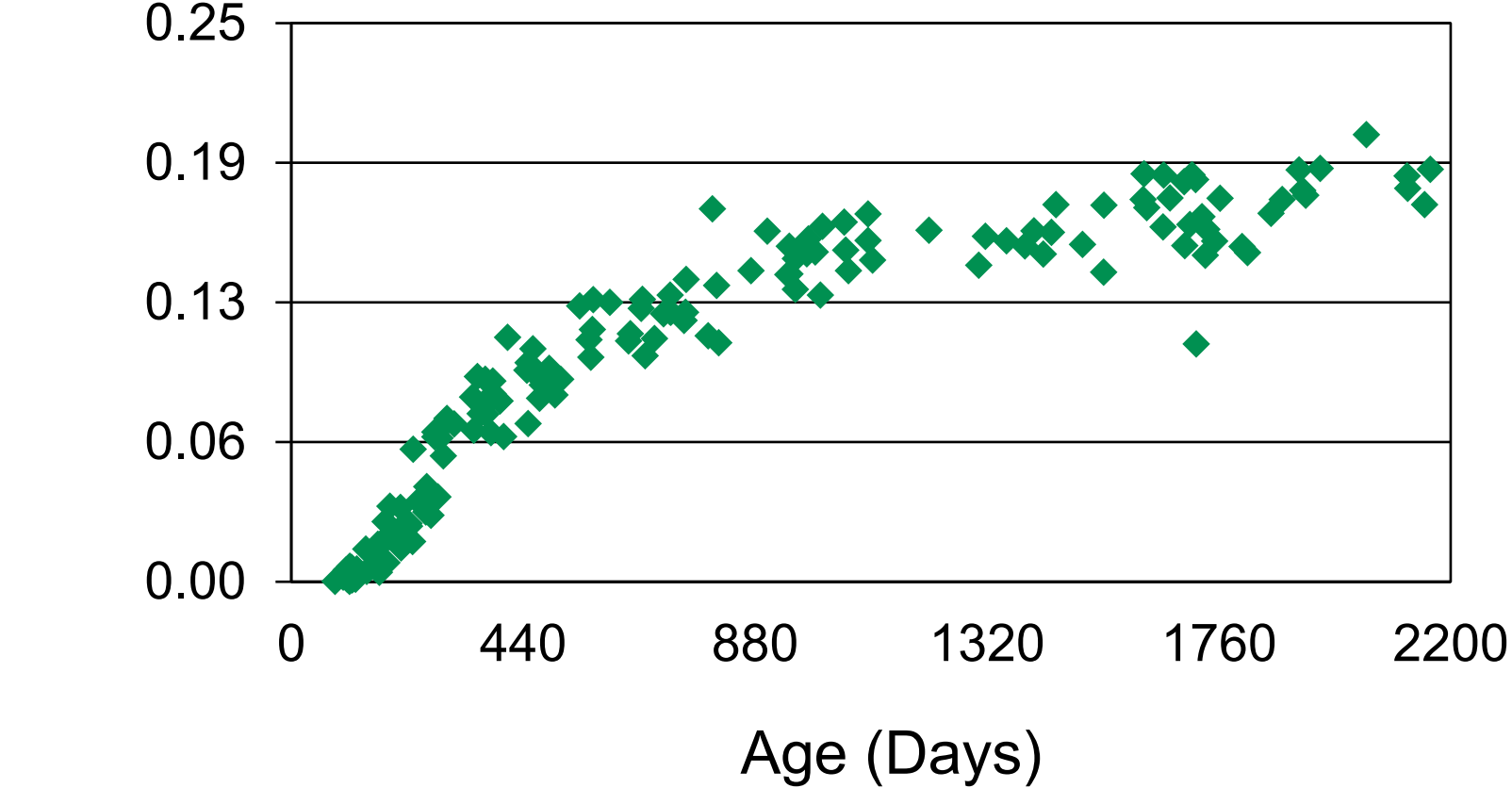
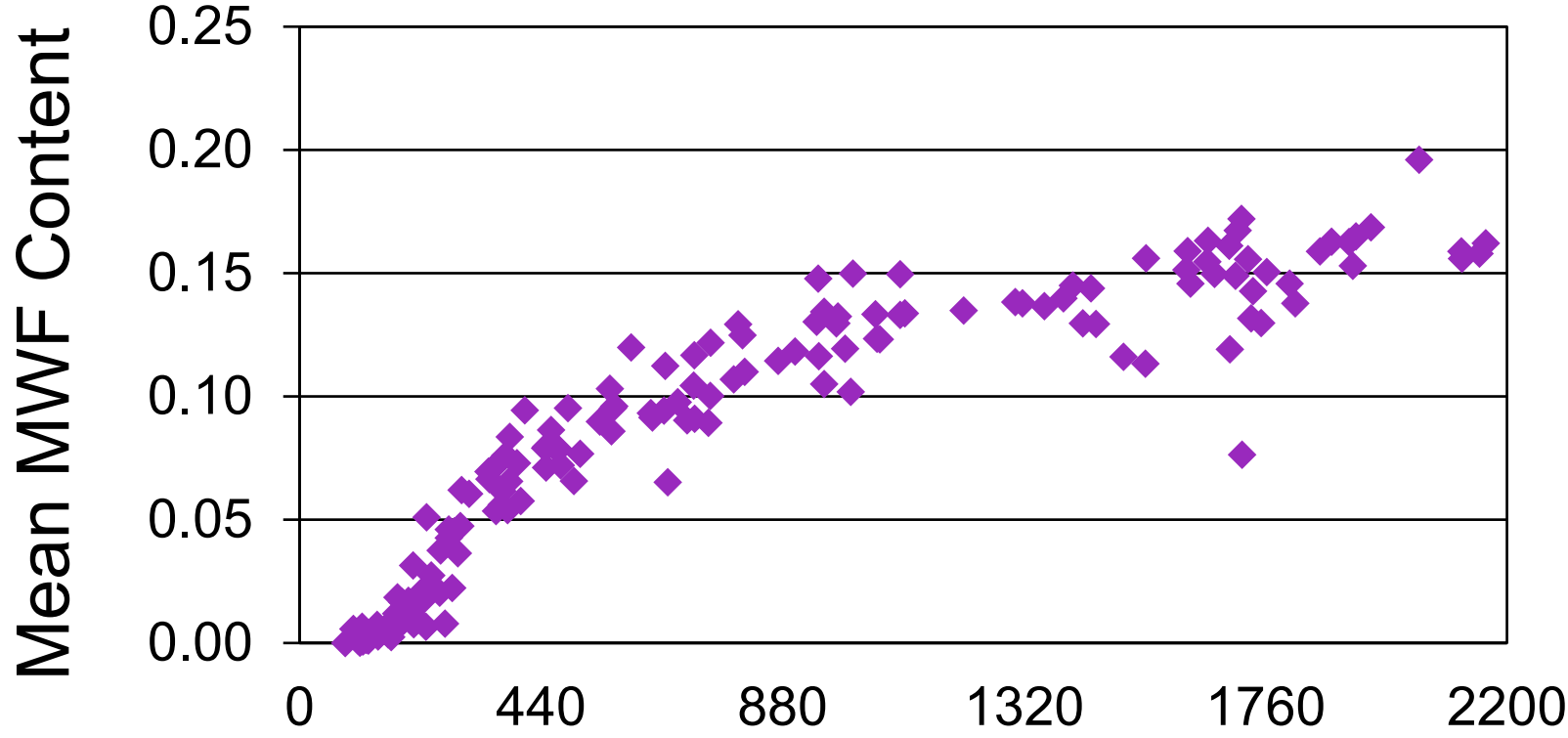
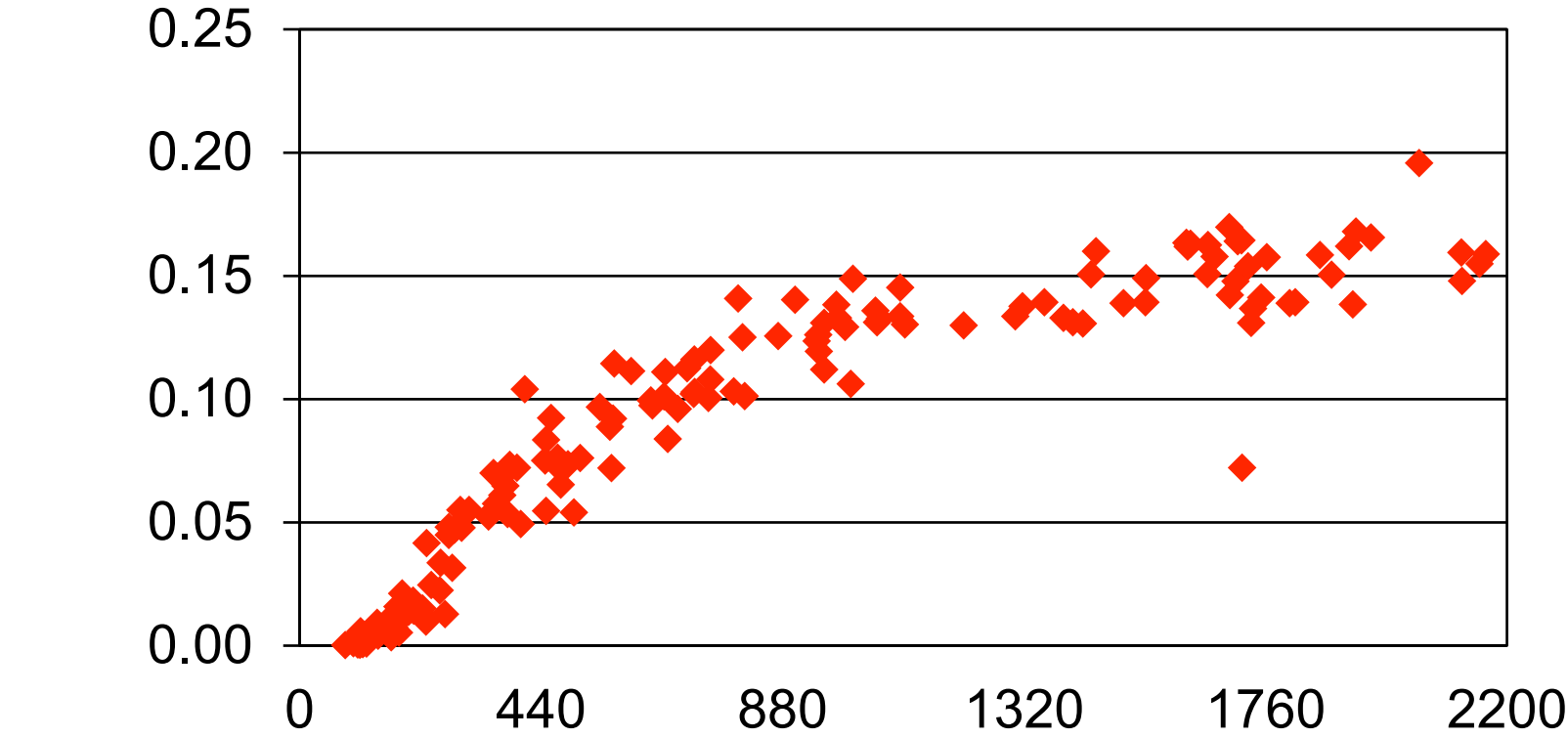
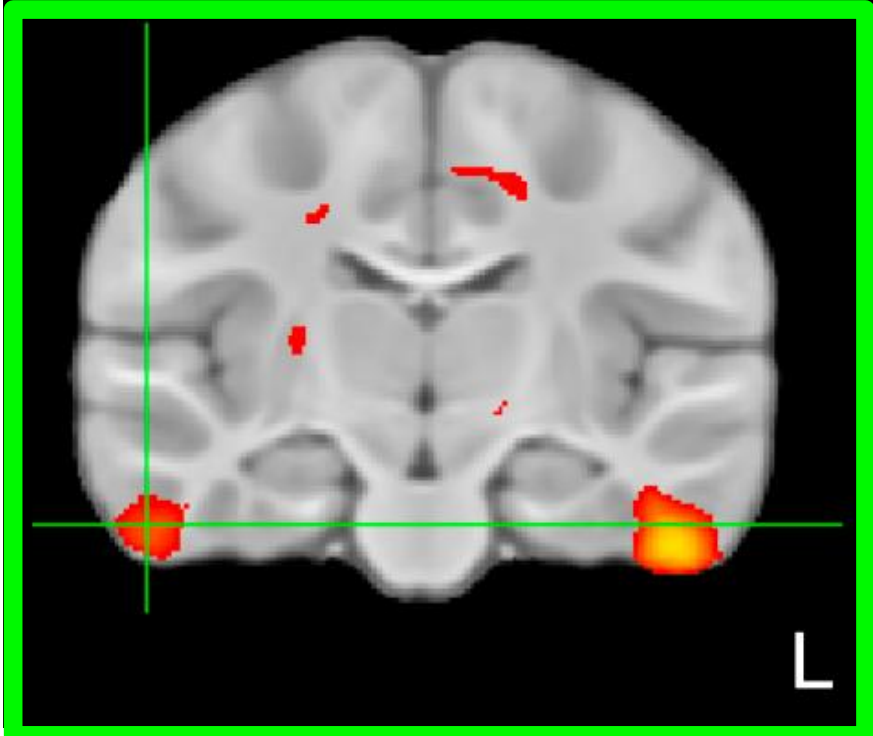
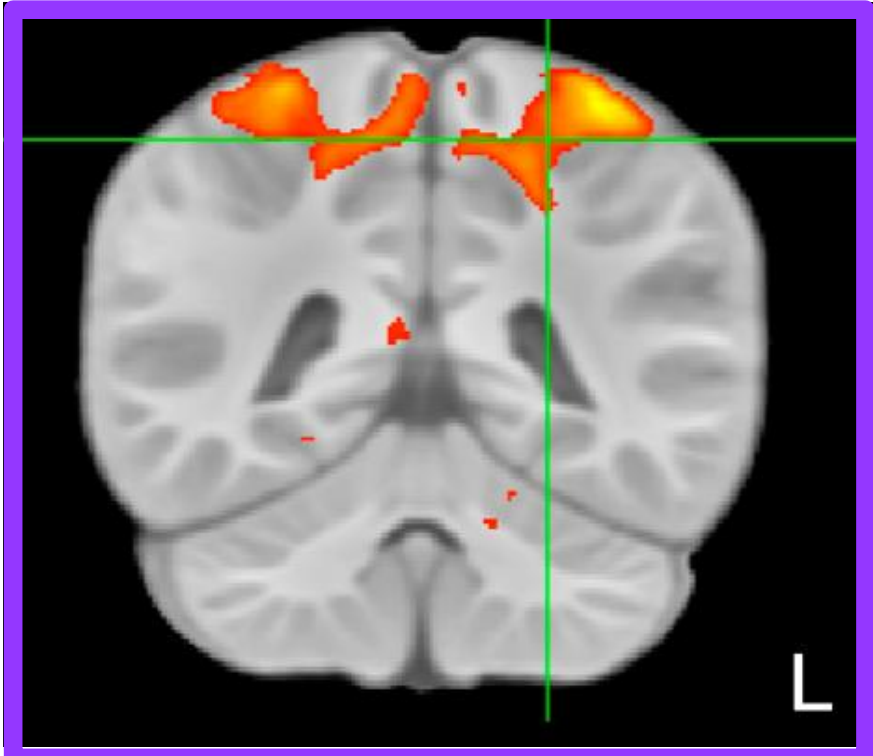
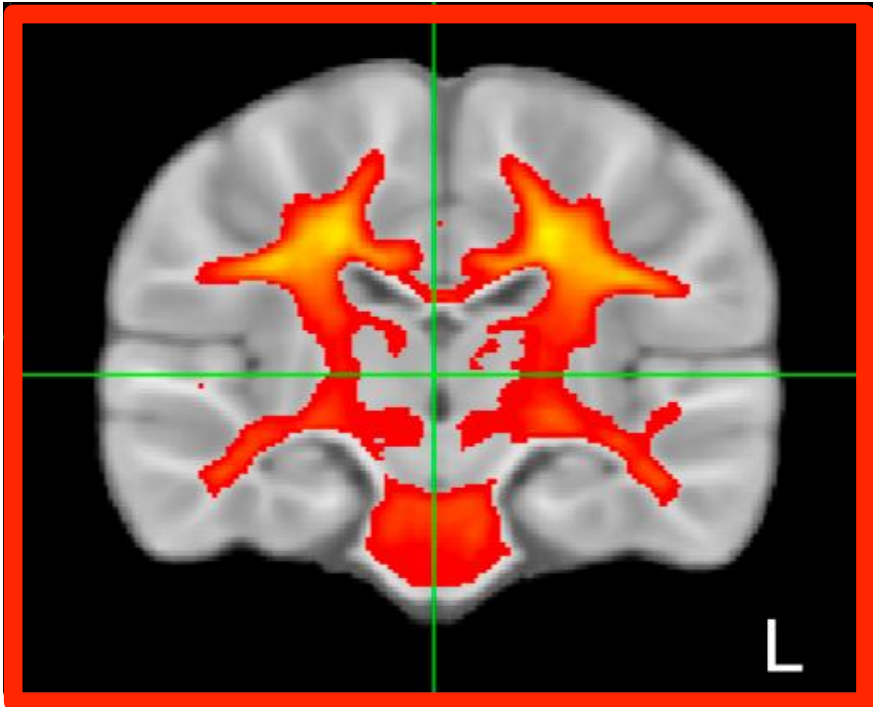
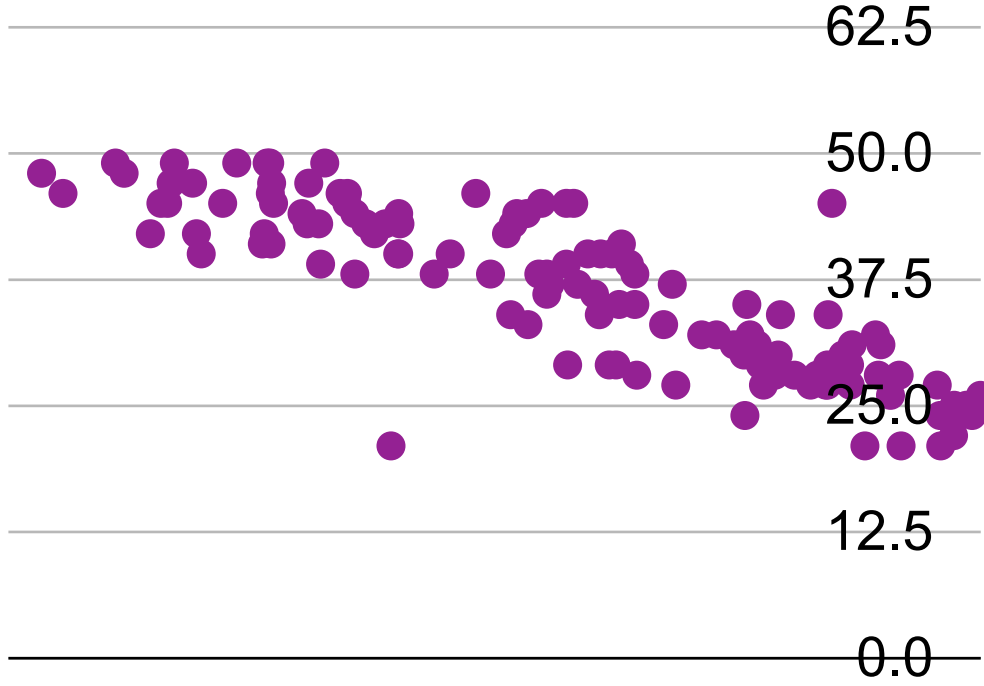


