

CIMMYT Series on Carbohydrates, Wheat, Grains, and Health

Carbohydrates and Their Grain Sources: A Review on Their Relationships to Brain Health^{1,2}

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ABSTRACT

Recent claims suggesting whole and refined grain-based foods should be omitted from the diet because the carbohydrates (CHOs) they contain negatively impact the brain's long-term health and functioning need to be evaluated in light of the scientific literature. This review reveals that grain-based foods are important sources of glucose for the brain, which preferentially uses glucose as a source of energy. The lipid-rich brain is very metabolically active and, therefore, requires a lot of energy. Further, CHO-rich foods such as whole grains contain a variety of antioxidant and bioactive compounds that counter oxidative stress and inflammation, helping to prevent damage to brain tissue and maintain optimal cognitive functioning. Such compounds become more important with aging because the brain becomes more susceptible to oxidative stress and inflammation—conditions that promote the development of neurological diseases and disorders. An overview of studies on the relationship between CHO-rich, grain-based foods and many different neurological conditions is presented. The body of scientific evidence shows that whole and refined grain-based foods contribute energy and needed glucose for brain metabolism and that whole grains have the potential to offer slow glucose release and the capacity to deliver vitamins, minerals, and phytonutrients that are important for brain health. Because refined grain-based foods often deliver rapidly available glucose and may contain fewer phytochemicals and nutrients and less fiber than whole grains, results described in the scientific literature on the effects of refined grains on cognitive health are mixed. For example, studies have found that too much refined grain, as well as too many calories or too much fat, in the diet can have adverse health effects. However, refined grains consumed as part of a balanced diet, including the minerals and vitamins contained in enriched and fortified grains, appear to contribute positively to cognitive capacity and brain health. The roles whole and refined grains and their CHOs play in brain metabolism and various neurological diseases and disorders when consumed as part of balanced dietary patterns (e.g., Mediterranean-style diets) and as part of unbalanced dietary patterns (e.g., typical Western diets) that include too many calories and grain-based desserts and too few fruits, vegetables, and whole grains are examined.

In the previous review articles in this series, carbohydrates (CHOs) and grains were introduced and established as important contributors of nutrition in the human diet and as promoters of a vast array of health benefits (1–3), such as reduced risk of cardiovascular disease (CVD), weight gain (4), type 2 diabetes (5), and both specific-cause and all-cause mortality (6–9). The relationship between

different types of CHOs and the development of neurological diseases and disorders is another area of interest, especially due to the links between oxidative stress and inflammation in the aging brain (10). Various bioactive, antioxidant, and fiber components found in refined and whole grains can aid in combatting inflammation and oxidative stress and regulating blood glucose response; all of which are beneficial for brain health. Refined grains contain less fiber and fewer vitamins than whole grains but often are enriched or fortified to provide key micronutrients, such as zinc, folic acid, and B vitamins, that are necessary to maintain a healthy brain. In prospective cohort studies, dietary intake scores that show high compliance with Mediterranean and DASH (Dietary Approaches to Stop Hypertension) style dietary patterns that include optimal amounts and types of grain products are associated with higher scores for cognitive function (11,12).

Despite the positive association between brain health and inclusion of grains as part of a balanced diet, many claims from authors and the media discourage the consumption of CHOs from grains, with specific accusations like “whole grain bread can slowly impinge on your brain's long-term health and functionality” (13). These sources further claim that consumption of carbohydrates, including those found in grains such as wheat, cause cognitive decline and numerous neurological disorders.

The purpose of this review is to provide an overview of common neurological disorders, evaluate the scientific literature on the important role of CHOs as fuel for the brain, and discuss existing evidence concerning the roles of CHOs and grains in the development and course of some common neurological diseases and disorders. An overview of the scientific evidence regarding common sources of CHOs and their relationships to different neurological outcomes will be provided.

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Overview of Common Neurological Diseases and Disorders

More than 600 neurologic diseases and disorders have been identified. These neurologic conditions can lead to problems with movement, speech, breathing, learning, memory, sensory perception, mood, and behavior. There are nearly as many causes as there are diseases and disorders. These include gene-related conditions such as Huntington's disease and muscular dystrophy; nervous system growth impairment and developmental conditions such as spina bifida; abnormal growths or injuries that impair the brain and spinal cord or other parts of the nervous system; infections such as meningitis; impaired blood supply to the brain, such as occurs with stroke; disordered chemical or electrical balances in the brain, such as those associated with depression, epilepsy, mental illness, and attention deficit hyperactivity disorder (ADHD); and degenerative diseases that are progressive and affect the nervous system, such as Parkinson's disease, or that cause irreversible changes in the brain, such as Alzheimer's disease.

Some common neurological disorders and diseases are listed in Table I. Some of these conditions, although minor in many forms or episodic, affect many people across the globe. According to data from the World Health Organization (WHO), depression is ranked as the fourth leading cause of disability worldwide, and the top four neurological disorders worldwide are migraine, epilepsy, dementia, and Parkinson's disease (23). The incidence of headache is likely underreported, but studies from North America, Europe, and Central America suggest that the percentage of the population experiencing tension headaches may be as high as 80%. These studies also suggest that severe headaches such as migraines affect 6–8% of men and 15–18% of women (18).

Depression affects nearly 16 million adults in the United States (24), whereas epilepsy and schizophrenia affect 2.9 and 3.5 million Americans, respectively (17). Some disorders are more common in children, such as ADHD, which affects 9% of American children 13–18 years of age, with boys at four times higher risk compared with girls (15). A number of conditions listed in Table I, such as Alzheimer's disease and dementia, occur more frequently as people age. Although Alzheimer's disease and other dementias can occur in younger adults, they are most prevalent in people over the age of 60.

The root causes of these conditions are still unknown.

Disorders such as mild cognitive impairment (MCI) cause some degree of decline in cognitive ability, including memory and thinking skills. Individuals with MCI have an increased risk of developing Alzheimer's disease or other dementias. Of the diseases and disorders listed in Table I, degenerative diseases such as Parkinson's and Alzheimer's are especially concerning because they are characterized by massive neuronal loss, loss of memory, and cognitive dysfunction (25). As these diseases progress, they lead to the inability to complete activities of daily living, which ultimately places a huge burden on their families and care givers.

