Highlights from 114th Abbott Nutrition Research Conference

- **Dr Neal Cohen (USA)** opened the conference with excitement about the role of nutrition in developing, protecting, and maintaining cognition across the life course (p 2).
- **Dr Bradley Sutton (USA)** introduced 3 magnetic resonance imaging techniques that promise to be sensitive enough to measure effects of nutrition on the brain—spectroscopy, diffusion tensor imaging, and elastography (pp 2-3).
- **Drs Cristina Campoy (Spain), Carol Cheatham (USA), and Elizabeth Johnson (USA)** addressed dietary nutrients important to infant brain development: lutein, iron, folic acid, and long-chain fatty acids (pp 3-4).
- **Drs Randy Hammond (USA), David Vauzour (UK), and Andrew Scholey (Australia)** presented evidence of nutrients in the adult diet that may offset aging processes by preventing and repairing cellular damage—lutein, flavonoids, and ginseng and Bacopa plant extracts (pp 5-7).
- **Dr Arthur Kramer (USA)** advised, "By combining nutrition and exercise, we have a remarkable opportunity to preserve memory across the lifespan" (p 7).
- **Drs Rodney Johnson (USA) and Anne Marie Minihane (UK)** tackled the question of how diseases impact cognitive health in adults (p 8).
- **Drs José Delgado-Garcia (Spain)** and **Milagros Gallo (Spain)** presented interesting animal models that can teach us about the complexities of nutrition and learning (p 9).

114th Abbott Nutrition Research Conference

Cognition and Nutrition

Abbott Nutrition Health Institute hosts global research conference at Ross Park

Dr Gary Fanjiang (USA), Abbott Nutrition Divisional Vice President of Scientific and Medical Affairs, welcomed 13 acclaimed speakers and more than 100 participants to the 114th Abbott Nutrition Research Conference on Cognition and Nutrition. Organized by the Abbott Nutrition Health Institute (ANHI), the meeting took place April 8 and 9, 2013, at Ross Park, Abbott Nutrition's research facility in Columbus, Ohio.

Unlocking the mysteries of the mind

The brain, the most mysterious of human organs, represents a fresh challenge in biomedical science in 2013. In April, US President Barack Obama proposed an ambitious $100 million project to map the brain. Such mapping will help scientists understand how the brain operates normally, and what happens when it behaves abnormally. Dr Fanjiang noted, "Because nutrition and cognition are inextricably linked from preconception to old age, we at Abbott Nutrition aim to be leaders in this advancing field."

Over the course of 1.5 days, the conference faculty addressed 5 key questions:

1. What tools are now available to assess brain structure and cognition?
2. What is presently understood about effects of maternal/infant nutrition on cognitive development of the child?
3. What are the roles of specific dietary nutrients and exercise in adult cognitive function?
4. How do diseases and aging impact cognitive health in adults?
5. What do we know about learning and nutrition from animal models?

Dr Gary Fanjiang, Abbott Nutrition Divisional Vice President of Scientific and Medical Affairs, welcomed participants to the 114th Abbott Nutrition Research Conference on Cognition and Nutrition, which was held April 8-9, 2013, in Columbus, Ohio.

Abbott Nutrition Health Institute® Science. Illuminated.

Abbott A Promise for Life

Learning, memory, and nutrition: an overview

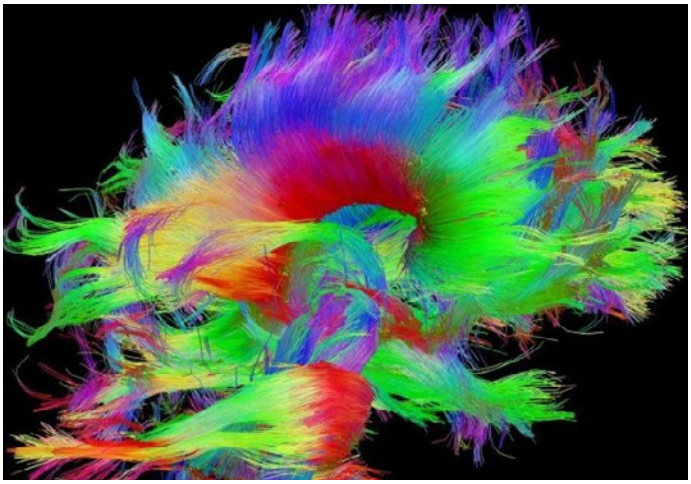
Neal Cohen, PhD, Director of the Center for Nutrition, Learning, and Memory at the University of Illinois (USA), has long recognized the close relationship between cognition and brain function.

In his words, "Cognition involves thinking and knowing, which are supported by acquiring, processing, and using information." 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 has been instrumental in identifying and characterizing multiple memory systems in the brain—declarative, procedural, and emotional memory.[1] *Declarative memory* refers to knowledge that is consciously acquired, the who-what-where-when-why information that we learn in school. *Procedural memory* refers to memory of skills and routines—riding a bicycle, performing a surgical procedure, or hitting a golf ball. *Emotional memory* is for remembering events associated with strong feelings such as fear or happiness. Each type of memory involves multiple brain regions, but the hippocampus region is critical to declarative memory, the brainstem and spinal motor outputs to procedural memory, and the amygdala to emotional memory.

As the conference began, Dr Cohen was eager and energized about the chance to hear researchers discuss how nutrition can help protect, maintain, and enhance cognition. Specifically, he touted potential benefits from antioxidants, omega-3 fatty acids, and flavonoids in the diet. At the same time, he cautioned about possible detrimental effects from dietary intake of refined sugar, saturated fat, and alcohol.[2,3]

Dr Neal Cohen, Director of the Center of Nutrition, Learning, and Memory at the University of Illinois (USA) has been instrumental in identifying and characterizing multiple memory systems in the brain.



As shown in this diffusion tensor image, different parts of the brain specialize in different functions, but the parts are extensively interconnected.

What tools do we have to image the brain?

