Cognition and mental wellbeing: From early life to adulthood

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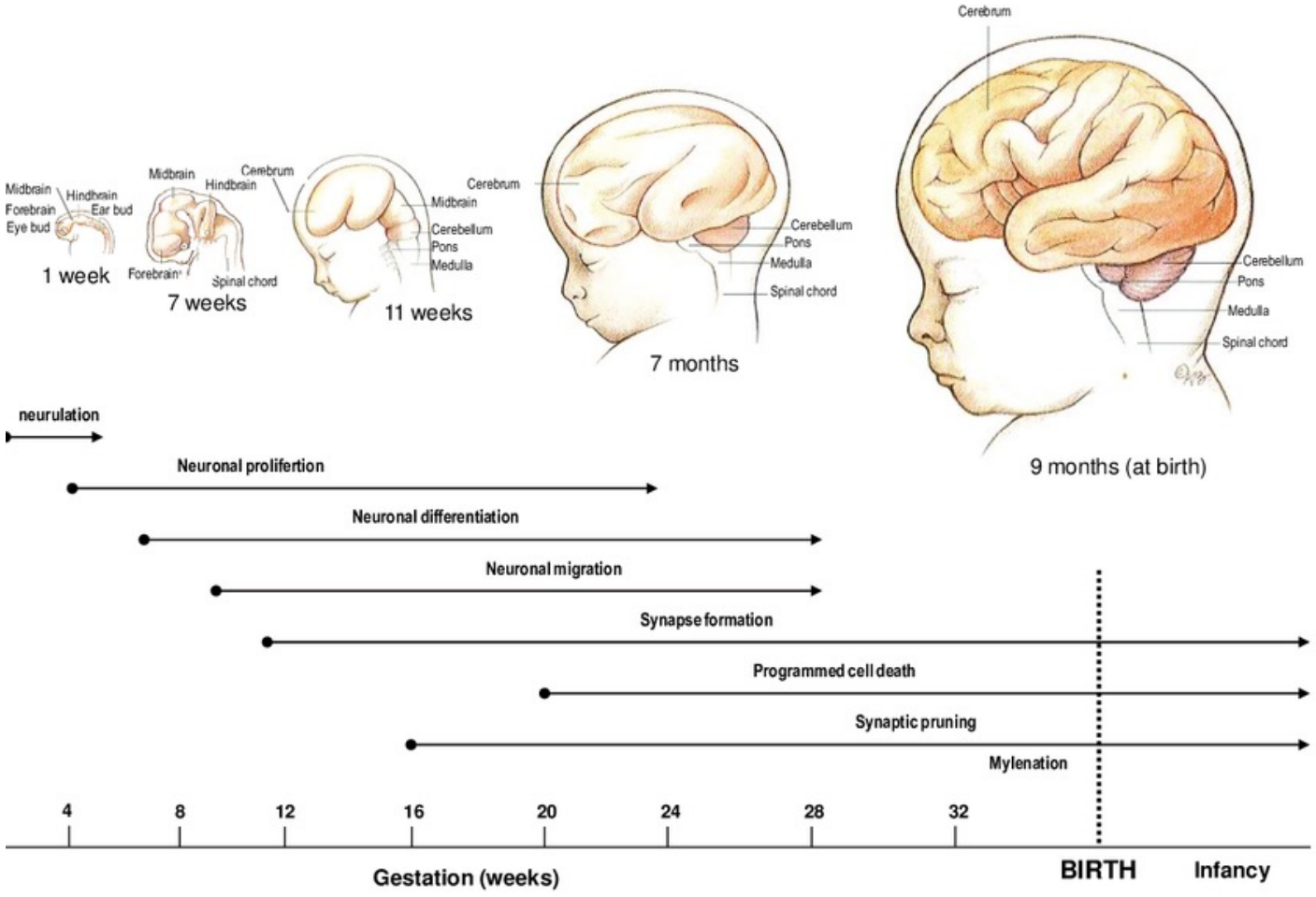
Disclosures

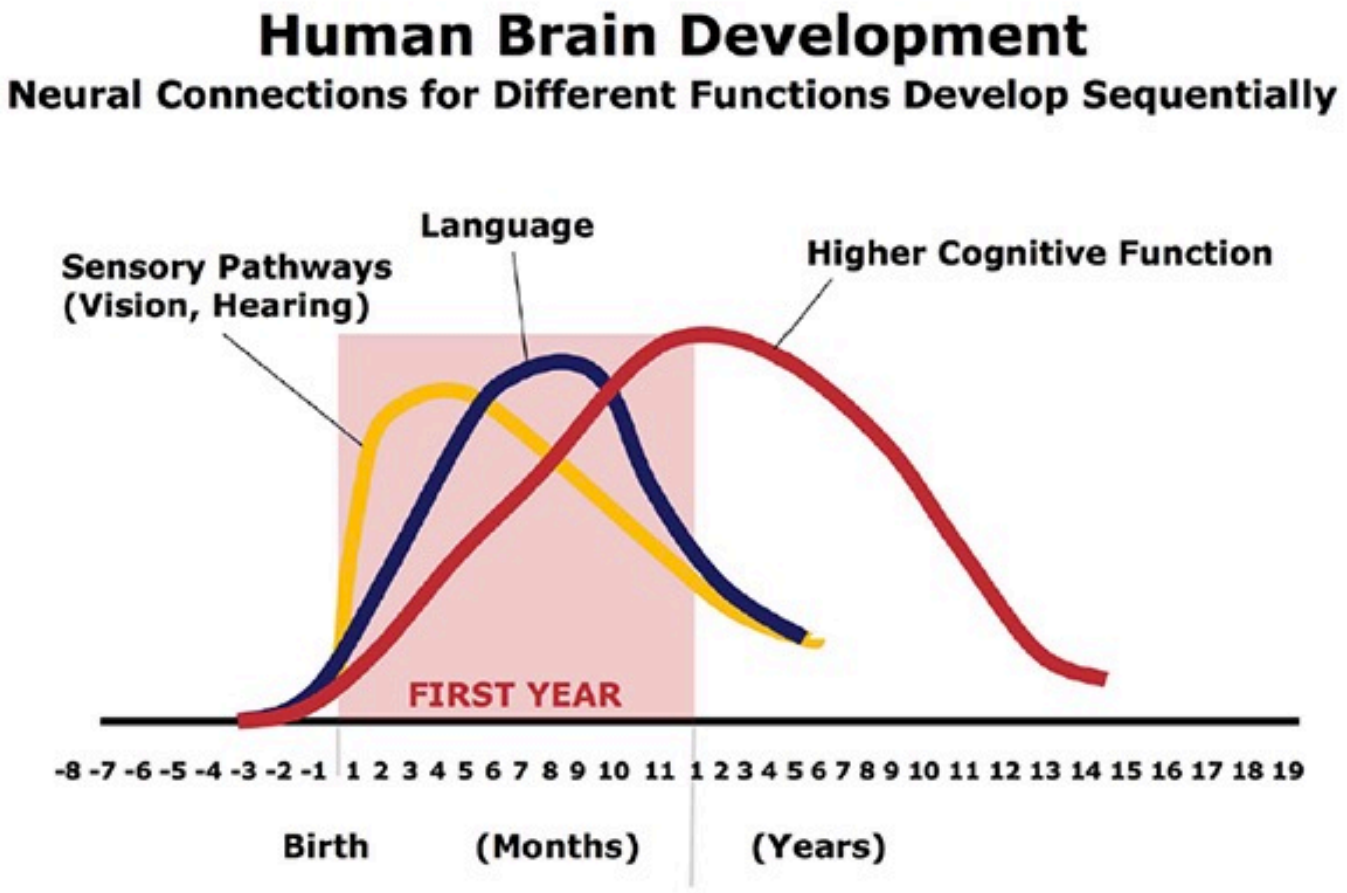
- The opinions shared and expressed in this presentation and webinar are my own and do not reflect the views and opinions of BASF.
- Within the last 12-months, in addition to federal, state and not-for profit foundation funding, I have received the following from commercial entities:
  - Research funding from Alcon Laboratories; Johnson and Johnson Vision Care, Inc.
  - Honoraria for research presentations from Abbott Laboratories and Kemin Health

We speak about the first year of life, but brain development begins earlier than birth