MCI, Parkinson's disease, Alzheimer's disease, and dementia are recognized as common consequences of the aging process (25). In the United States alone, about 5.3 million people have Alzheimer's disease, and about 10–20% of those 65 years of age and older have MCI (16,26,27). Globally, nearly 44 million people have Alzheimer's disease or a related dementia

(16,26), while Parkinson's disease affects 1 million Americans and 7–10 million individuals worldwide (27). Unfortunately, these numbers will continue to grow as the global population continues to age (28). A recent survey from the WHO projects that between one in four and one in six people in most countries will meet the criteria for a mental disorder during their lifetime (29).

Other less serious conditions have also been described. Some are controversial, including "brain fog," which is a reportedly frustrating disorder because those who suffer from it lose mental clarity and are unable to think coherently. Unfortunately, there is no general consensus as to whether brain fog is an actual condition, nor are there statistics to describe its prevalence. However, cancer patients undergoing certain treatments and celiac patients prior to following a gluten-free diet can experience a cognitive deficit referred to as "brain fog" (30,31). Although brain fog is a term commonly used in the popular press, unlike other neurological diseases and disorders scientific evidence

does not exist that relates it to changes in the brain that occur during aging.

The Brain and Aging

Senescence or "aging" is a natural physiological process that takes place over time. Eventually it can result in changes in metabolism, errors in DNA replication, loss of function, disease processes, and progressive deterioration of organs. As the brain ages, learning becomes more difficult, and memory impairment can lead to a decline in cognitive function.

Progressive changes in the brain with increasing age contribute to the decline in cognitive function. The first change generally is a decreased rate of neurogenesis that occurs because of reduced production of new neural cells with increasing age (10). The second change is decreased neuroplasticity of the cortex and hippocampus—the two regions that are most susceptible to the aging process (25). Neuroplasticity is defined as the brain's ability to reorganize itself by forming new neural connections throughout life. Neuroplasticity allows the neurons in the brain

Table I. An overview of some common neurological disorders and diseases^a

Disease or Disorder (Reference)	Definition
Alzheimer's disease (14)	A type of dementia that causes problems with memory, thinking, and behavior. Symptoms usually develop slowly and progress over time, becoming severe enough to interfere with activities of daily living. Alzheimer's disease is characterized by the presence of plaques and tangles that spread through the cortex as the disease progresses.
Attention deficit hyperactivity disorder (15)	Attention deficit hyperactivity disorder (ADHD) is most commonly diagnosed in children but can be diagnosed in adolescents and adults. Symptoms of ADHD include difficulty in staying focused and paying attention, difficulty controlling behavior, and hyperactivity (overactivity).
Dementia (16)	A group of disorders that cause cognitive decline as a result of death or damage to brain cells. Dementias cause a decline in at least two of four essential cognitive functions: 1) memory; 2) ability to speak or understand language; 3) capacity to plan, make sound judgments, and carry out complex tasks; and 4) ability to process and interpret visual information.
Epilepsy (17)	A central nervous system disorder in which nerve cell activity in the brain is impaired, causing seizures or periods of unusual behavior, sensations, and sometimes loss of consciousness. Epilepsies are a group of conditions characterized by recurring seizures, sometimes called seizure disorder.
Headache (18)	A pain in any part of the neck or head characterized by a dull ache, sharp pain, or throbbing sensation. The pain may be located in a specific area, occur on one or both sides of the head, radiate, or feel vice-like. Migraines, tension-type headaches, and cluster headaches are among the types of primary headaches whose incidence is unrelated to an identifiable cause, such as infection or trauma to the head and/or neck. Headaches caused by the latter are termed secondary headache disorders. Altogether headaches are among the most common disorders of the nervous system.
Major depressive disorder (19)	Depression is a catchall term for feelings of sadness. Major depressive disorder is a serious illness that involves a persistent feeling of sadness and loss of interest. It involves the body, mood, and thoughts and affects the way a person eats, sleeps, feels about themselves, and thinks about things. Depression alters brain chemistry. Major depressive disorders can be mild, moderate, or severe and include persistent depressive disorder and bipolar disorder.
Mild cognitive impairment (20)	Mild cognitive impairment is characterized by cognitive changes that are serious enough to be noticed by the individuals experiencing them or by other people but that are not severe enough to interfere with daily life or independent function. These are distinguishable from the cognitive changes of normal aging and other dementias.
Parkinson's disease (21)	A chronic, neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra and a deficiency of dopamine in the structures of the basal ganglia. This loss results in the slow and progressive loss of motor and nonmotor functioning.
Schizophrenia (22)	A long-term, disabling mental disorder involving a breakdown in the relationship between thought, emotion, and behavior, causing disordered or delusional thinking, inappropriate actions and feelings, withdrawal from reality and personal relationships, and an inability to sense what is real and what is not.

^a This table provides an overview of the most common neurological disorders and diseases discussed in this review; it does not provide a comprehensive review of all neurological disorders.

to compensate for injury and disease and to adjust their activities in response to new situations or changes in their environment. The cortex and hippocampus are two regions of the brain that are critical because they play important roles in both short- and long-term memory, as well as attention, perception, thought, and language.

Finally, with aging there is a decrease in the expression of specific neurotrophic factors that play important roles in synaptic and neuronal growth (25): brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and glial cell-derived neurotrophic factor (GDNF). BDNF, a small dimeric protein (structurally related to NGF) that is abundant in the adult mammalian brain, is responsible for regulating long-term potentiation (the ability of the brain to determine how frequently it sends signals to other brain cells), synaptic plasticity (the ability of the synapses to strengthen or weaken over time), axonal sprouting (the process in which fine nerve sprouts grow out from intact axons to reinnervate denervated muscle fibers), and differentiation of neuronal cells (32).

Studies have shown that levels of BDNF are low in Alzheimer's disease patients compared with healthy individuals (33–35), which suggests that neurotrophic factors also are affected in the aging process and may be associated with cognitive decline. Furthermore, there is evidence that aging is associated with impairment in episodic (i.e., working) and spatial memory (Table II). Spatial and working memory are largely dependent on the hippocampus, and Leal and Yassa (10) have de-

scribed how with aging the hippocampal network and its input pathways are altered. Collectively the changes associated with the brain and aging are multifaceted. To summarize, neurogenesis decreases with age, and the regions of the brain responsible for learning and memory decline in functionality (10,25). A lifetime of oxidative stress and inflammation also contributes to problems with neurological functioning and to diseases such as Alzheimer's and Parkinson's (36).

