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A Comprehensive Review of Eggs, Choline, and Lutein on Cognition Across the Life-span

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ABSTRACT

In 2030, one in five Americans will be older than 65 years, and with that an increase in the number of individuals who experience loss in cognitive capacity is to be expected. At the same time, nutrition within the first 1000 days postconception has been suggested to strongly influence cognitive outcomes across the life-span in humans. Eggs are a primary source of both choline and the xanthophyll carotenoid lutein in the western diet, and both have been suggested to influence cognitive function in humans. This comprehensive review critically examines the effects of eggs, choline, and lutein on cognition across the life-span. There seems to be clear scientific evidence to suggest that both choline and lutein play a vital role in brain and neurological development during the first 1000 days postconception. The extent to which higher intakes of choline have the potential to enhance or influence cognition during childhood, adulthood, and/or age-related cognitive decline needs further investigation. Emerging but consistent research suggests that lutein has the potential to influence cognition across the life-span and that sufficient intakes during mid to late adulthood may help to ward off age-related cognitive decline. Macular pigment optical density (MPOD) seems to be a reliable and consistent biomarker of brain lutein concentrations across the life-span and potentially one for clinically assessing cognitive status. This review summarizes the current peer-reviewed literature and existing gaps in research.

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Egg; choline; lutein; cognition

Introduction

The role of eggs in promoting cognitive function across the life-span is a source of great debate, with limited but emerging scientific evidence. Eggs are a primary source of both choline and the xanthophyll carotenoid lutein in addition to several essential amino acids, B vitamins, vitamin A, vitamin D, and iron (1). They have potential to contribute significant amounts of these nutrients to the diet, given that about 21% to 22% of the U.S. population consume whole eggs on a given day (2) and because they are also commonly consumed as a component of many prepared foods. Mean egg consumption has recently been shown to be about 24 g/d (about half of a whole egg) among the general population, which has increased across most subpopulations except food-insecure individuals and those participating in the Supplemental Nutrition Assistance Program (2). Egg consumption (1 egg/d for 6 months) has been shown to reduce stunting, which is highly associated with cognition, in mixed-indigenous rural Andean children in Ecuador by 47% (hazard ratio [HR], 0.53; 95% confidence interval [CI], 0.38–0.88) (3). Individual components of eggs, particularly choline and lutein, have been suggested to be associated with improved cognitive development as well as a reduced risk of cognitive decline (4,5). Egg yolks provide the greatest amount of choline to the U.S. diet (6), and the lipid-rich matrix has been shown to increase the bioavailability of lutein threefold as compared to dark green leafy vegetables and dietary supplements (7). Even though eggs are rich in lutein, colorful fruits and vegetables have been shown to be the major source in the diet.

Cognition represents a complex set of higher mental functions subserved by the brain and includes attention, memory, thinking, learning, and perception (8). Many studies report that the population of elderly people is growing and as the number of elderly persons increase, an increase in the number of people showing cognitive decline is to be expected. By the year 2030, 1 in 5 Americans will be older than 65 years (9). Loss of cognitive capacity is one of the major factors affecting quality of life in elderly individuals and their family members and is one of the main reasons for people entering nursing homes (10–12). Age represents the single most important predictor of cognitive decline in the developed world (13). At the same time, there is an increasing body of evidence that suggests a connection between improved maternal and early childhood nutrition and brain function across the life-span (14). Cognitive development in preschoolers is predictive of later school achievement (15). Thus, nutritional strategies to optimize cognitive development and maintenance throughout the life-span may have a tremendous public health, economic, and societal impact.

Since 1998, choline has been recognized by the National Academies of Medicine as an essential nutrient the metabolites

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of which have both structural and regulatory roles within the body (16). It can be (1) oxidized to betaine, an osmolyte and methyl donor; (2) acetylated to form acetylcholine, a neurotransmitter involved in learning, memory, and attention; or (3) phosphorylated and metabolized to phosphatidylcholine, a critical structural component of cellular membranes that ensures fluidity and integrity (16). Humans can endogenously produce small amounts of choline via the hepatic phosphatidylethanolamine N-methyltransferase (PEMT) pathway; however, the nutrient must be consumed exogenously to prevent symptoms of deficiency (16). The American Medical Association recently recommended the addition of choline to prenatal vitamins (17). There are two sensitive periods in rat brain development during which treatment with choline (about 1 mmol/d) produces long-lasting enhancement of spatial memory that is lifelong. The first occurs during embryonic days 12 through 17 (rats give birth on day 21) and the second during postnatal days 16 through 30 (4,18–27). Supplementation during these critical periods elicits a major improvement in memory performance of rats at all stages of training on a 12-arm radial maze (23). In rats, the choline-induced increase in spatial memory directly correlates with changes in the birth, death, and migration of cells in the hippocampus during fetal brain development and with the distribution and morphology of neurons involved in memory storage throughout the life-span (22,25). Evidence that suggests effects of choline on health in different stages of life is scarce and needs to be confirmed by human intervention studies. Currently there is no reliable nutritional biomarker of choline status. Free choline concentrations in the serum and plasma are common measures of status in the peer-reviewed literature. However, because choline is homeostatically regulated, plasma concentrations rarely reach below 50% of the normal fasting concentration range (7–20 μmol/L), making it a poor indicator of nutritional status (28).

