

## DEVELOPMENTAL EPIDEMIOLOGY

# Breastfeeding and brain structure in adolescence

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**Background** The purpose of this investigation was to evaluate an association between duration of exclusive breastfeeding and structure of cortical regions implicated in general intelligence.

**Methods** We studied adolescents ( $n = 571$ ; aged 12–18 years) participating in the Saguenay Youth Study; half of the participants were exposed to maternal cigarette smoking during pregnancy. Hierarchical linear modelling was used to assess whether breastfeeding is an important predictor of cortical thickness when other predictors, such as age, sex, parental education and exposure to maternal smoking during pregnancy, are also considered. Target cortical regions were identified using a meta-analysis of functional neuroimaging studies of cognitive abilities relevant for general intelligence.

**Results** We found that duration of exclusive breastfeeding was associated with cortical thickness in the superior and inferior parietal lobules ( $t = 2.31$ ,  $P = 0.02$ ). We also replicated the association between breastfeeding and general intelligence ( $t = 2.69$ ,  $P = 0.008$ ).

**Conclusion** In this study, we showed that breastfeeding is associated with variations in the thickness of the parietal cortex in a community-based sample of adolescents. We also found association of breastfeeding duration with full scale and performance IQ, as observed previously.

**Keywords** Human milk, development, cortical thickness, adolescence, intelligence

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## Introduction

The human brain grows the fastest during the second and third trimester of pregnancy and the first 2 years of post-natal life, reaching 83% of adult values by the end of the second year.<sup>1</sup> After birth, the infant's exclusive source of nutrients is breast milk or formula milk. The prevalence of breastfeeding differs across countries. In the United States, for example, 59.8% mothers ever

breastfeed, 25.4% breastfeed for at least 6 months and 17.5% breastfeed for at least 12 months.<sup>2</sup>

The effects of breastfeeding on brain structure are largely unknown. A recent study<sup>3</sup> showed that the amount of breast milk ingested by the infant correlated well with verbal intelligence and white-matter volume in adolescent boys born prematurely. Another report from the same group<sup>4</sup> described findings obtained in

76 adolescents born prematurely and assigned randomly, as infants, to a standard-nutrient diet (term formula or un-supplemented banked donor breast milk) vs a high-nutrient diet (formulated to meet the increased macronutrient and micronutrient needs of this population); the high-nutrient diet group had higher volume of the left and right caudate nuclei.

The present study was undertaken in a community-based sample of adolescents born at term to evaluate possible association between breastfeeding duration and cortical thickness in regions previously associated with cognitive abilities assessed by tests of general intelligence. This set of brain regions was considered, given the known beneficial effects of breastfeeding on these abilities.<sup>5–8</sup>

## Participants and methods

### Participants

Participants were 599 adolescents (aged 12–18 years, two or more siblings per family) recruited from a French Canadian population living in the Saguenay-Lac-Saint-Jean region of Quebec, Canada. The Saguenay Youth Study is a retrospective cohort study of the effects of maternal cigarette smoking during pregnancy on brain and cognition, and on cardiovascular and metabolic health during adolescence.<sup>9</sup>

Briefly, adolescents were recruited through regional high schools. Following a briefing of the teachers, the project team visited individual classrooms and presented a summary of the project. Concurrently, an information brochure, a letter from the principal and a consent form for a telephone interview were mailed to the parents. Then, a research nurse conducted a telephone interview with interested families to verify their eligibility. Additional information was acquired using a medical questionnaire completed by the child's biological parent. Details of the recruitment and testing procedures can be found elsewhere.<sup>9</sup> Exposure to maternal cigarette smoking was defined as smoking one or more cigarettes per day in the second trimester of pregnancy; mothers identified in this manner smoked throughout pregnancy.

The non-exposed adolescents were matched to the exposed ones based on the level of maternal education and the school attended. The main exclusion criteria for both exposed and non-exposed participants were as follows: (i) alcohol misuse during pregnancy; (ii) premature birth (<35 weeks); (iii) positive history of heart disease, brain trauma, brain tumour, meningitis or epilepsy; and (iv) severe mental illness (e.g. autism) or mental retardation (IQ < 70).

