



The influence of Sphingomyelin on Myelination: Fast and efficient brain connection and development.

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Elon Musk's future research-Neuralink

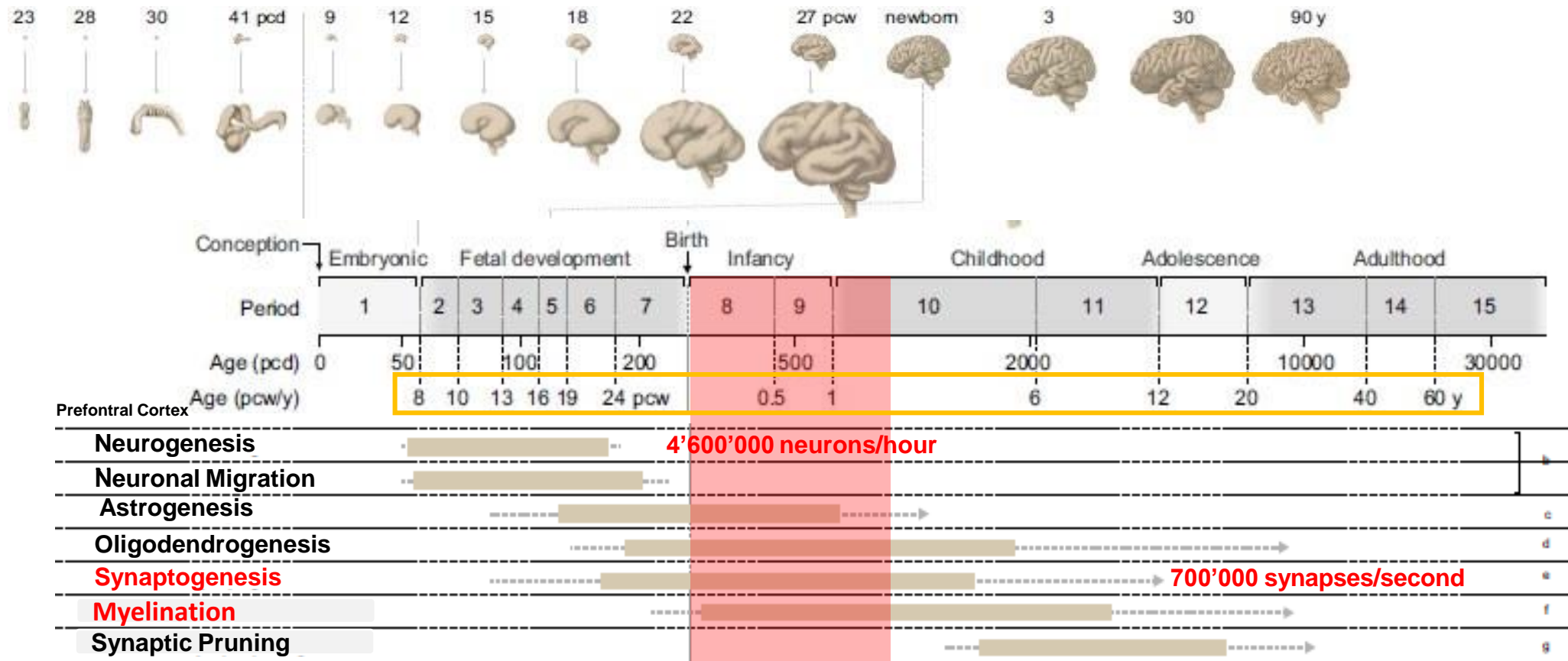


Neuralink:

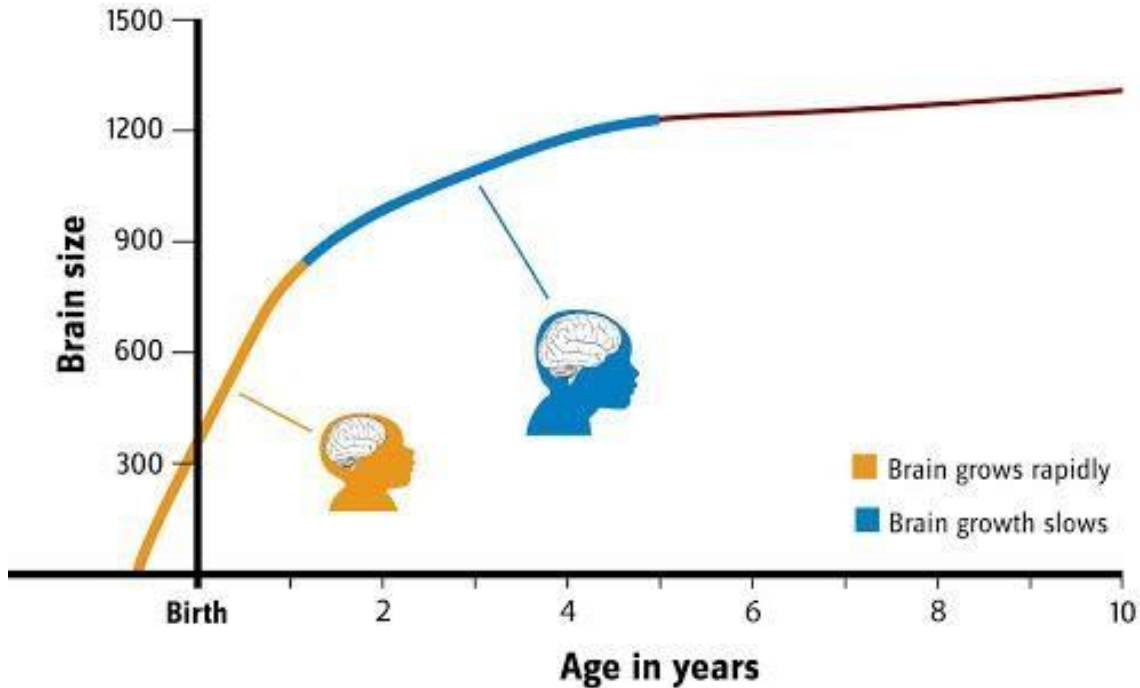
- 1,024 channels per link
- 23 x 8 mm, Flush with skull (invisible)
- Bluetooth Low Energy to communicate
- Robot does the surgery

- Neuralink:
 - increase the channels of communication with thousands of neurons in the brain
 - accessing more brain areas and new kinds of neural information and record the activity
- This technology has the potential to treat:
 - neurological disorders, severe spine injury
 - to restore sensory and movement function,
 - and eventually to expand how we interact with each other, with the world, and with ourselves.

