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Breastfeeding and Childhood IQ: The Mediating Role of Gray Matter Volume

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Abstract

Objective—A substantial body of literature has established the positive effect of breastfeeding on child developmental outcomes. There is increasing consensus that breastfed children have higher IQs after accounting for key variables, including maternal education, IQ, and socioeconomic status. Cross-sectional investigations of the effects of breastfeeding on structural brain development suggest that breastfed infants have larger whole brain, cortical, and white matter volumes. To date, few studies have related these measures of brain structure to IQ in breastfed versus nonbreastfed children in a longitudinal sample.

Method—Data were derived from the Preschool Depression Study (PDS), a prospective longitudinal study in which children and caregivers were assessed annually for 8 waves over 11 years. A subset completed neuroimaging between the ages of 9.5 and 14.11 years. A total of 148 individuals had breastfeeding data at baseline and complete data on all variables of interest, including IQ and structural neuroimaging. General linear models and process mediation models were used.

Results—Breastfed children had significantly higher IQ scores and larger whole brain, total gray matter, total cortical gray matter, and subcortical gray matter volumes compared with the nonbreastfed group in models that covaried for key variables. Subcortical gray matter volume significantly mediated the association between breast-feeding and children's IQ scores.

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Conclusion—The study findings suggest that the effects of breastfeeding on child IQ are mediated through subcortical gray volume. This effect and putative mechanism is of public health significance and further supports the importance of breastfeeding in mental health promotion.

Keywords

breastfeeding; IQ; brain development

A substantial body of literature has established the positive effect of breastfeeding on a variety of child health and developmental outcomes.[1] Although numerous studies have detected a positive relationship between breastfeeding and childhood IQ, many are confounded by the fact that in most wealthy societies, more educated women and those with higher incomes choose to breastfeed, making it unclear whether these correlates are driving the effects. However, the results of randomized controlled trials,[2,3] cross-population studies that eliminate social patterns of breastfeeding,[4] longitudinal cohort studies in several countries,[5,6] and meta-analyses[7] all offer support for positive associations between breastfeeding and child IQ when accounting for these critical confounds. At the same time, however, other work using sibling comparisons and designs that account for within-family effects fails to support this relationship.[8] Taken together, this body of work suggests that the impact of breastfeeding on child IQ is complex and likely involves contributions from genetics (e.g., maternal-to-child IQ), nutritional components of breast milk, the maternal–child relationship (e.g., maternal nurturance, close physical contact), and psychosocial factors (e.g., poverty, stimulation). Despite these conflicts and complexities in the behavioral literature, there is increasing consensus that breastfed children on average have higher IQs even after accounting for maternal education and IQ, socioeconomic status, and other key factors. This is of key public health importance, as childhood IQ is associated with adaptive outcomes including health (both mental and physical) and longevity later in life.[9]

Following these findings, investigations of the effects of breastfeeding on structural brain development have been of increasing interest as a possible mechanism for the positive effects of breastfeeding on cognitive development. Such studies begin to elucidate how breastfeeding affects IQ by addressing whether the structure of key brain regions involved in cognitive ability are enhanced by breastfeeding. Cross-sectional studies have shown that breastfed infants have enhanced early white matter development, as well as larger whole brain and cortical volume and thickness.[8,10-13] Furthermore, smaller ventricular volumes and larger head circumferences were evident in the first 2 months of life in breastfed versus bottle-fed infants.[14] However, despite the demonstrated effects of breastfeeding on cognitive outcomes and data showing enhanced brain development, to date few studies have related these measures of brain structure to IQ in breastfed versus nonbreastfed children in the same study sample longitudinally, a study design that is necessary to begin to elucidate the mechanism by which breastfeeding affects IQ. Given findings suggesting an important relationship between gray matter volume and IQ in healthy developing children,[15-17] the role of gray matter in this hypothesized relationship was of particular interest. Based on prior findings linking white matter tracts to IQ and studies demonstrating an effect of breastfeeding on IQ and white matter volume,[18] we also explored white matter volume.

Thus, we tested whole brain and subcortical brain volume as separate mediating mechanisms through which breastfeeding influences IQ.

