The Impact of Breastfeeding on Neurocognitive Outcome at Twelve Years – Secondary Analysis of a Prospective Cohort Study

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Research Article

Keywords: BREASTFEEDING, NEURODEVELOPMENT, COGNITION, BEHAVIOUR, GENRAL CONCEPTUAL ABILITY

Posted Date: July 30th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-612354/v1>

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Abstract

Background

The objectives of this secondary analysis were to compare the; (i) cognitive and (ii) behavioural outcomes in children born congenitally normal, non-preterm, and non-growth restricted that were breastfed beyond one month of age with those that were not breastfed or breastfed for <1-month.

Methods

An original prospective cohort study conducted on n=2097 fetuses compared children with normal fetal UAD PI (Umbilical Artery Doppler Pulsatility Index) against those with an elevated UAD PI and assessed neurocognitive development at twelve years of age using British Ability Scale Version II (BAS II) and the Achenbach Behavioural Checklist Parent Rated Version (CBCL). This secondary analysis included children where maternal breastfeeding status was known (n=252). Childhood cognitive and behavioural scores were analysed and compared for the breastfed versus the non-breastfed group. Linear regression analysis was performed, controlling for confounders including gender, age at assessment, Townsend Score, and UAD PI.

Results

Excluding congenitally abnormal, preterm and growth restricted babies, n=206 were included. The mean age at follow-up was 12.2 years (± 0.6 SD) for both groups with 43.5% (n=20) and 50.3% (n=81) of male gender in both groups respectively. When comparing those children who were breastfed against those who were not or for <1-month, the breastfed group score higher in spelling ($p < 0.001$) and reading ($p < 0.001$) assessments. As was also the case in verbal ($p < 0.001$), reasoning ($p < 0.001$) and spatial ability scores ($p < 0.001$). In relation to behavioural assessments, there was no difference between groups.

Conclusion

Term babies who are breastfed for >1-month have more optimal scores in neurocognition when analysed at 12-years with no differences in parent observed behaviour compared to non-breastfed/breastfed for <1-month counterparts. These findings must be interpreted with caution due to the presence of confounders with further research into the biological and physiological mechanisms by which breastfeeding may optimise brain development.

Background

Breastfeeding has consistently been proven to be an important and beneficial factor in health and nutritional input for children with an associated reduction in the incidence of childhood infections, chronic illnesses and cancer [1, 2, 3]. From 1929 the potential link between breastfeeding and improved childhood cognitive function has been postulated [4] and it has been demonstrated that Intelligence Quotient (IQ) scores differ significantly between breastfed, and formula fed babies and most notably so

in children delivered preterm with a low birth weight [5]. Potential physiological mechanisms for such differences have been attributed to the alternative nutritional composition of breastmilk and formula, with specific components of breast milk suggested to be particularly beneficial in childhood brain development [6, 7, 8].

It is not only breastfeeding but its' exclusivity and prolongation which lends itself to optimally improved scores in assessments of neurocognition [11, 12], with a duration of >3-months breastfeeding appearing significant [12]. Studies thus far display heterogeneity in design, notably in relation to assessment tools utilised as well as confounding variables considered including socio-economic status, gestation at delivery and the duration of child follow-up [4, 5, 12].

With most cohort studies assessing children to six to seven years and a paucity of evidence beyond this it is a challenge to deduce the long-term implications of breastfeeding on neurocognition [11]. Hence the objectives of this secondary analysis were to compare the (i) cognitive and (ii) behavioural outcomes in children born congenitally normal, non-preterm, and non-growth restricted that were breastfed beyond one month of age with those that were not breastfed or breastfed for <1-month.

Methods

The UAD PI (Umbilical Artery Doppler Pulsatility Index) is a measure of resistance within the fetoplacental circulation [14]. A historical study of $n = 2097$ fetuses evaluated if there was any effect on serial UAD PI testing at 28, 32 and 34 weeks' gestation on perinatal outcome [13]. The index prospective nested case-control compared two groups of children 11–12 years later, where at 28-weeks gestation they had an elevated (>90th centile) or normal (<10th centile) UAD PI [13, 15, 16]. Based on this cohort, results relating to the impact of UAD PI on cardiovascular, respiratory and neurocognitive outcome have been published previously [14, 15, 16]. Of the original cohort, $n = 252$ (12%) underwent neurocognitive assessment and following exclusion of growth-restricted (birthweight <10th centile), preterm (<37-weeks), congenitally or genetically abnormal babies, cases where retrospective maternal information had been gathered regarding breastfeeding status and duration were selected and a secondary analysis of the aforementioned objectives was performed. Following ethical approval from the Northern Ireland Research and Ethics committee, Queen's University Belfast, informed consent was obtained from parents and children.

