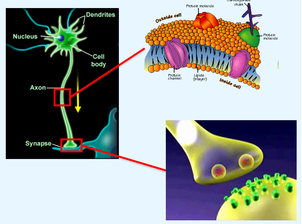
The omega-6 to omega-3 fatty acid ratio predicts declarative memory abilities in toddlers.

Kelly W. Sheppard,[1,2] Carol L. Cheatham,[1,2] Andrea L. Armer,[2] Grace Millsap [2]
[1]Department of Psychology & Neuroscience, University of North Carolina at Chapel Hill;
[2]Nutrition Research Institute, North Carolina Research Campus

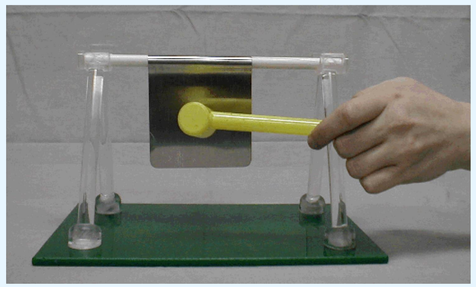
Fatty Acids in the Brain

- Omega-6 (n-6) and omega-3 (n-3) fatty acids are found throughout the brain in phospholipid membranes and concentrated in synaptic vesicles.
- Arachidonic acid (ARA, n-6) and docosahexaenoic acid (DHA, n-3) are related to neurite outgrowth in the hippocampus and prefrontal cortex, synaptogenesis, monoamine neurotransmission, long-term potentiation, and hippocampal volume.
- n-6 and n-3 fatty acids work together for brain function.
- n-6 and n-3 fatty acids are metabolized in the human body by the same desaturases and elongases.
- The mixture of fatty acids that a person consumes determines the production and availability of fatty acids further down the metabolic pathway - such as DHA and ARA.
- The ratio of n-6 to n-3 fatty acids provides a measure of the balance of fatty acids available to the brain.
- The ratio may be a better indicator than n-3 or n-6 fatty acids alone because of their complementary roles in the brain.



Participants and Methods

- One hundred twenty one 2- (n = 52) and 3- (n = 69) year-old children participated in a follow-up study of human milk nutrients and cognition.
- Ninety participants had full data including:
  - human milk levels of DHA obtained when infants were 3 months old,
  - dietary intake from two 24-hour recalls using the Nutrition Data System for Research (NDSR), and
  - elicited and deferred imitation task performance with immediate recall, a 20-minute delay recall, a one-week delay recall, and a relearning test.



The Gong

- The Gong is a classic imitation task.
- It can require 2 or 3 steps that involve placing the top bar, hanging the gong, and ringing it with the hammer.

Elicited and Deferred Imitation Methodology

- Four 4-step event sequences were employed.
- In Session 1, participants manipulated the props for each event, in turn, for a 2-minute baseline.
- After baseline for each event, researchers modeled the event twice.
- The 1st and 4th events were tested immediately; the 2nd and 3rd were tested after a 20-minute delay.
- Longer-term memory (7-day) was tested in Session 2 for all four event sequences.
- After the long-term memory test, events were modeled and participants were tested for relearning ability.
- Outcome variables were target actions (max=4) and ordered pairs of target actions (max=3).

Descriptive Statistics

	N	Mean (SD)		N	Mean (SD)
Milk DHA (nmol/L)	112	39.78 (2.83)	20-min delay target actions	114	3.58 (.64)
Dietary n-3 (g)	120	.94 (.46)	20-min delay ordered pairs	114	1.57 (.95)
Dietary n-6 (mg)	120	7.84 (3.46)	1-week delay target actions	108	3.56 (.57)
n-6 to n-3 ratio	120	8.95 (3.00)	1-week delay ordered pairs	108	1.54 (.72)
Immediate recall (target actions)	111	3.77 (.54)	Relearning target actions	109	3.88 (.32)
Immediate recall (ordered pairs)	111	1.91 (.92)	Relearning ordered pairs	110	2.15 (.69)

Data Reduction & Statistical Analyses

- Diet data were averaged across the two days reported.
- The fatty acid ratio was calculated as n-6 to n-3.
- Milk samples were analyzed for fatty acid content by gas chromatography in the NORC labs at UNC.
- Recall data (immediate, 20-min, 7-day, and relearning) were regressed in a multivariate model on the n-6 to n-3 ratio, n-3 intake, and n-6 intake with milk DHA and age at test as covariates for target actions and ordered pairs, in turn.
- Significance in the full model was followed with analyses of the two age groups (2- and 3-year-olds) separately.

Results

The n-6 to n-3 ratio predicted ordered pairs recalled at the 20-minute delay.

	B	Std. E	t
n-6 to n-3 ratio	.14	.07	2.03*
Dietary n-3	1.29	.77	1.70
Dietary n-6	-.12	.09	-1.35
Milk DHA (nmol/L)	-.003	.004	-1.07
Age	.002	.001	3.48*

Examining the role of the n-6 to n-3 ratio by age, the n-6 to n-3 ratio and dietary n-3 were significant predictor of ordered steps recalled at the 1-week delay for 3-year-olds.

	B	Std. E	t
n-6 to n-3 ratio	.12	.06	2.21*
Dietary n-3	1.30	.57	2.28*
Dietary n-6	-.12	.07	-1.69
Milk DHA (nmol/L)	- .005	.004	-1.29

*p < .05

Discussion

- The n-6 to n-3 ratio provides a measure of the balance of fatty acids available for incorporation into neurons.
- The balance of fatty acids affects brain function.
- The n-6 to n-3 ratio predicted recall of ordered steps after a 20-minute delay in 2- and 3-year-olds and after a 1-week delay in 3-year-olds.
- These recall measures are indicative of the quality of storage and retrieval as no additional modelling or cues were available to aid in performance.
- A higher n-6 to n-3 ratio has been found to predict improved performance on planning tasks in 7- to 9-year-olds who also consumed a high n-3 diet.
- n-3 intake was a positive predictor of ordered step recall after delay in 3-year-olds, and was a predictor as a trend for the entire sample.
- A higher n-6 to n-3 ratio (meaning more n-6 fatty acids) may be important in children who consume a high n-3 diet to avoid creating an imbalance between n-6 and n-3 fatty acids.
- In future work, we will explore genetic factors in fatty acid metabolism and will determine the optimal balance of fatty acids for optimal brain development, and subsequent cognition.

Acknowledgements: The authors would like to thank the families that made this research possible. This project was funded by NIH grant #DK56350 to the University of North Carolina at Chapel Hill Nutrition Obesity Research Center and Wyeth, a Nestle company. Correspondence and requests for reprints can be addressed to Carol L. Cheatham, Ph.D., Nutrition Research Institute, 500 Laureate Way, Rm 1101, Kannapolis, NC 28081 carol_cheatham@unc.edu