# Linking Structural and Cognitive Development



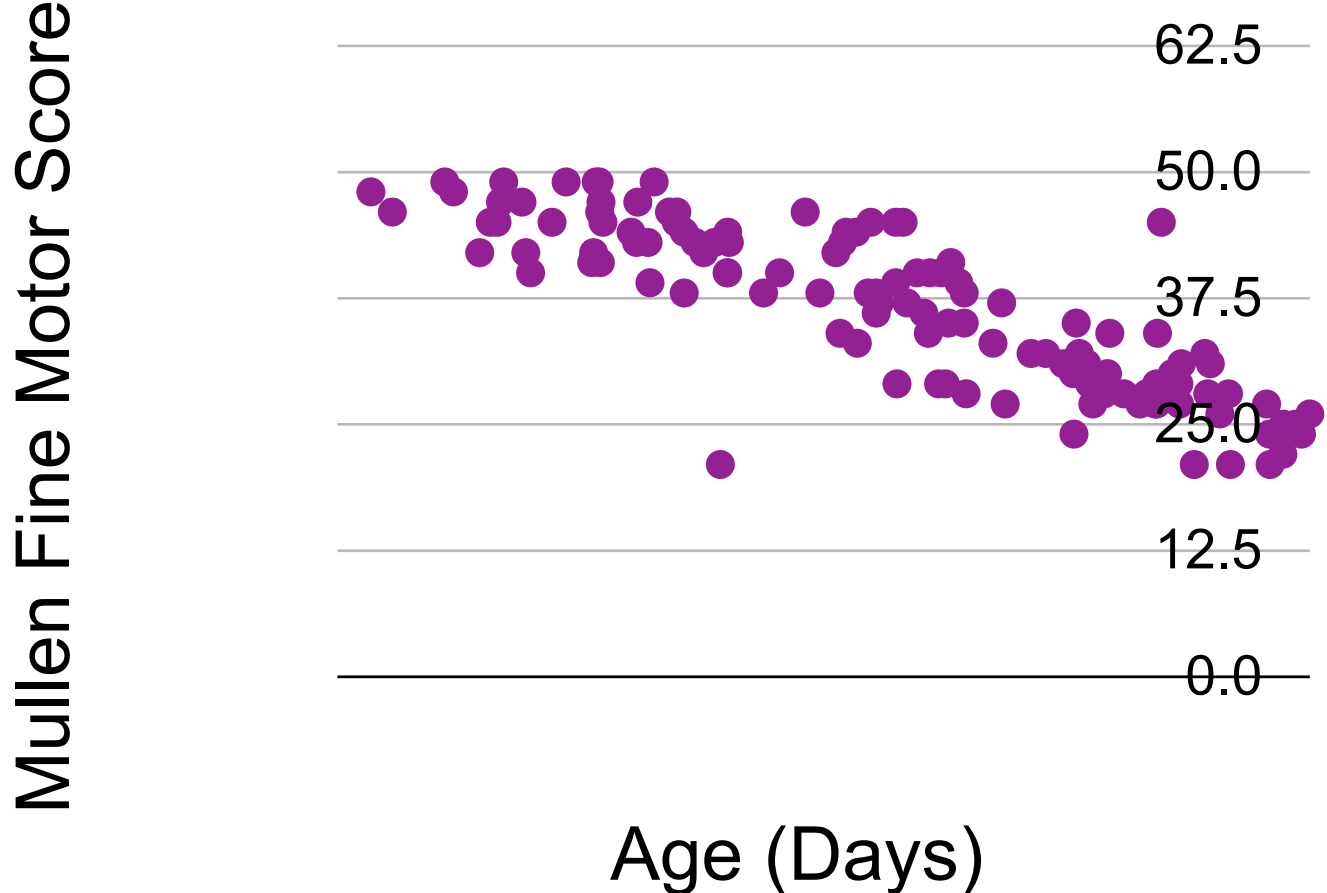
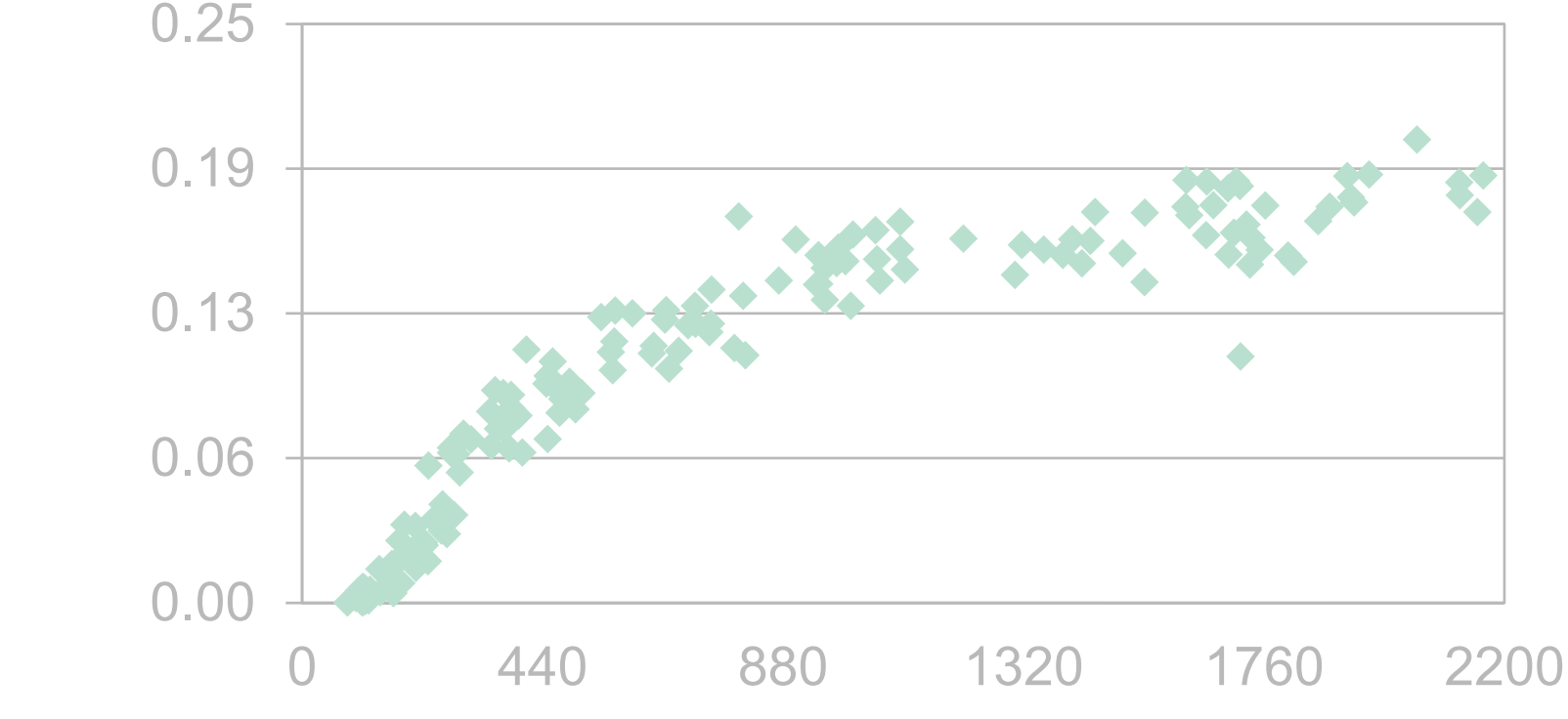
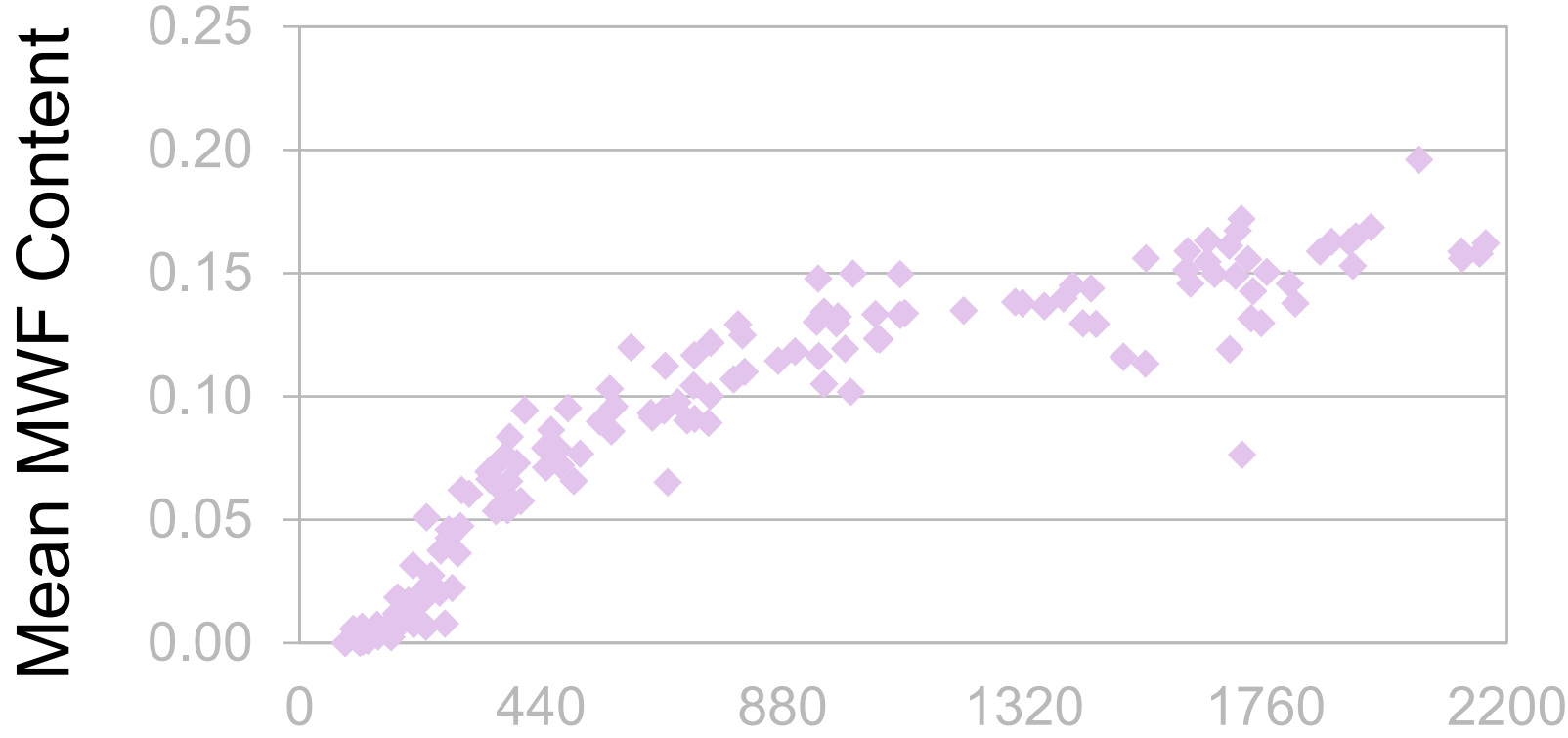
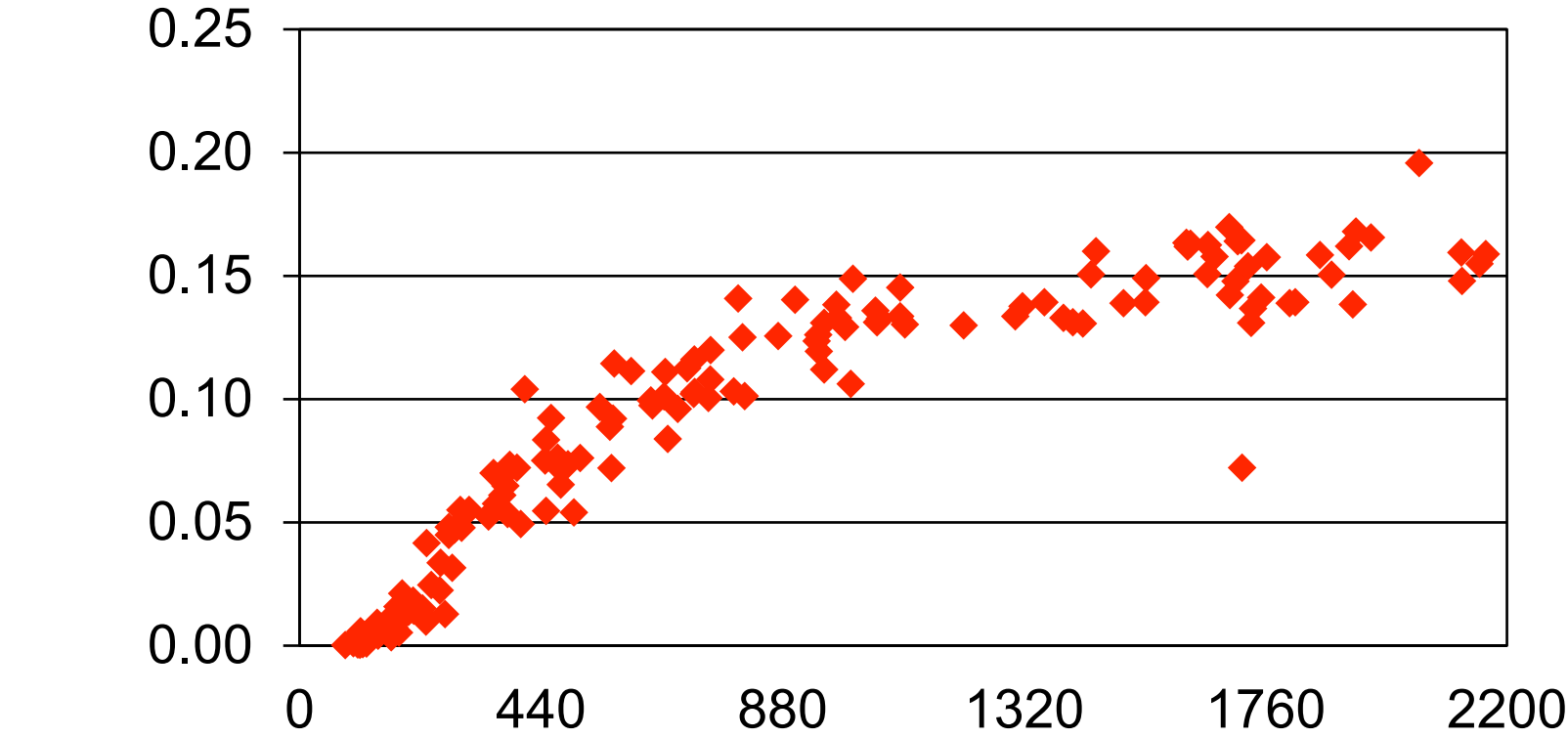
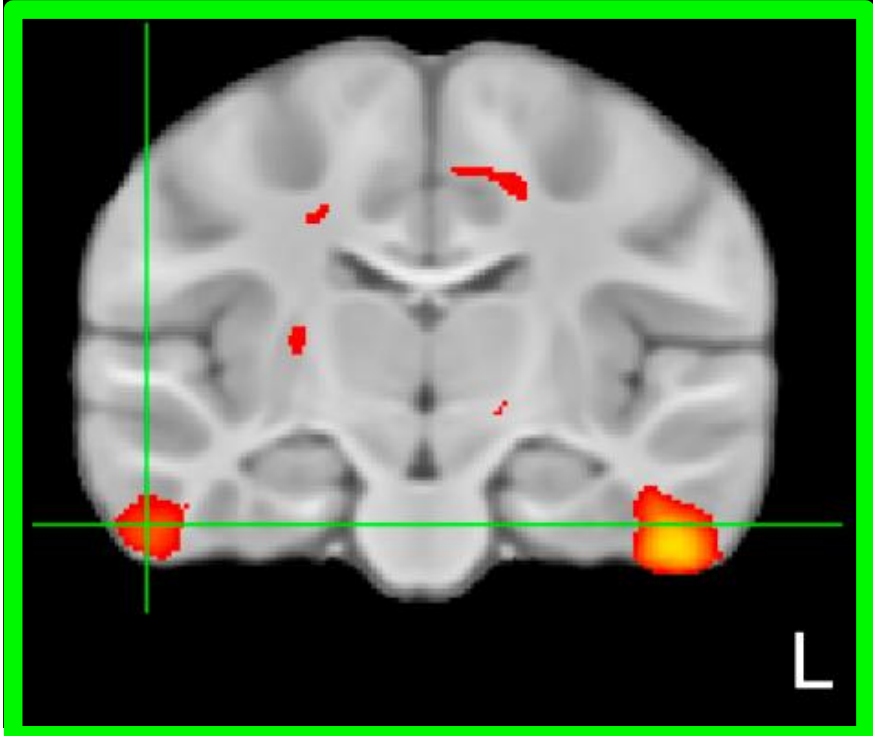
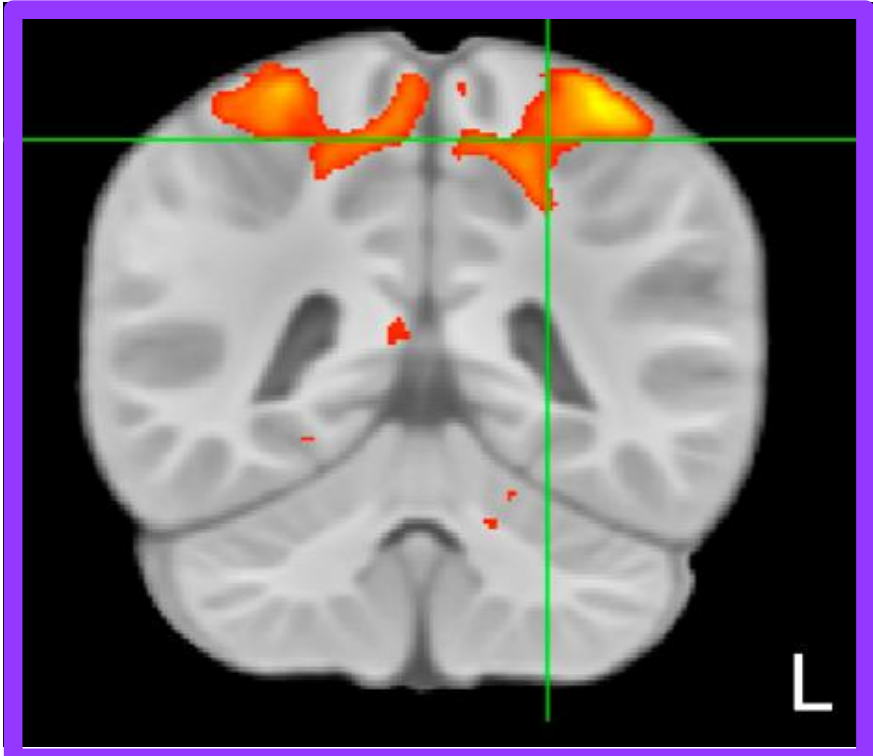
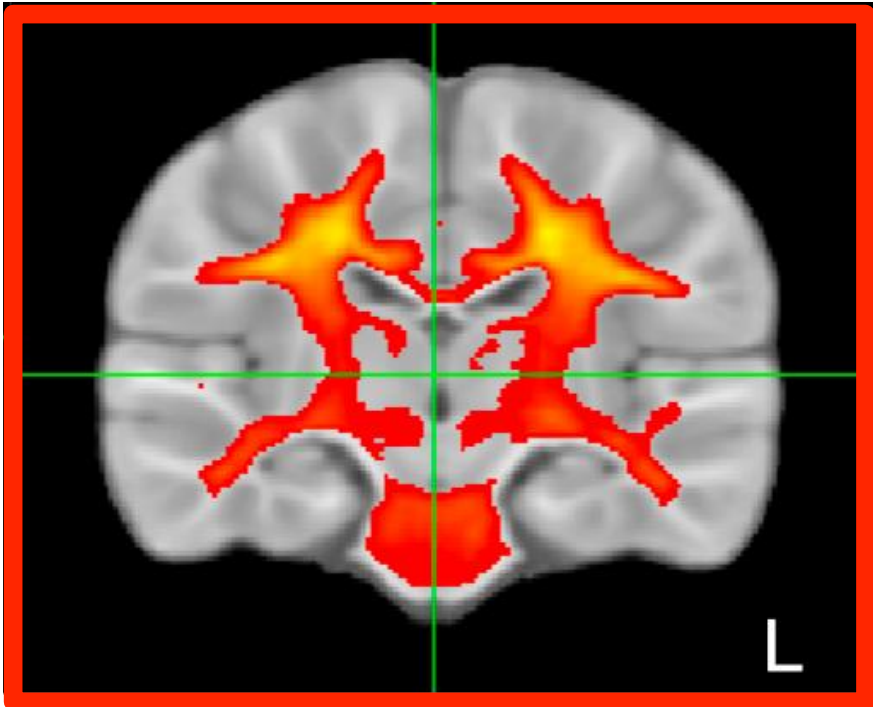
Mullen Fine Motor Score



Age (Days)

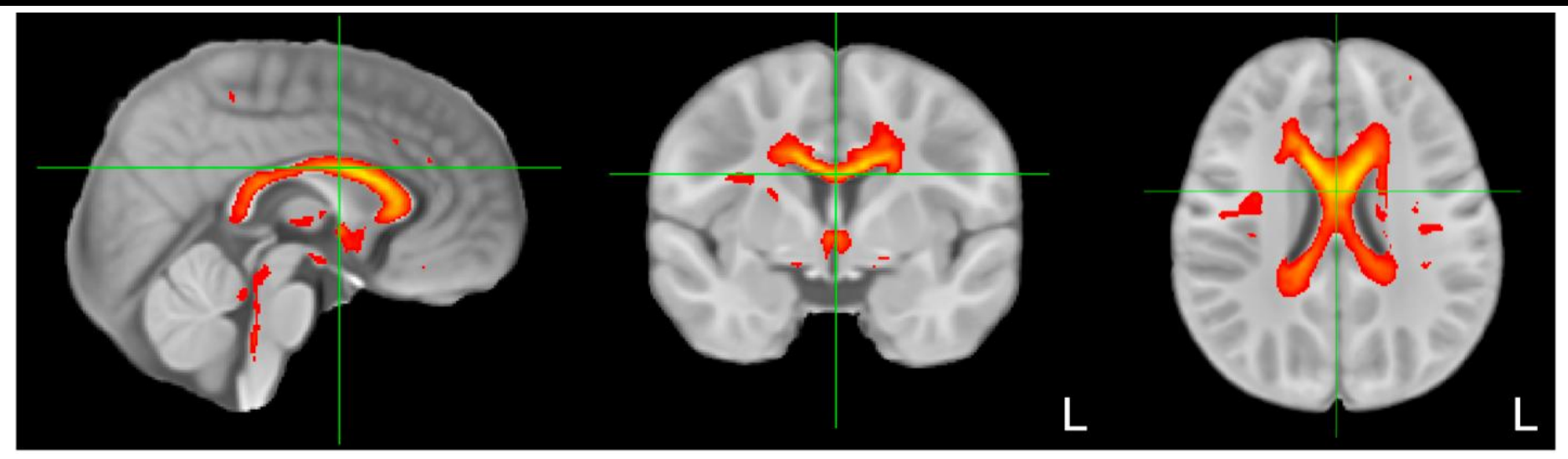
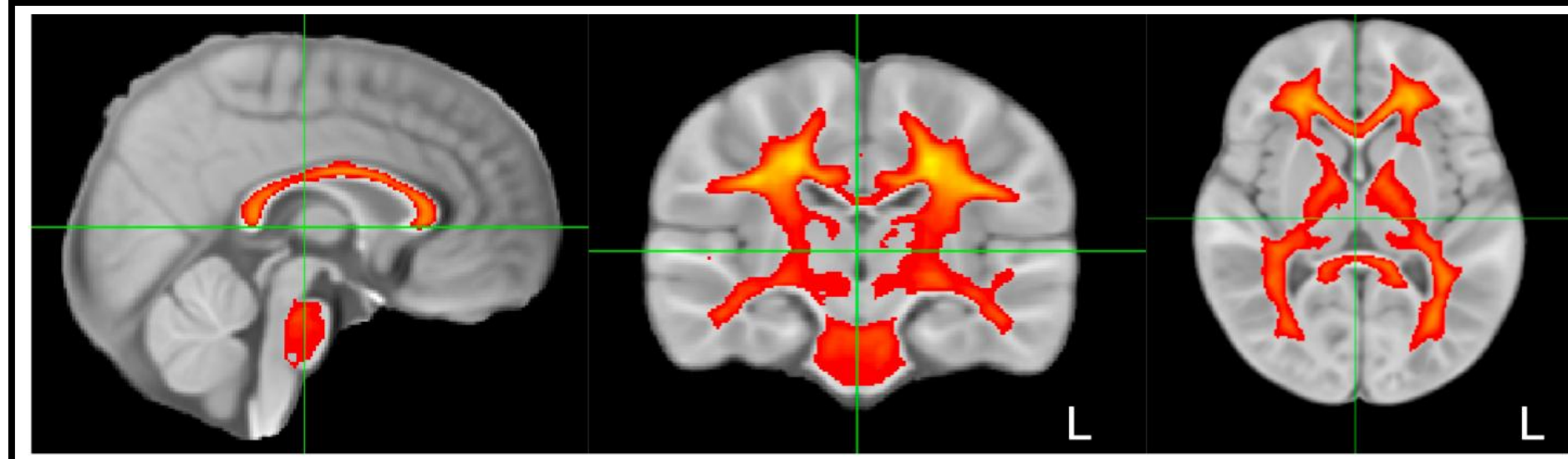


# Linking Structural and Cognitive Development

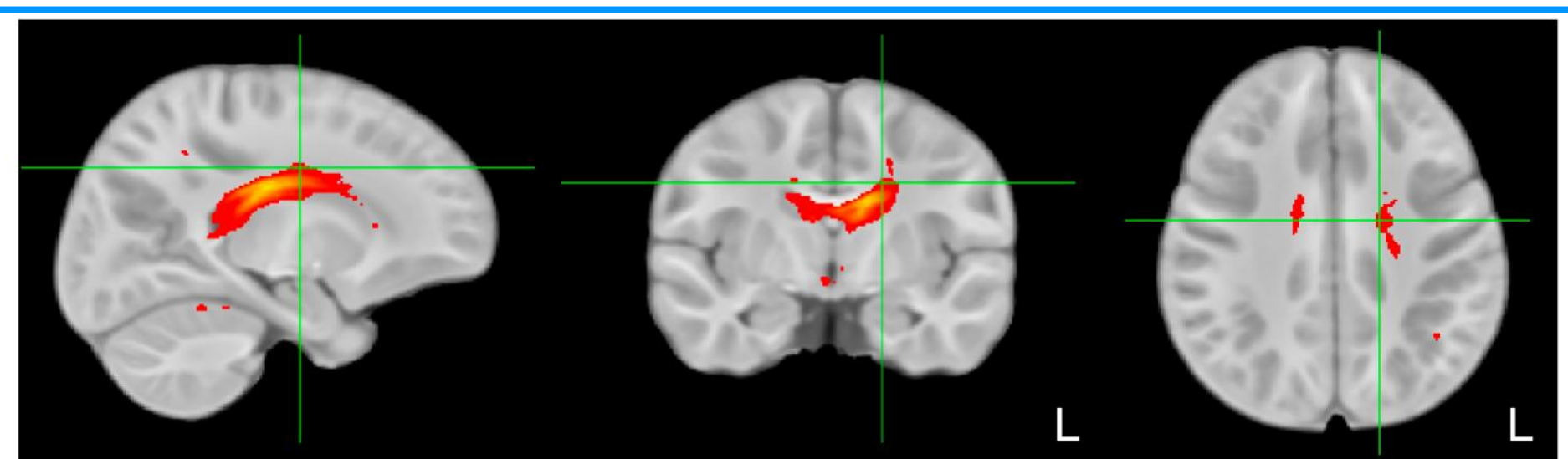
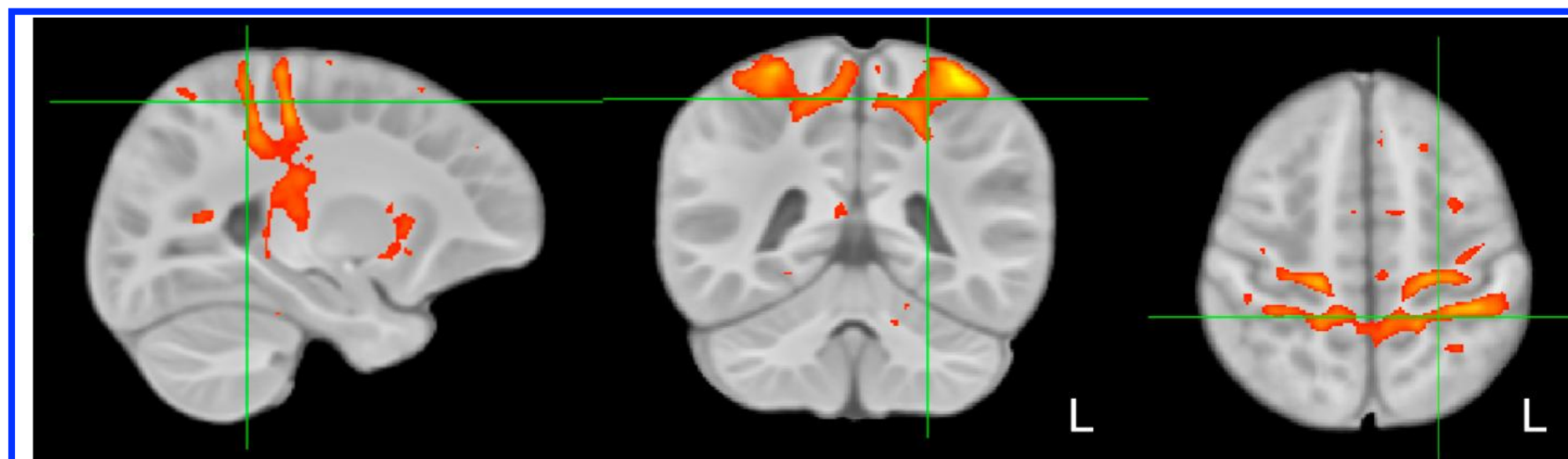


