THE LEARNING LEAD
Breakthrough nutrition and development news, now
Wyeth Nutrition SCIENCE CENTER
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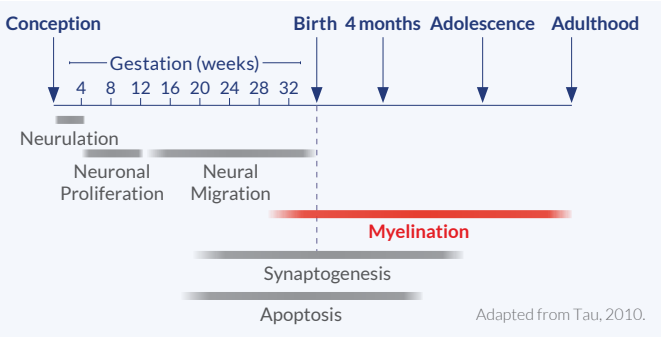
Can Early Life Nutrition Influence Myelination and Cognitive Outcomes in Healthy Infants?

Early life is an important foundational period to establish the basis for lifetime brain function. Brain development is at its fastest during this period with >1 million new connections forming every second. Myelination is a vital process supporting brain connectivity and has been positively associated with cognitive ability.[1,2] Studies have shown that myelination and cognition may be impacted by early life nutrition and that breastfeeding provides infants with the best outcomes.[3] However, data are limited on the window of opportunity to positively influence these outcomes (Figure 1) and the amount of specific nutrients that are needed to support optimal outcomes.

Figure 1: There may be a critical window for myelin development.[4]



Observational Data Have Suggested a Window of Opportunity Where Nutrition May Influence Myelination and Cognition

A longitudinal observational study by Deoni et al. used neuroimaging techniques as well as prospective and retrospective dietary data assessment to investigate the role of nutrition on early brain and cognitive growth.[3] This study recruited infants who were exclusively breastfed (n = 62) and exclusively formula-fed (n = 88) for at least the first 3 months of life.[3] As this was observational and parents chose the formula that their child was fed, there were differences in nutritional composition between the formula groups, which could then be further assessed.[3] Results from this study identified three main findings[3]:

- Children that were exclusively breastfed showed higher levels of myelin and better Early Learning Composite (ELC) scores compared with children that were exclusively formula-fed (Figure 2a)
- Variability in formula composition was linked with differences in myelin trajectories and ELC scores (Figure 2b)
- Higher intake of specific nutrients (docosahexaenoic acid [DHA], arachidonic acid [AA], folic acid, iron, choline and phospholipids [PLs]) were associated with higher brain myelin content. Specifically, DHA, AA, sphingomyelin (SM), and phosphatidylcholine (PC) were consistently and positively correlated with myelin in the parietal, occipital, frontal, and temporal lobes as well as the cerebellum ($P<0.05$).

Figure 2a: Longitudinal myelin curve for the corpus callosum (largest white matter structure of the brain) brain region between different formula compositions. Breastfeeding data are shown for reference.

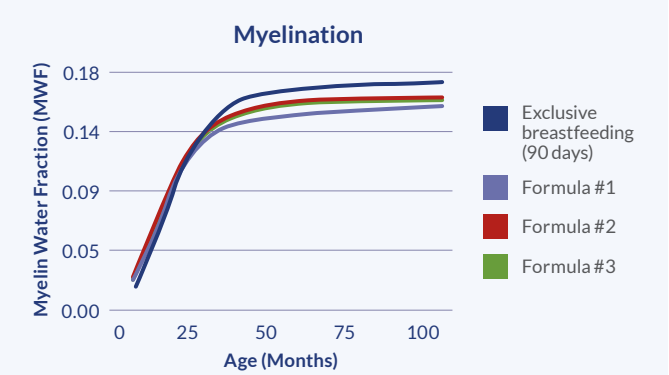
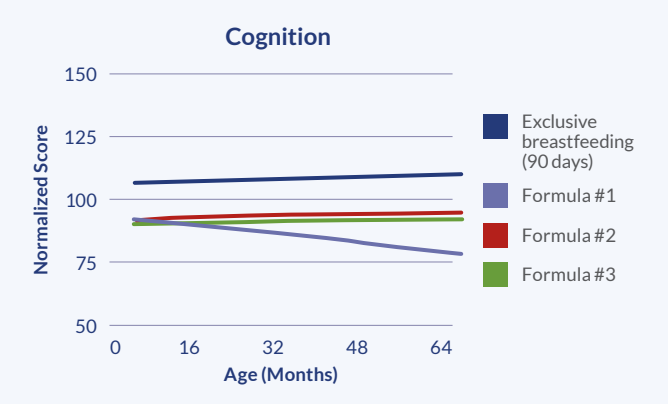


Figure 2b: Comparison of longitudinal maturation curves (Early Learning Composite [ELC] score of the Mullen Scales of Early Learning [MSEL]) between children who received different formula compositions. The trend for exclusively breastfed children is provided for reference.



These observational data provide strong insight into early life as a window of opportunity to support myelin development and cognitive outcomes in formula-fed infants, and suggests specific nutrients of interest.[3] These data are consistent with animal and *in vitro* studies where these nutrients promoted myelination.[5,6] While the available findings support the associations of these specific nutrients with developmental myelination, it is not possible to confirm a causal relationship.[3,5,6] Therefore, the efficacy of these nutrients on myelination and cognitive outcomes required a randomized, controlled clinical trial.

IMPORTANT NOTICE

The World Health Organization (WHO*) has recommended that pregnant women and new mothers be informed on the benefits and superiority of breastfeeding– in particular the fact that it provides the best nutrition and protection from illness for babies.

