Maternal and Early Postnatal Nutrition and Mental Health of Offspring by Age 5 Years: A Prospective Cohort Study

Felice N. Jacka, Ph.D., Eivind Ystrom, Ph.D., Anne Lise Brantsaeter, Ph.D., Evalill Karevold, Ph.D., Christine Roth, M.Sc., Margaretha Haugen, Ph.D., Helle Margrete Meltzer, Ph.D., Synnve Schjolberg, M.A., Michael Berk, Ph.D.

Objective: Diet quality is related to the risk for depression and anxiety in adults and adolescents; however, the possible impact of maternal and early postnatal nutritional exposures on children's subsequent mental health is unexplored. **Method:** The large prospective Norwegian Mother and Child Cohort Study recruited pregnant women between 1999 and 2008. Data were collected from mothers during pregnancy and when children were 6 months and 1.5, 3, and 5 years of age. Latent growth curve models were used to model linear development in children's internalizing and externalizing problems from 1.5 to 5 years of age as a function of diet quality during pregnancy and at 1.5 and 3 years. Diet quality was evaluated by dietary pattern extraction and characterized as "healthy" or "unhealthy." The sample comprised 23,020 eligible women and their children. Adjustments were made for variables including sex of the child, maternal depression, maternal and paternal age, maternal educational attainment, household income, maternal smoking before and during pregnancy, mothers' parental locus of control, and marital status. **Results:** Higher intakes of unhealthy foods during pregnancy predicted externalizing problems among children, independently of other potential confounding factors and childhood diet. Children with a high level of unhealthy diet postnatally had higher levels of both internalizing and externalizing problems. Moreover, children with a low level of postnatal healthy diet also had higher levels of both internalizing and externalizing problems. **Conclusion:** Among this large cohort of mothers and children, early nutritional exposures were independently related to the risk for behavioral and emotional problems in children. J. Am. Acad. Child Adolesc. Psychiatry, 2013;■(■):■–■. **Key Words:** anxiety, diet, depression, externalizing, internalizing

Although the World Health Organization has identified unipolar depressive disorders as accounting for the largest burden of disability in middle- and high-income countries,[1] psychiatry currently lacks effective universal public health strategies for the prevention of mental illness. Importantly, given that half of mental illnesses first manifest before 14 years of age,[2] identification of early-life risk factors and, hence, targets for prevention is imperative. This is particularly cogent in the context of the "double hit" hypothesis, wherein detrimental neonatal exposures may predispose to adult psychopathology in the presence of later environmental risk factors.[3]

The fundamental contribution made by habitual dietary behaviors to the risk for, and progression of, chronic noncommunicable physical illnesses is now well understood; however, it is only in the last 3 years that credible evidence has been generated indicating that dietary quality also contributes to the risk for the common mental illnesses, depression, and anxiety, in both adults and adolescents.[4-9] However, the possible impact of very early life nutritional exposures on children's subsequent mental health is unexplored. Given the known impact of maternal and early life nutrition on later physical health in offspring,[10] this is a notable gap in the knowledge base.

CG Clinical guidance is available at the end of this article.

Deficiencies of certain nutrients during critical phases in brain development may result in irreversible functional changes to the brain, the most vulnerable period being pregnancy and the first 2 to 3 years of life, in which there is rapid brain growth.[11] Maternal exposure to famine during pregnancy results in an elevated risk for major depression in offspring,[12,13] supporting a link between maternal nutrition and children's neurodevelopment. Moreover, a rapidly developing evidence base from preclinical studies indicates an important role for maternal diet in influencing the development of neurotransmitter systems in offspring,[14,15] while maternal and early infant nutrition modulates the immunologic development of offspring,[16] which may in turn influence the risk for later mental health problems.[17,18] A maternal "western" diet, high in fats and sugars, and obesity increased sympathetic nervous system activity and hyperactivity in rodent offspring that persisted into adulthood,[19] indicating a direct causal relationship between maternal dietary exposures and lifetime behavioral outcomes related to mood disorders.[20] Moreover, deficiencies in omega-3 fatty acids during in utero development and early life reduce brain plasticity and increase anxiety-like behaviors in adult mice.[21] Synaptic plasticity and neurotrophin levels are of particular relevance to mood disorders in human beings.[22,23]

Taken together with the previous observational findings, these data indicate a role for early-life nutritional exposures in the vulnerability to mental health problems in children. Therefore, in this study, we aimed to examine the relationship between the quality of both mothers' diets during pregnancy and children's diets in the first years of life, and behavioral markers of mental health problems in children, taking into account other variables that may explain such relationships. We hypothesized that both a low intake of healthy, nutrient-dense foods, and a high intake of unhealthy foods by mothers during pregnancy and children during early childhood would be independently related to children's internalizing and externalizing behaviors from 18 months to age 5 years.

METHOD

The large, ongoing Norwegian Mother and Child Cohort Study (MoBa) is conducted by the Norwegian Institute of Public Health.[24] Between 1999 and 2008, invitations were sent by mail to pregnant women across Norway concurrent with the routine ultrasound examination offered to all pregnant women at their local hospital around week 17 of pregnancy. The participation rate was 38.5%, with more than 108,000 births enrolled during the recruitment period. When pregnant mothers consented to participate, approximately 78% of the fathers also consented. Informed consents and approvals by the Regional Committee for Medical Research Ethics and Norwegian Data Inspectorate were obtained. Self-report questionnaires were sent to the mothers and fathers at 17 weeks of gestation, and to mothers only later in pregnancy and at intervals after birth when children were 6 months, 1.5, 3, and 5 years old. Response rates during pregnancy were 91% to 95%, and response rates for assessments after birth were 84.8%, 72.4%, 58.5%, and 53.4%, respectively. Pregnancy and birth records from the Medical Birth Registry of Norway (MBRN) were linked to the MoBa database.[25] The current study is based on version 6 of the data files, released for research in 2011. Our final sample comprised all of the 23,020 eligible women and their children that had received the 5-year questionnaire.