Oxidative Stress and Inflammation: Two Pathways Common to Neurodegenerative Diseases and Disorders

Oxidative stress is the result of an imbalance between reactive oxygen species, such as superoxide, hydrogen peroxide, and the hydroxyl radical, and a biological system's ability to detoxify them. The end result is damage to proteins, fat, DNA, and RNA and the release of transcription factors such as nuclear factor kappa B (NF- κ B) (44). The activation of NF- κ B activates pro-inflammatory cytokines, which include interleukin 1 (IL-1), tumor necrosis factor alpha (TNF α), and chemokines such as cyclooxygenase 2. Although all promote inflammation (44), TNF α has been shown to be overexpressed in Alzheimer's and Parkinson's disease patients (45,46).

The lipid-rich brain is highly susceptible to oxidative stress and inflammation compared with the rest of the body (44,47–50) because there is only a limited antioxidant defense system for this very metabolically active organ (51). As a result, the brain is vulnerable to lipid peroxidation, which

ultimately decreases cell membrane fluidity and can damage membrane proteins, enzymes, and ion channels (51). Patients with Alzheimer's or Parkinson's disease, when compared with the normal population, have impaired mitochondrial function and ATP generation, a lower antioxidant status, and greater oxidative damage to lipids, proteins, DNA, and RNA (52,53). Oxidative stress and inflammation are not the only aberrations found in neurological disorders—impaired glucose metabolism and insulin resistance also are common.

Fueling the Brain

Glucose Metabolism. Glucose is the main source of energy utilized by the brain (54–56). The human brain accounts for about 2% of body weight, but it consumes 20% of the energy and 25% of the body's glucose supply (57,58). Of all the cells in the adult body, brain neurons have the highest energy demand. They require a constant supply of glucose because they rely almost exclusively on glucose metabolism for energy generation. The demand for glucose is absolute, and while it cannot be replaced, it can be supplemented, as during periods of starvation, with ketone bodies. The average minimum amount of glucose utilized by the brain is 130 g/day (59).

The breakdown of glucose not only provides fuel for brain functions through the generation of adenosine triphosphate (ATP), but also yields metabolites that are used by the brain, including glycoproteins, glycolipids, amino acids, and one-carbon donors, for methylation reactions (57). Further, glucose metabolism is involved

Table II. Some terms used to describe or measure brain function^a

Term (Reference)	Definition
Attention (37)	The behavioral and cognitive process of selectively concentrating on a discrete aspect of information, whether subjective or objective, while ignoring other perceivable information.
Cognition (38)	The set of all mental abilities and processes related to knowledge, attention, memory and working memory, judgment, evaluation, reasoning, decision making, comprehension, and production of language.
Episodic (working) memory (39)	The ability to learn and retain new information. Episodic memory typically declines throughout life, and impairment is consistent with normal, healthy aging decline.
Executive functioning (40)	The ability to think abstractly and to plan, initiate, sequence, monitor, and stop complex behavior.
Foggy brain or brain fog (41)	A state of mental confusion or lack of mental clarity. Brain fog may cause a person to become forgetful, detached, and often discouraged and depressed. Currently, brain fog is not recognized as a clinical diagnosis because there is no agreed upon medical test, it is highly subjective, and it is affected by a variety of things, including lack of sleep.
Mental energy (42)	Mental energy consists of mood, motivation, and cognition. Optimal mental energy is characterized by an enthusiastic outlook, abundant energy, clear thinking, and a sharp memory.
Mini-mental state exam (43)	A widely used tool implemented by physicians to test for problems with memory or other mental abilities. The mini-mental state exam (MMSE) is used to test a number of different mental abilities, such as memory, language, and attention.
Spatial memory (10)	The part of memory that is responsible for recording information about an individual's environment and its spatial orientation.

^a This table provides an overview of some of the most common terms used to describe the aspects of neuroanatomy discussed in this review; it does not provide a comprehensive review of all terms.

in the formation of neurotransmitters such as acetylcholine and plays a critical part in the formation of memories, verbal and logical reasoning, and the ability to concentrate (54). Because the blood-brain barrier controls the entry of critical neuroactive compounds (e.g., glutamate, aspartate, glycine, D-serine) into the brain, these compounds must be synthesized from glucose within the brain.

Ketone Bodies as Alternative Fuel Sources. Dietary patterns that are very low in CHO, such as the paleo diet or periods of prolonged starvation, do not provide enough glucose to meet the energy needs of the brain, and the brain is unable to utilize fatty acids without breakdown products from CHO to enable metabolism through the Krebs cycle. Ketone bodies produced by the liver are able to fuel the brain when CHO is not available. The two main ketone bodies are acetoacetate and β -hydroxybutyrate; acetone is the least abundant ketone body (60). An overview of ketone bodies is provided in the text box below.

The long-term use of ketone bodies as an energy source for the brain in healthy individuals has been questioned. In a recent publication, Schönfeld and Reiser (61) describe multiple problems stemming from this scenario. The first is that the ATP generated from β -oxidation of fatty acids requires more oxygen compared with glucose, and the additional oxygen increases the risk of neurons becoming hypoxic (61). Second, harmful free radicals such as superoxide are generated from the β -oxidation of fatty acids, which causes severe oxidative stress. Finally, the rate of ATP generation is much slower for fatty

acids compared with glucose (61). Therefore, during periods of rapid neuron firing in the brain, the oxidation of fatty acids cannot guarantee ATP is generated quickly enough to be used by the neural cells. Collectively, all of this can lead to a decrease in brain function. In contrast, the metabolism of glucose generates more than twice as much ATP in the same amount of time as fat does (61).

In some cases, a ketogenic diet is used to treat specific medical conditions, such as epilepsy, especially epilepsy in children. This is because $\approx 30\%$ of epilepsies fail to respond to anticonvulsant drugs (62). A ketogenic dietary pattern is high in fat, adequate in protein, but low in CHO. The mechanism by which it helps control seizures is complex and largely still unknown, but it has been reported to lower blood glucose levels through the inhibition of glycolysis (63). This is helpful for those who are deficient in GLUT1—a transporter that facilitates the transport of glucose across the plasma membranes of cells (64,65). Statistics show that more than 10% of early-onset epilepsies and up to 1% of common idiopathic epilepsies are ascribed to a GLUT1 deficiency. Because glucose delivery to the brain is restricted in epileptic patients due to GLUT1 deficiency, the ketogenic diet is well suited for this population; however, vitamin and dietary fiber intakes must be monitored for potential deficiencies. Adverse effects can include acidosis, constipation, gastroesophageal reflux disease and other gut disorders, poor linear growth, renal calculi, changes in gut microbiota, and other metabolic abnormalities (66–68).