The goal of the current study was to address this gap in the literature by testing the hypothesis that the relationship between breastfeeding and IQ would be mediated by the effect of breastfeeding on structural brain development and, in turn, the effect of brain on IQ. To do so, we used data from an 11-year longitudinal study that was originally designed to investigate early childhood depression but that also included maternal report of breastfeeding obtained when children were between the ages of 3.0 and 5.11 years, as well as neuroimaging, IQ, and behavioral assessments at school age and early adolescence (ages 9–15 years). Importantly, key potential confounds such as income to needs (a measure of socioeconomic status [SES] in relation to the federal poverty level), maternal education, and other psychosocial variables were also measured. As breastfeeding is a modifiable health behavior across cultures, which could have a powerful impact on child IQ and other critical developmental outcomes, a greater understanding of the relationships between breastfeeding, brain development, and IQ is of great importance to health promotion and mental health and developmental disorder prevention. Importantly, enhancing child IQ could diminish the need for special educational services and mitigate the associated social impairment and psychiatric comorbidities that arise with cognitive delay.

METHOD

Overview of Study Design and Participants

At baseline (n = 306), children 3.0 to 5.11 years old and their primary caregivers were recruited from daycare, preschool, and primary care sites in the St. Louis area for a study of preschool depression. The sample was ascertained based on child characteristics, and a screening checklist[19] was used to oversample children with early-onset behavioral and emotional symptoms (specifically depression) as well as healthy controls. Children and their caregivers were assessed annually for 8 assessment waves over 11 years. A subset (those with any history of major depressive disorder [MDD] and healthy controls) completed 3 sessions of neuroimaging. From the original sample, 148 individuals had data on breastfeeding obtained at baseline from maternal report and had complete data on all variables of interest in the current analyses, including IQ and structural neuroimaging at scan 2 (Figure 1). Following minimal cut-offs used in the breastfeeding literature, participants with breastfeeding duration of less than 30 days were not included in the analyses. Three individuals with IQ scores of less than 75 were excluded from analyses due to being below the normative range and the possibility that a unique brain developmental process may be operative with IQs below the normative range. IQ scores ranged from 75 to 133 for participants included in the analyses. Parental written consent and verbal child assent (in children 4 years and older) were obtained before study participation. The Institutional Review Board at Washington University approved all procedures in accordance with the Health Insurance Portability and Accountability Act (HIPAA) and institutional ethical guidelines.

A total of 211 child participants (a subset of the 306 study participants ascertained at baseline and described above) were invited to complete 3 sessions of neuroimaging between

2008 and 2014. As the first step, we conducted multilevel models of subcortical gray volume across the 3 scan waves to test for an effect of breastfeeding on volumetric brain structure over time. Results indicated that the intercept differed significantly by breastfeeding status (B 1.81, standard error [SE] = 0.81, $t = 2.23$, $p = .0270$), with in greater volumes breastfed children. However, the interaction between breastfeeding and scan wave was not significant (B = 0.01, SE = 0.11, $t = 0.10$, $p = .9213$), indicating that the volumetric changes over the 3 scan waves were consistent between breastfed and nonbreastfed groups of children. Imaging data was taken from scan 2 (due to its temporal placement and superior scan quality) to allow us to address the mediation questions of interest (however, scan 1 was also tested). The current analyses included children with usable scan 2 data as well as complete data on all of the variables of interest. Of the total scan sample, 21 children were excluded because of poor-quality scan 2 data; 2 children did not have available IQ data; 3 children had IQ scores of <75; 5 children did not have data available for the breastfeeding variable; 7 had breastfeeding duration of less than 30 days; and 25 children never completed the scan at time 2 or had braces at the time of scan 2. Thus, the final sample included in the following analyses was based on 148 children who had high-quality and complete data on all of the variables of interest. At scan 2, participants were aged 9.5 to 14.11 years.

Measures

Breastfeeding—Information about breastfeeding was obtained at baseline, when the child was between the age of 3.0 and 5.11 years, from the primary caregiver (93.9% biological mother) using the psychosocial section of the Preschool Age Psychiatric Assessment (PAPA).[20] Dichotomous data about breastfeeding (Did you breastfeed your child, yes or no?) was used, as it was deemed to be more reliable than breastfeeding onset and offset data (which were also collected, but mothers often struggled to remember the exact dates/ duration of breastfeeding). However, those with breastfeeding durations of less than 30 days were excluded to ensure that participants who reported breastfeeding engaged in the practice for a meaningful duration.