Brain Development – early life

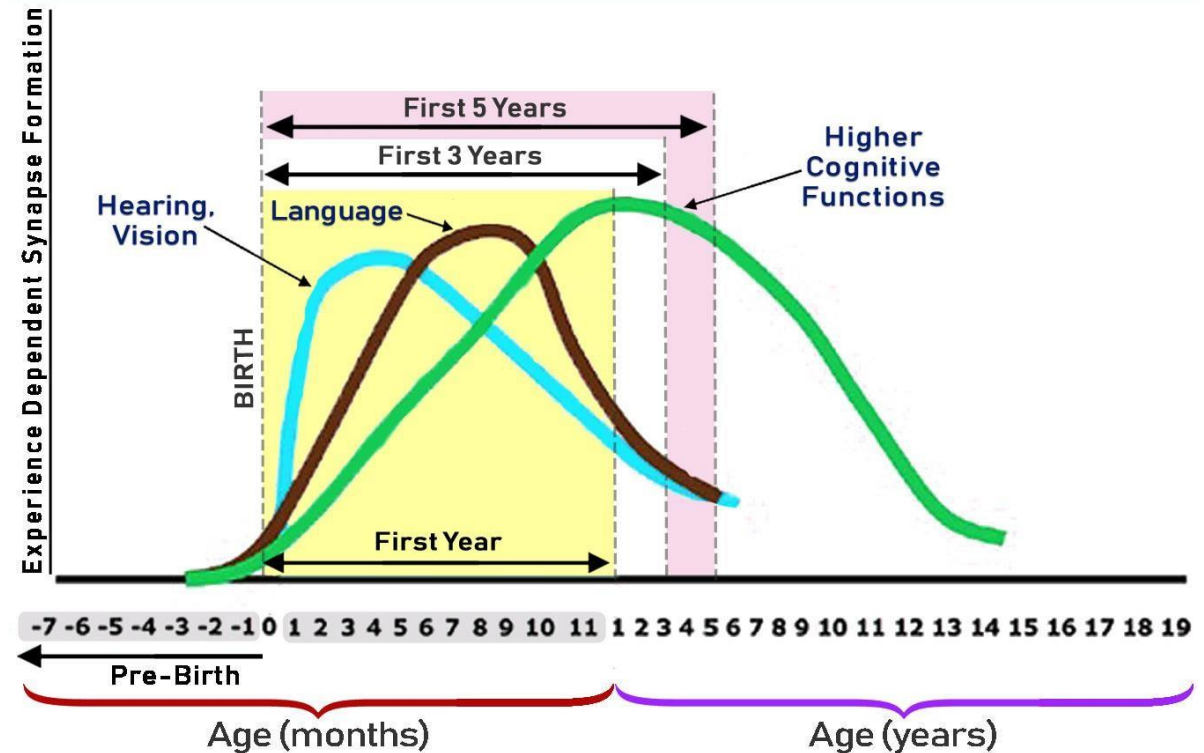


Critical Age Windows for Brain Development



Both structural and functional growth

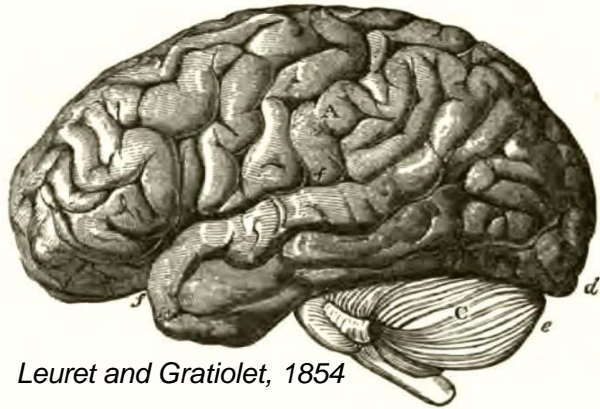
Human Brain Development



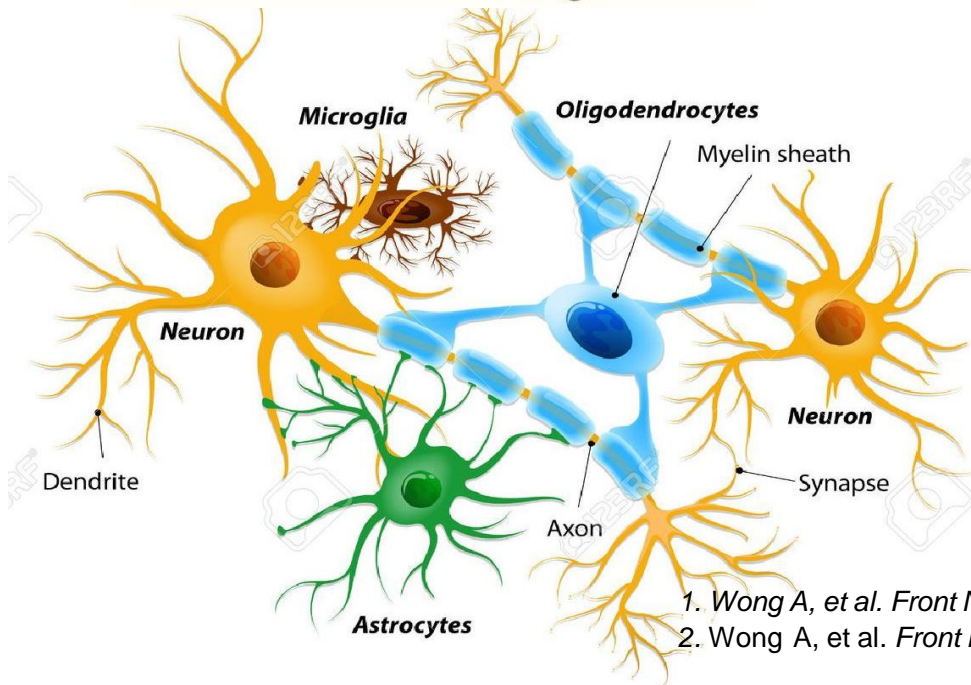
Source: Nelson C.A., In Neurons to Neighborhoods (2000)

