Impact of Minerals, Phytochemicals, Specific Grain-Based Foods, and Dietary Patterns on Mild Cognitive Impairment, Alzheimer’s Disease, and Parkinson’s Disease

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ABSTRACT

Incidence of mild cognitive impairment (MCI), Alzheimer’s disease, and Parkinson’s disease is increasing as the mean age of Western populations rises. This article, the second article of a two-part review, assesses the existing scientific literature addressing the role of minerals, phytochemicals, specific grain-based foods, and dietary patterns, with and without grains, to determine whether these foods and their constituents affect the onset or course of these common dementias, as has been alleged in various books, blogs, and other media. Intakes and serum markers of mineral and phytonutrient intakes in many cases have been documented as low or below recommended levels in elderly individuals and patients with MCI, Alzheimer’s disease, or Parkinson’s disease. However, it is not clear whether adequate intake of these minerals and phytonutrients from all sources, including grains, can impact the onset or course of these dementias. There are few published studies on specific grain-based foods and their relationships to common dementias, and the results have been mixed or shown a dose or total diet effect. Studies have shown an association between whole grain, cereal, and high-fiber grain-based foods and lower risk of cognitive impairment and dementias. Results of studies on specific grain-based foods indicate that higher bread intakes, especially high-fiber breads, are associated with better cognitive performance and lower rates of dementia; however, higher than recommended levels are associated with poorer performance and greater risk of impairment. Other studies have shown that high rice intake may be associated with poor cognitive performance but that this may be due to the lack of important components in the diet, rather than solely to rice intake, or to an interaction of the two factors. Studies have also shown an increased risk associated with excess white bread, rice, or indulgent grain intakes when the overall diet is out of balance. The results of most, but not all, studies show that grain-based foods that are eaten as part of a balanced dietary pattern do not increase the risk for developing MCI, Alzheimer’s disease, or Parkinson’s disease and, in fact, may reduce the risk.

The relationship between grain-based foods and brain health was introduced in a previous article (1) as part of the CIMMYT series on the role of grains in health (2–8). This is the second article in a two-part review on the impact of nutrients from grains and grain-based foods on mild cognitive impairment (MCI), Alzheimer’s disease, and Parkinson’s disease. Because both the causes and cures for these conditions are elusive, lifestyle and nutrition are being scrutinized to determine whether they play roles in prevention and therapy for these common dementias.

This article reviews the existing scientific literature on the impact of minerals, phytochemicals, specific grain-based foods, and grain-based foods in balanced and unbalanced dietary patterns on these disorders. The companion article to this review focused on the impact of macronutrients (CHOs) and vitamins from grains on MCI, Alzheimer’s disease, and Parkinson’s disease (9).

MINERALS FROM GRAINS: IMPACT ON BRAIN HEALTH

Mineral balance is crucial not only for overall health, but also for brain health. Copper, zinc, and iron, and to a lesser extent manganese and magnesium, are naturally abundant in the brain, where they play key roles in the activities of various enzymes, stabilization of DNA, and maintenance of synapse function, density, and plasticity. In addition, magnesium enables neurons to pass electrical and chemical signals to other neurons (neurotransmission) and is critical for learning and memory functions (10–14). Excess or inadequate levels of one or more of these metals upsets the overall balance of minerals, which may have a number of impacts, including altering the absorption or utilization of minerals, initiating changes in brain structure and function, changing the oxidative state of certain minerals, creating toxicity, and causing cell death. The net result can be diminished cognition and neurodegenerative disorders (15,16).

Alzheimer’s Disease and Parkinson’s Disease

Disordered mineral transport and tissue distribution can be markers of dementias and cognitive disorders. For example, zinc homeostasis is regulated, in part, by the zinc transporter mechanism. Abnormalities in this mechanism have been documented in the brains of mice and humans with Alzheimer’s disease.

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Alzheimer’s disease patients, compared to individuals without dementia, have elevated levels of iron, copper, aluminum, and zinc in their brains, as well as amyloid plaques (17). Patients with Parkinson’s disease, compared to healthy controls, have lower levels of serum zinc and iron transport proteins and higher levels of iron deposited in the substantia nigra (18), the area of the midbrain where the loss of cells results in a deficit of dopamine, which is characteristic of Parkinson’s disease. Lower plasma selenium and iron levels are associated with reduced risk for Parkinson’s disease (15,18). In addition, the brains of patients with Parkinson’s disease have higher levels of copper, zinc, and manganese (12,16,17,19). Excess zinc favors formation of zinc–Aβ (β-amyloid) complexes, β-amyloid precursor protein expression, and plaque burden (10,11,17). Furthermore, zinc deposition in amyloid in the brain appears to deplete zinc from other body systems, resulting in low hair and serum levels (10,11,16,17,20–23). Studies have also shown that copper and manganese levels in hair are higher and selenium level is lower in patients with Alzheimer’s disease than in healthy controls (21,22), and magnesium levels in cerebrospinal fluid in patients with Alzheimer’s disease is lower than in healthy controls (22).