Maternal Diet

A food frequency questionnaire (FFQ) was specifically developed for assessment of maternal diet in MoBa. The MoBa FFQ[26] has been used from February 2002 and onward. It is semiquantitative and designed to capture dietary habits and intake of dietary supplements during the first 4 to 5 months of pregnancy. The frequency of consumption was given per day, per week, and/or per month, depending on the food item. Food frequencies were converted into food amounts (g/day), and daily intakes of the 255 food and beverage items in the FFQ were aggregated into 58 nonoverlapping food groups and used as input variables for extraction of dietary patterns using principal components analysis.[27] Two major dietary patterns, a "healthy" pattern characterized by high intake of vegetables, fruit, high-fiber cereals, and vegetable oils, and an "unhealthy" pattern characterized by high intake of processed meat products, refined cereals, sweet drinks, and salty snacks. The dietary patterns identified in the current study parallel those identified and described in more detail in a previous MoBa study.[28] The MoBa FFQ has been thoroughly validated against a dietary reference method and several biological markers.[29]

Child Diet

Mothers described the current diets of their children at 18 months using a 36-item FFQ comprising dietary items on types of foods and drinks such as dairy products, cereal-based porridge, and fruit juice.[30] Response categories ranged from "never" to "5 or more times a day" for drinks, and from "never" to "3 or more times a day" for foods. At 3 years, mothers answered questions on a food frequency questionnaire with 37 items. For each food and drink item, mothers

reported the frequency of consumption in a usual month using response categories ranging from "never or less than 1 serving per week" to "4 or more servings per day" for nondinner foods and drinks and "once or less per month" to "5 or more times per week" for dinner foods. To assess children's diet quality at 1.5 and 3 years, we combined the 1.5- and 3-year data in a common factor with fixed effects (i.e., equal factor loadings) across time. The common factor had a variance of unity and mean of 0. We used these data to replicate 2 dietary patterns previously identified in MoBa with factor scores from factor analysis for ordinal data.[30,31] The factor loadings were 0.70 for the unhealthy and 0.73 for the "healthy" dietary pattern. The "unhealthy" factor described a pattern of eating characterized by consumption of chips, buns, cakes, waffles, chocolate, cookies, sweets, soda, ice cream, popsicles, bread with jam or honey, pizza, and soda with artificial sweeteners. The "healthy" factor describes a pattern characterized by consumption of white fish, oily fish, boiled vegetables, raw vegetables, fruit, bread with fish products, egg, bread with meat, Norwegian brown cheese, and fish products. The 2 factors, "unhealthy" and "healthy" diet, were modestly inversely associated ($r = -0.11$; 95% CI $= -0.09$ to -0.12).

Child Behavior Checklist

At ages 1.5, 3, and 5 years, we used a short form of the Child Behavior Checklist (CBCL) to assess internalizing (5 items) and externalizing (8 items) problems.[32] The CBCL is the most renowned parental report tool of behavioral problems for young children. Adequate sensitivity (71%) and specificity (92%), and prediction of psychiatric disorders has been found in a Norwegian sample.[33] Latent factor analysis of the MoBa subset of CBCL questions loaded clearly on the 2 expected constructs of internalizing and externalizing, and the subset of 11 items at 36 months in MoBa was found to correlate 0.92 with the full original externalizing scale using data from the National Institute of Child Health and Human Development (NICHD) Study of Early Child Care and Youth Development.[34] Internalizing behaviors capture symptoms of anxiety and depression, whereas externalizing behaviors encompass symptoms of oppositional defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder. The same items were used at all time points; as such, we combined the data across the 3 time points, using factor analysis, to create a common factor with fixed effects across time.

Covariates

To assess possible confounding, we included the following variables in our analyses chosen a priori on theoretical grounds: sex of the child; maternal and paternal age; parity and length of gestation; maternal educational attainment; household income; maternal smoking before and during pregnancy; mothers' parental locus of control (at 3 years)[31]; stay-at-home mother (1.5 and 3 years); and marital status (1.5 and 3 years). We also adjusted for maternal depressive symptoms at week 30 of pregnancy, and 1.5 and 3 years postpartum using data from a short version of the Hopkins Symptom Checklist (SCL-8).[35]