Brain structure: the brain is more than neurons

Fig. 68



Leuret and Gratiolet, 1854



80 - 100 billions neurons¹

- **Neuron**: information transmission and processing

100 billions non-neuronal cells

- **Astrocyte**: supports BBB, brain energy, damage repair
- **Oligodendrocyte**: myelination
- **Microglia**: primary immune cells of the brain, guardian of the brain

- 1 quadrillion synapses (1,000,000,000,000,000)
- 100 km of nerves
- 600 km of blood vessels²
- Adult brain comprises 2% of total body weight but consumes 20% of total energy

1. Wong A, et al. *Front Neuroengineering* 2013;6:1–22

2. Wong A, et al. *Front Neuroengineering* 2013;6:1–22;

Brain Lipids

- Among the body organs, the brain is one of the richest in lipids

Water (77-78%)

Lipids (10-12%) ►

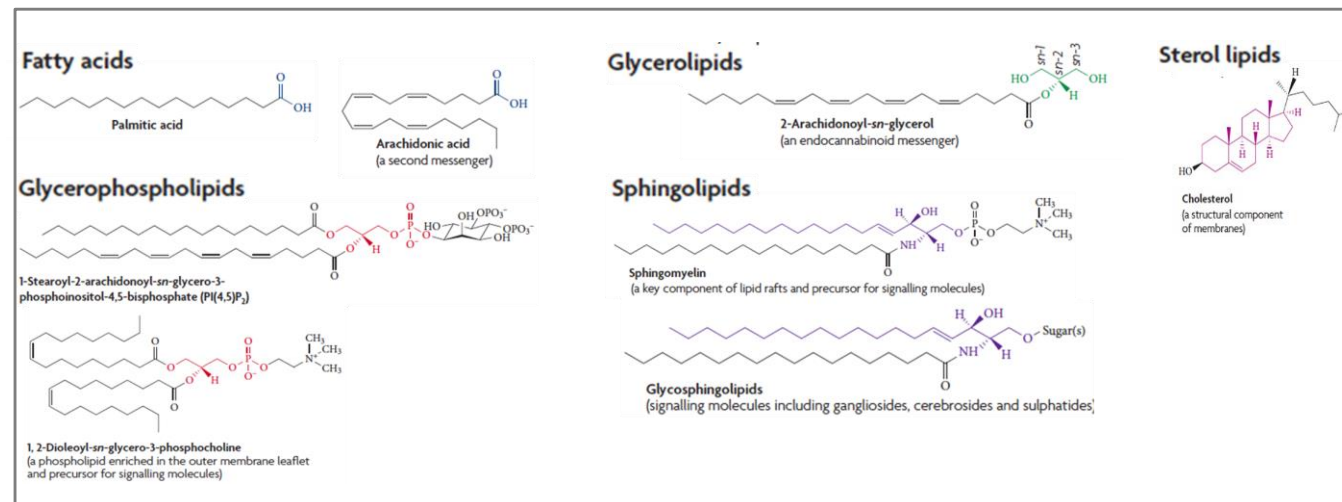
Protein (8%)

Carbohydrate (2%)

Soluble Inorganics (2%)

Inorganic Salts (1%)

Brain Lipids = ~ 100'000 different molecular species, e.g.



Nutrients that influence brain development & functions

Breast Milk & Physiological Benefits:

- Less risk respiratory and gastrointestinal infections
- Less risk for obesity and diabetes
- Less risk for allergies, possibly
- Optimal brain and cognitive development



What are the specific breast milk components that provide the observed benefits?

Nutrients that influence brain development & functions

- DHA → Brain and eye development
- Choline → Mental functioning
- Lutein → Eye and retina
- Iron → Red blood cell
- **Phospholipids (PLs)**
 - PLs includes;
 - Sphingomyelin (SM),
 - Phosphatidylethanolamine (PE),
 - Phosphatidylcholine (PC),
 - Phosphatidylinositol (PI) and
 - Phosphatidylserine (PS)

Macronutrients

Protein^a
Specific fats (eg, LC-PUFAs)^a
Glucose
Micronutrients
Zinc^a
Copper^a
Iodine^a
Iron^a
Selenium
Vitamins and cofactors
B vitamins (B₆, B₁₂)
Vitamin A
Vitamin K
Folate^a
Choline^a

LC-PUFA, long-chain polyunsaturated fatty acid. Reprinted with permission from Georgieff MK, Brunette KE, Tran PV. Early life nutrition and neural plasticity. *Dev Psychopathol.* 2015;27(2):415.

^a Nutrients that meet the principles for demonstrating a critical or sensitive period during development.