Redox-active minerals such as copper and iron can promote oxidation, which is thought to occur early in the process of neurodegeneration and is a hallmark of both Alzheimer’s disease and Parkinson’s disease (15–17,24,25). This not only impairs function, but also decreases the number of neurons and can catalyze aggregation and hyperphosphorylation of tau protein, the main component of the neurofibrillary tangles associated with Alzheimer’s disease (26). In addition, the mineral–amyloid complex formed is active and furthers oxidation (1,26,27). For both Alzheimer’s and Parkinson’s disease, it is unclear whether the effects of minerals are due to altered utilization, caused by disease processes, or result from a combination of low intakes or changed metabolism.

MCI

Proper mineral nutriture throughout life appears to be important for cognitive health, especially because magnesium can counter insulin resistance and reduce the risk of type 2 diabetes, which is known risk factors for dementia and poorer cognition (28). Studies have specifically iden-
defined the association of higher magnesium intakes with reduced risk for developing MCI and low magnesium levels with increased risk (29–31). In a Japanese cohort, those who had the highest magnesium intakes showed nearly a 75% reduction in risk for vascular dementia, including MCI and Alzheimer’s disease (30). The 17 year Personality and Total Health (PATH) Through Life Project also showed that adequate dietary mineral intake by cognitively healthy individuals was associated with a lower risk for developing MCI (31).

Mineral Status and Grain-Based Foods

Because adequate mineral status may impact cognitive functioning, appraisal of mineral intakes is important. Data from food intake surveys in the United States, Canada, and Europe show that iron intakes are adequate for most individuals, even the elderly (32–35). For example, the European Nutrition and Health Report II showed that the mean prevalence of iron inadequacy was below 11% (35). Yet, there are minerals for which intake by elderly individuals may be low. This was shown in a small Polish cohort of postmenopausal women (36), and in India, where only 59% of male and 43% of female elderly individuals, mostly vegetarians, had adequate intakes of iron (37). Further, iron absorption studies on Indian diets have shown that a much smaller portion of iron is available from a mixed cereal–pulse vegetarian diet. Among different types of cereal grains, iron was better absorbed from rice than from wheat, and absorption from both of these grains was better than absorption from millet.

Zinc. Elderly individuals are particularly prone to zinc deficiency because of the lower energy requirements and physiological vulnerabilities associated with aging (38). About 25% of older U.S. males and females (51–70 years of age) failed to meet the EAR (estimated average requirement) for zinc from food alone; however, with the addition of supplements the number was reduced to <5% (32). Similar data were reported for Canadians (33), where as European data showed only 10% prevalence of inadequate zinc intake (35).

The overall European intake data may hide inadequate intakes in the elderly populations in certain countries, however. In a sample of free-living elderly Spanish individuals (mean age ~79 years) inadequate intakes of zinc were observed, with men having lower intakes than women (39). Intake data for elderly Irish individuals showed a similar pattern (40). Among older Polish adults 44% had deficits in zinc, and a small study of Polish postmenopausal women found that nearly 70% of the women had inadequate intakes (36). Among elderly Indian adults (mostly vegetarians), only 39% of the males and 26% of the females had adequate zinc intakes (37,41). In parts of Southeast Asia and South Africa, more than 70% of elderly adults are at high risk of developing zinc deficiency (38,42). In a random national survey of Australian adults, daily intakes of zinc were marginal, with intake for 67% of men and 85% of women below recommended levels (43). To add to the problem of inadequate intake, some elderly individuals have a reduced capacity to absorb or utilize zinc due to drugs or disease, which exacerbates the effects of low intakes (44). Low zinc levels in serum were correlated with oxidative stress and cellular aging (45).

Magnesium. Magnesium intake seems to be low in most surveys. Surveys in North America show that a significant portion of the population failed to meet the EAR through food intake (32,33). More than 85% of adults in the United States over the age of 70 failed to meet the EAR for magnesium through diet alone; however, that percentage was reduced in supplement users to around 40% for males and 30% for females (32). In Canada for those 51 years of age and older, 61% of males and 46% of females had inadequate magnesium intakes from their diet alone. Supplementation brought these percentages down to levels similar to those seen in the United States (33). The prevalence of obesity is a complicating factor as well (46). Compared with normal weight adults in NHANES data, obese adults had lower intakes of micronutrients (about 5–12%) and a higher prevalence of nutrient inadequacy, especially for men (46). In an elderly population in India (mostly vegetarian), 88% of the males and 76% of the females had adequate intakes (37).