Statistical Analysis

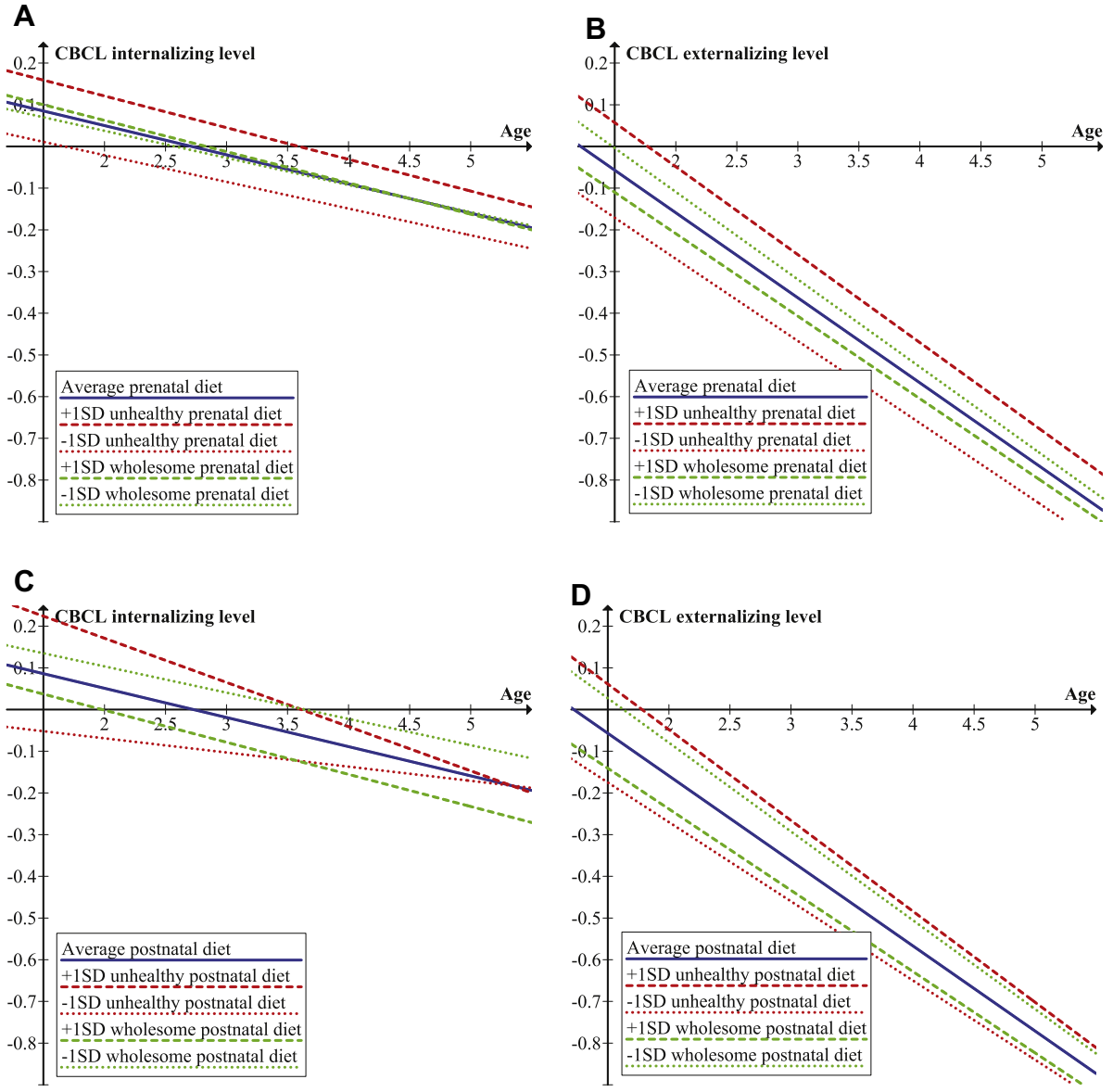
In behavioral sciences, nonresponse is seldom completely missing at random. Therefore, we estimated nonresponse in the data for all mother–child dyads having received the 5-year questionnaire using multiple imputation with 50 data sets. In multiple imputation, bias due to missingness as a function of measured variables, the so-called "missing at random assumption," is corrected for. When using multiple imputation, standard errors are not deflated due to data imputation. To improve interpretability of effect sizes, the child internalizing/externalizing scales and maternal depressive symptoms scales were standardized according to the variance at the first time point. We used latent growth curves to model linear development in internalizing and externalizing problems from 1.5 to 5 years of age.[36] In latent growth curves, 2 outcome factor variables were constructed: an intercept factor, comprising all individual differences at time 0; and a slope factor, comprising all individual differences in growth from there on. The intercepts of the mental health variables were set to 0, and the means of the intercept factor and slope factor were estimated.

We regressed the intercept and slope factors of the latent growth curves on covariates using linear regression. All the adjusting variables were entered into the regression analysis at the same time as the dietary factors. However, to have a reference point for the effect sizes, we particularly show the effect of 1 covariate: maternal depression. After initial adjustments for listed covariates, further adjustment was made for dietary patterns at the other time points (i.e., either prenatal or postnatal diet). This was done to assess the independent contribution of the pre- or postnatal dietary exposures to the variance in children's internalizing and externalizing. Analyses were computed in Mplus version 6.1 and estimated using maximum likelihood with robust standard errors.

RESULTS

Figure 1 provides a graphical depiction of the children's externalizing and internalizing behaviors as a function of both maternal and child dietary patterns. The intercept describes the level of internalizing or externalizing behaviors at 18 months, whereas the slopes describe the trajectory of such behaviors over the ensuing assessment periods to age 5. The lines in Figure 1 depict both "healthy" dietary patterns (in green) and

FIGURE 1 Relationship between healthy and unhealthy dietary pattern scores 1 standard deviation above and below the mean, and internalizing and externalizing (y axis) in children from 18 months to 5 years (x axis). Note: (A) Prenatal (mothers') diet quality and internalizing; (B) prenatal (mothers') diet quality and externalizing; (C) postnatal (children's) diet quality and internalizing; (D) postnatal (children's) diet quality and externalizing. Blue line indicates mean of internalizing/externalizing behaviors. CBCL = Child Behavior Checklist.



"unhealthy" dietary patterns (in red), as well as the mean of the internalizing or externalizing behaviors (in blue), and are presented for both 1 SD above and 1 SD below the mean dietary pattern score. Before standardization according to the mean and SD at 1.5 years for analyses, the mean ± SD for short form CBCL at 1.5 years was 1.33 ± 0.30 for internalizing and 1.53 ± 0.30 for externalizing. The means ± SD before standardization for SCL at week 30 of gestation, 1.5 years postpartum, and 3 years postpartum were 1.26 ± 0.36, 1.29 ± 0.37, and 1.28 ± 0.40, respectively. The dietary factors are originally computed as standardized variables with a variance of 1 and a mean of 0.