Bradley Sutton, PhD, Associate Professor of Engineering at the University of Illinois (USA), reviewed how magnetic resonance imaging (MRI) techniques are increasingly used to study the brain, including investigations of how nutrition affects normal development and pathology across the lifespan. The brain develops rapidly during the perinatal period and, in infancy, continues to mature into the 2nd and 3rd decade of life, may be changed by illness or injury, and ultimately undergoes changes due to aging.[4]

MRI has long been used to measure changes in the macrostructure of different regions of the brain. Now several new MRI techniques provide information about microstructures of the brain. Dr Sutton focused on 3 techniques that promise to be sensitive enough to measure very minute changes in the brain—spectroscopy, diffusion tensor imaging, and elastography. These highly sensitive methods will allow measurement of nutrition-associated changes that were not detectable with earlier imaging technologies or with assessments of cognitive behavior.

Dr Brad Sutton (USA) identified elastography as a sensitive measure expected to diagnose disease onset and monitor response to nutrition treatment.

Magnetic resonance spectroscopy (MRS) is unique among MRI techniques because it can measure the chemical composition of tissue. Radio-frequency pulses perturb nuclei within various molecules, and the resultant resonant signal is measured. Specifically, MRS can be used to quantify the neuronal marker N-acetylaspartate (NAA) as well as brain metabolites choline, creatine, glucose, and lactate.[5] Changes in amounts or ratios of brain chemicals can predict brain abnormalities,[6] sometimes even before symptoms become evident.

Diffusion tensor imaging (DTI) is a semi-quantitative magnetic resonance technique used to measure the magnitude and direction of water diffusion.[4] DTI images reflect the functional status of neural tracts or pathways in the brain, especially those established by the myelinated coating of neurons. DTI has proven useful for detecting changes in developing infant brains,[4] identifying regions of speech and language processing,[7] and observing age-related changes in connectivity of brain regions. Aging is associated with deterioration of brain white matter, which appears to be a consequence of myelin degeneration.[8]

Magnetic resonance elastography (MRE) is a technique that determines the shear modulus (stiffness) of tissues *in vivo.*[9] According to Dr Sutton, the brain is subjected to micro-palpations in MRE, ie, a rocker within the MRI scanner creates micron-sized shakes of the subject's head. MRE detects the magnitude of brain movement in response to shaking, which serves as a measure of its elasticity. Since the brain loses stiffness or gets softer with neurodegeneration (as in Alzheimer's disease, multiple sclerosis, and normal physiological aging), MRE is expected to serve as a way to diagnose disease onset and monitor response to treatment.

Imaging technique	Use in cognition research
Magnetic resonance spectroscopy (MRS)	• MRS measures neurochemicals and their metabolites in the brain, eg, N-acetylaspartate (NAA), choline (Cho), creatine (Cr). • MRS allows early detection of pathologic changes before clinical symptoms are evident.
Diffusion tensor imaging (DTI)	• DTI measures the magnitude and direction of water diffusion in the brain, thus reflecting pathways such as myelinated neuronal structures. • This method is used to determine structural connectivity of brain regions, including increasing connectivity in the developing brain and deterioration of connectivity with aging.
Magnetic resonance elastography (MRE)	• MRE combines mechanical wave propagation with MRI to create a visual map, or elastogram, showing the stiffness (elasticity) of brain regions. • This sensitive measure is expected to identify disease onset and monitor response to nutrition treatment.

Nutrition and cognitive development in infants and children

Cristina Campoy, MD, PhD, Professor, Department of Pediatrics, School of Medicine, University of Granada (Spain), **Carol Cheatham, PhD,** Assistant Professor of Psychology, University of North Carolina, Nutrition Research Institute (USA), and **Elizabeth Johnson, PhD,** Associate Professor, School of Nutrition, Tufts University, Jean Mayer USDA Human Nutrition Research Center on Aging (USA), reviewed influences of specific nutrients, both alone and in combination, on brain development in infants and children.

Brain development occurs at a remarkable pace in the fetus and in infancy. Dr Campoy advised, "An infant's brain triples in weight during the first 3 years of life—from 400 to 1200 grams." 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.[10] Adequate energy and protein intake, as well as intake of other specific nutrients, is necessary for this rapid structural growth of the brain.

Iron, folic acid, and long-chain polyunsaturated fatty acids

Drs Campoy and Cheatham agree that nutrition is important for maturation of brain function (vision, motor activity, memory, language). Specifically, results of certain animal and clinical studies suggest that prenatal supplies of iron, folic acid, and long-chain polyunsaturated fatty acids (LC-PUFAs; docosahexaenoic acid DHA and arachidonic acid AA) are involved in brain development. Drs Campoy and Cheatham likewise agree that definitive data are lacking regarding roles, doses, and timing for intake of specific nutrients. For many years, researchers have been challenged to find infant performance measures that were sufficiently sensitive to support or refute links between the mother's intake before and during pregnancy/lactation and cognitive or visual development of her offspring in infancy and childhood.[11-15]

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.

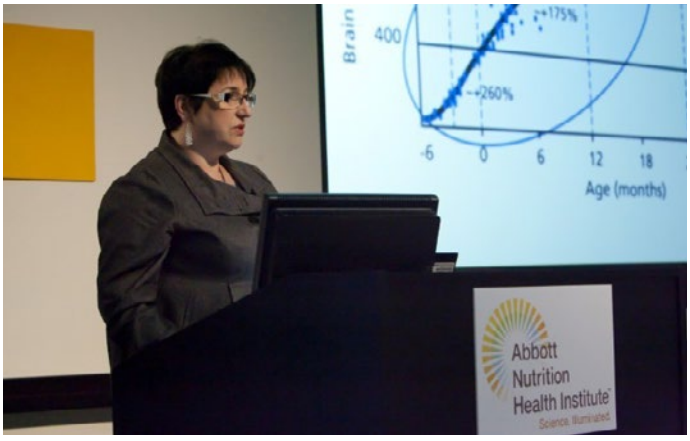
Lutein is an important carotenoid in breast milk, and it represents more than half of all carotenoids in the infant brain.

