negative emotionality in infancy; no treatment effect was detected among children with normal temperament.[62] The same pattern is apparent with cognitive outcomes. Infants of difficult temperament enrolled in the enrichment program were 5 times less likely to exhibit cognitive impairments (IQ <75) than those in the control group; there were no treatment effects on cognitive development among children with a normal or positive infant temperament. Children with a history of negative mood and irritability in infancy were most affected by parental care. Evaluative research conducted with the Abecedarian Project shows that early (years 1 to 4) enrichment interventions have profound effects, in the order of 1.0 to 1.5 standard deviations on IQ tests, in

Table 1 Preliminary profile of MAVAN sample retention

	Time point, months								
Variable	3[a]	6	12	18	24	36	48	60	72
Possible data available	402	551	548	540	528	504	460	427	309
Actual data collected	402	551	512	464	448	390	329	260	161
Any laboratory data	n/a	338	n/a	343	n/a	287	251	233	122

This table represents a preliminary overview and approximation of the MAVAN retention data. Data available include whether the dyad had any data at the given time point. Whether all or part of laboratory data were collected is included in Any laboratory data from the laboratory assessments at that time point. This table is a work-in-progress as data collection and entry are ongoing.

[a] No 3-month data were collected for the first cohort.

MAVAN = Maternal Adversity, Vulnerability and Neurodevelopment;
n/a = no laboratory administered at this time point

children from seriously disadvantaged homes.[63] There was little effect on children from more advantaged, better-educated families. These findings suggest that the effective targeting of prevention programs will require a more effective definition of the determinants of vulnerability at the level of the individual child. An obvious challenge is to identify phenotypic markers in early life that better predict intervention outcomes. To meet this challenge, the MAVAN project emphasizes the importance of gene–environment interactions over time to define better predictors of vulnerability.

Genotype

Individual differences in complex traits are heritable and reflect the influence of genomic variation. There is considerable research examining the role of candidate genes on the expression of endophenotypes associated with psychopathology. Although the results of genome-wide association studies are often controversial, there is emerging evidence for gene–environment interdependence, especially for genes that encode for proteins implicated in serotonergic and dopaminergic signalling. We focus on studies of a priori hypotheses considered within a relevant developmental context that includes genomic sequence variation. We adopted a candidate gene approach, focusing on selected polymorphisms previously associated with either target endophenotypes or disorders. In general, the genomic polymorphisms included in the MAVAN project, to date, focus on classic neurotransmitter systems associated with emotional and (or) cognitive function as well as for those regulating stress responses.

The Maternal Adversity, Vulnerability and Neurodevelopment Project

The MAVAN project addresses the hypothesis that functional outcomes associated with vulnerability, defined by gene–environment interactions, are determined by the quality of subsequent environmental conditions. MAVAN is a multidisciplinary, collaborative study that includes several Canadian laboratories.

Sample

The MAVAN sample was drawn from Montreal, Quebec, and Hamilton, Ontario. The sample was enriched for 2 sources of developmental adversity: fetal growth, examining birth weight corrected for gestational age, and maternal emotional distress. Our emphasis is on the influence of fetal growth across the entire population, and thus the birth weights of all MAVAN children fell within the normal range, using Canadian norms.[64] In Montreal, there was an attempt to recruit families with children born with lower birth weights. The Hamilton sample was also recruited from the general population, with a subsample of high-risk women recruited from a mental health clinic (undergoing treatment for depression or anxiety).

Therefore, pregnant women are recruited (usually at 13 to 20 weeks' gestation) from obstetric clinics in hospitals. Women were included in the study if they were 18 years of age and older, and fluent in either English or French. Exclusion criteria include serious obstetric complications during the pregnancy or delivery of the child, extremely low birth weight, prematurity (≤37 weeks' gestation), or any congenital diseases. Ethical approval for this study was obtained from the Douglas Mental Health University Institute (Montreal) and St-Joseph's Hospital (Hamilton).

The study is ongoing. However, we are beginning to get an idea of the sample's retention rate, outlined in Table 1. In light of several time points having multiple assessments, some dyads may be missing information. Additionally, it is possible that some families have skipped assessment. These data should be considered preliminary. Based on the calculations from other longitudinal studies, we consider official participants after the child's birth. The sample is predominantly Caucasian.

