Conference Summary

The emerging field of cognition and nutrition explores ways that nutrition can enhance brain structure and physiology, cognitive development, and learning and memory across the lifespan. The right nutrition at the right time is key to cognitive development early in life and to the protection or enhancement of cognition in later years.

Dr Gary Fanjiang, Abbott Nutrition Divisional Vice President of Scientific and Medical Affairs, said in his opening remarks that nutrition and cognition are inextricably linked from preconception to old age. Cognitive development is especially critical in infants and children because the infant's brain triples in weight during the first 3 years of life. Specific nutrients support this rapid brain development. Investigations of the roles of lutein, docosahexaenoic acid (DHA), arachidonic acid, iron, folic acid, choline, and iodine in early neural development and cognition in the preconception, fetal and infant stages, and early childhood are important strategies toward favorable long-term health outcomes. A growing body of evidence also suggests the potential for dietary lutein, DHA, flavonoids, and extracts from botanical sources along with physical activity and exercise for preserving and enhancing cognitive function during aging, while reducing the risk for cognitive impairment, Alzheimer's disease, and other dementias.

The participants of the 114th Abbott Nutrition Research Conference described translational and clinical research that will help identify those nutrients that influence cognition across the lifecycle, including the type, form, dose, and timing of intake, as well as the potential for synergistic effects with exercise. With advances in magnetic resonance imaging, researchers now can analyze the physiology of the brain, providing a sensitive measure to assess the efficacy of nutrition interventions.

This publication offers 13 presentation summaries that address 5 key questions:

- How can we assess cognition, brain function, and efficacy of nutrition interventions?
- What is the impact of nutrition on cognitive development?
- What does emerging science tell us about the impact of lutein on the brain?
- How can nutrition and exercise help protect cognitive function in aging and illness?
- What can animal models tell us about nutrition effects on learning and memory?

Assessing Cognition, Brain Function, and Efficacy of Nutrition Interventions

Science has long recognized the close relationships between cognition and brain function. The first two summaries lay the groundwork for the conference: The first explains the relationships between cognition, memory, and brain function; and the second describes the tools that are now available to measure brain structure and physiology and the effects of nutrition intervention on the brain.

Assessing Cognition and Brain Function

"Cognition involves thinking and knowing, which are supported by acquiring, processing, and using information," Dr Neal Cohen stated in his keynote presentation. He added that these actions are variously driven by mental processes in different brain regions. Different parts of the brain specialize in different functions, but the parts are extensively interconnected. Dr Cohen also described multiple memory systems in the brain and the brain regions in which those systems are expressed. He introduced the topic of nutrition and cognition by describing potential benefits from antioxidants, omega-3 fatty acids, and flavonoids in the diet. Furthermore, he presented research on the potential benefits of exercise in reducing the negative effects of dietary intake high in refined sugar and saturated fat on memory performance.

Advances in MR Imaging and the Questions They Answer

Magnetic resonance imaging (MRI) techniques are used increasingly to study the brain, including investigations of how nutrition affects normal development and pathology across the lifespan. Dr Bradley Sutton discussed three particularly promising techniques—magnetic resonance spectroscopy (MRS), diffusion tensor imaging (DTI), and magnetic resonance elastography (MRE)—that allow researchers to monitor changes in brain metabolism, neuronal connectivity, and tissue structure. He stated that MRS can be used to examine localized brain chemistry and metabolism, DTI to assess white matter axonal connectivity and integrity of the membranes and myelin, and MRE to provide information on the overall structural integrity of brain tissue. These highly sensitive methods allow measurement of nutrition-associated changes that were not detectable with earlier imaging technologies or with assessments of cognitive behavior.

Impact of Nutrition on Cognitive Development

Brain development occurs at a remarkable pace in the fetus and in infancy. In terms of energy utilization, 74% of a newborn infant's energy intake fuels the brain and its growth, while just 23% of resting energy intake is consumed by the adult brain. Adequate energy and protein intake, as well as intake of other specific nutrients such as iron, folic acid, and long-chain polyunsaturated fatty acids are necessary to support this rapid structural growth of the brain.

Early Programming of Brain Development

Prof Cristina Campoy advised that an infant's brain triples in weight during the first 3 years of life—from 400 to 1200 grams. Exposure to diet, drugs, and adversity during such sensitive windows of early life can lead to lasting changes in gene expression that contribute to the display of physiological and behavioral phenotypes. Diet is a potent modulator of epigenetic marks, especially during prenatal and early postnatal life. Diets high in choline, methionine, folate, and vitamins B_6 and B_{12} increase DNA and histone methylation, alter gene expression, and can result in permanent changes in development. Prof Campoy described studies that, using new and more sensitive measures, have identified some of the mechanisms associating early nutrition with later brain developmental outcomes. She concluded that understanding these mechanisms may have an enormous preventive potential, given the major public health implications, including opportunities for an improvement of cognition and an effective primary prevention of childhood and adult behavior and mental diseases.