Maternal Education—Information about maternal education was obtained from the psychosocial section of the Child and Adolescent Psychiatric Assessment (CAPA) at the scan 2 assessment.

Family Income-to-Needs Ratio—Mothers reported family income at each annual assessment. The income-to-needs ratio[21,22] was computed as the total family income at the time of scan divided by the federal poverty level, based on family size, at the time of data collection (i.e., at the scan 2 assessment).

Intelligence Quotient (IQ)—The Kaufman Brief Intelligence Test (KBIT)[23] or the Wechsler Abbreviated Scale of Intelligence (WASI)[24] (depending upon study wave) was used to assess verbal and nonverbal intelligence during school age (range, 8.10-11.10 years for the WASI and 9.11-15.2 years for the KBIT). There was no difference in the rate of completing the WASI compared with the KBIT in breastfed versus nonbreastfed children (WASI used for 15% of the breastfed group and 11% of the nonbreastfed group, $p = .44$).

History of Child Depression and/or Anxiety Diagnoses—The PAPA was administered at baseline and subsequent assessment waves up to age 8 years to obtain information from parents about the child's psychiatric diagnoses. After age 8, the CAPA[25] was used and both parent and child report were obtained, and data were combined using the “or” rule. Because children with early-onset emotional and behavioral problems were oversampled, this information was used as a control variable (see below).

Magnetic Resonance Image Acquisition

Structural images were collected as part of a longer scan session that also included acquisition of task-based and functional connectivity data. Imaging data were collected using a 3T TIM TRIO Siemens scanner. Two T1-weighted structural images were acquired sagittally using an MPRAGE 3D sequence (TR = 2400 milleseconds, TE = 3.16 milliseconds, flip angle = 8°, 160 slices, matrix size = 256 × 256, field of view = 256mm, voxel size = 1 × 1 × 1 mm). The 2 MPRAGE scans were assessed visually, and the best one was selected for further processing by a rater blinded to participant characteristics.

The selected MPRAGE for the second scan wave was processed using the longitudinal stream in FreeSurfer v5.3[26] as part of a broader analysis involving 3 scan waves.[27] The white and pial surfaces generated by FreeSurfer were visually inspected, and, when necessary, appropriate edits were performed and the surfaces regenerated. Total cortical and subcortical gray matter volumes and cerebral white matter volume were obtained from the “CortexVol,” “SubCortGrayVol,” and “CorticalWhiteMatterVol” measures, respectively, in FreeSurfer's “aseg.stats” report. Whole brain volume was the sum of all 3 of these measures.

Descriptive Analysis and Potential Covariates

Differences between breastfed and nonbreastfed children on demographic and clinical/ psychological variables were examined using *t* tests and χ^2 tests (see Table 1). Given the importance of age and sex in relation to structural brain development, these variables were included as covariates in all mediation models. Furthermore, given the known associations between brain structure and IQ with familial income and caregiver education, these variables were also considered as covariates in the models. Finally, given that the current sample was originally recruited based on the likelihood of having or being at risk for depression, children's history of being diagnosed with depression and/or anxiety disorders from baseline until the time of scan was also included as a covariate in all final models.

The PROCESS macro for SPSS[22] was used to determine whether brain volumes mediated the hypothesized association between breastfeeding and IQ score.

Analysis Plan

Hypothesis 1 and Analytical Approach—Hypothesis 1 was that breastfed children would have significantly higher IQ scores compared with nonbreastfed children, even when children's age, sex, and history of depression and/or anxiety diagnoses from baseline until the time of scan, caregiver's highest level of education achieved by the time of scan, and familial income-to-needs ratio at the time of scan were included in the models as covariates. Hierarchical linear regression was conducted to test whether breastfeeding predicted children's IQ scores and accounted for a significant portion of the variance above and beyond that explained by the covariates entered in step 1 of the model.

Hypothesis 2 and Analytic Approach—Hypothesis 2 was that breastfed children would have significantly larger whole brain volumes (WBV) compared with nonbreastfed same-age peers, even when including the same covariates as tested in hypothesis 1. Hierarchical linear regression was conducted to test whether breastfeeding (entered at step 2 of the model) predicted children's WBV and accounted for a significant portion of the variance above and beyond that explained by the covariates entered in step 1 of the model.