Silburn et al, 2011

Brain development is lifelong, but year 1 is particularly important



Nelson, 2000

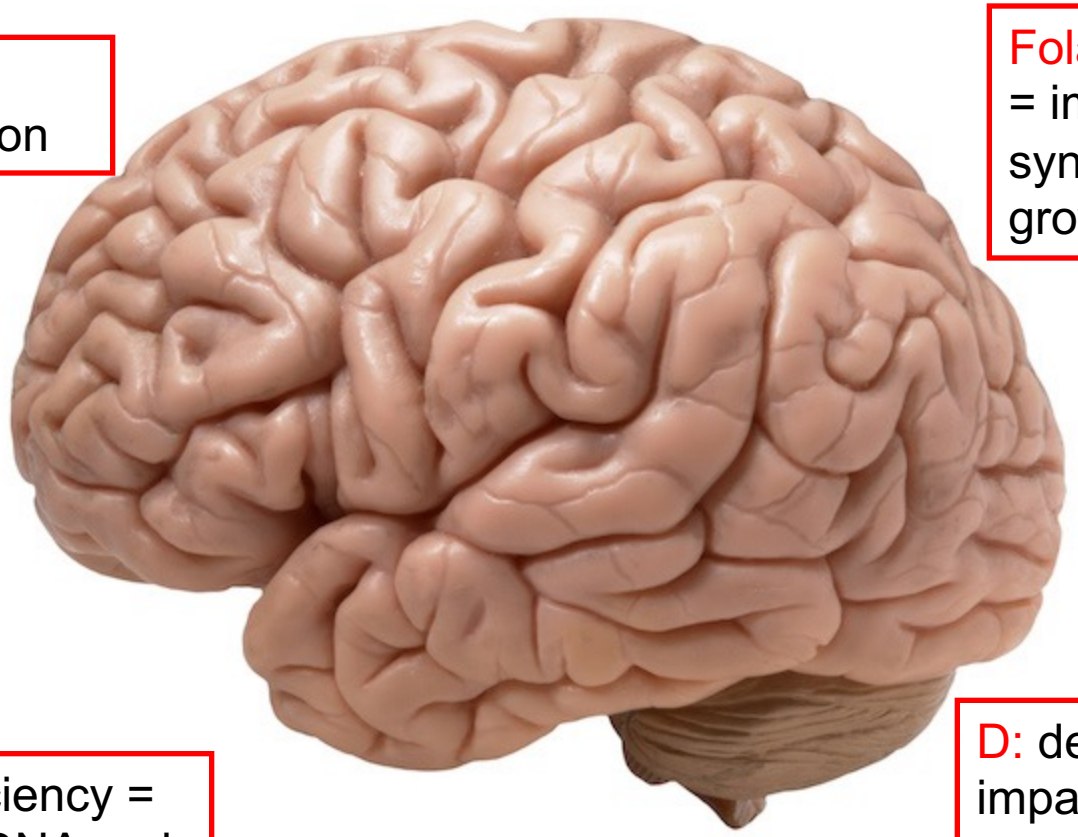
Iodine: deficiency = 13 IQ points lost

Iron: deficiency during first 6 months = irreversible consequences

B12: deficiency = reduced myelination

Folate: deficiency = impaired DNA synthesis, brain growth

Choline: deficiency = phospholipid formation, reductions in acetylcholine levels

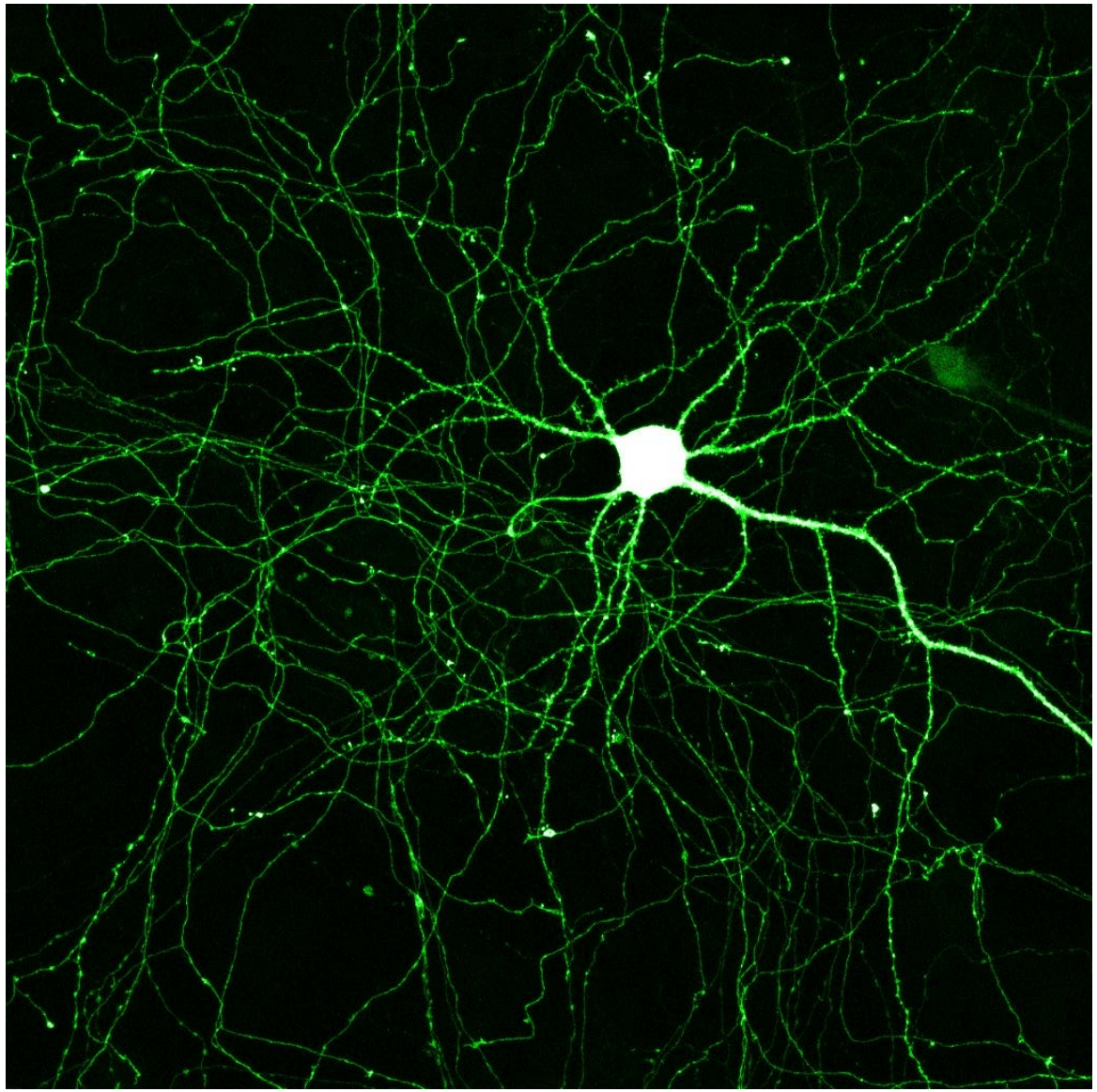


Zinc: deficiency = impaired DNA and RNA synthesis

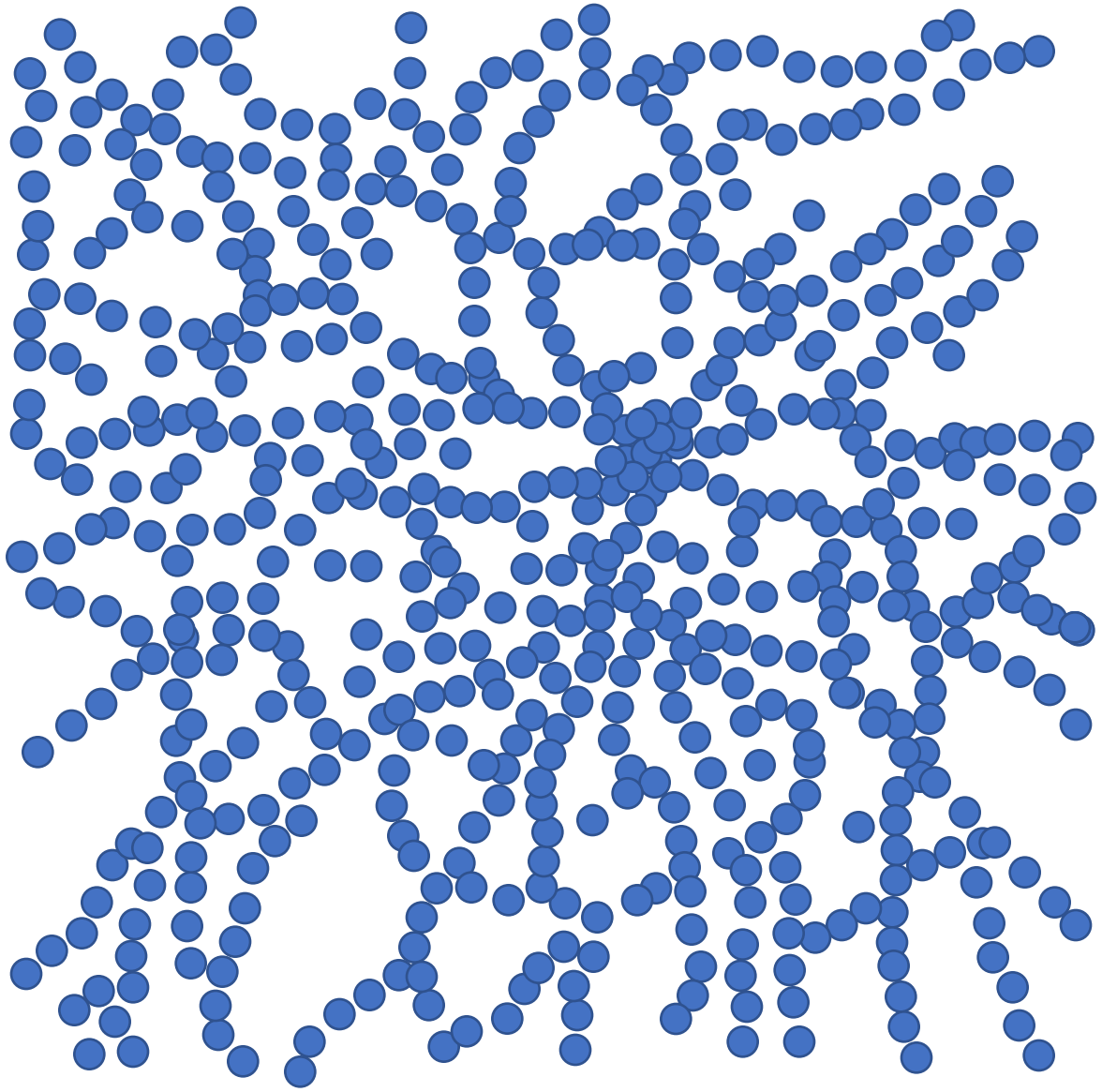
D: deficiency = impaired hippocampal and motor function

Brain-specific nutrients (1993)

What’s in a neuron?

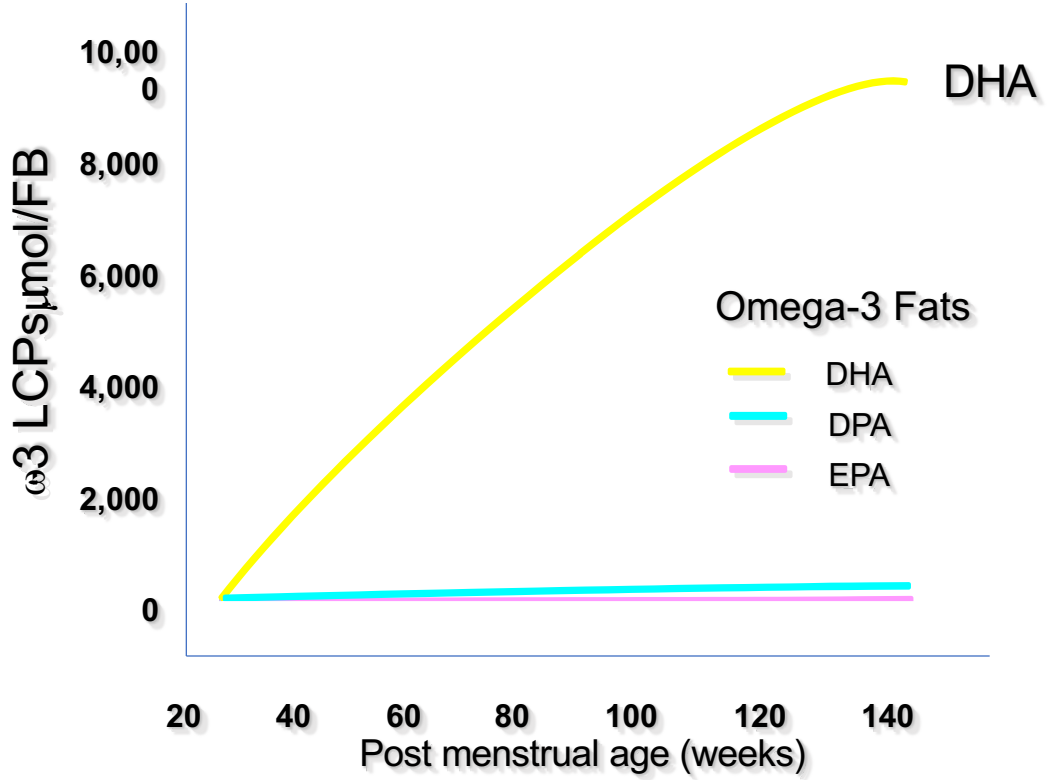


What's in a neuron?



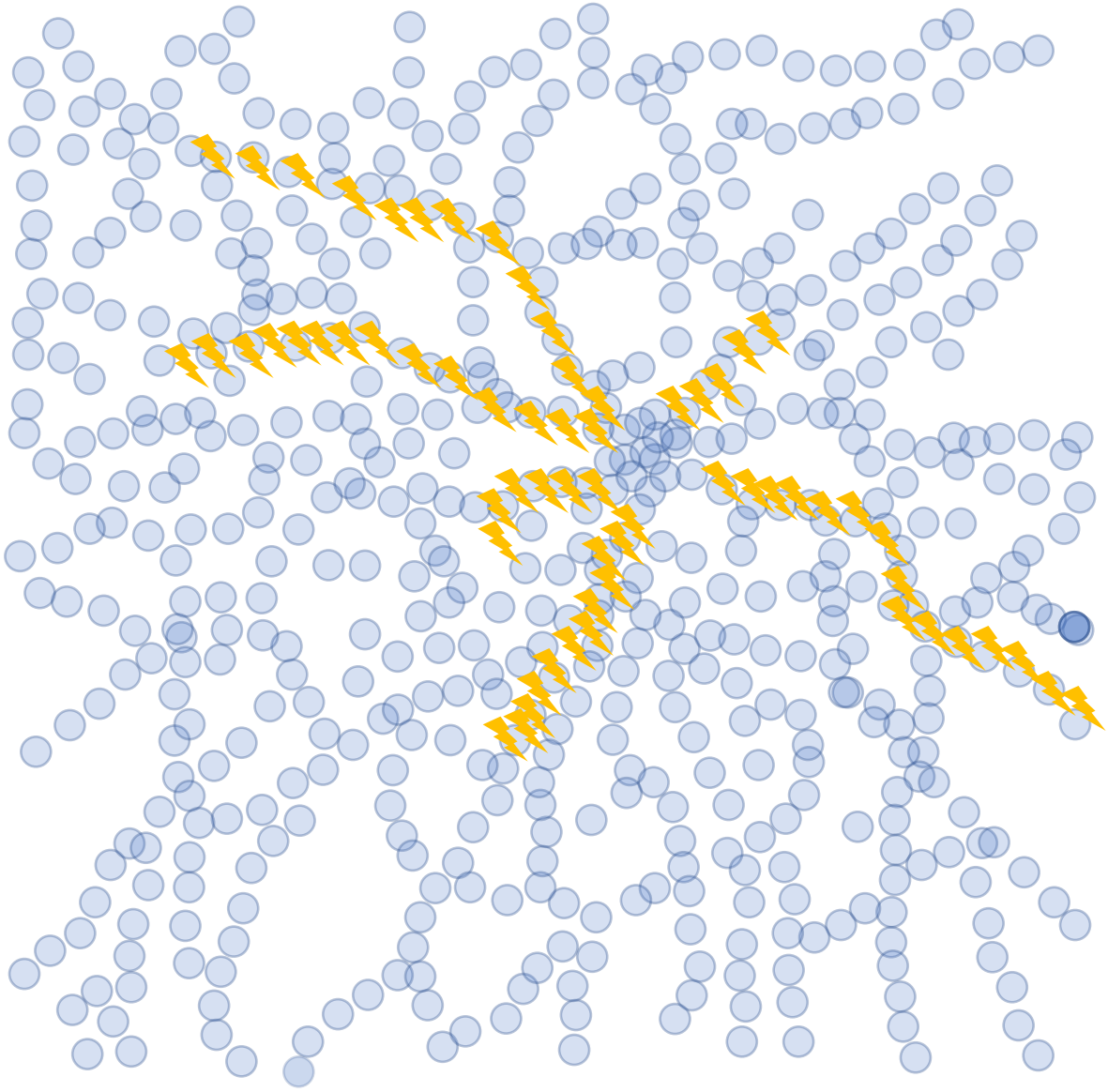
Fatty acids (lipid bilayers)

Preferential accumulation of DHA in frontal cortex



Martinez, J Pediatr, 1992, 120, S129-38

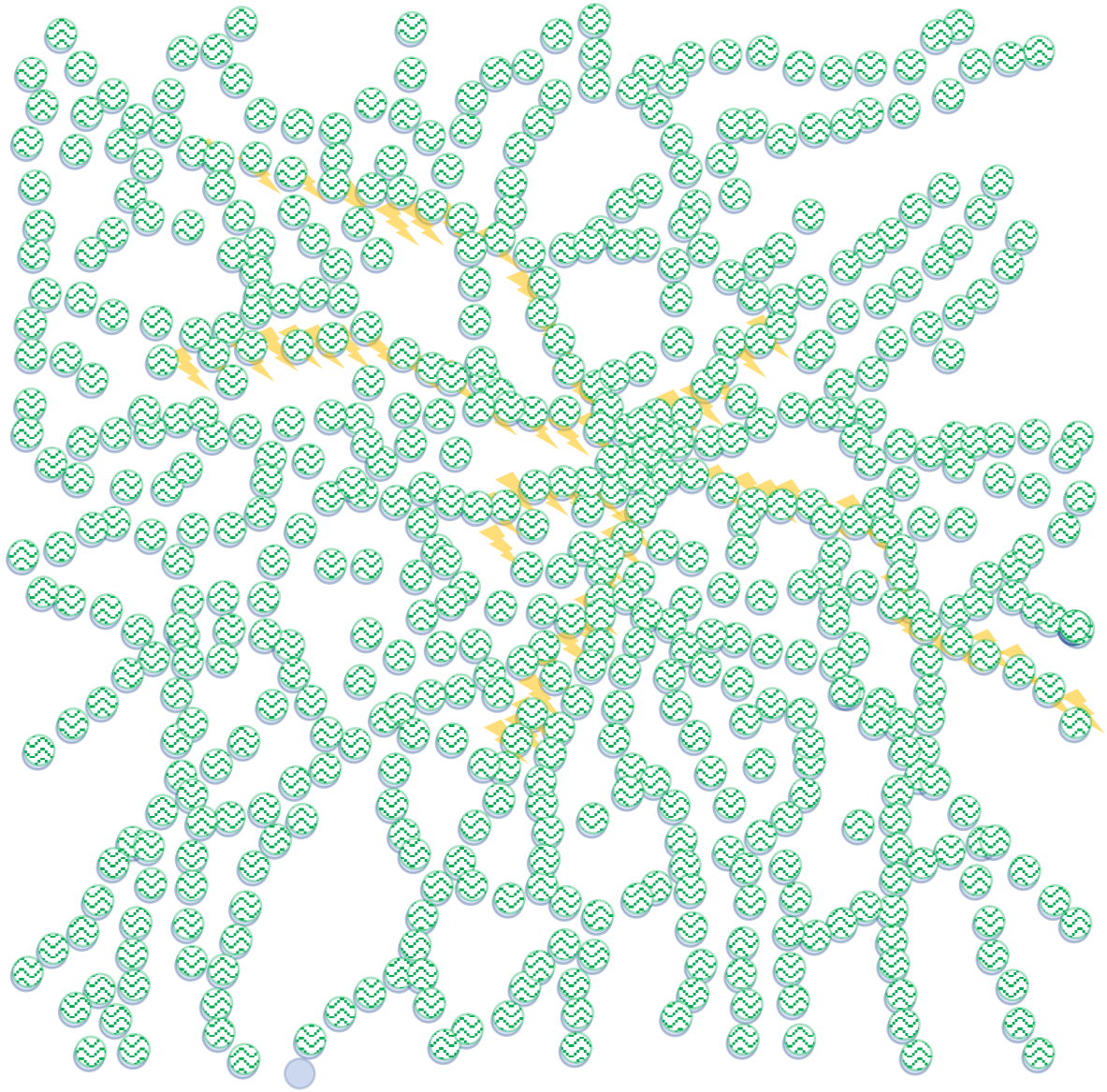
What's in a neuron?



Fatty acids (lipid bilayers)

Electrolytes (ion channels)

What's in a neuron?