Dr Campoy introduced a large and ongoing European research initiative called NUTRIMENTHE, which aims to study the roles, mechanisms, risks and benefits of specific nutrients and food components on the mental performance of children.

NUTRIMENTHE is using the newest and most sensitive measures available today in order to study babies from fetal stage onward through childhood. In particular, NUTRIMENTHE is evaluating how LC-PUFA intake affects mental performance in infancy and early childhood (http://www.nutrimenthe.eu).

To date, the lack of clear links between specific nutrient intake and developmental measures may be confounded by other factors. Dr Cheatham reported that genetic studies in mothers have shown that mutations in genes encoding enzymes for synthesis of fatty acids DHA and AA (fatty acid desaturase enzymes, FAD) can limit supplies of these long-chain fatty acids during pregnancy and lactation,[16] ultimately resulting in impaired cognitive development of the infant.[17, 18] Then again, the mother's health influences pregnancy outcomes; Dr Campoy advised that mothers who are obese during pregnancy may be at greater risk than healthy weight mothers to have babies with birth anomalies, including deficits in function of the brain and nervous system.[19]

Taking all the evidence together, Drs Campoy and Cheatham concluded that there is a complicated interplay between genetics and diet in control of infant brain development. Further studies are needed to probe these relationships and the underlying mechanisms by which nutrients modulate brain development.



Dr Cristina Campoy (Spain) advised that mothers who are obese during pregnancy may be at greater risk than healthy weight mothers to have babies with birth anomalies, including deficits in development of the brain and nervous system.

Lutein

Dr Johnson presented fascinating new findings on 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.

Infants are born with carotenoids acquired during gestation, but because lutein cannot be made by the body, infants and children depend on dietary sources throughout life. In one study, lutein levels were similar at birth in all infants.[20] After one month, however, levels increased in breastfed infants but fell below baseline in infants fed formula without lutein supplementation.[20] According to Dr Johnson, "Lutein is an important carotenoid in breast milk, and it represents more than half of all carotenoids in the infant brain." Dietary intake of lutein increases with the child's age, starting as toddlers adopt a more varied diet; lutein intake continues to increase well into adulthood.[21] Dietary sources of lutein include egg yolk, fruits, and vegetables, especially leafy greens such as spinach and kale.

Lutein crosses the blood-retina barrier and accumulates preferentially in the macular region of the retina. Here lutein becomes part of the macular pigment that protects the retina as the eye matures.[22] The precise role for lutein in the infant brain is not yet known, but it may be involved in neural development and cognition. As such, more studies of lutein-supplemented infant formulas are needed. In older people, lower levels of brain lutein are associated with poorer cognitive function.[23]

The level of lutein in the macula of primates correlates with the level of lutein in the brain; macular lutein may thus serve as a biomarker for cognitive function.[24] Research studies are needed to confirm and extend this association, but Dr Johnson enthusiastically imagined a time when non-invasive measurements of macular lutein can be used to monitor brain development and detect disease- or age-related changes.

Dr Elizabeth Johnson (USA) discussed lutein in the retinal macula and in the brain of infants.

Dr Carol Cheatham (USA) noted that prenatal supplies of iron, folic acid, and long-chain polyunsaturated fatty acids are involved in brain development.

Nutrition and exercise affect adult cognition

With an aging world population in the 21st century, it is important to understand what lifestyle factors contribute to the longevity of a healthy mind. There is no doubt that diet and exercise are important.

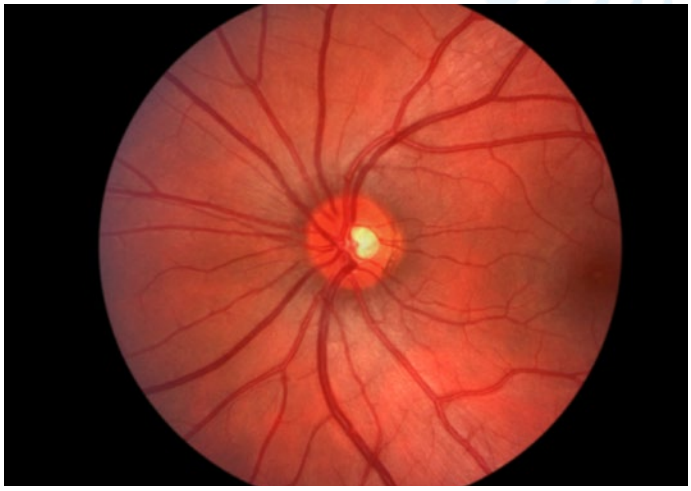
Lutein and other carotenoids

Just as lutein is important for infant vision and brain development, it is also important for the function of the adult brain and retina. **Randy Hammond, PhD,** Professor of Brain and Behavioral Sciences, University of Georgia (USA), discussed the influence of lutein on neural processing speed—including evidence of its roles in preventing and treating cognitive decline in older adults. In addition, lutein intake (from fruits, vegetables, and egg yolks) is particularly important in the diet of young women, as they need sufficient lutein intake to meet their babies' needs during gestation and lactation.

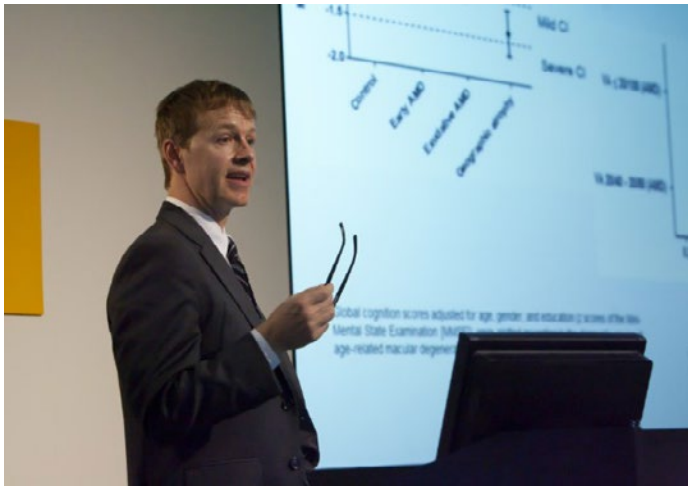
Lutein is a yellow carotenoid pigment that absorbs blue light; lutein is heavily concentrated in the macular region of the central retinal area.[25] Light must pass through macular pigment before reaching retinal receptors. While macular pigment is known to protect the retina by absorbing potentially damaging short-wave light, lutein also appears to inactivate highly reactive free radicals that are the by-product of light-driven cellular activity.[25] This latter action can help prevent buildup of damage over time.