Some preliminary studies, mainly with rodents, have caused some researchers to hypothesize that intermittent fasting and other methods of inducing ketosis may be useful for maintaining hippocampus size, addressing some neurological conditions, and delaying impacts of aging in many tissues, especially the brain. However, several points must be noted. First, because the data are from animal studies direct extrapolation of the findings is limited due to metabolic differences. Second, energy-restricted diets or intermittent fasting plans reduce all types of calories, not just those from CHO and grains. Third, the few human studies conducted have had small sample sizes and limitations in design and tended to include subjects with a specific disorder, further restricting their applicability. Most data from low-CHO diets are based on diets

with much higher levels of CHO than those found in either therapeutic ketogenic diets or those used in animal studies, so these may not be directly applicable. Nevertheless, the findings all emphasize that diets with excess calories or that are unbalanced nutritionally are not ideal for the general health and functioning of the body and brain (58,69–73).

Effects of Excess Energy Intake and Insulin Resistance on Brain Function

The body responds to intake of macronutrients, especially CHO and protein, by causing the pancreas to secrete insulin in order to utilize the ingested macronutrients. Under normal conditions, insulin binds the resulting blood glucose and delivers it to cells needing energy. However, if energy needs have been met, insulin activates metabolic machinery that promotes the synthesis of the excess glucose into triglycerides. In conditions such as chronic hyperglycemia and excess circulating insulin, which can occur with excess body weight or insulin resistance, insulin does not bind with the glucose effectively, and excess circulating glucose is not removed from the bloodstream. Any impairment of glucose entry into cells is concerning, and its impact is greater as insulin resistance increases. Excess circulating glucose can trigger an inflammatory response, lead to glycosylation of proteins, impair the functioning of all tissues (74), and lead to a variety of chronic conditions such as diabetes. The brain, like the rest of the body, is adversely affected by excess circulating glucose (1), and the aging brain is even less able to deal with excess glucose and conditions that impair glucose entry into cells (75).

Excess CHO intake in individuals with impaired glucose tolerance and insulin resistance has been shown to be problematic, but CHO intake is not the sole cause (1). Excess intake of fat or calories and inadequate intake of nutrients and phytonutrients also are known causes of inflammation, insulin resistance, and their attendant adverse effects (76–78). However, intake of the right balance of available CHO and dietary fiber, especially some dietary fibers from whole grains and other CHOs, has the ability to attenuate glucose and insulin response (79). Thus, consumption of cereal fibers and whole grains is recommended to the public in dietary guidance (80). These dietary components are important not only because they can help achieve the right balance of available CHO, but they also con-

Overview of Ketone Bodies

Ketone bodies include acetone, acetoacetate, and β -hydroxybutyrate and are produced by the liver from fatty acids during periods of low food intake. Of the three, acetone is the least abundant and is produced from the decarboxylation of acetoacetate. Acetone is slowly excreted via the lungs and generates the distinct smell on the breath of patients with diabetic ketoacidosis. Acetoacetate and β -hydroxybutyrate serve as an energy source for peripheral tissues, such as skeletal muscle, cardiac muscle, the renal cortex, and the brain.

tain many components in their matrices that may also be important for brain health. Whole and enriched grains are examples of CHO sources that contain additional nutrients and bioactive components that are beneficial for brain health.

Optimal Fuel for Brain Health: Whole and Enriched Grains

Antioxidants and Anti-inflammatory Agents. Whole and enriched grains contain nutrients that provide protection to the brain through different mechanisms

Nuclear Factor Kappa B

Nuclear factor kappa B (NF- κ B) is a protein complex that controls DNA transcription and cytokine production. It is produced in response to infections, stress, cytokines, free radicals, oxidized metabolites (including oxidized LDL), and bacterial or viral antigens. Its full name is nuclear factor kappa light-chain enhancer of activated B cells, in which the kappa light chains are critical components of immunoglobulins. Overexpression of NF- κ B has been linked to cancer and other autoimmune diseases. NF- κ B has also been implicated in synaptic plasticity and memory processes.

(Tables III and IV). Further, many whole grains are rich sources of phenolics that function as antioxidants and anti-inflammatory agents that have the potential to mediate oxidative stress throughout the body and combat pro-inflammatory proteins (81,82). For example, akyresorcinols, a class of phenolic lipids that act as plant estrogens, have high antioxidant activity (83,84). Both rye and wheat contain akyresorcinols, but they are found in higher quantities in rye. Akyresorcinols are used in some studies as markers of whole grain intake. In addition, lignans are changed by bacteria in the gut to enterolactone, which in animal experiments has been found in various parts of the body, including the brain, after eating grains (83).

Bioactives. While certain bioactives are found to some degree in nearly all grains, others are unique to only a few grains. For example, most grains contain some phenolics. Highly colored grains such as purple corn and red rice are very rich in these compounds, and antioxidant potential is correlated with total phenolic content (84). Various yellow or orange grains such as corn (maize) and wheat contain carotenoids, which also act as antioxidants. Because few of the carotenoids found in grains are vitamin A precursors, grains contribute only slightly to vitamin A status. Many whole grains are rich in tocopherols and tocotrienols, with wheat germ containing particularly high levels of

these components (82,85). Rice is one of the few grains that contain oryzanol. Oats, on the other hand, are rich in avenanthramides, tocopherols, tocotrienols, β -glucan, and phenolic compounds (85–87). Avenanthramides are polyphenol compounds that can decrease inflammation and block the activity of NF- κ B. The role of NF- κ B is discussed in the text box to the left.

