The Long-Term Effects of Breastfeeding on Development

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1. Introduction

The link between breastfeeding duration and subsequent development, cognition, educational, mental, psychomotor and behavioural functioning of the infant has been the subject of much scientific enquiry. Indeed, the effect of feeding on infant health and development was first discussed more than half a century ago when breastfed babies were reported to have better cognitive outcomes in childhood than artificially fed babies (Hoefer and Hardy 1929).

Some studies have found striking results pertaining to the relative advantages that breastfeeding can confer on child neurodevelopment (Oddy, Kendall et al. 2003; Vohr, Poindexter et al. 2006; Kramer, Aboud et al. 2008). Breastfeeding has previously been associated with improvements across neurodevelopmental domains for low birthweight babies in comparison with not breastfeeding at all (Vohr, Poindexter et al. 2006). One study reported results from a large randomized controlled trial and found that breastfeeding for a longer duration and exclusive breastfeeding were associated with significant increases in the child's IQ by age six years (Kramer, Aboud et al. 2008).

Breastfeeding is more common among women of social advantage and confounding complicates study interpretation (Bauchner, Leventhal et al. 1986). The question of whether breastfeeding and formula feeding have differential effects on development, cognitive and language has not yet been comprehensively answered (Drane and Logemann 2000), largely due to lack of sample size resulting in inadequate statistical power and failure to obtain prospective data on a wide range of variables. These include infant feeding, the relevant covariates and validated outcome tests later in childhood. While language development in

humans is under substantial genetic control (Stromswold 2001; Spinath, Price et al. 2004), there is accumulating evidence that environmental factors such as early nutrition can alter the expression of the genome and lead to enduring phenotypic changes.

Breastfed infants have cognitive advantages over formula-fed infants in a meta-analysis of 20 studies of children, after adjusting for confounders (Anderson, Johnstone et al. 1999). Studies that examined developmental time points have observed advantages of breastfeeding in comparison with not breastfeeding for infant development that can be observed from the neonatal period (Hart, Boylan et al. 2003), through to infancy (Vestergaard, Obel et al. 1999), early childhood (Fergusson, Beautrais et al. 1982), mid-childhood (Oddy, Robinson et al. 2011), adolescence (Oddy, Kendall et al. 2010) and into midlife (Richards, Hardy et al. 2002). Some reviews and individual studies have found the protective effect of a longer duration of breastfeeding on child behaviour and cognition to be an artifact of sociodemographic confounding rather than a true association. Zhou and colleagues (Zhou, Baghurst et al. 2007) suggested that the benefits of breastfeeding were diminished when improvements in the home environment were taken into consideration and concluded that socioeconomic factors mediate the relationship between breastfeeding and child cognitive development. The authors of a meta-analysis of studies on breastfeeding and child intelligence argued that the relationship between breastfeeding and child development is heavily mediated by maternal IQ and studies that do not adjust for maternal IQ will observe biased results (Der, Batty et al. 2006). However, other studies have found that controlling for maternal education and IQ does not eliminate the positive effects of breastfeeding, suggesting that maternal IQ is not always an alternative explanation for results (Bartels, van Beijsterveldt et al. 2009).

To ascertain the true effect of breastfeeding on infant development, adequate study design is essential. A review of 24 studies found that almost all studies contained a methodological flaw; either inadequate control for confounders; insufficient definition of outcomes; or inconsistent definition of breastfeeding (Drane and Logemann 2000) concluding that the benefits of breastfeeding for development and cognitive IQ could not be determined due to study design limitations. Many studies are limited by insufficient methodological rigour, as suggested by a review of 40 studies on breastfeeding and intelligence between 1929-2001 that concluded no convincing evidence existed regarding the effects of breastfeeding versus formula feeding in relation to intelligence. The major challenge is to adequately control for the considerable confounding of parental and family characteristics also strongly associated with both breastfeeding for longer periods and good developmental outcomes for children. Given controversy in this area, efforts must be concentrated towards study design that allows for the appropriate determination of any relationship between breastfeeding and early developmental outcomes whilst allowing adjustment for factors that are closely associated with both. Future investigations must use more rigorous methods and criteria in the design of breastfeeding studies (Drane and Logemann 2000; Jain, Concato et al. 2002).

Breastfeeding is promoted as beneficial to both the mother and newborn and exclusive breastfeeding for at least six months is recommended (World Health Organisation 2003). Although there are many reasons to encourage breastfeeding, its benefits for cognitive ability, intelligence and academic achievement have received increasing scientific scrutiny (Horwood and Fergusson 1998; Der, Batty et al. 2006; Silva, Mehta et al. 2006; Kramer, Aboud et al. 2008).

Neurobehavioural development is an essential aspect of childhood development and an estimated one in five children have some mental health problem in Australia (Zubrick, Silburn et al. 2000). Between ten and twenty percent of children globally have emotional or behavioural problems and these have been listed as one of the six priority areas for future strategic directions for improving the health and development of children and adolescents (Belfer 2008). Although evidence shows that family, social, economic and psychological disadvantages associated with poverty, low parental income and education, single-parenthood and living in deprived areas are key risk factors for child mental health problems (Robinson, Oddy et al. 2008), little is understood about the potential impact of early infant feeding on subsequent mental health.

Compelling evidence exists for a relationship between breastfeeding, developmental milestones (Sacker, Quigley et al. 2006) and cognition from longitudinal (Drane and Logemann 2000), experimental (Koletzko, Aggett et al. 1998) and neurodevelopmental studies (Farquharson, Cockburn et al. 1992). However there has been conflicting evidence as to the psychological and behavioural outcomes associated with breastfeeding, potentially caused by inherent methodological challenges in this area including inadequate adjustment for confounding factors and problems with study design (Der, Batty et al. 2006; Kramer, Aboud et al. 2008).