Measuring the Impact of Nutrition on Cognitive Development

Human brain development begins at conception. However, the influence of nutrition on brain development begins before conception and continues for many years. Dr Carol Cheatham reviewed the most important nutrients for brain development and discussed their cognitive effects. She outlined the rationale for studying the effects of nutrition on two specific cognitive abilities—memory and speed of processing. Dr Cheatham argued that the importance of nutrition to cognition in general cannot be overstated because memory is central to learning, and speed of processing underlies all cognitive abilities. Yet definitive data are lacking regarding roles, doses, and timing for intake of specific nutrients. Dr Cheatham concluded that nutrition researchers should work with developmental cognitive neuroscientists to use behavioral and electrophysiological methodologies to determine the effects of nutrition on brain development and help ensure that children have a chance to achieve their cognitive potential.

Lutein's Influence on Cognitive Development and Function

New research is revealing the potential importance of dietary carotenoids to visual and brain development in infants and children. Lutein is a carotenoid that plays a key role in development and function of the human retina, especially in infants. The retina is a neural tissue; as such, retinal development may provide insights into development and function of the brain. Furthermore, lutein may protect the brain from cognitive decline related to aging.

Emerging Science on Lutein in the Brain

Lutein is the predominant carotenoid in pediatric and adult brain tissue. Infants are born with carotenoids acquired during gestation, but because the body cannot make lutein, humans depend on dietary sources throughout life. Lutein in neural tissue has biological effects including antioxidant, anti-inflammatory, and structural actions. In infants' brains, the contribution of lutein to the total carotenoids is twice that found in adults, accounting for more than half the concentration of total carotenoids. In the adult, a variety of evidence supports a role for lutein in cognition. Therefore, Dr Elizabeth Johnson argued, the greater proportion of lutein in the pediatric brain suggests a need for lutein during neural development. Infant formula is not routinely supplemented with lutein, whereas breast milk is a highly bioavailable source of lutein. Given that the 1st year of life is a time of neural growth and development for which nutrition can have significant consequences, the addition of this dietary plant pigment to infant formulas could be an important strategy toward favorable long-term health outcomes.

Lutein's Influence on Neural Processing Speed

Just as macular carotenoids such as lutein are important for infant vision and brain development, they also are important for the function of the adult brain and retina. Lutein, for instance, influences many aspects of central nervous system function. These effects extend from optical filtering within the eye to physiological activity of neurons within the brain. A growing body of evidence suggests that lutein can enhance neural processing speed. This is particularly important for the elderly because slowing appears to be a central feature of cognitive decline and impairment. Dr Billy R. Hammond Jr described the mechanisms by which lutein could produce these effects (eg, by reducing oxidative and inflammatory stress, improving neural collective processing, and preserving brain white matter). He concluded that lutein likely serves multiple functions within the central nervous system and that these functions seem optimally suited to the preservation and

perhaps even enhancement of cognitive performance. Thus, carotenoids are important to protecting both vision and cognition against age-related decline.

Protecting Cognitive Function in Aging and Illness With Nutrition and Exercise

In 2010, there were 36 million people in the world living with dementia, and the number is expected to double every 20 years—reaching an alarming 115 million people in 2050. In the words of one conference participant, however, "By combining nutrition and exercise, we have a remarkable opportunity to preserve memory across the lifespan." Use of bioactive ingredients such as flavonoids that have anti-inflammatory properties, combined with a program of physical activity, may help protect cognitive function during aging.

Nutrigenetics and Cognitive Health

People are living longer than ever before and therefore are more likely to experience age-related diseases and conditions. However, living longer is not matched by an increase in healthy life expectancy. The aging population demographic is having a dramatic impact on dementia incidence worldwide, with prevalence approximately doubling every 20 years and estimated to increase to 115 million by 2050. In the context of these demographic changes, Dr Anne Marie Minihane reviewed the acute and chronic impact of eicosapentaenoic acid and docosahexaenoic acid and the interaction with the apolipoprotein 4 genotype. According to Dr Minihane, lifestyle, diet, and genetics interact to confer risk for cognitive decline with aging, and two of these factors are modifiable.

The Role of Flavonoids in Preventing Neuroinflammation and Cognitive Decline

Plant-based compounds called flavonoids have powerful anti-inflammatory and anti-neurotoxic properties, which means they may help offset aging processes in the brain by preventing and repairing cellular damage. The potential of dietary flavonoids for aiding in the preservation of cognitive function during aging, while reducing the risk of Alzheimer's disease and other dementing disorders, has gained great interest in research literature during the past decade. Dr David Vauzour discussed the impact of nutritional antioxidants on neuroinflammation and neurocognitive performance, and the role of flavonoids and their anti-inflammatory properties in cognitive protection. He also described the effects of flavonoids on the vascular system, which may induce increases in cerebral blood flow capable

of having an impact on acute cognitive performance or may lead to an increase in hippocampal vascularization capable of inducing new neuronal growth.

