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Headline

The critical window of intervening neurodevelopment

Vivian Tsang Nutritionist, MSc, BSc

A recent publication revealed neurogenesis in human hippocampus drops sharply throughout early years to undetectable levels in adults, which challenged the conventional view that adult human brain continues to produce new neurons[1]. This finding also raised the query of how the human brain may continue to evolve throughout life cycle without adding new cells, while the critical period of brain development and maturation falls into early life stages[1].

When looking into brain developmental progress, it is a continuous trend commencing from the 3rd gestational week[2], consisting of a series of neurodevelopmental process from neurogenesis, synaptogenesis, and myelination to synaptic pruning[3]. **This is a sophistically well-organized process where the newly formed neurons migrate to different areas of the brain and become myelinated, which enabling efficient brain connections and building the foundation of high cognitive functions**[3].

The below table illustrated how myelination of the brain coincides with an overall developmental progress in early life.

In the meanwhile, myelination was shown to be associated with cognitive development, with individual researches observed that:

- General cognitive function was correlated with white matter architecture during childhood and adolescence[11]
- White matter maturation in breastfed infants was corresponded to improved cognitive performance in early years, with significantly improved receptive language scores ($p < 0.05$) as compared to formula-fed infants, and positively correlated to breastfeeding duration[12]

(Continued on P.2)

Stages	Key progression of myelination*	Overall developmental progress
In utero	Myelination first begins in the spinal cord at around 12 weeks of gestation, followed by the brain stem[4]	Brain stem that is connected to the spinal cord develops which controls vital functions such as breathing and heart rate[5]
At birth	Myelination progressively increases and proceeds to the medulla[6]	Medulla controls movement of shoulders and head, salivation and swallowing, as well as hearing and equilibrium[7]
2 months	Increases in deep cerebellar white matter[6]	Infants are able to lift their head while lying on their tummy by the end of the 3rd month[8]
4 months	The entire cerebellum appears to be myelinated[6]	
6 months	The entire corpus callosum appears to be myelinated[6]	Corpus callosum is proposed to play an important role in mediating complex behaviors and integrating information[9]
12 months	The brain achieves adult appearance, while ongoing myelination can still be detected[6]	Children are demonstrating fine and gross motor coordinations[10]

**As per T1-weighted images from MRI*

- Structural integrity of white matter pathways was closely related to the speed of cognitive processing abilities[13]

All of the above may hence draw the attention to healthy progression of white matter or myelination, where nutrition is playing an essential role in supporting this process of the growing child. The following summarizes some examples of nutrients that may impact brain development in early life[14]:

Nutrient	Roles of the nutrition in the brain	Impacted brain region
Protein-Energy	Cell proliferation Cell differentiation	Global Cortex Hippocampus
Long-chain polyunsaturated fatty acids e.g. DHA	Myelination Synaptogenesis	Cortex Visual
Iron	Myelination Dopamine synthesis	White matter Striatal-frontal Hippocampal-frontal
Zinc	DNA synthesis Neurotransmitter release	Autonomic nervous system Hippocampus Cerebellum

On top of the above nutrients, **phospholipids are also critical components comprising the brain cell membrane and supporting myelination, these include sphingomyelin (SM), phosphatidylcholine (PC), phosphatidylethanolamine (PE) and phosphatidylserine (PS), where the composition of phospholipids changes notably with age**[15]. At birth, PC predominates at 50% of the brain phospholipids, followed by a substantial decline with SM increases from 2% to 15% by the age of 3 years, showing a consistency with the role of SM in myelin sheath and mature membranes formation[15].

A longitudinal observational study conducted by Deoni *et al* (2017) has shown that early nutrition is associated with myelination and cognition in infants and young children, where neuroimaging and cognitive tests were applied to explore the impact of feeding practice on the longitudinal trajetories of myelination and cognitive development, which oberserved that[16]:

- Exclusively breastfed infants had significantly enhanced myelination as well as higher cognitive scores (within normal ranges), which persisted throughout early childhood, as compared to those exclusively formula-fed for the first 3 months ($p < 0.0001$)
- For formula-fed infants, myelin development differences were found to be associated with individual nutrients, including DHA, AA, folic acid, iron, SM and PC. Among these nutrients, SM and PC appeared to possess the most diffuse influence in the brain

Myelination is an integral part of brain connectivity that supports cognitive and behavioral functioning throughout the neurodevelopmental process, where the potential influencing factors including the roles of nutrition worth more attention in future researches.