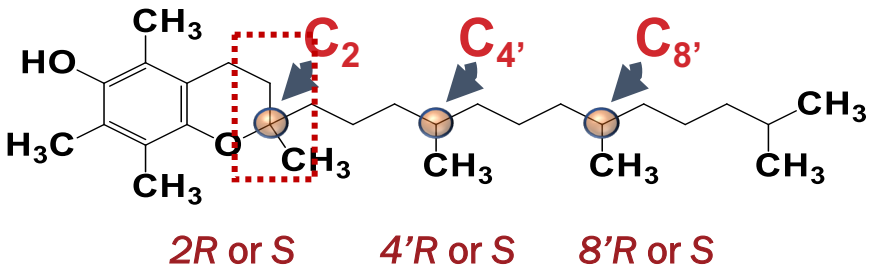
Fatty acids (lipid bilayers)

Electrolytes (ion channels)

Vitamins (fat and water soluble)

Natural Vitamin E

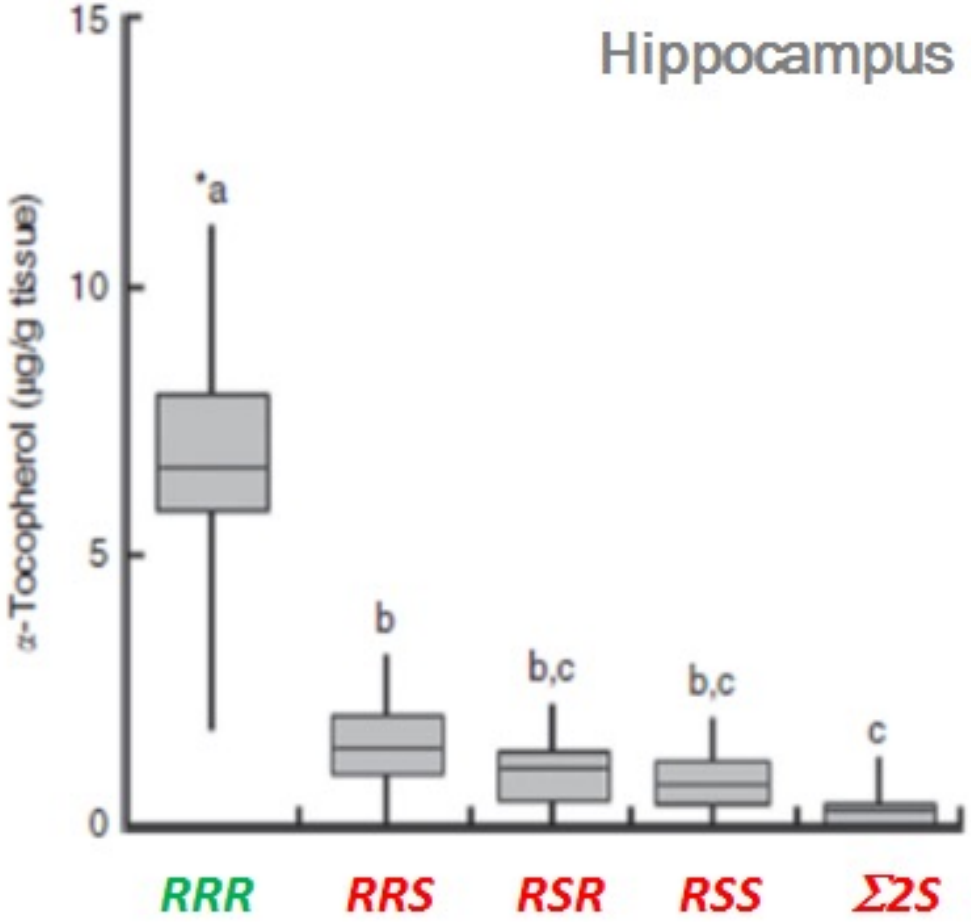
A Closer Look at α-Tocopherol Chemistry



- <u>ONLY</u> *RRR*-α-tocopherol is found in foods – plants – Natural vitamin E
- Synthetic α-tocopherol consists of 8 different stereoisomers

	Natural	Synthetic
RRR	8/8	1/8
RRS	-	1/8
RSR	-	1/8
RSS	-	1/8
SRR	-	1/8
SRS	-	1/8
SSR	-	1/8
SSS	-	1/8

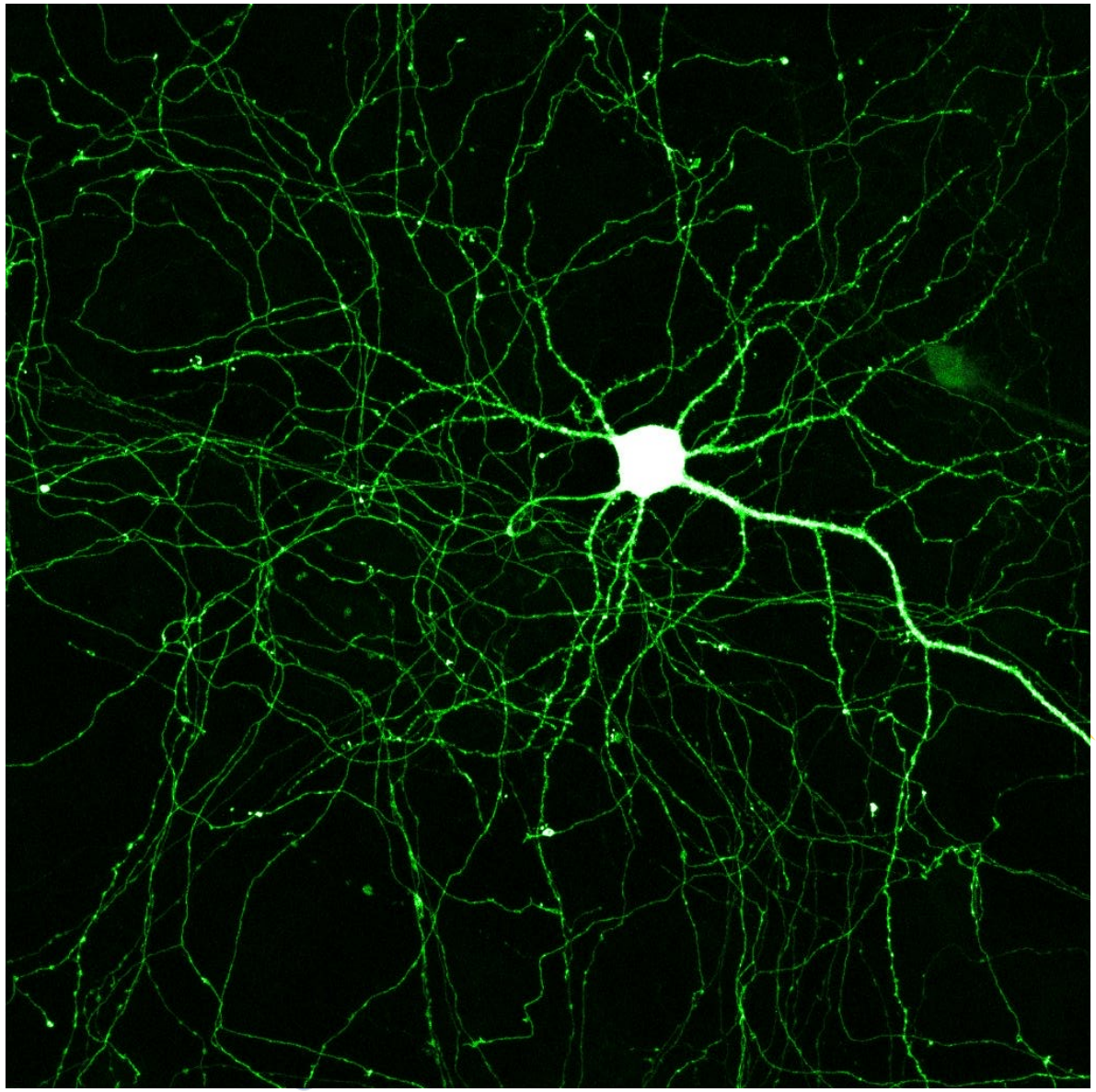
RRR-α-tocopherol is the dominant form in infant brain



Kuchan MJ et al. Br J Nutr 2016;116:126-131.

[a-c] Unlike values statistically different. n=36 decedents.
2S, RSS, RRS, and RSR are synthetic forms of vitamin E.

What's in a neuron?



Fatty acids (lipid bilayers)

Electrolytes (ion channels)

Vitamins (fat and water soluble)

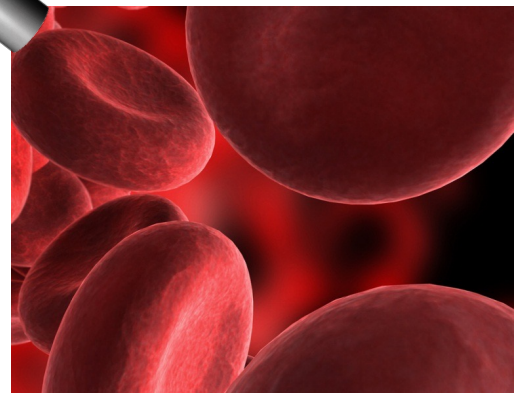
Proteins and carbohydrates (cytoskeleton, receptors)

Carotenoids.

Carotenoids

~700 carotenoids

~50-60 carotenoids



~20 carotenoids

Lutein and isomers

How does nutrition impact cognitive performance?

Academic Achievement

Hear and see teachers

Attend or ignore

Process quickly

Make new associations

Rehearse and use

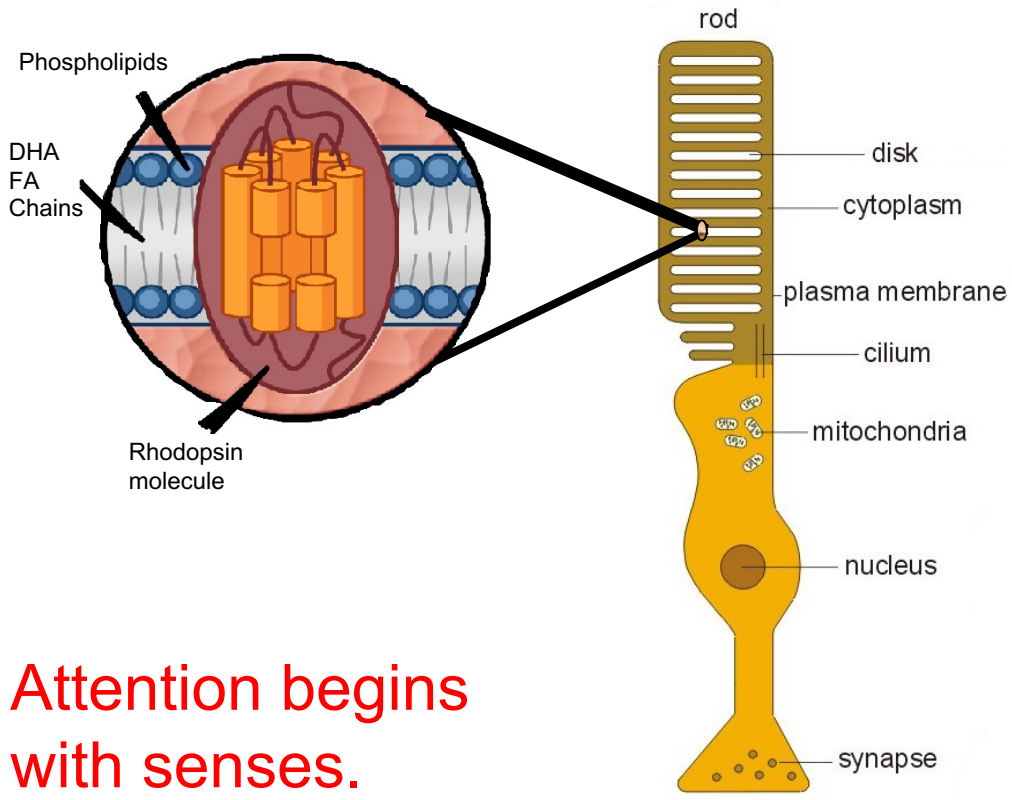
Rest and exercise

Sleep

Wake-up refreshed

1. Attend or ignore

1. Attend or ignore



Attention begins with senses.

DHA is the dominant fat in photoreceptor membranes

DHA deficiency is associated with visual processing deficits

Lien & Hammond, 2011

1. Attend or ignore

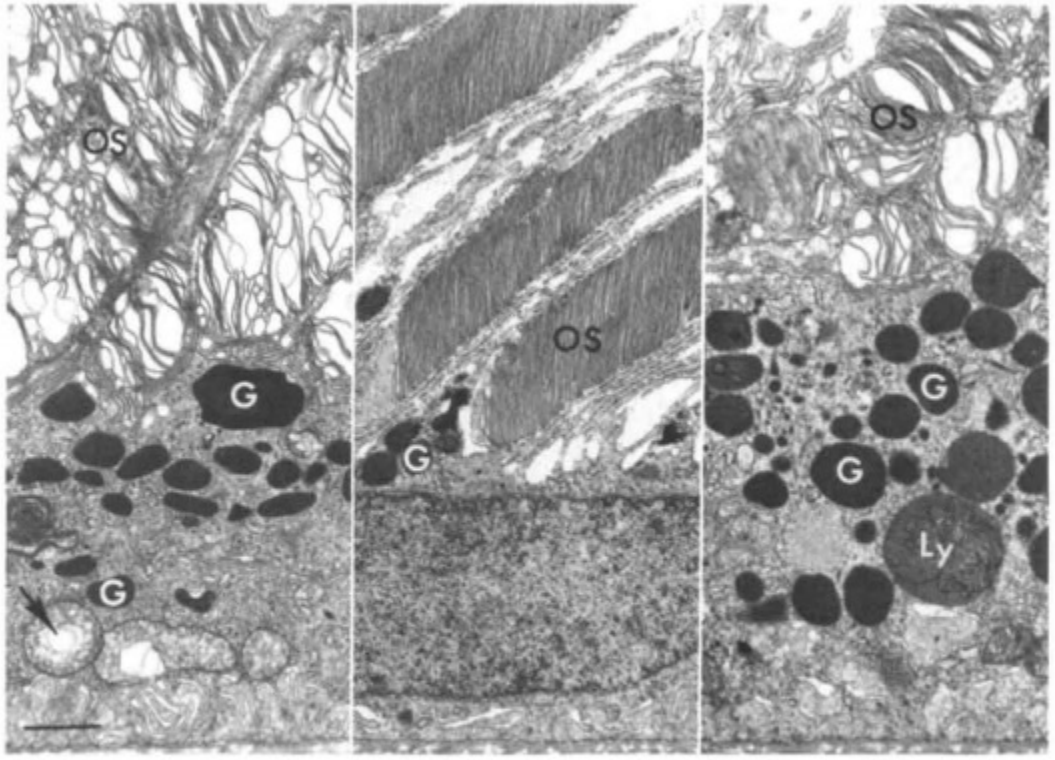
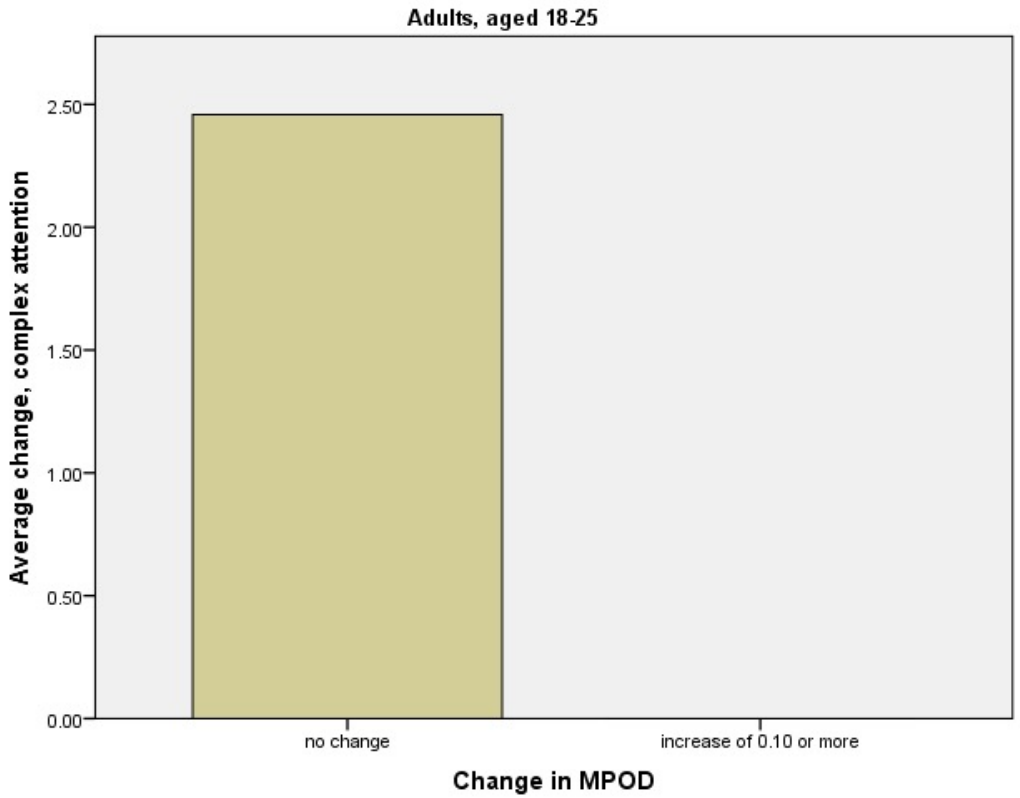


Fig. 3. Retinal pigment epithelium and portions of outer segments *(OS)* from rats fed an E-free, A-marginal diet for 5 months (left), an E-adequate, A-adequate diet for 8 months (middle), or an E-free, A-adequate diet for 8 months (right). E-deprived rats accumulated unusual quantities of lipofuscin pigment granules *(G)* and secondary lysosomes *(Ly)* in their swollen retinal pigment epithelium. They showed some mitochondrial changes (arrow) of undetermined origin and consequence. (Calibration bar: 1.0 μm.)