For young adults in Poland, magnesium intakes from food were below recommended levels (47), and nearly 70% of postmenopausal women had inadequate intake levels (36). Low intake levels were also found among elderly adults in Ireland (40) and free-living elderly adults in Spain (mean age ~79 years) (39). Of the elderly Spanish adults more than 90% did not meet 80% of the European Food Safety Authority (EFSA) magnesium intake requirements (48).

Copper. The European Nutrition and Health Report II showed that the mean prevalence of inadequacy for copper intake was 11–20% for adult and elderly populations (35). Once again, however, the overall means fail to tell the whole story for some specific regions. For example, among Polish postmenopausal women, more than 85% had inadequate copper intakes (36).

Selenium. The European Nutrition and Health Report II showed that the mean prevalence of inadequacy for selenium was higher than 20% (35). In a systematic review of free-living older adults, intakes of selenium were low enough to be considered a public health concern (49). Grain-based foods can be important sources of selenium, depending on the selenium content of the soil in which the crop is grown. Selenium content is high in shale soils; thus, it is naturally high in wheat-growing regions of North America, such as Kansas and North and South Dakota (50). Soil biofortification with selenium, which is done in parts of Europe and elsewhere, has proven to be a successful method for addressing mineral inadequacies, including selenium (51).

Role of Grain-Based Foods in Brain Function

Consumers of breakfast cereals (n = 3,728, aged 2 years and older) in the U.K. Low Income Diet and Nutrition Survey (2003–2005) had higher intakes of iron and zinc than nonconsumers (52). Cereals and grain products also were the major dietary contributor of magnesium (22.6%) in a cohort of elderly Spanish adults (48).

Adequate intakes of a variety of grain-based foods are very helpful for maintaining a healthy mineral status, with whole grains providing higher levels of minerals and enriched grains allowing easier absorption of minerals. A systematic review found that zinc intakes were higher among consumers of exclusively whole grain and high-fiber breakfast cereals compared with consumers of other breakfast cereals (53). Enriched, fortified, and whole grains contribute 31% of the iron, 16% of the zinc, 14% of the magnesium, 13% of the phosphorus, and 7% of the potassium in a balanced diet (54).

The outer layers of whole grains can also be a source of heavy metals if they are present in the environment (55). Adequate intake of other minerals and nutrients is the best defense against absorption and the negative impacts of many of these toxic
minerals (56). In addition, phytonutrients from grains, such as phytate, may chelate heavy metals, and animal studies suggest that they may work together with other components to reduce metal-induced oxidation (57). Animal models suggest that this may have a positive impact on cognition and reduce or delay development of some dementias (58).

**PHYTONUTRIENTS FROM GRAINS: IMPACT ON BRAIN HEALTH**

Other phytonutrients contained in grain-based foods, especially those found in the outer layers of whole grains, can impact oxidative state and cognitive functioning. This review addresses only those components that have been shown to have a bearing on cognition or delaying MCI, Alzheimer’s disease, or Parkinson’s disease, i.e., choline, betaine, avenanthramides from oats, and polyphenolics as ferrulate (59). This is not to say that further studies may not show that all phytonutrients have some impact or that they may work together in synergy; however, many are present in small amounts and may not act directly on neural tissues but instead may impact the microbiome.

**Choline and Betaine**

Choline and betaine (a related compound found in many grains and especially high amounts in wheat germ and quinoa) play many roles in human metabolism, including neural tissue development and functioning. Choline deficiency is thought to have an impact on diseases and neurological disorders (60,61). It plays a key role in formation of the neurotransmitter acetylcholine and is a significant player in one-carbon transfers. In conjunction with many B vitamins, choline plays a role in determining fasting homocysteine (fHcy) concentrations (Fig. 1). (The role of B vitamins in fHcy concentrations is discussed in the companion review on the impact of macronutrients and vitamins on MCI, Alzheimer’s disease, and Parkinson’s disease (9).) Lower fHcy concentration is associated with better cognitive functioning. In the Framingham Offspring cohort, higher intakes of dietary choline and betaine were related to lower fHcy concentrations (independent of other factors, including folate and other B vitamins) and better verbal and visual memory (62,63). Similarly, older adults (70–74 years of age) with high plasma concentrations of free choline (versus low) exhibited significantly better performance on cognitive tests ranging from motor and perceptual speed to executive function and global cognition (64). A study of Australian women of childbearing age showed that only 16% met the adequate intake (AI) recommendation for choline. In terms of diet (65), the top five food contributors of choline were eggs, red meat, milk, bread, and chicken, and the top five food contributors of betaine were bread, breakfast cereals, pasta, grains, and root vegetables. In a Norwegian population, dietary fiber and high-fiber bread intake were strongly associated with betaine intake and lower fHcy (66). The role of grain-based foods and their betaine and choline contributions with respect to cognition looks promising but requires further study.