Table 1 gives the correlations between the dietary factors and children's behavioral problems. Table 2 shows the coefficients for the intercept and slope: the intercept describing the relationship between the dietary pattern and the level of

TABLE 1 Correlations Between Dietary Factors and Child Behavior Problems at 1.5, 3, and 5 Years (y)

	Internalizing Problems			Externalizing Problems		
	1.5 y	3 y	5 y	1.5 y	3 y	5 y
Prenatal unhealthy diet	0.07**	0.06**	0.06**	0.11**	0.11**	0.09**
Prenatal healthy diet	0.01	0.01	−0.01	−0.05**	−0.05**	−0.05**
Postnatal unhealthy diet	0.07**	0.06**	0.01	0.06**	0.05**	0.04**
Postnatal healthy diet	−0.04**	−0.04**	−0.04**	−0.05**	−0.04**	−0.03*

Note: *p < .05; **p < .01.

internalizing and externalizing behaviors at 18 months, whereas the slope gives an indication of whether the level of behavior problems increase, decrease, or remain consistent over the follow up period as a function of dietary patterns. The intercept coefficients can be interpreted in the same way as beta coefficients in standard regression analyses. All reported coefficients are mutually adjusted for each other and standardized, meaning that they are directly comparable.

In Figure 1 A and B, it can be seen that children whose mothers had an unhealthy dietary pattern that was 1 standard deviation above the mean had consistently higher internalizing and externalizing scores compared to those whose mothers' scores were 1 SD below the mean on the unhealthy dietary pattern. The positive relationship between higher maternal unhealthy diet and externalizing behaviors was not confounded by other factors, nor explained by children's diets in the postnatal period (intercept coefficients Table 2). For these children exposed to a higher intake of unhealthy diet during pregnancy, the high level of externalizing problems also lasted throughout the period of follow-up. On the other hand, the initial positive relationship between higher scores on maternal unhealthy diet and internalizing behaviors was fully explained by the contribution to internalizing by children's diets at 18 and 36 months (intercept coefficients shown in Table 2).

In regard to maternal healthy diet and internalizing and externalizing behaviors (Figure 1 A and B), the results were divergent. Children of mothers with higher intakes of healthy foods had lower externalizing scores compared to children of mothers with lower intakes, both before and after adjustments for potential confounders; however, this relationship was explained by children's diets in the postnatal period (intercept coefficients Table 2). Conversely, children of mothers with higher intakes of healthy foods had higher internalizing scores compared to children of mothers with lower intakes, and this relationship was maintained after all adjustments (intercept coefficients Table 2).

Figure 1 C and D graphically display the relationships between children's dietary patterns at 18 and 36 months and both internalizing and externalizing behaviors between 18 months and 5 years. In regard to unhealthy diets, children with higher scores had both higher internalizing and externalizing behaviors compared to those with lower scores, although the strength of the relationship between unhealthy diets and internalizing problems diminished over the follow-up period. Children with a low level of healthy diet also had higher levels of both internalizing and externalizing problems compared to those with higher scores. Neither the effect of unhealthy diet nor the effect of healthy postnatal diet could be explained by maternal depressive symptoms, other confounding factors, or prenatal diet (intercept coefficients shown in Table 2).

DISCUSSION

In this study, we report highly novel data suggesting that maternal and early postnatal dietary factors play a role in the subsequent risk for behavioral and emotional problems in children. Both an increased intake of unhealthy foods and a decreased intake of nutrient-rich foods in early childhood were independently related to higher internalizing and externalizing behaviors in young children. These behaviors are established early markers for later mental health problems.[37] In addition, children whose mothers had higher intakes of unhealthy foods during pregnancy displayed higher levels of externalizing behaviors, and this effect was independent of the contribution made by postnatal diet to the variance in externalizing. Importantly, the size of the standardized coefficients for many of the dietary exposures was of a similar magnitude to those for maternal depression, a well-established contributor to the mental health of offspring.[38]

TABLE 2 Change and Stability in Internalizing and Externalizing Problems From 1.5 to 5 Years Predicted by Pre- and Postnatal Diet Adjusted for Maternal Depression and Other Confounding Factors

		Internalizing[a]					
		Unadjusted		Adjusted for Covariates[c]		Adjusted for Covariates and Diet at Other Time Points	
		Intercept Factor	Slope Factor	Intercept Factor	Slope Factor	Intercept Factor	Slope Factor
Prenatal diet	Unhealthy	0.074**	−0.006*	0.034**	−0.002	0.003	0.004
	Healthy	0.015*	−0.005	0.018*	−0.006	0.046**	−0.007*
Maternal depressive symptoms	Week 30 of pregnancy	—	—	0.095**	0.012	0.093**	0.012
Postnatal diet	Unhealthy	0.138**	−0.036**	0.109**	−0.026**	0.110**	−0.028**
	Healthy	−0.049**	−0.007	−0.026**	−0.007	−0.048**	−0.003
Maternal depressive symptoms[d]	1.5 y postpartum	—	—	0.174**	−0.013	0.172**	−0.013
	3 y postpartum	—	—	0.091**	0.028*	0.088**	0.028**
		Externalizing[b]					
		Unadjusted		Adjusted for Covariates[c]		Adjusted for Covariates and Diet at Other Time Points	
		Intercept Factor	Slope Factor	Intercept factor	Slope factor	Intercept factor	Slope factor
Prenatal diet	Unhealthy	0.114**	−0.007*	0.052**	−0.006*	0.036**	−0.002
	Healthy	−0.053**	0.006*	−0.021**	0.003	−0.005	−0.001
Maternal depressive symptoms[d]	Week 30 of pregnancy	—	—	0.106**	0.000	0.105**	−0.001
Postnatal diet	Unhealthy	0.118**	−0.014**	0.071**	−0.012**	0.057**	−0.011**
	Healthy	−0.084**	0.009**	−0.033**	0.008*	−0.030**	0.008*
Maternal depressive symptoms	1.5 y postpartum	—	—	0.242**	−0.018	0.241**	−0.018
	3 y postpartum	—	—	0.067**	0.030**	0.067**	0.030**

Note: All coefficients are standardized and directly comparable. The intercept factor represents the problem level at 1.5 years (y) and stability from there on. The slope factor represents linear change in problems from 1.5 years to 5 years.