Fine Motor Function	B	T	p
Age	0.010349	5.772304	0.000000
Biological Sex (Male)	0.274504	1.050498	0.293808
Birth Weight	-0.137721	-1.228163	0.219749
Maternal Education	0.010809	0.088453	0.929539
<b>Fine Motor Function</b>	<b>50.442363</b>	<b>16.519220</b>	<b>0.00169</b>

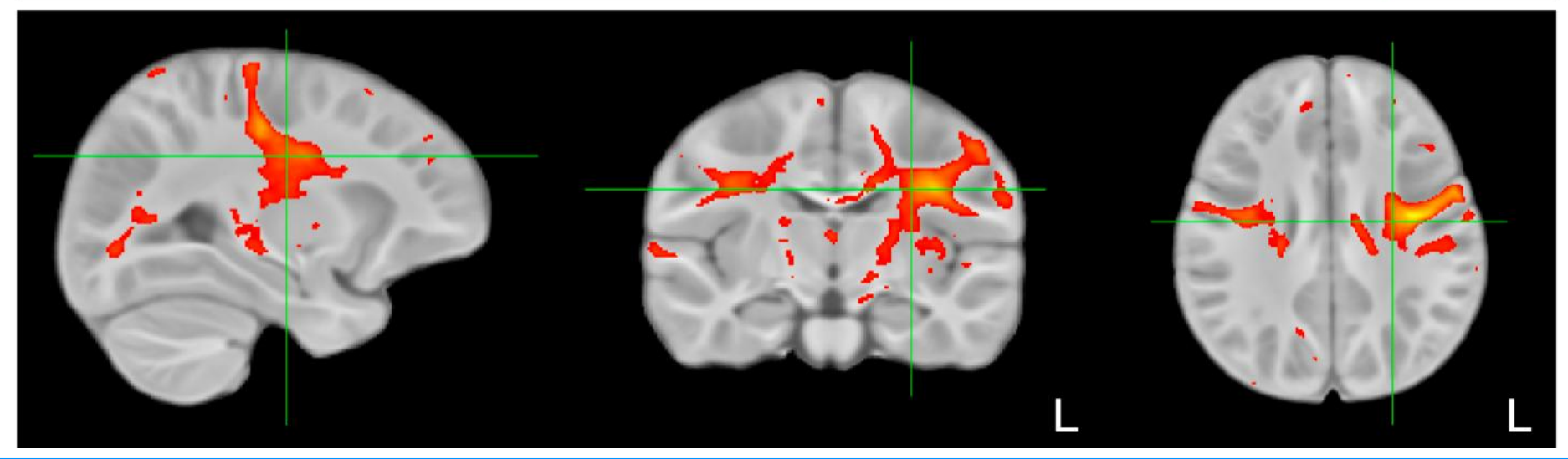
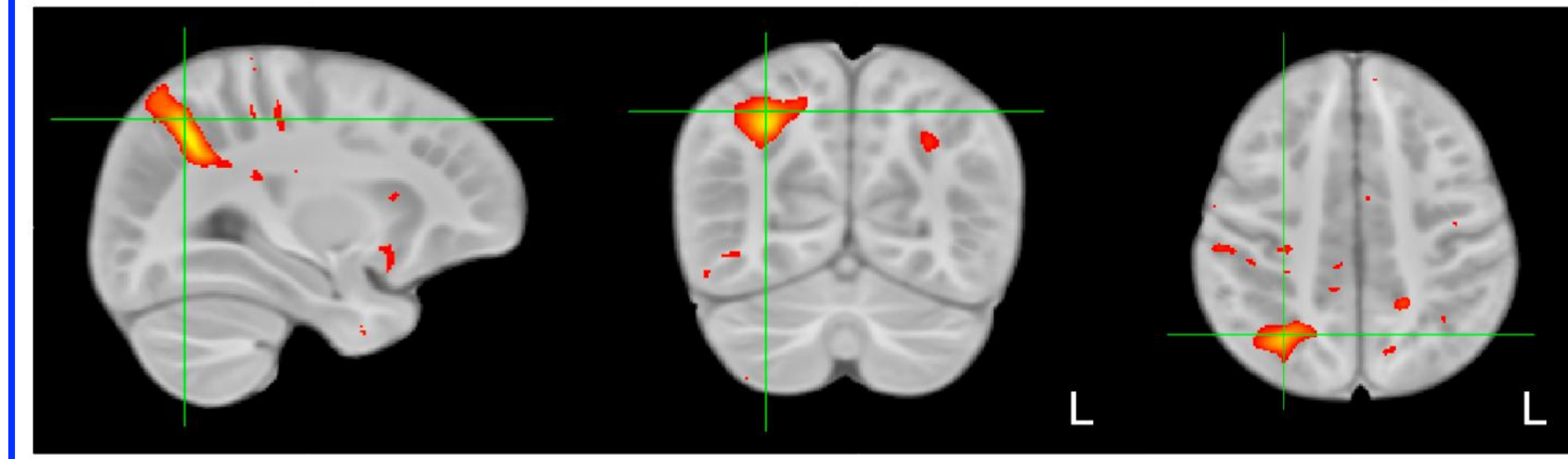




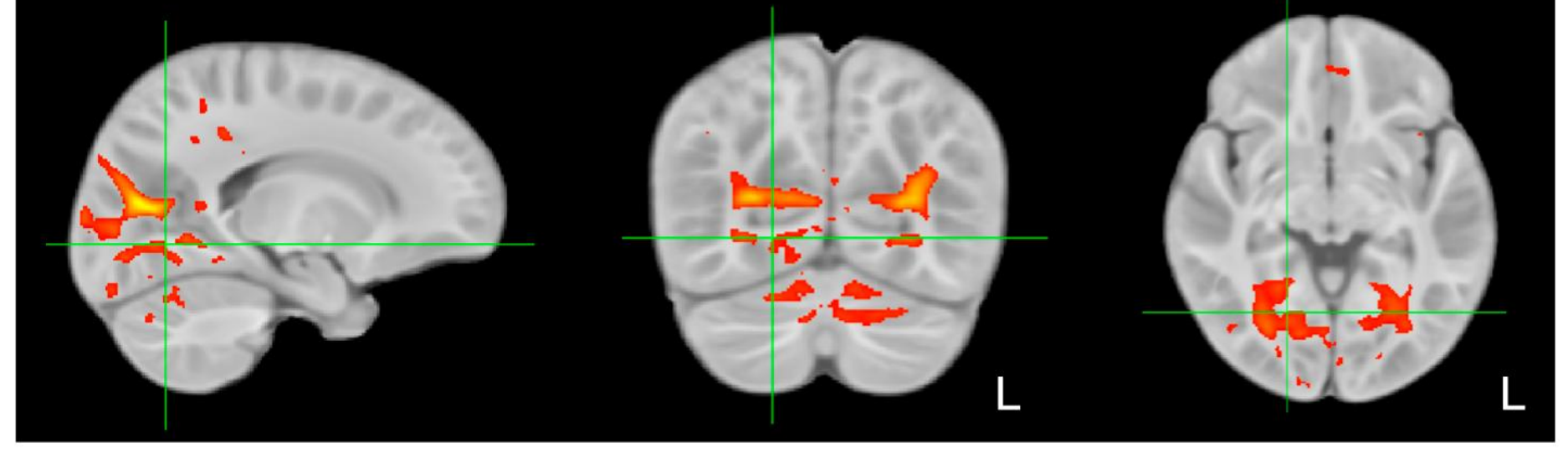
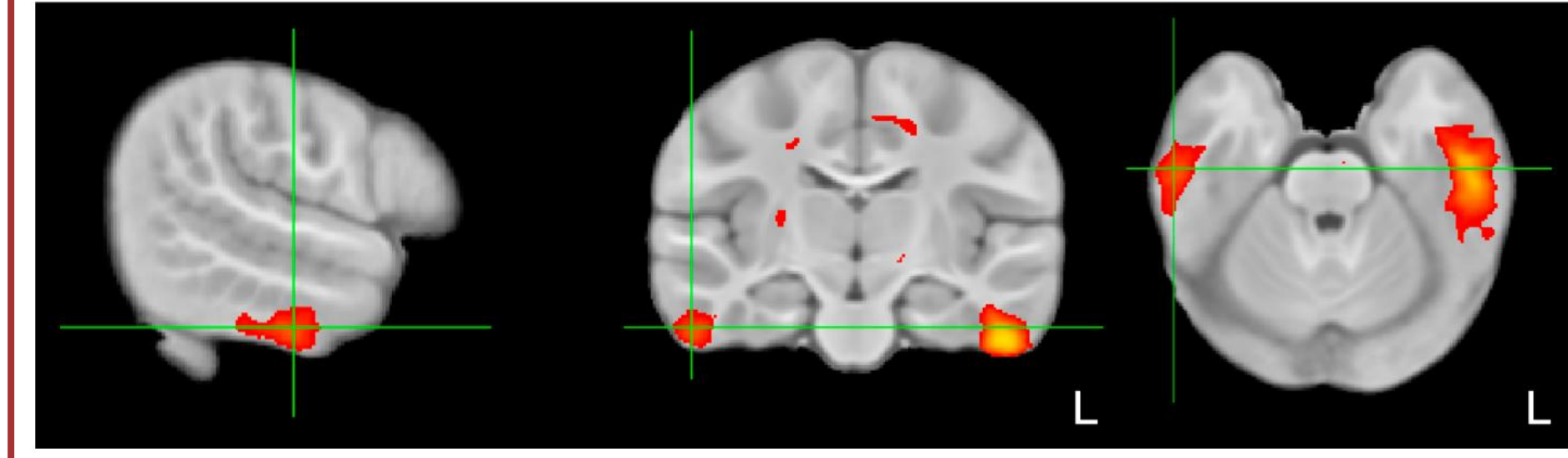
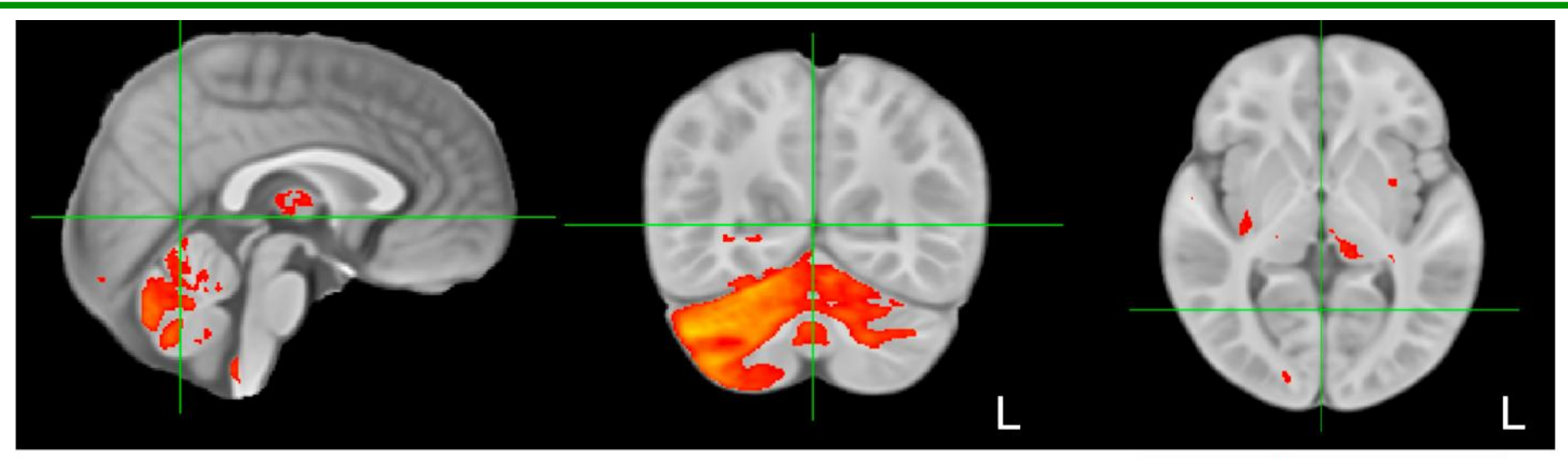
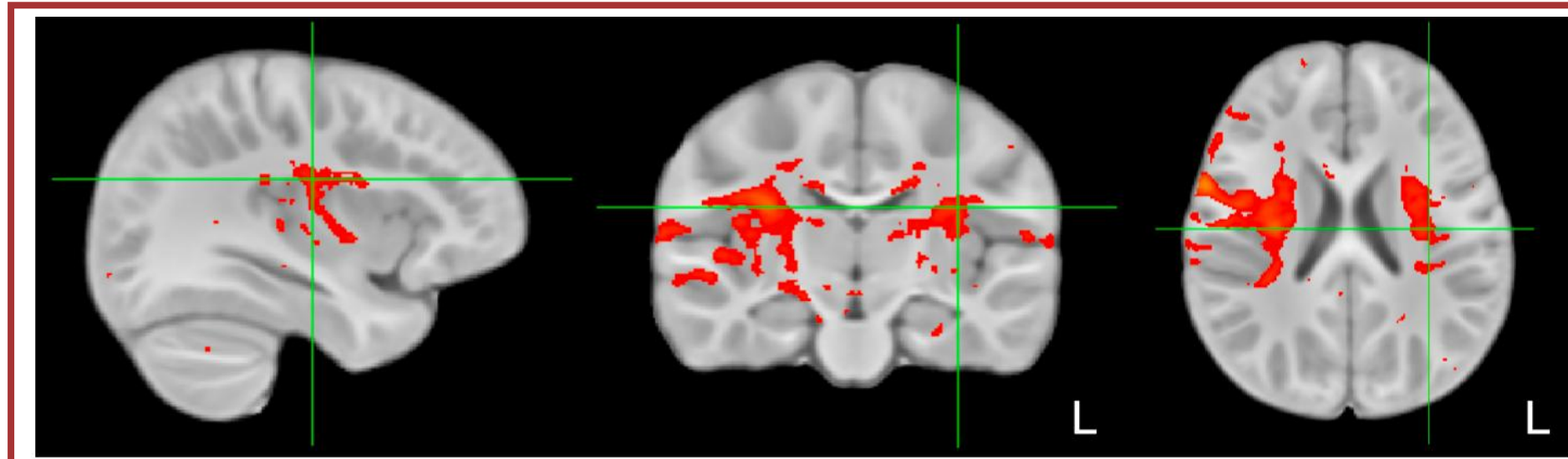
“Core”: All Functions



Gross Motor  
Fine Motor



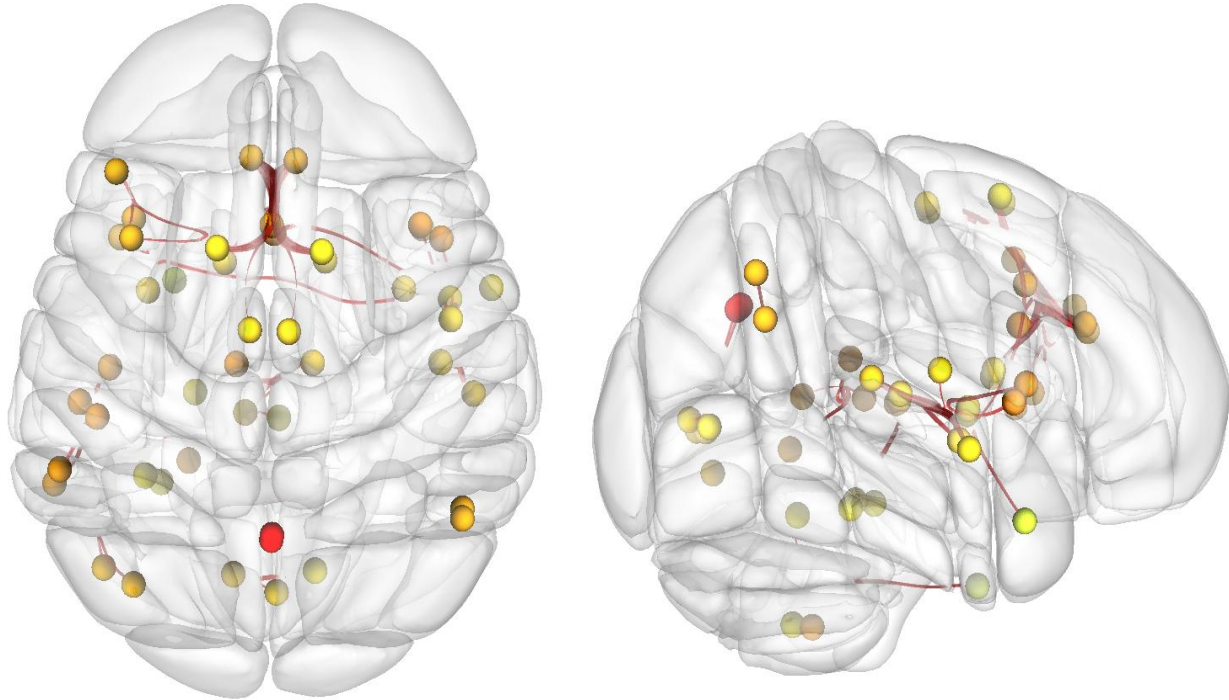
Expr. & Recept. Language  
Visual Reception



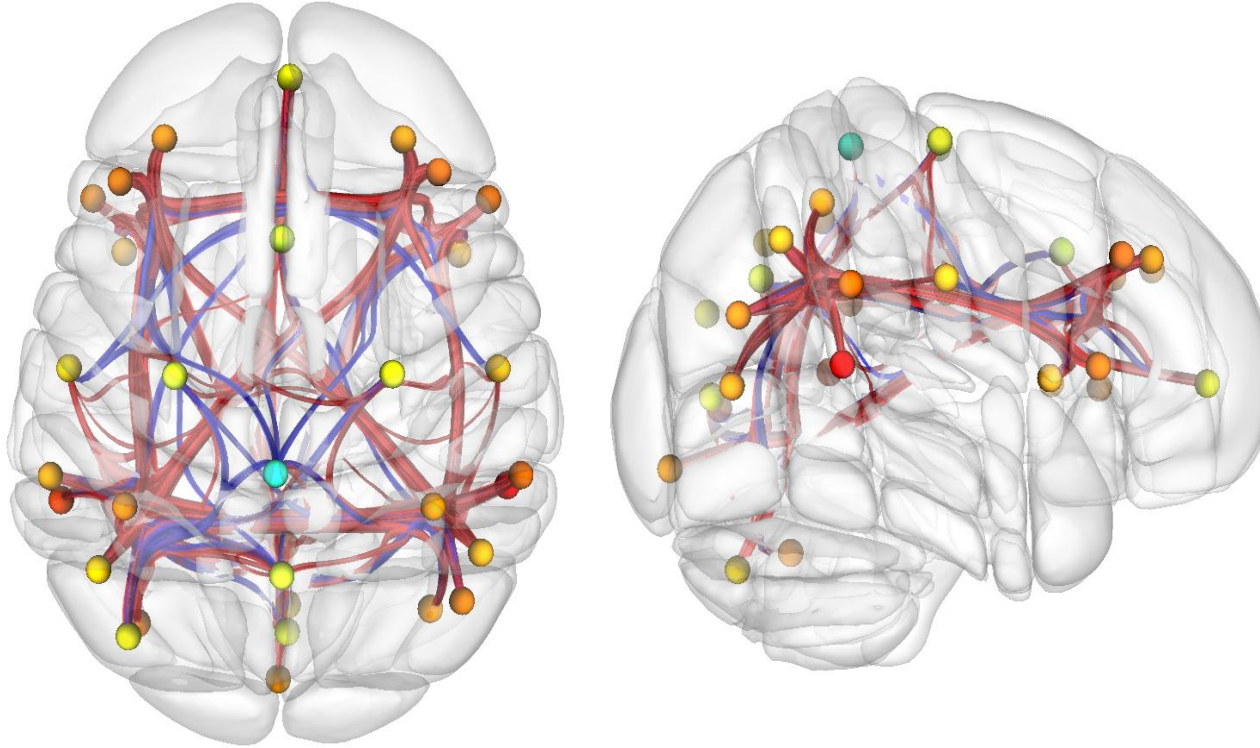
# Developmental Milestones



Cruising / Pre-Walking



First Step



# The Importance of Nutrition



# Nutritional Needs of the Developing Brain

Brain development requires the carefully orchestrated delivery of key nutrients at key timepoints.

## Lipids & Fatty Acids:

LC-PUFAs (e.g., DHA, ARA) promote healthy neural growth and development, regulate membrane function, and are involved in lipid biosynthesis and myelination. Make up ~20% of the fatty acid content of the brain.

Phospholipids, such as phosphatidylcholine, make up ~10% of the lipid weight of myelin.

Sphingolipids, specifically **sphingomyelin**, are critical components of the myelin sheath.

Cholesterol is an essential constituent of myelin and is necessary for myelin membrane synthesis.

## Minerals:

Iron is utilised by the oligodendrocytes (myelin producing cells).

Zinc helps bind myelin basic proteins to the myelin membrane.

## Vitamins:

B12 helps convert L-methylmalonyl coenzyme A into succinylcholine coenzyme A, and is required for synthesis of myelin phospholipids

Vitamin K can increase sulfatides, which are incorporated into the myelin sheath and help maintain structure & function

## Micronutrients:

CDP-Choline helps promote oligodendrocytes and their precursors, influencing myelination and remyelination.







18.99

OVER 30% MORE!  
Similac

go grow

go grow

18.99

NEW LARGER SIZE  
go grow

NEW LARGER SIZE  
go grow

NEW LARGER SIZE  
go grow

NEW LARGER SIZE  
go grow

19.99

PRELADY

PRELADY

PRELADY

PRELADY

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Mark Hyman, M.D. ✓

@drmarkhyman

This is HUGE. Many infant formulas contain corn syrup and inflammatory seed oils as primary ingredients.

Heavy metals, glyphosate, and other contaminants have been found in infant formula, yet regulations have remained outdated and inadequate. We NEED cleaner, healthier alternatives.