Phospholipids - Human milk

In Human Milk fat accounts for ~50% of the total energy contribution, of which 0.2–2.0% are phospholipids^(1, 2)

There are 5 major phospholipids:

- 3 predominant phospholipids (62–80%)⁽¹⁾
 - Phosphatidylethanolamine (PE)
 - Phosphatidylcholine (PC)
 - **Sphingomyelin (SM) a sphingolipid**
- 2 minor phospholipid (12–15%)⁽²⁻⁴⁾
 - Phosphatidylinositol (PI)
 - Phosphatidylserine (PS)

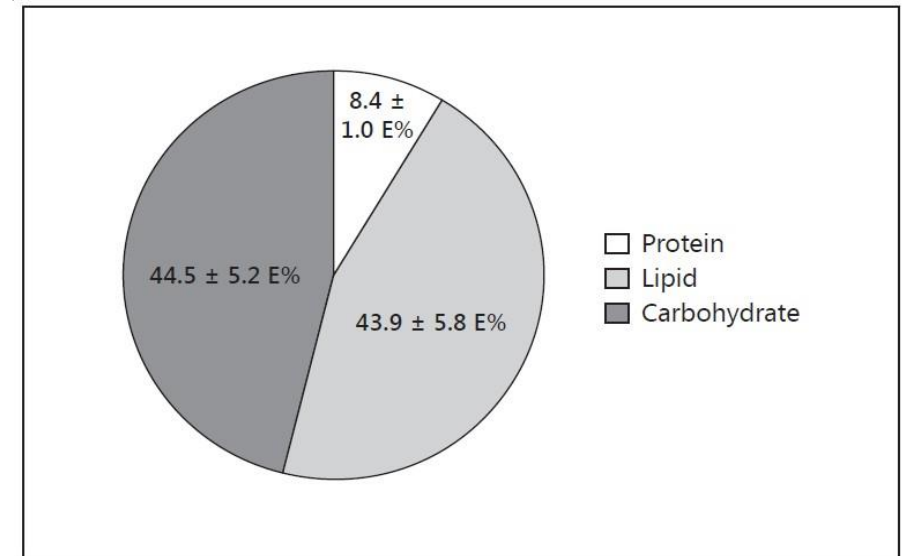
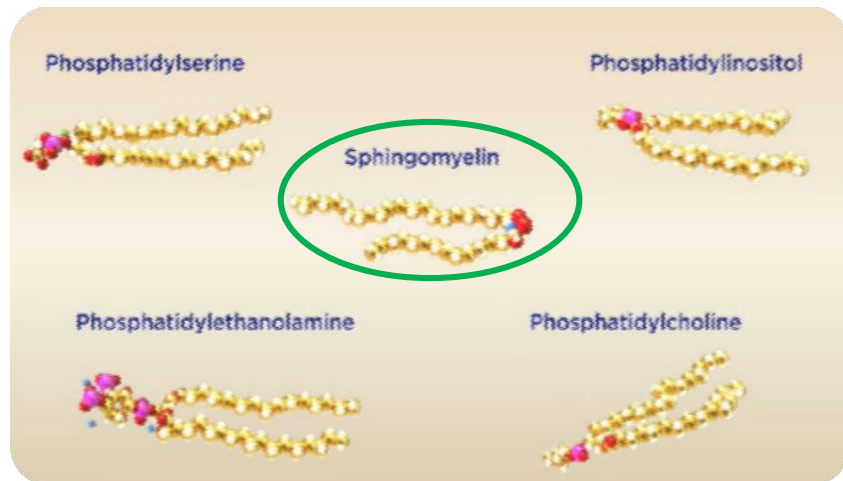


Fig. 1. Contribution of macronutrients to total energy intake in breastfed infants aged 1 month. Drawn from data of Grote et al. [4]. E%, percentage of energy supply.

1. Jansson et al., 1981, 2. Bitman et al., 1984
3. Braun et al., 2010, 4. Garcia et al., 2012

Polar Lipids



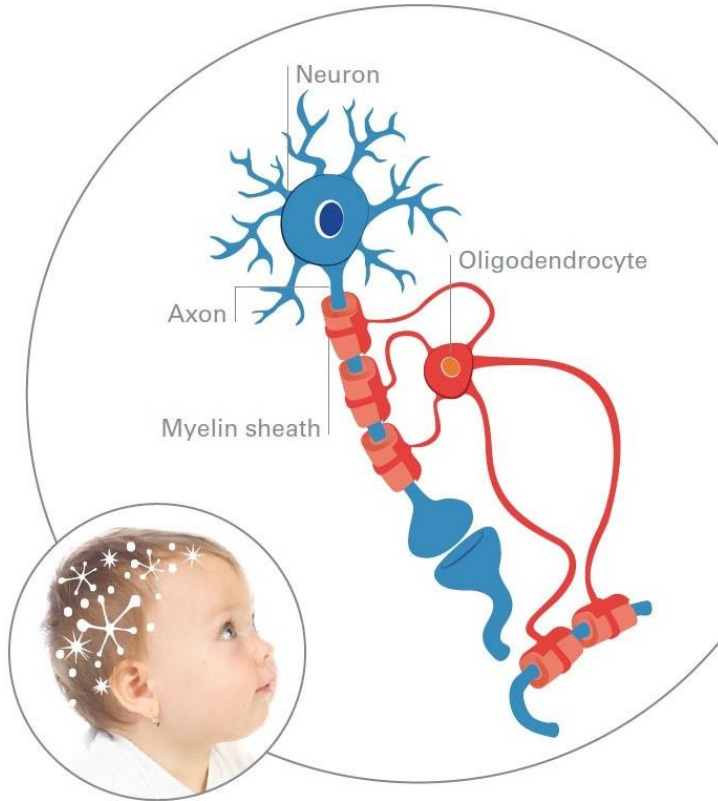
Function of Polar Lipids

- Naturally present in Human Milk
- Structural components of neural tissues
- Neuronal outgrowth and morphology Energy Metabolism
- **Synaptogenesis and synaptic transmission**
- **Myelination**