[a]*Mean and variance of growth factors for internalizing: intercept = 0.085 and 0.537; slope = −0.070 and 0.048.*

[b]*Mean and variance of growth factors for externalizing: intercept = 0.057 and 0.596; slope = −0.204 and 0.052.*

[c]*Sex of child; maternal and paternal age; parity and length of gestation; maternal educational attainment; household income; maternal smoking before and during pregnancy; mothers' parental locus of control (at 3 years); stay-at-home mother (1.5 and 3 years); marital status (1.5 and 3 years); and maternal depression.*

[d]*Standardized coefficients for maternal depression shown separately to provide comparison of size of effect.*

*p < .05; **p < .01.

To our knowledge, this is the first study to explicitly examine the relationship between early life nutritional exposures and measures of vulnerability to mental health problems in children, and the results were largely concordant with our hypotheses. The only outcome that was discordant with our expectations was the finding that higher intakes of healthy foods by mothers during pregnancy were related to higher levels of internalizing behaviors in children. It is unclear as to why this relationship was apparent, although it may suggest a possible confounding effect of maternal anxiety. It is plausible to hypothesize that anxious mothers would be more likely to adhere to good dietary behaviors in pregnancy, and that such anxiety in the mothers would be, in turn, related to children's internalizing symptoms. Previous research has shown that women with higher anxiety levels are more likely to report weight-restrictive behaviors during pregnancy.[39] In this study, we controlled for maternal depression with the Hopkins Symptom Checklist—8 (HSCL-8), which captures symptoms of psychological distress including anxiety; however, it may be that aspects of anxiety were not fully captured by this questionnaire.

Of note were the slopes describing the trajectory of internalizing behaviors in children both high and low in unhealthy dietary intakes. These slopes showed convergence over the period to the age of 5 years (indicated visually in Figure 1 C and by the coefficients for slopes in Table 2), suggesting that the impact of unhealthy foods on internalizing may be most evident in early life but may diminish over time as the impact of other environmental exposures come into play. This was not the case for the relationship between unhealthy foods and the trajectory of externalizing behaviors, which remained consistent and significant over the follow-up period. It is unclear as to why there might be differences between internalizing and externalizing in the the relationship of these children to unhealthy foods. In contrast, the trajectory of the slopes for internalizing and externalizing in children high and low in nutrient-dense foods tended to suggest a divergence over time (observable visually in Figure 1 C and D and statistically in Table 2). This suggests that the impact of inadequate nutrition in early childhood on mental health vulnerability may be more profound the longer the period of exposure to such a diet.

The finding that dietary patterns were related to markers of mental health in children is concordant with previous research showing that measures of diet quality (both healthy and unhealthy) are related to mental health and depression in adolescents and to common mental disorders, depression and anxiety, in adults. For example, we have previously reported that adolescents reporting a diet habitually low in nutrient-dense foods were more likely to report case-level depressive symptomatology, whereas those consuming diets high in unhealthy and take-out/take-away foods were more likely to be depressed.[5] These relationships between measures of diet quality and the likelihood of adolescent depression were independent of numerous measures of parental sociodemographic factors, familial factors, and other health behaviors. Similarly, in a study of approximately 3,000 adolescents, we found independent dose–response relationships between both lower intakes of healthy foods and higher intakes of unhealthy foods and poorer mental health cross-sectionally, whereas over time, lower intakes of healthy, nutrient-dense foods predicted poorer mental health outcomes 2 years later, even after adjustment for mental health at baseline. Perhaps most importantly, dietary improvement over the 2-year period was linked to improvements in mental health, whereas individuals whose diet quality diminished over the same period had poorer mental health at the end of the study.[7] More recently, a study in German children reported that higher intakes of confectionary, but not sugar-sweetened drinks or savory snacks, was associated with increased emotional problems, whereas higher diet quality scores were related to reduced odds for such problems.[40] Our findings are also concordant with the numerous studies now published reporting both cross-sectional and prospective relationships between dietary patterns and common mental disorders in adults.[4,6,8,9]

Of particular interest is the relative contribution of each dietary pattern to the variance in internalizing and externalizing, in that there was a consistently great effect of unhealthy diets compared to that of healthy diets. These dietary patterns were only weakly correlated, indicating that they are not just the inverse of each other. An individual can be high or low on both dietary patterns (for example, one might eat a diet high in nutrient-dense foods but may also consume many processed and unhealthy foods). Both dietary patterns may, theoretically, independently influence pathophysiologies relevant to mental

disorders.[41] In animal models, sugary, high-fat diets, independently of nutrient deficiencies, reduce plasticity in areas of the brain highly salient to mental health,[42,43] and this may be one pathway by which both maternal and early childhood nutrition influences children's mental health. In nonhuman primates, maternal high-fat (HF) diet caused disturbances in fetal central serotonergic systems, including an increase in the gene expression for the rate-limiting enzyme for serotonin synthesis.[14] Maternal HF diet also resulted in increased anxiety-like behaviors in female primate offspring and increased aggression in male offspring. Also in animal models, maternal HF diet has been shown to alter the expression of dopaminergic signaling molecules in key brain regions of offspring, along with altered expression of opioid-related genes and global hypomethylation across all studied brain regions.[15] Weaning of offspring onto a HF diet resulted in the upregulation of inflammatory and oxidative stress pathways and mitochondrial dysfunction,[16] which may also be of relevance, given the data indicating a role for each of these factors in depression.[17,18] Finally, maternal HF diet has also been shown to result in reduced maternal care by dams during the early life of offspring, suggesting another possible pathway by which maternal diet may influence the mental health of children.[44]

The human genome is most vulnerable to environmental factors during early development and disturbances of epigenetic gene regulation as a result of intrauterine exposures during pregnancy are likely play a role in the developmental programming of mental health vulnerability in offspring.[45] However, although it is becoming clear that epigenetic mechanisms influence the risk for later metabolic and cardiovascular disorders in human beings,[46] the existing research supporting such mechanisms in brain development is primarily to be found in animal models to date. As such, future research should also focus on the epigenetic mechanisms that may mediate links between early life nutrition and later mental health.