Dr Hammond noted that patients with age-related macular degeneration had lower global cognition scores than did those with normal vision,[26] and he speculated, "Sensory decline may be the gateway to cognitive decline." In addition, he presented evidence that oxidative and inflammatory stresses lead to impairment of the central nervous system.[27] He showed data from studies in animals and human newborns to suggest that dietary lutein intake may protect against oxidative stress in the retina and other tissues.

At the next level, Dr Hammond discussed new and intriguing evidence that dietary lutein intake has potential for treatment of cognitive decline. His newest research findings suggest that lutein and other carotenoids can improve aspects of the visual stimulus, such as glare disability and photostress recovery.[28] Further, retinal carotenoid levels were positively correlated with cognitive function as assessed by numerous tasks including visuospatial and constructional ability, language, attention, and memory (unpublished data).



Lutein is a yellow carotenoid pigment in the macular region of the central retina. Lutein absorbs potentially damaging short-wave blue light, thus protecting the retina from oxidative stress.



Dr Randy Hammond (USA) noted that patients with age-related macular degeneration had lower global cognition scores than did those with normal vision.

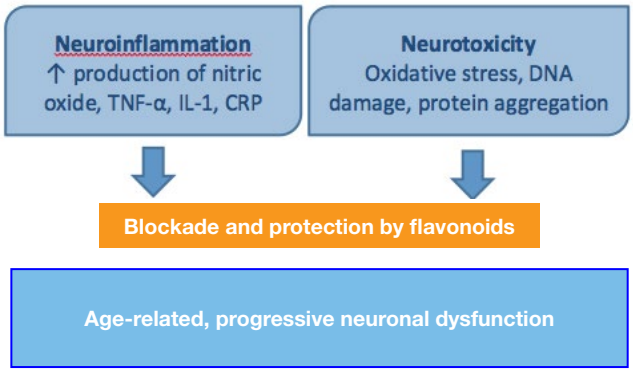
Taken together, Dr Hammond found a correlation between levels of lutein in the macular region of the retina and both visual and cognitive function, eg, low retinal carotenoids were associated with low cognitive function. Such findings indicate that carotenoids such as lutein are important to protect both vision and cognition against age-related decline.

Flavonoids

David Vauzour, PhD, Senior Research Associate, Department of Nutrition, University of East Anglia, Norwich Medical School (UK), introduced flavonoids, plant-based polyphenolic compounds. 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.[29] Flavonoids—classified as flavonols, flavones, flavanones, isoflavones, catechins, anthocyanidins—are sourced from the diet and have properties that provide protection against dementia, Alzheimer's disease, and Parkinson's disease. Tea, red wine, citrus fruits, dark chocolate, and berries are all rich in flavonoids.

How do flavonoids protect against age-related dementia? Polyphenols have been reported to exert neuroprotective actions by (1) protecting against injury induced by neurotoxins, (2) suppressing neuroinflammation, and (3) promoting memory, learning, and cognitive function.[29] Mechanisms for these beneficial effects variously involve decreases in inflammatory stress signaling, increases in protective signaling, and increased expression of genes that encode antioxidant enzymes, phase-2 enzymes, neurotrophic factors, and cytoprotective proteins. Flavonoids also induce vascular changes leading to angiogenesis and neurogenesis.

Consumption of flavonoid-rich foods is effective at reversing age-related memory deficits in both animals and humans. Dr Vauzour discussed a fascinating animal experiment, which showed improved performance of aged rats in spatial working memory tasks when their diet was supplemented with blueberries for 12 weeks.[30] Likewise, when older adults (with or without mild cognitive impairment) consumed blueberry or grape juice for 12 weeks, memory function improved significantly.[29]



Flavonoids help prevent age-related damage to the brain by decreasing neuroinflammation and protecting against neurotoxins.

Dr David Vauzour (UK) described the powerful anti-inflammatory and anti-neurotoxic properties of flavonoids.

Dr Andrew Scholey (Australia) asked, "Are we barking up the wrong tree in our search for cognitive enhancers?"

Nutraceuticals

Andrew Scholey, PhD, Professor of Behavioral and Brain Sciences, Swinburne University (Australia), directs a world-renowned program exploring the relationship between different natural medicines and neurocognition. At his Australian Centre for Human Psychopharmacology, researchers can take a big-picture view of the brain by assessing changes in cognition, mood, and stress, as well as structural and chemical markers of brain activity. He is particularly interested in age-related changes in brain structure and performance.

Brain performance assessment

- Cognitive testing
- Mood assessment
- Stress evaluation

Brain structure and chemical assessment

- Brain imaging
- Metabolite measurements
- Inflammatory mediator detection
- Measures of oxidative stress
- Assessment of cardiovascular function

Dr Scholey stated, "The list of factors contributing to dementia is long and complicated—including disease processes, specific risk factors, and lifestyle aspects." Examples of dementia-inducing disease processes are acetylcholine degeneration, abnormal amyloid processing, inflammation, cortical atrophy, free radical damage, and compromised glucose metabolism. Risk factors include aging, *APOE* genotype, head trauma, toxin exposure, and hormonal status. Harmful lifestyle factors include diet, alcohol consumption, and nicotine consumption. As a result, multiple proprietary drugs and nutraceuticals (herbal supplements) are now being used for prevention and treatment of dementia.