### Measurements

#### Breastfeeding status

Breastfeeding was measured using a questionnaire in which mothers were asked whether they had breastfed their child, and, if yes, for how long

**Table 1** Exclusive breastfeeding duration characteristics [non-breastfed adolescents ( $n = 301$ ) are not included]

Breastfeeding characteristics ( $n = 270$ )	
Median number of weeks exclusively breastfed	8
Min-max weeks breastfeeding	1–60
Interquartile range (25–75%)	4–16
Distribution of breastfeeding duration	
<4 weeks	18%
4–16 weeks	61%
≥16 weeks	21%

(weeks) had they exclusively breastfed; they were asked at what age they introduced water or unsweetened liquids, at what age they first introduced formula or milk of any kind, at what age they introduced cereals, fruits and other solid foods and, lastly, at what age did they completely stop breastfeeding. In the current analysis, we used duration of exclusive breastfeeding. Exclusive breastfeeding duration was analysed as a categorical variable with four levels: (i) never breastfed; (ii) breastfed for <4 weeks; (iii) breastfed for 4–16 weeks; and (iv) breastfed for >16 weeks. These ranges reflect the inter-quartiles range (25–75%) of the 'exclusive breastfeeding duration', as shown in Table 1.

#### Prenatal, perinatal and family environment measures

A number of pregnancy and birth-related variables, such as birthweight, maternal age at delivery, alcohol during pregnancy, number of pregnancies and *in utero* exposure to second-hand smoking, were assessed using a structured telephone interview and a set of questionnaires answered by the biological mother in the majority of participants. A number of socio-economic indicators, such as household income and parental education, were also obtained.

#### Intelligence

The Wechsler Intelligence Scale for Children III (WISC-III)<sup>10</sup> was used to measure intelligence (IQ). The WISC-III consists of 12 subtests, six measuring verbal IQ and six measuring performance IQ.

#### Magnetic Resonance Imaging: Acquisition

For each participant, T1-weighted magnetic resonance (MR) images of the brain were collected on a Phillips 1.0-T superconducting magnet using the following parameters: three-dimensional radio-frequency-spoiled gradient echo scan, 140–160 sagittal slices, 1-mm isotropic resolution, a repetition time of 25 ms, an echo time of 5 ms and a flip angle of 30°.

#### Magnetic Resonance Imaging: Analysis

Cortical thickness was calculated using FreeSurfer;<sup>11</sup> triangular meshes computed by this suite of algorithms recover the geometry and the topology of the

pial surface and the grey/white interface of the left and right hemispheres. The local cortical thickness is estimated from the difference between the position of equivalent vertices in the pial and grey/white surfaces. Finally, a correspondence between the cortical surfaces across the participants is established using a non-linear alignment of the principal sulci in each participant's brain with an average brain.<sup>12</sup> A 30-mm (full width at half maximum) smoothing kernel is applied to the cortical surface before extracting the values of cortical thickness at each vertex corresponding to the X, Y and Z coordinates identified in the activation-likelihood estimation (ALE) maps (see next section). These measurements are automatic and, as such, unaffected (unbiased) by the infant feeding history.

#### *Identification of 'intelligence-related' cortical regions*

To identify cortical regions previously associated with cognitive functions assessed by tests of general intelligence, we carried out a meta-analysis of functional neuroimaging studies using the ALE method.<sup>13</sup> Functional MRI and positron emission tomography studies related to intelligence were selected for this meta-analysis. Studies published from 1997 to 2009 were selected from the ISI Web of Knowledge and Sleuth (BrainMap database) using the following terms: intelligence, reasoning, Raven's matrices, WISC/WAIS, processing speed and cognitive control. Only studies clearly describing their methodology and reporting 3-D stereotaxic coordinates were included in the meta-analysis. Studies that did not report results based on whole-brain analysis were excluded. In this meta-analysis, 23 fMRI and positron emission tomography studies reporting a total of 30 analyses were included, yielding a total of 328 'foci' of brain 'activation'. [Supplementary Table S1 \(available as Supplementary data at IJE online\)](#) presents a summary of these studies.<sup>13-35</sup>

The ALE maps were created using a 10-mm full-width half-maximum Gaussian function to model each coordinate.<sup>36</sup> The likelihood of each voxel in standard space representing each primary locus of activation was combined to generate a map of the ALE score at each voxel. ALE maps were thresholded by a permutation test controlling the false discovery rate at  $P < 0.05$ , and clusters of supra-threshold voxels superior to  $200\text{ mm}^3$  in volume were defined as loci of brain activation across all studies included in the meta-analysis. ALE meta-analysis was carried out using a Java version of GingerALE.