**@diaryofacruchymom** “So much of the formula marketing is predatory ..... There's **so many things wrong with infant formula, I mean, it's filled of high fructose corn syrup, right now they call it “corn syrup solids” and seed oils, which are very unhealthy,** especially for babies bodies you know, they are only a few days old and they are filling them with this highly inflammatory make up of these, just these chemical ingredients”



iamjasyra ✓ Edited • 80w

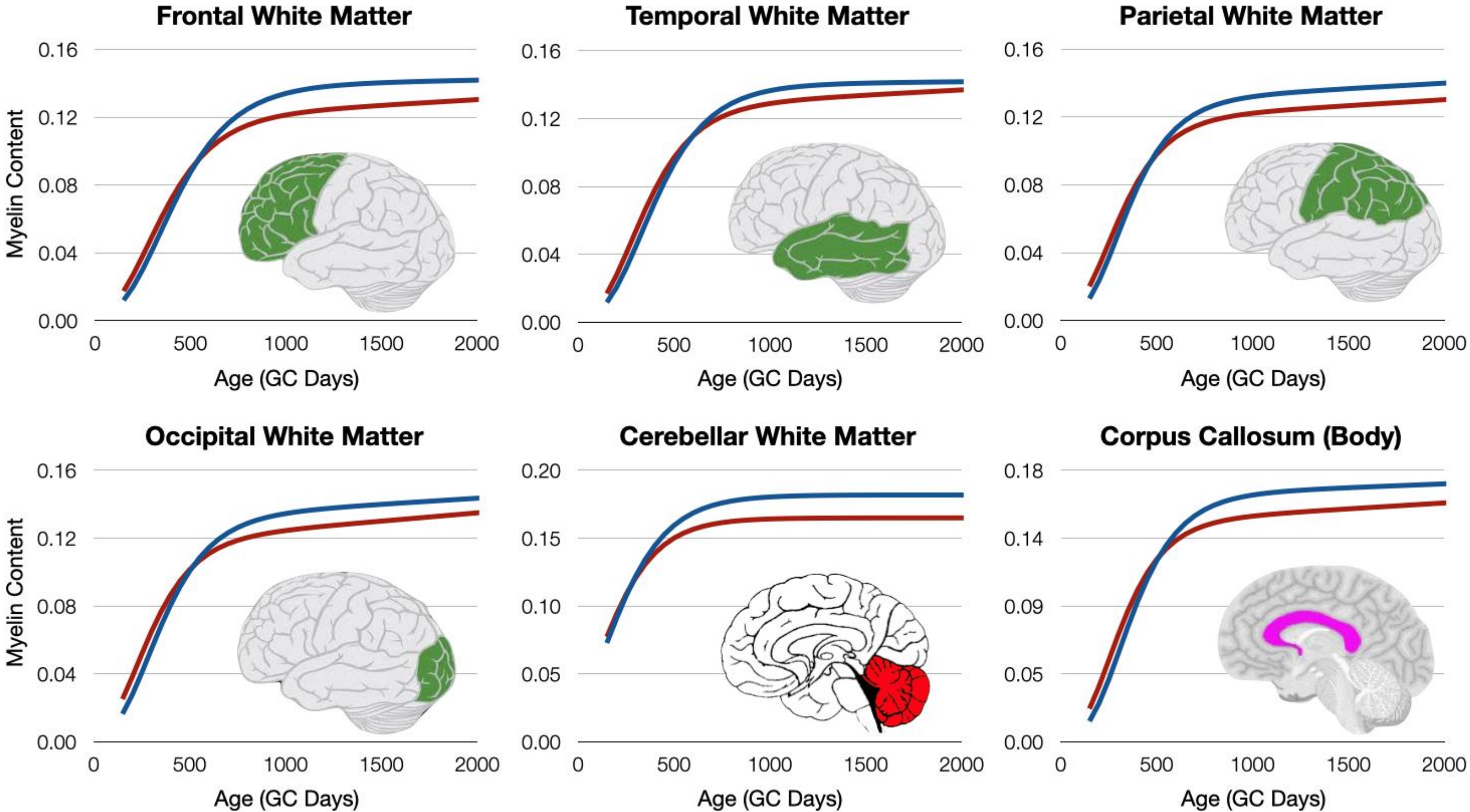
There is no perfect formula because majority still have seed oils in it but if you are struggling with breastfeeding these brands will be your better options if you need formula. As a mom who struggled with breastfeeding and had to stop breastfeeding due to my pharmaceutical injury I can understand how hard it is to make a decision on formula so I hope this post helps you make a decision you feel good about. I forgot to add [@myserenitykids](#) toddler milk to my last slide. It's actually one of the best options and can be used for babies too. Doing a graphic with an awake toddler who was rushing me is never a good idea lol. Code JASYRA15 to save for serenity



# Breastfeeding & Neurodevelopment: Longitudinal

150 Toddlers (2-76 months of age).  
62 Breast-Fed / 88 Formula-Fed.  
Exclusive feeding for at least 3 months  
Cohorts were matched for:

- Mean Age;
- Male/Female ratio;
- Parent Marital Status;
- Maternal Age, Education & Income;
- Birth Weight and Gestation Duration;
- Family Size, Birth Order;
- Language Spoken in Home;



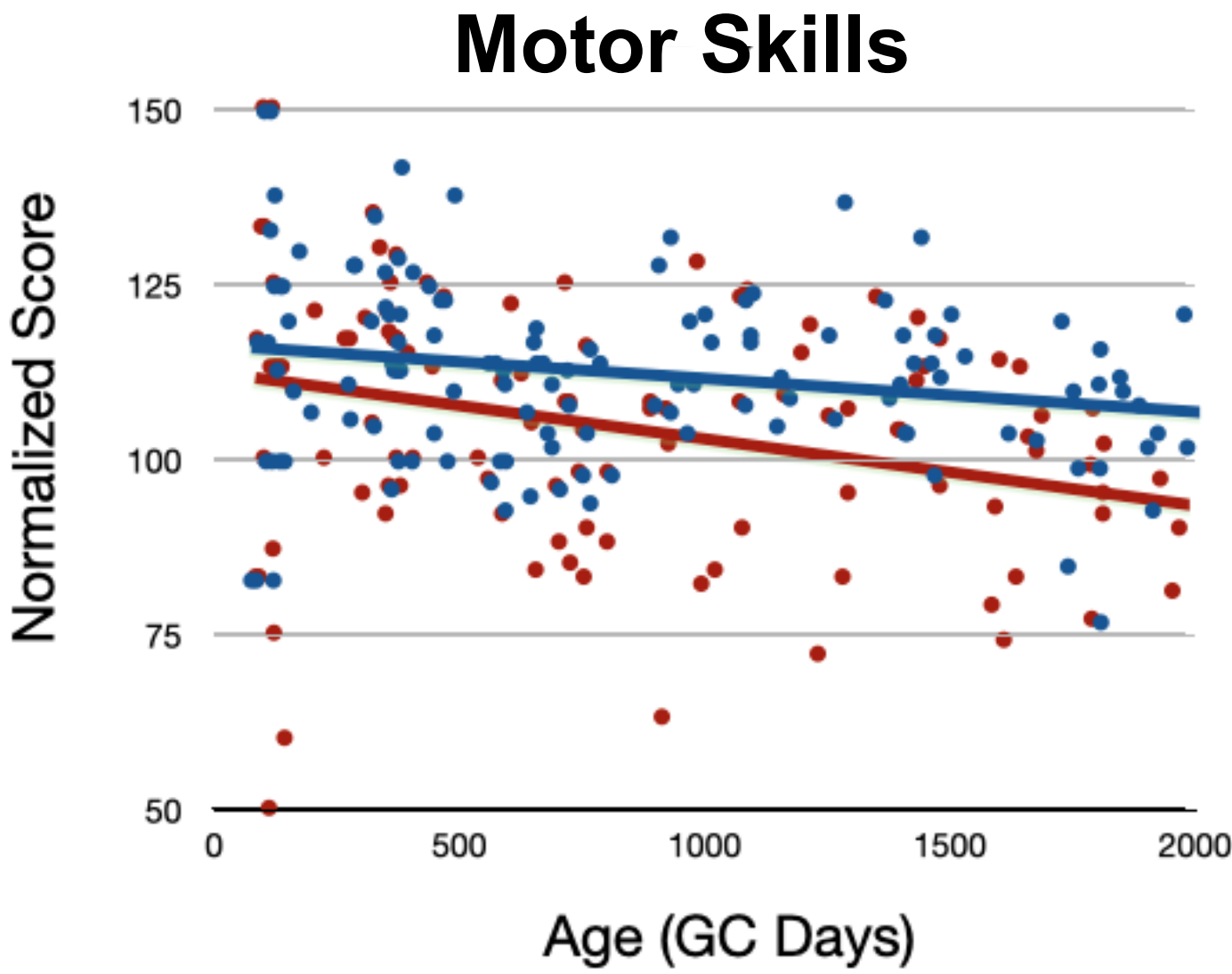
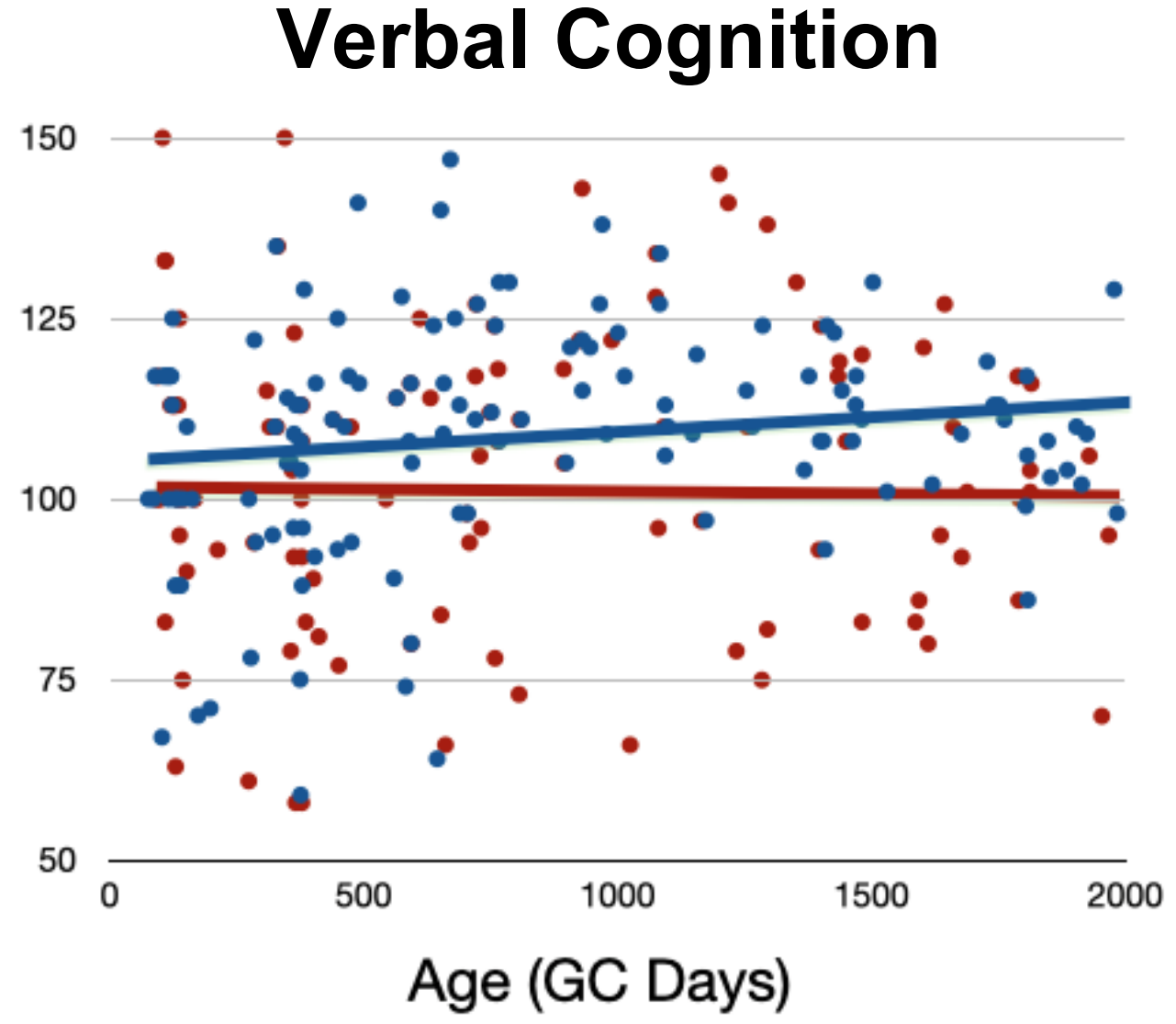
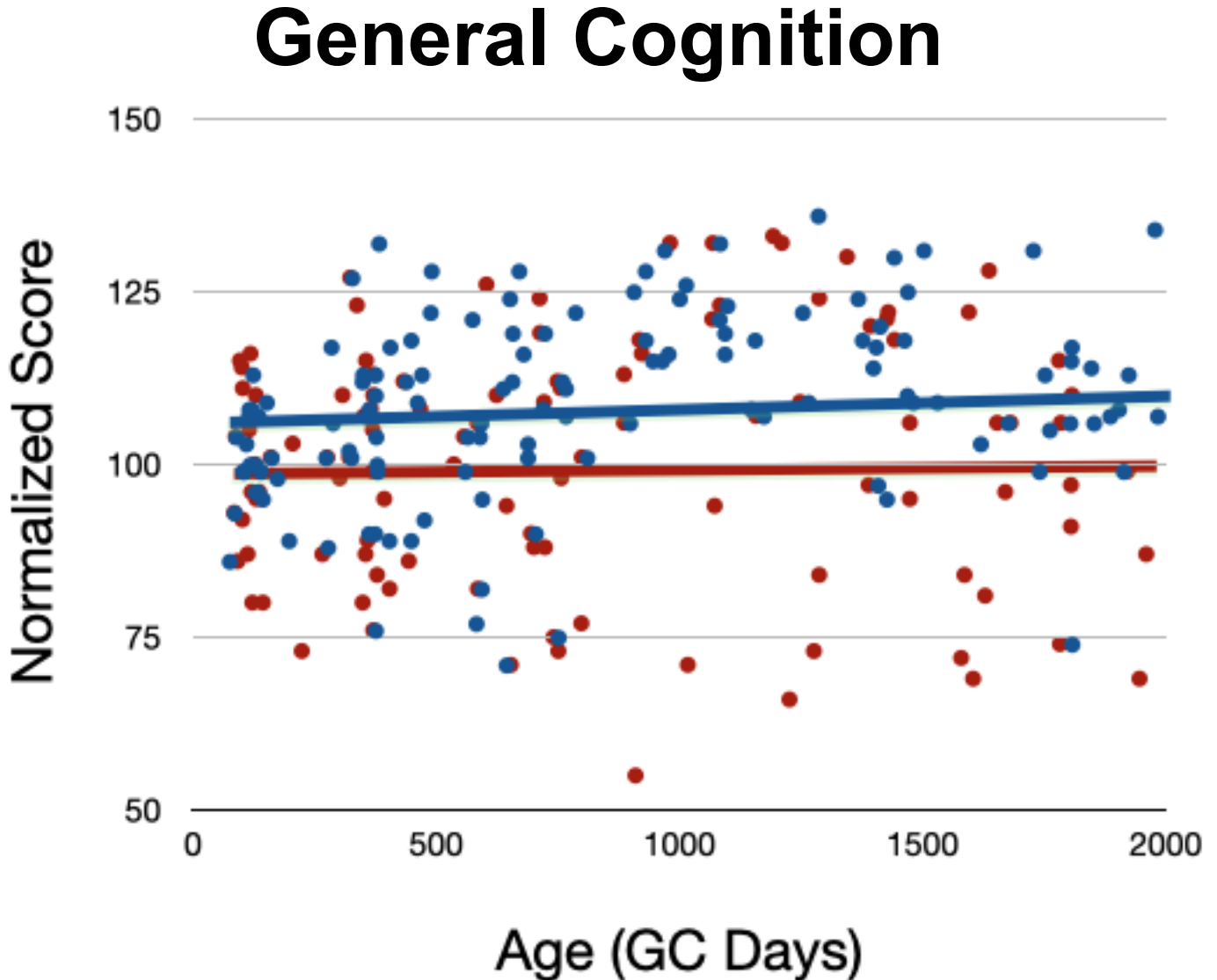
**\*Significant differences in all growth model parameters between groups**

■ Breastfeeding  
■ Formula Feeding



# Breastfeeding & Neurodevelopment: Longitudinal

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■ Breastfeeding  
■ Formula Feeding



# Breastfeeding & Neurodevelopment: Longitudinal

Of the ~1800 emails and other messages received, some common comments:

“I’ll never believe your results. You need to do a proper double-blind randomised control trial.”

“I didn’t breastfeed my children and one is a Professor at Columbia. There are so many other effects that you’ve not accounted for.”



# Breastfeeding & Neurodevelopment: Longitudinal

Of the ~1800 emails and other messages received, some common comments:

“I’ll never believe your results. You need to do a proper double-blind randomised control trial.”

I don’t know how to blind mum to whether she is breastfeeding or not.

“I didn’t breastfeed my children and one is a Professor at Columbia. There are so many other effects that you’ve not accounted for.”

Too bad, if you had breastfed they could have been on faculty here at Brown.

 I did not send this, but desperately wanted to.

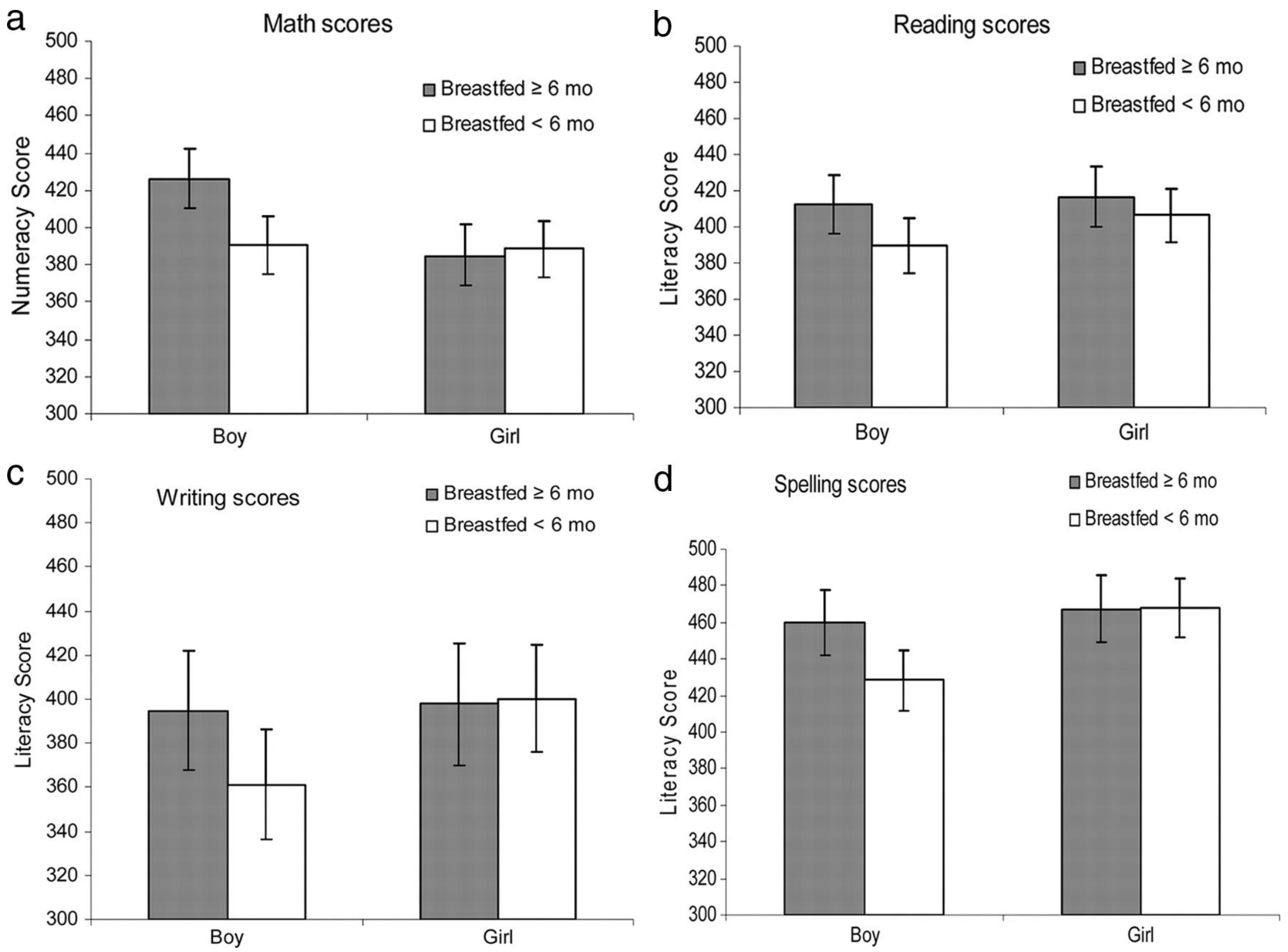


Nutrition Facts	
Serving Size 1 cup (240 g)	
Amount Per Serving	
Calories 172	Calories from Fat 15
% Daily Value	
Total Fat 11g	22%
Saturated Fat 5g	10%
Trans Fat	
Cholesterol 42mg	84%
Sodium 42mg	84%
Total Carbohydrate 17g	34%
Dietary Fiber 0g	0%
Sugars 17g	34%
Protein 3g	6%
Vitamin A	10%
Calcium	8%
*Percent Daily Values are based on a diet of other people's secrets.	
© www.NutritionData.com	