Cognitive and behavioural assessments using validated questionnaires were performed by a single accredited, developmental child psychologist. Each child's cognitive function was assessed using the British Ability Scale (BAS) II questionnaire [17]. This includes diagnostic scales which assess information processing and memory; academic performance and core scales making up the General Conceptual Ability (GCA score), which serves as an overall assessment of mental processing and reasoning. Behavioural function was assessed via a parent questionnaire using the Achenbach Child Behavioural Checklist Parent Rated Version (CBCL) which evaluates specific behaviours on a three-point rated scale. The published study relating to UAD PI and childhood neurocognition and behaviour showed that an

elevated UAD PI at 28 weeks' gestation was associated with lower scores in cognitive assessments of information processing and memory with no impact on academic ability or behaviour [14].

In addition to CBCL, developmental histories were taken from mothers, including breastfeeding initiation and duration. Mothers who stated they breastfed for more than one month were compared to those who did not breastfeed or breastfed for less than one month. Instances where neurocognitive assessments were incomplete were excluded. Demographics were summarised using N (percentage) and mean (standard deviation) where appropriate. Linear regression analysis was performed with adjustment for gender, age at assessment, Townsend score (a measure of socioeconomic status) [19] and UAD PI group (elevated (> 90th centile) and normal (< 90th centile)). Analysis was performed using IBM SPSS V.27, 2020.

Results

In total n=252 children were recruited to undergo neuro-cognitive assessment. Of this cohort, instances of birthweight <10th centile, pre-term delivery (<37-weeks' gestation), incomplete assessment and post-natal diagnoses of a congenital anomaly and or suspected genetic syndrome were excluded, leaving a final cohort of n=206 (n=45 (21.8%) breastfeeding for >1-month and n=161 (78.2%) breastfeeding <1-month, or not at all. Of mothers that breastfed for >1-month, n=11 (24.4%) and n=7 (15.6%) breastfed for > 3-months and > 6-months respectively. The demographics of both groups are demonstrated in Table 1.

Unadjusted (crude) and adjusted linear analysis revealed a significant difference in almost all parameters in cognitive assessments of the GCA and BAS II scales (Tables 2 and 3 respectively). There was no difference between groups in behavioural assessments

Achenbach Child Behavioural Checklist (Supplementary Table 1).

Discussion

This secondary analysis of a prospective cohort study demonstrates that when appropriately grown, congenitally normal, term babies are breastfed beyond one month of age they have significantly greater scores in cognitive assessment with no difference in behavioural assessment.

The findings of this study are consistent with existing evidence, demonstrating a positive impact of breastfeeding on neurocognitive function [21, 24, 25, 28, 32]. Our study supports this further by separating the areas for assessment into verbal, non-verbal, spatial and standard, facilitating a more thorough assessment of each area of neurocognition. When looking at these in more detail we can see significantly greater scores between groups in relation to assessments of GCA which led to an overall difference in the collective ultimate GCA score. This suggests a more optimal ability to perform complex transformations of information and is a combination of verbal, non-verbal reasoning and spatial skills [17]. In relation to the BAS II assessment, while spelling and reading scores were greater in the breastfed

group, there was no significant difference in relation to numerical assessment. This contradicts existing evidence assessing mathematical ability in breastfed children [27] and hence should be interpreted with caution. The CBLC (behavioural assessments) in this study showed no difference between groups. This has been reproduced in other studies with variable findings. Some studies have reported improved behavioural scores when also using the CBLC in breastfed children, and one in particular used a diagnosis of ADHD as a marker of behavioural difficulties and demonstrated that this is less likely in those who are breastfed [42, 43, 44].

As expected, mothers in the breastfeeding group had a greater maternal age and lower Townsend score (degree of social deprivation) the latter being taken into consideration as part of the adjusted analysis [22, 23, 24, 25, 31]. A previous systematic review looked at the effect of confounders and its impact on the results of breastfeeding and neurocognitive scores [45]. Many previous studies have not controlled for confounders as thoroughly as this study and therefore may have contributed to skewed results [45].