Do current mental performance-enhancing pharmaceutical and nutraceutical drugs actually work? Dr Scholey and others have put them through rigorous testing, as reported at this symposium. Modafinil is a memory-enhancing prescription drug; ginseng, Bacopa, and ginkgo are plant-derived supplements used in Chinese medicine and around the world for memory enhancement. In a systematic review, Dr Scholey and colleagues benchmarked the cognitive effects of ginseng and Bacopa against modafinil in terms of cognitive effects.[31] With strict criteria for studies on healthy human subjects and a double-blind, placebo-controlled design, the highest effect sizes for cognitive outcomes were 0.77 for modafinil (visuospatial memory accuracy), 0.86 for ginseng (simple reaction time), and 0.95 for Bacopa (delayed word recall). These data confirm that neurocognitive enhancement from well-characterized nutraceuticals can produce cognition enhancing effects of similar magnitude to those from pharmaceutical interventions. Future research should compare these effects directly in clinical trials.

Dr Scholey concluded, "Are we barking up the wrong tree in our search for cognitive enhancers?"[32]

Dr Art Kramer (USA) presented study findings on how physical activity improves cognition in children and older adults.

Exercise and cognition

Physical fitness is associated with better cognitive performance and reduced incidence of Alzheimer's disease in older adults.

Arthur Kramer, PhD, Professor of Psychology and Neuroscience, University of Illinois (USA) summarized a wealth of information presently known about how physical activity benefits cellular and molecular actions in the brain.

Results of animal studies have shown that exercise:

- Increases production of neurotrophins and neurotransmitters
- Enhances formation of synapses and blood vessels
- Down-regulates genes associated with oxidative stress
- Reduces production of beta amyloid
- Enhances learning and memory

By combining nutrition and exercise, we have a remarkable opportunity to preserve memory across the lifespan.

In human studies, fitness training had broad benefits for cognition across the lifespan, including robust effects on executive and control processes.[33] In children, fitness enhanced relational memory and increased hippocampus volume.[34] Similarly in older adults, aerobic exercise increased the size of the hippocampus and improved memory.[35] Further, aerobic exercise improved functional connectivity between brain regions in adults,[36,37] and resistance training likewise yielded benefits.[38] Dr Kramer presented early evidence that fitness training can help delay decline in neurological function in patients with early Alzheimer's disease, Parkinson's disease, and multiple sclerosis.

Dr Kramer concluded, "By combining nutrition and exercise, we have a remarkable opportunity to preserve memory across the lifespan." Findings from a study by Chytrova and colleagues revealed how a diet enriched with docosahexaenoic acid (DHA), together with exercise, elevated the capacity of the adult brain for axonal growth, synaptic plasticity, and cognitive function.[39]

How does disease impact cognitive health in adults?

Though the connection may not seem obvious at first, good health is crucial to preserving good memory. **Rodney Johnson, PhD,** Professor of Integrative Biology, University of Illinois (USA) and **Anne Marie Minihane, PhD,** Professor, Nutrigenetics, University of East Anglia, Norwich Medical School (UK), described how specific acute and chronic health conditions can affect cognitive function.

Acute disease or injury

Dr Johnson reported substantial evidence for an association among infection, inflammation, and altered immune function, which is, in turn, associated with cognitive dysfunction.[40-44]

Infectious diseases (eg, influenza), autoimmune diseases (eg, rheumatoid arthritis), tissue trauma (eg, injury or surgery), and some chronic disease conditions (eg, obesity) elicit peripheral inflammation. As a result, peripheral immune cells release proinflammatory cytokines, which subsequently activate brain microglia (~15% of the cells in the brain). The microglial cells then release local proinflammatory cytokines that cause neuroinflammation in the brain. Mechanistically, such inflammation leads to atrophy of dendrites, impaired neurotransmitter signaling, and inhibited neurogenesis in the hippocampus. This inflammatory cascade ultimately leads to well-known "sickness" behaviors—increased sleep, lethargy, fever, social isolation, reduced appetite, and cognitive impairment.

Further, the increased neuroinflammation initiated by infection or injury is similar to the inflammation associated with aging. Specifically, Dr Johnson noted that the inflammatory cytokine, interleukin-6 (IL-6) is expressed to a much higher degree in the glial cells of old mice compared to young mice.[45]

Dr Rodney Johnson (USA) cautioned, "The negative effects of infection on cognition may last much longer than the infection itself."

In 2010, there were 36 million people in the world living with dementia. The number is expected to double every 20 years—reaching an alarming 115 million people in 2050.

Chronic cardiovascular disease

Dr Minihane drew attention to alarming new evidence on the rising prevalence of dementia in older populations globally.[46] Among people older than 60 years, the prevalence of dementia is 5%-7% around the world. 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.[46]

Why the increase, and what can we do about it? In part, people are living longer than ever before, so they are more likely to experience age-related diseases and conditions. In addition, many people have poor dietary practices and sedentary lifestyles, which increase risk for cardiovascular conditions, in turn raising risks for dementia. Dr Minihane specifically noted that hypercholesterolemia, obesity, metabolic disease, and diabetes increase risk of cognitive impairment and Alzheimer's disease.[47-49] The numbers on dementia prevention tell an interesting story. If we can delay the onset of Alzheimer's disease by 5 years, the prevalence will decline by half; with a delay of one year, prevalence will decline by 5%.[50]

A person's genetic background also plays a role in predicting risk for Alzheimer's disease. In fact, people with the apolipoprotein *APOE*-ε4 gene are at major risk for late-onset Alzhemier's disease; a double dose of this gene (homozygous *APOE*-ε4) makes Alzheimer's disease a certainty by age 80 years.[51, 52]

For protection against dementia, convincing evidence continues to accumulate in support of consuming fish or fish oil (active ingredients omega-3 fatty acids eicosapentaenoic acid EPA and docosahexaenoic acid DHA) as a means to improve vascular tone, increase longevity, and prevent or delay cognitive decline.[53-57] Unfortunately, fish oil provides little protection against development of dementia in individuals with the *APOE*-ε4 gene.[58]

In summary, lifestyle, diet, and genetics interact to confer risk for cognitive decline with aging; 2 of these factors are modifiable.