Since breastfeeding predicted WBV after covariates were included in the model (see below), we conducted a series of additional regression models to better understand the specificity of the effect of breastfeeding on structural brain volumes. Thus, we first tested whether breastfeeding predicted the 2 components that comprise WBV, which are total gray matter volume and cortical white matter volume. Given that the effect of breastfeeding on total gray matter volume was significant (see below), we then tested whether this finding was specific to cortical gray matter volume and/or subcortical gray matter volume.

Hypothesis 3 and Analytic Approach—Hypothesis 3 was that the association between breastfeeding and higher IQ would be mediated by WBV and the components that comprise WBV. The PROCESS macro was used to test volume as a mediator of the hypothesized relationship between breastfeeding and higher IQ. Models were tested using a bootstrapped sample of 10,000, confidence intervals (CI) set at 95%, and covariates were applied to both the mediator and the outcome variables of the models.

RESULTS

Demographic, Developmental, and Clinical Characteristics of the Sample

As seen in Table 1, breastfeeding (yes versus no) was not related to children's age at scan, sex, gestational age, or birth weight (all p values >.05). Breastfed compared with nonbreastfed children were marginally less likely to have been diagnosed with depression and/or anxiety from baseline up until the time of scan ($p = .09$). African American children were less likely to have been breastfed compared with children of white and other ethnicities ($p < .0001$). Breastfed children were more likely to be from families with significantly greater income ($p < .0001$) and caregivers who had completed significantly more years of education ($p < .0001$) compared with nonbreastfed children.

It is important to note that when examining the association between breastfeeding and caregiver education, as well as family income-to-needs ratio, the correlation between the income and education variables was high in the current sample ($r = .63$, $p < .0001$). Thus, given concerns of multi-collinearity (variance inflation factor [VIF]; VIF tolerance = 0.57) when including these 2 variables as covariates in the final models, we chose to use only 1 of these variables. We used the variable that was most strongly correlated with child IQ, and thus most important to account for its effects when considering the role of breastfeeding and brain volume on child IQ. Findings indicated that the correlation between caregiver education and child IQ was $r = 0.42$, whereas family income-to-needs ratios and child IQ correlated at $r = 0.41$. Thus, for all proceeding analyses, caregivers' highest level of education completed at the time of scan was included as the covariate.

Breastfeeding as Predictor of Higher IQ Scores When Covarying for Child Age, Sex, Diagnostic History, and Caregiver Education

As seen in Table 2, step 1 of the regression equation included the covariates of interest and accounted for a significant proportion (~17%) of the variation in children's IQ scores. Greater caregiver education was the only significant demographic predictor of children's higher IQ scores. When entered at step 2, breastfeeding accounted for an additional and significant increase in the variance accounted for in the model ($R^2_{change} = 0.03$, F_{change} [1, 142] = 5.16, p .03). Breastfed children had significantly higher IQ scores than nonbreastfed children, even when controlling for the robust effect of caregivers' education.

Breastfeeding as Predictor of Whole Brain Volume and Its Components When Covarying for Key Variables

Whole Brain Volume—Results from the hierarchical regression indicated that, as seen in Table 3, children's sex and age were significant ($p < .05$) predictors of WBV at step 1. When breastfeeding was added to the model at step 2, it resulted in a significant increase in the amount of variance accounted for in children's WBV ($R^2_{change} = 0.02$, F_{change} [1, 142] = 4.57, $p = .03$), with breastfeeding associated with greater WBV. We then further analyzed WBV by examining its 2 subcomponents separately (i.e., cortical white matter volume and total gray matter volume).

Cortical White Matter Volume—Results indicated that breastfeeding was not a significant predictor of children's white matter volume ($R^2_{change} = 0.01$, F_{change} [1, 142] = 1.78, $p = .18$) (Table 3).

Total Gray Matter Volume—Breastfeeding again accounted for a significant and additional portion of the variance in total gray matter volume at step 2, even after accounting for the significant effect of children's sex at step 1 ($R^2_{change} = .03$, F_{change} [1, 142] = 6.40, $p = .01$). Breastfed children had larger total gray matter volume than nonbreastfed children.