References (Latest Science article):
1. Food and Environmental Hygiene Department, HKDOH. Hong Kong population-based food consumption survey 2005-2007 final report. 2010. 2. Agnoli C et al. Nutr Metab Cardiovasc Dis. 2017;27:1037-1052. 3. Hever J. Perm J. 2016;20(3):15-082. 4. Centre for Health Protection, HKDOH. Guidelines for vegetarian diet. Available at: https://www.chp.gov.hk/en/static/90050.html. Accessed on: 19Apr2018. 5. Vesanto M et al. J Acad Nutr. 2016;116(12):1970-1980.

Info Card 2018 Issue 2

Child Immune Health Fact Sheet

An overview of nutrients and foods important for immune health

Distribution of the Info Card by healthcare professionals is welcomed. Electronic copy is available on the WNSC HK website under "WNSC Publications" for download and reprint.

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Latest Science

Guidelines for a nutritionally adequate vegetarian diet

Danica Yau *Accredited Practising Dietitian (DAA), MSc, BSc (Hons)*

While approximately 1% of the Hong Kong population were vegetarian in 2007[1], you may have observed an increasing trend in recent years. **There are often concerns on the nutritional adequacy of vegetarianism** as these diets may omit whole food groups such as meat or dairy[2].

(Continued on P.3)

Guidelines from a recent position paper by the Italian Society of Human Nutrition[2]

- Consume more protein than recommended for the normal population as digestibility of plant protein is relatively lower
- Routinely consume good sources of calcium, iron and zinc, with low phytate and oxalate levels

- Ensure adequate omega-3 fat intake by consuming good sources of α-linolenic acid such as seeds and nuts, while limiting linoleic acid intake such as corn and sunflower oils
- Supplementation of vitamin B_{12} may be needed

Below are some **potential at-risk nutrients and examples of plant-based food sources** that should be encouraged to vegetarians.

Nutrient[2]	Food sources[3]
Protein	Legumes (beans, lentils, peas), nuts, seeds, soy foods such as tofu
Vitamin B_{12}	Fortified foods such as plant milks and cereals
Vitamin D	Fortified plant milks
Calcium	Low-oxalate green leafy vegetables (broccoli, bok choy, cabbage, kale, watercress), calcium-set tofu, almonds, fortified plant milks, sesame seeds, figs
Iron	Legumes (beans, lentils, peas), soybean and soy foods, quinoa, potatoes, dried fruit, seeds (pumpkin, sesame, sunflower)
Zinc	Legumes (beans, lentils, peas), soy foods, nuts, seeds, oats
Omega-3 fats	Seeds (chia, flax), soybeans and soy foods, walnuts, green leafy vegetables

Nutritional gaps can be filled by selecting foods wisely, with the exception of vitamin D and vitamin B_{12} that require extra attention[3]. Individuals should have **ample sunlight exposure for the skin to produce vitamin D**[3]. While eggs and dairy foods are good vitamin B_{12} sources for lacto-ovo-vegetarians[3], **supplementation may be needed for vegans,** where some plant-based nutrition experts have recommended a total supplementation of 2,000 to 2,500 mcg per week[3].

While in Hong Kong, the Department of Health also highlights the importance of **a balanced vegetarian diet with wholegrains and a variety of fruit and vegetables in rainbow colours without overcooking**[4]. The Academy of Nutrition and Dietetics stated **well-planned vegetarian diets with reliable sources of vitamin B_{12} can be nutritionally adequate** and appropriate for all stages of the life cycle, while conferring health benefits in the **prevention and treatment of diseases such as ischemic heart disease, type 2 diabetes, hypertension, cancers and obesity**[5].