1.1 Aims of our study

The aim of our study was to overcome some of the main methodological challenges that have limited previous research and in so doing determine whether independent effects of breastfeeding on early child development, cognitive IQ, academic attainment and mental health were apparent using data collected from the Western Australian Pregnancy Cohort (Raine) Study, a large prospective pregnancy cohort study followed to fourteen years of age.

We examined the association between early infant feeding and developmental outcomes at ages one, two and three years after adjusting for confounders. We hypothesized that developmental outcomes would be improved for children who were breastfed for a longer duration (Oddy, Robinson et al. 2011).

We examined the association between the duration of full breastfeeding and cognitive outcome (cognitive IQ) measured at six (Oddy, Kendall et al. 2003) and at ten years (Whitehouse, Robinson et al. 2011), taking into account perinatal, social and family factors. We conducted a longitudinal follow-up investigation of previous positive findings of breastfeeding (Oddy, Kendall et al. 2003) on language ability among children, whether the association persists until middle childhood, and whether any effect was of comparable magnitude at ten years (Whitehouse, Robinson et al. 2011).

We aimed to determine if the duration of breastfeeding was associated with numeracy and literacy achievement in children at ten years (Oddy, Li et al. 2011). We hypothesised that children breastfed for longer compared to those breastfed for a shorter duration would achieve higher scores in numeracy and literacy, independent of maternal and demographic factors, and early cognitive stimulation received in the home.

Finally, we aimed to investigate the duration of breastfeeding with child and adolescent mental health (Oddy, Kendall et al. 2010). We hypothesised that infants breastfed for longer would have improved mental health outcomes throughout childhood and adolescence.

2. Methods

2.1 Study population

The Western Australian Pregnancy Cohort (Raine) Study commenced as a randomized controlled trial to study the effects of repeated ultrasound during pregnancy in which 2,900 pregnant women were enrolled from the public antenatal clinic at the major obstetric hospital in Perth, Western Australia, and nearby private practices. This became a longitudinal study following 2,868 children born over a three year period with approximately 100 women per month enrolled from May 1989 to November 1991 (Newnham, Evans et al. 1993). The criteria for enrolment were gestational age between 16 and 20 weeks, sufficient proficiency in English to understand the implications of participation, an expectation to deliver at the hospital and an intention to remain in Western Australia so that follow-up would be possible.

2.2 Data collection during pregnancy and subsequent follow-ups

Comprehensive data on social and demographic factors, and medical and obstetric history were obtained from the parent at enrolment and, in the mother's case, updated during the 34th week of pregnancy. The babies were examined at two days of age by a paediatrician or midwife. Follow-ups at the first (N=2,441), second (70% follow-up; N=1,988) and third years (N=2,280) involved a structured interview and clinical examination of participating children in the cohort. A questionnaire was administered and information from a clinical examination was collected at around the intended age of one (mean age= 14 months), two (mean age= 26 months) and three years (mean age= 37 months) and at six (mean age= 71 months), eight (mean age=97 months), ten (mean age=126 months) and fourteen (mean age=168 months) years. For all follow-up assessments, parents were contacted and a questionnaire was posted for completion as soon as possible. Parents were asked to return the questionnaire at the time of the physical examination. The questionnaire collected information about parental sociodemographic factors (housing, family structure, employment, income), family functioning, and information about their child such as the development of speech and language, cognitive development, behaviour and history of illnesses, injuries and admissions to hospital.

2.3 Infant feeding

Infant feeding data were collected at one, two, and three years. Information about 'age at which milk other than breast milk was introduced' was applied to obtain a continuous measure of predominant breastfeeding in months. In a similar way, information about the age at which breastfeeding stopped was used to obtain measures of any breastfeeding. These data were categorised as 'less than four months' versus 'four months or longer', and 'less than six months' versus 'six months or longer'.

2.4 Covariate measures

We considered a wide range of pregnancy, antenatal, obstetric and postnatal variables throughout the child's life. Perinatal covariates included gender; gestational age (weeks)

and; percentage of expected birthweight,. Social covariates were maternal age at child's birth; parental smoking; and presence of other siblings. In addition we considered fathers education, family income and parental employment status. Language stimulation was measured at three and five years by asking the parent how often she reads a story to the child. Maternal postnatal depression, diagnosed by a doctor, was measured retrospectively at the ten year follow-up.

2.5 Outcome measures

2.5.1 Infant/Child Monitoring Questionnaires (IMQ)

The IMQ (now known as the Ages and Stages Questionnaire (ASQ)) is a series of parent completed questionnaires designed to be used as a screening tool to assist in the monitoring of child development in the early years (Squires, Bricker et al. 1990). Each questionnaire measures communication, gross and fine motor, adaptive and social/personal development. IMQ was administered at 12, 24 and 36 months and scored as per the manual (Squires, Bricker et al. 1990). Scoring below the cutpoint was classified as having an "atypical score" for that domain. We also created a variable representing the presence of any atypical score across domains for each age and categorised the outcomes according to the total number of atypical scores for all follow-ups in each domain

2.5.2 Cognitive IQ

At both the six and ten year follow ups, children completed a clinical assessment that included administration of the Peabody Picture Vocabulary Test – Revised (PPVT-R). This was an achievement test of receptive vocabulary in English that provides an estimate of one major aspect of verbal ability for subjects who have grown up in an English speaking environment (Dunn and Dunn 1981). The PPVT-R was administered by the two child health nurses according to the manual and supervised by a registered psychologist. A child with a score less that the first negative standard deviation for the group was deemed to have a "below average verbal ability" irrespective of the language spoken at home. There were significant tester effects and these were adjusted in all analyses.

2.5.3 Educational assessment

The Western Australian Literacy and Numeracy Assessment (WALNA) was administered annually to all students across Western Australia in grades three, five and seven (approximately 75% of West Australian children from public schools completed the assessment). The assessment consists of multiple-choice, short-response, and open-response questions in four areas: mathematics, reading, writing and spelling. WALNA records were linked for 1,038 Raine study children who were in grade five and attending government schools at the time of assessment.