Cortical and Subcortical Gray Matter Volumes—Finally, we examined whether breastfeeding predicted increased cortical and/or subcortical gray matter volume when controlling for key variables. Results indicated that breastfeeding significantly predicted cortical gray matter volume after covarying for the significant effect of child sex ($R^2_{change} = .02$, F_{change} [1, 142] = 3.92, $p = .05$). In addition, results indicated that breastfeeding significantly predicted subcortical gray matter volume after covarying for the significant effects of child sex and age on subcortical gray matter volume ($R^2_{change} = .03$, F_{change} [1, 142] = 5.99, $p = .02$).

Based on the results of the separate regression analyses, we proceeded to test whether subcortical gray matter volume functioned as a mediating mechanism of the identified association between breastfeeding and higher IQ scores. Given that analyses indicated that subcortical gray matter volume was the most significant subcomponent of the identified effect in WBV and total gray matter volume, we focused on subcortical gray matter volume and did not test other variables as mediators, to limit the number of comparisons.

Subcortical Gray Matter Volume as Mediator of the Relationship Between Breastfeeding and Higher IQ Scores

As seen in Figure 2, subcortical gray matter volume mediated the association between breastfeeding and higher IQ scores. That is, the significant effect of breastfeeding on IQ scores was not as strong when accounting for the effect of breastfeeding on subcortical volume and the association between larger subcortical volume and higher IQ scores. Thus, the relationship between breastfeeding and IQ was better explained by the indirect effect via subcortical gray matter volume (bootstrap 95% CI = 0.04–2.86). It is important to note that to further validate the mediation findings, we conducted the same analyses using data from scan 1. Results indicated highly consistent effects sizes in both mediation models. However, the indirect effect only approached significance when tested using scan 1 subcortical gray matter. Specifically, the indirect effect via subcortical gray matter volume at scan 1 using n 5,000 bootstrap and 95% CI was −0.0071 to 2.3123 compared with scan 2 subcortical gray matter volume with CI = 0.0426 to 2.8557.

DISCUSSION

These data demonstrate an indirect relationship between breastfeeding and IQ through the development of gray matter volume, specifically subcortical gray matter. The relationship held even after accounting for key variables known to influence IQ, including primary caregiver education, sex, and internalizing diagnoses. Importantly, the effects of breastfeeding on IQ were mediated by subcortical gray matter. To the best of our knowledge, these findings are the first showing a putative mechanistic pathway among breastfeeding, brain development, and IQ in the same participants.

The question of whether and how breastfeeding affects cognitive development has tremendous importance for health promotion and prevention. Evidence for large and long-lasting effects is most clear from a Brazilian epidemiological study in which 3,500 participants were followed up into adulthood.[6] In this population, in which breastfeeding is common across all social classes, individuals who were breastfed for more than 1 month displayed a greater than 4- point increase in IQ. Importantly, IQ explained 72% of economic achievement in adulthood in the sample. Findings from this study also suggested an important potential for change in adult economic achievement and related adaptive outcomes related to breastfeeding. Underscoring the potential public health cost–benefit implications of breastfeeding, Michaelson *et al.*[28] have estimated that increasing the frequency of breastfeeding from 20% to 50% would save an estimated half a billion dollars annually in special education costs in the United States alone.

Although the exact etiology of the relationship between breastfeeding and neural development remains unclear, there has been broad speculation and some evidence for the role of long-chain polyunsaturated fatty acids present in human breast milk in enhancing neurodevelopment.[29] However, in addition to such physiological processes, there may also be an important epigenetic role of the psychosocial effects of enhanced early parent–infant contact and nurturance afforded by breastfeeding on brain development. In addition, breastfed infants may also receive more psychosocial stimulation in the process of being fed, which in turn may contribute positively to brain development. The finding that subcortical gray matter emerged as the mediator of the effect is consistent with animal and some human literature demonstrating powerful effects of early nurturance and deprivation on subcortical structures (e.g., the amygdala and hippocampus[30-32]) and suggest a role for enhanced maternal support; however, this is entirely speculative. Furthermore, this finding contrasts with the results reported by Isaacs *et al.*,[13] who found a great effect in white matter, particularly in boys. Based on this discrepancy and the dearth of studies designed to investigate mechanisms, future studies are now needed that are specifically designed to investigate the differential contributions of these mechanisms as well as the regional specificity of effects.