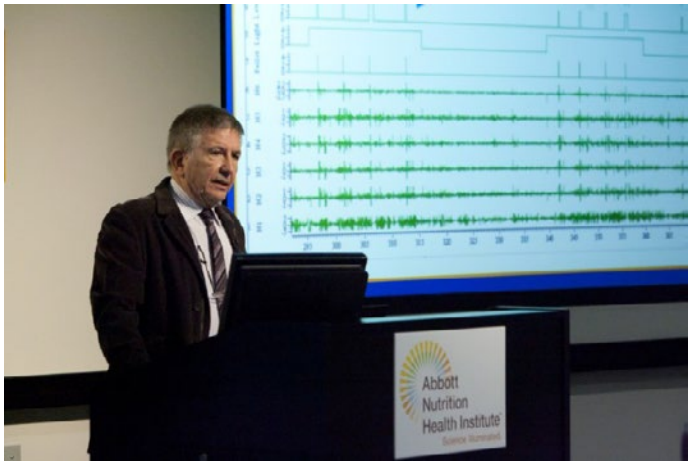
Dr Anne Marie Minihane (UK) drew attention to alarming evidence of the rising prevalence of dementia around the world.

What do animal models teach us about nutrition and learning?

Contemporary neuroscientists **José Delgado-Garcia, MD, PhD,** Professor of Physiology, University of Pablo de Olavide (Spain) and **Milagros Gallo, PhD,** Institute of Neurosciences Federico Olóriz (Spain), 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.

Dr Delgado-Garcia and colleagues have developed exquisitely sensitive methods for eliciting and recording learning behaviors of rodents. They can measure activity-dependent neural changes taking place at the moment of learning. Using operant conditioning, a type of associative learning, Dr Delgado-Garcia's research team has studied pathways involved in learned feeding behaviors and appetite. They have pinpointed conditioned behaviors for food rewards to hippocampal synapses,[59] and they can modulate learning by stimulation of the medial prefrontal cortex or the nucleus accumbens.[60]

Similarly, Dr Milagros Gallo and colleagues have studied taste-aversion learning in rodents as a model for memory acquisition and its reorganization across the lifespan.[61] The perirhinal cortex and the hippocampus appear to play different but complementary roles in taste-aversion learning and memory, and these region-specific functions are altered by aging. Development of conditioned taste aversions takes longer in older rats than in young rats, and aging impairs memory and recognition of safe-taste foods. Hippocampus-based memory is less involved in new learning for old rats, but prior hippocampus-centered memory can be reactivated. Dr Gallo concluded that the effect of aging on taste memory is actually a complex mix of impaired, preserved, and enhanced functions.



Dr José Delgado-Garcia (Spain) demonstrated learned feeding behaviors and appetite through animal models.

Dr José Delgado-Garcia (Spain), Dr Jeff Baxter (Abbott Nutrition Discovery R&D), and Dr Milagros Gallo (Spain) discussed research strategies between conference faculty and Abbott Nutrition research scientists.

Coming soon to the all new anhi.org site: Videos of the presentations and proceedings from the 114th Abbott Nutrition Research Conference on Cognition and Nutrition.

This new site will feature the highest quality educational materials, along with new resources for our partners who specialize in research and development.

Left to right, front: Elizabeth Johnson, Carol Cheatham, José Delgado-Garcia, Andrew Scholey, Arthur Kramer **Left to right, back:** Rodney Johnson, David Vauzour, Neal Cohen, Milagros Gallo, Randy Hammond, Cristina Campoy, Anne Marie Minihane, Bradley Sutton

Table 1.
Presenters at 114th Abbott Nutrition Research Conference: Cognition and Nutrition

Neal J. Cohen, PhD (USA)
Assessing Cognition and Brain Function

Bradley P. Sutton, PhD (USA)
Advances in MR Imaging and the Questions They Answer

Cristina Campoy, Prof, MD, PhD (Spain)
Early Programming of Brain Development

Carol L. Cheatham, PhD (USA)
Measuring the Impact of Nutrition on Cognitive Development

Elizabeth J. Johnson, PhD (USA)
Emerging Science on Lutein in the Brain

Randy Hammond Jr, PhD (USA)
Lutein's Influence on Neural Processing Speed

David Vauzour, PhD (UK)
The Role of Flavonoids in Preventing Neuroinflammation and Cognitive Decline

Andrew Scholey, PhD (Australia)
Neurocognitive and Mood Effects of Nutrition and Nutraceuticals

Arthur F. Kramer, PhD (USA)
Exercise and the Aging Brain

Rodney W. Johnson, PhD (USA)
From Inflammation to Sickness and Cognitive Dysfunction: When the Immune System Subjugates the Brain

Anne Marie Minihane, PhD (UK)
Nutrigenetics and Cognitive Health

José M. Delgado-García, MD, PhD (Spain)
Associative Learning and Long-term Potentiation in Rodents: Effects of Nutrition

Milagros Gallo, PhD (Spain)
Taste Learning and Memory in Aging

At Abbott Nutrition Health Institute, we illuminate the power of science-based nutrition through education, advocacy, and collaboration to help people throughout the world live healthier lives. To gain knowledge and information about nutrition solutions that support your efforts in providing better patient care, visit **ANHI.org** today.

Abbott Nutrition Health Institute®
Science. Illuminated.