Lutein and natural vitamin E (NVE) protect retinal tissue.

Robison et al, 1979

1. Attend or ignore



Supplementing lutein improves complex attention in healthy college students.

Renzi-Hammond et al, 2017

1. Attend or ignore

International Journal of Psychophysiology 118 (2017) 1–8

Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho

Registered Reports

From neuro-pigments to neural efficiency: The relationship between retinal carotenoids and behavioral and neuroelectric indices of cognitive control in childhood

Anne M. Walk[a], Naiman A. Khan[a,b,*], Sasha M. Barnett[c], Lauren B. Raine[d], Arthur F. Kramer[d,e], Neal J. Cohen[e,f], Christopher J. Moulton[g], Lisa M. Renzi-Hammond[h], Billy R. Hammond[h], Charles H. Hillman[d,i]

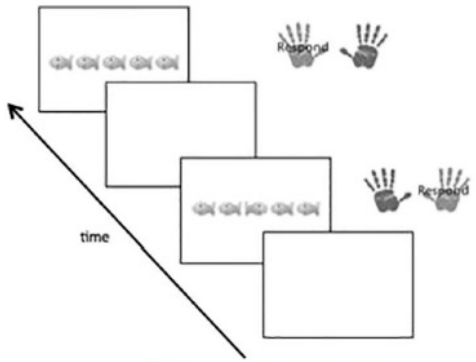


Fig. 1. Sample of stimuli from the revised flanker task.

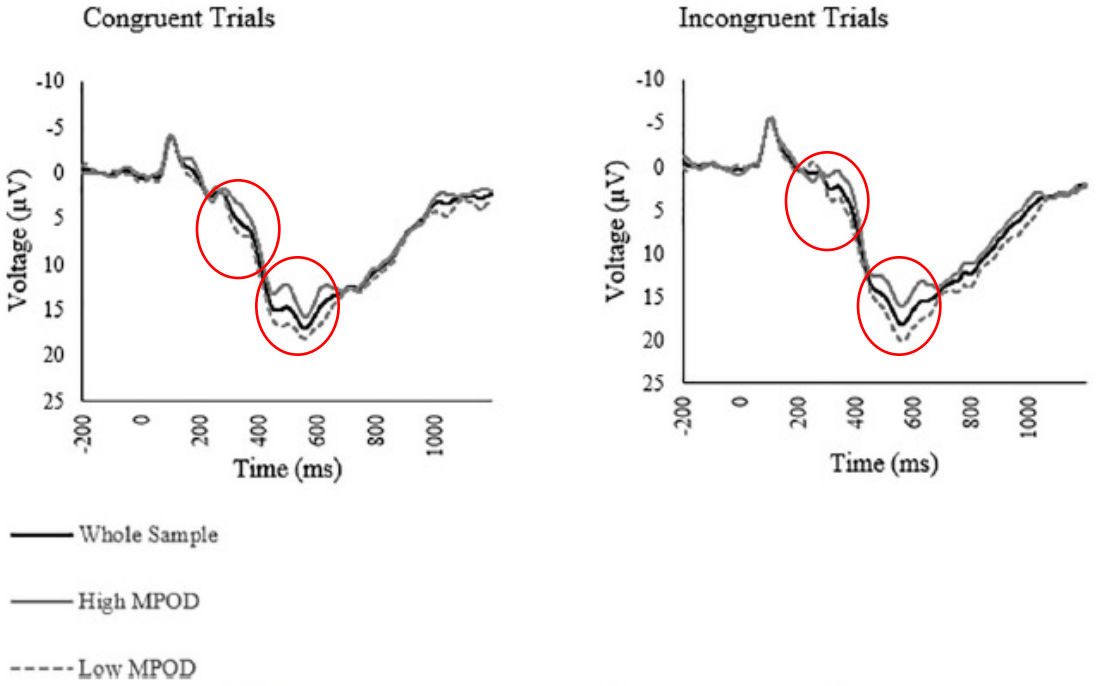
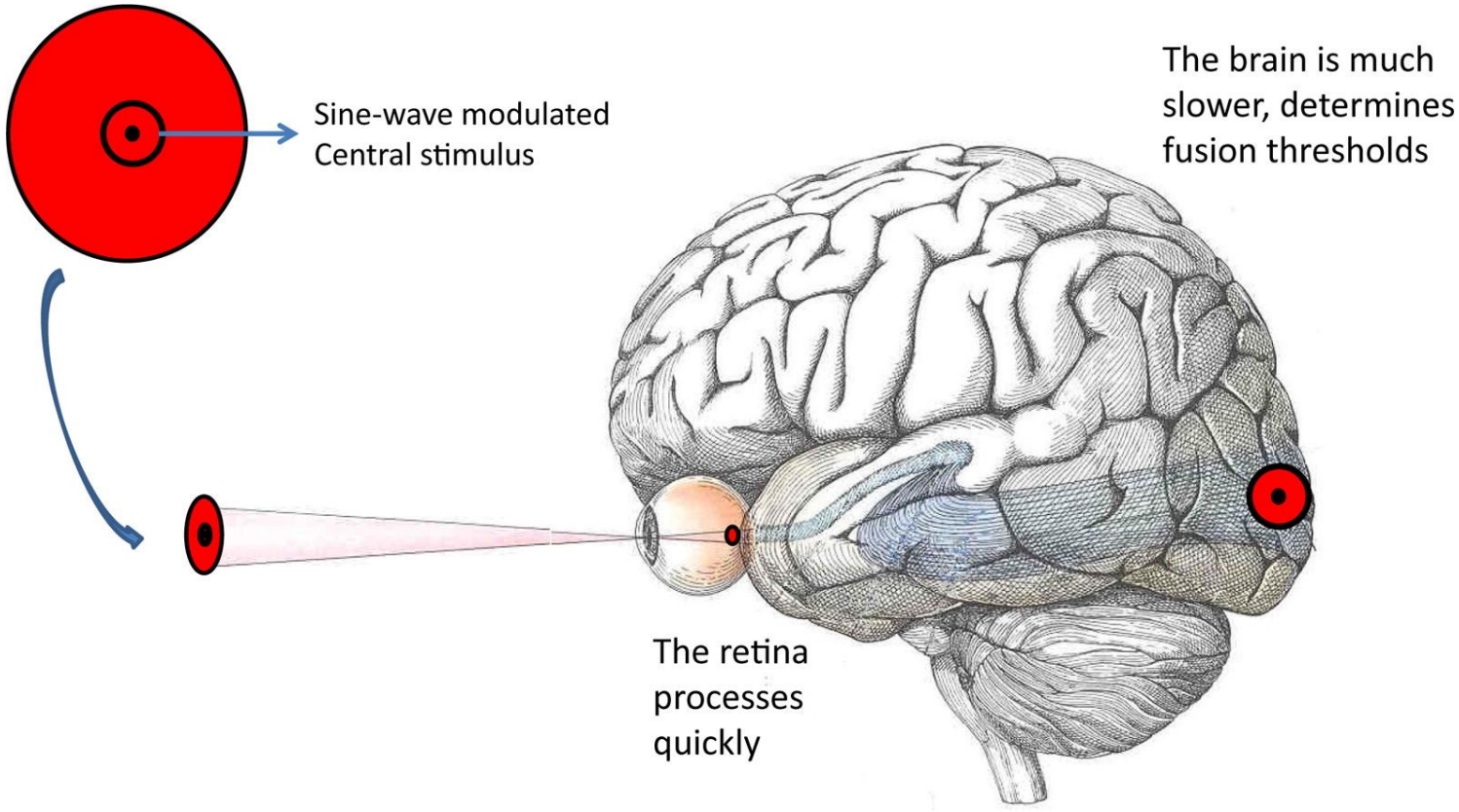


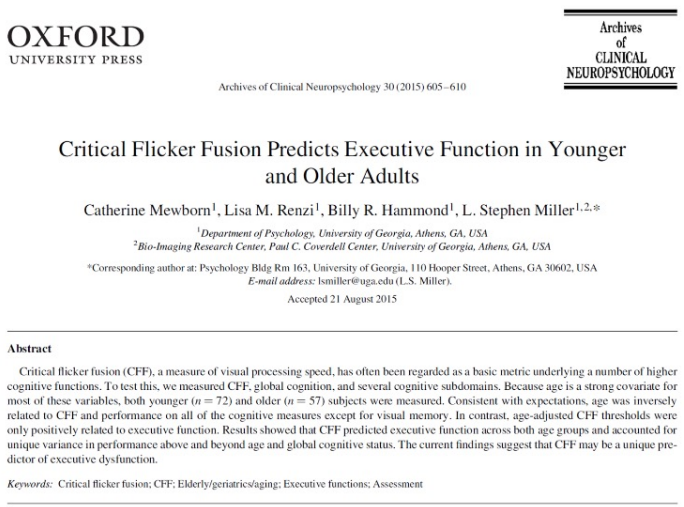
Fig. 2. ERP waveforms for congruent and incongruent flanker trials.

2. Process quickly



Bovier & Hammond, 2015;
Arch Biochem Biophys

2. Process quickly



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Archives of Clinical Neuropsychology 30 (2015) 605–610

Archives of CLINICAL NEUROPSYCHOLOGY

Critical Flicker Fusion Predicts Executive Function in Younger and Older Adults

Catherine Mewborn[1], Lisa M. Renzi[1], Billy R. Hammond[1], L. Stephen Miller[1,2,*]

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[2]*Bio-Imaging Research Center, Paul C. Coverdell Center, University of Georgia, Athens, GA, USA*

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E-mail address: lsmiller@uga.edu (L.S. Miller).

Accepted 21 August 2015

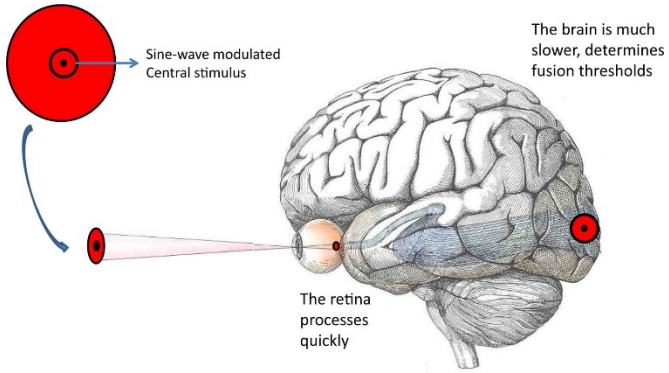
Abstract

Critical flicker fusion (CFF), a measure of visual processing speed, has often been regarded as a basic metric underlying a number of higher cognitive functions. To test this, we measured CFF, global cognition, and several cognitive subdomains. Because age is a strong covariate for most of these variables, both younger ($n = 72$) and older ($n = 57$) subjects were measured. Consistent with expectations, age was inversely related to CFF and performance on all of the cognitive measures except for visual memory. In contrast, age-adjusted CFF thresholds were only positively related to executive function. Results showed that CFF predicted executive function across both age groups and accounted for unique variance in performance above and beyond age and global cognitive status. The current findings suggest that CFF may be a unique predictor of executive dysfunction.

Keywords: Critical flicker fusion; CFF; Elderly/geriatrics/aging; Executive functions; Assessment

Measure	Relationship to Processing Speed (r)
GLOBAL COGNITION	0.377
REASONING	0.386
EXECUTIVE FUNCTIONING	0.465

2. Process quickly

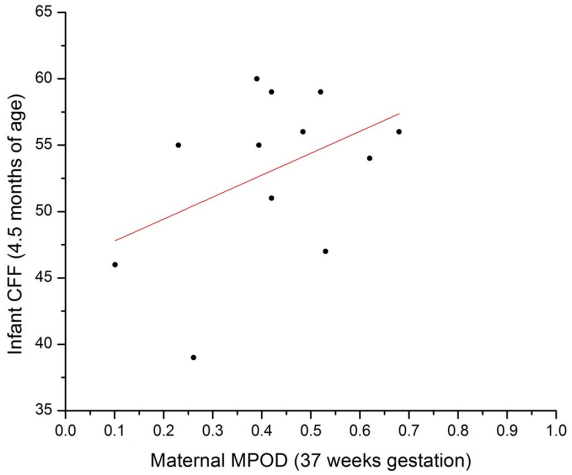


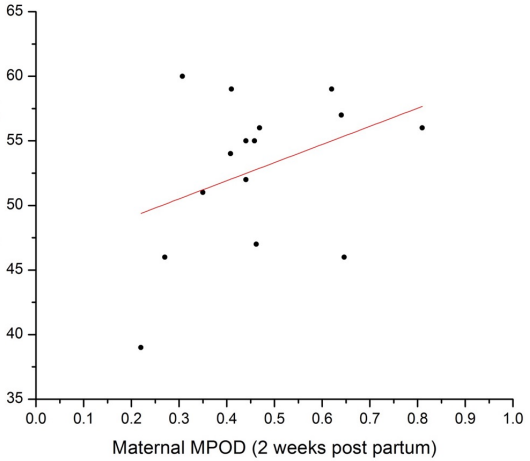
Measure	Relationship to Processing Speed (r)
COGNITIVE EFFICIENCY	0.272
PROCESSING SPEED	0.193
EXECUTIVE PROCESSES	0.217

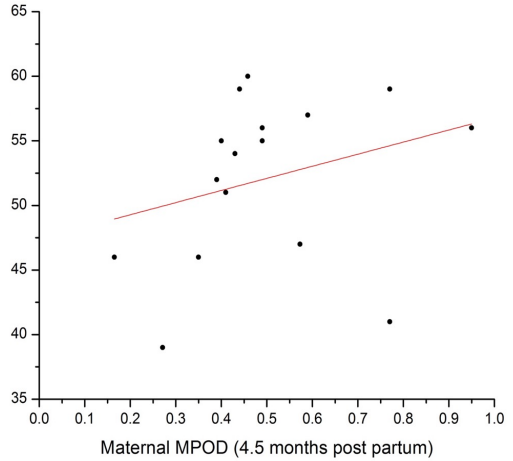
Saint et al, under reviww

Infant processing speed

Infant processing speed







- Saint, Renzi-Hammond, Hammond et al, in preparation

3. Process quickly

OPEN ACCESS Freely available online

PLOS ONE

A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency

Emily R. Bovier[1], Lisa M. Renzi[1,2], Billy R. Hammond[1]*

1 Vision Sciences and Human Biofactors Laboratories, Department of Psychology, The University of Georgia, Athens, Georgia, United States of America, 2 Abbott Nutrition, Columbus, Ohio, United States of America

Abstract

Lutein and zeaxanthin are major carotenoids in the eye but are also found in post-receptoral visual pathways. It has been hypothesized that these pigments influence the processing of visual signals within and post-retina, and that increasing lutein and zeaxanthin levels within the visual system will lead to increased visual processing speeds. To test this, we measured macular pigment density (as a biomarker of lutein and zeaxanthin levels in brain), critical flicker fusion (CFF) thresholds, and visual motor reaction time in young healthy subjects (n = 92). Changes in these outcome variables were also assessed after four months of supplementation with either placebo (n = 10), zeaxanthin only (20 mg/day; n = 29) or a mixed formulation containing 26 mg/day zeaxanthin, 8 mg/day lutein, and 190 mg/day mixed omega-3 fatty acids (n = 25). Significant correlations were found between retinal lutein and zeaxanthin (macular pigment) and CFF thresholds ($p<0.01$) and visual motor performance (overall $p<0.01$). Supplementation with zeaxanthin and the mixed formulation (considered together) produced significant ($p<0.01$) increases in CFF thresholds (~12%) and visual motor reaction time (~10%) compared to placebo. In general, increasing macular pigment density through supplementation (average increase of about 0.09 log units) resulted in significant improvements in visual processing speed, even when testing young, healthy individuals who tend to be at peak efficiency.