The major strengths of this study comprise the large and representative cohort of mothers and children, the detailed data gathered, and the prospective design, which limits the problems associated with recall bias and reverse causality. An additional strength is the use of dietary patterns as measures of diet quality, which avoids the potential pitfall of ascribing preconceived values to "healthy" and "unhealthy" dietary components. Measurement of markers of childhood mental health was made using a well-established and widely used tool. Finally, the use of latent growth curves to model the trajectories of internalizing and externalizing behaviors as a function of diet quality is a statistical method that affords a valuable diagrammatic depiction of the relationships under examination and a sensitive measure of the relationships that minimizes the impact of measurement error.

On the other hand, although we adjusted for numerous variables determined a priori to be potential confounders, we cannot exclude the possibility of residual or unmeasured confounding. For example, although we controlled for important variables that have the potential to confound the diet–mental health relationship, such as maternal depression, parental locus of control, and measures of education and socioeconomic status (SES), we may not have captured salient aspects of maternal psychopathology, SES, the home environment, or other factors that may have an impact on both mothers' and children's diets and children's mental health. However, it should be noted that previous studies examining the relationship between diet quality and mental health in young adolescents have not found factors such as SES, family conflict, and poor family management to explain the relationships observed.[5] Another potential explanation of the observed relationships relates to response bias; mothers with mental health problems may answer questions regarding their own diets, their children's diets, and/or their children's behaviors differently from mothers without such problems. Also potentially problematic is the reliance on maternal reports only to assess children's mental health. Data from multiple informants may be a more reliable method of assessment. Another concern is selection bias, given that less than 40% of women who were approached participated in the MoBa. Previous investigation of this issue has identified that mothers participating in the MoBa have higher levels of education, are slightly older, less likely to smoke, and are more likely to be first-time mothers compared to the broader population. Although an examination of 8 exposure–outcome associations in this cohort with the associations in the Medical Birth Registry of Norway found no evidence of selection bias on association estimates,[47] it may be that the results that we have reported here are not necessarily representative of the entire population. On the

other hand, the nature of the differences in the MoBa cohort compared to the general population, given that higher education, increased age, and nonsmoking are related to both better dietary habits and less depression, would likely bias our results toward the null. Finally, we were not able to examine the mechanisms by which maternal or child diet may have affected child mental health.

Diet quality is a key modifiable risk factor for the development of other noncommunicable somatic diseases, and the discussion regarding the need for policy initiatives targeting unhealthy,diets[48,49] including taxation,[50,51] is becoming more strident. In 2011, a consortium of researchers, advocates, and clinicians nominated the identification of "modifiable social and biological risk factors across the life course" as their number one priority among the grand challenges in global mental health.[52] The second major goal was to "advance prevention and implementation of early interventions." These new data suggest that a population health approach to the problem of the common mental disorders focused on dietary improvements and food policies may support these goals.[53]

CG Clinical Guidance

- Consuming a diet higher in unhealthy foods during pregnancy may increase the vulnerability for later mental health problems in children.
- Young children consuming a diet high in unhealthy foods, and/or a diet low in nutrient-dense foods, such as vegetables, display increased behaviors signifying mental health problems.
- Clinicians should discuss the possibility that good nutrition for mothers during pregnancy and for children in early life is important for children's mental health as well as for their physical health.

In conclusion, our study data support the hypothesis that early life nutritional exposures play a role in modulating early vulnerability factors for mental health problems in children. These findings offer further support for the contention that good dietary practices are of considerable importance to mental health, as well as to physical health, across the lifespan.[54] &

Accepted July 12, 2013.

Dr. Jacka is with the IMPACT Strategic Research Centre, Deakin University, and the University of Melbourne. Dr. Ystrom is with the Norwegian Institute of Public Health. Drs. Brantsaeter, Meltzer, and Haugen are with the Division of Environmental Medicine, Norwegian Institute of Public Health. Dr. Karevold, Ms. Roth, and Ms. Schjolberg are with the Division of Mental Health, Norwegian Institute of Public Health. Dr. Karevold is also with the University of Oslo. Dr. Berk is with the School of Medicine at Deakin University, the Florey Institute of Neuroscience and Mental Health, and the Orygen Research Centre at the University of Melbourne.

The Norwegian Mother and Child Cohort Study is supported by the Norwegian Ministry of Health and the Ministry of Education and Research, the National Institutes of Health (NIH)/National Institute of Environmental Health Sciences (NIEHS) (contract no NO1-ES-75558), NIH/National Institute of Neurological Disorders and Stroke (NINDS) (grants UO1 NS 047537-01 and UO1 NS047537-06A1), and the Norwegian Research Council/Functional Genomics in Norway (FUGE) (grant 151918/S10).

This study was funded by the Brain and Behaviour Research Institute (formerly NARSAD). Dr. Jacka also gratefully acknowledges current and previous grant/research support from the National Health and Medical Research Council (NHMRC); Australian Rotary Health; the Geelong Medical Research Foundation; the Ian Potter Foundation; and the University of Melbourne. Dr. Jacka is currently supported by an NHMRC fellowship (#628912).

Dr. Ystrom served as the statistical expert for this research.