BAS II is not an assessment tool that has been used to examine neurocognitive function in relation to breastfeeding previously. This test gives a General Conceptual Ability to give the overall abilities of the child, not just based upon IQ. Scales such as BAS II are key to ensuring full assessment of children beyond IQ to assess for executive functioning, attention, processing and memory and thus facilitate selection for further assessment for dyslexia, autistic spectrum disorder and attention-deficit/hyperactivity disorder [26, 30]. A review into the BAS II edition demonstrated its ability through psychometric assessments to contribute to a 'holistic analysis of the child's functioning' [29]. Hence, our study evaluates the effect of breastfeeding on the child's neurocognitive development as a whole and not just on an intellectual level. CBLC has been studied before and a systematic review reflects studies that have demonstrated that children who have been breastfed for at least three or four months may have behaviour and conduct scores using this system. These same studies indicated that a longer time period of breastfeeding seems to be more important than the initiation itself [33].

Strengths of the study include its prospective nature and robust methodology. The study is novel in that it is, to our knowledge one of the longest follow-up in specifically appropriately grown, term, breastfed children published to date, as well as being one of the first to use the aforementioned scales for assessment in relation to breastfeeding and neurocognition. Study limitations include the reliability upon maternal retrospective recall of breastfeeding status and duration as well as lack of information regarding breast-feeding exclusivity. However, existing evidence suggests that such maternal recall is a reliable and valid method of assessment, although its application up to 12-years has not been formally assessed [31].

Existing evidence demonstrates more optimal myelination and cerebral cortex maturation in the brains of breastfed versus those who are not [9, 39]. The nutritional elements that are linked to these differences include lutein, long chain fatty acids, sphingolipid and α -tocopherol [7, 8, 9, 10]. Carotenoids such as lutein and zeaxanthin have been found to be one of the few nutrients present in breastmilk yet only in trace amounts in formula and are vital in the development of the nervous system and vision [46]. Lutein

is selectively deposited in the brain promoting corpus callosum and cerebral cortical gray matter maturation [9]. This has been demonstrated on brain imaging by MRI (Magnetic Resonance Imaging) and correlates with the shown significant differences seen in the white and subcortical gray matter when comparing breast fed and non-breastfed children [9]. The corpus callosum is responsible for cognitive processing, motor function and helps with the transfer of visual, auditory and somatosensory information to the temporal, occipital and parietal lobes of the brain [10]. Some studies have shown that formula that has been supplemented with long chain fatty acids can produce a similar improvement in children's cognitive abilities [41]. This could be extrapolated to indicate that certain nutritional elements of breastmilk could be the cause of improved neurocognitive scores and therefore further studies into this and addition to formulas could replicate these findings.

The findings of our study provide a further incentive for mothers to breastfeed. At the time of this study, breastfeeding rates among mothers in Northern Ireland were some of the lowest in the UK at 36% [20]. Reasons for this may have included poor initiation prior to discharge, lack of education and cultural differences [34]. Since the subsequent implementation of the first Northern Ireland regional breastfeeding strategy and the more recent 'Ten Year Breastfeeding Strategy', rates have significantly improved due to improved hospital and community training and service provision and therefore maternal education and support [20, 35, 36, 37, 38]. Providing education antenatally and maternal support in relation to breastfeeding has been shown to improve uptake [39]. NICE (National Institute for Health and Care Excellence) encourage this uptake through the fostering of training, education and support as a key part of postnatal care for all mothers [40].

While the findings of this study support breastfeeding, due to the nature of the scoring systems and the influence of an abundance of confounding variables, particularly as children get older, one cannot directly imply that that breastfed children are more intelligent but simply objectively interpret the findings in relation to existing evidence. Further studies at this age considering the interaction of additional confounders must be performed to support this.

Conclusion

This study demonstrates that breastfeeding beyond one month of age in appropriately grown, term babies lead to significantly improved scores in neurocognition at 12-years. There were no differences in behavioural assessments between groups. One must apply caution to interpretation due to the presence of confounders and a paucity of supporting evidence at this age. More research is required into the physiological and biological mechanisms by which breastfeeding optimises brain development and function.