Citation: Bovier ER, Renzi LM, Hammond BR (2014) A Double-Blind, Placebo-Controlled Study on the Effects of Lutein and Zeaxanthin on Neural Processing Speed and Efficiency. PLoS ONE 9(9): e108178. doi:10.1371/journal.pone.0108178

Editor: Kevin McGraw, Arizona State University, United States of America

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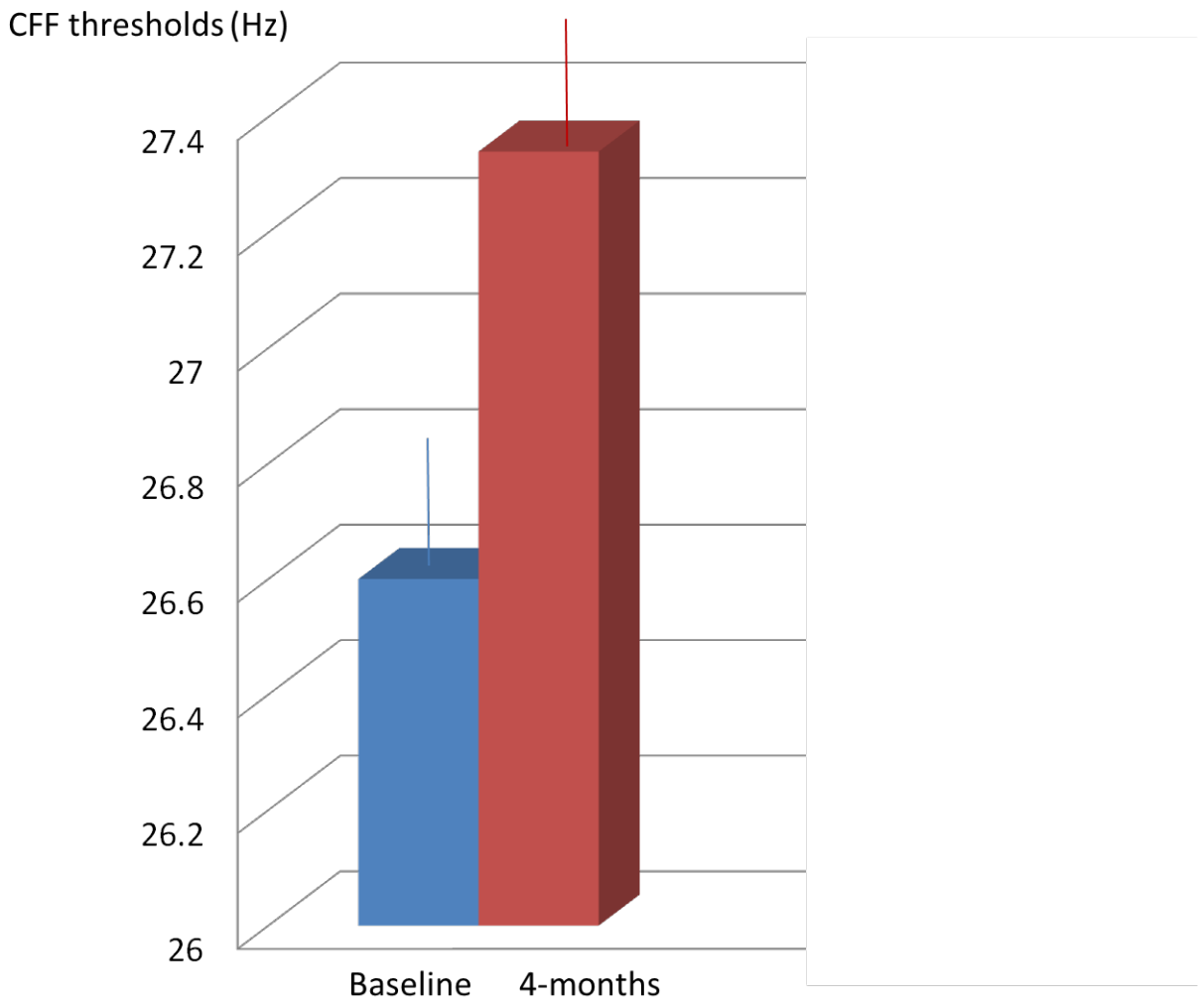
Data Availability: The authors confirm that all data underlying the findings are fully available without restriction. All data underlying the findings in the study are freely available in the manuscript (averages and standard deviations are listed in the tables). Individual raw data points for each participant are available upon request by contacting the corresponding author.

Funding: This study was funded by ZeaVision, LLC. http://www.zeavision.com/. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have read the journal's policy and the authors of this manuscript have the following competing interests: ERB, none; BRH has received speaker fees from ZeaVision, LLC; and LMR is currently an employee of Abbott Nutrition. Abbott Nutrition did not contribute to this study in any way. At the time the work was completed, LMR was solely an employee of the University of Georgia. Information listed in the "Competing Interests" section of this submission does not alter the authors' adherence to all PLOS ONE policies on sharing data and materials.

* Email: bhammond@uga.edu

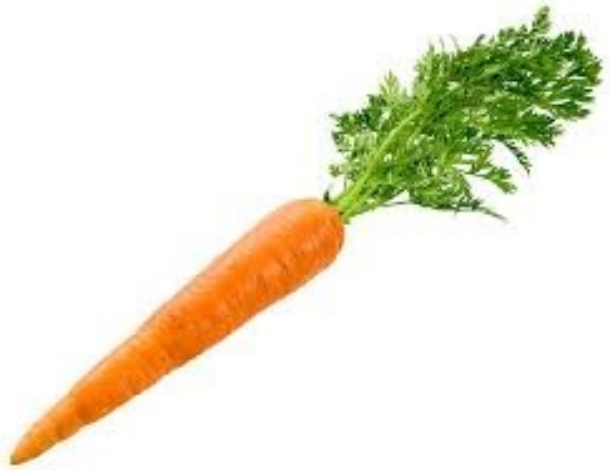


3. Make new associations

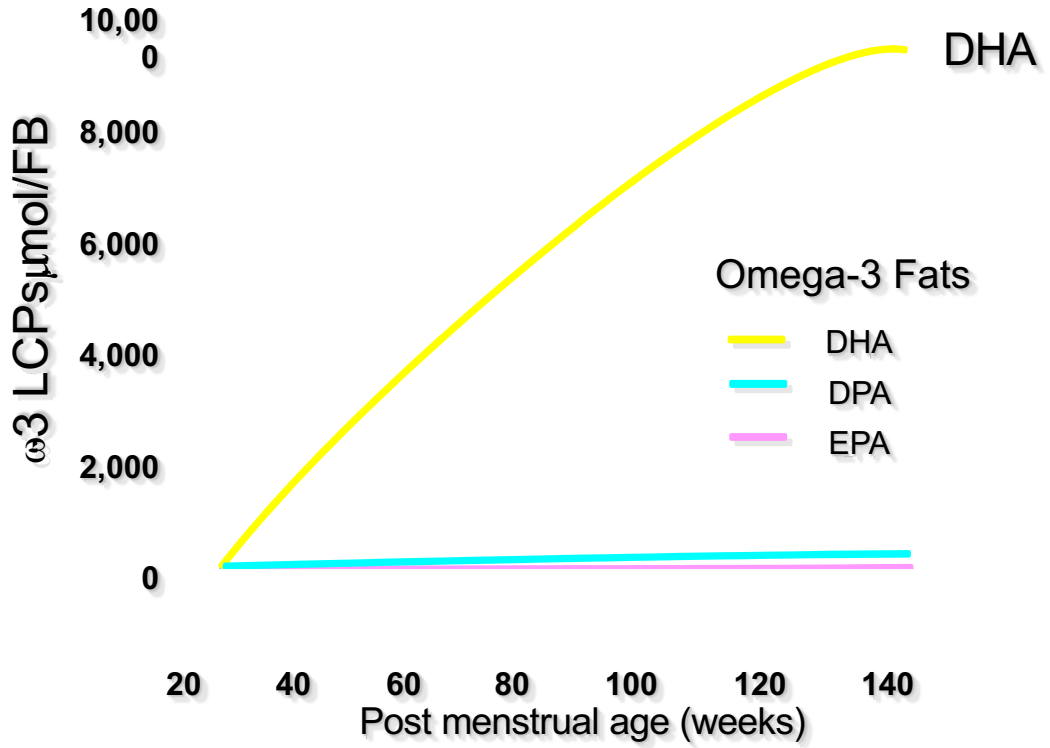
What is:

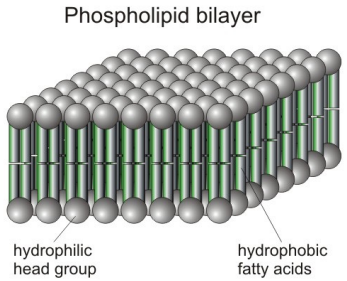
7+7
8+6
15-1
4+10
2+12
17-3
9+5

Now, think of a vegetable



3. Make new associations





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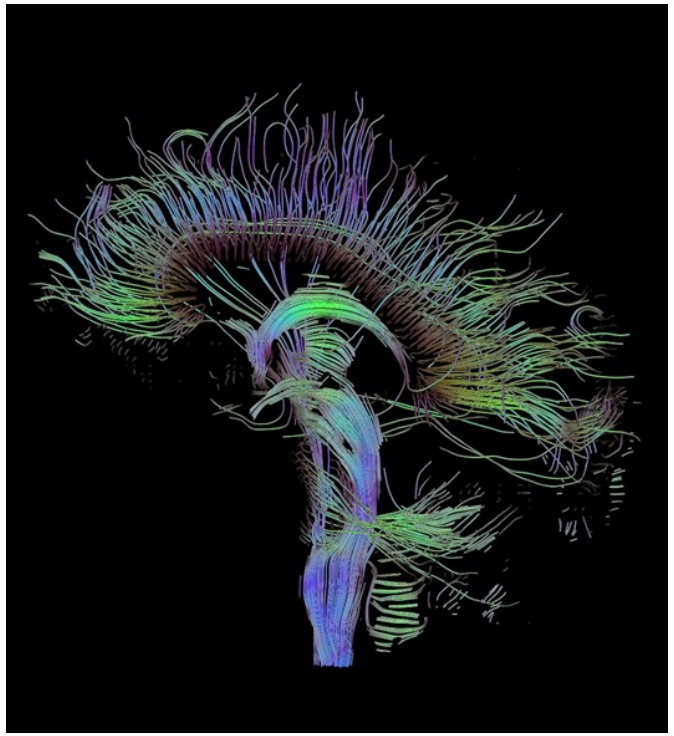
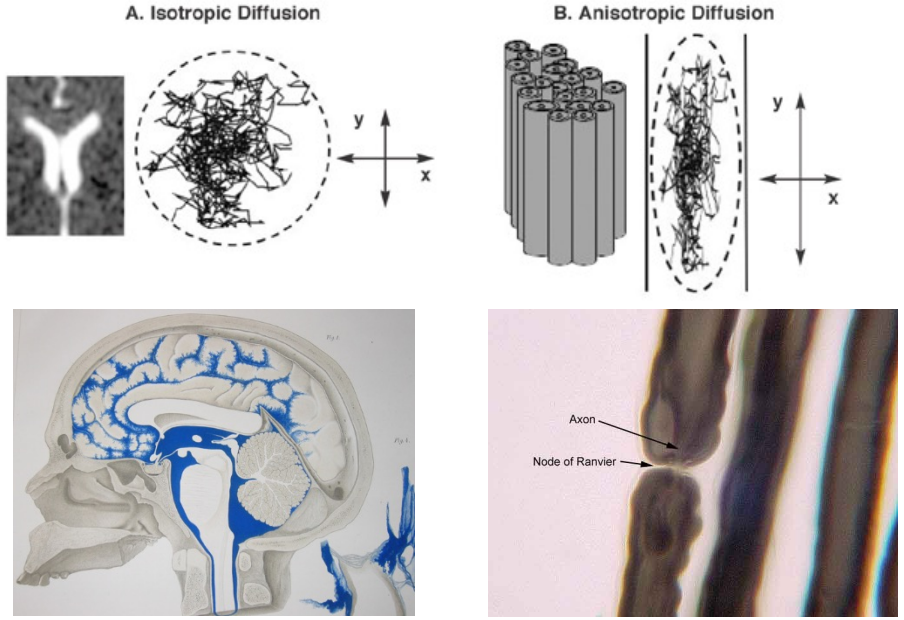


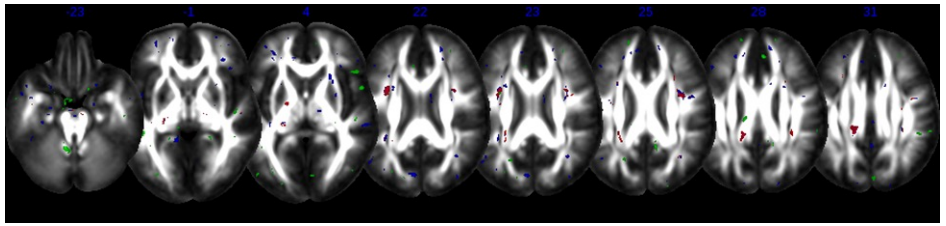


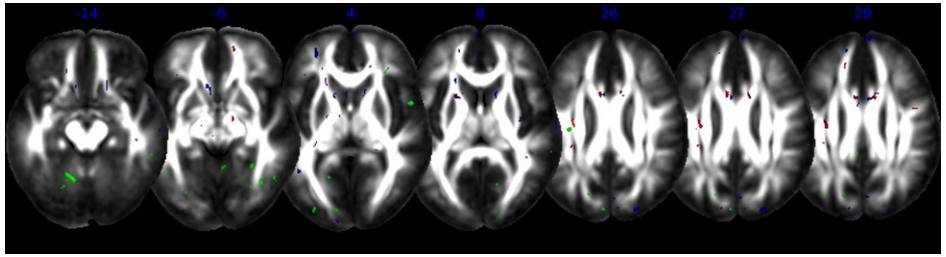
e.g., cerebrospinal fluid

e.g., a mylelinated axon

Images: Rosenbloom et al, 2004; Key & Gustav, 1875; SUNY virtual lab

3. Make new associations





MPOD

serum L+Z

Significant relationships in areas affected in dementia, as well as whole brain white matter, younger and older adults

Lutein in brain relates to improved white matter integrity

Mewborn et al, in press

Relational Memory Paradigm – Study Phase

10 Seconds…

Relational Memory Paradigm – Test Phase

Self-paced

Improved associative memory in children

The Journal of Pediatrics
Volume 183, April 2017, Pages 108–114.e1

Original Articles

Macular Carotenoids, Aerobic Fitness, and Central Adiposity Are Associated Differentially with Hippocampal-Dependent Relational Memory in Preadolescent Children