Brain Connectivity for fast & efficient brain communication

Myelination facilitates information processing

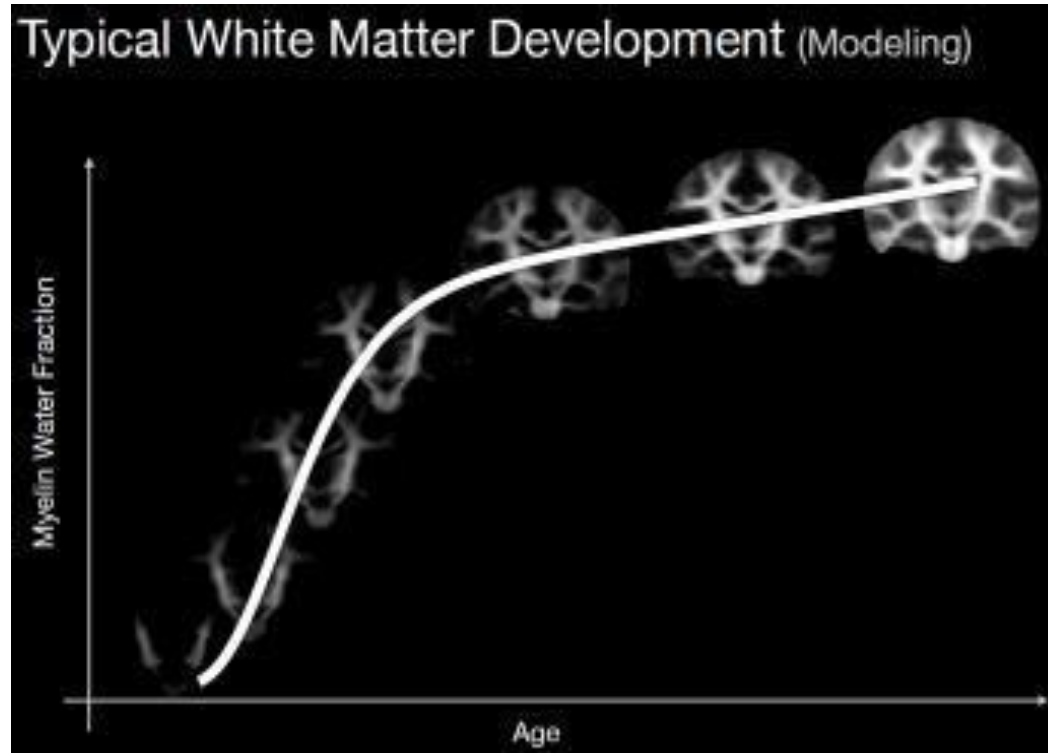


Myelination is a hallmark of neurodevelopment

- Wrapping of nerve fibers (axons) with a lipid-rich sheath (**Sphingomyelin**)
- Ensures fast, efficient & synchronized communication between cells and networks
 - Velocity of unmyelinated axon¹: **5m/sec**
 - Velocity of myelinated axon¹: **100 m/sec**
- Matures alongside cognitive and behavioral development

Myelination & Cognition

Clinical studies demonstrate the link between myelination and cognition, including:

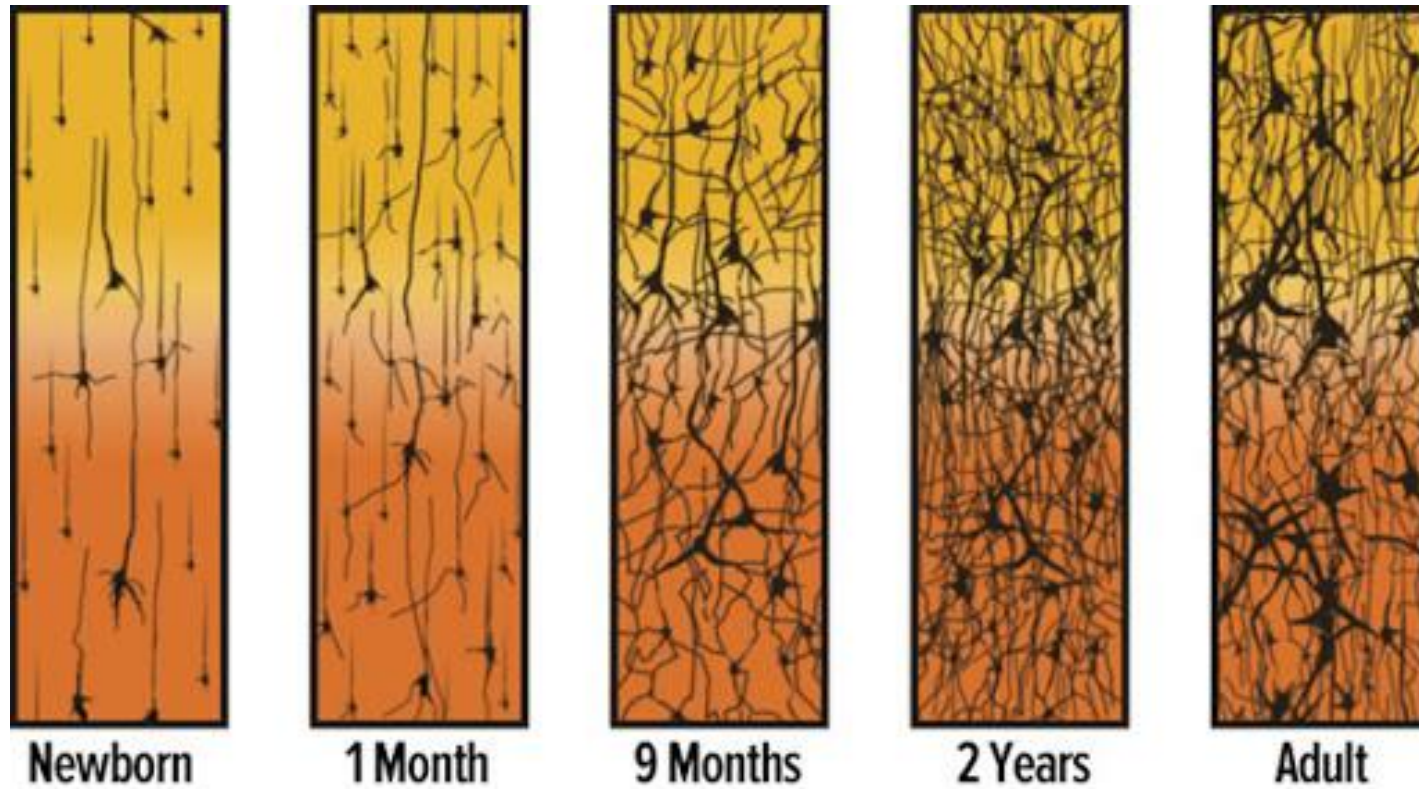


Modeling of myelin development in first 5 years of life & measurable brain marker for myelination.