Table 2 Maternal measures in the MAVAN protocol

Measure, study	Time point administered, months									
	PN	3	6	12	18	24	36	48	60	72
Arizona Social Support Interview Schedule[67]	PN		PN	PN		PN	PN	PN	PN	PN
Beck Depression Inventory[68]								PN	PN	PN
Breastfeeding Questions	PN	PN	PN	PN	PN	PN				
Center for Epidemiologic Studies Depression Scale[69]	PN		PN	PN		PN	PN	PN	PN	PN
Cambridge Neuropsychological Test Automated Battery[70]								H	H	H
Childbearing Attitudes Questionnaire[71]	PN	PN	PN							
Childhood Trauma Questionnaire[72]	H					PN				
Dutch Eating Behaviour Questionnaire[73]									PN	
Edinburgh Postnatal Depression Scale[74]	PN	PN	PN	PN	PN	PN	PN			
Family History–Research Diagnostic Criteria Data Sheet[75]	H									
Hamilton Anxiety Rating Scale[76]	H	H								
Health behaviours	PN		PN	PN		PN	PN	PN	PN	PN
Home observation for measurement of the environment[77]			PN		PN			PN		
Implicit Association[78] and Lexical Decision Task									PN	
The Job Content Instrument[79]	PN		PN	PN		PN	PN	PN	PN	PN
Life Orientation Test[80]	PN		PN	PN		PN	PN	PN	PN	PN
Marital strain[81]	PN		PN	PN		PN	PN	PN	PN	PN
MINI International Neuropsychiatric Interview[82]	H									
Montgomery Åsberg Depression Rating Scale[83]	H	H								
Parental Authority Questionnaire[84]								PN		
Parental Bonding Inventory[85]		PN	PN							
Parental Health Beliefs Scale[86]	PN									
Parenting Stress Index[87]	PN		PN	PN		PN	PN	PN	PN	PN
The Prenatal Life Events Scale[88]	PN									
Perceived Stress Scale[89]	PN		PN	PN		PN	PN	PN	PN	PN
Quality of Marriage Index[90]	PN		PN	PN		PN	PN	PN	PN	PN
Rosenberg Self-Esteem Scale[91]	PN		PN	PN		PN	PN	PN	PN	PN
Seasonal Pattern Assessment[92]									PN	
Socioeconomic status information	PN		PN	PN		PN	PN	PN	PN	PN
State-Trait Anxiety Inventory[93]	H	PN	PN	PN	PN	PN			PN	

H = Hamilton cohort; MAVAN = Maternal Adversity, Vulnerability and Neurodevelopment;
PN = prenatal assessment was administered at that time point

Procedure and Measures

Mothers were interviewed between 24 and 36 weeks of pregnancy. Dyads were assessed at 3, 6, 12, and 18 months, and yearly from age 24 months onwards. We assessed maternal health and well-being annually using a questionnaire composed of validated short versions of multiple measures (Table 1), as well as standardized measures of mental health focusing on mood. Children were assessed with age-appropriate measures. Children at 6, 12, and 18 months were administered the Bayley Scales of Infant Development for motor, socioemotional and cognitive development.[65] There is an emphasis on school readiness using a validated test battery[66] at 48 months as well as a series of psychopathology screening tools (Table 2). MAVAN examines developmental trajectories in endophenotypes for psychopathology to associate differences in laboratory- or parent-based measures with those that more directly predict mental health outcomes. Thus assessment at 72 months includes validated screening tools for child mental health.

We worked with Brad Sheese to develop computer-based tests of cognitive function in children at 18 and 36 months of age, focusing on attention, habituation, and visual expectation (that is, the ability to anticipate the location of a target in a fixed sequence of presentations).[94] The performance of the children was registered using eye-gaze coding, and the tests emphasize early features of executive functions.[95] An obvious objective of any longitudinal study is that of establishing developmental trajectories within specific functional domains. The challenge is that of selecting tests that permit sufficient variation to meaningfully compare performance