**Anthocyanins, Ferulic Acid, and Avenanthramides**

Anthocyanins, ferulic acid, and avenanthramides are important phenolic phytochemicals found in grain-based foods; higher concentrations are found in the bran and germ layers of whole grains (1). The actual amounts and specific molecules vary within and among grain varieties, with highly pigmented varieties containing higher levels. These grain bioactives function as antioxidants and anti-inflammatory agents and impact antioxidant status throughout the body, helping to protect lipid-rich neural tissues and, thereby, reducing the risk for MCI, Alzheimer’s disease, and Parkinson’s disease (67,68). A review of food-based anthocyanins suggests they may have positive impacts on cognition, but variability from study to study is marked, making it difficult to draw firm conclusions (69).

Ferulic acid, which is present in high amounts in the outer layers of many grains, acts as a free-radical scavenger and anti-inflammatory agent (70). Animal studies suggest that it inhibits or disaggregates amyloid and may have other positive effects that could impact Alzheimer’s disease (70,71). Supplemental ferulic acid given to model animals with Alzheimer’s disease showed a protective effect, but much more research is needed on how these doses relate to those achieved by eating grain-based foods (72).

Avenanthramides from oats when given in high doses as supplements (3 mg/day) have been shown to increase serum levels of natural body antioxidants (superoxide dismutase and glutathione) and reduce serum malonaldehyde, a marker of oxidative stress (68). In addition, high concentrations have been shown in in vitro studies to affect formation of β-amyloid fibrils, leading to the suggestion that they be used as therapeutic agents for the treatment of neurodegenerative diseases (67,73).

Despite these initial findings, further studies on the impact of all of these phytonutrients is required to determine whether the amount delivered through daily con-
The amount and type of bread consumed may also have an impact on cognition. For example, cognitive test scores for the elderly Norwegian Hordaland Health Study cohort were highest after consumption of certain foods, one of which was high-fiber bread (75), whereas very high intakes of white bread were associated with lower scores. However, this study showed that there was an optimal intake level for grain-based foods. Cognitive scores increased as intakes of grain products (and potatoes) increased to between 100 and 150 g/day and then plateaued or decreased at higher intake levels. The study showed that consumption of excess amounts of grain and white bread products and inadequate amounts of dietary fiber were problematic, underscoring the need for dietary balance (75). The benefits of dietary balance were also demonstrated in a study of 4,000 elderly adults in the 12 year Cache County (Utah) Study on Memory Health and Aging (78). Cognitive scores were higher, both at baseline and subsequently, for those consuming ready-to-eat (RTE) cereals more frequently than weekly but less frequently than daily. Daily and non-consumers of RTE cereals had lower scores (78). In the Women’s Health Study, higher whole grain intake (2.2 servings/day) was associated with higher average cognition scores compared with women whose daily intake of whole grains was lower (0.8 servings/day) (79). In a European cohort, higher whole grain bread and cereal intakes provided higher mineral intakes from the diet (80). Findings such as these suggest that when eaten in the right balance grain-based foods are associated with better cognitive functioning (75,81).

The literature on the impact of grain-based foods on Parkinson’s disease is limited. In Sweden, intake of Swedish white and French breads in a small case-control study was associated with lower risk for Parkinson’s disease. In contrast, a U.S. study conducted in Washington State found that neither bread nor cereal intake was associated with risk for Parkinson’s disease (82,83). In a case-control study, Parkinson’s disease patients reported eating significantly larger quantities of sweet foods and eating more snacks than control subjects (84). (Studies with Alzheimer’s disease patients point to similar trends.) The authors suggest that the findings may be the result of illness-related changes in dietary habits and perhaps were not causal (84).

Rice

Study findings on rice intake and its impact on MCI, Alzheimer’s disease, and Parkinson’s disease show mixed results. Higher total cereal (primarily rice) and carbohydrate (CHO) intakes among older Korean women (n = 239) were positively associated with higher scores on cognitive tests, whereas lower cereal intake was associated with lower scores for cognitive functioning (85).