The benefits of these grain bioactives depend on their bioaccessibility, absorption in the gastrointestinal tract, bioavailability, and overall impacts on oxidation throughout the body and in nervous system tissue. Bioactives such as betaine and choline are found in the bran and germ of most grains. In fact, cereal grains are the main source of betaine in the diet, providing 60–67% of the betaine in the typical Western diet (88). Betaine, a methyl derivative of glycine, functions as an osmolyte and methyl donor, functions in the brain as part of the γ -amino butyric acid (GABA) metabolic pathway, has antidepressant and other effects, and is a precursor to choline (89). As an osmolyte, betaine helps maintain water balance and protects cells from dehydration. As a methyl donor, betaine, like choline, provides the one-carbon units for DNA methylation reactions. Although choline participates in DNA methylation reactions, it also is required for the synthesis of the neurotransmitter acetylcholine and

Table III. Bioactive compounds found in whole grains and their health-protective mechanisms^a

Bioactive Compound(s)	Grain(s) High in Bioactive Compound(s)	Potential Protective Mechanisms	Health Benefits
Polyunsaturated fatty acids (PUFAs)	Whole grain wheat, rice, oats, maize, and most grains	Regulate neurotransmission, cell survival, and inflammation	Improve mood and cognition
Alkyresorcinols	Whole grain wheat, rice, rye, and oats	Function as antioxidants	Antioxidants and estrogenic
Anthocyanins	Colored rices (including brown rice) and colored maize	Suppress iNOS (inducible nitric oxide synthase) expression and scavenge free radicals	Antioxidants and anti-inflammatories
Avenanthramide	Oats	Decreases inflammation-related cytokine production	Antioxidant and anti-inflammatory
Choline	Whole grain wheat, rice, quinoa, most cereal grains, and oats	Supports intracellular signaling, methyl donor for DNA methylation, epigenetic regulator of gene expression, and accelerates synthesis and release of acetylcholine	Aids brain development and normal learning and memory functions
Ferulic acid	Whole grain wheat, rye, oats, maize, and rice	Scavenges free radicals and decreases inflammatory cytokines	Antioxidant and anti-inflammatory
Methionine	Whole grain wheat, rice, and oats	Functions as an antioxidant, precursor to S-adenosyl methionine, and methyl and glutathione donor	Prevents neural tube defects and cognitive impairment
Tocotrienols	Whole grain wheat, wheat germ, rice, maize, and oats	Function mainly as antioxidants, act directly to inhibit formation of carcinogenic compounds, and act as anti-inflammatories	Protect neurons and prevent neurodegeneration
Oryzanol	Brown rice, Korean rice, and rice bran oil	Functions as an antioxidant that prevents cell death in neuronal cells	Helps lower cholesterol, anti-inflammatory, and possesses anticancer and antidiabetic properties

^a Adapted from Fardet, "A New Hypothesis for the Health-Protective Mechanisms of Whole-Grain Cereals: What Is Beyond Fiber?" *Nutr. Res. Rev.* 23:65, 2010.

an array of phospholipids, which are components of brain lipids and membranes such as the myelin sheath (90). In addition, choline plays a critical role during periods of neonatal development and can have a long-term effect on memory (90). Fetal development of the hippocampus (the memory center of the brain) requires choline, and the presence of betaine may reduce the impact of alcohol exposure during fetal development (91,92). Rodent studies have shown that lack of choline in the diet causes detrimental changes to brain structure and function at all stages of life (93).

Because choline plays diverse roles, from formation of cell structure to neurotransmitter synthesis, adequate choline in the diet is critical for prevention of neurological disorders (94). Choline, in tandem with folate and the essential amino acid methionine, is critical for DNA methylation and gene expression. These are critical processes throughout the body, as well as for proper brain and nervous system functioning (91). Alzheimer's disease is associated with acetylcholine neuronal deficit (93). In the Framingham cohort, better verbal and visual memory were associated with higher choline. Furthermore, an inverse association was observed between

past choline intakes and the presence of greater white-matter hyperintensity, measures associated with impaired cognitive function and Alzheimer's disease (95). Sadly, recent research shows that only 1–3% of females in the United States over 14 years of age and 2–13% of males meet the AI (adequate intake) guideline for choline (96).

Vitamins. A healthy nervous system relies on the closely interrelated functions of the eight B vitamins working together. They function as coenzymes throughout the body in various key cycles, such as the Krebs cycle, which is crucial for utilizing energy provided to the brain. They also are involved in antioxidant generation, tissue repair, methylation of DNA and RNA and other components, and synthesis of neurochemicals and other signaling molecules. Their importance is underscored by the fact that a specific carrier for crossing the blood-brain barrier has been found for each of these vitamins. Serious neurological complications ensue when these vitamins are lacking, including peripheral neuropathy, cognitive impairment, dementia, and depression.

For example, thiamin (vitamin B1) plays an essential role in maintaining the func-

tional integrity of neuronal cells, including neuroglia. It also plays a key role as a cofactor for enzymes that are critical for brain functioning. Thiamin-dependent transketolase helps synthesize the antioxidant glutathione, which provides protection for cells, including brain cells. Two other thiamin-dependent enzymes are involved in the synthesis of neurotransmitters, including acetylcholine. Thiamin also is necessary for production and maintenance of the myelin sheath, which must function properly to carry electrical impulses (97). Lack of thiamin leads to mitochondrial dysfunction in regions of the brain and other impairments, such as increased oxidative stress and inflammation, decreased neurogenesis, and blood-brain barrier disruption (97). An animal study has shown that short-term depletion of thiamin drastically affects plasma, liver, and cerebellum concentrations, whereas repletion of thiamin from consumption of whole wheat bread or white (refined) bread restores thiamin levels in the cerebellum and kidneys (98). Data from human studies reveal that the brains and peripheral tissues of patients with Alzheimer's disease have reduced thiamin levels and thiamin-dependent enzyme activity (99).

Table IV. Vitamins and minerals found in whole grains and their health-protective mechanisms^a