Mothers should be given guidance on the preparation for, and maintenance of, lactation, with special emphasis on the importance of a well-balanced diet both during pregnancy and after delivery. Unnecessary introduction of partial formula-feeding or other foods and drinks should be discouraged since it will have a negative effect on breastfeeding.

Similarly, mothers should be warned of the difficulty of reversing a decision not to breast-feed.

Before advising a mother to use an infant formula, she should be advised of the social and financial implications of her decision: for example, if a baby is exclusively formula-fed, more than 400g per week will be needed, so the family circumstances and costs should be kept in mind. Mothers should be reminded that breast-milk is not only the best, but also the most economical food for babies.

If a decision to use an infant formula is taken, it is important to give instructions on correct preparation methods, emphasizing that unboiled water, unsterilized bottles or incorrect dilution can all lead to illness.

*See: International Code of Marketing of Breast Milk Substitutes, adopted by the World Health Assembly in Resolution WHA 34.22, May 1981.

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The First Pediatric Nutritional Neuroimaging Study Demonstrates the Efficacy of a Unique Myelin Blend on Developmental Myelination in Well-nourished, Term Infants

In March 2017, Wyeth Nutrition, in collaboration with NR Lausanne, Switzerland, began the Project CONNECT Clinical Trial, a multicenter, double-blind, randomized, controlled trial in healthy infants to study the effects of key nutrients on brain myelin content using magnetic resonance imaging (Image 1), and on cognitive development up to 24 months of life.[7] Infants were recruited in the first 5 weeks of life and randomized to receive an intervention or control formula until 12 months of age.[7] A breastfed reference group was recruited in parallel.[7] The intervention formula contained a myelin blend* containing: a uniquely processed alpha-lactalbumin PL/SM-enriched whey protein concentrate, DHA, AA, vitamin B12, folic acid, and iron.[7] The control formula was a standard formula.[7]

Information on the Project CONNECT Clinical Trial can be found on ClinicalTrials.gov (identifier NCT03111927), a database of publicly and privately supported human clinical studies, which is provided as a service by the U.S. National Institutes of Health.[8]

Image 1: View of an example magnetic resonance imaging scanner similar to that used in the CONNECT Clinical Trial.

The first data from the CONNECT Clinical Trial have recently been published.[7] The recruitment and intervention periods have been completed for all participants, with follow-up visits ongoing.[7] The results from the 6-month data set demonstrate the efficacy of a formula with a unique myelin blend* of nutrients compared to a standard formula.[7]

Infants fed formula supplemented with a unique myelin blend,* vs. standard formula, had[7]:

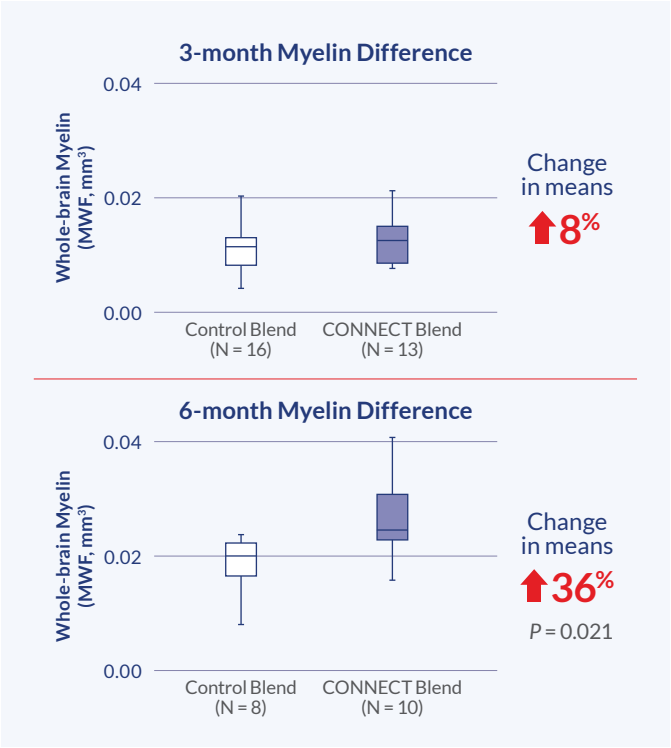
- 36% increase in whole-brain myelin content at 6 months ($P = 0.021$)
- 2.5x faster myelin growth rate ($P = 0.013$) by 9 months
- Significant whole-brain myelin content increases in brain regions involved in sensory, motor, cognitive, and language functions by 6 months

*Clinically-proven combination of a uniquely processed whey protein concentrate ingredient (containing alpha-lactalbumin and PLs including SM), DHA, AA, vitamin B12, iron, and folic acid.

The intervention formula was well tolerated and supported age-appropriate growth in infants.[7] There was also a trend towards fewer night awakenings in infants fed the formula with the myelin blend compared to the control.[7] However, the study was not powered to detect a difference in this outcome and so a larger sample size may have shown significance.[7]

This is the first study of its kind to demonstrate the efficacy of a unique myelin blend on developmental myelination, which may support cognitive abilities including learning.[7]

Figure 3: Infant formula supplemented with a unique myelin blend shows increases in myelination at 3 and 6 months.



Key Takeaways

- Early life nutrition is a modifiable factor that influences myelination, a foundational process for learning abilities
- First-of-its-kind research demonstrates that a formula supplemented with a unique myelin blend can increase whole-brain myelin content by 36%, compared to the control ($P < 0.05$), in healthy term infants
- These first results add to nutritional neuroscience research by demonstrating early nutritional benefits for brain architecture, which are foundational for later cognitive and learning outcomes

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