In contrast, two Japanese studies implicated rice in increased risk for Alzheimer’s disease. One study showed that total energy, meat, and rice intakes were associated with risk for Alzheimer’s disease (86). Further, in more than 1,000 Japanese subjects, a balanced dietary pattern that included a mix of soybean-based foods and vegetables and lower intakes of rice was associated with lower risks for Alzheimer’s disease and cognitive decline (87).

However, the authors of the paper stress that the association between rice intake and Alzheimer’s disease and cognitive decline might be the result of unbalanced dietary patterns (i.e., high rice intake might mean that foods that could help prevent dementia were lacking) rather than any harmful effects of the rice itself (87).

GRAIN-BASED FOODS AS PART OF HEALTHY DIETARY PATTERNS

The impact of a specific grain-based food or group of foods on brain health is often difficult to determine because grains are not (nor should they be) eaten in isolation. Healthy dietary patterns such as the Mediterranean Diet, Dietary Approaches to Stop Hypertension (DASH) Diet, and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) Diet all include grain-based foods as part of a balanced pattern (88,89). The basic components and recommended servings for each of these diets are provided in Table 1. Study findings have shown that these diets are associated with lower risks for cognitive impairment, cognitive decline, and dementia or Alzheimer’s disease compared with typical “Western” diets that are high in red meat, dairy products, and sweets; are low in foods that provide key nutrients; and have minimal intakes of fruits, vegetables, fish, legumes, and whole grains (88,90). The Mediterranean, DASH, and Mind Diets, as well as other patterns that focus on dietary balance and diversity, are thought to promote general health because they include nutrients and phytonutrients in beneficial proportions. In a study on dietary quality, an association between dietary diversity and higher cognitive scores was shown for elderly Taiwanese adults (91).

This review focuses primarily on the Mediterranean and DASH Diets, but their similarity to other health-promoting diets suggests they are all likely to have similar

IMPACT OF SPECIFIC GRAIN-BASED FOODS ON COGNITION AND BRAIN HEALTH

Only a few studies have looked at grain-based foods, collectively or individually, and their impact on cognition, brain health, and MCI, Alzheimer’s disease, and Parkinson’s disease. There are a number of studies that have examined these foods as part of dietary pattern research, and these will be reviewed after looking at the impact of specific foods.

Breads and Cereals

Studies on the impact of breads and cereals on cognition and cognitive decline in elderly adults suggest that the outcome depends on the types and amounts of bread eaten and the background dietary pattern. However, the results from most of these studies indicate that these staple grain-based foods, especially those containing dietary fiber, are associated with improved cognition and lower risk for developing MCI and other dementias. Several studies of elderly populations indicate that cognitive function is related to higher intakes of grain-based foods. In more than 2,000 elderly Norwegian subjects (70–74 years of age), those who had the highest intakes of grain products (as well as fruits, vegetables, and mushrooms) performed significantly better on cognitive tests than those with very low or no intake (75).

Institutionalized elderly Spanish subjects (N = 178) with higher cereal and dietary fiber intakes had fewer errors on memory tests and showed improved cognition (76). The results of a statewide survey of elderly adults in Alabama (n = 1,056) showed bread/cereal intake was inversely associated with cognitive impairment, whereas dessert intake was positively associated with cognitive impairment (77). Cereals were one of the foods associated with lower risk for Alzheimer’s disease in populations from Europe and North America (75).

The amount and type of bread consumed may also have an impact on cognition. For example, cognitive test scores for the elderly Norwegian Hordaland Health Study cohort were highest after consumption of certain foods, one of which was high-fiber bread (75), whereas very high intakes of certain foods, one of which was high-fiber bread (75), whereas very high intakes of
impacts. The MIND Diet is also discussed.

The Mediterranean Diet was recognized more than 50 years ago by Ancel Keys and colleagues (92) as being associated with heart health and longevity. More recently, an association between the diet and lower risk for cognitive decline has been shown. The DASH Diet was developed by the U.S. National Heart, Lung, and Blood Institute to determine whether healthy eating patterns could have positive impacts on blood pressure. Subsequent research has shown that the diet can improve not only blood pressure but many health outcomes, including cognition (93). Such diets emphasize inclusion of vegetables, fruits, whole grains, fat-free or low-fat dairy products, fish, poultry, beans, and healthy oils and recommend moderate consumption of foods that are high in saturated fat, red meat, and wine (79,88).

There are a few differences between the two diets. The DASH Diet limits sodium and the Mediterranean Diet emphasizes olive oil and nuts; however, they both recognize the role of cereal grains (both refined and whole in balanced amounts) as part of a balanced diet. The MIND Diet is a blend of these two diets, but recommends consumption of only whole grains and fewer servings of grain. The diet was designed to specifically address cognitive functioning and delay dementia.