#### *Cortical thickness: factor analysis*

ALE meta-analyses resulted in 36 'intelligence-related' regions; these regions were grouped by the ALE algorithm into 22 clusters ([Supplementary Table S2, available as Supplementary data at IJE online](#)). To obtain a global view of the data, we conducted a principal components analysis with direct oblimin (oblique) rotation. Four out of the 36 regions [( $x=56, y=32, z=24$ ), ( $x=-32, y=-62, z=-12$ ), ( $x=-50,$

$y=-66, z=-10$ ) and ( $x=12, y=-90, z=-10$ )] were excluded owing to low extracted communalities<sup>37</sup> ( $<0.2$ ). Principal components analysis was then repeated. Kaiser's criterion was used to identify the number of derived components. The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.922, reflecting the proportion of variance explained by the derived factors. According to the total variance explained, seven components have eigenvalues  $>1.0$  and together explain 64.4% of the variance. [Supplementary Table S3 \(available as Supplementary data at IJE online\)](#) shows which regions load on each principal component. The seven components identified in this manner represent the following cortical regions: bilateral frontal eye field; left medial prefrontal cortex; bilateral ventrolateral prefrontal cortex; left mid dorsolateral frontal cortex; left and right superior and inferior parietal lobule; left angular gyrus and right lateral occipital cortex ([Supplementary Table S3, available as Supplementary data at IJE online](#)). For each of these regions, we have extracted values of cortical thickness for all vertices corresponding to X, Y and Z coordinates of the three-dimensional locations constituting a given cluster (as listed in [Supplementary Table S3, available as Supplementary data at IJE online](#)) and averaged these values to obtain one measure of cortical thickness for each of the seven regions in each participant.

For further analysis, items loaded above  $0.40$ <sup>38</sup> on a component were selected, and, for each component, the weighted sum of included items was calculated for each individual.

#### *Statistical approaches*

In all analyses, outliers, defined as values three standard deviations from the mean, were excluded. Statistical analyses were carried out using JMP (version 9), SPSS 17 (for Windows) and hierarchical linear modelling (HLM statistical software, version 6.0; Scientific Software International, Lincolnwood, IL). Using HLM, we accounted for the clustering of sibling pairs ( $n=279$ ) within families.

Further statistical analyses began by assessing the association between each potential confounder and exclusive breastfeeding duration ([Table 2](#)). Potential confounders were separated into two levels. Level-1 confounders included those related to pregnancy, namely exposure (to maternal cigarette smoking during pregnancy) status, maternal age at delivery, pregnancy duration, alcohol during pregnancy and second-hand smoking during pregnancy, and post-natal confounders, namely sex, age, birthweight and birth order. Level-2 confounders were household income and parental education. Confounders were selected after examining for multicollinearity using a correlation matrix of all of the predictor variables. For variables that were highly correlated (e.g. number of pregnancies and maternal age at delivery), only one was included for further analysis.

**Table 2** Sample characteristics separated by exclusive breastfeeding status

Sample characteristics	Non-breastfed	Breastfed <4 weeks	Breastfed 4–16 weeks	Breastfed >16 weeks	P
Level 1					
Age (years)	14.5 ± 0.1 (301) <sup>a</sup>	15 ± 0.26 (48)	14.7 ± 0.15 (164)	14.7 ± 0.22(58)	0.249
Pregnancy					
Exposure status (maternal smoking during pregnancy)	30.8% (176)	2.28% (13)	11.2% (64)	2.45% (14)	<0.0001
Non-exposed percentage	21.8% (125)	6.13% (35)	17.5% (100)	7.71% (44)	
Maternal age at delivery	26.9 ± 0.2 (301)	26.3 ± 0.5 (48)	26.9 ± 0.3 (164)	28.2 ± 0.4 (58)	0.068
Pregnancy duration	39 ± 0.08 (300)	39 ± 0.2 (48)	39.2 ± 0.1 (164)	39.5 ± 0.1 (58)	0.287
Alcohol during pregnancy	12.3% (70)	1.7% (10)	7.4% (42)	2.6% (15)	0.89
Second-hand smoking (no. cigarettes)	7.4 ± 0.6 (296)	4.2 ± 0.9 (44)	7.1 ± 0.8 (163)	3.2 ± 0.8 (58)	0.0002
Post-natal					
Sex					
Females (n)	28.7% (164)	4.3% (25)	12.7% (73)	5.4% (31)	0.224
Males (n)	23.9% (137)	4% (23)	15.9% (91)	4.7% (27)	
Birthweight	3328.3 ± 30.1 (298)	3404.3 ± 58.7 (48)	3462.6 ± 38.9 (163)	3543.1 ± 56.9 (57)	0.003
Birth order	1.8 ± 0.04 (301)	1.7 ± 0.1 (48)	1.9 ± 0.07 (164)	2.3 ± 0.1(58)	0.004
Level 2 <sup>b</sup>					
Income	53 076 ± 1944.1 (143)	56 956.9 ± 4318 (23)	53 231 ± 2706.9 (82)	61 458 ± 4065.6 (24)	0.369
Mother education <sup>c</sup>	4.5 ± 0.1 (140)	4.6 ± 0.3 (23)	4.9 ± 0.2 (82)	5.3 ± 0.3 (24)	0.071
Father education	4.8 ± 0.1 (133)	4.7 ± 0.1 (23)	5.1 ± 0.2 (76)	5.6 ± 0.4 (23)	0.123