The authors are grateful to all of the participating families in Norway who take part in this ongoing cohort study.

Disclosure: Drs. Jacka, Ystrom, Brantsaeter, Karevold, Haugen, Meltzer, and Berk, and Ms. Roth and Ms. Schjolberg report no biomedical financial interests or potential conflicts of interest.

Correspondence to Felice N. Jacka, Ph.D., Deakin University, P.O. Box 281, Geelong 3220, Australia; e-mail: felice@barwonhealth.org.au

http://dx.doi.org/10.1016/j.jaac.2013.07.002

REFERENCES

1. World Health Organisation (WHO). The Global Burden of Disease: 2004 Update. Geneva: World Health Organisation; 2004.
2. Kessler RC, Berglund P, Demler O, Jin R, Merikangas KR, Walters EE. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. Arch Gen Psychiatry. 2005;62:593-602.
3. Walker AK, Nakamura T, Byrne RJ, *et al*. Neonatal lipopolysaccharide and adult stress exposure predisposes rats to anxiety-like behaviour and blunted corticosterone responses: implications for the double-hit hypothesis. Psychoneuroendocrinology. 2009;34:1515-1525.
4. Jacka FN, Pasco JA, Mykletun A, *et al*. Association between western and traditional diets and depression and anxiety in women. Am J Psychiatry. 2010;167:305-311.
5. Jacka FN, Kremer PJ, Leslie E, *et al*. Associations between diet quality and depressed mood in adolescents: results from the Healthy Neighbourhoods study. Aust N Z J Psychiatry. 2010;44:435-442.
6. Jacka FN, Mykletun A, Berk M, Bjelland I, Tell GS. The association between habitual diet quality and the common mental disorders in community-dwelling adults: the Hordaland Health study. Psychosom Med. 2011;73:483-490.
7. Jacka F, Kremer PJ, Berk M, *et al*. A prospective study of diet quality and mental health in adolescents. PLoS One. 2011;6:e24805.
8. Akbaraly TN, Brunner EJ, Ferrie JE, Marmot MG, Kivimaki M, Singh-Manoux A. Dietary pattern and depressive symptoms in middle age. Br J Psychiatry. 2009;195:408-413.