- general cognitive ability¹
 - language² & reading³
 - working memory⁴
 - processing speed⁵
 - sensory reactivity⁶
- Important skills for learning

¹Schmithorst et al., 2005; Deoni et al., 2015; ²Büchel et al., 2004; O'Muircheartaigh et al., 2013; ³Nagy et al., 2004; Beaulieu et al., 2005; ⁴Nagy et al., 2004; Short et al., 2013; ⁵Turken et al., 2008; Bartzokis et al., 2010; Lu et al., 2013; ⁶Weinstein et al., 2014

Development of Synapse (Intelligence)



The vast majority of synapses are formed during the first 3 years of life and pared down after the age of 10

Adapted from Corel, JL. 1975.

Sphingomyelin (SM)

- 70% to 85% of the Myelin sheath is comprised of lipids.
- One integral component of myelin is the phospholipid sphingomyelin. This nutrient accounts for up to 36% of the total lipid content of breastmilk ²
- Sphingomyelin, a major sphingolipid in human and bovine milks, is an important structural component of neurons, myelin function and supports axonal maturation¹

Sphingomyelin in human milk

Original Research Article

Dynamics of Human Milk Nutrient Composition of Women from Singapore with a Special Focus on Lipids

- Experimental design: observatory, single center, longitudinal trial with human milk collection at 30, 60, and 120 days postpartum from 50 mothers

Variable	Visit (days)	Milk secreted for female infants	Milk secreted for male infants	Combined data	
Sphingomyelin (mg/100 ml)	30	8.07	8.86	8.47	Average = 8.28 mg /100 ml
	60	6.93	8.49	7.71	
	120	7.89	9.37	8.66	
Total phospholipids (mg/100 ml)	30	22.01	24.03	23.02	
	60	18.73	22.83	20.78	
	120	22.02	28.29	24.24	

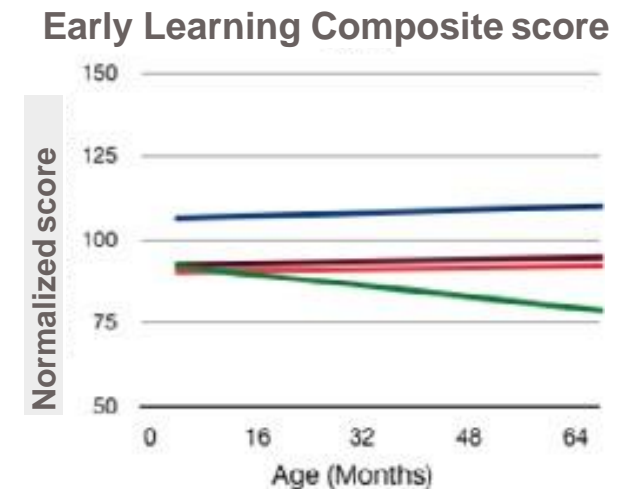
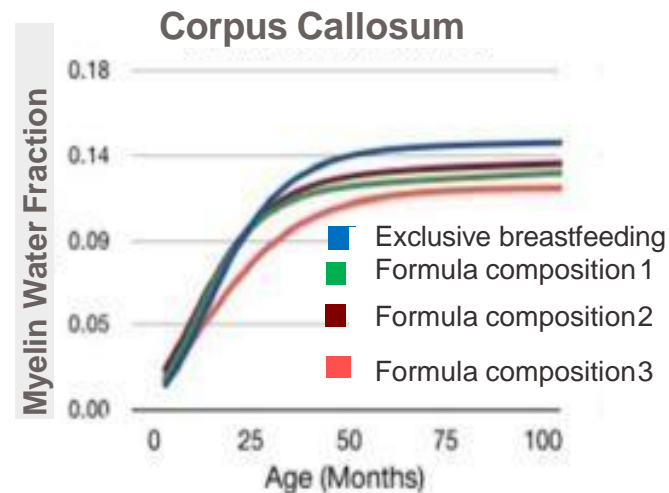
Nutrients and Brain Development

- The positive association between early sphingomyelin intake (0-3 months) and brain development as well as neurocognitive outcomes.