<sup>a</sup>Numbers in brackets state *n*.

<sup>b</sup>Parental data are specified as Level-2 variables, which estimate between-family effects; thus they have '*n*' approximately half to that of Level-1 variables. Sibling data are specified as Level-1 variables, estimating within-family variability.

<sup>c</sup>Parental education was measured starting from the lowest level, which is ≤8th grade, and going up to a doctoral degree.

Note that percentages (Exposure status to maternal smoking during pregnancy, Alcohol during pregnancy, Sex) were calculated with the total number of adolescents (*n* = 571) in denominator.

Hierarchical linear modelling was used to account for sibling pairs and to assess whether breastfeeding is an important predictor of cortical thickness when other predictors are also considered. Confounders were selected a priori. Offspring-based predictors such as age, sex and exposure (to maternal cigarette smoking during pregnancy) status were included in all models. Family-based predictors (family income and parental education) were also included in all models. As such, the final model used for the seven different cortical regions included offspring-based predictors (age, sex, exposure status to maternal smoking during pregnancy and exclusive breastfeeding duration) and parental variables (family income and parental education). As an example, the final model for Component A is given below:

$$\begin{aligned} \text{Component A} = & \gamma_{00} + \gamma_{01} * (\mathbf{Income}) \\ & + \gamma_{02} * (\mathbf{Maternal\_Education}) \\ & + \gamma_{03} * (\mathbf{Paternal\_Education}) \\ & + \gamma_{10} * (\text{Exposure to Maternal Smoking}) \\ & + \gamma_{20} * (\mathbf{Age}) + \gamma_{30} * (\mathbf{Sex}) \\ & + \gamma_{40} * (\text{Exclusive Breastfeeding Duration}) \\ & + u_0 + r \end{aligned}$$

in which  $\gamma_{01}$  to  $\gamma_{03}$  are the level-2 variables,  $\gamma_{10}$  to  $\gamma_{40}$  are the level-1 variables and  $r$  is the level-1 random effect. Predictors in boldface type represent group-mean centered variables, whereas predictors in bold-italic type represent grand-mean centred variables.

For comparison with other studies, we also examined the associations of exclusive breastfeeding duration with full scale IQ, performance IQ and verbal IQ (WISC-III):

$$\begin{aligned} \text{Full scale IQ} = & \gamma_{00} + \gamma_{01} * (\mathbf{Income}) \\ & + \gamma_{02} * (\mathbf{Maternal\_Education}) \\ & + \gamma_{03} * (\mathbf{Paternal\_Education}) \\ & + \gamma_{10} * (\text{Exposure to Maternal Smoking}) \\ & + \gamma_{20} * (\mathbf{Age}) + \gamma_{30} * (\mathbf{Sex}) \\ & + \gamma_{40} * (\text{Exclusive Breastfeeding Duration}) \\ & + u_0 + r \end{aligned}$$

in which  $\gamma_{01}$  to  $\gamma_{03}$  are the level-2 variables,  $\gamma_{10}$  to  $\gamma_{40}$  are the level-1 variables and  $r$  is the level-1 random effect. Predictors in boldface type represent group-mean centred variables, whereas predictors in bold-italic type represent grand-mean centred variables.

## Results

### Sample characteristics

From 599 adolescents, 20 adolescents were excluded owing to registration failure during MRI analysis, and

eight adolescents were excluded owing to missing data, hence the final sample size of 571 adolescents. Table 2 separates breastfed (three groups) and non-breastfed adolescents and describes the adolescents' age, sex and exposure status (to maternal smoking during pregnancy), as well as household income and parental education.