2.5.4 Mental health measures

We focused on the parent-report Child Behaviour Checklist (CBCL/4-18) (Achenbach 1991) as the mental health outcome variable at the two, five, eight, ten and fourteen year follow-

ups. The CBCL/2-3, validated for use with two year old children, was applied at the two-year follow-up (Achenbach, Edelbrock et al. 1987). The CBCL/4-18 is a 118-item instrument that assesses behavioural psychopathology in children according to syndrome scales. The scales of withdrawn, anxious/depressed and somatic complaints are grouped and scored as internalizing problems while the syndrome scores of delinquent behaviour and aggressive behaviour are grouped and scored as externalizing problems. A total score of overall mental health morbidity, representing the sum of all the items, is derived for the entire scale. Higher scores represent more disturbed behaviour. In accordance with the normative criteria, we applied the recommended clinical cut-off scores ($T \geq 60$) to total, internalizing, and externalizing T-scores to distinguish those children with a 'mental health problem' of clinical significance (Achenbach 1991). Therefore we were able to analyse mental health outcomes at   all years using continuous CBCL T-scores and a binary variable reflecting clinical significance.

2.6 Statistical analysis

(See references (Oddy, Kendall et al. 2003; Oddy, Kendall et al. 2010; Oddy, Li et al. 2011; Oddy, Robinson et al. 2011; Whitehouse, Robinson et al. 2011) for detail)

Numerous statistical methods were used for these analyses. They included T-tests to assess differences in mean scores for each of the early developmental outcomes of gross motor skills, fine motor skills, adaptability, sociability and communication at ages one, two and three according to breastfeeding status. The predictor variables were entered into a multivariable logistic regression model, with an outcome of any atypical scores at each age, adjusting for the confounding factors. Finally, we examined IMQ outcomes as total atypical scores across follow-ups in a multinomial logistic regression model with a reference category of no atypical scores at any follow-up. For the cognitive IQ investigation, basic chi square tests for association, Spearman's correlations and multiple linear regression were conducted. Adjustment was made for the factors correlated with each outcome and breastfeeding (gestational age, maternal age, maternal education and presence of other siblings). PPVT-R scores across breastfeeding groups were compared and hierarchical multivariable linear regression analyses were conducted.

Associations between breastfeeding duration and educational outcomes were estimated using linear models with adjustment for gender, family income, maternal factors and early stimulation at home through reading. For mental health, chi-square tests for trends were conducted using standard bivariate models between the primary exposure and the outcomes. To look at the estimated effect of breastfeeding on child mental health over time, we constructed binary outcomes, which provided information on clinical relevance. Factors were adjusted as potential confounders (maternal age, education, smoking in pregnancy, stress in pregnancy, proportion of optimal birthweight, family income, and family structure) (Robinson, Oddy et al. 2008). Chi square tests and generalised estimating equations that generate odds ratios, confidence intervals and p-values are given.

3. Results

3.1 Development at one, two and three years

The frequency characteristics for our predictor and control variables are presented for the cohort who provided data at the one-year follow-up (n=2,375). Approximately 63% of the

cohort was breastfed for four months or longer, 41% of mothers had completed high school education, and 29% had a family income below the poverty line during pregnancy. When the baby was one year, more than one in five infants had at least one atypical score for an early developmental domain, increasing to 32% with at least one atypical score at age two and reducing to 29% at age three. Infants breastfed for four months or longer had significantly higher mean scores for fine motor skills at one, two and three years (Table 1).

N=2,375	Breastfeeding Mean (SD)		Sig 2 tailed*	Cohen's D
Year 1	<4months	4+ months		
Gross Motor	5.39 (1.10)	5.41 (1.10)	0.647	-0.02
Fine Motor	5.33 (0.90)	5.44 (0.80)	0.002	-0.13
Adaptability	4.84 (1.27)	5.14 (1.09)	<0.001	-0.25
Sociability	4.72 (1.14)	4.81 (1.12)	0.058	-0.08
Communication	4.08 (1.49)	4.25 (1.38)	0.005	-0.12
Year 2				
Gross Motor	5.58 (0.72)	5.59 (0.71)	0.645	-0.01
Fine Motor	5.35 (0.75)	5.44 (0.74)	0.009	-0.12
Adaptability	5.02 (1.00)	5.14 (0.90)	0.007	-0.13
Sociability	4.51 (0.99)	4.52 (0.95)	0.888	-0.01
Communication	5.24 (1.16)	5.34 (1.09)	0.076	-0.09
Year 3				
Gross Motor	5.57 (0.68)	5.60 (0.75)	0.356	-0.04
Fine Motor	5.19 (1.07)	5.38 (0.92)	<0.001	-0.19
Adaptability	5.46 (0.84)	5.51 (0.83)	0.198	-0.06
Sociability	5.16 (0.81)	5.22 (0.77)	0.121	-0.08
Communication	5.34 (0.80)	5.44 (0.73)	0.007	-0.13

*equal variances not assumed

Table 1. Mean Infant Monitoring Questionnaire (IMQ/ASQ) scores (with standard deviations) and breastfeeding for less than four months and four months or longer (Oddy, Robinson et al. 2011)

The risk of any atypical score for all developmental outcomes was significantly increased for infants who were breastfed for less than four months at age one (OR=1.49, 95%CI= 1.16, 1.92), two (OR=1.29, 95%CI= 1.01, 1.65) and three years (OR=1.34, 95%CI= 1.06, 1.70) (Table 2).

The results of multinomial logistic regression analyses showed that breastfeeding for less than four months increased the risk for two or more atypical scores across all domains over the three years of the study except for gross motor skills (Table 3).