Abbott
A Promise for Life

References

1. Eichenbaum H, Cohen N. *From Conditioning to Conscious Recollection: Memory Systems of the Brain.* Oxford: Oxford University Press; 2001.
2. Molteni R, Wu A, Vaynman S, et al. Exercise reverses the harmful effects of consumption of a high-fat diet on synaptic and behavioral plasticity associated to the action of brain-derived neurotrophic factor. *Neuroscience.* 2004;123:429-440.
3. Molteni R, Barnard RJ, Ying Z, et al. A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning. *Neuroscience.* 2002;112:803-814.
4. Wozniak JR, Lim KO. Advances in white matter imaging: a review of in vivo magnetic resonance methodologies and their applicability to the study of development and aging. *Neurosci Biobehav Rev.* 2006;30:762-774.
5. Soares DP, Law M. Magnetic resonance spectroscopy of the brain: review of metabolites and clinical applications. *Clin Radiol.* 2009;64:12-21.
6. Garcia Santos JM, Gavrila D, Antunez C, et al. Magnetic resonance spectroscopy performance for detection of dementia, Alzheimer's disease and mild cognitive impairment in a community-based survey. *Dement Geriatr Cogn Disord.* 2008;26:15-25.
7. Roberts RE, Anderson EJ, Husain M. White matter microstructure and cognitive function. *Neuroscientist.* 2013;19:8-15.
8. Davis SW, Dennis NA, Buchler NG, et al. Assessing the effects of age on long white matter tracts using diffusion tensor tractography. *Neuroimage.* 2009;46:530-541.
9. Kruse SA, Rose GH, Glaser KJ, et al. Magnetic resonance elastography of the brain. *Neuroimage.* 2008;39:231-237.
10. Cunnane SC, Crawford MA. Survival of the fattest: fat babies were the key to evolution of the large human brain. *Comp Biochem Physiol A Mol Integr Physiol.* 2003;136:17-26.
11. Campoy C, Escolano-Margarit MV, Anjos T, et al. Omega 3 fatty acids on child growth, visual acuity and neurodevelopment. *Br J Nutr.* 2012;107 Suppl 2:S85-106.
12. Gould JF, Smithers LG, Makrides M. The effect of maternal omega-3 (n-3) LCPUFA supplementation during pregnancy on early childhood cognitive and visual development: a systematic review and meta-analysis of randomized controlled trials. *Am J Clin Nutr.* 2013;97:531-544.
13. Szajewska H, Ruszczynski M, Chmielewska A. Effects of iron supplementation in nonanemic pregnant women, infants, and young children on the mental performance and psychomotor development of children: a systematic review of randomized controlled trials. *Am J Clin Nutr.* 2010;91:1684-1690.
14. Skorka A, Gieruszczak-Bialek D, Piescik M, et al. Effects of prenatal and/or postnatal (maternal and/or child) folic acid supplementation on the mental performance of children. *Crit Rev Food Sci Nutr.* 2012;52:959-964.
15. Cheatham CL, Goldman BD, Fischer LM, et al. Phosphatidylcholine supplementation in pregnant women consuming moderate-choline diets does not enhance infant cognitive function: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr.* 2012;96:1465-1472.
16. Xie L, Innis SM. Genetic variants of the FADS1 FADS2 gene cluster are associated with altered (n-6) and (n-3) essential fatty acids in plasma and erythrocyte phospholipids in women during pregnancy and in breast milk during lactation. *J Nutr.* 2008;138:2222-2228.
17. Glaser C, Lattka E, Rzehak P, et al. Genetic variation in polyunsaturated fatty acid metabolism and its potential relevance for human development and health. Matern Child Nutr. 2011;7 Suppl 2:27-40.
18. Steer CD, Hibbeln JR, Golding J, et al. Polyunsaturated fatty acid levels in blood during pregnancy, at birth and at 7 years: their associations with two common FADS2 polymorphisms. *Hum Mol Genet.* 2012;21:1504-1512.
19. Stothard KJ, Tennant PW, Bell R, et al. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA.* 2009;301:636-650.
20. Zimmer JP, Hammond BR, Jr. Possible influences of lutein and zeaxanthin on the developing retina. *Clin Ophthalmol.* 2007;1:25-35.
21. Johnson EJ, Maras JE, Rasmussen HM, et al. Intake of lutein and zeaxanthin differ with age, sex, and ethnicity. *J Am Diet Assoc.* 2010;110:1357-1362.
22. Hammond BR, Jr. Possible role for dietary lutein and zeaxanthin in visual development. *Nutr Rev.* 2008;66:695-702.
23. Johnson EJ. A possible role for lutein and zeaxanthin in cognitive function in the elderly. *Am J Clin Nutr.* 2012;96:1161S-1165S.
24. Vishwanathan R, Neuringer M, Snodderly DM, et al. Macular lutein and zeaxanthin are related to brain lutein and zeaxanthin in primates. *Nutr Neurosci.* 2013;16:21-29.
25. Hammond BR, Jr., Fletcher LM. Influence of the dietary carotenoids lutein and zeaxanthin on visual performance: application to baseball. Am J Clin Nutr. 2012;96:1207S-1213S.
26. Woo SJ, Park KH, Ahn J, et al. Cognitive impairment in age-related macular degeneration and geographic atrophy. *Ophthalmology.* 2012;119:2094-2101.
27. Craft S, Foster TC, Landfield PW, et al. Session III: Mechanisms of age-related cognitive change and targets for intervention: inflammatory, oxidative, and metabolic processes. *J Gerontol A Biol Sci Med Sci.* 2012;67:754-759.
28. Hammond BR, Jr., Fletcher LM, Elliott JG. Glare disability, photostress recovery, and chromatic contrast: relation to macular pigment and serum lutein and zeaxanthin. *Invest Ophthalmol Vis Sci.* 2013;54:476-481.
29. Vauzour D. Dietary polyphenols as modulators of brain functions: biological actions and molecular mechanisms underpinning their beneficial effects. *Oxid Med Cell Longev.* 2012;2012:914273.
30. Williams CM, El Mohsen MA, Vauzour D, et al. Blueberry-induced changes in spatial working memory correlate with changes in hippocampal CREB phosphorylation and brain-derived neurotrophic factor (BDNF) levels. *Free Radic Biol Med.* 2008;45:295-305.
