Brain Imaging and Human Nutrition: Which Measures to Use in Intervention Studies?

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Brain Imaging and Human Nutrition: Which Measures to Use in Intervention Studies?[1,2]

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ABSTRACT

Throughout the life span, the brain is a metabolically highly active organ that uses a large proportion of total nutrient and energy intake. Furthermore, the development and repair of neural tissue depend on the proper intake of essential structural nutrients, minerals, and vitamins. Therefore, what we eat, or refrain from eating, may have an important impact on our cognitive ability and mental performance. Two of the key areas in which diet is thought to play an important role are in optimizing neurodevelopment in children and in preventing neurodegeneration and cognitive decline during aging. From early development to aging, brain imaging can detect structural, functional, and metabolic changes in humans and modifications due to altered nutrition or to additional nutritional supplementation. Inclusion of imaging measures in clinical studies can increase understanding with regard to the modification of brain structure, metabolism, and functional endpoints and may provide early sensitive measures of long-term effects. In this symposium, the utility of existing brain imaging technologies to assess the effects of nutritional intervention in humans is described. Examples of current research showing the utility of these markers are reviewed. *Adv. Nutr. 4: 554–556, 2013.*

Introduction

The current article summarizes the research presented at the symposium "Brain Imaging and Human Nutrition: Which Measures to Use in Intervention Studies," held on April 23 at the 2013 Experimental Biology meeting in Boston and organized by the European Branch of the International Life Science Institute (ILSI Europe) in collaboration with the American Society for Nutrition. A more extensive review on the topic of the symposium, including references of this summary, can be found elsewhere (1).

The importance of understanding brain function is illustrated by the magnitude of the economic and societal burden related to brain dysfunction. A recent study by the European Brain Counsel and European College of Neuropsychopharmacology indicated that 38.2% of the European Union population, or 168 million people, suffer from a mental disorder. This was estimated to cost €798 billion in 2010, more than cancer, cardiovascular disease, and diabetes put together. Many studies suggest that nutrition can play a role in improving brain function throughout the life span. However, progress in this field is challenged by methodologic and practical constraints, including the feasibility of conducting intervention studies with a long duration and the collection of data regarding mechanisms of action in humans. The current expert group was established to review whether brain imaging biomarkers can provide sensitive measures that predict long-term effects earlier, thereby shortening the required trial duration, and to explore how neuroimaging measures may help improve our understanding of mode of action as part of nutritional interventions.

Understanding Brain Imaging and Translating Outcomes: Structural and Functional Magnetic Resonance Techniques in Early Development

Stephane V. Sizonenko, MD, PhD, School of Medicine and University Hospital, Geneva. By means of different MRI techniques and postprocessing analysis, cerebral macrostructure (3D-volumetry), microstructure (diffusion MRI),

[1] This article is a summary of the symposium "Brain Imaging and Human Nutrition: Which Measures to Use in Intervention Studies?" held April 24, 2013, at the ASN Scientific Sessions and Annual Meeting at Experimental Biology 2013 in Boston, MA. The symposium was sponsored by the American Society for Nutrition and supported in part by the Nutrition and Mental Performance Task Force of the International Life Sciences Institute, European Branch.

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metabolism [magnetic resonance spectroscopy (MRS)],[7] and function (fMRI) can be acquired, analyzed, and evaluated in regard to development and aging and in intervention studies, including nutrition.

Noninvasive MRI was a breakthrough to assess the human brain structure and function in vivo during development. It is now clear that preterm infants or newborns showing intrauterine growth restriction (nutritional deficits) show changes in brain development trajectories seen with MRI that are correlated to motor and/or cognitive deficits later in life. In this high-risk population, altered white and gray matter development is seen at the macro- and microstructural amounts and is more prominent with injury. Similarly, MRS measures changes in the brain metabolic status that show neuronal, astrocyte, and axonal maturation and is able to measure injury-induced changes. At this stage, fMRI in newborns and early in childhood remains at the experimental amount but can show the functional changes in relation to psychomotor development and in regard to injury or early development care intervention, including nutrition.

Structural and cognitive outcomes at adolescence in neurologically normal preterm infants in a randomized perinatal feeding trial have been reported (2). Compared with a standard diet, a high-nutrient diet was associated with larger caudate nuclei volumes and higher verbal IQ in boys (3). In a later report, maternal breast milk was associated with greater white matter volume and with higher verbal IQ in boys (4).

A powerful feature of the MRI multimodal approach is its translational research capabilities. Applied to animal models of developmental brain injury, it has allowed improved correlation of the changes seen in human imaging with the neuropathological changes seen in the animal. Furthermore, this imaging approach has been used to test for neuroprotective strategies in injury, including nutritional intervention.

Therefore, we believe that the use of advanced MRI for the study of early alteration of brain development and future therapeutic interventions, including nutritional trials, represents a major research tool.