Neurocognitive and Mood Effects of Nutrition and Nutraceuticals

Dr Andrew Scholey stated, "The list of factors contributing to dementia is long and complicated—including disease processes, specific risk factors, and lifestyle aspects." Nutrients and extracts from botanical sources, unlike mainstream pharmacological agents, may contain many active components with a combination of properties that may affect multiple neuronal, metabolic, and hormonal systems with direct effects on cognitive processes. Dr Scholey described the role of specific herbal extracts such as ginseng and lemon balm on adult cognitive function, as well as techniques for mood and cognitive assessment—eg, magnetoencephalography, which measures changes in magnetic fields associated with postsynaptic potentials. He also discussed the need for future research to discover synergistic nutrition interventions to optimize day-to-day cognitive function, maintain psychological well-being throughout life, and treat conditions in which mental function becomes fragile, including dementia.

From Inflammation to Sickness and Cognitive Dysfunction: When the Immune System Subjugates the Brain

Dr Rodney Johnson reported substantial evidence for an association among infection, inflammation, and altered immune function, which is, in turn, associated with cognitive dysfunction. Microglial cells, resident macrophages in the central nervous system, are relatively quiescent but can respond to signals from the peripheral immune system and induce neuroinflammation. In aging, microglia tend to transition to a proinflammatory state and become hypersensitive to messages emerging from immune-to-brain signaling pathways. Thus, in older individuals with an infection, microglia overreact and produce excessive levels of inflammatory cytokines causing behavioral pathology, including cognitive dysfunction.
Dr Johnson described recent studies that indicate dietary flavonoids have anti-inflammatory properties and are capable of mitigating microglial cells in the brain of aged mice. Thus, he argued that dietary or supplemental flavonoids and other bioactive compounds have the potential to restore the population of microglial cells in the aging brain to a more quiescent state.

Exercise and the Aging Brain

Dr Arthur Kramer summarized a wealth of information about how physical activity benefits cellular and molecular actions in the brain. He described observational and randomized controlled human studies that have established the relationship between physical activity and cognitive maintenance in normal adults or in adults diagnosed with neurodegenerative diseases such as Alzheimer's or Parkinson's disease. Dr Kramer also cited more recent studies that have reported similar cognitive and brain benefits, as a function of exercise and physical activity, for children. Such findings are important to the understanding of lifestyle choices on cognitive and brain development as well as the impact of the increasing sedentary nature and levels of obesity observed for children in today's society. However, he said, many important questions remain unanswered, such as can a combination of nutrition and exercise bestow greater benefits to healthy minds and brains than either of these factors alone?

Nutrition Effects in Learning and Memory in Animal Models

Neuroscientists are looking closely at cellular, molecular, and electrophysiological mechanisms underlying learning and memory processes. Animal models provide a unique opportunity to examine complex details of the relationship between nutrition and learning.

Associative Learning and Long-Term Potentiation in Rodents: Effects of Nutrition

Many excellent in vitro studies describe the electrophysiological processes and molecular events supporting activity-dependent synaptic changes. However, little information is available on synaptic changes in strength during actual learning in behaving animals. Dr José Delgado-García and his research team have shown that classical conditioning of eyelid responses in behaving mice increased the synaptic strength of the hippocampal CA3-CA1 synapse. He described technical procedures used to study the firing and synaptic activities of selected brain sites during different types of associative learning tasks. He stated that long-term potentiation evoked experimentally in laboratory animals shares some synaptic properties and molecular mechanisms with learning-dependent changes in synaptic strength. Synaptic changes evoked by learning can be modified by environmental, social, and emotional factors, as well as by certain drugs and putative dietary ingredients.

Taste Learning and Memory in Aging

Dr Milagros Gallo and colleagues have studied taste aversion learning in rodents as a model for memory acquisition and its reorganization across the lifespan. The effect of aging on taste memory is a complex mix of impaired, preserved, and enhanced functions. Research on safe taste recognition memory has pointed to the amygdala's role in the taste neophobic response and its habituation when the taste is recognized as familiar and safe. However, the results are controversial regarding the impact of aging in taste neophobia, indicating a critical role of previous aversive experiences. Dr Gallo shared her research on the effect of aging in rodent taste memory and compared the brain mechanisms of taste and visual recognition memory. She concluded by explaining the need for further research involving the functional and anatomical dissociation among shared and independent recognition memory processes involving the temporal lobe and related areas.

Conclusion

We hope this conference report encourages you to explore new strategies and tools to help ensure that your patients are receiving optimal nutrition that, combined with adequate physical activity, supports cognitive development in early life and protects cognitive function throughout the adult years.