In contrast with these balanced dietary patterns, unbalanced patterns often include excess saturated fat and very inadequate fruit, vegetable, and fiber consumption. Unbalanced patterns may also include a high proportion of refined sugars and snack foods with low nutritional value. There are many names for unbalanced diets, such as “Western,” “meat and potatoes,” and “red meat and white bread” patterns. They are not only linked with higher risks for obesity, heart disease, and diabetes, but also with higher risk for Alzheimer’s disease (77,79,88–90,94–97). In contrast, balanced dietary patterns that include lower intakes of white bread, sugars, and red meat and higher intakes of fruits, vegetables, fish, and whole grains are termed “prudent” diets.

Results of studies from several countries show that lower cognitive scores and greater risk of Alzheimer’s disease occur with diets that are high in meat, fat, and white bread and low in vegetables and grains. In a Polish case-control study (n = 71 patients and matched controls), patients with Alzheimer’s disease had high intakes of meat, butter, eggs, refined sugar, and high-fat dairy products, whereas the control group had high intakes of grains, cereals, bread, and vegetables (95). In a study of more than 1,000 elderly British adults over 85 years of age, dietary patterns high in meat, butter, gravy and potatoes were associated with poorer cognitive scores than other dietary patterns (98–100). However, the pattern was not associated with cognitive decline. Further, intake of whole and refined grains differed little among the dietary patterns and had little impact on outcomes despite the fact that cereals and cereal products were the top contributors to energy and CHO intakes.

In elderly Irish subjects following “prudent” dietary patterns, which specifically were noted as being low in red meat and white bread, had higher cognitive function scores than those following “Western” dietary patterns described as high in red meat and white bread and low in fruits and vegetables (96).

In Asian cultures unbalanced dietary patterns are sometimes characterized by very high intakes of white rice and low intakes of other foods. Among more than 750 older Korean adults, those following a “multigrain rice, fish, dairy products, fruits and fruit juices” pattern, compared to those following a pattern with higher intakes of “white rice, noodles, and coffee,” had lower risk for cognitive impairment (85).

Dietary pattern research does contain some degree of confounding. Those who follow a Western pattern may ingest excess calories and have sedentary lifestyles, which are associated with a number of adverse health conditions, such as diabetes, that contribute to cognitive impairment (101–105). On the other hand, those following a “prudent” diet often have a number of dietary and lifestyle patterns that may lower disease risk, making the attribution of risk to a specific food, nutrient, food group, or combination of nutrients difficult.

Since the first published studies showing the cognitive benefits of adherence to

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### Table 1. Dietary patterns associated with cognitive health: Dietary components and recommended servings for the DASH, Mediterranean, and MIND Diets

<table>
<thead>
<tr>
<th>DASH Dieta</th>
<th>Mediterranean Diet</th>
<th>MIND Diet</th>
<th>Food Group</th>
<th>Frequency or Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grains (mostly whole) per day</td>
<td>Grains/cereals (mostly whole)</td>
<td>Whole grains</td>
<td>Every meal</td>
<td>≥3/day</td>
</tr>
<tr>
<td>Meat, poultry, and fish per day ≤2</td>
<td>Meats and sweets</td>
<td>Green leafy vegetables</td>
<td>Less often</td>
<td>≥6/week</td>
</tr>
<tr>
<td>Vegetables per day 4–5</td>
<td>Poultry, eggs, cheese, and yogurt</td>
<td>Other vegetables</td>
<td>Moderate portions, daily to weekly</td>
<td>≥1/day</td>
</tr>
<tr>
<td>Fruits per day 4–5</td>
<td>Fish and seafood</td>
<td>Berries</td>
<td>Often, ≥2/week</td>
<td>≥2/week</td>
</tr>
<tr>
<td>Low-fat or fat-free dairy products per day 2–3</td>
<td>Fruits, vegetables, nuts, legumes, and seeds</td>
<td>Red meat</td>
<td>Base every meal on these foods</td>
<td>&lt;4/week</td>
</tr>
<tr>
<td>Nuts, seeds, legumes per week 4–5</td>
<td>Fats, vegetables, nuts, legumes, and seeds</td>
<td>Fish</td>
<td>Replace butter with olive oil at each meal</td>
<td>≥1/week</td>
</tr>
<tr>
<td>Fats and oils per day 2–3</td>
<td>Fats (i.e., olive oil)</td>
<td>Beans</td>
<td>Base every meal on these foods</td>
<td>&gt;3/week</td>
</tr>
<tr>
<td>Sodium per day 2,300 mg</td>
<td>Herbs and spices</td>
<td>Nuts</td>
<td>Use to flavor foods</td>
<td>≥5/week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fast/fried foods</td>
<td>Olive oil</td>
<td>&lt;1/Tbsp/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Butter/margarine</td>
<td>&lt;1/Tbsp/day</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cheese Pastries and sweets</td>
<td>&lt;5/week</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Alcohol/wine</td>
<td>1 glass/day</td>
</tr>
</tbody>
</table>

