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NUTRITION

Nutrition and infant cognitive development

The right nutrients at the right time to support cognitive development.

Introduction

The first years of life are critical for strong foundations. The human brain is the most complex organ in the human body. The nutritional status of a woman at pre-conception, her diet during pregnancy and lactation, and her infant's nutrition all play a role in shaping the growth and development of the infant for later health and optimal cognitive performance.

The role of the environment

Brain development in utero is mainly driven by genetics but the developing brain of the fetus remains vulnerable to the environment (i.e. is subject to epigenetic changes) such as maternal diet, maternal stress and exposure to harmful substances. In contrast, brain development after birth is predominantly driven by experience and infant nutrition. Environmental input through the senses drives the organisation of the brain's neural networks and is the foundation of learning and memory in the first years and beyond.

COGNITIVE DEVELOPMENTAL STAGES IN EARLY LIFE

In Utero

Brain development begins early in pregnancy (Figure 1). The neural plate begins to fold 18 days after conception and, by day 27, the neural tube is formed (O'Rahilly and Muller, 1994). Neurogenesis is mainly a prenatal event and is complete by 20 wk of gestation (Innis, 2014).

In the last trimester of pregnancy, there is a rapid accumulation of specific lipids in the fetal brain, such as the polyunsaturated fatty acid (PUFA) docosahexaenoic acid DHA (Innis, 2014) and gangliosides (Mendez-Otero et al., 2013). Studies showed that DHA and gangliosides can be transferred from the maternal diet to the fetal brain via the placenta (Innis, 2014; Mitchell et al., 2012). During the first 5 months of gestation, the lipid concentration in the fetal brain varies slightly. In the second period of gestation, the concentration of cholesterol, gangliosides and phospholipids rapidly increased in the fetal brain (Svennerholm and Vanier, 1972).

The cerebral cortex is the largest part of the brain and is responsible for conscious experience, voluntary actions, thinking, remembering and feeling. It is the final part of the fetal brain to develop and can only function at a basic level at birth (Dobbing and Sands, 1973). The basic architecture of the brain is established prior to birth (Figure 1) with the number of neurons at birth being roughly the same as in the adult brain (Stiles and Jernigan, 2010).

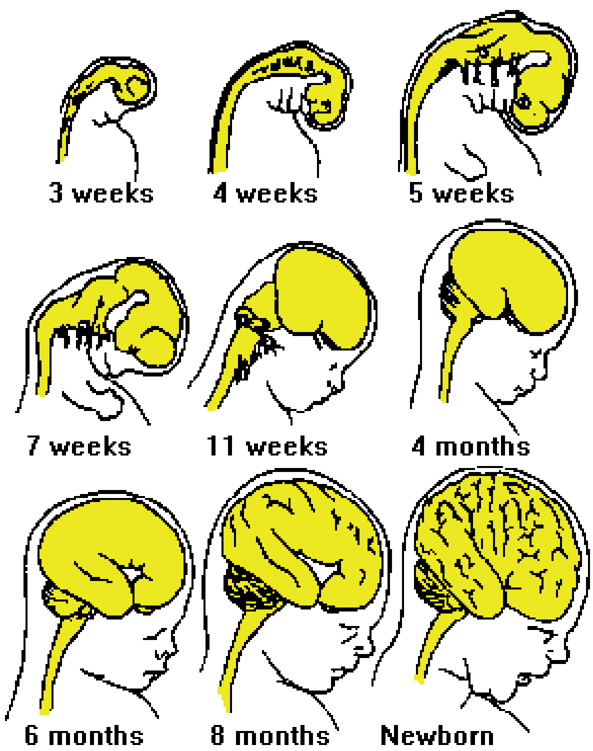

Figure 1: Brain growth and development in the fetus.

Infancy and toddlerhood

Despite the presence of most of the required neurons at birth, the neonatal brain is immature in its organisation and complexity. The brain at birth weighs on average 350g and rapidly grows up to 925 g, or 70% of the adult brain weight, by 1 year of age (Innis, 2014; Figure 2). Amazingly the infant brain at birth is about 10% of the infant body weight, while in contrast the adult brain represents 2% of the adult body weight (Innis, 2014). The structural and functional development, the high metabolism of resting energy (~ 50%) and the metabolic activity of the infant brain makes it extremely sensitive to nutrient and energy deficiencies or inadequacies.

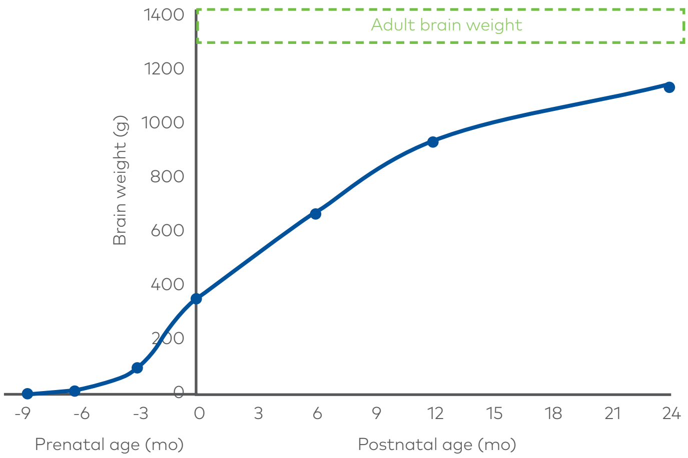

Figure 2: Brain growth in utero and postnatally up to 24 months of age. Adapted from Innis (2014).