	Breastfeeding duration <4 months[μ]		
	Atypical score at year 1, 2 or 3		
	Year 1	Year 2	Year 3
	OR (95% CI) § p-value		
Atypical score on 1 or more domains	**1.49**[**] 1.16, 1.92 .002	**1.29**[*] 1.01, 1.65 .041	**1.34**[*] 1.06, 1.70 .016

* p<0.05, ** p<0.005 [μ] Reference category breastfeeding 4+ months
§ Adjusted for child's age at examination, maternal age at conception, maternal education, total stress events experienced during pregnancy, maternal smoking during pregnancy, biological father living with family, family income, Apgar scores at 5 minutes, gestational age and child gender

Table 2. Adjusted binary logistic regression analyses for the risk of any atypical scores on the total score of the IMQ/ASQ by breastfeeding < 4 months compared to breastfeeding 4+ months (Oddy, Robinson et al. 2011)

	Breastfeeding duration <4 months[μ]		
	No atypical scores (reference category)	One atypical score at any time point	Atypical scores at two or more time points
IMQ Domains	OR (95% CI) § p-value		
Gross motor	1.00	**1.52**[*] 1.03, 2.23 .035	1.23 0.60, 2.51 .577
Fine Motor	1.00	1.35 0.96, 1.90 .085	**1.81**[*] 1.05, 3.15 .034
Adaptability	1.00	**1.49**[*] 1.07, 2.07 .019	**1.91**[*] 1.10, 3.31 .021
Sociability	1.00	1.11 0.82, 1.50 .492	**2.09**[**] 1.31 3.33 .002
Communication	1.00	**1.53**[*] 1.10, 2.14 .013	**1.97**[*] 1.22, 3.17 .006

* p<0.05, ** p<0.005

[μ] Reference category breastfeeding 4+ months
§ Adjusted for child's age at examination, maternal age at conception, maternal education, total stress events experienced during pregnancy, maternal smoking during pregnancy, biological father living with family, family income, Apgar scores at 5 minutes, gestational age and child gender

Table 3. Adjusted multinomial logistic regression analyses for the risk of atypical scores at one or two or more time points compared with no atypical scores for domains of the IMQ/ASQ by breastfed< 4 months compared to breastfed 4+ months (Oddy, Robinson et al. 2011)

3.2 Cognitive development

Table 4 gives the adjusted mean IQ scores for each level of breastfeeding, the F test for linearity from the fitted model and corresponding significance test at six years. After adjustment for covariates there remained a significant association between duration of breastfeeding and cognitive IQ (F=8.59 p=0.003) with a 3.56 point advantage for those children fully breastfed for more than six months compared with children never breastfed.

| Mea-sure | Duration of full breastfeeding | | | | | F test for linearity | p-value | max-min |
	Total group	Never breastfed (n=117)	Fully breastfed < 4 months (n=495)	Fully breastfed 4-6 months (n=378)	Fully breast-fed > 6 months (n=412)			
Cogni-tive IQ†	106.88 (12.86)	105.19 (12.98) (n=79)	105.55 (12.73) (n=348)	107.18 (12.44) (n=272)	108.67 (13.15) (n=299)	8.59	.003	3.56

† Cognitive IQ measured by 'Peabody Picture Vocabulary Test – Revised' at six years adjusted for gestational age, maternal age, maternal education, parental smoking and older siblings.

Table 4. Mean (SD) standardised cognitive IQ scores at six years by duration of full breastfeeding after adjustment for covariates (Oddy, Kendall et al. 2003)

There was a strong positive association between PPVT-R scores at six and ten years for the 1067 children who provided data at both time-points, r = 0.601, p <0.01. A one-way ANOVA revealed a significant difference between the PPVT-R scores of the groups representing different predominant breastfeeding durations, F(3,1193) = 12.32, p <0.01. Bonferroni post-hoc tests found that the children who had been breastfed predominantly for between 4 and 6 months or for greater than 6 months, had greater language scores than children who had been breastfed predominantly for 0 to 4 months or not at all (for all comparisons, p <0.05) at ten years.

	B (95%CI)	P*
Duration of predominant breastfeeding		
< 4 months	2.94 (0.51, 5.36)	0.02
4 to 6 months	3.98 (1.45, 6.5)	<0.01
> 6 months	4.39 (1.88, 6.9)	<0.01

*Significant covariates only are presented
†Adjusted for maternal age at conception, gender, maternal education, smoking during pregnancy, alcohol during pregnancy, parity, reading to child

Table 5 Adjusted† multivariate linear regression models showing the effect of the duration of predominant breastfeeding on receptive vocabulary at ten years (Whitehouse, Robinson et al. 2011).

Children who had been breastfed predominantly for less than four months had higher language scores than children never breastfed (B = 2.33, 95% CI = 0.51, 5.36, p = 0.02), while the effect was stronger for children breastfed predominantly for between 4 to 6 months (B = 3.98, 95% CI = 1.45, 6.5, p <0.01) (Table 5), and stronger still for children who were breastfed

predominantly for more than 6 months (B = 4.39, 95% CI = 1.88, 6.9, p <0.01). Of the confounders included in the

model, a higher maternal age at conception, male gender and low levels of alcohol during pregnancy were associated with small increases in language scores. Lower levels of maternal education, maternal smoking of 11+ cigarettes per day during pregnancy, and having at least one older sibling were significantly associated with poorer language scores at ten years. A progressively stronger positive association was observed between the frequency of reading to the child at three years and language ability in middle childhood.

3.3 Educational outcomes

Data for 1,038 children were matched with West Australian Literacy and Numeracy Assessment (WALNA) grade five records. Of 1,038 children, complete data were available on most key outcome and exposure variables for 980 children.