# Breastfeeding & Child Neurodevelopment

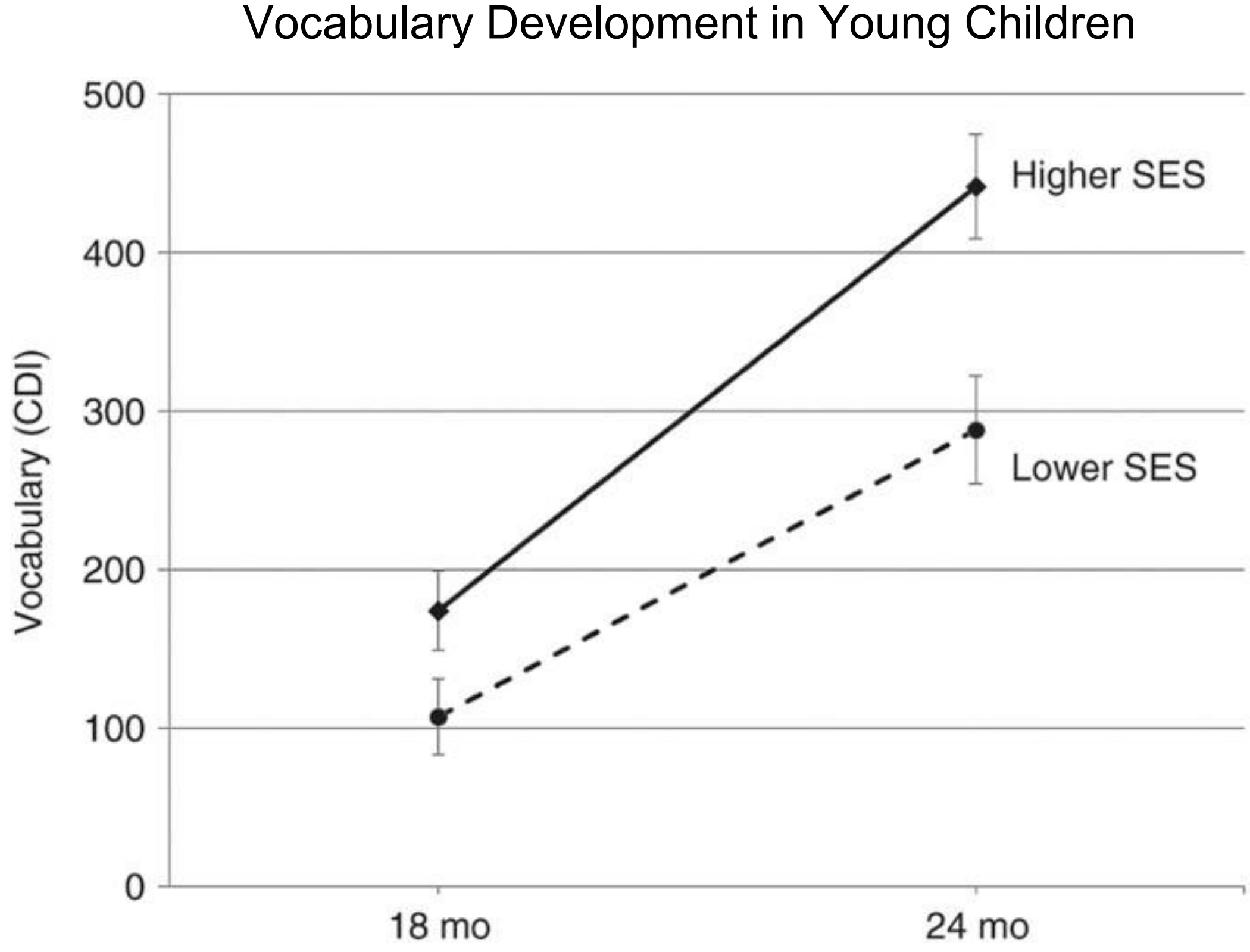
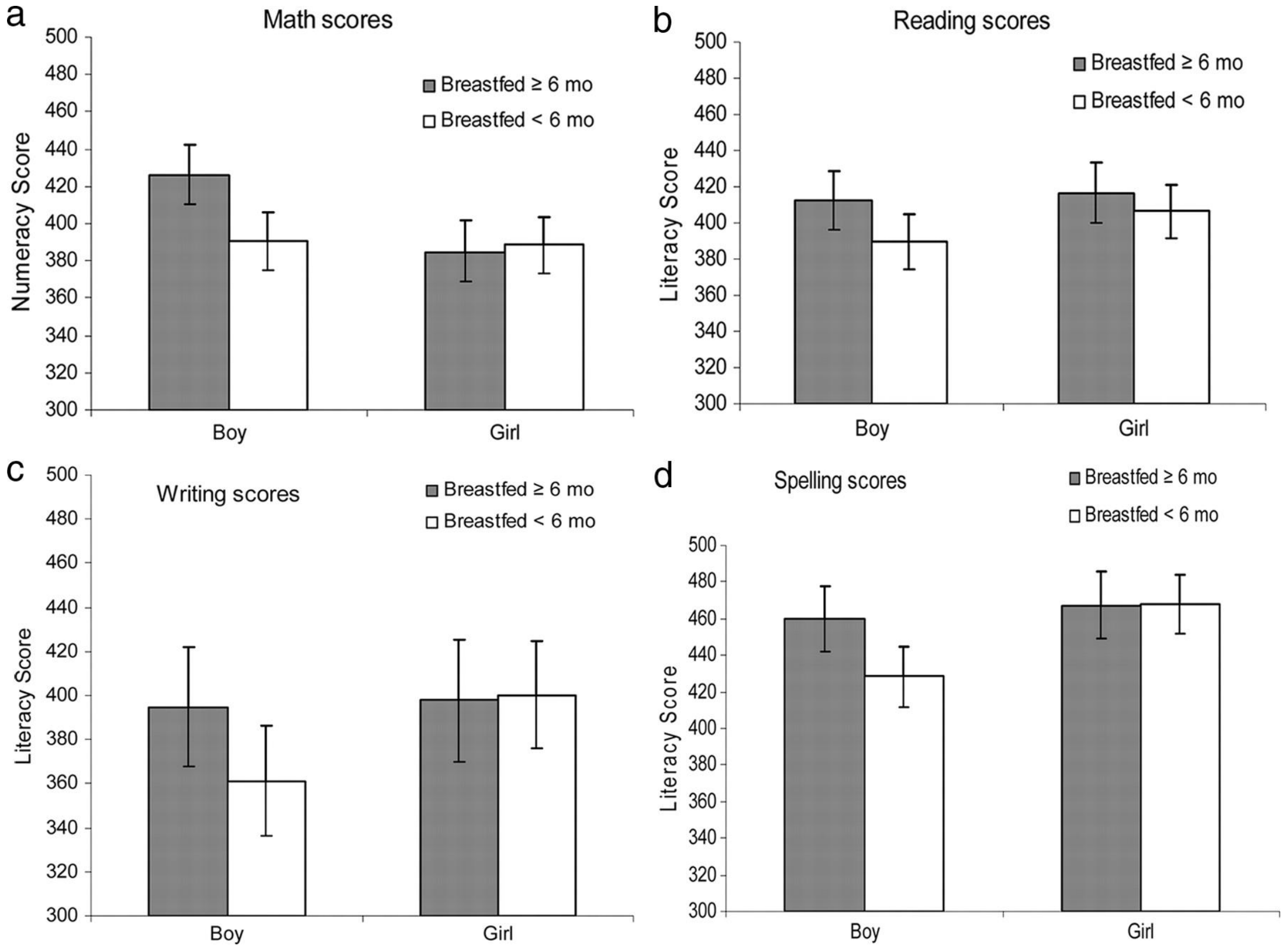
Studies consistently show improved cognitive development and academic outcomes in individuals who were breastfed as infants; enhanced as a function of breastfeeding duration.



# Breastfeeding & Child Neurodevelopment

Studies consistently show improved cognitive development and academic outcomes in individuals who were breastfed as infants; enhanced as a function of breastfeeding duration.

**BUT**, other health and environmental factors (e.g., mother-child bonding, care-giving quality, family education, family income, home stress, sleep, etc.) can also contribute to these cognitive differences.



# Does Nutrition Shape Neurodevelopment?

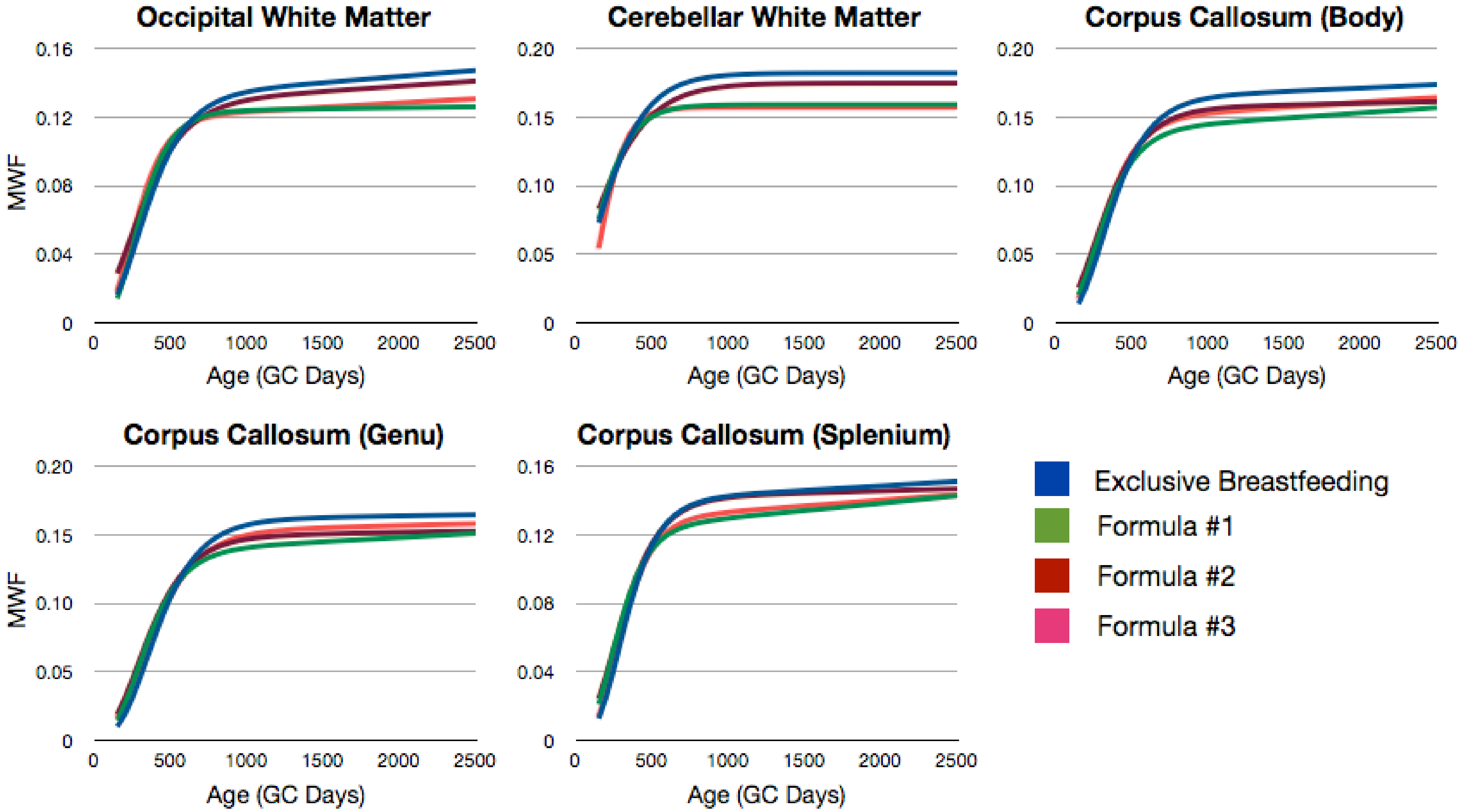
	Units	Formula #1	Formula #2	Formula #3	% Difference (Min-Max)
ARA	mg / L	173	238	255	32
DHA	mg / L	62.2	117	120.6	48
Folic Acid	mcg / L	304	232	146.2	52
Phosphatidylcholine	mg / L	85	58	60	29
Sphingomyelin	mg / L	28.1	62	28.1	55
Iron	mg / 100g	10.6	8.42	11.65	28
Choline	mg / 100g	170	92.5	144	46

A series of GLMs were used to regress nutrient values against individual growth trajectory parameters.

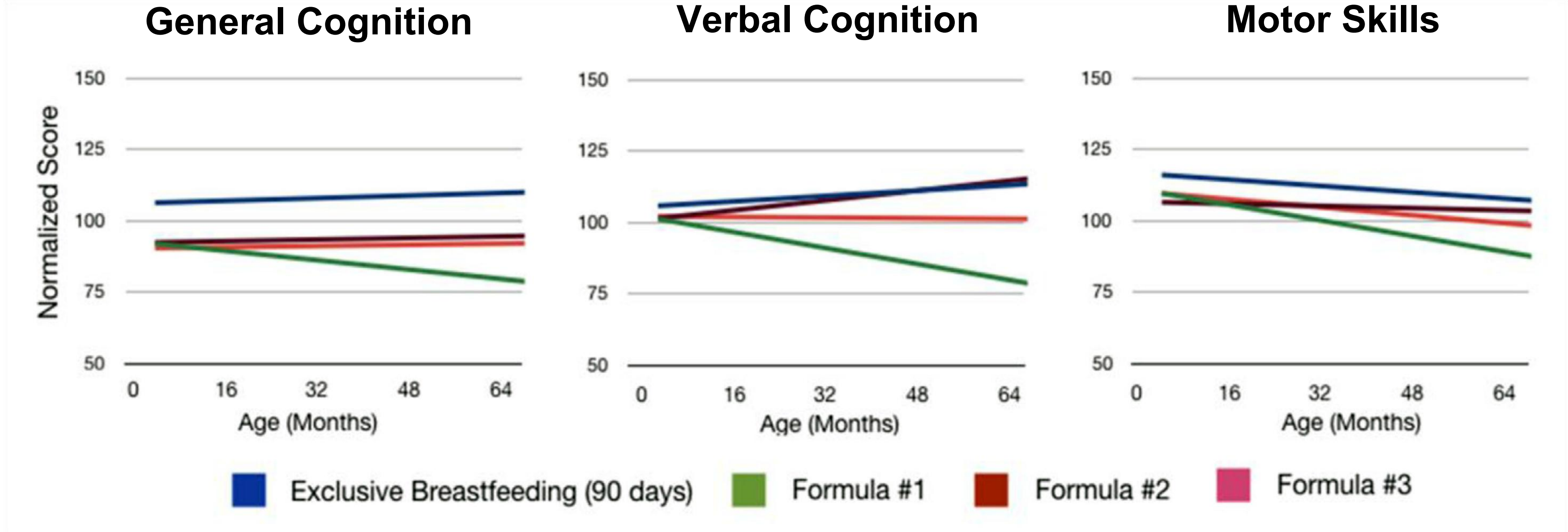
# Does Nutrition Shape Neurodevelopment?

		BreastFed	All Formula	Formula #1	Formula #2	Formula #3
Gender	Male (n)	25	50	8	18	24
	Female (n)	15	30	5	10	15
Age Range (days)		86 - 3384	88 - 4009	103 - 4009	98 - 3308	88 - 3384
Mean Gestation (days)		276 ± 7	281 ± 19	278 ± 6	275 ± 11	285 ± 12
Mean Birth Weight (g)		3376 ± 675	3313 ± 540	3164 ± 589	3179 ± 555	3446 ± 508
Mean Birth Height (inches)		20 ± 1.6	21 ± 3.5	20 ± 0.5	20 ± 1.8	21 ± 4.9
Mean Maternal Education		6 ± 1.3	5.6 ± 1.5	5.8 ± 1.2	5.4 ± 1.1	5.6 ± 1.8
Mean Paternal Education		5.9 ± 1	5.5 ± 1.6	5.8 ± 1.3	5.1 ± 1.1	5.5 ± 1.6
Mean Family Size (# Children)		2.3 ± 1.1	2.3 ± 1.5	2 ± 2	2.1 ± 1.5	2.2 ± 1
# Scans / Child		3.4 ± 1.2	2.5 ± 1.3	2.2 ± 1.4	3 ± 1.2	2.1 ± 1.3
Mean Inter-Scan Period (days)		423 ± 234	380 ± 250	439 ± 250	407 ± 299	330 ± 190
Marital Status	Married / Living Together (n)	36	62	10	21	29
	Divorced / Single (n)	4	18	3	7	9

# Does Nutrition Shape Neurodevelopment?



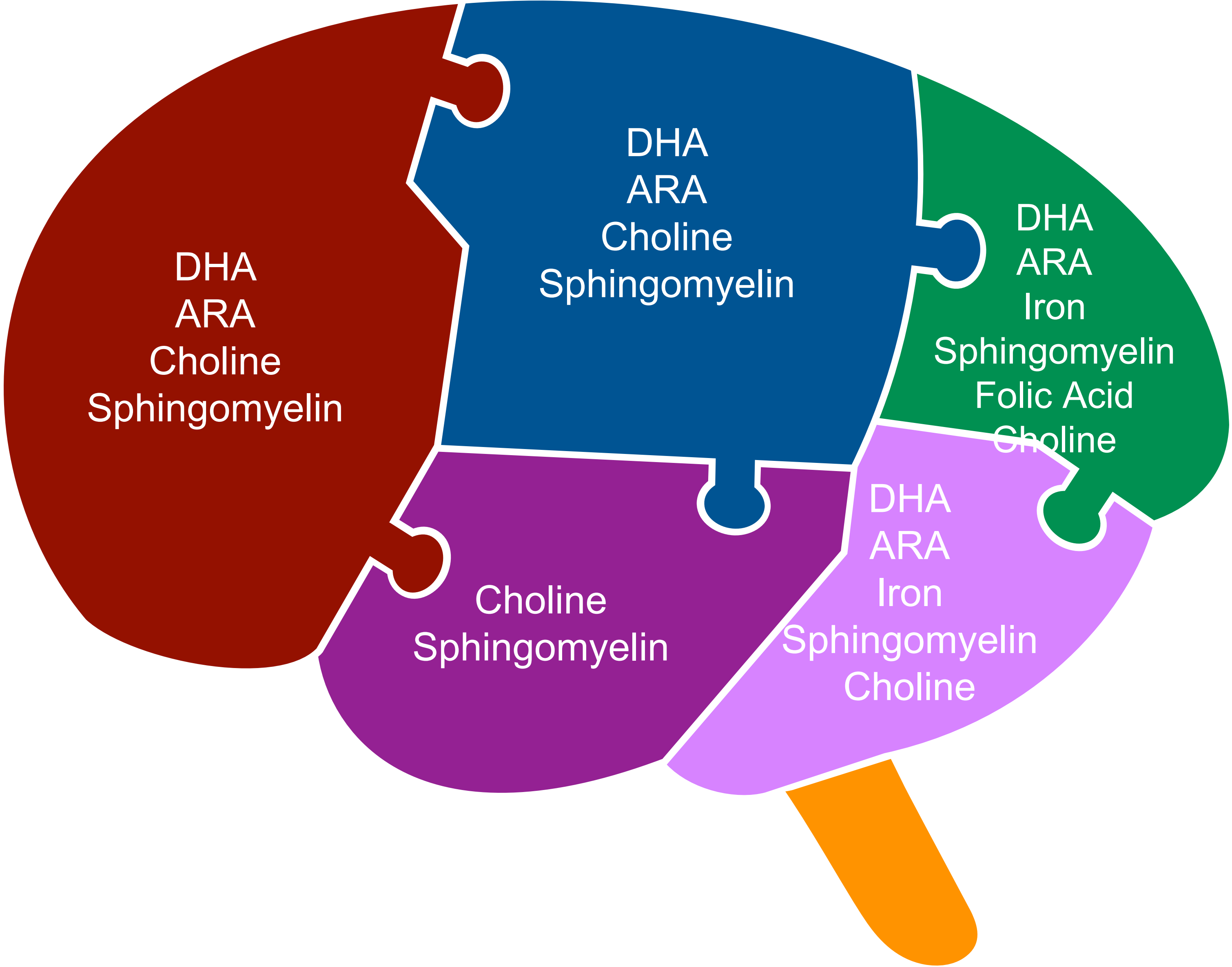
# Does Nutrition Shape Neurodevelopment?



\*Significant differences in intercept and slope between formula #1 and breastfeeding and other formulas;

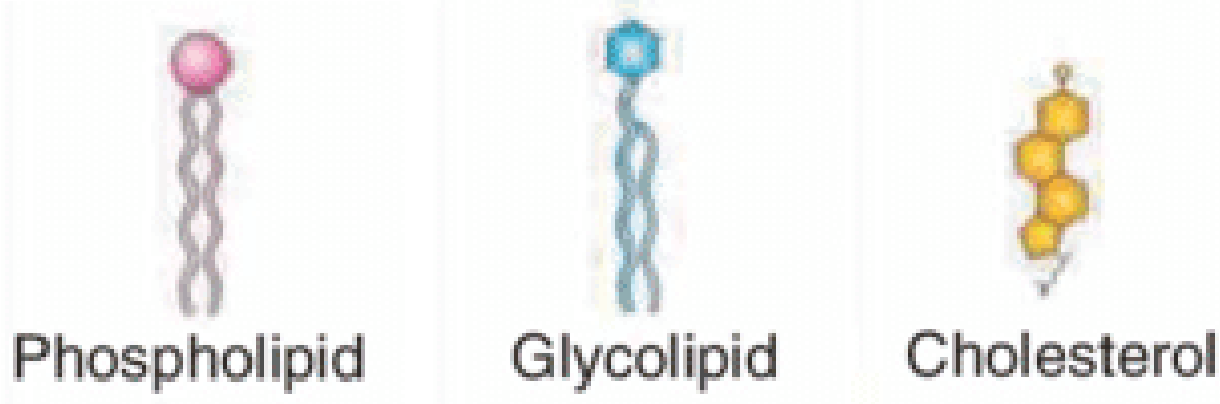
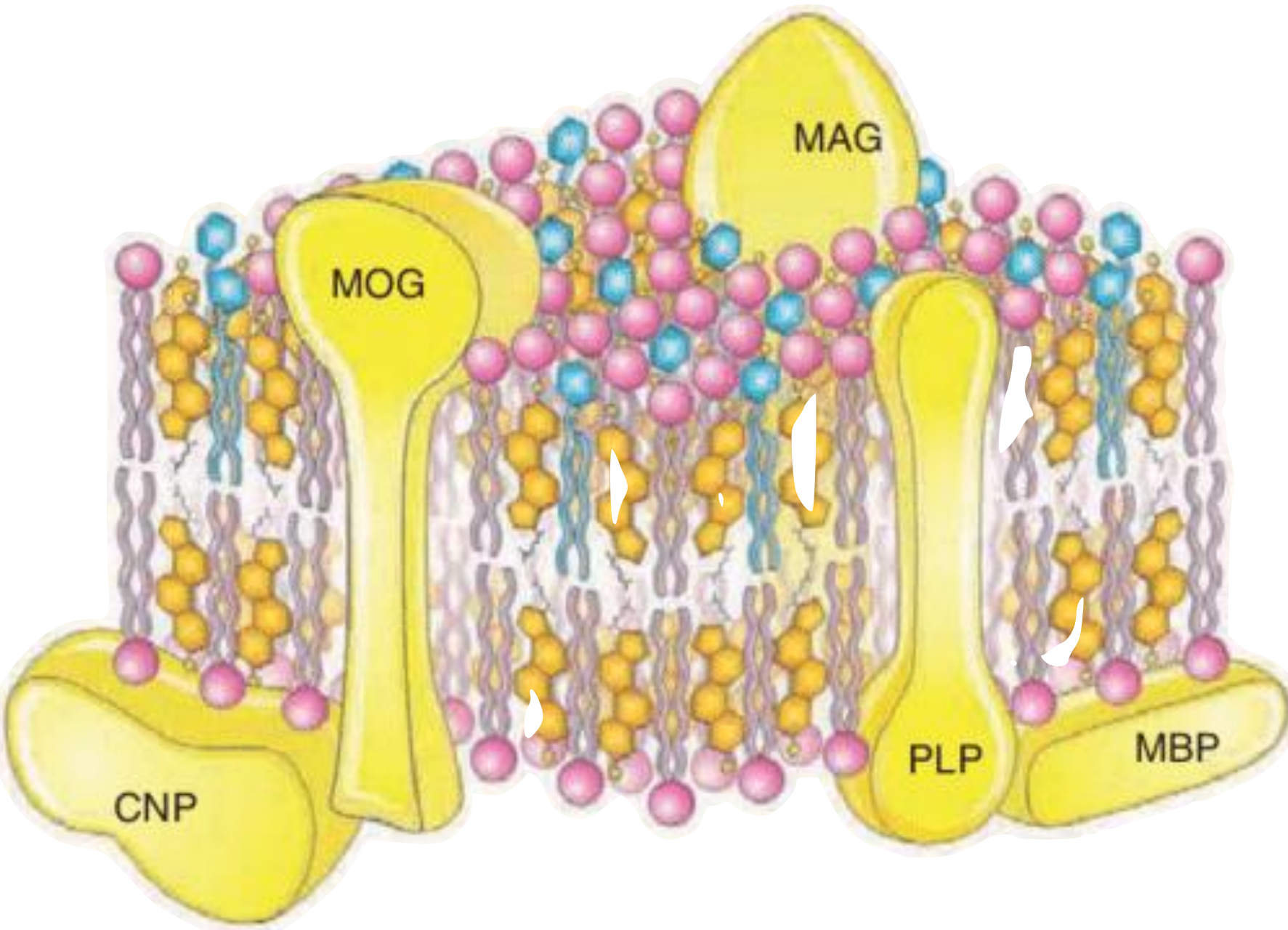
\*General difference in intercept of each formula and breastfeeding in ELC scores.