Applying Structural Magnetic Resonance Brain Imaging in Nutrition Studies: Uses and Limitations—Life Span Perspectives

Kristine B. Walhovd, PhD, University of Oslo. A number of changes in brain structure and cognition take place across the life span. Such changes as follows: 1) continuous throughout life, 2) of an individual nature, 3) coordinated and regionally variable, 4) often of a dimensional rather than categorical nature, and 5) influenced by both endo- and exogenous factors. For instance, whereas overall cortical thickness tends to show a linear decline with age and from an early age, white matter volume shows prolonged increase followed by accelerated decline in older age. Whereas age is a major explanatory variable, there are marked individual differences transcending age groups: e.g., temporal atrophy differences can be found not only in dementia but also in cognitively stable individuals. Changes can be influenced by a number of factors, including nutrition.

Nutrition studies using imaging techniques have been used to relate natural variation in dietary intake or nutritional markers to brain measures or to study the effect of nutritional interventions, as in randomized controlled trials. There are relatively few examples of the latter. MRI nutrition studies have tended to focus on extremes of the age spectrum, studying how nutrition may enhance brain development or protect the brain from age-associated atrophy or disease. Examples of both types of studies were presented, including data on a dietary intervention and percentage of maternal breast milk consumed in prematurely born infants (3,4) and levels of long-chain PUFAs as well as B-vitamin and folate supplementation in aging and mild cognitive impairment (5,6). Effects have been identified in different brain regions.

MRI does not directly inform on the molecular mechanisms underlying the observed changes. Animal and human studies using imaging and histologic techniques are needed, along with additional longitudinal studies to inform on a possible chain of causation. Preliminary data were presented on longitudinal brain aging changes in relation to nutrition, regional cortical thinning and BMI, cholesterol, DHA, and vitamin D.

Individual variation across the life span necessitates large or age-homogenous samples. Regional variance in effects implies inclusion of multiple neuroanatomic regions. Furthermore, because effects have been found by different imaging modalities, a multimodal approach is preferred. Future longitudinal studies have the potential to reveal how different nutritional factors may interact with each other and with individual characteristics.

Understanding Functional Brain Imaging and Translating Outcomes: fMRI, Positron Emission Tomography–^{18}F-Fluoro-2-deoxy-D-glucose, Electroencephalography, and Magnetoencephalography

Claudio Babiloni, PhD, University of Rome "La Sapienza," and IRCCS San Raffaele Pisana. Enhancement of the BOLD signal measured via fMRI approximately reflects the increase in oxygenated hemoglobin in the blood accompanying local neural activity. In past years, fMRI has been applied to identify a food-related functional recruitment in both sensory processing and emotion-related structures, including prefrontal, orbitofrontal temporal, cingulate, amygdala, and insula. On the other hand, few fMRI studies have tried to determine the role of nutrition on brain function.

Electroencephalography (EEG) and magnetoencephalography (MEG) measure brain electrical and magnetic activity recorded from scalp electrodes and extracranial sensors, respectively. EEG and MEG signals have the highest temporal resolution compared with all current brain imaging

[7] Abbreviations used: EEG, electroencephalography; MEG, magnetoencephalography; MRS, magnetic resonance spectroscopy; PET, positron emission tomography.

techniques (<1 ms), whereas spatial resolution is of centimeters with EEG and of millimeters to a few centimeters with MEG. EEG is more diffuse and less expensive (~$65,000) than MEG (several times the cost of EEG).

Many articles on EEG report resting state, evoked potential or magnetic field, and event-related potential or magnetic field, which capture short-term (acute) and long-term (chronic) effects of nutrients on brain activity in healthy infants, children, and adults. MEG techniques are used sporadically in nutritional studies.

Positron emission tomography (PET) enables in vivo visualization of regional cerebral glucose metabolism, blood flow, and neurotransmitter metabolism in a variety of physiologic conditions and in neurological or psychiatric disorders. PET scanning is useful for understanding adult brain function, but the use of short-life radioactive compounds poses a strict ethical limitation to the number of PET scan examinations, especially in healthy children and adolescents.

The number of nutrition studies using PET techniques is limited. This is not surprising due to the high cost of the technology, its limited availability, and the short half-life of the radiotracers. Due to the high radiation, most of the studies available either examine the effect of nutrition in the adult brain or are clinical studies in children.

Overall Conclusions

Brain imaging markers can reliably reflect neurostructural, neurophysiologic, neurochemical, and functional cerebral changes occurring over the life span and potentially after nutritional interventions. Furthermore, these markers may increase the understanding of changes in brain and cognitive function associated with nutritional interventions and can be used as surrogate instrumental endpoints in intervention studies. They are also suitable to construct translational models to be used in both animals and humans to validate preclinical research. However, these markers cannot be considered as a substitute for clinical endpoints in terms of cognitive or behavioral response to a task or challenge.

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