In univariate associations between breastfeeding and educational outcomes at ten years, parameter estimates from linear regression showed that continuous breastfeeding was associated with an increase in scores with each additional month of breastfeeding for mathematics (Beta 1.21; 95% CI 0.30, 2.13; P=0.010), reading (Beta 1.68; 95% CI 0.78, 2.58; P<0.001), writing (Beta 2.13; 95% CI 0.68, 3.59; P=0.004) and spelling (Beta 1.46; 95% CI 0.44, 2.48; P=0.005). Results were attenuated when adjusted for confounding factors and we concluded that breastfeeding as measured in months was weakened in multivariate models.

Predominant breastfeeding for six months or longer was a significant predictor for improved academic scores in multivariable models for mathematics, reading and spelling and approaching significance for writing (Table 6).

	Mathematics			Reading			Writing			Spelling		
Predominant breastfeeding 6+months**	Beta	95% CI	P value†	Beta	95% CI	P value †	Beta	95% CI	P value†	Beta	95% CI	P value†
	15.79	1.04, 30.55	0.036	18.28	3.92, 32.64	0.021	18.00	5.68, 41.67	0.136	15.60	-0.03, 31.24	0.050

* Adjustment was made for child gender, maternal age, maternal education, family income, marital status, parent looks at book with child; also adjusted for maternal race: Aboriginal, Asian/other, or Caucasian.
** Reference for predominant breastfeeding for 6 or more months was predominant breastfeeding for less than 6 months.
† Test of between-subjects effects

Table 6. Multivariable linear regression model between predominant breastfeeding for six months or longer and educational outcomes at 10 years of age* (N=980) (Oddy, Li et al. 2011)

We observed increased mathematics, reading, writing and spelling scores for boys but no effect of breastfeeding was apparent on the educational attainment of girls. Significant observed interactions for mathematics (p=0.007) and spelling (p=0.047), revealed that boys were more likely than girls to have improved academic scores if they were breastfed for longer (Oddy, Li et al. 2011).

3.4 Mental health outcomes

Children breastfed for six months or longer had significantly lower mean behavioural scores (meaning improved behaviour) across total, internalizing and externalizing domains of mental health morbidity (Table 7). Younger mothers, those with 12 years education or less, those who were stressed, with low incomes, or who smoked during pregnancy were more likely to breastfeed for less than six months. Postnatal depression and inappropriate fetal growth were associated with a shorter duration of breastfeeding. There were significant downward trends in the proportions of children above the behavioural cut-off score at all ages as duration of breastfeeding increased. These trends were most pronounced in the total and externalizing domains.

Multivariable generalized estimating equations with binary mental health outcomes across the years revealed similar trends (Table 8), with a shorter duration of breastfeeding being consistently associated with increased risks for mental health problems of clinical significance through childhood and into adolescence. Prenatal risk factors such as smoking, experience of multiple stress events, low family income, younger maternal age and the absence of the biological father in the family home, plus postnatal depression, were also associated with increasing CBCL scores and in some cases mental health morbidity, as has been previously identified (Robinson, Oddy et al. 2008).

Breastfeeding duration	Age 2 N=1899	Age 5 N=2036	Age 8 N=1938	Age 10 N=1895	Age 14 N=1695
Total morbidity					
Never breastfed	16.1	26.3	19.4	15.2	16.7
<3 mo‡	16.4	31.2	29.8	20.9	18.9
3 mo - <6 mo	9.6	20.6	20.3	16.4	12.6
6 mo-<12 mo	9.3	18.4	16.2	12.1	12.6
12+ mo	9.6	16.0	13.5	12.6	10.9
Test for trend*	0.001	<0.001	<0.001	0.004	0.004
Internalizing morbidity					
Never breastfed	12.8	21.6	18.9	18.2	19.4
<3 mo	11.3	21.8	25.6	21.2	16.4
3 mo - <6 mo	5.6	17.6	20.6	19.9	11.3
6 mo-<12 mo	7.3	16.7	15.8	15.1	12.2
12+ mo	7.2	16.0	18.0	15.8	9.3
Test for trend*	0.007	0.013	0.022	0.037	<0.001
Externalizing morbidity					
Never breastfed	16.7	21.1	20.0	13.3	20.8
<3 mo	21.2	30.9	25.6	18.4	20.4
3 mo - <6 mo	10.5	18.4	18.6	13.2	14.6
6 mo-<12 mo	12.1	17.9	16.0	10.4	13.2
12+ mo	9.8	16.4	12.2	9.4	12.3
Test for trend*	<0.001	<0.001	<0.001	0.001	0.001

*P-value for linear by linear association; ‡ mo= month

Table 7. Percentage of children in mental health morbidity groups (total, internalizing and externalizing) and breastfeeding duration (never, < 3 mo, 3 mo- <6 mo, 6 mo -<12 mo, 12+ mo) (Oddy, Kendall et al. 2010).

Multivariable Generalised Estimating Equation Model- Years 2 to 14 Inclusive			
	Total Morbidity	**Internalizing Morbidity**	**Externalizing Morbidity**
Exposure variables	Odds Ratio 95% Confidence Interval p-value		
Breastfeeding duration < 6 months: 6+ months	1.33 1.09, 1.62 0.005	1.21 1.00, 1.46 0.054	1.23 1.01, 1.49 0.044

** Adjusted for maternal age, education, marital status, smoking in pregnancy, family income, life stress events, postnatal depression. Also adjusted for proportion of optimal birth weight and child gender.