The study findings are limited by the relatively small sample sizes, lack of prospective and detailed duration data on breastfeeding (including whether breast and bottle feeding were combined), and the absence of measures of maternal IQ. However, caregiver education and income-to-needs ratios are both variables that are well established to be highly related to IQ, and the current study found that breastfeeding predicted IQ even after controlling for maternal education and child's age, sex, and history of ever being diagnosed with depression and/or anxiety disorders. Generalizability of the findings may be limited by the fact that the study used a clinically enriched sample of children. However, related to this, this is also the first study, to the best of our knowledge, to account for the effect of childhood psychopathology on the relationship between breastfeeding and IQ.

The current findings build on the available extant literature linking breastfeeding to IQ and brain development independently, by elucidating a possible mechanistic pathway between these variables and quantifying an effect on IQ in breastfed compared with nonbreastfed children. Study findings further underscore the potential importance of breastfeeding as a key factor in the facilitation of healthy brain and cognitive development in children, an issue critical to health promotion and prevention. Elucidating this pathway between breastfeeding, brain development, and IQ while accounting for other key variables known to affect both IQ and brain development adds further support to the principle that greater efforts to encourage breastfeeding in human infants should be a public health priority.[1]

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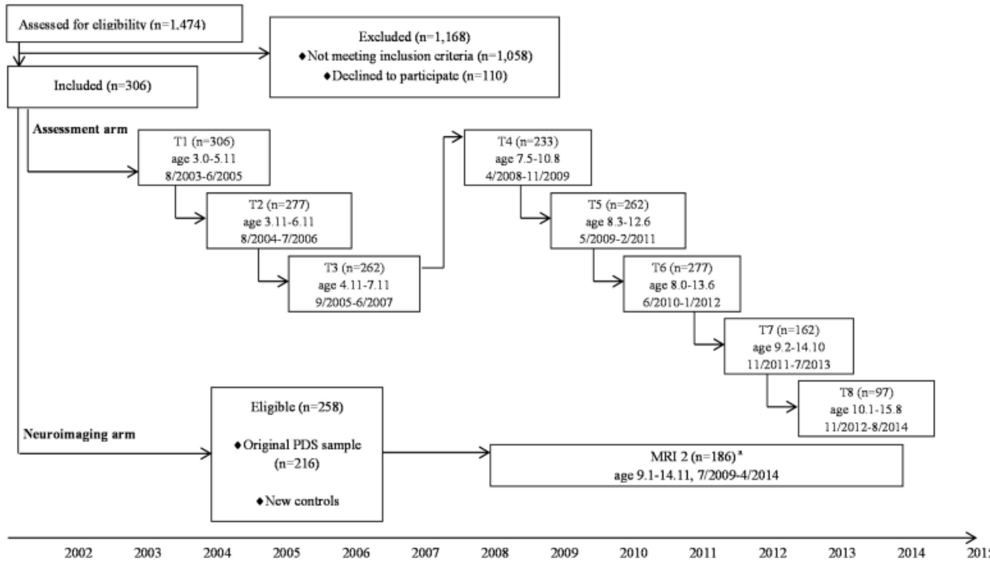

FIGURE 1.

Flow of the Preschool Depression Study (PDS). Note: MRI = magnetic resonance imaging. [a]Of 211 potential scan 2 participants, 21 had unusable scan data, 2 did not have IQ data, 3 had an IQ score < 5, 5 did not have breastfeeding data, 7 had breastfeeding duration of less than 1 month, 18 refused participation, and 7 had braces; therefore scan 2 data were included in the analyses for 148 participants.