Postnatal organisation of the brain (Stiles and Jernigan, 2010) occurs via a complex combination of:

- Synaptogenesis: formation of neuron-neuron connections or synapses which is greatest in the last trimester of pregnancy and the first 2-3 years of life.
- Synaptic pruning: driven by learning resulting in the removal of unused synapses and stabilisation of frequently used synapses. Pruning is one of the primary mechanisms of brain plasticity allowing adaptation to the environment and recovery from injury (Prado and Dewey).
- Myelination: encapsulation of the axons of frequently used neurons with a myelin sheath for a more efficient transduction of the electrical signal along the axon.

The brain contains about 100 billion neurons, from birth and throughout life, that communicate with each other through more than 100 trillion synapses formed with the right stimulation and adequate nutrition (Cowan, 1979).

The proliferation of neural synapses increases logarithmically in the first year of life and peaks at 8 months of age, reaching rates of 40,000 synapses formed per second (Innis, 2014). These synapses are rich in lipids such as DHA (Innis, 2014) and gangliosides (Mendez-Otero et al., 2013), both important for neurite outgrowth, metabolism of neurotransmitters and dendritic complexity. DHA and gangliosides make up 10% and 6-10% of human brain lipids, respectively (Mendez-Otero et al., 2013; Innis, 2014). DHA is largely present in the phospholipids of neural synapses. An increase in cholesterol, gangliosides and phospholipids is also observed in the cerebral cortex during the first 2–3 months of postnatal life, after which their concentrations do not vary significantly (Svennerholm and Vanier, 1972). In the white matter, a steady increase by 3-fold for phospholipids, 5-fold for cholesterol and 70-fold for cerebrosides was observed from birth to 2 years of age. Interestingly in the first couple of years, there is a continuous decrease in phosphatidylcholine, in particular in the white matter, while sphingomyelin concentration increases (Svennerholm and Vanier, 1972).

While neural synapses grow and strengthen in the first year of life, synaptic density in the prefrontal cortex peaks at 4-5 years of age. In postnatal life, the cerebral growth is associated with cognitive function and IQ development (Dobbing and Sands, 1973). Myelination happens largely in the postnatal period up to 8 years of life and is largely responsible for the increased size and weight of the brain (Cowan, 1979).

Different functions of the brain develop over the first 3 years of life (Figure 3). The touch sense develops prenatally and is enriched postnatally through experience and sensory input. In the first 2 months of life, crying is the way the newborn communicates feelings and needs, and the feeding experience creates a special mother-infant bond. Vision is the least mature sense at birth while hearing is well developed. From 2 months of age, babies begin to make sounds and learn how to balance and gain control of their body. Cognition and learning develop from 6 months of age with repeat experiments to learn about their physical and social environment. Social and emotional functions are strengthened by social interactions. From one year of age, the baby's first steps represent the start of complex motor skills which develop all through the second year of life. Receptive language also develops rapidly in the first year of life. By 1 year of age, the hippocampus of toddlers has matured enough for them to recall actions. Cognition, learning, movement, language and social functions keep developing through experience and interactions with the environment throughout the first years of life.

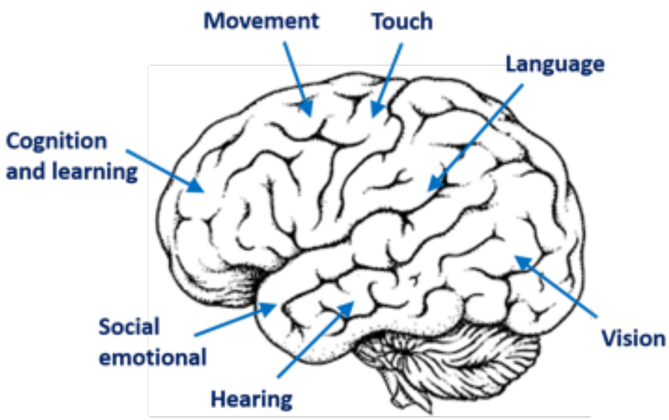

Figure 3: Key brain regions and functions developing in the first 36 months of life.

KEY NUTRIENTS FOR A HEALTHY BRAIN

In Utero

Adequate intake of both macro- and micro-nutrients during pregnancy is vital for normal brain development. Requirements for folate, iron, essential fatty acids, protein, iodine, vitamin B_{12} and choline increase during pregnancy, partly in relation to demands from the developing fetal nervous system. Deficiencies in vitamin B_{12} and folic acid are strongly linked to an increased risk of neural tube defects (O'Rahilly and Muller, 1994). Folic acid plays a role in the synthesis of DNA and RNA, and vitamin B_{12} is necessary for the production of myelin and certain neurotransmitters. Vegan mothers are prone to vitamin B_{12} deficiency as it can only be obtained by eating animal foods, including dairy products.