Table 3 Measures of Child Outcomes in the MAVAN protocol

	Time point administered, months								
Measure, study	3	6	12	18	24	36	48	60	72
APGAR scores	S								
Attachment Security				PN[98]		PN			PN[99]
Bayley Scales of Infant Development II[66]		PN	PN	PN		PN			
Behavioral Evaluation Strategies and Taxonomies[100]	PN	PN							
Body Composition						PN	PN	PN	PN
Cambridge Neuropsychological Test Automated Battery[70]							PN	PN	PN
Children's Attributional Style Interview[101]								PN	
Child Behaviour Checklist[102]							PN	PN	
Children's Eating Behaviour Questionnaire[103]							PN		
Child's Health Questions	PN	PN	PN	PN	PN	PN	PN	PN	PN
Children's Sleep Habits Questionnaire[104]							PN	PN	PN
Conners' Rating Scales—Revised[105]								PN	PN
Conners' Kiddie Continuous Performance Test[106]							PN	PN	
Dominic/que[107]									PN
Early Childhood Behavior Questionnaire[108]				PN		PN			
Infant Behaviour Questionnaire[109]	PN	PN							
Infant-Toddler Social and Emotional Assessment[110]				PN	PN				
Koala Fear Questionnaire[111]								PN	
Lollipop Test[112]							PN	PN	
NEPSY[113]							PN		
Number Knowledge[114]							PN	PN	
Peabody Picture Vocabulary Test[115]									
Pediatric Sleep Questionnaire[116]								PN	PN
Preschool Age Psychiatric Assessment[117]									PN
Questions About Sleeping Habits[118]	PN	PN	PN	PN	PN				
Response to Challenge Puzzles[119]								PN	
Random Object Span Task[120]							PN	PN	PN
Separation Questionnaire	PN	PN	PN	PN	PN	PN	PN	PN	PN
Sensitivity to Punishment & Sensitivity to Reward[121]								PN	
Snack Delay[122]						PN			
Snack Test[123]							PN		
Strengths and Difficulties Questionnaire[124]								PN	PN
Theory of Mind[125]								PN	
Visual Expectation Task[94]		PN		PN		PN			
Visual Cued Recall[126]					PN	PN	PN	PN	
Wechsler Preschool and Primary Scale of Intelligence—Revised[127]							PN		

PN = prenatal assessment was administered at that time point; Apgar = Appearance, Pulse, Grimace, Activity, Respiration; MAVAN = Maternal Adversity, Vulnerability and Neurodevelopment; NEPSY = A Developmental NEuroPSYchological Assessment; S = telephone screening at 3 weeks' postpartum

across multiple ages. A test for 6-year-olds may be too difficult for 5-year-olds and too simple for 8-year-olds, and thus preclude the analysis of developmental changes in function. We selected the Cambridge Neuropsychological Testing Automated Battery (commonly referred to as CANTAB),[70] which includes a series of tests derived from clinical neuropsychology, focusing largely on executive functions, and with a range that extends from normal adult to severely impaired patients. Executive functions are critical intermediate phenotypes associated with academic performance,[96] and are better predictors of such than IQ.[97]

Measures of Mother–Child Interactions

MAVAN examines mother–child interactions as a potential mediator or moderator of the influence of specific environmental and genomic factors using various approaches

Table 4 Correlations between subscales of the Ainsworth Scales at age 6 and 18 months

	Month, correlation (*n*)							
Measure, month assessed	1	2	3	4	5	6	7	8
1) Sensitivity, 6	—	0.95[a] (363)	0.94[a] (363)	0.95[a] (363)	0.26[a] (204)	0.27[a] (204)	0.23[a] (204)	0.27[a] (204)
2) Cooperation, 6		—	0.93[a] (363)	0.93[a] (363)	0.26[a] (204)	0.29[a] (204)	0.22[a] (204)	0.29[a] (204)
3) Availability, 6			—	0.94[a] (363)	0.28[a] (204)	0.30[a] (204)	0.25[a] (204)	0.29[a] (204)
4) Acceptance, 6				—	0.31[a] (204)	0.32[a] (204)	0.27[a] (204)	0.33[a] (204)
5) Sensitivity, 18					—	0.91[a] (248)	0.93[a] (248)	0.92[b] (248)
6) Cooperation, 18						—	0.87[a] (248)	0.92[a] (248)
7) Availability, 18							—	0.88[a] (248)
8) Acceptance, 18								—

All correlations are based on the Pearson product–moment correlation

[a] $P < 0.01$; [b] $P < 0.05$

(Table 3). These include quantitative analyses of infant-directed behaviour, as well as measures of inferred maternal qualities, including sensitivity and attunement, using well-validated coding procedures of mother–infant interactions in the home environment as well as structured situations at the laboratory. These measures are acquired at various periods during development. A question of considerable interest is that of interrelation of such measures.

The measures included for comparison are a small selection of behaviours coded using the Behavioral Evaluation Strategies and Taxonomies (commonly referred to as BEST)[100] coding system (Educational Consulting, Inc, Hobe Sound, FL) at 6 months, postpartum. For the purpose of our paper, we focused on behaviours related to maternal sensitivity, that is, the duration the mother spends looking away from the infant (related to inattention) and maternal vocalization toward the child (related to prosocial speech). Also included are Ainsworth Maternal Sensitivity Scales[128] coded from home-videotaped mother–child interaction at 6 and 18 months, concurrently). The Ainsworth scales consist of 4 scales: Acceptance, Availability, Cooperation, and Sensitivity (for operational definitions see Ainsworth[128]). As is typical, these scales were highly correlated at each time point (Table 4), with correlations of more than 0.91 at each time point, thus we used the mean scores in our analyses to represent Maternal Sensitivity. At age 18 and 36 months, we assessed children's attachment security. The present analyses include a measure of attachment at 36 months assessed using the modified Strange Situation paradigm designed for preschool-aged children. The task starts with a 5-minute habituation stage (dyad together), followed by four 5-minute separation and reunion episodes between the child and their mother. Lastly in this matrix is a measure of mother–child interaction at age 48 months based on a laboratory task where the dyad is instructed to produce the image of a house together using an EAS toy. The mother and child each manipulated one of the EAS knobs. A coding system developed by Susan Pawlby and Gesine Schmücker, to measure child, maternal, and dyadic variables, scores included maternal attunement, engagement, and control. We hypothesized that measures of maternal sensitivity would be positive correlated.