References (Headline article):
1. Sorrells SF et al. Nature. 2018;doi:10.1038/nature25975 [Epub ahead of print]. 2. Stiles J and Jernigan TL. Neuropsychol Rev. 2010;20:327-348. 3. Semple BD et al. Prog Neurobiol. 2013;0:1-16. 4. Linderkamp O et al. Int J Prenat Perinat Psycho Med. 2009;21(1):4-16. 5. PubMed Health. Brain Steam. Available at: https://www.ncbi.nlm.nih.gov/pubmedhealth/PMHT0024736/. Accessed on 23Apr2018. 6. Welker KM and Patton A. Semin Neurol. 2012;32:15-28. 7. Ackerman S. Major Structures and Function of the Brain. Discovering Brain. Washington (DC): National Academies Press (US). 1992. 8. Family Health Service. HK DOH. Child Development 3 – One to Three Months. Available at: http://www.fhs.gov.hk/english/health_info/child/15650.html. Accessed on 23Apr2018. 9. Hinkley LBN et al. PLoS ONE. 2012;7(8):e39804. 10. Family Health Service. HK DOH. Child Development 5 – Eight to Twelve Months. Available at: http://www.fhs.gov.hk/english/health_info/child/15697.html. Accessed on 23Apr2018. 11. Schmithorst VJ et al. Hum Brain Mapp. 2005;26(2):139–147. 12. Deoni SCL et al. Neuroimage. 2013;82:77–86. 13. Turken A et al. Neuroimage. 2008;42(2):1032-1044. 14. Georgieff MK et al. Dev Psychopathol. 2015;27(2):411-423. 15. Dawson G. Biochem Biophys Acta. 2015;1851(8):1026-1039. 16. Deoni S et al. Neuroimage. 2017;doi: 10.1016/j.neuroimage.2017.12.056 [Epub ahead of print].

Poll Corner – Do you know?

Question: What is the top rejected food category by Hong Kong children with picky eating habit?

A. Rice B. Water C. Meat D. Vegetables

Interested in knowing more?

Read the WNSC HK Bulletin 2018 Issue 1 to discover more about:

- Local Research – Studying Impact of Nutrition on Growth (SING) Study

Available at: https://hongkong.wyethnutritionsc.org/en/publications/bulletin/2018-issue-1

Scan to view more:

Answer: D

Reference: Lee A et al. BMJ Open. 2017;7:e018380.

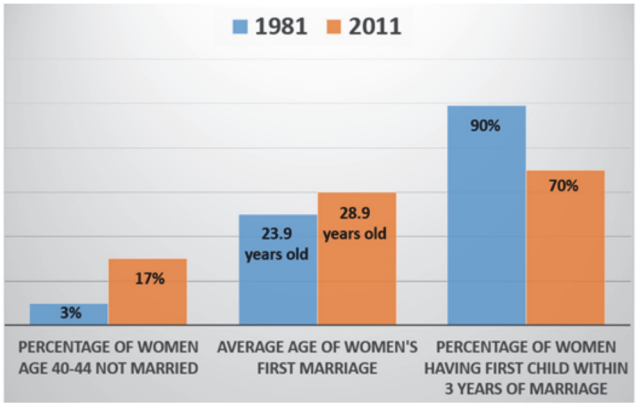
Monthly Health Focus

Infertility Awareness Week - The role of dietary intervention

Peter Chiu *Registered Dietitian (Canada), MHSc (Community Nutrition), BSc, eMBA*

This past April 22-28 was the National Infertility Awareness Week (NIAW) in the United States[1]. The NIAW movement started in 1989 by a US non-profit organization aimed to reduce the stigma surrounding reproductive health issues and to empower those struggling to build a family due to infertility[1,2]. **In Hong Kong, infertility affects 1 in every 6 couples**[3].

Over the past three decades, due to various socio-economic reasons, **the fertility trend in Hong Kong has generally been on a decline**[4,5]. Likewise, a trend of **postponing marriage and childbearing** was observed[4,5]:



(Source: *Public Engagement Exercise on Population Policy 2013-2014. Chapter 5*)

(Continued on P.4)

While the delay in childbearing age may be suggestive for the decline in a women's fertility, **epidemiological data shows that both male and female are each accountable** for approximately 30% of subfertility problems, while the remaining 40% are joint or unexplainable causes[3,5].

Promoting a proper diet and normal body weight, among other healthy lifestyle factors remain some of the common recommendations complementing infertility management[3].

However, nutrition research in this domain has mostly been focusing on the correlation of specific nutrients and food groups, while **data looking at the holistic role of dietary patterns on fertility has generally been scarce**[6,7]. Until recently, a study conducted in Athens, Greece, looking at the association of the Mediterranean dietary pattern on *In-vitro* Fertilization (IVF) success rate was published in the journal - *Human Reproduction*[6]. Results concluded that among non-obese women <35 years, higher adherence to the Mediterranean diet was associated with ~2.7 time higher chance of achieving pregnancy and live birth undergoing IVF[6]. Although the current literature may be very limited, and far from identifying a perfect 'fertility diet', results from this study, among others, may still provide implications strengthening the **importance of dietary and lifestyle interventions as some of the most promising strategies in managing infertility**[6,7].