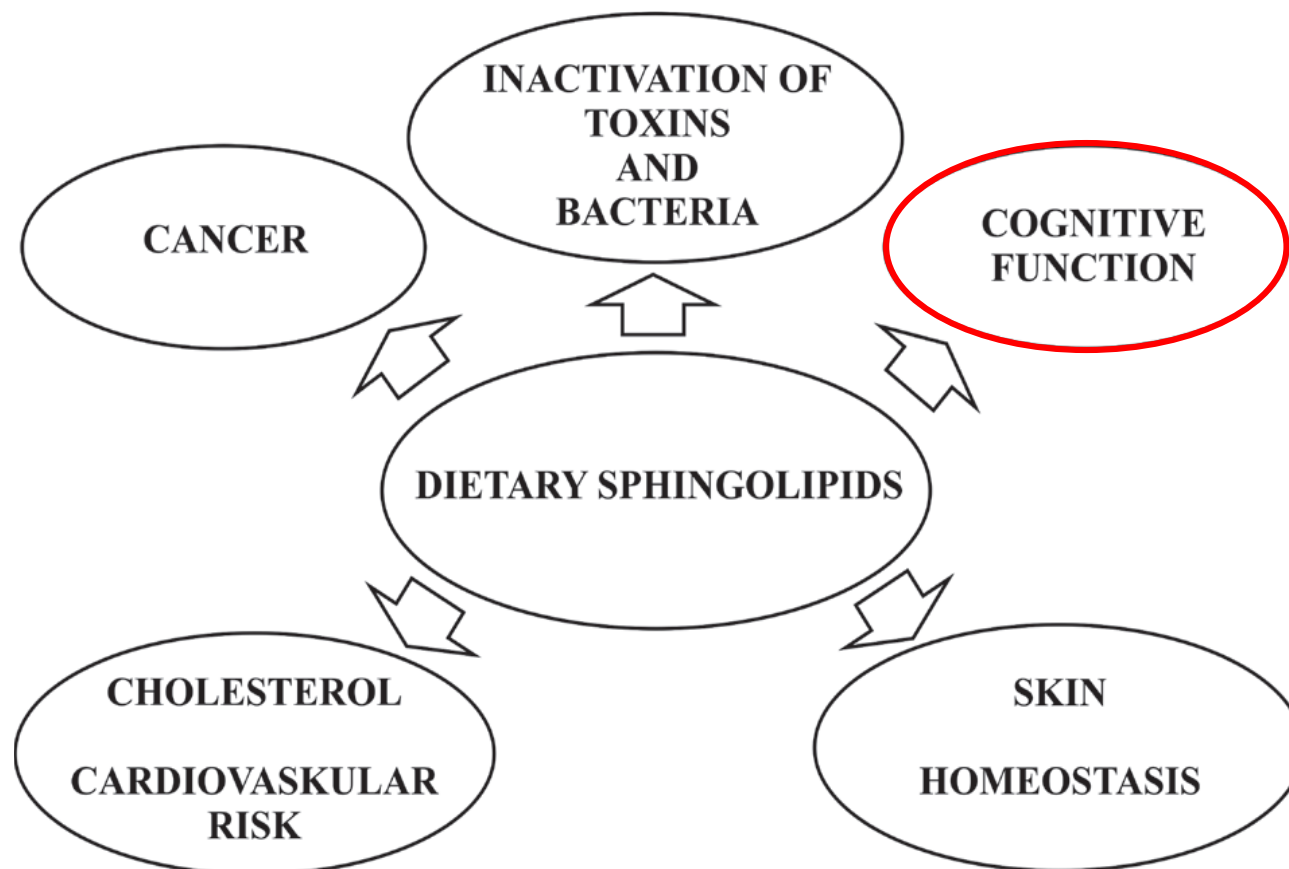


Different composites of infant nutrition appear in different myelin development.