Preliminary results (Table 5) indicate that maternal sensitivity significantly correlate with measures made 1.0 and 3.5 years later. The Ainsworth score at 18 months also modestly correlated with the 4-year assessment. This is consistent with research showing the stability of maternal care behaviours over time.[129] However, we extend the literature from previous findings, by showing the stability of maternal sensitivity, during a longer period of time and across types of tasks (for example, free-play and structured laboratory-based tasks). Note that we did not replicate the correlation between maternal sensitivity and child attachment security.[60] This is consistent with meta-analytic evidence that temporally distal assessments of maternal sensitivity and child attachment are a statistically sufficient condition for low effect size linking the 2 constructs.[130] The finding has been interpreted as evidence of low stability in the child's cognitive and (or) emotional models of their world, and an explanation of why well-timed interventions may have dramatic impact on parent–child relations.[130]

The strength of the maternal care analyses are the multiple types of assessment, and independent raters, blinded to child and maternal characteristics. However, these correlations were not exceptionally strong, suggesting that multiple

Table 5 Correlations between measures of maternal care, over time

Measure, month assessed	Month, correlation (*n*)							
	1	2	3	4	5	6	7	8
1) BEST: Look Away, 6	—	–0.08 (335)	0.14[a] (304)	–0.23[b] (212)	–0.07 (124)	–0.07 (124)	–0.00 (125)	–0.03 (256)
2) BEST: Vocalization, 6		—	0.03 (304)	–0.13 (212)	0.09 (109)	–0.05 (124)	0.03 (125)	0.04 (125)
3) Ainsworth Maternal Sensitivity, 6			—	0.29[b] (204)	0.01 (213)	0.36[b] (115)	0.17 (116)	0.26[b] (116)
4) Ainsworth Maternal Sensitivity, 18				—	0.07 (162)	0.34[b] (121)	–0.11 (122)	0.35[b] (122)
5) Attachment, 36					—	0.02 (156)	0.12 (157)	0 (157)
6) EAS Attunement, 48						—	–0.12 (149)	0.79[b] (149)
7) EAS Control, 48							—	–0.28[b] (150)
8) EAS Engagement, 48								—

All correlations are based on the Pearson product–moment correlation, except the correlations with attachment security, which are Spearman

[a] $P < 0.05$; [b] $P < 0.01$

BEST = Behavioral Evaluation Strategies and Taxonomies; EAS = Etch A Sketch

factors influence the stability of maternal care. It will be important to examine what factors influence the stability or change in maternal care and how these changes influence child outcomes within the full sample. Moreover, in the MAVAN sample, we have some sibling data, with which we may eventually compare within-family changes as well.

Conclusion

In sum, the MAVAN project has accumulated considerable data on children 3 months to 6 years of age, using a mixture of traditional rating scales and laboratory-based measures, targeting phenotypes associated with the risk for psychopathology. The present research is drawn from a hypothesis-driven, prospective longitudinal study. The strengths of the MAVAN project are its annual use of detailed laboratory-based measures and the ability to relate such findings to measures of the risk for psychopathology. The sample size of the MAVAN project is growing and will allow the replication of current studies with larger samples. Moreover, the MAVAN study has also come to include the siblings of our participants, providing unique opportunities for mother–child studies within the same family.

MAVAN is also expanding in relation to the current state of knowledge and technology. We have recently completed a genome-wide methylation examining the epigenetic state of about 500K CpG (cytosine and guanine separated by only 1 phosphate) dinucleotides using epithelial cells of buccal origin. There are clearly limitations associated with such so-called proxy measures, but embedding such data within the rich environmental and phenotypic information available within MAVAN and genotyping provides an ideal platform for the integration of epigenetics. This approach certainly complements the overriding Gene × Environment theme. As with other measures of phenotype, there are unique opportunities to use longitudinal strategies, allowing researchers to examine changes in epigenetic marks in relation to selected forms of experience and in concert with phenotypic variation. Taken together, these data allow for a comprehensive and nuanced understanding of the different types of maternal experiences and effects on offspring phenotypes.

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