Kelsey M. Hassevoort, BA[1, 2], Sarah E. Khazoum, BA[3], John A. Walker, PhD[2, 3], Sasha M. Barnett, MA[4], Lauren B. Raine, PhD[5], Billy R. Hammond, PhD[6], Lisa M. Renzi-Hammond, PhD[6],
Show more

https://doi.org/10.1016/j.jpeds.2017.01.016

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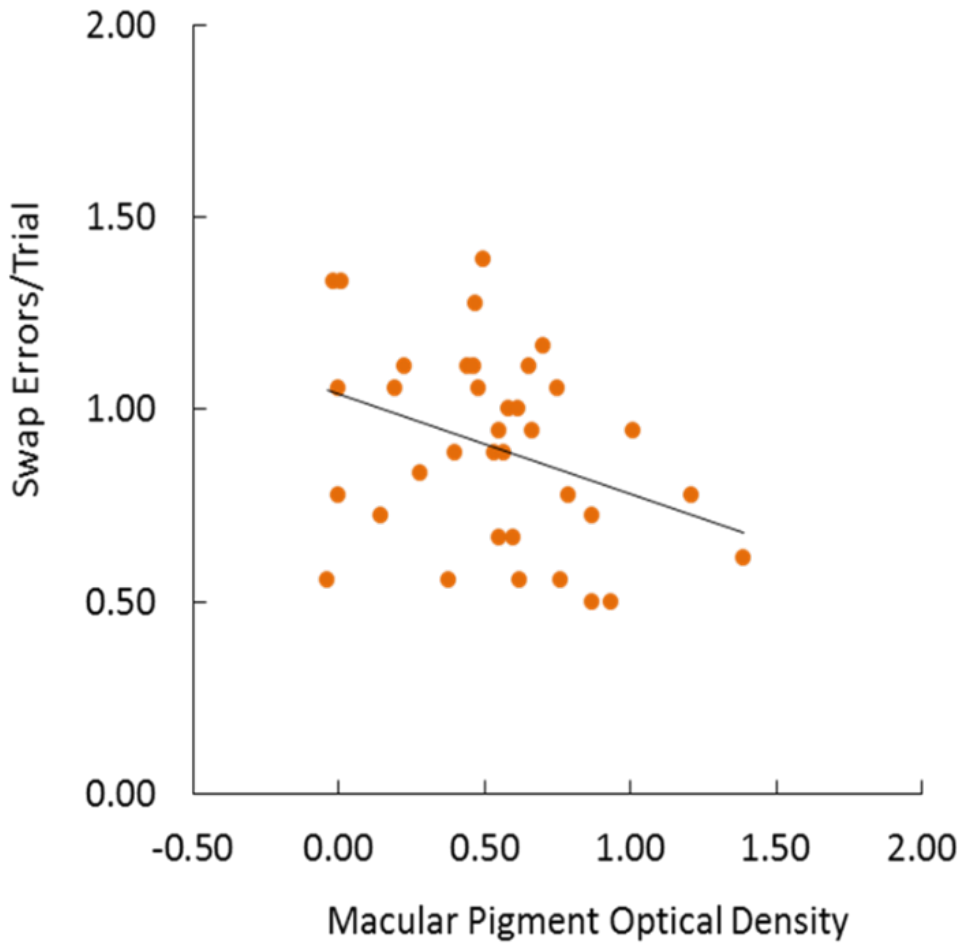
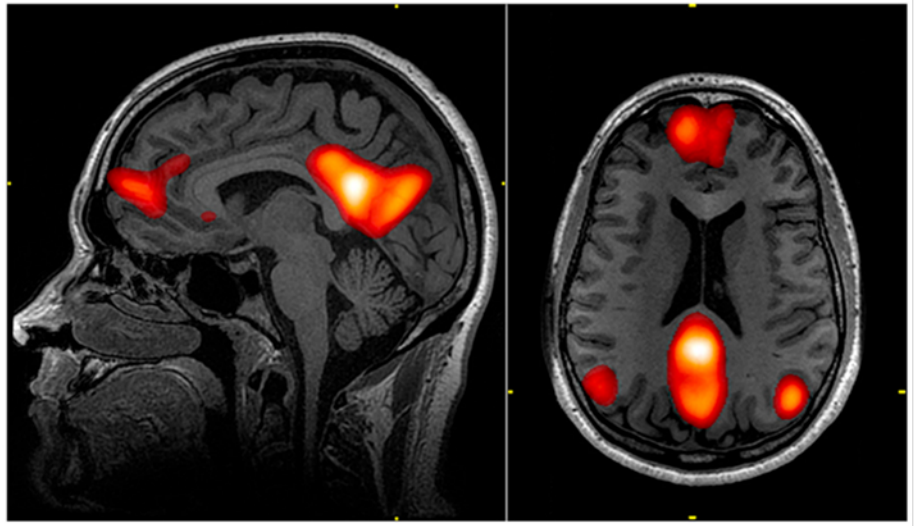
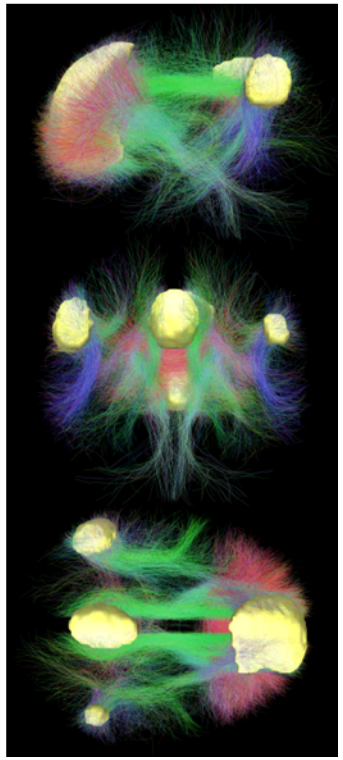


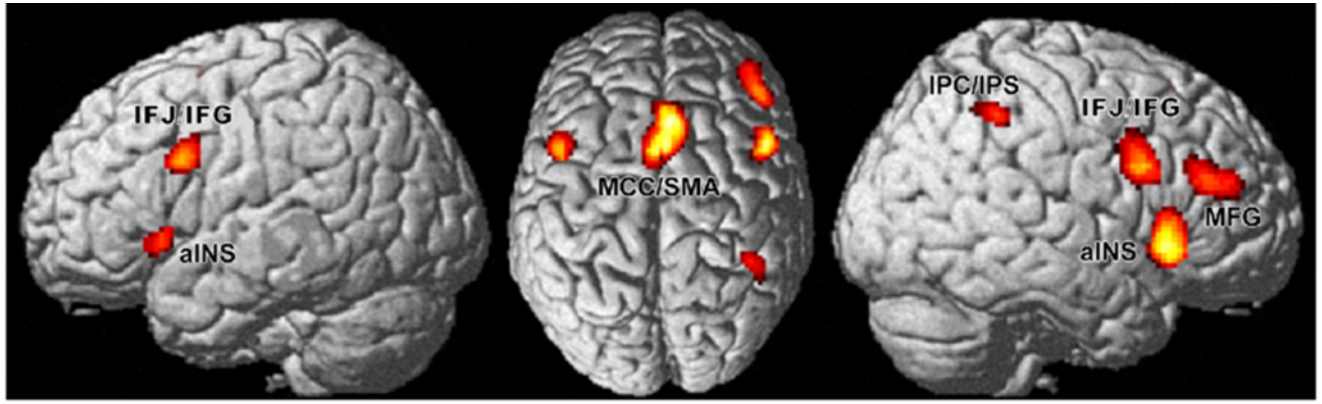
4. Rehearse and use



Default mode network (DMN) in absence of sensory – and goal-directed behavior

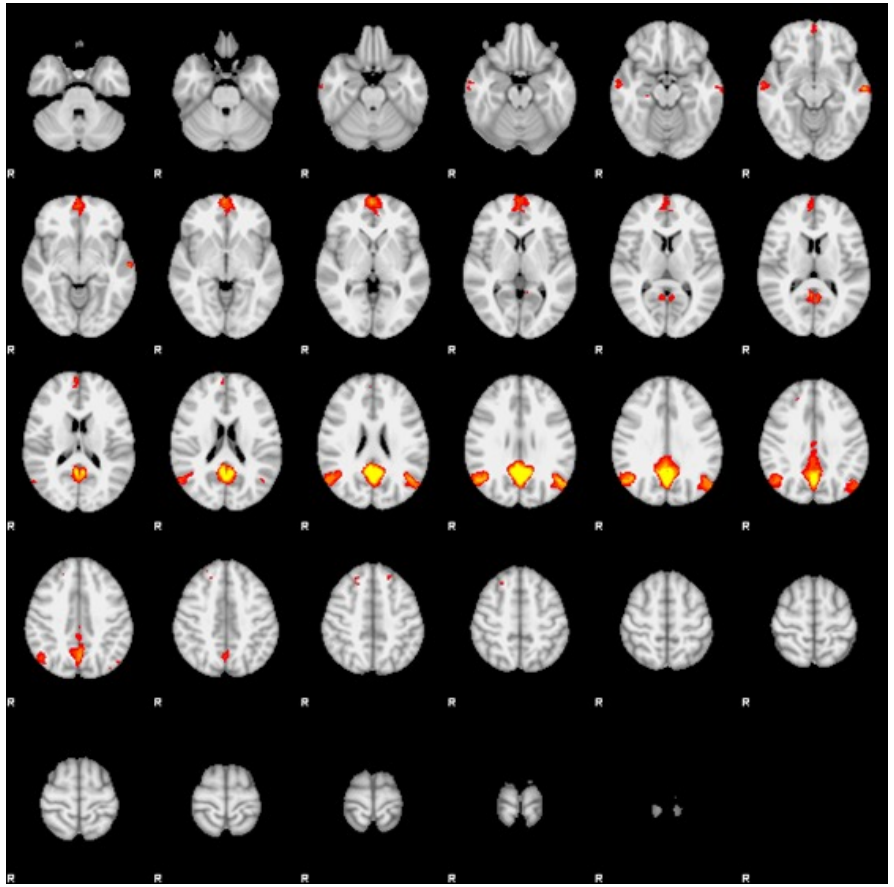


4. Rehearse and use



Multiple demand network (MDN): stimulus detected, attention must shift to accomplish a goal.

4. Rehearse and use

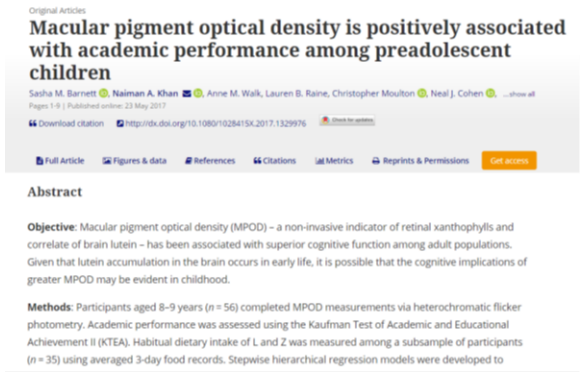


Supplementation with lutein increases inter-network connectivity

True even in older adults

Lindbergh et al, 2017

4. Rehearse and use



Original Articles

Macular pigment optical density is positively associated with academic performance among preadolescent children

Sasha M. Barnett, **Naiman A. Khan**, Anne M. Walk, Lauren B. Raine, Christopher Moulton, Neal J. Cohen, ...show all

Pages 1-9 | Published online: 23 May 2017

Download citation http://dx.doi.org/10.1080/102841SX.2017.1329976

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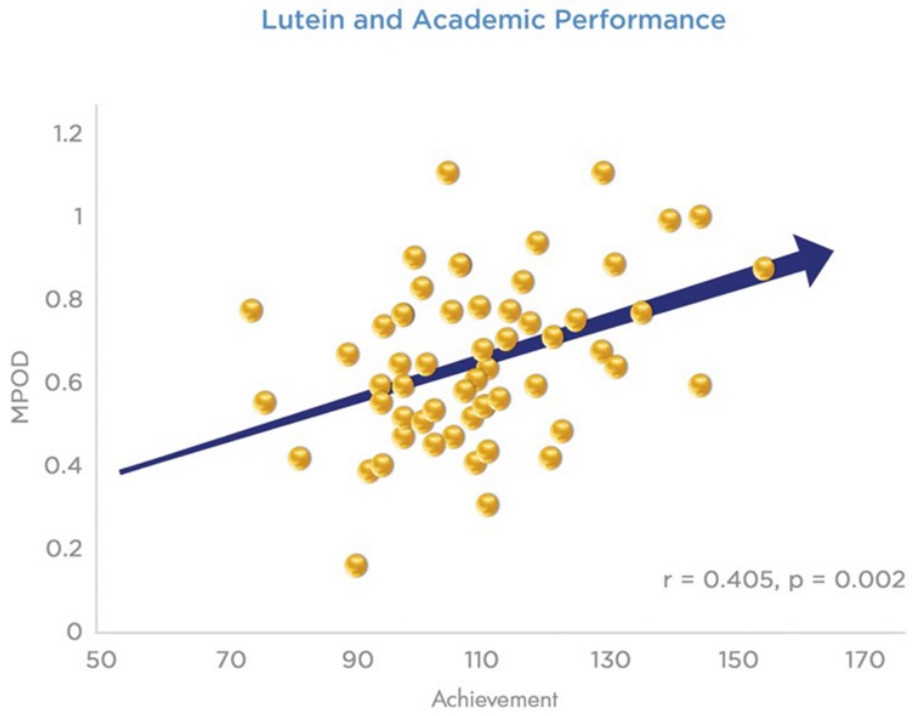
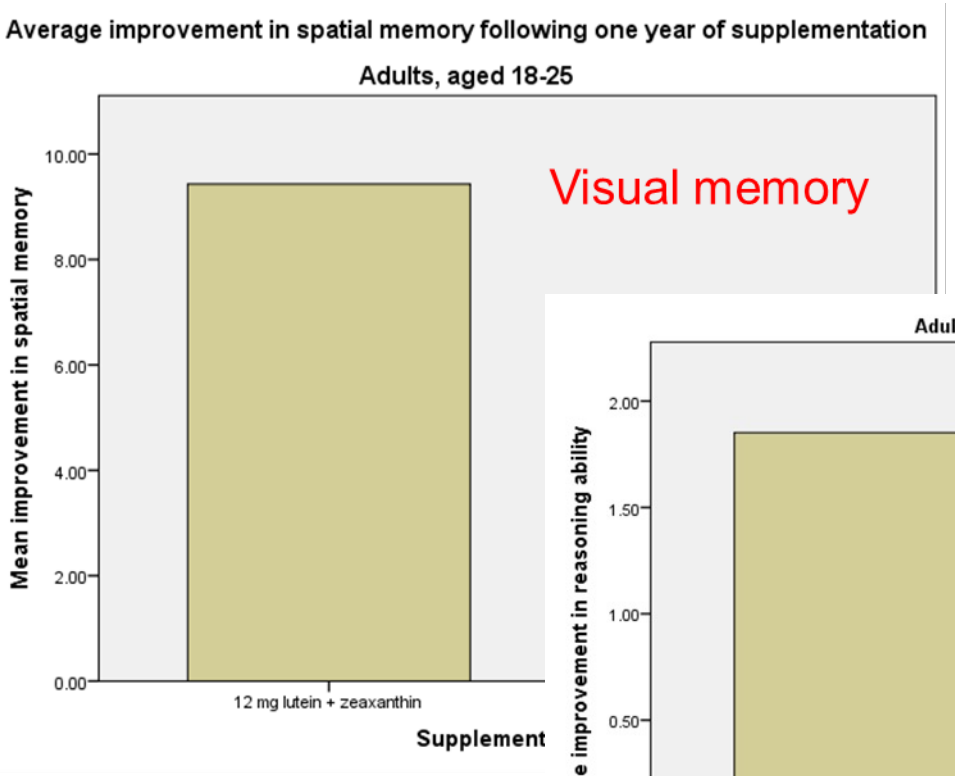
Abstract

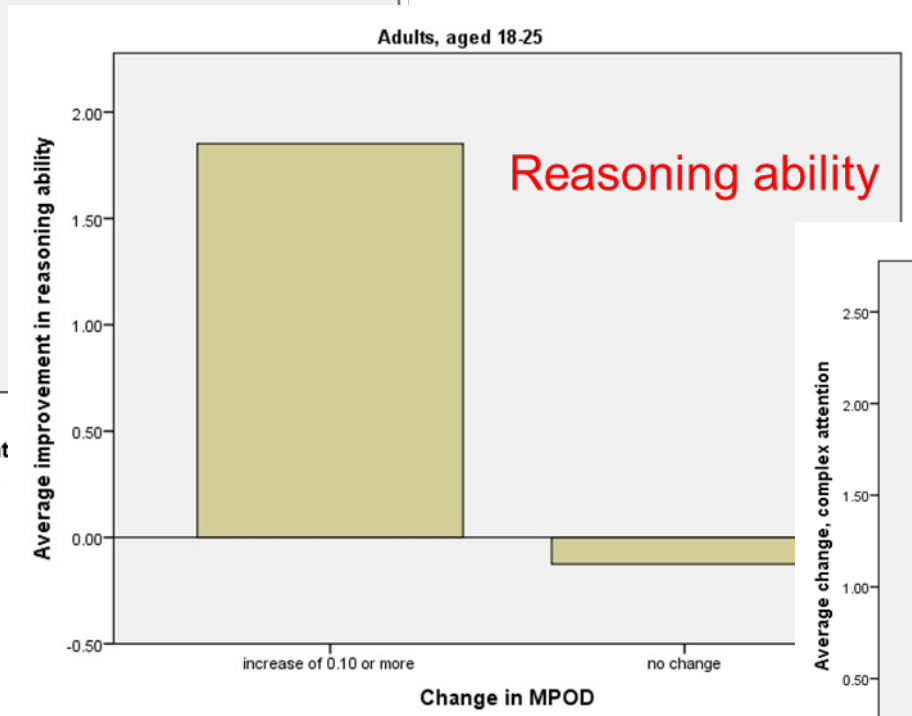
Objective: Macular pigment optical density (MPOD) – a non-invasive indicator of retinal xanthophylls and correlate of brain lutein – has been associated with superior cognitive function among adult populations. Given that lutein accumulation in the brain occurs in early life, it is possible that the cognitive implications of greater MPOD may be evident in childhood.