# Nutrients for Neurodevelopment

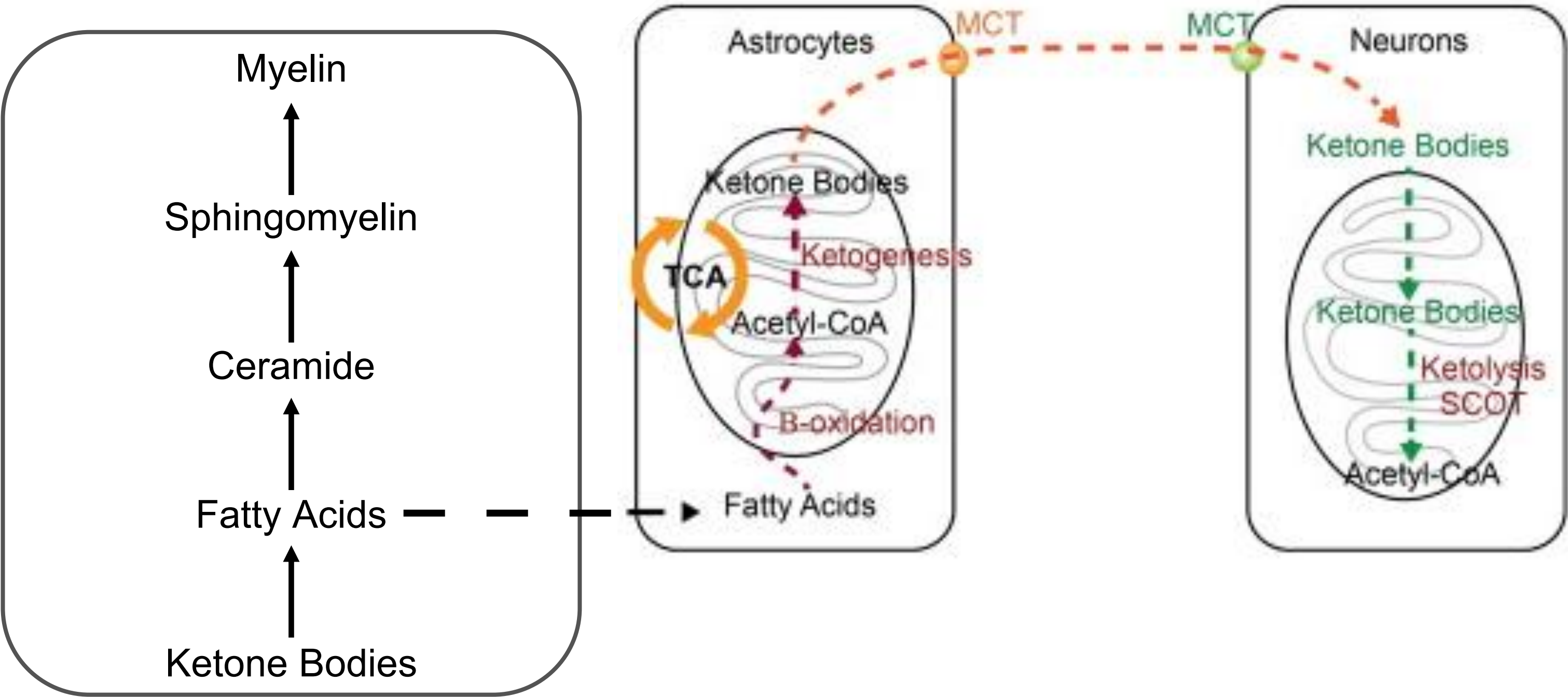


# Nutrients for Neurodevelopment

## The Myelin Sheath

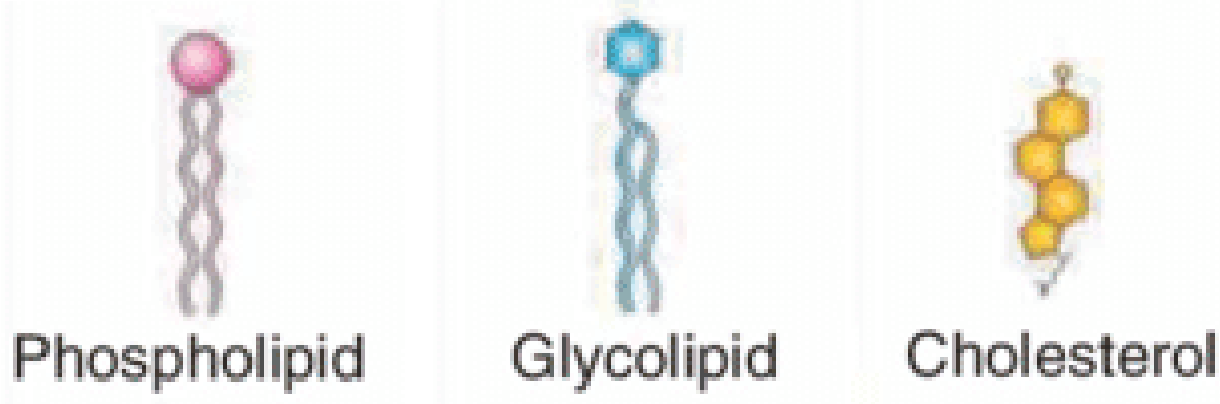
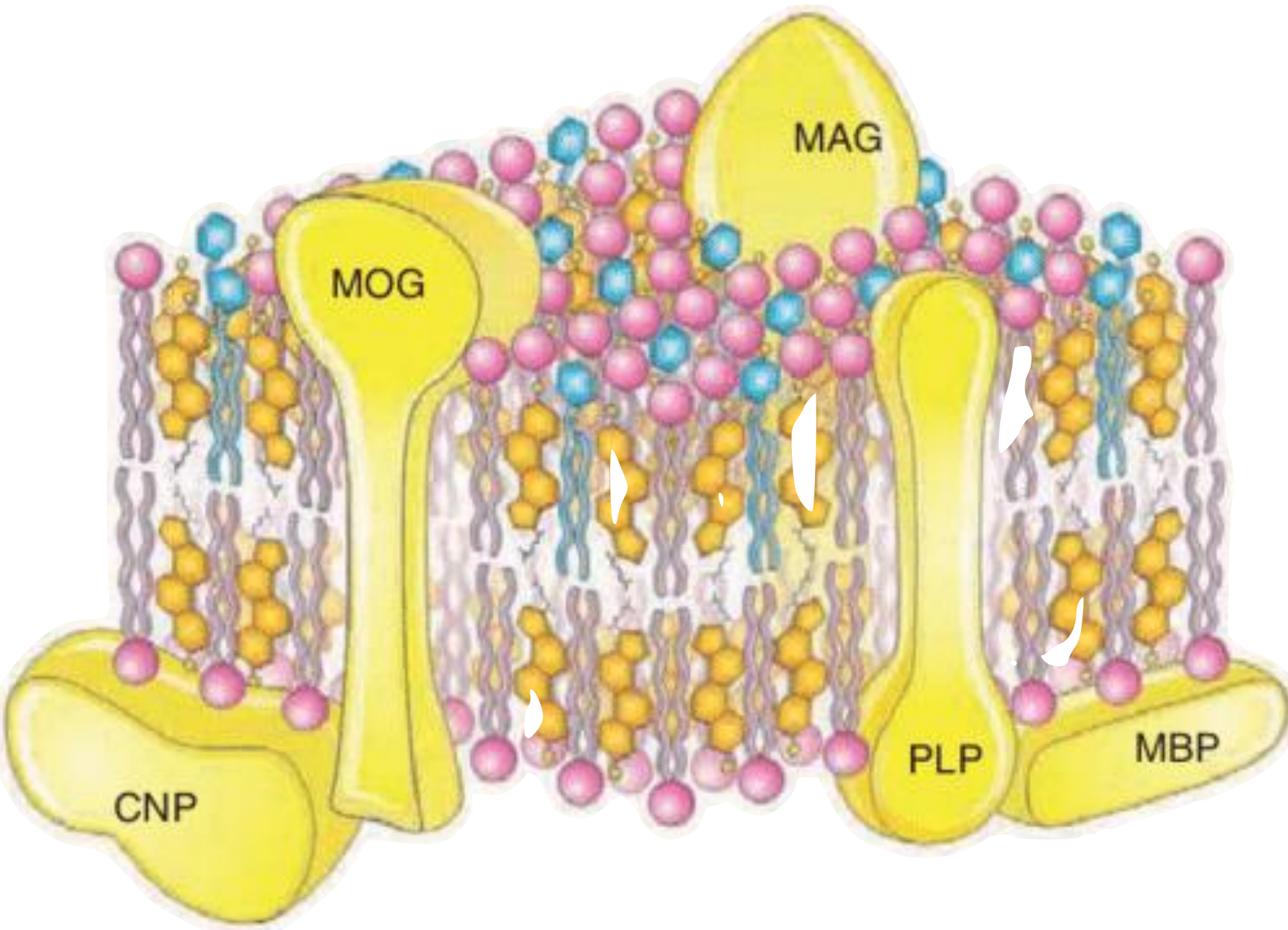


## Building the Myelin Sheath

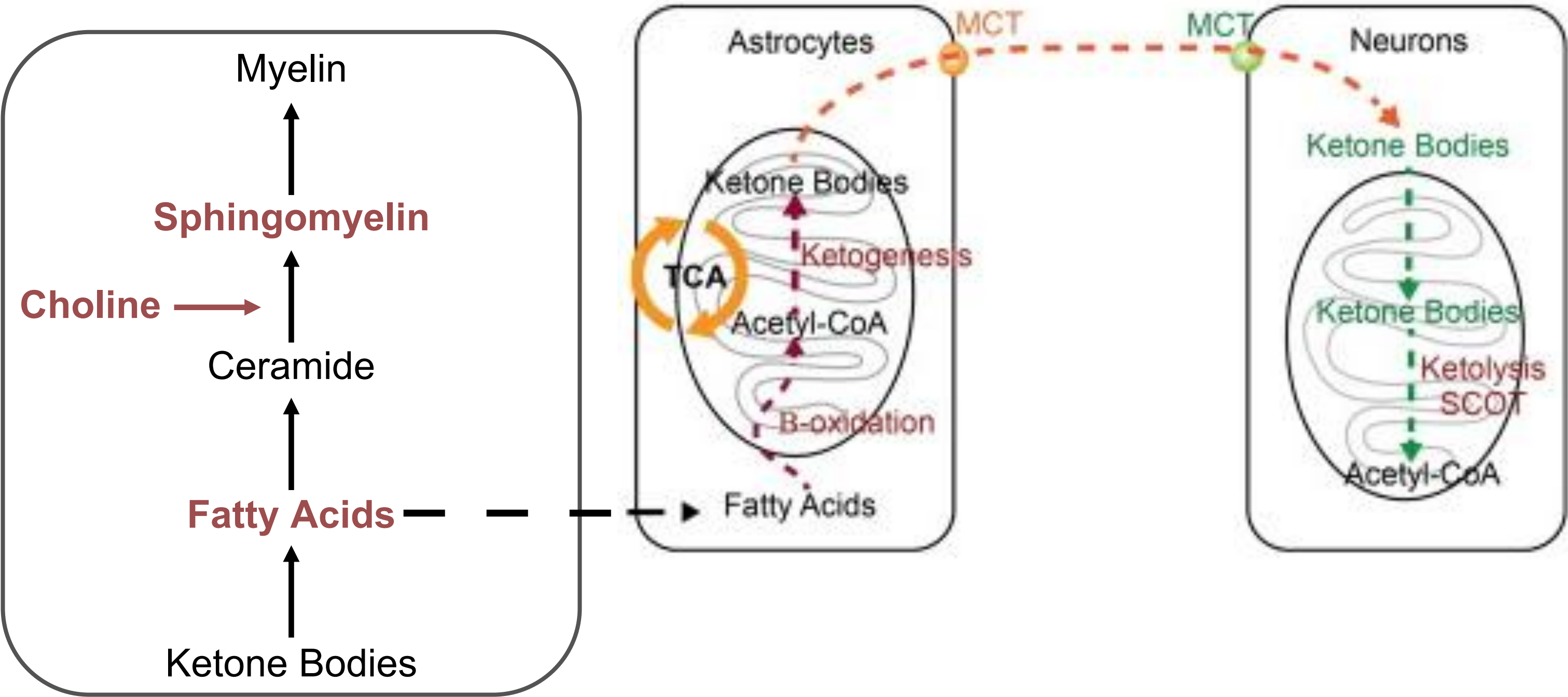


# Nutrients for Neurodevelopment

## The Myelin Sheath



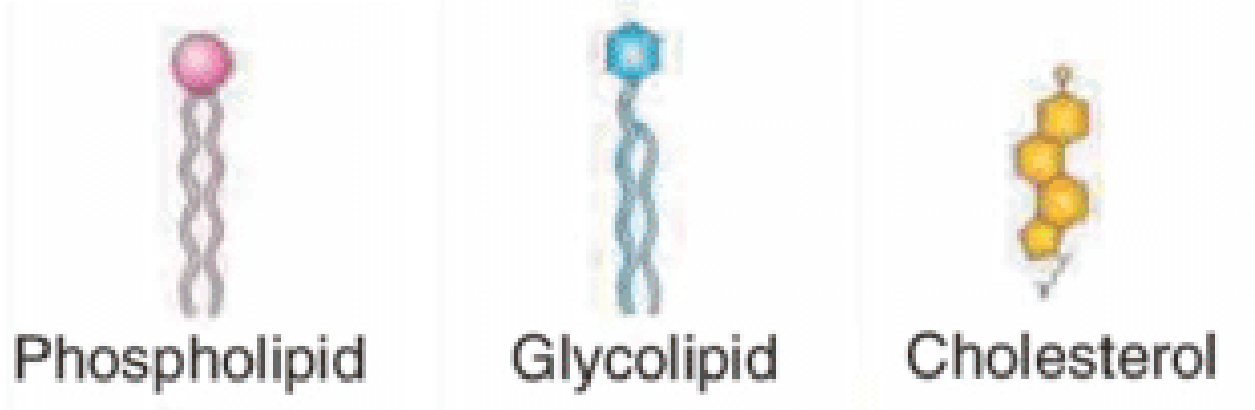
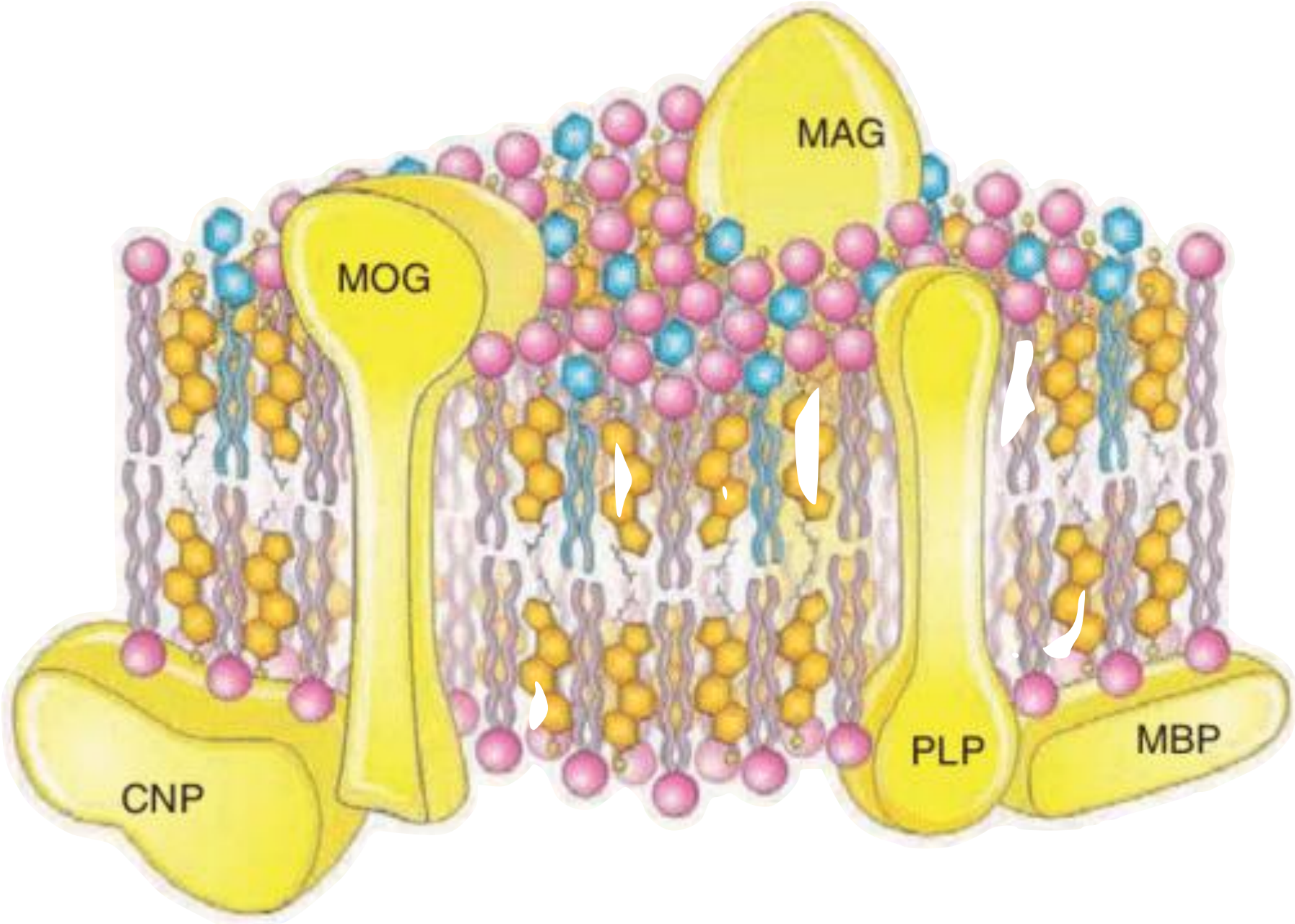
## Building the Myelin Sheath