Deoni et al., 2018

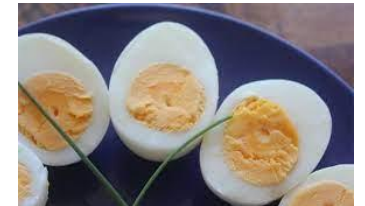


Health benefits of dietary sphingolipids

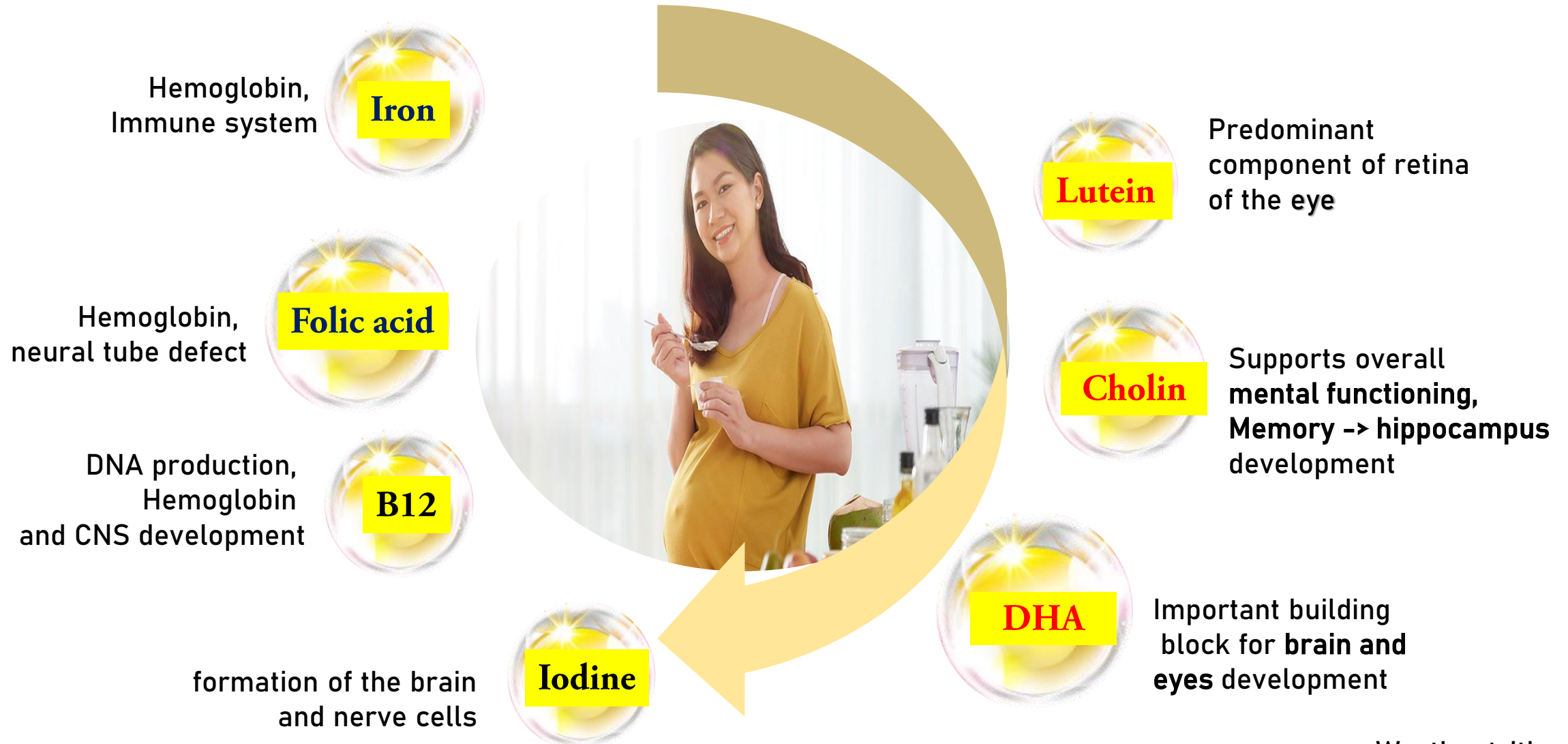


Foods rich in Sphingomyelin

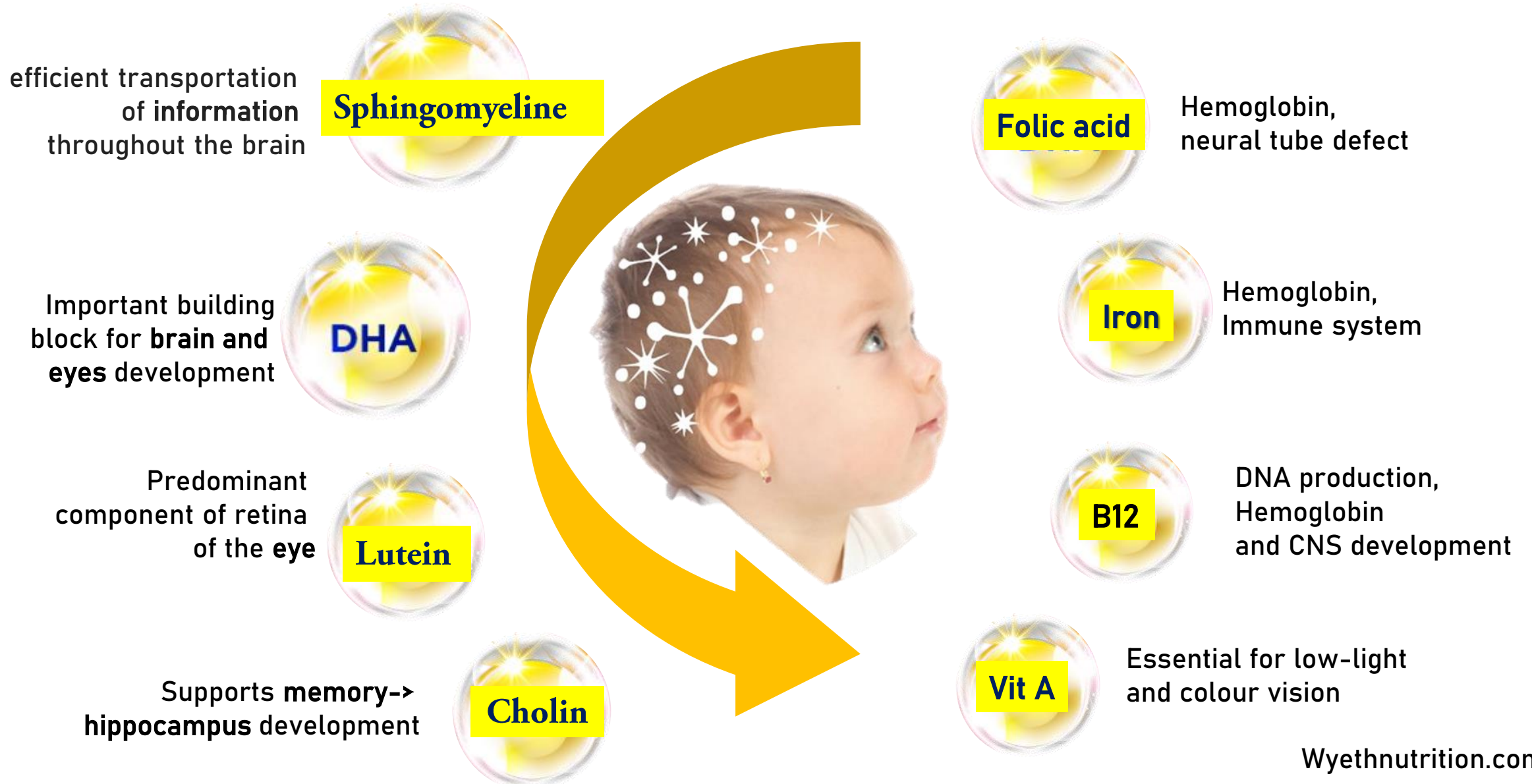
Dietary sources	Content (mg/100g)
Bovine milk, whole	9
Beef	44-69
Egg (yolk)	82
Cottage cheese	139
Mackerel	224
Chicken liver	291



Intake recommendation for pregnancy



Intake recommendation for young children



Nutrient	Role in supporting physical growth and development
Proteins	<ul style="list-style-type: none">• High quality protein alpha-lactalbumin supports growth and developmental processes as well as digestive health• May facilitate the absorption of essential minerals and provides essential amino acids to support growth and development
Carbohydrates	An essential source of energy for growing babies and children
Fats	Main source of energy for babies; necessary for absorption of fat-soluble vitamins; essential for normal growth and maturation of many organ systems
Oligofructose	Supports digestive health as a source of prebiotic fiber
Calcium	Essential for bone mineralization and growth
Iodine	Necessary for the production of hormones that play a role in growth and development; especially important for brain development
Nucleotides	Important for normal development, maturation, and repair of the digestive system and other rapidly growing tissues
Selenium	Plays a role in both the immune and endocrine systems. It is also an antioxidant.
Vitamin E	Antioxidant that helps support immune system function
Vitamin C	Important for immune system function and helps with iron absorption
Zinc	Critical for normal physical growth, neurologic development, and immune system function

Take home messages

- The first years of life are a rapid & dynamic period for brain maturation.
- Most brain processes during that period are primarily focused on connecting the brain, e.g. myelination, synaptogenesis...
- Many factors influence brain growth and myelination; early life nutrition is an important. Especially lipids play an important role in brain, myelin and cognitive development, particularly polar lipids e.g. phospholipids and sphingomyelin
- Sphingomyelin, the major phospholipid in breast milk, is the specific lipid molecule in myelin sheath.

Thank you for your attention!