Abbreviations

BAS II – British Ability Scale Version II

CBCL- Child Behavioural Checklist Parent Rated Version (Achenbach)

GCA- General Conceptual Ability

IQ- Intelligence Quotient

MRI- Magnetic Resonance Imaging

NICE- National Institute for Health and Care Excellence

UAD PI – Umbilical Artery Doppler Pulsatility Index

Declarations

Ethics approval and consent to participate

Ethical approval for this research was obtained from the Northern Ireland Research and Ethics Committee and Queens University Belfast and prospective written informed consent was obtained from the parents and children participating.

Consent for publication

Participant and parental consent included authorisation for publication of respective anonymized findings and consent was provided by all co-authors for publication following review of the final manuscript.

Availability of data and material

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

Competing interests

The authors have no competing interests as defined by BMC, or other interests that might be perceived to influence the results and/or discussion reported in this paper.

Funding

This research was funded by the Tiny Life organisation, formerly known as NIMBA.

Authors' contributions

K.M.R and F.M wrote the main manuscript text and F.M performed the analysis. B.McC, A.T, P.H, M.C.S, M.D.S and F.M conceived the original study and collated the original data. All authors reviewed and approved the final manuscript.

Acknowledgements

None

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Tables

Table 1: Demographic characteristics of study cohort [PI, pulsatility index; SD, standard deviation; UAD, Umbilical artery Doppler]

Variable	Breastfed > 1-month Mean (SD) or N (%) N = 45	Not breastfed or < 1-month Mean (SD) or N (%) N = 161
Gender (male)	20 (44.4%)	81 (50.3%)
Age of child (years)	12.2 (0.6)	12.3 (0.6)
Body mass index (Kg/m ²)	19.0 (3.0)	19.1 (3.6)
Townsend score*	-0.7 (3.3)	2.5 (3.2)
Tanner Pubic hair staging		
1	21 (46.7%)	99 (61.5%)
2	11 (24.4%)	29 (18.0%)
3	5 (11.1%)	21 (13.0%)
4	8 (17.8%)	10 (6.2%)
5	0 (0%)	2 (1.3%)
Crowding index	0.82 (0.3)	0.87 (0.3)
Birthweight	3547.4 (502.7)	3481.9 (496.6)
Ponderal index	2.7 (0.5)	2.8 (0.5)
Gestation	39.9 (1.2)	39.9 (1.6)
UAD PI at 28-weeks	1.2 (0.4)	1.32 (0.5)
Maternal age (years)*	42.5 (4.8)	39.7 (5.0)

(* = significant difference between groups).

Table 2

Adjusted and unadjusted linear regression analysis for mothers breast-feeding for > 1-month vs. <1-month/non-breastfeeding for GCA scale parameters. This analysis was adjusted for gender, age at assessment, Townsend score and Umbilical artery Doppler pulsatility index group (elevated (> 90th centile) and normal (< 90th centile)).

BAS II Score	Breastfed > 1-month Mean score (SD) N = 45	Not breastfed or < 1- month Mean score (SD) N = 161	Unadjusted analysis p-value	Adjusted analysis p-value
Number standard score	115.9 (12.3)	109.5 (15.1)	0.009	0.640
Spelling standard score	109.2 (14.9)	99.6 (15.5)	< 0.001	0.043
Reading standard score	106.6 (16.3)	95.7 (15.1)	< 0.001	0.039

Table 3

Adjusted and unadjusted linear regression analysis for mothers breast-feeding for > 1-month vs. <1-month/non-breastfeeding for validated British Ability Scales II achievement scale parameters. This table was adjusted for gender, age at assessment, Townsend score and Umbilical artery Doppler pulsatility index group (high (> 90th centile) and normal (< 90th centile)).

GCA Scale	Breastfed > 1-month Mean score (SD) N = 45	Not breastfed or < 1-month Mean score (SD) N = 161	Unadjusted analysis p-value	Adjusted analysis p-value
Verbal sums of scores	113.5 (16.5)	99.2 (18.7)	< 0.001	0.035
Non-verbal reasoning sums of scores	104.9 (16.1)	93.2 (16.9)	< 0.001	0.027
Spatial sums of scores	107.7 (17.4)	96.7 (17.5)	< 0.001	0.03
Standard verbal ability scores	110.7 (13.0)	99.4 (15.0)	< 0.001	0.038
Standard non-verbal reasoning ability	103.9 (13.4)	94.1 (14.2)	< 0.001	0.026
Standard spatial ability	106.2 (15.3)	96.5 (15.4)	< 0.001	0.028
Standard GCA	108.3 (14.6)	95.8 (14.9)	< 0.001	0.008

Supplementary Files

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