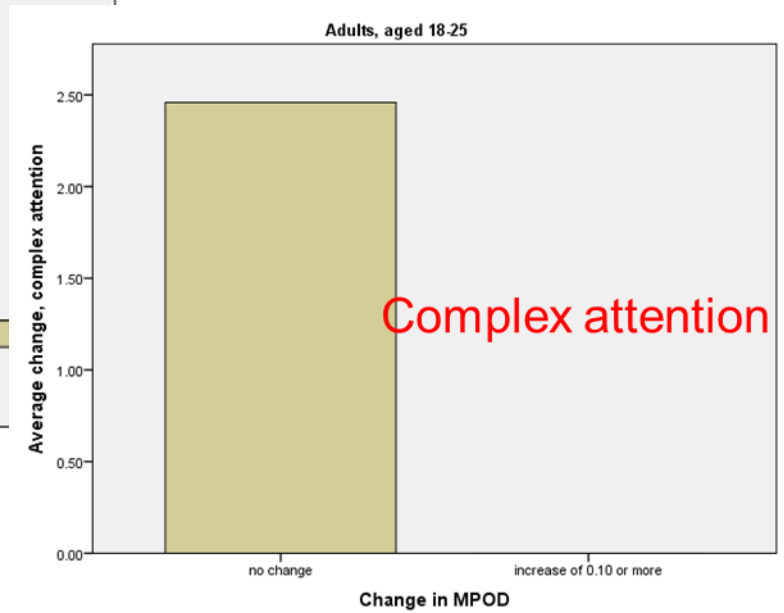
Methods: Participants aged 8–9 years (n = 56) completed MPOD measurements via heterochromatic flicker photometry. Academic performance was assessed using the Kaufman Test of Academic and Educational Achievement II (KTEA). Habitual dietary intake of L and Z was measured among a subsample of participants (n = 35) using averaged 3-day food records. Stepwise hierarchical regression models were developed to



Cognition in young adults





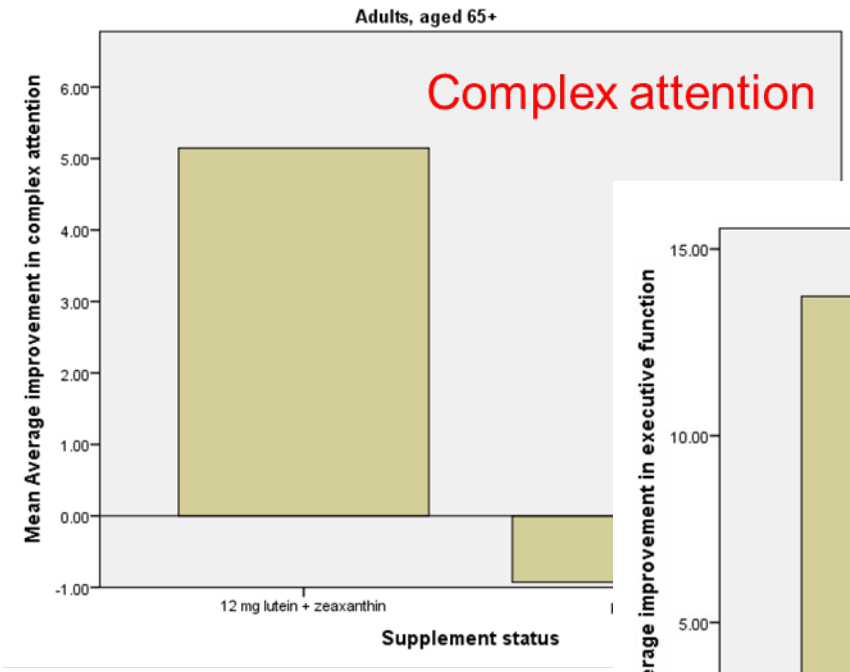


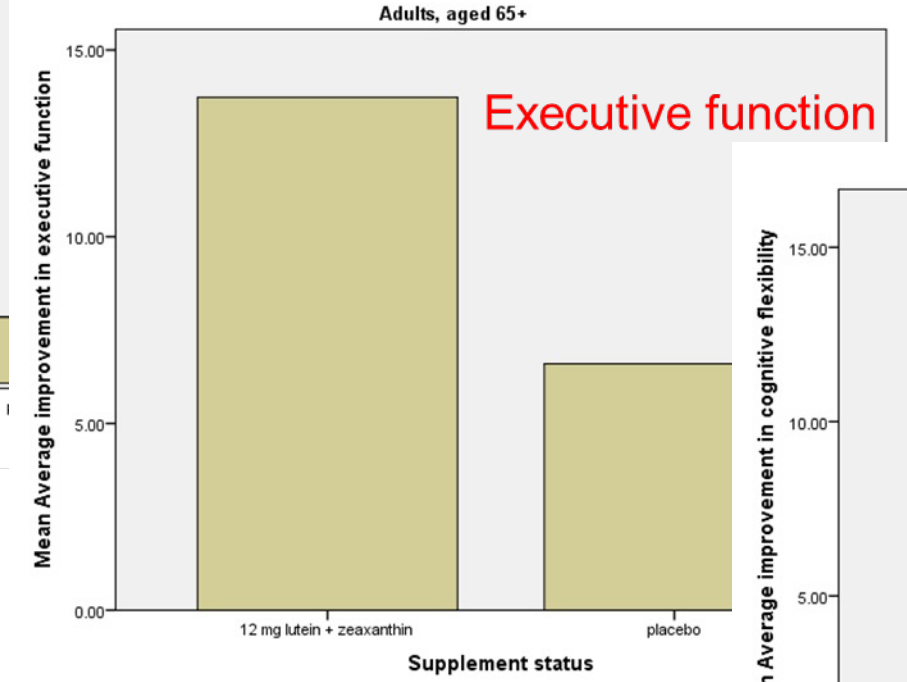
Supplementation with 10 mg lutein, 2 mg zeaxanthin for one year

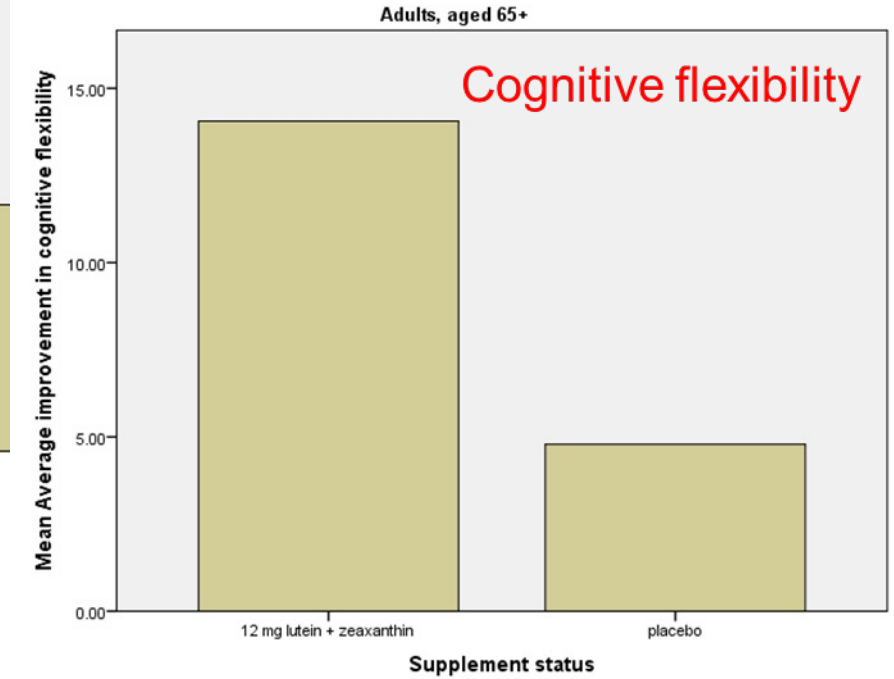
Renzi-Hammond et al, 2017

And to foreshadow, cognitive function in older adults

Supplementation with 10 mg lutein, 2 mg zeaxanthin for one year

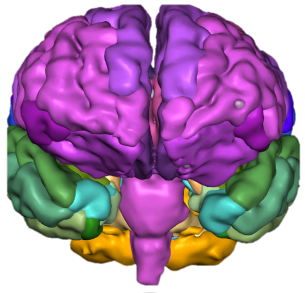






Hammond et al, 2017

Key nutrients in brain structure and function



Protein

Choline

Natural Vitamin E (NVE)

Lutein

Vitamin D

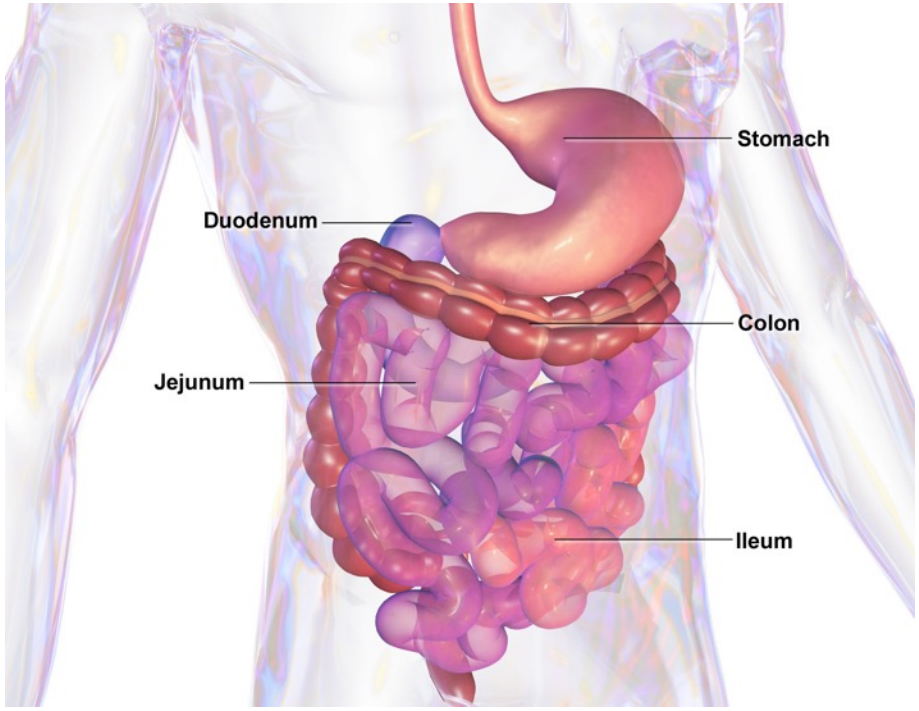
Iron

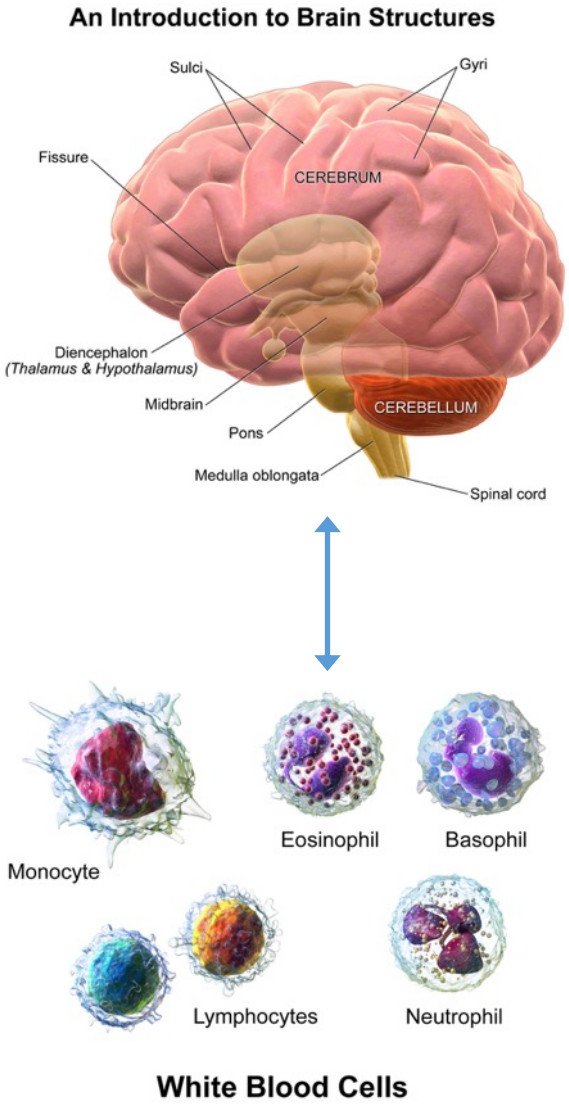
Electrolytes

DHA

Other phospholipids

The problem with silos





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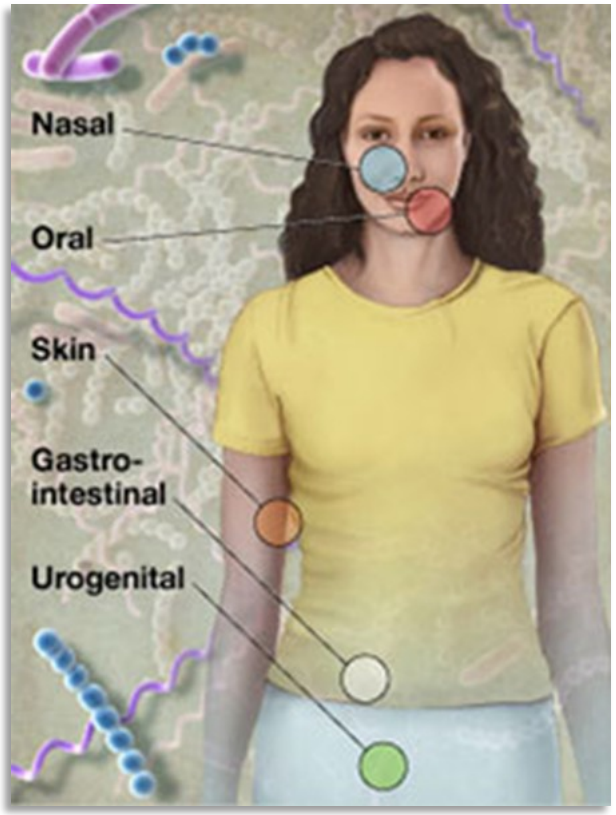
We are holobionts