The four 'breastfeeding' groups showed no differences in family socio-economic status (SES) (income, parental education). There was a noteworthy difference between the four groups in exposure status (to maternal smoking during pregnancy) [ $\chi^2(3, n=571) = 39.91, P < 0.0001$ ], birthweight [ $F(3,565) = 4.50, P = 0.003$ ], birth order [ $F(3,570) = 4.40, P = 0.004$ ], and second-hand smoking exposure [ $Welch F(3,560) = 7.18, P = 0.0002$ ]. Non-breastfed adolescents were more likely to be exposed to second-hand prenatal smoking and to weigh less at birth than breastfed adolescents. The majority of these group differences reflect the expected differences associated with the exposure status: adolescents who had been exposed (vs non-exposed) to prenatal maternal smoking were less likely to be breastfed [ $\chi^2(3, n=571) = 39.91, P < 0.0001$ ].

### Exclusive breastfeeding duration and cortical thickness

We found that exclusive breastfeeding duration was a predictor of cortical thickness in the superior and inferior parietal lobules (Table 3).

Analysis with measures of general intelligence as outcomes showed that exclusive breastfeeding duration was also predicting performance and full scale IQ, but not verbal IQ (Supplementary Table S4, available as Supplementary data at *IJE* online).

Finally, we did not observe any correlations between cortical thickness and IQ, either in the overall sample or in any of the breastfeeding subgroups.

## Discussion

In the present study, we evaluated the association of exclusive breastfeeding duration with brain structure of adolescents born at term. We assessed cortical thickness in a number of cortical regions identified by a meta-analysis of functional neuroimaging studies of cognitive abilities related to general intelligence. We found a positive association between exclusive breastfeeding duration and the thickness of the parietal cortex. As expected, we also found a positive association of exclusive breastfeeding duration with general intelligence.

### Breastfeeding and cortical thickness

All seven cortical regions showed age-related decreases during adolescence, consistent with other studies carried out in typically developing children and adolescents<sup>39,40</sup>. We also observed sex differences in six out of the seven cortical regions, with the

**Table 3** Effects of Level 1 and Level 2 predictors on cortical thickness

Models	Level 1 predictors Total sample ( <i>n</i> = 571)		Level 2 predictors Total sample ( <i>n</i> = 279)		
	T-ratio	<i>P</i>		T-ratio	<i>P</i>
Frontal eye field					
Exposure <sup>a</sup>	-2.61	0.010	Income	-2.01	0.045
Sex	4.88	<.0001	Maternal education	0.86	0.389
Age	-5.85	<.0001	Paternal education	1.60	0.109
Breastfeeding	0.45	0.652			
L medial prefrontal cortex					
Exposure	-1.73	0.083	Income	-1.11	0.267
Sex	2.61	0.010	Maternal education	0.13	0.897
Age	-9.35	<.0001	Paternal education	1.45	0.147
Breastfeeding	0.65	0.516			
Ventrolateral prefrontal cortex					
Exposure	-1.39	0.165	Income	-1.68	0.094
Sex	3.43	0.001	Maternal education	0.78	0.433
Age	-7.7	<.0001	Paternal education	0.80	0.423
Breastfeeding	-0.31	0.755			
L mid dorsolateral frontal cortex					
Exposure	-0.97	0.330	Income	-1.37	0.172
Sex	5.26	<.0001	Maternal education	0.77	0.441
Age	-7.70	<.0001	Paternal education	1.65	0.098
Breastfeeding	0.77	0.439			
Superior and inferior parietal lobule					
Exposure	-0.07	0.938	Income	-1.39	0.165
Sex	3.86	<.0001	Maternal education	1.27	0.203
Age	-8.27	<.0001	Paternal education	-0.03	0.971
Breastfeeding	2.31	0.021			
L angular gyrus					
Exposure	0.73	0.462	Income	-1.51	0.130
Sex	3.42	0.001	Maternal education	-0.29	0.772
Age	-6.62	<.0001	Paternal education	0.52	0.600
Breastfeeding	1.58	0.114			
R occipital cortex					
Exposure	1.18	0.237	Income	-2.01	0.045
Sex	1.78	0.074	Maternal education	0.33	0.741
Age	-4.24	<.0001	Paternal education	1.17	0.240
Breastfeeding	0.41	0.685			

<sup>a</sup>Term 'exposure' is used as such to denote exposure of foetus to maternal cigarette smoking during pregnancy.

cortex thicker in female than in male adolescents; these results are also consistent with other studies of cortical thickness.<sup>41,42</sup> Exclusive breastfeeding duration was associated with the cortical thickness in the superior and inferior parietal lobules: the longer the duration, the thicker the cortex,

even after adjustment for age and sex. However, the observed association between cortical thickness and breastfeeding duration did not survive correction for multiple (seven) comparisons. It is important to replicate this finding in future studies, both in humans and experimental animals.