Vitamin or Mineral	Grains High in Vitamin or Mineral	Potential Protective Mechanisms	Health Benefits
Biotin	Whole grain wheat, rice, barley, and oats	Functions as a coenzyme in bicarbonate-dependent carboxylation reactions, necessary for cell growth and production of fatty acids, and helps maintain a steady blood sugar level	Mental and nervous system health (helps prevent certain neurological disorders)
Copper	Whole grain wheat, rice, and oats	Serves as a cofactor for superoxide dismutase and functions as an antioxidant	Brain and mental health (helps prevent central nervous system dysfunction)
Folate	Whole grain wheat, rice, and oats; quinoa; wild rice; and many enriched or fortified flours, cereal grains, and meals	Functions as a coenzyme in single-carbon transfers in metabolism of nucleic amino acids and prevents depletion of brain membrane phosphatidylcholine	Prevents neural tube defects and promotes mental health (reduces risk of cognitive impairment and depression)
Iron	Whole, enriched, and fortified cereal grains	Functions as an antioxidant in prevention of diseases arising from increased oxidative stress	Brain health (helps prevent development of certain neurodegenerative diseases and disorders)
Magnesium	Whole grain wheat, rice, oats, flours, cereal grains, and meals	Improves glucose uptake and clearance, can act as an antioxidant against lipid peroxidation, and plays a role in neurotransmission	Mental health (helps prevent fatigue, stress, and anxiety)
Riboflavin	Whole grain wheat, rice, and oats; quinoa; and many enriched or fortified flours, cereal grains, and meals	Participates as a coenzyme in numerous redox reactions in metabolic pathways and energy production via respiratory chain and assists fat, protein, and carbohydrate metabolism	Mental health (helps prevent neurodegeneration and peripheral neuropathy)
Thiamin	Whole grain wheat, rice, and oats and many enriched or fortified flours, cereal grains, and meals	Involved in glucose metabolism and Krebs cycle through thiamin-dependent enzymes and promotes healthy nerves (i.e., neuromodulation in brain and involvement in neurotransmitter synthesis)	Helps prevent alcohol-induced Wernicke-Korsakoff syndrome and beriberi; low levels are associated with diseases such as Alzheimer's
Zinc	Whole grain wheat, rice, and oats and many enriched or fortified flours, cereal grains, and meals	Antioxidant effect mainly as a cofactor for superoxide dismutase, role in neurotransmission and DNA stabilization, and regulates mechanisms of inflammatory disease pathologies	Mental health

^a Adapted from Fardet, "A New Hypothesis for the Health-Protective Mechanisms of Whole-Grain Cereals: What Is Beyond Fiber?" *Nutr. Res. Rev.* 23:65, 2010.

Other B vitamins, such as riboflavin (vitamin B2), also play essential roles in the brain. Riboflavin is a precursor for flavin coenzymes, which are involved in generation of energy. Not only is it critical for the metabolism of other B vitamins, it is involved in the synthesis of heme proteins, which carry oxygen, generate energy through electron transport to the brain's energy-demanding cells, and detoxify xenobiotics and active oxygen species. Dysregulation of any of these processes due to riboflavin deficiency has adverse effects on brain and nervous tissue functioning. A recent review described the role of riboflavin in iron absorption, tryptophan metabolism, mitochondrial dysfunction, and brain dysfunction (100). Further research is needed to gain a deeper understanding of its role and potential for nutrition therapy and brain dysfunction in the future (100).

Niacin (vitamin B3) plays a role in brain health as well, mirroring the role of riboflavin in the niacin-derived processes and enzymes that are involved in a vast array of brain and nervous tissue reactions. Niacin receptors are downregulated in people with schizophrenia and upregulated in the substantia nigra of people with Parkinson's disease, in which niacin levels are generally low. Other B vitamins, such as B6 (pyridoxine), are involved in the folate cycle. Vitamin B6 is a rate-limiting cofactor in the synthesis of neurotransmitters such as dopamine, serotonin, GABA, and noradrenaline.

Many other vitamins are found in grains as well. While some are lost in milling, others are added to refined grains to replace these losses. The important contribution of grain-based foods is shown in the Multiethnic Cohort Study of U.S. adults 45–75 years of age. In the study, whole and refined grain-based foods contributed one-third to one-half of the thiamin; one-fourth of the riboflavin, vitamin B6, and folic acid (vitamin B12); and about one-third of the niacin in the diets consumed (101). Because the interaction of these B vitamins is important for nervous system tissue integrity and functioning, the vitamin contribution of grain-based foods is critical (102). Low levels of these B vitamins can impact neural functioning and result in decreased cognitive functioning. Poor dietary choices in developed countries can result in marginal intake of many B vitamins, which may cause mild learning or other neurological and brain function issues. Because grain-based foods are an important source of B vitamins, elim-

ination of whole and refined grains from the diet can have a negative impact on the intake of these and other vitamins.

Minerals. Whole and refined grains are also a source of minerals. Although whole grains contain more minerals, in some cases absorption from refined grains is better than from whole grains. Minerals such as magnesium and zinc play a vital role in synaptic plasticity, learning, and memory (103,104). Animal studies have shown that zinc is involved in enabling communication between neurons and the hippocampus and, therefore, plays a role in memory. Supplementation of magnesium and zinc in rats with Alzheimer's disease reversed impairments in synaptic proteins and dendrites (103–105). Low levels of magnesium are associated with a variety of neurological problems, including migraine headaches, Alzheimer's disease, and cerebrovascular accident (stroke) (105).

Zinc is important not only for prevention of low-level inflammation throughout the body and nervous system associated with its deficiency, but also as a cofactor in a variety of neurological functions (106). It is found in the presynaptic vesicles and is needed for neuronal signaling and proper synaptic functioning. Throughout the lifespan, starting with fetal development, zinc is involved in neuronal plasticity. At the cellular level, zinc modulates synaptic activity. Alterations in brain zinc status are implicated in a wide range of neurological disorders, including impaired brain development and neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, and prion diseases, as well as mood disorders, including depression. In addition, zinc has been implicated in neuronal damage associated with traumatic brain injury, stroke, and seizure. Because of differences in bioavailability due to grain type and processing, it is difficult to accurately quantify the contribution of bread and cereal products to the nutritive value of these minerals. However, their contribution is thought to be important (107,108).

Fatty Acids. Polyunsaturated fatty acids (PUFAs) found in the germ of most cereal grains are important for cell membrane and brain functioning (109). Throughout the body they function as anti-inflammatories. Both arachidonic acid and the n-3 family of long-chain fatty acids from fish and seeds are esterified and found in nerve cell membranes as phospholipids. Either directly or after conversion these compounds participate in signal transduction

compounds and regulate several processes within the brain, such as neurotransmission, cell survival and inflammation, and, thereby, mood and cognition. PUFA levels and the signaling pathways they regulate are altered in various neurological disorders, including Alzheimer's disease and major depression. As a result, they appear to be important for the prevention and treatment of brain disorders (110).

Finally, tocotrienols are antioxidants with neuroprotective effects, as shown in a recent trial. Volunteers with risk factors for CVD received 200 mg of mixed tocotrienols twice a day for 2 years. The results showed that mixed tocotrienols attenuated progression of white-matter lesions compared with a placebo treatment (111).