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1. National Infertility Awareness Week. About NIAW. Available at: https://infertilityawareness.org/about-niaw/. Accessed on 24Apr2018. 2. RESOLVE: The National Infertility Association. Home. Available at: https://resolve.org/. Accessed on 24Apr2018. 3. The Family Planning Association of Hong Kong. Subfertility. Available at: https://www.famplan.org.hk/en/health-info/subfertility. Accessed on 24Apr2018. 4. Census and Statistics Department. The Fertility Trend in Hong Kong, 1981 to 2014. Available at: https://www.statistics.gov.hk/pub/B71512FB2015XXXXB0100.pdf. Accessed on 24Apr2018. 5. Public Engagement Exercise on Population Policy 2013-2014. Chapter 5 - Fostering a Supportive Environment for our People to Form and Raise Families. Available at: https://www.hkpopulation.gov.hk/public_engagement/pdf/chapter5_eng.pdf. Accessed on 24Apr2018. 6. Karayiannis D et al. Hum Reprod. 2018;33(3):494-502. 7. Fontana R et al Nutrients. 2016;8(2):87.

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Allergy Q&As – What is the latest suggestion on weaning and prevention of food allergy for Asian babies?

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Featured News

Maternal DHA status - Its role in programming future generations

***Emily Tai** PhD, Mphil, MSc, BSc (Hons)*

DHA is a principal element of cell membranes. Its intake during pregnancy and lactation contributes to brain and eye development of the fetuses and breastfed infants[1,2].

Recent science additionally suggested a favorable programming effect that interferes body composition in early childhood[3]. Children of the Kansas DHA Outcomes Study (KUDOS), whose mothers were provided with 600 mg algae oil DHA or placebo during pregnancy, were followed to monitor their growth and development[3,4]. DHA supplementation strongly impact maternal DHA status. The maternal red blood cell (RBC) phospholipid (PL) DHA increased 81% from enrollment to delivery in the intervention group whereas the value was 6% in the placebo group[3]. More importantly, **the increase in intrauterine DHA exposure was correlated to greater child fat-free mass at 5 years of age** ($p = 0.0088$)[3]. This observation is analogous to those from a previous research that linked maternal plasma DHA with higher lean mass in the children[5].

The influences of maternal DHA supplementation on child development have also been revealed. Infants born to mothers participated in the KUDOS cohort were tested on visual habituation at 4, 6 and 9 months[6]. **Consistent levels of sustained attention (SA), a high-quality attentional state closely associated with stimulus processing, were maintained throughout the first year among infants of supplemented mothers** whereas SA declined in the placebo group, although no impact on look duration or habituation parameters was noted[6]. The maintenance of consistent levels of SA throughout the first year may program later development because this profile has been associated with higher preschool vocabulary and intelligence scores at 4 years[6,7].

Following the advice from European experts helps provide mothers with proper DHA intake to support desirable health outcomes,

- Additional supply of ≥200 mg DHA daily should be achieved during pregnancy[8]
- Higher DHA intake (600 – 800 mg daily) may offer greater protection versus early preterm birth[8]

References:
1. Koletzko B et al. J Perinat Med. 2008;36(1):5-14. 2. European Commission.EU register of nutrition and health claims made on foods. Available at: http://ec.europa.eu/food/safety/labelling_nutrition/claims/register/public/?event=register.home. Accessed on 25Apr2018. 3. Hidaka BH et al. Am J Clin Nutr. 2018;107(1):35-42. 4. Carlson SE et al. Am J Clin Nutr. 2013;97(4):808-815. 5. Moon RJ et al. J Clin Endocrinol Metab. 2013;98(1):299-307. 6. Colombo J et al. Pediatr Res. 2016;80(5):656-662. 7. Colombo J et al. Infant pathways to language: Methods, models and research directions. New York, NY, US: Psychology Press; 2009. P. 143-167 . 8. Koletzko B. Ann Nutr Metab. 2014;65(1):49-80.