### Possible mechanisms

The mechanism for the observed associations is unclear. Recently, it has been suggested that long-chain polyunsaturated fatty acids (LC-PUFAs), mainly docosahexaenoic acid (DHA), underlie neurodevelopmental benefits of breast milk. Breast milk is rich in essential fatty acids, namely linoleic and  $\alpha$ -linolenic acids and their LC-PUFA derivatives, including arachidonic acid, dihomo- $\gamma$ -linolenic and eicosadienoic acids for the  $\omega$ -6 series, as well as DHA and docosapentaenoic acid of the  $\omega$ -3 series. The  $\omega$ -6 arachidonic acid and  $\omega$ -3 DHA contribute the highest proportions of LC-PUFA in human milk.<sup>43</sup> Before birth, the foetus obtains all the EFAs and LC-PUFAs from the maternal circulation through placental transfer. After birth, all  $\omega$ -6 and  $\omega$ -3 fatty acids are derived from breast or formula milk. *Post mortem* studies of infants who died from sudden infant death syndrome showed that DHA levels in the cerebral and cerebellar cortex of breast-fed infants are higher than those in formula-fed infants.<sup>44–47</sup>

No previous studies have examined an association between breastfeeding duration and cortical thickness in humans. Animal studies have illustrated that a diet deficient in  $\omega$ -3 (DHA) was associated with smaller size of neurons in the parietal cortex, hippocampus and hypothalamus at weaning, and in the piriform cortex in mature rats.<sup>48</sup> Furthermore, the mean thickness of cortical plate and mean sectional area of the primordial dentate gyrus have been reported to be lower in  $\omega$ -3 deficient embryonic rats, whereas the mean thickness of the cortical ventricular zone and the primary dentate neuroepithelium were higher, thus indicating a delay or inhibition of normal brain development.<sup>49</sup> Supplementation with DHA was found to improve/restore DHA levels in the brain of baboon neonates,<sup>50</sup> to increase the population of neurons with longer neurites and a higher number of branches in hippocampal culture<sup>51</sup> and to promote the differentiation of neural stem cells into neurons.<sup>52</sup> Taken together, these animal studies suggest that DHA supports neurogenesis. An addition of DHA to infant formulas increases the DHA content in the blood lipids of infants<sup>53,54</sup> and facilitates maturation of the visual system in term infants.<sup>55,56</sup> Further, DHA levels during breastfeeding correlates with cognitive abilities measured later in early childhood.<sup>57</sup> Finally, a recent study<sup>3</sup> demonstrated a dose-response relationship between breast-milk intake and later intelligence and whole brain volume of adolescents born prematurely.

The thickness of the cortex reflects characteristics of the neuropil, including the density and size of neurons, dendrites, axons and glial cells.<sup>58</sup> In the first year of life, when breast milk or formula milk are the main (and often exclusive) sources of nutrition, grey matter increases by 149%, with very little change in white matter during this period.<sup>1</sup> Intake of LC-PUFAs via breastfeeding during the first year of life may promote growth in several cellular compartments in the cortical

grey-matter, with long-lasting consequences not affected by subsequent age-related decreases in cortical thickness during adolescence. Animal studies have illustrated that DHA supplementation increases the population of neurons with longer neurites and higher number of branches in hippocampal culture.<sup>51</sup> As such, thicker parietal cortex in adolescents who were exclusively breastfed for longer periods may suggest that, during the first year of life, breast milk in general and DHA in particular facilitated such neuronal growth, possibly accompanied by an increased number of glial cells and increased vascularization. Finally, DHA may also reduce apoptosis during the early post-natal period,<sup>59</sup> thus leading to a higher number of neurons present later in life.