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a DASH = Dietary Approaches to Stop Hypertension; MIND = Mediterranean-DASH Intervention for Neurodegenerative Delay. Other similar dietary patterns include the French National Nutrition and Health Programme (Programme National Nutrition Santé [PNNS]); Recommended Food Score (RFS); Healthy Eating Index (HEI); and Alternate Healthy Eating Index (AHEI) (88).

b Based on a 2,000 calorie/day diet.
the Mediterranean Diet, studies from New York, rural Utah, and Australia have shown that greater compliance with such dietary patterns from the middle decades of life and beyond is associated with reduced risk for MCI and Alzheimer's disease and slower progression of the disease (89,90,93-97,106-117). Similarly, high adherence to DASH and other balanced dietary patterns that emphasize intake of fruits, vegetables, cereals, and whole grains have also been associated with a lower likelihood of developing Alzheimer's disease (90,97,110,115). A few examples, such as the Washington Heights–Inwood Columbia Aging Project involving 2,364 nondemented individuals in New York, have shown adherence to the Mediterranean Diet to be associated with a borderline reduction in risk for developing MCI and a reduction in risk for progression from MCI to Alzheimer’s disease. Even in individuals with increased genetic risk for development of Alzheimer’s disease due to the apolipoprotein E (APOE) e4 allele, long-term adherence to the DASH Diet for more than 16,000 women over 70 years of age in the Nurses’ Health Study was associated with better than average cognitive functioning (118). High adherers had cognitive scores that measured them as an average of one year younger than their actual ages.

The positive impact the Mediterranean Diet has on cognitive function has not only been shown in cohort and case-control studies, but also in the large PREDIMED intervention trial with participants (N = 522) at high risk for vascular disease (119). In the intervention trial, those following the Mediterranean Diet had higher mean Mini-Mental State Examination (MMSE) and other cognitive test scores compared with those following a low-fat diet (119).

Although the findings from many studies support the benefits of these balanced dietary patterns, there are three large cohort studies that failed to show that adherence to healthy patterns helped to prevent cognitive decline. For example, in the Women's Health Study with more than 6,000 U.S. women over 65 years of age adherence to the Mediterranean Diet did not impact cognition measures, but intake of whole grain was one factor that appeared to lower risk for cognitive decrement (79). In addition, adherence to the DASH Diet, Mediterranean Diet, or any other of four healthy dietary plans for 9 years among more than 6,000 postmenopausal women over 65 years of age in the Women's Health Memory Initiative project was not associated with risk for cognitive impairment (120). (The latter study was criticized because diets may not remain stable over time, and diet measures were only recorded at baseline (121).)

Concerns about maintaining optimal cognitive functioning resulted in the creation of a hybrid of the Mediterranean and DASH Diets—the MIND Diet (122). The MIND Diet focuses on foods and nutrients that scientific research has shown to be associated with prevention of dementia (123–125). This diet emphasizes inclusion of green leafy vegetables, nuts, berries, beans, whole grains (at least 3 servings/day), oily fish, poultry, olive oil, and wine and recommends limiting inclusion of red meat, butter/stick margarine, cheese, pastries, and sweets, as well as fried or fast foods (126). In a prospective cohort study of 923 participants (ages 58–98 years) those with high adherence to the MIND Diet lowered their risk for Alzheimer’s disease by about 50% over those with poor adherence (127). Interestingly, even those who modestly adhered to the diet lowered their risk for developing Alzheimer’s disease by about 35%.

Thus, the majority of studies show that balanced dietary patterns are most beneficial for maintaining or improving cognition, and they may reduce the risk for or delay the onset of MCI and Alzheimer’s disease. It is also true that unbalanced patterns that include high intakes of red meat, saturated fat, and CHO, as well as bread and grain-based desserts, and inadequate intakes of fish, fruits, vegetables, and dietary fiber promote oxidation, insulin resistance, and other metabolic reactions that do not favor optimal cognitive functioning and may increase the risk for developing MCI and Alzheimer’s disease.