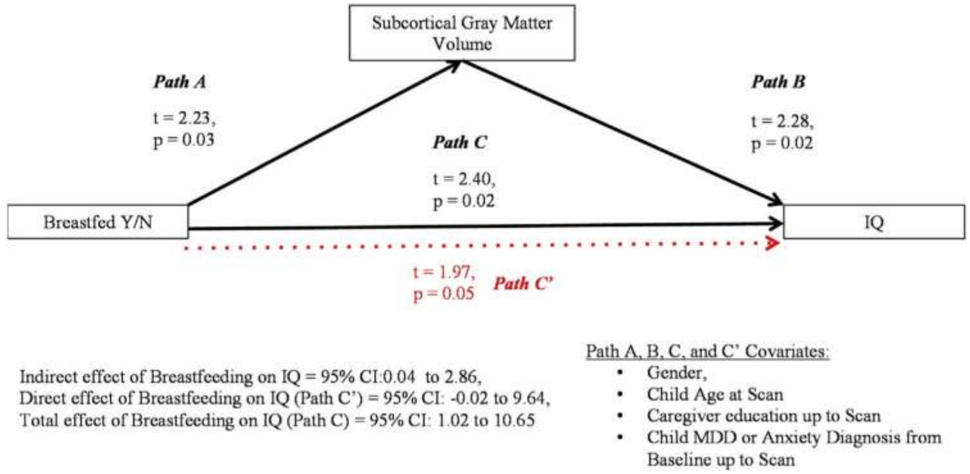

FIGURE 2.

Subcortical gray matter volume as a mediator of the relationship between breastfeeding and IQ. Note: N = no; Y = yes.

TABLE 1

Characteristics of the Sample (N = 148)

	Breastfed n = 56	Not Breastfed n = 92	*p* Value
Age at Scan			
Mean (SD), y	11.88 (1.08)	11.86 (1.24)	.94
Income-to-Needs at Scan			
Mean (SD)	1.25 (0.96)	2.00 (0.78)	< .0001
IQ			
Mean (SD)	99.11 (13.18)	109.03 (13.06)	< .0001
IQ Measure			
% WASI (n)	11% (6)	15% (14)	.44
% KBIT-II (n)	89% (50)	85% (78)	
Primary Caregiver			
Education			
Mean (SD)	6.48 (2.39)	8.74 (2.06)	< .0001
Gestational Age			
Mean (SD), wk	38.65 (2.37)	39.02 (2.08)	.33
Birth weight			
Mean (SD), lb and oz	7.14 (1.31)	7.31 (1.24)	.44
Sex			
% Female (n)	41% (23)	54% (50)	.12
MDD or Anxiety by Time of Scan			
% Yes (n)	71% (40)	58% (53)	.09
Ethnicity			
% African American (n)	64% (36)	27% (25)	
% White (n)	30% (17)	61% (56)	.0001
% Other (n)	5% (3)	12% (11)	

Note: KBIT-II = Kaufman Brief Intelligence Test; WASI = Wechsler Abbreviated Scale of Intelligence.

TABLE 2

Hierarchical Linear Regression Models of IQ Scores in 148 Participants

DV: IQ Score	R^2 adjusted	Nonstandardized Coefficients B	Nonstandardized Coefficients SE	Standardized Coefficient β	*t*	*p*
Step 1	0.17**					
Intercept		76.81	10.34		7.43	.00
Child Sex (M = 1, F = 0)		–0.37	2.10	–0.01	–0.18	.86
Child Age, y		1.00	0.88	0.09	1.13	.26
Caregiver Education		2.36	0.43	0.41	5.48	.00
Child History of MDD or Anxiety		–1.99	2.17	–0.07	–0.92	.36
Step 2	0.19*					
Intercept		76.25	10.19		7.48	.00
Child Sex (M = 1, F = 0)		0.22	2.08	0.01	0.11	.92
Child Age, y		1.02	0.87	0.09	1.17	.24
Caregiver Education		1.87	0.48	0.33	3.94	.00
Child History of MDD or Anxiety		–1.34	2.16	–0.05	–0.62	.54
Breastfed		5.49	2.42	0.19	2.27	.03

Note: DV = dependent variable; F = female; M = male; MDD = major depressive disorder.