Many other dietary components such as gangliosides, sialic acid, sphingomyelin, phosphatidylserine, ceramides, DHA and arachidonic acid have been shown to play an important role in brain development, structure and function pre- and post-natally (Cutler and Mattson, 2001; Mendez-Otero et al., 2013; Prado and Dewey, 2014). Maternal dietary supplementation of bovine milk gangliosides has been shown to increase the ganglioside content in fetal brain (Gustavsson et al., 2010).

Infancy and toddlerhood

Breast milk is the optimal sole source of infant nutrition in the first 4-6 months of life, after which time complementary foods should be added to the diet in combination with breastfeeding. Breastfeeding improves the infant's neurodevelopment due to its composition and through the breastfeeding experience. Breast milk fatty acids, vitamin A, some water-soluble vitamins such as vitamin B_6, vitamin B_{12} and folate, iodine and selenium play a role in the infant's neurodevelopment and are affected by maternal nutrition (Innis, 2014). Linoleic acid (LA) in breast milk varies from 7 to 26% and DHA varies 10-fold between <0.1% and >1% of total fatty acids (Innis, 2014). All n-6 and n-3 fatty acids in breast milk derive from maternal dietary fat with little interconversion to PUFAs before secretion into milk. Therefore dietary intake of animal-sourced foods during lactation will greatly determine DHA levels in breast milk (Innis, 2014). Breast milk from vegan and vegetarian lactating women has very low levels of DHA, while milk from lactating women with high fish, seafood or DHA supplements has greater DHA levels.

Breast milk lipids are present in the form of triglyceride globules surrounded by the milk fat globule membrane (MFGM), which contains key complex milk lipids, such as phospholipids, sphingomyelin, gangliosides and cerebrosides, that may help support brain development and maintenance (Mendez-Otero et al., 2015; Gurnida et al., 2012). Human milk oligosaccharides, lactoferrin and gangliosides are sources of sialic acid, an important nutrient for brain development.

Breast milk is low in iron (0.3–0.4 mg/L). However, iron found in breast milk has high bioavailability with 40-50% being absorbed (Lönnerdal, 2017). Due to the role of iron in growth and development and oxygen delivery, iron deficiency in infants and children is associated with impaired cognitive development, gross and fine motor skills, and social and emotional development (Prado and Dewey, 2014; Lönnerdal, 2017).

Iodine is required for the synthesis of thyroid hormones, which are critical for the development of the central nervous system (Prado and Dewey, 2014). Zinc is abundant in the brain and plays a role in the DNA and RNA synthesis and metabolism of macronutrients (Prado and Dewey, 2010).

Medium-chain fatty acids (MCFAs) represent 4-27% of human milk fatty acids (Innis, 2014). During digestion, MCFAs are rapidly absorbed and directed towards ß-oxidation in the liver, resulting in the production of ketones. The developing brain uses ketones as a source of energy and acetyl-CoA (Innis, 2014).

From 4-6 months of age, solid foods are introduced. Vegetable and fruit purees are a good source of vitamins, minerals and fibers, with breast milk or a suitable infant formula as a predominant source of nutrition for the first 12 months of life. After 12 months of age, dairy products such as milk, yoghurt or toddler milks can provide essential amino acids and MFGM complex milk lipids, contributing to the continuous development of the toddler's brain.

Conclusion

Gestation and infancy are foundational periods that are critical for lifetime brain function. Nutritional deficiencies during these periods may result in the infant failing to reach the full potential in cognitive, motor and socioemotional skills. Breast milk contains growth factors, hormones and critical building blocks for brain cells, such as DHA, choline and complex milk lipids from the milk fat globule membrane, contributing to brain development.

As gut maturation occurs simultaneously with brain development in early life, it is likely that the signalling between the gut and the brain, i.e. the gut-brain axis, play a key role in neurodevelopment of the infants.

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CONTACTS

Fonterra Co-operative Group
109 Fanshawe Street
Auckland 1010, New Zealand
+64 9 374 9000

Fonterra (USA) Inc
9525 West Bryn Mawr Ave
Rosemont 60018, Illinois, USA
+1 847 928 1600

Fonterra (Europe) Coöperatie U.A.
Barbara Strozzilaan
Amsterdam 1083HN, Netherlands
+31 20 707 5300

Fonterra (Japan) Limited
20F 2-16-2 Konan Minato-ku
Tokyo 108-0075
+81 3 6737 1800

Fonterra Commercial Trading (Shanghai)
268 Middle Xizang Road
Shanghai 200001, China
+86 21 6133 5999

Fonterra (SEA) Singapore
1 George Street
Singapore 049145
+65 6879 2977

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