### Breastfeeding and intelligence

Results from the HLM analysis revealed that exclusive breastfeeding duration was predicting performance and full scale IQ after controlling for possible confounders, including parental education. These results are consistent with previous studies indicating that breastfeeding is positively related with later cognitive outcome, even after adjusting for potential confounders.<sup>5–8</sup> The effect size of associations between IQ and breastfeeding observed in our sample [FIQ:  $B(SE) = 1.30 (0.48)$ ,  $P = 0.008$ ; PIQ:  $B(SE) = 1.77 (0.54)$ ,  $P = 0.002$ ] is comparable with that reported in a number of previous studies. For example, in a prospective study,<sup>60</sup> duration of breastfeeding was found to have small, but noteworthy, effect on children's IQ scores [ $B(SE) = 0.11 (0.05)$ ,  $P = 0.025$ ]. Overall, there is universal agreement that breastfeeding duration is associated with small positive outcomes on cognition. Although the LC-PUFA hypothesis has been proposed as a key explanation for neurodevelopmental benefits of breast milk,<sup>61</sup> breast milk consists of many ingredients besides fatty acids. Therefore, fatty acids may not be the only mediator in the relationship between breastfeeding and brain structure and function. Furthermore, other possible mechanisms include the physical contact and psychological interactions between the mother and the child during breastfeeding.<sup>62</sup> As Drane and Logemann<sup>63</sup> have stated, lactating women have higher circulating levels of prolactin and oxytocin than non-lactating women, perhaps activating feelings of calmness and nurturing behaviour and facilitating positive mother-child interactions.

In general, the parietal cortex is critical for cognitive processes tapped by performance IQ, namely visuospatial skills and perceptual organization. Performance IQ reflects the ability to integrate perceptual stimuli with appropriate motor responses, evaluate visuospatial information and—in general—work quickly and efficiently with information present in the surrounding physical and social environment.<sup>64</sup> But, we did not observe a direct relationship between the thickness of the parietal cortex and any of these components

of the performance IQ in our sample. These results suggest that the beneficial impact of breastfeeding on IQ may not be mediated, at least not entirely, by promoting the development of grey matter. In fact, Isaacs *et al.* (2010)<sup>3</sup> showed that the effects of breast milk were seen more strongly on white matter than grey matter in the brain of adolescent boys born prematurely, and that IQ itself was strongly related to white matter volume. As such, we suggest that effects of total breastfeeding duration on cortical thickness of bilateral superior and inferior parietal lobules, as shown in this study, may not promote intelligence as such, but perhaps support other functions of the parietal lobe, such as awareness of the spatial qualities of the world. This remains to be tested with appropriate neuropsychological tools in the future.

Our study has a number of limitations and strengths. The SYS is a retrospective cohort of a modest size ( $n = 571$ ); the breastfeeding status was determined by maternal reports and, as such, it is subject to recall bias. Furthermore, duration of breastfeeding maybe related to quality of prenatal care—an important confounder not measured in this study. Also, although parental education and household income were controlled for statistically, a direct measure of maternal intelligence was not included; although useful, education may not be an adequate proxy for intelligence. Finally, we do not know why mothers stopped breastfeeding; perhaps mothers in the <4 weeks group intended to breastfeed, but their infants failed to thrive, and, thus, they switched to bottle feeding. On the other hand, this is the first study to examine associations of breastfeeding with cortical thickness in adolescents born at term, with a reasonable sample size, given the objective and quantitative nature of the main outcome measure (cortical thickness), careful ascertainment of participants and detailed assessments of cognition and family environment in a population characterized by a relatively high genetic and cultural homogeneity.<sup>9</sup>

## Conclusion

In summary, we found that continuous exclusive breastfeeding is associated with thicker parietal cortex and improved cognitive performance in typically developing adolescents. Perhaps the constituents of mothers' milk and mother-child attachment are

underlying the consistent observations that breastfeeding is associated with a positive impact on brain and cognitive development. This may help us improve our scientific and clinical knowledge vis-a-vis dietary practices that could enhance brain development.

## Supplementary Data

Supplementary Data are available at *IJE* online.

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**Conflict of Interest:** None declared.

### KEY MESSAGES

- Breast-feeding is promoted by clinicians in part due to the beneficial effects on cognitive development.
- To date, only one study investigated the effect of breastfeeding on brain structure; this study was carried out in children born prematurely.
- Here we report findings obtained in term-born adolescents. We show that exclusive breastfeeding is associated with thicker parietal cortex and better cognitive performance.



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