* $p < .05$

** $p < .0001$.

TABLE 3

Hierarchical Linear Regression Models of IQ Score in 148 Participants

		Nonstandardized Coefficients				
Whole Brain Volume (cm^3)	$R^2_{adjusted}$	**B**	**SE**	**Standardized Coefficient β**	***t***	***p***
Step 1	0.24**					
Intercept		862.75	78.74		10.96	.00
Child Sex (M = 1, F = 0)		95.73	15.97	0.43	5.99	.00
Child Age, y		20.16	6.73	0.22	2.99	.00
Caregiver Education		3.93	3.28	0.09	1.20	.23
Child History of MDD or Anxiety		–25.60	16.54	–0.11	–1.55	.12
Step 2	0.26*					
Intercept		858.75	77.80		11.04	.00
Child Sex (M = 1, F = 0)		99.95	15.90	0.45	6.29	.00
Child Age, y		20.33	6.65	0.22	3.06	.00
Caregiver Education		0.43	3.63	0.01	0.12	.91
Child History of MDD or Anxiety		–20.92	16.48	–0.09	–1.27	.21
Breastfed		39.46	18.45	0.17	2.14	.03
Cortical White Matter (cm^3)						
Step 1	0.23**					
Intercept		224.99	37.48		6.00	.00
Child Sex (M = 1, F = 0)		36.55	7.60	0.35	4.81	.00
Child Age, y		15.03	3.20	0.34	4.69	.00
Caregiver Education		1.16	1.56	0.05	0.74	.46
Child History of MDD or Anxiety		–9.05	7.87	–0.08	–1.15	.25
Step 2	0.24					
Intercept		223.79	37.39		5.99	.00
Child Sex (M = 1, F = 0)		37.82	7.64	0.36	4.95	.00
Child Age, y		15.08	3.20	0.34	4.72	.00
Caregiver Education		0.11	1.74	0.01	0.06	.95
Child History of MDD or Anxiety		–7.65	7.92	–0.07	–0.97	.34
Breastfed		11.83	8.87	0.11	1.33	.18
Total Gray Matter (cm^3)						
Step 1	0.22**					
Intercept		637.76	46.89		13.60	.00
Child Sex (M = 1, F = 0)		59.17	9.51	0.46	6.22	.00
Child Age, y		5.13	4.01	0.09	1.28	.20
Caregiver Education		2.77	1.95	0.10	1.42	.16
Child History of MDD or Anxiety		–16.55	9.85	–0.12	–1.68	.10
Step 2	0.25*					
Intercept		634.96	46.04		13.79	.00

Whole Brain Volume (cm³)	R^2 adjusted	Nonstandardized Coefficients B	Nonstandardized Coefficients SE	Standardized Coefficient β	*t*	*p*
Child Sex (M = 1, F = 0)		62.13	9.41	0.48	6.60	.00
Child Age, y		5.25	3.94	0.10	1.33	.18
Caregiver Education		0.32	2.15	0.01	0.15	.88
Child History of MDD or Anxiety		–13.27	9.75	–0.10	–1.36	.18
Breastfed		27.63	10.92	0.21	2.53	.01
Total Cortical Gray Matter (cm³)						
Step 1	0.19**					
Intercept		501.47	39.16		12.81	.00
Child Sex (M = 1, F = 0)		46.21	7.94	0.43	5.82	.00
Child Age, y		3.07	3.35	0.07	0.92	.36
Caregiver Education		1.85	1.63	0.09	1.14	.26
Child History of MDD or Anxiety		–14.61	8.22	–0.13	–1.78	.08
Step 2	0.21*					
Intercept		499.62	38.77		12.89	.00
Child Sex (M = 1, F = 0)		48.16	7.92	0.45	6.08	.00
Child Age, y		3.15	3.31	0.07	0.95	.34
Caregiver Education		0.24	1.81	0.01	0.13	.89
Child History of MDD or Anxiety		–12.45	8.21	–0.11	–1.52	.13
Breastfed		18.20	9.20	0.17	1.98	.05
Total Subcortical Gray Matter (cm³)						
Step 1	0.23**					
Intercept		46.54	3.62		12.87	.00
Child Sex (M = 1, F = 0)		3.86	0.73	0.38	5.26	.00
Child Age, y		1.16	0.31	0.27	3.74	.00
Caregiver Education		0.28	0.15	0.14	1.87	.06
Child History of MDD or Anxiety		–0.64	0.76	–0.06	–0.85	.40
Step 2	0.26*					
Intercept		46.33	3.56		13.03	.00
Child Sex (M = 1, F = 0)		4.08	0.73	0.40	5.61	.00
Child Age, y		1.17	0.30	0.27	3.83	.00
Caregiver Education		0.10	0.17	0.05	0.60	.55
Child History of MDD or Anxiety		–0.40	0.75	–0.04	–0.53	.60
Breastfed		2.06	0.84	0.20	2.45	.02

Note: F = female; M = male; MDD = major depressive disorder

* $p < .05$

** $p < .0001$.