31. Neale C, Camfield D, Reay J, et al. Cognitive effects of two nutraceuticals Ginseng and Bacopa benchmarked against modafinil: a review and comparison of effect sizes. *Br J Clin Pharmacol.* 2012;75:728-737.
32. Scholey A, Stough C, Verster JC. Editorial: Cognitive enhancement: are we barking up the wrong tree? *Curr Drug Abuse Rev.* 2012;5:255-256.
33. Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci.* 2003;14:125-130.
34. Chaddock L, Erickson KI, Prakash RS, et al. A neuroimaging investigation of the association between aerobic fitness, hippocampal volume, and memory performance in preadolescent children. *Brain Res.* 2010;1358:172-183.
35. Erickson KI, Voss MW, Prakash RS, et al. Exercise training increases size of hippocampus and improves memory. *Proc Natl Acad Sci U S A.* 2011;108:3017-3022.
36. Voss MW, Erickson KI, Prakash RS, et al. Functional connectivity: a source of variance in the association between cardiorespiratory fitness and cognition? *Neuropsychologia.* 2010;48:1394-1406.
37. Voss MW, Prakash RS, Erickson KI, et al. Plasticity of brain networks in a randomized intervention trial of exercise training in older adults. *Front Aging Neurosci.* 2010;2:32. doi: 10.3389/fnagi.2010.00032.
38. Cassilhas RC, Viana VA, Grassmann V, et al. The impact of resistance exercise on the cognitive function of the elderly. *Med Sci Sports Exerc.* 2007;39:1401-1407.
39. Chytrova G, Ying Z, Gomez-Pinilla F. Exercise contributes to the effects of DHA dietary supplementation by acting on membrane-related synaptic systems. *Brain Res.* 2010;1341:32-40.
40. Elderkin-Thompson V, Irwin MR, Hellemann G, et al. Interleukin-6 and memory functions of encoding and recall in healthy and depressed elderly adults. *Am J Geriatr Psychiatry.* 2012;20:753-763.
41. Jefferson AL, Massaro JM, Beiser AS, et al. Inflammatory markers and neuropsychological functioning: the Framingham Heart Study. *Neuroepidemiology.* 2011;37:21-30.
42. Trollor JN, Smith E, Agars E, et al. The association between systemic inflammation and cognitive performance in the elderly: the Sydney Memory and Ageing Study. *Age (Dordr).* 2012;34:1295-1308.
43. Trollor JN, Smith E, Baune BT, et al. Systemic inflammation is associated with MCI and its subtypes: the Sydney Memory and Aging Study. *Dement Geriatr Cogn Disord.* 2010;30:569-578.
44. Reichenberg A, Yirmiya R, Schuld A, et al. Cytokine-associated emotional and cognitive disturbances in humans. *Arch Gen Psychiatry.* 2001;58:445-452.
45. Daynes RA, Araneo BA, Ershler WB, et al. Altered regulation of IL-6 production with normal aging. Possible linkage to the age-associated decline in dehydroepiandrosterone and its sulfated derivative. J Immunol. 1993;150:5219-5230.
46. Prince M, Bryce R, Albanese E, et al. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement.* 2013;9:63-75 e62.
47. Profenno LA, Porsteinsson AP, Faraone SV. Meta-analysis of Alzheimer's disease risk with obesity, diabetes, and related disorders. *Biol Psychiatry.* 2010;67:505-512.
48. Yaffe K, Weston AL, Blackwell T, et al. The metabolic syndrome and development of cognitive impairment among older women. *Arch Neurol.* 2009;66:324-328.
49. Gamba P, Testa G, Sottero B, et al. The link between altered cholesterol metabolism and Alzheimer's disease. *Ann N Y Acad Sci.* 2012;1259:54-64.
50. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. *Am J Public Health.* 1998;88:1337-1342.
51. Bertram L, McQueen MB, Mullin K, et al. Systematic meta-analyses of Alzheimer disease genetic association studies: the AlzGene database. *Nat Genet.* 2007;39:17-23.
52. Corder EH, Saunders AM, Strittmatter WJ, et al. Gene dose of apolipoprotein E type 4 allele and the risk of Alzheimer's disease in late onset families. *Science.* 1993;261:921-923.
53. Beydoun MA, Kaufman JS, Satia JA, et al. Plasma n-3 fatty acids and the risk of cognitive decline in older adults: the Atherosclerosis Risk in Communities Study. *Am J Clin Nutr.* 2007;85:1103-1111.
54. Schaefer EJ, Bongard V, Beiser AS, et al. Plasma phosphatidylcholine docosahexaenoic acid content and risk of dementia and Alzheimer disease: the Framingham Heart Study. *Arch Neurol.* 2006;63:1545-1550.
55. van Gelder BM, Tijhuis M, Kalmijn S, et al. Fish consumption, n-3 fatty acids, and subsequent 5-y cognitive decline in elderly men: the Zutphen Elderly Study. *Am J Clin Nutr.* 2007;85:1142-1147.
56. Stonehouse W, Conlon CA, Podd J, et al. DHA supplementation improved both memory and reaction time in healthy young adults: a randomized controlled trial. *Am J Clin Nutr.* 2013;97:1134-1143.
57. Jackson KG, Armah CK, Doman I, et al. The impact of age on the postprandial vascular response to a fish oil-enriched meal. *Br J Nutr.* 2009;102:1414-1419.
58. Huang TL, Zandi PP, Tucker KL, et al. Benefits of fatty fish on dementia risk are stronger for those without APOE epsilon4. *Neurology.* 2005;65:1409-1414.
59. Vega-Flores G, Rubio SE, Jurado-Parras MT, et al. The GABAergic Septohippocampal Pathway Is Directly Involved in Internal Processes Related to Operant Reward Learning. *Cereb Cortex.* 2013; Mar 10:[Epub ahead of print].
60. Jurado-Parras MT, Gruart A, Delgado-Garcia JM. Observational learning in mice can be prevented by medial prefrontal cortex stimulation and enhanced by nucleus accumbens stimulation. *Learn Mem.* 2012;19:99-106.
61. Gamiz F, Gallo M. Taste learning and memory: a window on the study of brain aging. *Front Syst Neurosci.* 2011;5:91.

87379/August 2013 LITHO IN USA