EVIDENCE OF THE PROTECTIVE ROLE OF BALANCED DIETARY PATTERNS IN PARKINSON’S DISEASE

Balanced dietary patterns may be useful in reducing the risk for Parkinson’s disease, but only a limited number of studies have been published. Higher adherence to a Mediterranean-type diet, as assessed in a case-control study (n = 257 Parkinson’s disease patients and 198 controls), was associated with reduced risk for Parkinson’s disease (128), whereas lower adherence was associated with earlier onset. Similarly, a “prudent” diet with high intakes of fruits, vegetables, and fish was inversely associated with Parkinson’s disease risk in the Health Professionals Follow-Up Study and the Nurses’ Health Study (n = 49,692 men and 81,676 women), whereas a Western dietary pattern was not (129). Adherence to the Japanese healthy dietary pattern (characterized by high intakes of vegetables, seaweed, pulses, mushrooms, fruits, and fish) was inversely related in a case-control study to risk for Parkinson’s disease (130). Although other identified patterns did not increase the risk for Parkinson’s disease, patterns with a high glycemic load (GL) were inversely associated with risk for Parkinson’s disease. The latter may mean that when rice is included in the right amount as part of a health-promoting pattern that it contributes to GL but does not increase risk. This suggests the right balance of grains, both whole and refined, and a balanced dietary pattern are required to reduce risk. More research is need to determine how balanced patterns impact Parkinson’s disease.

CONCLUSIONS

Grain-based foods are important contributors not only of macronutrients and vitamins (1,2,9), but also of minerals and phytonutrients that impact brain health and cognitive function. Maintaining an optimal balance of minerals, nutrients, and phytonutrients is critical for minimizing creation of free-radical products from oxidation and inflammation. In addition, phytochemicals from whole grains, such as phytate or ferulate, may act as anti-inflammatory, antioxidant, and chelating agents, which are all activities that help protect brain functioning (58). In addition, betaine may work with certain B vitamins to inhibit tHcy, a known risk factor for MCI and Alzheimer’s disease. Inadequate intakes of grain-based foods may lead to mineral imbalance or insufficient antioxidant protection, which is associated with higher risks for MCI, Alzheimer’s disease, and Parkinson’s disease. Although whole grains fed to high-risk individuals, even when part of an otherwise unbalanced diet, reduced inflammation (131), it appears that the beneficial components in grain-based foods are more useful when they are consumed as part of a health-promoting dietary pattern. Higher risks for MCI, Alzheimer’s disease, and Parkinson’s disease have been linked to habitual consumption of “Western” diets that are high in red meat and refined carbohydrates and grains and low in fruits, vegetables, and whole grains. Lower risks are associated with habitual
consumption of balanced dietary patterns such as the DASH or Mediterranean Diet. Because of much confounding, it is not possible to attribute the cause of common dementias to excessive intakes of refined CHO-rich staple foods such as bread, rice, and cereal- or grain-based desserts and snacks or animal products that are high in saturated fat; to low intakes of recommended fats, fish, fruits and vegetables, whole grains, nuts, seeds, low-fat dairy products, or dietary fiber; or to a combination of nutrient inadequacy in the face of excess calories or overall dietary imbalance.

What is clear is that there are many components found in both whole and enriched refined grains that contribute to cognitive health and reduced risk for developing MCI, Alzheimer’s disease, and, perhaps, Parkinson’s disease. Dietary fiber, vitamin E, and magnesium are all provided by grain-based foods and are nutrients of concern because many people fail to ingest adequate amounts. Further, it is important that enriched and refined grain-based staples not be placed in the same category as grain-based indulgent foods such as snacks and desserts in dietary recommendations.

The prevention of dementias is a growing public health concern because there is no effective cure and rising global prevalence (86). Because MCI seems to be part of the continuum from normal aging to development of Alzheimer’s disease and other dementias, identifying dietary patterns that can help delay this progression is important (114,132). Dietary approaches that include grains and whole grains and their beneficial components as part of a balanced pattern appear to be associated with reduced risk (not with increased risk as has been alleged by some) and delayed onset of MCI, Alzheimer’s disease, and Parkinson’s disease.

References
112 / MAY–JUNE 2017, VOL. 62, NO. 3


44. Linus Pauling Institute. Micronutrients for Older Adults. Published online at http://lpi.oregonstate.edu/mic/life-stages/older-adults. LPI, Oregon State University, Corvallis, OR, 2017.


65. Mygind, V. L., Evans, S. E., Peddie, M. C.,


89. Schwingshackl, L., and Hoffmann, G. Diet quality as assessed by the Healthy Eating Index, the Alternate Healthy Eating Index, the Dietary Approaches to Stop Hypertension score, and health outcomes: A systematic review and meta-analysis of cohort studies. J. Acad. Nutr. Diet. 115:780, 2015.