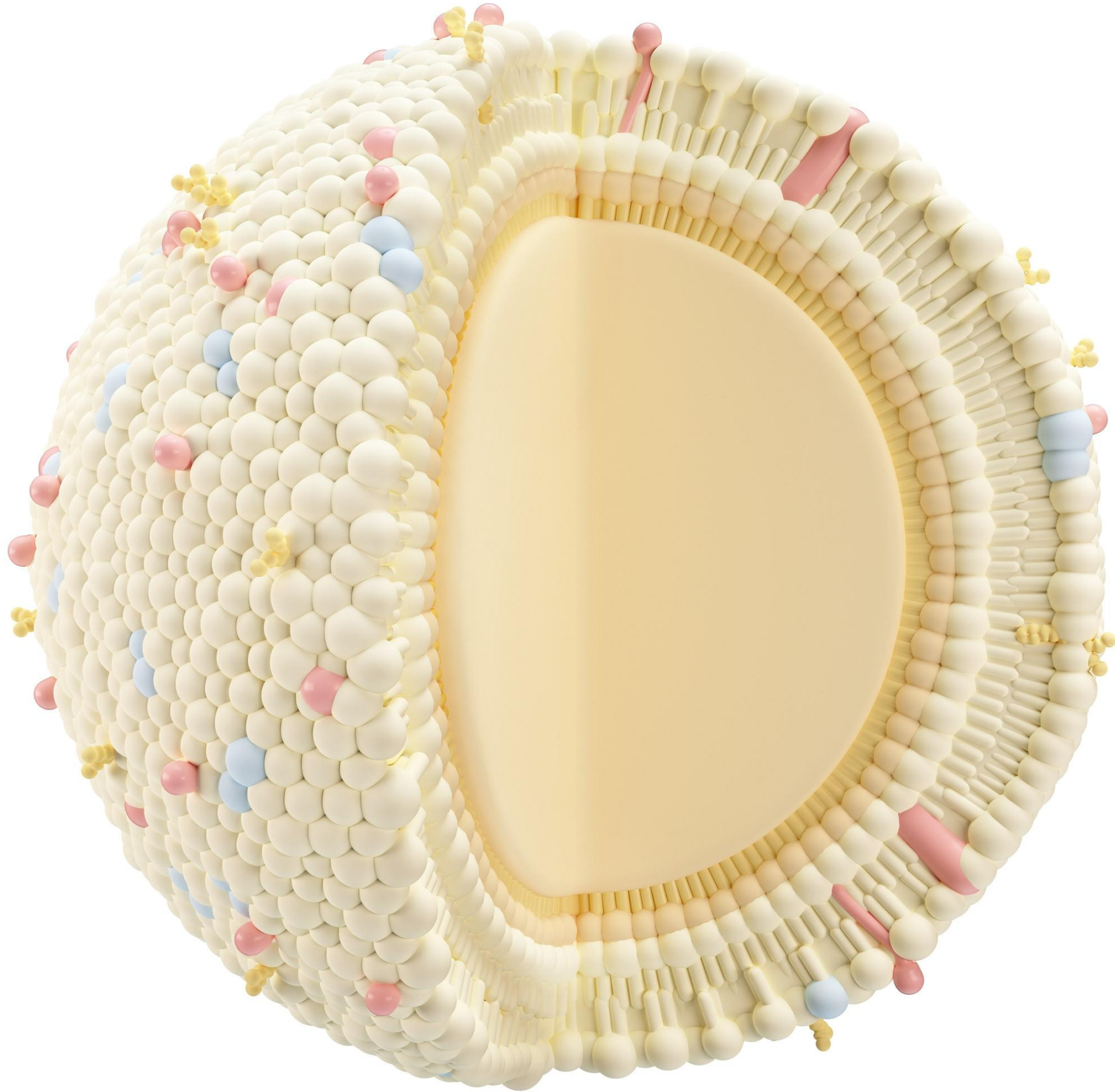


# MFGM as a Source of Neurodevelopment Nutrients

Myelin Sheath

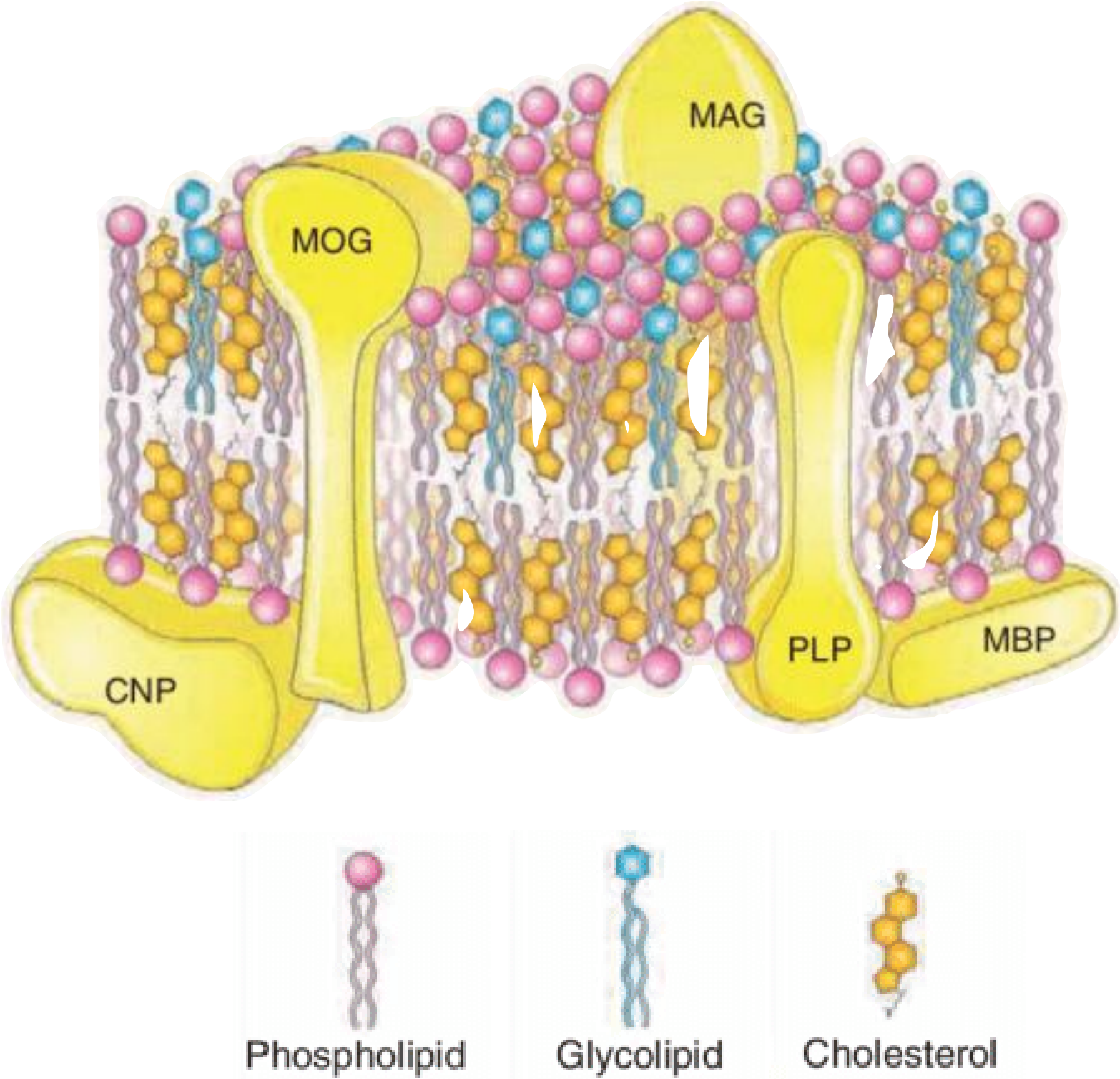


Milk Fat Globule

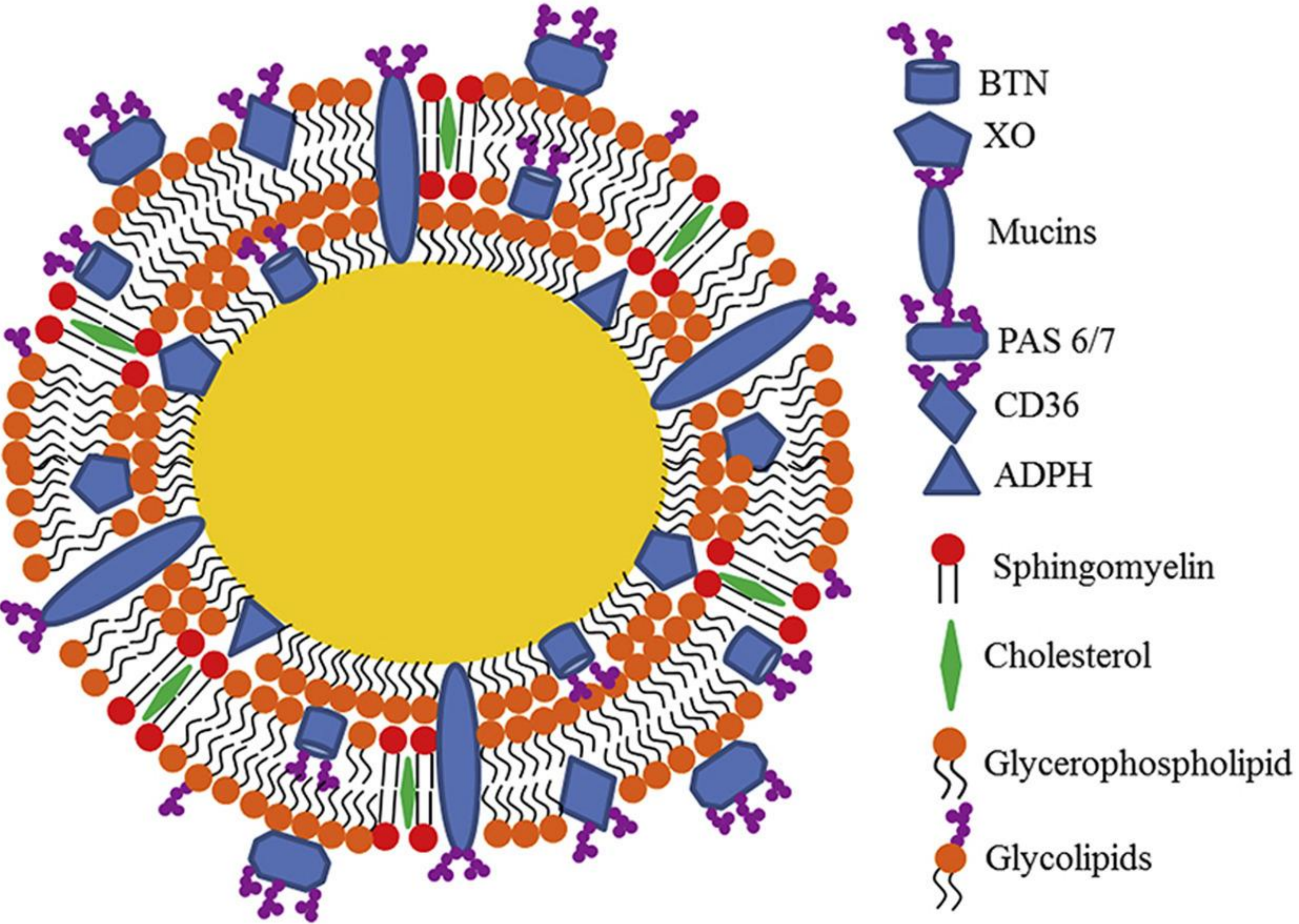


# MFGM as a Source of Neurodevelopment Nutrients

## Myelin Sheath

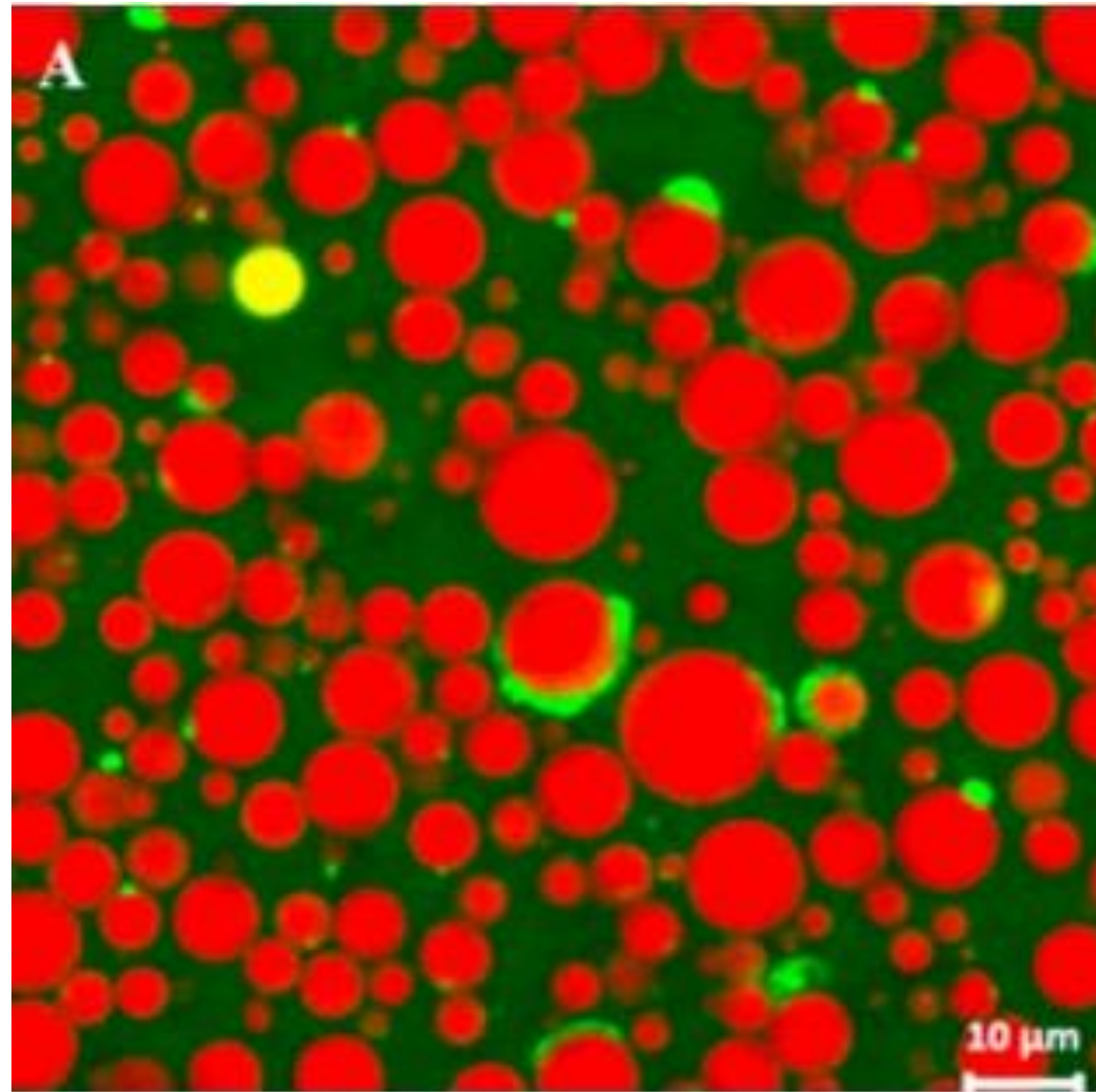


## Milk Fat Globule Membrane



# Lipid Differences in Human Milk and Infant Formula

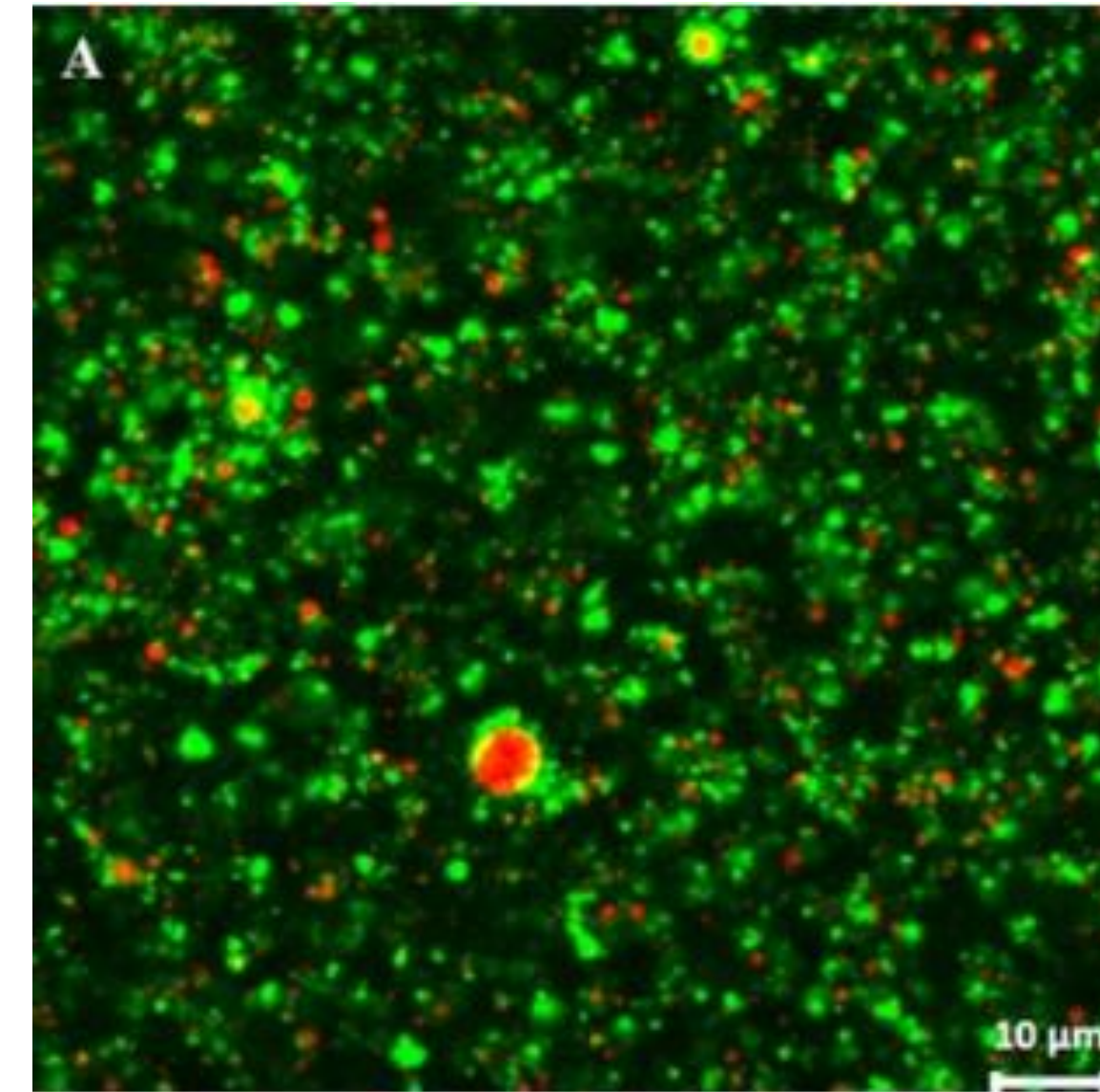
## Human Milk



### Characteristics of Human Milk Fat Droplets<sup>2</sup>

- High sphingomyelin content
- Dynamic across lactation stages
- Large fat globules (~5 μm)
- Phospholipid bilayer membrane

## Infant Formula



### Characteristics of Standard Infant Formula Fat Droplets<sup>2</sup>

- High phospholipid content
- High phosphatidylcholine content
- Small fat globules (~0.2 μm)
- No phospholipid bilayer membrane

# Improving Brain Development Through Nutrition?



# Importance of Sphingomyelin for Neurodevelopment

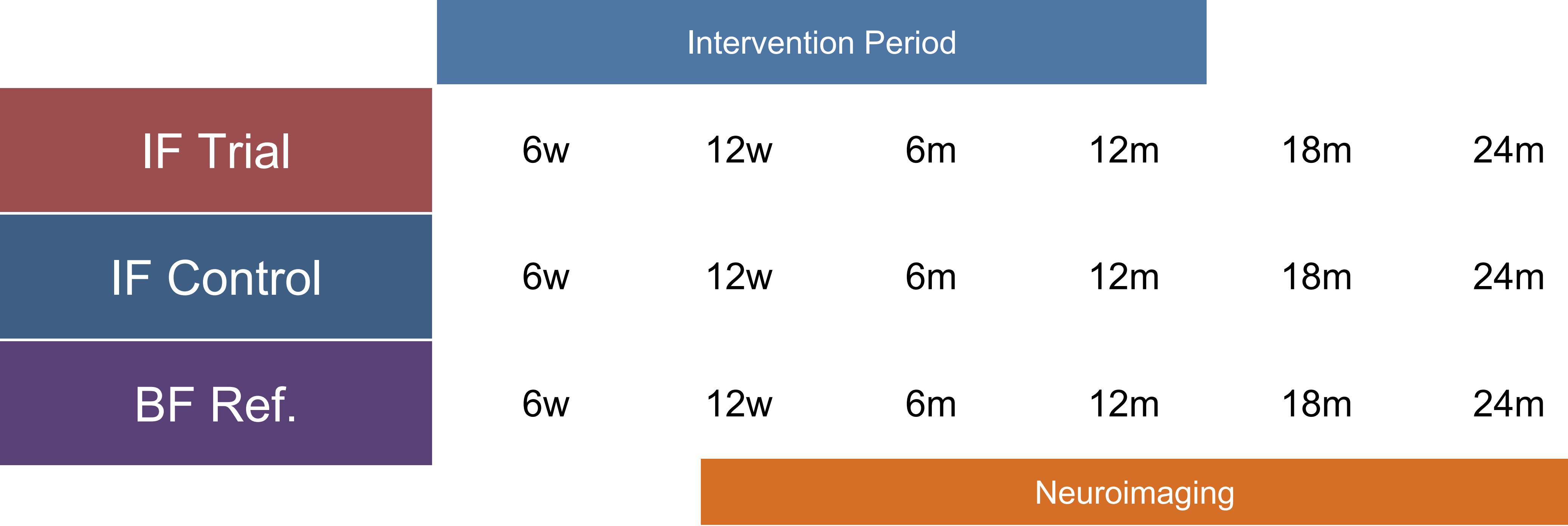
A Nutritional RCT Investigating Sphingomyelin Intake and Myelination

	<b>Trial Formula</b>	<b>Control Formula</b>	<b>Breast Milk Levels (3 &amp; 6m Average))</b>
Energy (kcal per 200 ml serving)	132	132	
<b>Myelin Blend</b>			
Sphingomyelin (mg/L)	105	22	86.7
DHA (mg/L)	132	71	89.8
ARA (mg/L)	132	71	172.0
Iron (mg/L)	8.6	4.0	0.3
Folate (mcg/L)	219	85	24.5



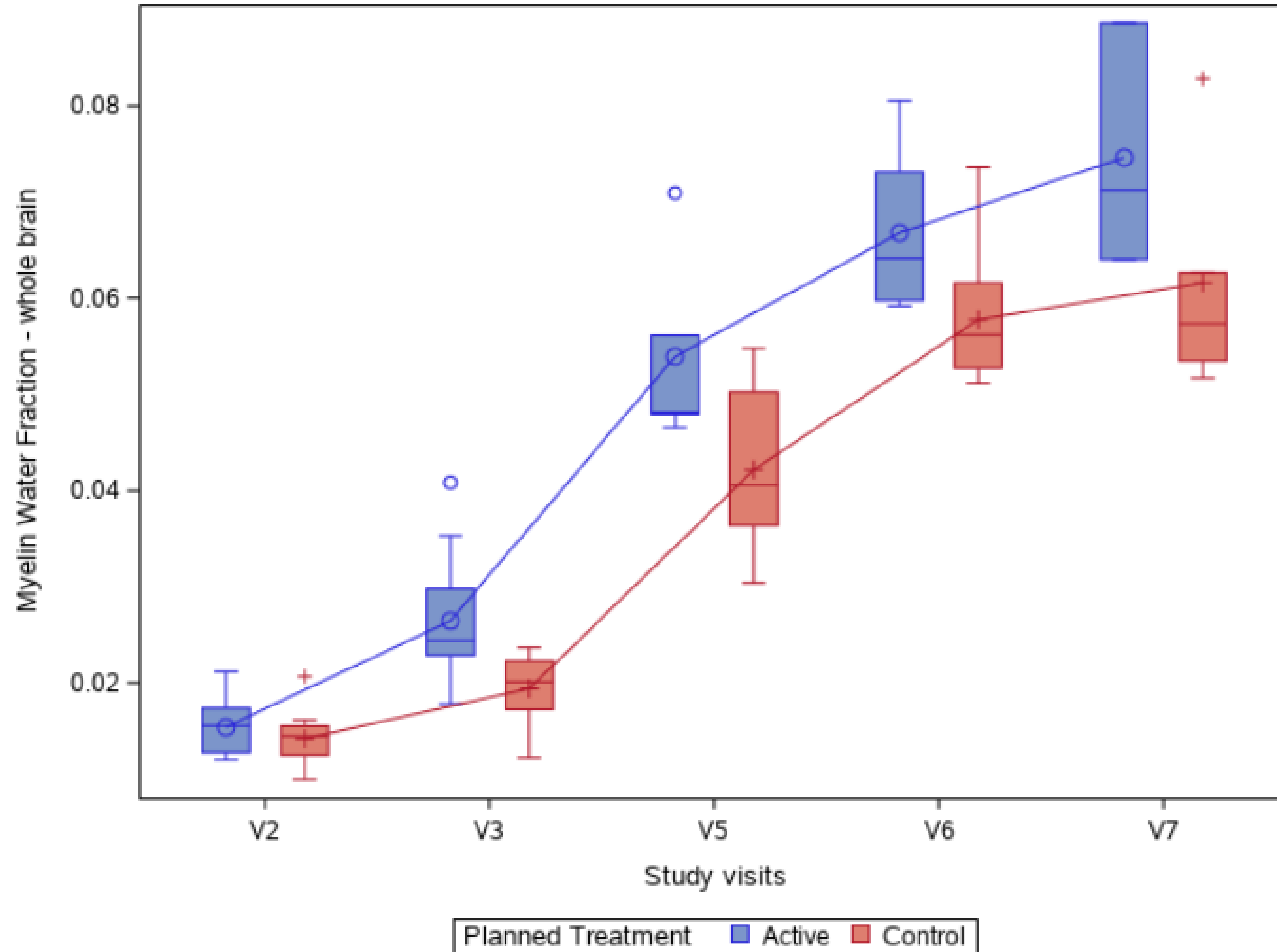
# Importance of Sphingomyelin for Neurodevelopment

A Nutritional RCT Investigating Sphingomyelin Intake and Myelination



# Importance of Sphingomyelin for Neurodevelopment

Longitudinal trends from 3 Months through to 2 Years



- Significantly increased brain myelin content at 3, 6, 12, and 24 months of age.
- Significantly increased rate of myelination throughout the first year of life.



# Impact of Added MFGM to Infant Formula

Continuous enrollment of 150-200 families per year

2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021 2022 2023

Study Launch

COVID-19 Pandemic

Introduction of  
MFGM-Added  
Formula

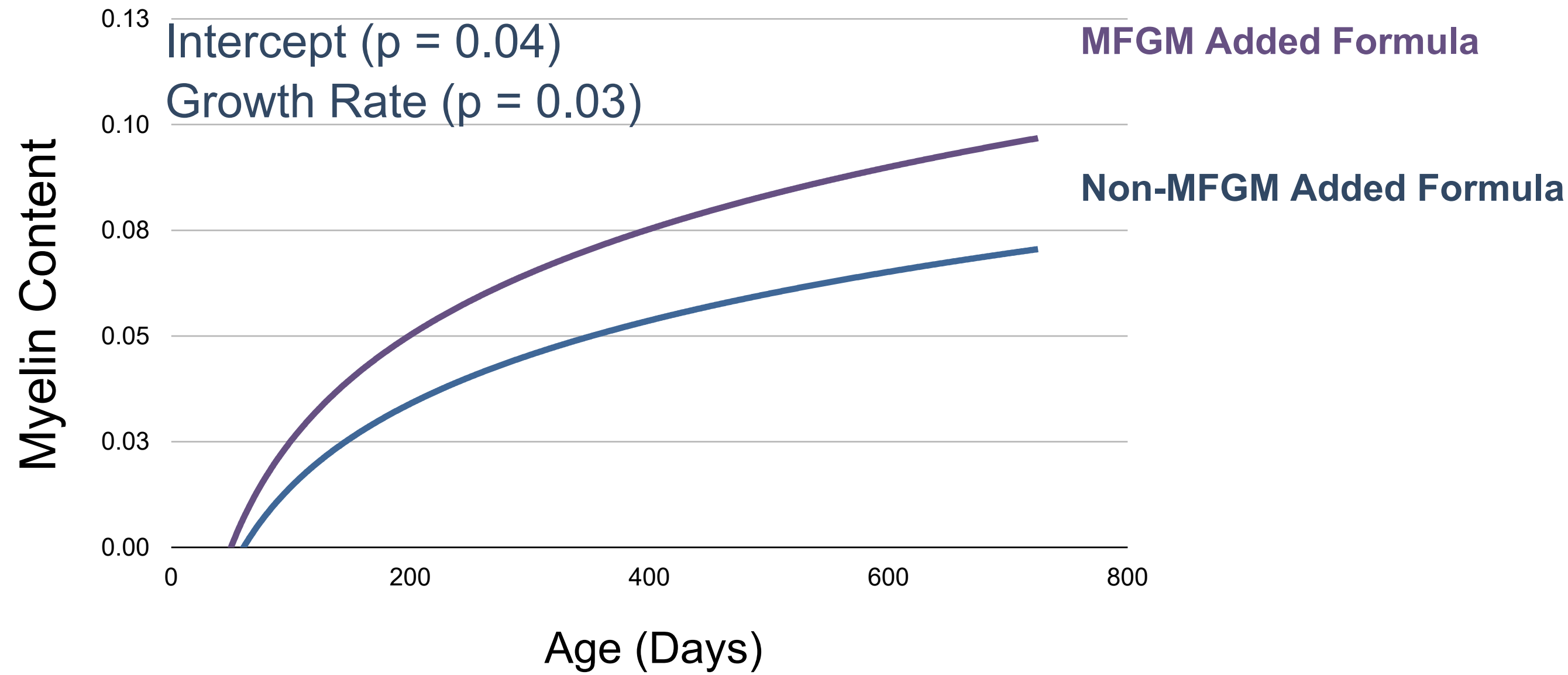
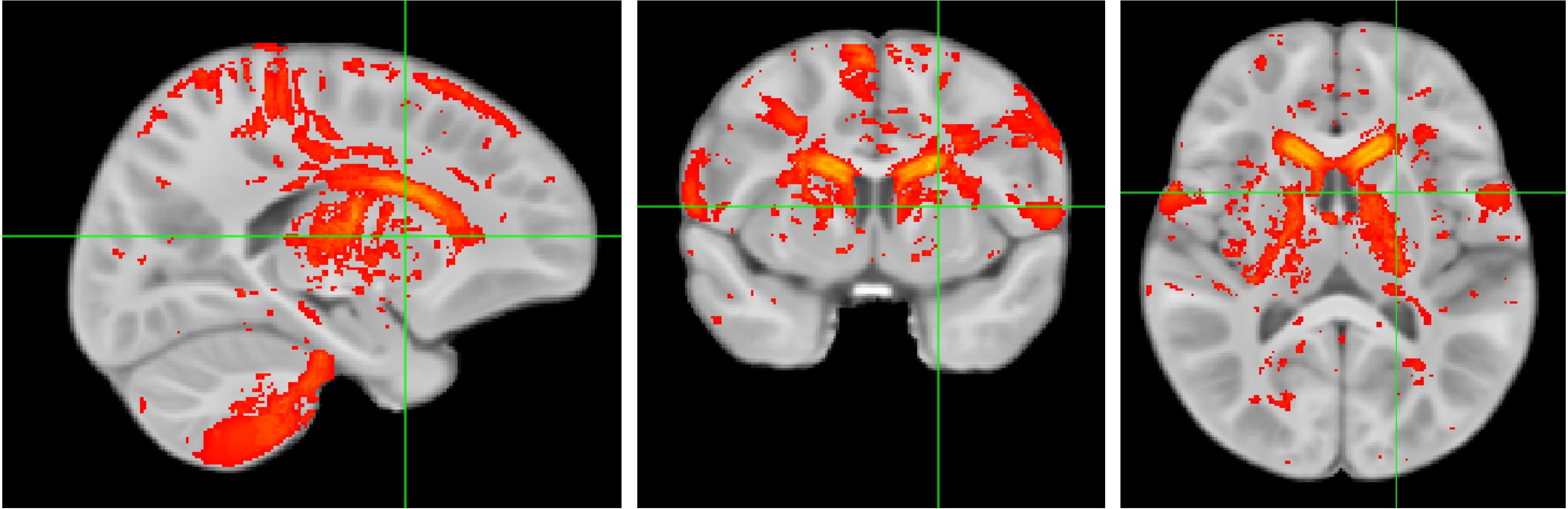
Formula-fed children receiving the same formula brand without Added MFGM