Table 8. Association between breastfeeding duration and mental health morbidity of clinical significance † (Oddy, Kendall et al. 2010)

4. Discussion

We have shown convincing evidence that breastfeeding for less than four months was associated with lower developmental scores in the first three years of life. We observed a clear and significant dose response relation between duration of full breastfeeding in infancy and cognitive IQ as measured at six and ten years of age. The magnitude of the association at ten years was comparable to the effect observed at six years and indicates long-term advantages of breastfeeding. Predominant breastfeeding for six months or longer was associated with significantly higher scores for mathematics, reading and spelling in ten-year-old children when adjusted for the socio-demographic characteristics of the mother and family, and early stimulation of the child in the home at age five through reading. However, significant interaction effects were shown between gender and breastfeeding. We showed that a shorter duration of breastfeeding (less than six months) compared with a longer duration (≥ six months) was associated with increased mental health morbidity from early childhood to adolescence. This association was evident for the continuous measures of total, externalizing and internalizing behaviours as well as for dichotomous measures of morbidity which reflect clinically significant behavioural problems. Further, these associations persisted after adjustment for social, economic, birth and psychological factors in early life. Hence, we suggest that breastfeeding impacts on development, cognitive IQ, educational attainment and mental health from infancy to adolescence and potentially beyond.

A number of domains of early child development were sensitive to a longer duration of breastfeeding, following adjustment for confounding factors. In particular, we observed that the developmental domains of adaptability and communication were most responsive to the effects of breastfeeding duration, with children breastfed for longer than four months being more likely to have higher scores in these domains. Our findings pertaining to the communication domain of early development are consistent with a previous study that has found a link between an increased length of breastfeeding and mastery of developmental milestones including polysyllabic babbling (Vestergaard, Obel et al. 1999). These results also support findings from a New Zealand cohort study that demonstrated benefits for infants breastfed for four months or longer in the domains of intelligence, comprehension and

expression (Fergusson, Beautrais et al. 1982). A recent study of infants from the Millennium Cohort Study (Sacker, Quigley et al. 2006) found that those who were never breastfed were 30% more likely to have developmental delays for gross motor skills (Montgomery, Ehlin et al. 2006). Unexpectedly, we found that gross motor skills were least sensitive to duration of breastfeeding and a shorter duration of breastfeeding was associated with an increased risk of atypical gross motor scores for boys at age one and two years.

Gender differences are apparent in the effect of breastfeeding on early development whereby girls appear to be less responsive to extended breastfeeding than boys. A longer duration of breastfeeding remained predictive for academic achievement in ten-year-old boys for mathematics and spelling with a small but insignificant benefit for reading in girls. We suggest that gender ought to be considered in explanations of the link between breastfeeding and neuro-cognitive development. Boys may be more vulnerable to adversity during critical periods than girls (Catalano, Bruckner et al. 2005), possibly due to the neuro-protective effect of estrodiols (Garcia-Segura, Azcoitia et al. 2001) at higher concentration in females. The neuro-protective components in breast milk – and the downstream consequences for development – may have greater benefits for boys. Compelling evidence exists for sexual dimorphism in the developing brain, giving rise to gender differences in cognition and behaviour (Baron-Cohen, Knickmeyer et al. 2005). For example, males generally do better on tests of mental rotation, map reading, targeting, and embedded figures, whereas females do better on tests of emotional recognition, social sensitivity, and verbal fluency and they start to talk earlier than males (Baron-Cohen, Knickmeyer et al. 2005). Only one previous study has examined gender differences in the association between breastfeeding and child development. Breastfeeding was associated with improved clarity of speech in boys and girls but significantly more so in boys and better speech was associated with improved reading ability (Broad 1972). The effect of breastfeeding on speech and reading in boys was reported in a later follow-up, suggesting that breastfeeding accelerates the rate of maturation of boys (Broad 1972; Broad 1975). Significant gender differences were observed in the association between breastfeeding and educational outcomes in our study. Therefore we analysed our data by boys and girls separately.

Our studies were based on a prospective birth cohort study reasonably representative of the general population and has a number of strengths. Firstly, although controlling for every potential confounding in the child's developmental trajectory is not possible, we were able to adjust for a range of socio-demographic, biological and psychological factors that share a relationship with breastfeeding duration and child developmental, in particular maternal education, family income and maternal stress (Jain, Concato et al. 2002; Der, Batty et al. 2006) to minimise the possibility of confounding being responsible for any observed results.

The ten year findings extend those of a previous investigation in the same cohort (Oddy, Kendall et al. 2003), and have implications for our understanding of the longitudinal effects of breastfeeding on development. At six years, children breastfed predominantly for more than six months had an adjusted increase in PPVT-R scores of 3.56 points compared with children who were never breastfed. This increase in PPVT-R score at ten years was 4.39 points. We suggest that our findings provide evidence for a beneficial effect of breastfeeding on language development in middle childhood of at least equivalent magnitude to the association in early childhood at six years.

A growing literature suggests that a relationship between breastfeeding and cognitive development exists (Silva, Buckfield et al. 1978; Clandinin, Chappell et al. 1980; Fergusson, Beautrais et al. 1982; Taylor and Wadsworth 1984; Doyle, Rickards et al. 1992; Wharton 1992; Makrides, Neumann et al. 1994; Michaelson, Larsen et al. 1994; Malloy and Berendes 1998; Quinn, O'Callaghan et al. 2001; Oddy, Kendall et al. 2003). In a recent critical evaluation (Drane and Logemann 2000) of the three methodological standards described by Bauchner(Bauchner, Leventhal et al. 1986), definition of outcome, correct classification of infant feeding type and control of potential confounding variables were determined in relation to cognitive development. The evaluation found that adherence to an infant feeding standard was poor with most studies classifying partial and exclusive breastfeeding together and only five considering feeding as a continuous variable (Taylor and Wadsworth 1984; Morrow-Tlucak, Haude et al. 1988; Bauer, Ewald et al. 1991; Lucas, Morley et al. 1992; Horwood and Fergusson 1998). Most studies adjusted for confounding factors including maternal education, socioeconomic status, birthweight and birth order. Few studies had well-defined and consistent outcome measures. Only five studies met all three methodological standards (Lucas, Morley et al. 1992; Lucas, Morley et al. 1994; Pollock 1994; Horwood and Fergusson 1998; Malloy and Berendes 1998); three of these found consistent advantages to breastfed infants (Lucas, Morley et al. 1992; Lucas, Morley et al. 1994; Horwood and Fergusson 1998) but two did not find significant associations (Lucas, Morley et al. 1994; Pollock 1994). The lack of association in these two studies may be explained by design issues. One study found differences for the Bayley Scale Psychomotor Index but not for Mental Development Scale Scores, when comparing infants fed donor breast milk with infants fed formula milk. In this study the low birthweight breastfed infants were fed 'drip' milk rather than own mothers' milk, which had a higher calorific value and fat content (Lucas, Morley et al. 1994). In relation to intelligence, the breastfed infant has been shown to have an advantage over the non breastfed infant (Pollock 1994), although some studies have been criticised for neglecting the possible genetic influence of maternal intelligence (Der, Batty et al. 2006).