CHOs, Grain Intake, and Brain Health

Grains provide a large portion of dietary CHO, and they enter the diet in many ways. Although CHOs, as mentioned earlier, are critical for brain functioning, it has to be emphasized that diets high in CHOs and sugars in general represent a higher risk for Alzheimer's disease (112). This is because excess circulating glucose, particularly when connected to insulin resistance and impaired glucose tolerance conditions, may create underlying patterns of inflammation and play havoc with brain and cognitive functioning. In fact, poor glucose regulation is an established risk factor for impaired cognitive function in patients with diabetes (113). A recent systematic review concluded that poor glucose tolerance affects several domains of cognitive function, such as verbal memory, working memory, vigilance, and attention. These functions are most vulnerable to the adverse impacts of hyperglycemia and insulin resistance conditions (114).

Some suggest that the glycemic index (GI) or glycemic load (GL) of CHOs is a good way to predict their impact on the body and brain. However, attempts to associate either GI or GL with cognitive or other outcomes have often produced mixed results. For example, one review concludes that studies assessing the effect of GI on domains of cognitive function are inconsistent (113). The authors further conclude that although a low-GI meal may favor cognitive function in adults, the findings collectively are inconclusive (114).

Another area in which data are inconclusive is the long-term effect of ketosis on cognitive health. Some studies have suggested that dietary ketosis can enhance memory in individuals with MCI

(115); however, they were short-term (6 weeks) studies and did not test the effects of long-term ketosis. Proving that dietary ketosis is effective for cognitive health will require longer interventions and a better understanding of the metabolic changes and neurocognitive effects that occur during ketosis over the long term (115).

Effects of CHOs and Grains on Cognitive Performance and Mental Health. CHOs and grains have recently been attacked by some bloggers, media personalities, book authors, and health professionals who claim that all grains and most CHOs should be removed from the diet. Statements such as these that target CHOs and cereal grains need to be evaluated in light of the available scientific evidence. Other statements have attacked specific whole grain food sources, such as bread. For example, one author states, “Whole grain breads and favorite comfort foods are slowly impinging on your brain’s long-term health and functionality” (13). Such controversial assertions need to be scrutinized and supported with scientific evidence. The Whole Grains Council (part of the Harvard Oldways Trust) recently reviewed popular arguments made for avoiding grains in the diet and stated, “There is no evidence for the idea that we should avoid all grains in the diet” (116). Grains have been a staple in the human diet for thousands of years, and claims that “all grains are injurious to brain health” (13) are not substantiated by the scientific evidence (116).

Furthermore, scientific evidence supporting the health benefits of whole grains has been discussed in the previously published reviews in this series (1–5) with regard to lowering the risks for CVD, overweight, type 2 diabetes, and specific and all-cause mortality (6–9). Whole grains have also been shown to decrease markers of inflammation (i.e., TNF α) in a randomized trial in which participants were asked to replace portions of refined wheat with whole grain wheat or refined wheat products for 8 weeks (117). New evidence also confirms that whole grains were important to the evolution of the human brain (118). More specifically, Hardy et al. (118) looked at the role of diet in the development of early humans and found that CHOs, including whole grains, other starchy plant foods, and certain root vegetables, were necessary to accommodate the increased metabolic demands of the growing brain and that cooking of CHO-rich and other foods in-

creased their digestibility and palatability, allowing for increases in brain size (118).

Relationship between Breakfast Consumption and Cognitive Performance and Mental Health. Cognitive performance during the day has been associated with consumption of breakfast, including ready-to-eat cereals (RTEC), especially in school-aged children. Studies have been conducted to assess the effects of consuming breakfast on cognition and academic performance, as well as the effects of breakfasts differing in energy and macronutrient composition. However, the scientific evidence on this subject is not conclusive for either children or adults.

In a systematic review conducted by Hoyland et al. (119), the majority of the evidence demonstrates positive effects of eating breakfast on certain measures of cognitive performance in school-aged children compared with not eating breakfast. These include positive associations between some aspects of memory and attention, although not verbal memory. For spatial memory, some studies show a benefit of breakfast consumption, whereas other studies show no difference. The review concludes that it is difficult to recommend an optimal breakfast for cognitive function based on current research findings (119).

Another review looking at the relationship between cognitive and academic performance and energy intake at breakfast and breakfast composition found little consistency (120). Even though some of the evidence indicates that a lower glycemic response is beneficial for cognitive performance in children, this finding needs to be substantiated by further trials.

Consumption of RTECs and other cereals at breakfast compared with no breakfast was associated in one study with improvements in some areas of cognition, including spatial memory in both boys and girls and short-term memory in children 6–11 years of age (121). Compared with children who did not eat breakfast younger children in the cohort (6–8 years old) showed improved spatial memory and better auditory attention after consuming oatmeal. Girls also displayed better short-term memory skills after consuming oatmeal (121). In addition, deportment was improved in those children who ate a nutritionally balanced breakfast.

In another study, compared with those who skipped breakfast children who had eaten a high-quality breakfast consisting of milk and fortified breakfast cereal or bread showed better scores on the child

behavior checklist (122). However, RTEC consumption for those over 65 years of age was not associated with improved measures of cognitive functioning as assessed by the MMSE (123). In fact, in this 11 year prospective cohort of 3,381 men and women in the Cache County Study on Memory, Health and Aging (CCMS) (123), daily RTEC consumption resulted in better micronutrient intake compared with more or less frequent consumption but was associated with poorer cognitive performance both at baseline and after the 11 years of follow-up (123). This finding is puzzling, because both higher and lower consumption levels were associated with better cognitive performance. Further analyses are needed before a conclusion can be drawn.

Some studies, however, have shown that breakfast and breakfast cereal consumption positively impact mental health in adults (124,125). One study divided adults ($N = 126$), 20–79 years of age, into irregular breakfast consumers, low breakfast cereal consumers, and high breakfast cereal consumers (124). Individuals who were high breakfast cereal consumers were less depressed and less emotionally distressed and had a lower level of perceived stress than irregular breakfast consumers (124). These findings were replicated in another study of similar design using a larger sample size ($N = 262$) and a slightly older population (21–85 years of age) (125). In another study examining the dietary habits of 1,252 men and 4,991 women (40–60 years of age), those with poor mental health were less likely than their healthier counterparts to report consuming fresh fruits, vegetables, low-fat milk, cheese, and cereals, including porridge (126). Thus, most studies confirm that the inclusion of breakfast and cereals generally results in better cognitive performance and mental health in both children and adults, especially when they are consumed as part of a balanced dietary pattern.