Organ / System
Eyes
Nose
Mouth
Lungs
Vagina
Skin
Intestines



Microbes outnumber native cells 10:1

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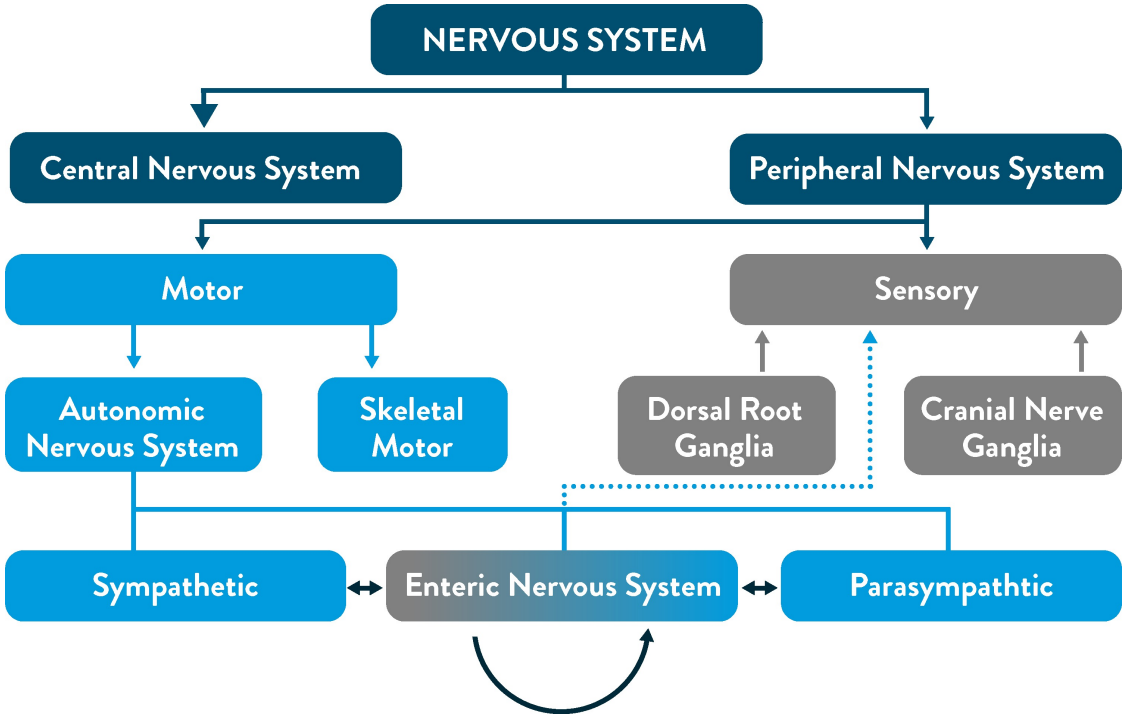
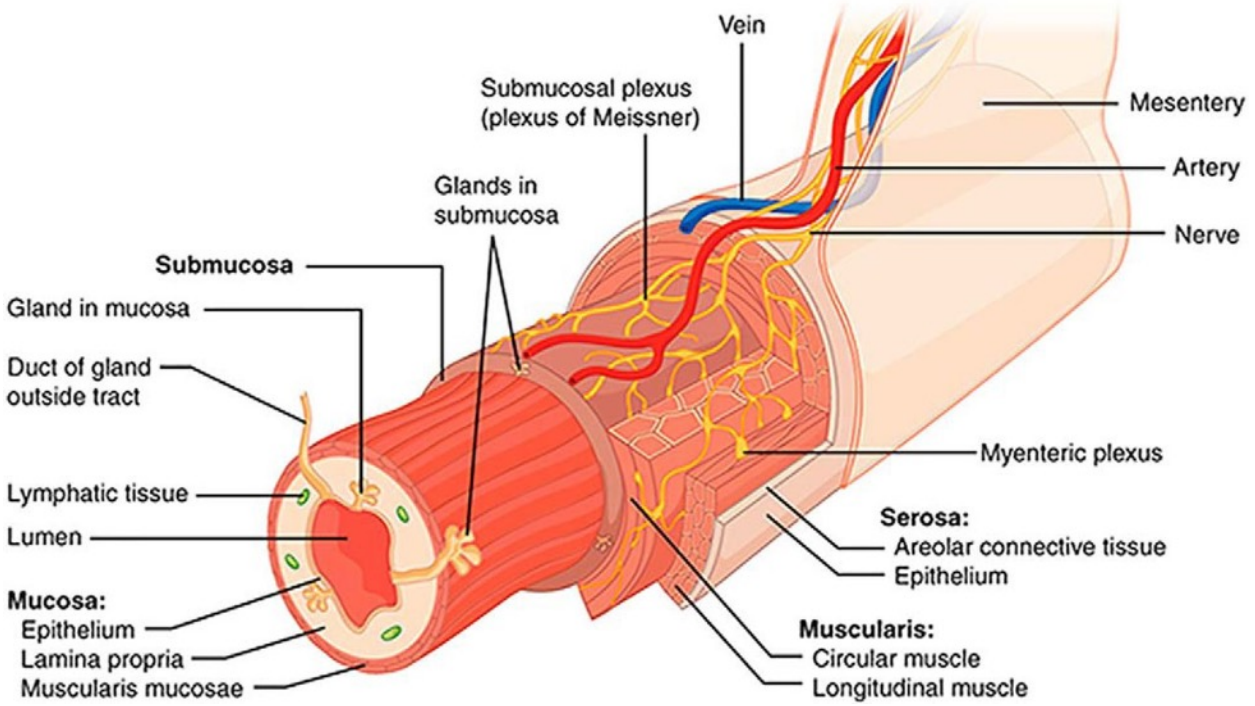
The “other” brain





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Microbiota affect brain development via multiple mechanisms

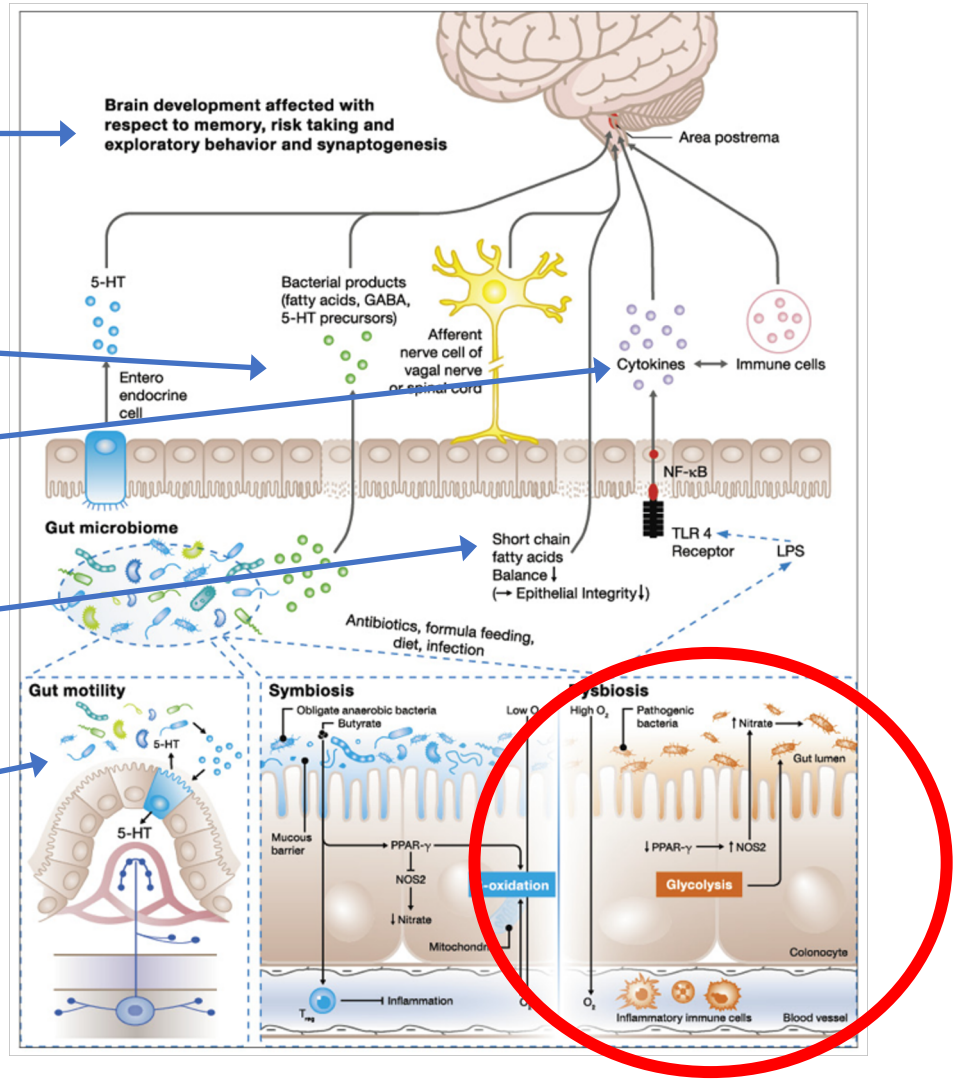
Produce neurotransmitters and their precursors

Vagus nerve signaling

Influence cytokine signaling to the brain

Synthesize short-chain fatty acids that change permeability

Influence gut motility via enteric nervous system, which signals brain



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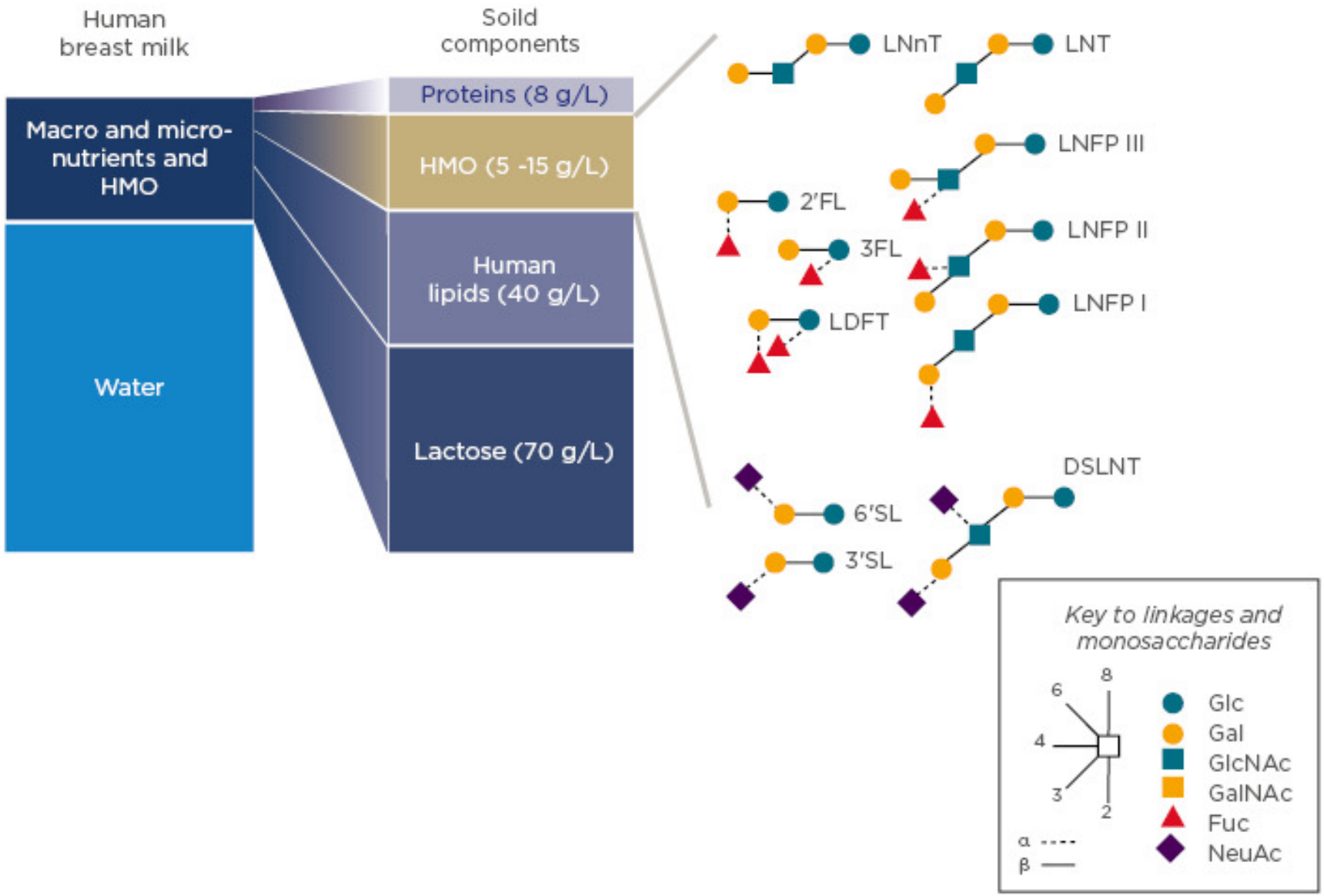
Human Milk Oligosaccharides (HMO)



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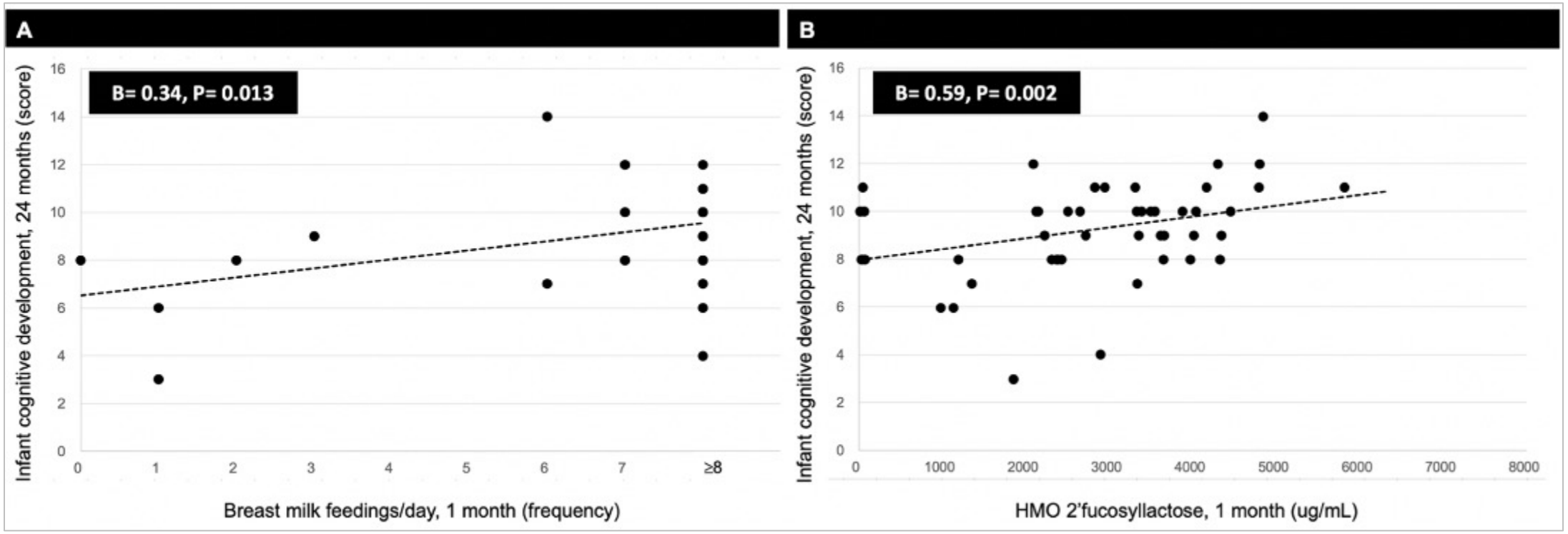
HMO and cognition in humans



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