In prospective studies after adjustment for numerous confounding variables, children breastfed for longer performed better on tests of cognition, verbal ability and school performance. Similar results have been observed in term and pre-term infants (Horwood and Fergusson 1998; Horwood, Darlow et al. 2001) and extend beyond adolescence (Lucas 2005). In a study to examine the association between duration of breastfeeding and cognitive ability at 7-8 years in a birth cohort of very low birthweight infants (Horwood, Darlow et al. 2001), increasing duration of breast milk feeding was associated with increases in both cognitive IQ ($p<0.001$) and performance ($p<0.05$). The effects on cognitive IQ are in the range of 2-5 points and may be as large as 10 points in low birthweight babies (Lucas, Morley et al. 1992; Lucas, Morley et al. 1994; Horwood, Darlow et al. 2001). The results of our study agree with this and other reports and adds to a growing body of evidence for an association between breastfeeding and cognitive development.

An early study showed small but significant increases in later intelligence and educational attainment between breast and formula-fed infants (Rodgers 1978). Fergusson et al combined males and females and tested for differences in intelligence, comprehension, expression and articulation and found significantly increased scores in infants breastfed for four months or longer for intelligence and comprehension at three, five and seven years, and expression at three and five years (Fergusson, Beautrais et al. 1982). Quinn et al speculated the observed that cognitive differences between breast- and formula-fed infants observed in

their birth cohort of 3,880 infants followed to five years was due to unique constituents of breast milk (Quinn, O'Callaghan et al. 2001).

Available meta-analyses reflect a less conclusive pattern of breastfeeding effect on developmental outcomes. A meta-analysis of studies published up to 1996 found that breastfed children had higher cognitive scores, compared to bottle-fed children (Anderson, Johnstone et al. 1999) although some studies adjusted for few confounders. Another meta-analysis showed that only two studies met stringent criteria for inclusion, such as adequate adjustment for socioeconomic status of the family and stimulation of the child (Jain, Concato et al. 2002). Of these two studies, one reported a positive association between breastfeeding and intelligence (Johnson, Swank et al. 1996), while the other found no benefit (Wigg, Tong et al. 1998).

The majority of previous studies have focused on the association between breastfeeding and cognitive ability, and only a few have examined academic achievement. Where this has been studied, positive associations have been observed (Horwood and Fergusson 1998; Anderson, Johnstone et al. 1999; Jain, Concato et al. 2002). For example, Richards (Richards, Hardy et al. 2002) found a positive impact of breastfeeding on educational attainment in midlife independent of early background in 1,739 participants from the British 1946 birth cohort. Further analyses found that the association was largely mediated through adolescent cognition and educational attainment.

Despite the evidence for an impact of breastfeeding on cognitive development, there have been few published papers on mental health outcomes since the early theorists working within a developmental psychopathological framework (Hoefer and Hardy 1929) which is surprising given the popularity of attachment theory in relation to healthy psychological development (Rutter 2006). There is reluctance to suggest an association between breastfeeding and later mental health partly due to the possibility of alternative explanations such as parenting behaviours and cognitive ability (Anderson, Johnstone et al. 1999) and concern for creating guilt in women who do not breastfeed. In developed nations breastfeeding is more likely in communities with greater economic and social resources (Pollock 1994; Vohr, Poindexter et al. 2006), and the confounding socioeconomic effects complicate interpretation of this association (Li, Kendall et al. 2008). Our study addresses this issue by adjusting for many of these underlying factors, although we acknowledge that not all potential confounders (such as maternal IQ) were measured with sufficient validity and precision to fully control for all potential confounding effects.

Existing research tends to focus on infant and early childhood behaviour (Golding, Rogers et al. 1997) and consistent with our findings, infants who are breastfed for at least six months have a distinct developmental advantage over non breastfed infants and infants breastfed for a short period of time (Horne, Parslow et al. 2004). One study found that low birthweight infants fed breast milk had significantly higher scores for engagement and emotional regulation on the Bayley Developmental Scale than low birthweight infants not given breast milk (Vohr, Poindexter et al. 2006). However, this study did not differentiate the effects of feeding at the breast versus feeding of breast milk through a tube or bottle (Lucas, Morley et al. 1994). Another study found that breastfed infants were more able to face adverse stimuli with greater degrees of control, show more appropriate amounts of change in arousal levels, and were more able to return to moderate states of arousal than formula fed infants (Hart, Boylan et al. 2003). However, much of this research is based on

small and non-random samples with a few exceptions to this (Sacker, Quigley et al. 2006). One exception includes the results from a large, cluster-randomized trial, whereby the authors did not find significant differences in behavioural outcomes at age six for those infants whose mothers were encouraged to breastfeed exclusively and for longer durations; however, the age at follow-up was considerably less than in our study, the children were only assessed at one point in time and a short form behavioural measure was used (Kramer, Aboud et al. 2008). Later childhood outcomes in breastfed children include greater resilience against stress and anxiety associated with parental separation and divorce at ten years in a study of 8958 children (Montgomery, Ehlin et al. 2006).

