Young Brain – Big Appetite

Weili Lin

Biomedical Research Imaging Center, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

The first few years of life represent one of the most dynamic and critical time periods in brain development. The total brain volume of a 2-week-old is roughly 35% of the adult brain volume, and it increases by ~101% and 15% during the first and second year of life, respectively. By the age of 2 years, brain volume reaches about 80% of the adult brain volume. In addition to the rapid increase in brain size, critical brain functions also emerge during the first years of life and continue to mature into adulthood. Underlying these morphological changes and functional development are complex cellular and molecular processes, which require an extraordinarily high demand for energy (food) to ensure adequate maturation of our brains during early infancy. Although the “young brain” is relatively small when compared to the entire body, it has a “big appetite” for energy (food) to support these cellular and physiological processes underpinning the rapid increase in brain size and the emergence of brain functions. Specifically, an infant brain consumes about 60–75% of the total daily intake of calories, which is in marked contrast to an adult brain consuming roughly 20–25% of the total energy intake. Therefore, it is not surprising that malnutrition during pregnancy as well as in early postnatal life could lead to a cascade of negative impacts on the long-term health of our brains.

Dr. Steiner’s chapter offers insights into the underlying cellular and physiological processes of brain structural and functional development. The critical metabolic pathways to meet

the energy demands for supporting these important developments are introduced. In particular, in order to meet the extraordinarily high energy demands to support early brain development, glucose and ketone bodies work synergistically to support not only the energetic, but also anabolic demands and provide the carbon backbones used to synthesize lipids, nucleic acid, and cholesterol, which are indispensable building blocks of neuronal cell proliferation during early brain development.

Following Dr. Steiner’s chapter, Dr. Cheatham’s chapter describes how different nutrients, providing energy to the brain, may play different roles during preconception, pregnancy, and after birth. Reviewing the effects of different nutrients at different stages is clearly important since cellular processes of early brain development vary throughout pregnancy and postnatal life. Thus, important nutrients are likely to vary depending on the stage of brain development. The importance of 6 nutrients that have been studied extensively with respect to maternal nutrition and subsequent offspring brain development, namely folate, iodine, iron, vitamin D, choline, and docosahexaenoic acid (DHA; 22:6n-3), are comprehensively discussed. More importantly, the timing, doses, and duration of different nutrients along with the sequelae of nutrient deficiencies on brain development are provided. For example, vitamin D deficiency during pregnancy could potentially lead to morphological differences in brain size. Children

of mothers who were diagnosed with anemia in the first 30 weeks of pregnancy exhibited a higher incidence of autism spectrum disorder, attention deficit hyperactivity disorder, and intellectual disability relative to children of mothers who were diagnosed later in pregnancy, or not diagnosed. Postnatally, iron deficiency at 9 months of age has been related to concurrent delays in memory and attention development. Together, it should be noted that the effects of nutrients on brain development depend on timing, dose, and duration.

In addition to the “big” appetite for energy/food to support early brain development, a young brain also exhibits a craving for learning. Learning through interacting with the external environment is one of the keys to ensuring proper maturation of cognition. Similar to the importance of tailoring nutrients at different stages of early brain development, brain functional development is also age dependent, with the basic brain functions maturing earlier, while higher-order brain functions follow a protracted developmental process. The chapter by Colombo et al. links the notion of fetal/neonatal programming – a common concept within the nutrition field – to the notion of “critical period” of brain development, a topic that has been extensively studied in biobehavioral and developmental sciences. Specifically, the history of and criteria for critical periods are first provided with important distinctions between “critical” and “sensitive” periods. Subsequently, the links between the fetal/neonatal programming within the framework of critical periods and developmental science are discussed. Finally, building on the understanding of the critical/sensitive periods, the implications of these time periods for the design of future preclinical research and clinical trials are offered.

An infant spends most of the time sleeping during early infancy; that is, a “young brain” has a “big appetite” for sleep. Therefore, it is not surprising that the quality of sleep can greatly impact the development of the young brain. Dr. Jiang’s chapter first reviews the architectural organization of sleep, including non-rapid eye movement (NREM) sleep, rapid eye movement (REM) sleep, and wakefulness. The transition from

early infancy to a more adult-like sleep pattern is also discussed. In particular, early childhood could be an important time period to establish a healthy sleep rhythm. Interestingly, through a systematical review of 102 studies with 167,886 children aged 0–3 years from 26 different countries across the world, Dr. Jiang’s team revealed an apparent cross-cultural disparity in the sleep parameters in early childhood. More importantly, it appears that parental sleep-setting behaviors may be one of the main contributors to the observed cultural disparity of the sleep parameters, underscoring the potential parental influence on establishing a healthy sleep pattern for children. The potential links between sleep and cognition are extensively reviewed by Dr. Jiang. It has been widely implicated that sleep plays a critical role in memory functions of the adult brain. In contrast, current evidence on the links between memory functions and sleep in infants is inconclusive and warrants additional studies. Furthermore, sleep appears to also play a key role in mental health, psychosocial adjustment, general cognitive development, and language development. Imaging studies further elucidate the potential interplay between sleep and brain structures, although more studies are needed to further determine the neural substrates underpinning the observed relations.

In summary, the first years of life, undoubtedly, are an important time period of brain development. While the “young brain” is relatively small when compared to the entire body, it has a “big appetite” for food, learning, and sleep. The chapters included in this volume provide some insights into the complex cellular processes and the neural substrates underpinning the highly dynamic processes of early brain development. Nevertheless, we have only seen the tip of the iceberg of these complex processes and their implications for how one could potentially enrich the development of a healthy brain. Future studies integrating noninvasive imaging methods, such as magnetic resonance imaging, during early infancy could further shed new light on how these complex factors work synergistically to improve the total health of our brain.