Impact of Balanced Dietary Patterns on Brain Health. Adherence to balanced dietary patterns, especially those that emphasize inclusion of a variety of grains and whole grains, such as Mediterranean, DASH, or New Nordic diets, has been associated in epidemiological studies with improved cognitive performance and positive impacts on brain health and functioning (127). For example, for the 1,393 U.S. adults who participated in a 4.5 year multiethnic community study, those individuals in the middle and high-

est tertiles of adherence to the Mediterranean Diet, when compared with those in the lowest tertile, over the study period had a 17 and 28% lower risk, respectively, of developing MCI (127). Similar findings were reported in a cross-sectional study of 806 Korean older adults (>60 years of age), in which a “prudent” pattern incorporating a mix of grains and foods was not associated with cognitive impairment and a “bread, egg, and dairy” pattern was inversely related to risk for cognitive impairment. In contrast the “white rice only” pattern (high consumption of white rice, low consumption of multigrain rice, and little dietary diversity) was positively associated with risk for cognitive impairment (128).

Balanced dietary patterns, such as DASH- and Mediterranean-style diets, are replete with adequate intakes of fruits, vegetables, grains, and whole grains that provide antioxidants and other components that are likely to support brain health (129) and are associated with better cognitive function (11). Another balanced pattern, the New Nordic Diet, is based on common Scandinavian food items such as fruits, rapeseed oil, berries, vegetables, fish, and whole grain products, including oats, barley, and rye, and a low to moderate intake of alcohol and meat (130). Like the Mediterranean Diet, the measures of cognitive functioning assessed by MMSE and other tests for more than 1,000 men and women in Scandinavia between the ages of 57 and 78 years show that dietary pattern alignment with the New Nordic Diet at baseline was positively associated with verbal fluency and word list learning (130). Further, in those cognitively normal at baseline, the New Nordic Diet also was positively associated with better performance on MMSE and neuropsychological tests (130).

Finally, a recent study published on the MIND (Mediterranean–DASH Intervention for Neurodegenerative Delay) Diet, a hybrid of the Mediterranean and DASH diets, found that the risk for Alzheimer’s disease was reduced by ≈50% in participants who strictly adhered to the diet compared with a 35% reduction in Alzheimer’s disease risk for those who followed the diet moderately (131). The MIND Diet recommends consumption of at least 3 servings of whole grains daily, along with green leafy vegetables, nuts, beans, fish, poultry, olive oil, and wine.

Effects of Grain-Based Food Intake on Mental Health. A few studies have focused on grain-based food intake and mental health. For example, a Japanese

study looked at the association between dietary patterns and depressive symptoms among 791 individuals (132). Patterns that included bread and pasta or high intake of noodles did not differ in their depression scores (132). Data from a larger cohort, such as the Women’s Health Initiative, indicate an association between diets that are high GI and risk for incident depression (133). More specifically, those women who consumed diets high in lactose, fiber, fruit, and vegetables had significantly lower risk for depression, whereas those who consumed diets high in refined grain from sweets, cookies, and cake had increased risk for depression (133). Determining the difference between refined and whole grains and their relationship to cognitive health is difficult, however, because most of the evidence in this area is epidemiological and focuses on subsets of cognitive and mental health issues, such as stress and depression (133). The type of grain-based food, frequency of selection, amount of fiber, and glyce-mic response may, in fact, all be related to one or more aspects of mood and mental health. Further research is needed to clarify the relationships.

Conclusions

Grain-based foods and the CHOs they contain are critical to supporting overall health when included in the proper amounts as part of a balanced diet such as DASH- or Mediterranean-style dietary patterns. It is clear that overconsumption of calories or macronutrients, including those from grains, especially in a diet in which other essential components are lacking, can be problematic for brain health, especially for those with impaired glucose tolerance and insulin resistance. In fact, CHO and/or calorie restrictions are being used clinically to treat certain conditions.

Recent claims that CHOs should be removed from the diet and that whole grain bread and comfort foods negatively impact the long-term health and functioning of the brain run counter to the evidence reported in the scientific literature. Such claims fail to consider data documenting that the brain preferentially uses glucose as its primary source of fuel and that CHOs are best suited to provide this fuel (59). Although alternative sources of energy, such as ketone bodies, can be used by the brain, these are most beneficial for those who suffer from GLUT1 deficiencies, such as those with epilepsy (64,65). Furthermore, the long-term efficacy of dietary ketosis for maintaining

brain health are largely unknown because research in this area is focused on acute intervention studies in people with various brain disorders (115). In short, the elimination of CHO foods and the many nutritional advantages they provide the body and brain could have unintended negative consequences. The nutrients and phytonutrients in whole and enriched grains can help counter the oxidative stress and inflammation that occurs in aging and contributes to many neurological diseases and disorders (36).

Whole grains are a key contributor of dietary fiber, and some, such as oatmeal, are particularly good sources of soluble fiber, which works to attenuate blood glucose and insulin levels. This is important because elevated blood glucose and insulin resistance are contributors of inflammation in the body and impair glucose entry into the brain (134). Refined grains contain lower amounts of fiber because much of it is removed during processing, and they are, therefore, not associated with a blood glucose and insulin benefit. However, enriched and fortified refined grains provide key micronutrients such as minerals, folic acid, and B vitamins—nutrients that are essential for brain health. There is a gap in the literature, however, and it is unclear whether the CHOs from refined or enriched grains have an effect on cognitive health. Diets with too many calories and too many refined CHOs from all sources, including those from grains, together with low dietary fiber, phytochemical, and micronutrient intakes, are problematic for a variety of health endpoints.

The scientific evidence linking various grains and cognitive health outcomes is mostly epidemiological, with the exception of a few randomized trials (11,12,59,117,121–128,130–136). Although epidemiological data do not prove cause and effect, they are the best data currently available. Studies continue to show that grains consumed as part of healthy, balanced dietary patterns that are culturally appropriate are beneficial for cognitive health as well. In an upcoming review, the health benefits of grains as part of these specific dietary patterns will be described.

For all of the reasons discussed in this review, there should be a continued effort to incorporate healthy CHO-rich foods, including grain-based foods, as part of a balanced diet, as well as continued efforts to combat false claims concerning CHOs and cereal grains made in the media.

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