Formula-fed children receiving the same formula brand with Added MFGM

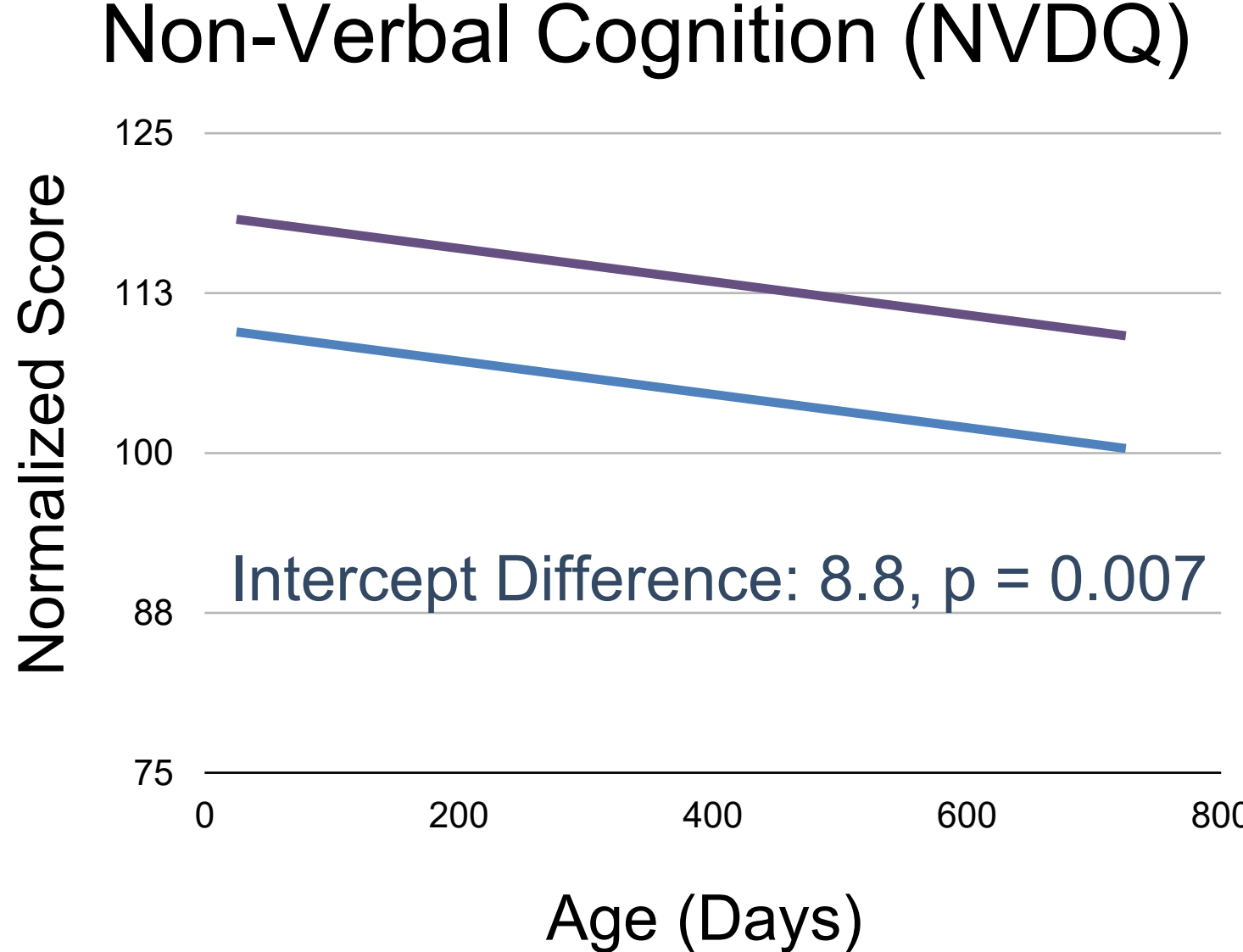
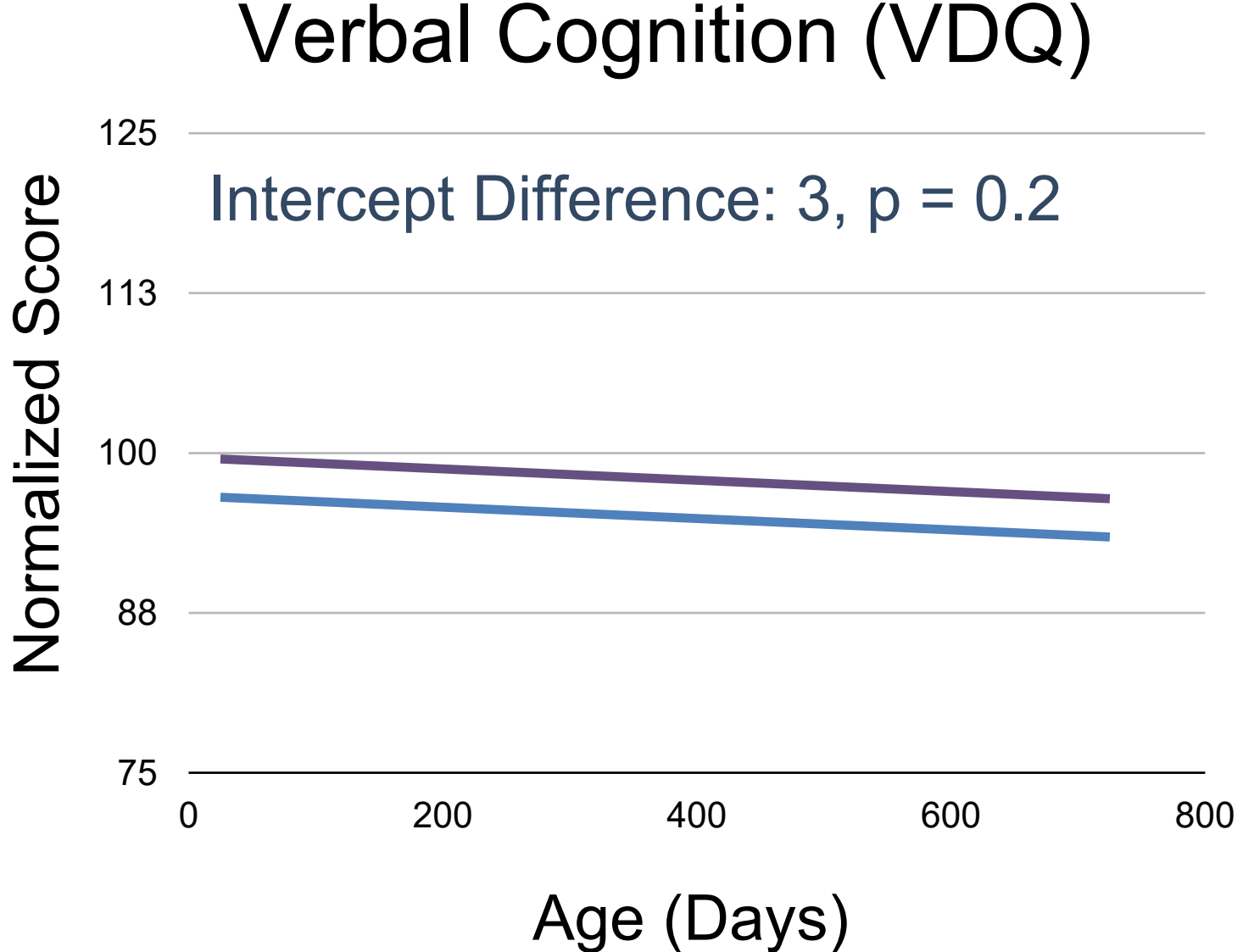
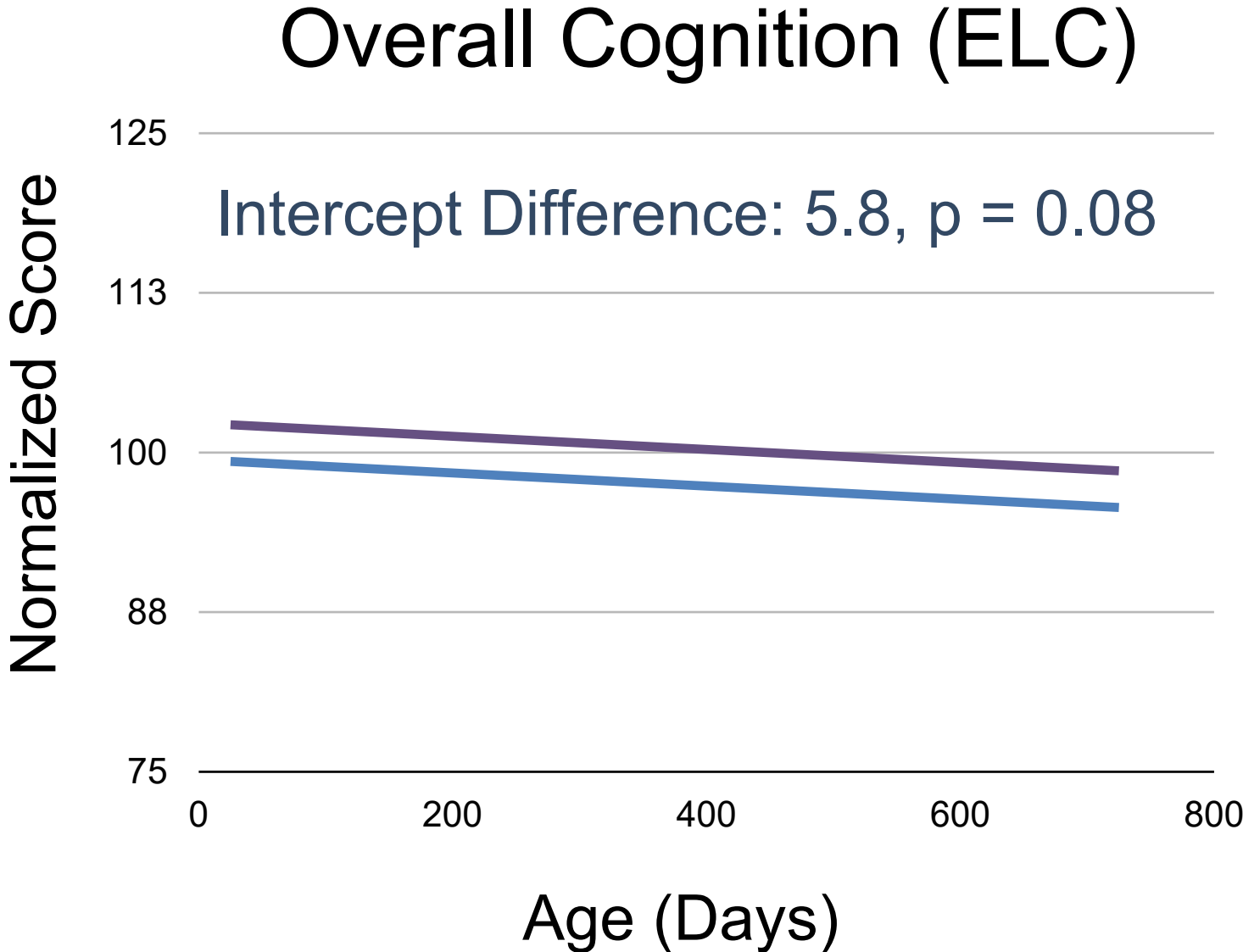
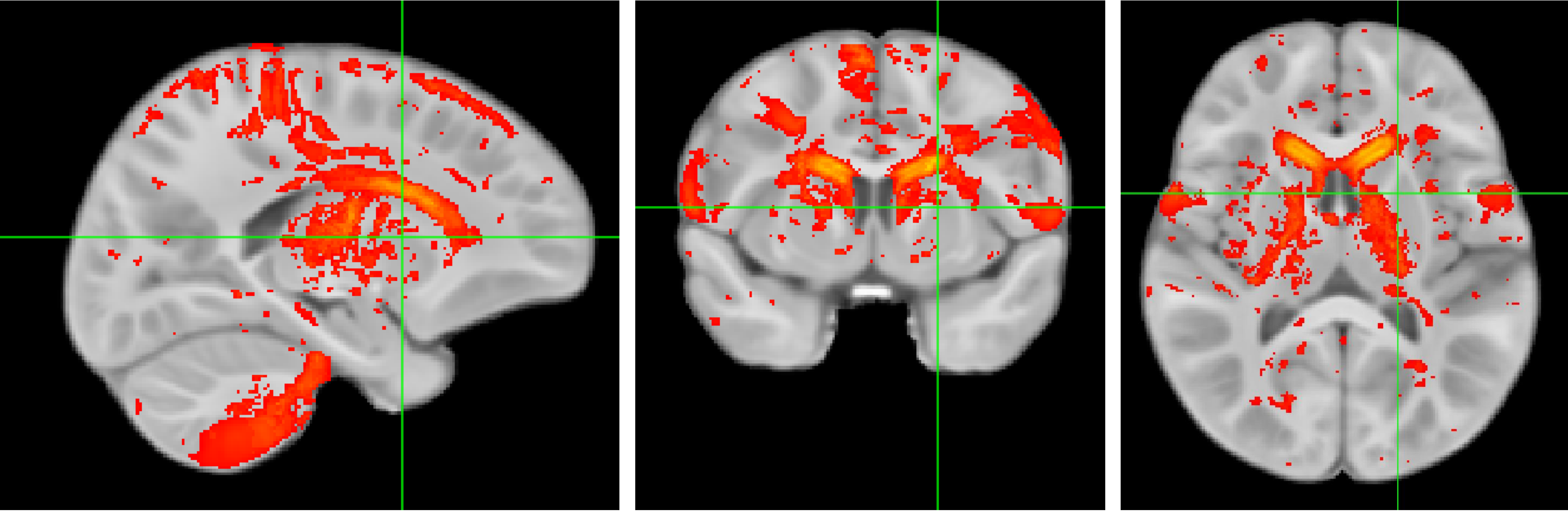
Children growing up in a pandemic environment

Temporally Controlled Trial of Convenience (TcToC) examining the impact of Added MFGM on infant brain development and myelination

# Impact of Added MFGM to Infant Formula



# Impact of Added MFGM to Infant Formula



# Alignment with other MFGM Outcomes

Improved longterm neurodevelopment outcomes in children who received MFGM-supplemented formula at >5 years of age.

**Table III.** Wechsler Preschool & Primary Scale of Intelligence 4<sup>th</sup> Edition composite scores (mean  $\pm$  standard error) at 5.5 years of age

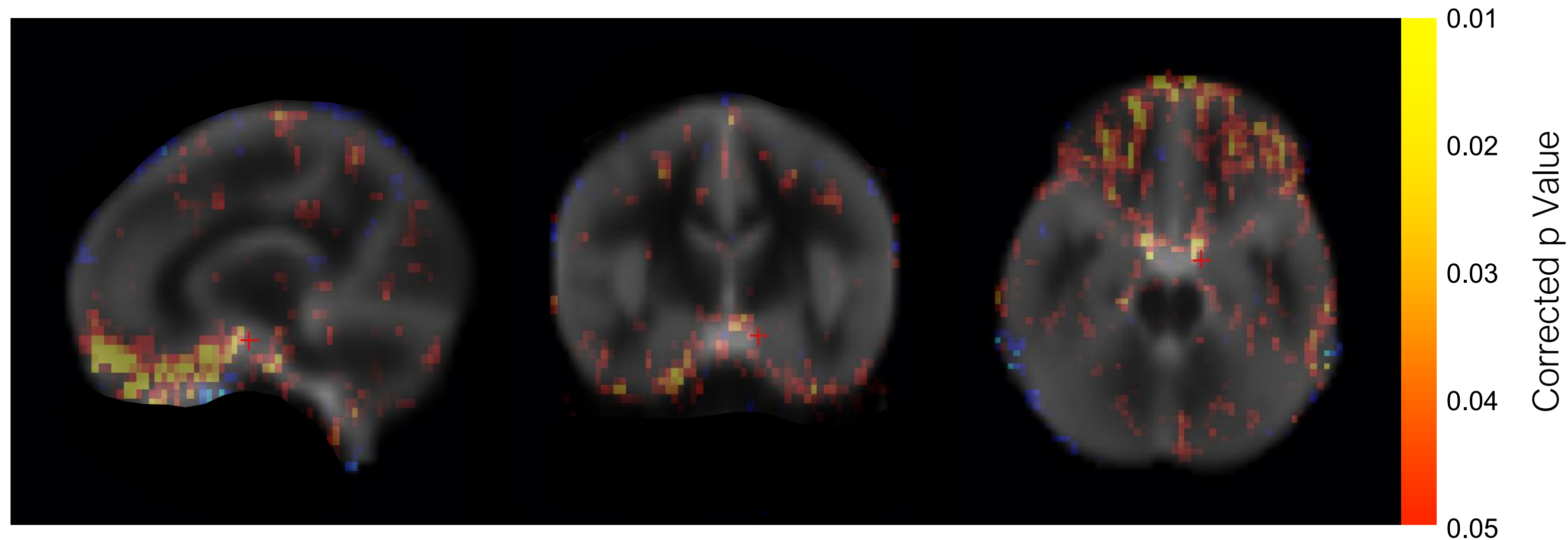
WPPSI-IV composite scores*	ANOVA			ANCOVA <sup>†</sup>		
	Control	MFGM + LF	<i>P</i>	Control	MFGM + LF	<i>P</i>
Verbal Comprehension Index	93.5 $\pm$ 1.4	96.4 $\pm$ 1.4	.139	92.3 $\pm$ 2.7	94.3 $\pm$ 2.9	.287
Visual Spatial Index	95.3 $\pm$ 1.7	100.6 $\pm$ 1.7	.027	92.3 $\pm$ 3.4	98.2 $\pm$ 3.6	.014
Fluid Reasoning Index	97.5 $\pm$ 1.4	101.1 $\pm$ 1.4	.067	94.0 $\pm$ 2.8	97.3 $\pm$ 3.0	.094
Working Memory Index	101.4 $\pm$ 1.7	102.0 $\pm$ 1.7	.820	102.6 $\pm$ 3.5	103.2 $\pm$ 3.8	.831
Processing Speed Index	100.0 $\pm$ 1.4	107.1 $\pm$ 1.4	<.001	98.6 $\pm$ 2.8	105.4 $\pm$ 3.0	<.001
FSIQ	93.5 $\pm$ 1.5	98.7 $\pm$ 1.4	.012	90.9 $\pm$ 2.9	95.6 $\pm$ 3.0	.020

# Long-Term Impact of MFGM Intake in Infancy

## Chilean infant Nutrition Trial (ChiNuT)

- Based in Institute of Nutrition and Food Technology (INTA), University of Chile, Santiago, Chile
- Original RCT 2016-2018** compared growth, nutritional status, and brain development in children fed an infant formula with added bovine MFGM (bMFGM) vs. a control formula or exclusively human breast milk.
- At age 9 years:** Low-Field MRI results suggest ongoing improvements in frontal white matter myelination (reduced  $qT_1$ ) and cortical development in infants who received formula with added bMFGM

## Reduced $qT_1$ in Children who Received Added Bovine MFGM Formula vs. Control



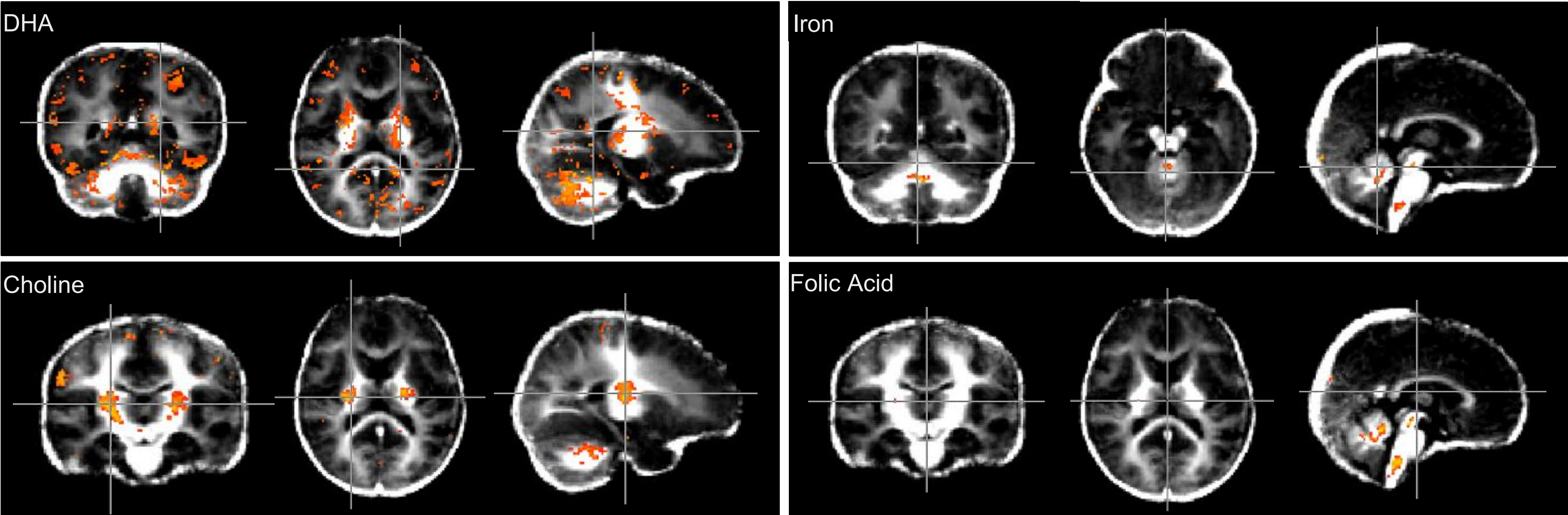
## Cortical Thickness

Cortical Region	Control	Added Bovine MFGM	p Value
Right Orbital Frontal	2.6 (0.35)	2.9 (0.43)	0.01
Right Anterior Occipital	2.6 (0.21)	2.8 (0.26)	0.02
Right Cingulum	2.65 (0.13)	2.76 (0.15)	0.02
Left Insula	2.66 (0.14)	2.8 (0.12)	0.001
Left Interior Frontal	2.89 (0.13)	2.98 (0.15)	0.04
Left Cingulum	3.16 (0.21)	3.3 (0.18)	0.02



# Importance of Supporting Maternal Nutrition

Linking maternal intake of key brain nutrients at 3 months with corresponding myelination values in their breastfeeding children



# Take Home Messages

- Infant Nutrition plays an important and *modifiable* role in early brain development.
- Nutrients, including Folic Acid, Iron, Choline, DHA, and Sphingomyelin are essential for white matter development and brain function.
- These nutrients are amply provided in breastmilk but are not present in high amounts in many infant formulas.
- Formulas with high DHA and Sphingomyelin content appear to promote improved myelination and brain maturation along with improved cognitive development.
- Observational and RCT findings suggest we can improve infant neurodevelopment through improved nutrition even in a generally healthy child population.
- Improvements in brain development are observed early in the first two years of life (5-8 point IQ increase) and extend into later childhood and early adolescence.
- **BUT!** Nutrition is only one factor that shapes a child's development. Love, read, and play with your child!

# Advanced Baby Imaging Lab



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## ECHO

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A program supported by the NIH

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