9. Sanchez-Villegas A, Delgado-Rodriguez M, Alonso A, *et al*. Association of the Mediterranean dietary pattern with the incidence of depression: the Seguimiento Universidad de Navarra/University of Navarra follow-up (SUN) cohort. Arch Gen Psychiatry. 2009;66:1090-1098.
10. Barker DJ. Maternal nutrition, fetal nutrition, and disease in later life. Nutrition. 1997;13:807-813.
11. Benton D, a.i.s.b.l IE. Micronutrient status, cognition and behavioral problems in childhood. Eur J Nutr. 2008;47(Suppl 3):38-50.
12. Brown AS, Susser ES, Lin SP, Neugebauer R, Gorman JM. Increased risk of affective disorders in males after second trimester prenatal exposure to the Dutch hunger winter of 1944-45. Br J Psychiatry. 1995;166:601-606.
13. Brown AS, van Os J, Driessens C, Hoek HW, Susser ES. Further evidence of relation between prenatal famine and major affective disorder. Am J Psychiatry. 2000;157:190-195.
14. Sullivan EL, Grayson B, Takahashi D, *et al*. Chronic consumption of a high-fat diet during pregnancy causes perturbations in the serotonergic system and increased anxiety-like behavior in nonhuman primate offspring. J Neurosci. 2010;30:3826-3830.
15. Vucetic Z, Kimmel J, Totoki K, Hollenbeck E, Reyes TM. Maternal high-fat diet alters methylation and gene expression of dopamine and opioid-related genes. Endocrinology. 2010;151:4756-4764.
16. Bruce KD, Cagampang FR, Argenton M, *et al*. Maternal high-fat feeding primes steatohepatitis in adult mice offspring, involving mitochondrial dysfunction and altered lipogenesis gene expression. Hepatology. 2009;50:1796-1808.
17. Maes M, Fisar Z, Medina M, Scapagnini G, Nowak G, Berk M. New drug targets in depression: inflammatory, cell-mediated immune, oxidative and nitrosative stress, mitochondrial, antioxidant, and neuroprogressive pathways. And new drug candidates—Nrf2 activators and GSK-3 inhibitors. Inflammopharmacology. 2012;20:127-150.
18. Pasco JA, Nicholson GC, Williams LJ, *et al*. Association of high-sensitivity C-reactive protein with de novo major depression. Br J Psychiatry. 2010;197:372-377.
19. Fernandes C, Grayton H, Poston L, *et al*. Prenatal exposure to maternal obesity leads to hyperactivity in offspring. Mol Psychiatry. 2012;17:1159-1160.
20. Sachs GS, Baldassano CF, Truman CJ, Guille C. Comorbidity of attention deficit hyperactivity disorder with early- and late-onset bipolar disorder. Am J Psychiatry. 2000;157:466-468.
21. Bhatia HS, Agrawal R, Sharma S, Huo YX, Ying Z, Gomez-Pinilla F. Omega-3 fatty acid deficiency during brain maturation reduces neuronal and behavioral plasticity in adulthood. PLoS One. 2011;6:e28451.
22. Duman RS. Pathophysiology of depression: the concept of synaptic plasticity. Eur Psychiatry. 2002;17(Suppl 3):306-310.
23. Malberg JE, Eisch AJ, Nestler EJ, Duman RS. Chronic antidepressant treatment increases neurogenesis in adult rat hippocampus. J Neurosci. 2000;20:9104-9110.
24. Magnus P, Irgens LM, Haug K, Nystad W, Skjaerven R, Stoltenberg C. Cohort profile: the Norwegian Mother and Child Cohort Study (MoBa). Int J Epidemiol. 2006;35:1146-1150.
25. Irgens LM. The Medical Birth Registry of Norway; a source for epidemiological and clinical research. Scand J Rheumatol Suppl. 1998;107:105-108.
26. MoBa. Food Frequency Questionnaire. Available at: http://www.fhi.no/dokumenter/011fbd699d.pdf. Accessed August 1, 2013.
27. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. Curr Opin Lipidol. 2002;13:3-9.
28. Brantsaeter AL, Haugen M, Samuelsen SO, *et al*. A dietary pattern characterized by high intake of vegetables, fruits, and vegetable oils is associated with reduced risk of preeclampsia in nulliparous pregnant Norwegian women. J Nutr. 2009;139:1162-1168.
29. Brantsaeter AL, Haugen M, Alexander J, Meltzer HM. Validity of a new food frequency questionnaire for pregnant women in the Norwegian Mother and Child Cohort Study (MoBa). Matern Child Nutr. 2008;4:28-43.
30. Ystrom E, Niegel S, Vollrath ME. The impact of maternal negative affectivity on dietary patterns of 18-month-old children in the Norwegian Mother and Child Cohort Study. Matern Child Nutr. 2009;5:234-242.
31. Ystrom E, Barker M, Vollrath ME. Impact of mothers' negative affectivity, parental locus of control and child-feeding practices on dietary patterns of 3-year-old children: the MoBa Cohort Study. Matern Child Nutr. 2012;8:103-114.
32. Achenbach TM, Ruffle TM. The Child Behavior Checklist and related forms for assessing behavioral/emotional problems and competencies. Pediatr Rev. 2000;21:265-271.
33. Novik TS. Validity of the Child Behaviour Checklist in a Norwegian sample. Eur Child Adolesc Psychiatry. 1999;8:247-254.
34. Zachrisson HD, Dearing E, Lekhal R, Toppelberg CO. Little evidence that time in child care causes externalizing problems during early childhood in Norway. Child Dev. 2013;84:1152-1170.
35. Strand BH, Dalgard OS, Tambs K, Rognerud M. Measuring the mental health status of the Norwegian population: a comparison of the instruments SCL-25, SCL-10, SCL-5 and MHI-5 (SF-36). Nord J Psychiatry. 2003;57:113-118.
36. McArdle JJ, Epstein D. Latent growth curves within developmental structural equation models. Child Dev. 1987;58:110-133.
37. Jaffee SR, Moffitt TE, Caspi A, Fombonne E, Poulton R, Martin J. Differences in early childhood risk factors for juvenile-onset and adult-onset depression. Arch Gen Psychiatry. 2002;59:215-222.
38. McLaughlin KA, Gadermann AM, Hwang I, *et al*. Parent psychopathology and offspring mental disorders: results from the WHO World Mental Health Surveys. Br J Psychiatry. 2012;200:290-299.
39. Dipietro JA, Millet S, Costigan KA, Gurewitsch E, Caulfield LE. Psychosocial influences on weight gain attitudes and behaviors during pregnancy. J Am Diet Assoc. 2003;103:1314-1319.
40. Kohlboeck G, Sausenthaler S, Standl M, *et al*. Food intake, diet quality and behavioral problems in children: results from the GINI-plus/LISA-plus studies. Ann Nutr Metab. 2012;60:247-256.
41. Jacka FN, Berk M. Food for thought. Acta Neuropsychiatrica. 2007;19:321-323.
42. Wu A, Molteni R, Ying Z, Gomez-Pinilla F. A saturated-fat diet aggravates the outcome of traumatic brain injury on hippocampal plasticity and cognitive function by reducing brain-derived neurotrophic factor. Neuroscience. 2003;119:365-375.
43. Agrawal R, Gomez-Pinilla F. 'Metabolic syndrome' in the brain: deficiency in omega-3 fatty acid exacerbates dysfunctions in insulin receptor signalling and cognition. J Physiol. 2012;590:2485-2499.
44. Connor KL, Vickers MH, Beltrand J, Meaney MJ, Sloboda DM. Nature, nurture or nutrition? Impact of maternal nutrition on maternal care, offspring development and reproductive function. J Physiol. 2012;590:2167-2180.
45. Knopik VS, Maccani MA, Francazio S, McGeary JE. The epigenetics of maternal cigarette smoking during pregnancy and effects on child development. Dev Psychopathol. 2012;24:1377-1390.
46. Chen M, Zhang L. Epigenetic mechanisms in developmental programming of adult disease. Drug Discov Today. 2011;16:1007-1018.
47. Nilsen RM, Vollset SE, Gjessing HK, *et al*. Self-selection and bias in a large prospective pregnancy cohort in Norway. Paediatr Perinat Epidemiol. 2009;23:597-608.
48. Ludwig DS. Technology, diet, and the burden of chronic disease. JAMA. 2011;305:1352-1353.
49. Gortmaker SL, Swinburn BA, Levy D, *et al*. Changing the future of obesity: science, policy, and action. Lancet. 2011;378:838-847.
50. Brownell KD, Farley T, Willett WC, *et al*. The public health and economic benefits of taxing sugar-sweetened beverages. N Engl J Med. 2009;361:1599-1605.
51. Lustig RH, Schmidt LA, Brindis CD. Public health: the toxic truth about sugar. Nature. 2012;482:27-29.
52. Collins PY, Patel V, Joestl SS, *et al*. Grand challenges in global mental health. Nature. 2011;475:27-30.
53. Jacka FN, Mykletun A, Berk M. Moving towards a population health approach to the primary prevention of common mental disorders. BMC Med. 2012;10:149.
54. Berk M, Jacka FN. Preventive strategies in depression: gathering evidence for risk factors and potential interventions. Br J Psychiatry. 2012;201:339-341.