Breastfeeding may influence children's academic achievement by promoting brain development and general health. Nutrients in breast milk that are essential for optimum brain growth, such as long-chain polyunsaturated fatty acids (LCPUFA), may not be contained in formula milk (Larque, Demmelmair et al. 2006). LCPUFAs are structural elements of cell membranes and are essential in the formation of new tissue, including neurons. Makrides et al. noted an increased docosahexanoic acid (DHA; 22:6n-3) content of brain cortex with breastfeeding (Makrides, Neumann et al. 1994). Breastfed infants had a greater proportion of DHA in their erythrocytes and brain cortex and scored better on visual and developmental tests than did formula-fed infants. Crawford highlighted arachidonic acid (AA; 20:4n6) and DHA as vital components of breast milk that support development of the newborn brain (Crawford 1993) and research supports this (Crawford, Bloom et al. 1999; Crawford, Bloom et al. 2001).

Animal studies have found that LCPUFA may also play a neuroprotective role in early development, eliminating the build-up of neurotoxic levels of certain molecules (e.g., Ca^{2+}) and inhibiting glutamatergic synaptic transmission (Lauritzen, Blondeau et al. 2000). Further studies (Das 2002; Farkas, de Wilde et al. 2002; Das 2003) have identified that certain LCPUFAs, including eicosapentaenoic acid, docosahexaenoic and arachidonic acid, act as secondary messengers, inducing the release of acetylcholine and noradrenaline, which are neurotransmitters known to be involved in cognitive development (Sarter and Bruno 1997; Dalley, McGaughy et al. 2001). The specific fatty acid content of breast milk is essential for central nervous system development, including the brain in the neonate. Breastfeeding may have long-term consequences for child mental health outcomes because of the maternal fatty acids and other bioactive components essential for neurodevelopment (Keating and Hertzman 1999; McCain and Mustard 1999; Yehuda, Rabinovitz et al. 1999). Further, breast milk may contain elements relevant to the stress response. For example, the hormone leptin in breast milk may reduce stress in infants through its action on the hippocampus, hypothalamus, pituitary gland, and adrenal gland (Montgomery, Ehlin et al. 2006), whereas formula milk may have a depressant effect on newborn behavior (DiPietro, Larson et al. 1987).

Breastfeeding may also promote growth and development by facilitating the mother-child bonding, interaction and, indirectly, cognitive growth (Quinn, O'Callaghan et al. 2001). Positive maternal contact may induce a biological response in offspring. In rats, variations in maternal licking and grooming have been shown to promote the development of neural systems that mediate hypothalamic–pituitary–adrenal axis and behavioral responses to stress in offspring as well as certain forms of learning and memory (Caldji, Tannenbaum et al. 1998; Liu, Diorio et al. 2000). Stimulation associated with maternal contact during

breastfeeding may have a positive effect on the development of neuroendocrine aspects of the stress response, which may affect development (Huizink, Robles de Medina et al. 2003). There is some evidence to date in human studies (Strathearn, Mamun et al. 2009), but this hypothesis is largely informed by rat models (Uvnäs-Moberg 1998). Rat pups who experienced a greater frequency of maternal contact during nursing in the first ten days after birth (licking and grooming) exhibited a more controlled response to acute stress as adults (e.g. a lower magnitude of hypothalamic-pituitary-adrenal (HPA) response) (Liu, Diorio et al. 2000). In humans the pattern of mother-infant interaction differs between breastfeeding and bottle-feeding. The amount of mutual touch, tactile stimulation and mother's gaze to infant were significantly elevated during breastfeeding compared with bottle-feeding (Lavelli and Poli 1998). Breastfeeding helps promote attachment between the mother and the infant which is known to have a positive influence on the child's psychological development into adulthood (Crowell and Waters 2005).

4.1 Directions for future research

More rigourous research is required to investigate the plausible biological mechanisms discussed above and any other factors we have not considered, eg, since we have not adjusted for maternal IQ in any of the studies, there is a possibility that this factor confounds or mediates some of the breastfeeding effects we have shown.

4.2 Conclusion

Breastfeeding for a longer duration appears to have significant benefits for the development, cognitive IQ, educational attainment and mental health of the child into adolescence. Our study has demonstrated that following adjustment for socioeconomic, psychological and maternal exposures in early life, a longer duration of breastfeeding was positively associated with the developmental, cognitive, educational and psychological health and wellbeing of children and adolescents. Therefore, public health programs aimed at increasing breastfeeding duration could be of long-term benefit for child and adolescent health.

5. Key findings

Breastfeeding for six months or longer is preferable to shorter breastfeeding or formula feeding because it is independently and longitudinally associated with better development, cognition, educational attainment and mental health throughout childhood and into adolescence.

Mothers should be encouraged, enabled and supported to continue breastfeeding for six months and longer in order to promote the optimum developmental health and well-being of their infants into childhood and adolescence

6. Information on contributors

Professor WH Oddy developed the hypotheses, statistical analyses, wrote the main drafts of the manuscript, and is responsible for correspondence and requests for reprints. Associate Professor Li played a lead role in the conceptualisation of the chapter, undertook statistical analyses and with Associate Professor Whitehouse and Dr Robinson contributed to the interpretation and discussion of the results and other sections.

We declare that none of the co-authors have competing interests.

7. Abbreviations

AA	Arachidonic acid
DHA	DocosaHexanoic acid
LCPUFA	Long-Chain Polyunsaturated Fatty Acids
PPVT	Peabody Picture Vocabulary Test
WALNA	Western Australian Literacy and Numeracy Assessment

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10. References

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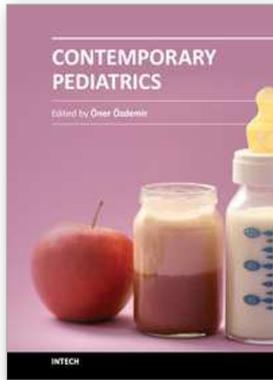
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Edited by Dr. Öner Özdemir

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