The relationship between lutein and cognitive health is particularly compelling because it is selectively taken up in to the eye and brain tissue (29–31). To date, scientific research supports the role of lutein in visual health, while emerging evidence suggests that it plays an important role in cognition across the life-span. A recent review suggests that lutein is ready to be considered for DRI-like intake recommendations based on its putative role in visual performance and reducing the risk of age-related macular degeneration (32).Given that the eye is an extension of the neural system, it makes sense that lutein, similar to omega-3 fatty acids, could affect both visual and cognitive functions early in life and extend into adulthood. Lutein is the predominant brain carotenoid in both early and late life, despite that it is much less consumed as compared to other carotenoids such as beta-carotene and lycopene (30–31). Vishwanathan and others collected hippocampus, frontal, auditory, occipital cortices from infants who died within the first year of life and showed lutein to represent about 58% of total brain carotenoids (31).The same group used the NHANES 1988–1994 data sets to show that dietary intakes of lutein represent only about 12% of total carotenoid intakes in this age group (31). Serum levels of lutein have also been shown to be lower relative to other carotenoids compared to those in the brain tissues of elderly individuals (i.e., lutein was the most predominant brain but not serum carotenoid) (30). Lutein and zeaxanthin are the only two carotenoids that cross the blood-brain barrier to form macular pigment in the eye, which is significantly correlated with levels in matched brain tissue among primates (5) and humans (34). Therefore, MPOD may serve as a reliable, noninvasive biomarker of brain carotenoid concentrations.

This article (1) reports the findings of a nonsystematic, evidence-based comprehensive review of the current scientific literature on the effect of eggs, choline, and lutein on cognition; (2) outlines a research agenda to address current gaps; and (3) identifies implementation strategies.

Methodology

A search strategy was developed in consultation with two librarians first using nomenclatures for Ovid MEDLINE and then adjusted for other electronic databases. The searches were implemented through July 1, 2017, in three databases: PubMed, Ovid MEDLINE, and BIOSIS. The searches were limited to the English language and human studies that examined the relationships of egg, choline, or lutein intake (food or supplemental sources) with cognitive outcomes. The complete search strategies are presented in Table 1. I included human studies among individuals of all ages that examined the effects of varying doses of egg, choline, and/or lutein intake from any source on cognitive outcomes. Other studies are included within the review as relevant. This article is not intended to serve as a systematic review but more as a comprehensive review of the scientific literature to date.

Current status of knowledge

Whole eggs and cognition

One intervention and four observational studies assessing the impact of whole egg consumption on cognitive outcomes in middle age to older adulthood were identified through the literature search (3,35–38). The most recent randomized controlled trial of Andean children aged 6 to 9 months (i.e., the Lulun Project) found that consumption of one egg/d for 6 months was associated with a 47% reduced incidence of stunting, a marker that is highly associated with suboptimal cognitive development. The results also showed a partial mediating effect by choline (3). Investigation of the Kuopio Ischaemic Heart Disease Risk Factor Study examined the role of cholesterol and egg intakes with incident dementia, Alzheimer's disease, and cognitive performance in 2427 dementia-free men aged 42 to 60 years at baseline. Higher egg intake was associated with better performance on neuropsychological tests of frontal lobe and executive functioning, the Trail Making Test, and the Verbal Frequency Test during the 21.9 years of follow-up. Each additional 0.5 eggs (27g/d) per day was marginally associated with a decrease in incident dementia (HR, 0.89; 95% CI, 0.78–1.01). Egg intake did not affect the apolipoprotein E4 gene, which has been identified as a "risk gene" for both Alzheimer's disease and cardiovascular disease (35). This suggests that egg consumption patterns in midlife may be associated with later-life cognitive function, but it is currently unknown whether intakes later in life can impact those already experiencing age-related cognitive decline. Although this study was the first and only

study to longitudinally evaluate the impact of egg intake on dementia risk over a significant time span, inverse associations of egg intake with mild cognitive impairment have been shown among elderly individuals in other types of observational studies (36–38). Analysis of a population-based prospective, nested case-controlled study of 5691 elderly individuals aged 65 and older with normal cognitive function enrolled in the Chinese Longitudinal Health Longevity Study showed cognitive decline that was inversely associated with egg consumption (odds ratio [OR], 0.73; 95% CI, 0.59–0.89) in bivariate analysis. There were no significant associations identified after adjusting for demographic variables (37). Cross-sectional analysis of 178 institutionalized elderly men and women aged 65 and older found that participants who incurred no errors on the Short Portable Mental Status Questionnaire had a greater intake of eggs (36). Similarly, a case-controlled analysis of 404 elderly people in Beijing aged 60 and older found that higher daily intake of eggs resulted in significantly decreased odds of experiencing mild cognitive impairment (OR, 0.975; 95% CI, 0.959–0.992) (38). We did not identify any studies assessing the effects of eggs in children or younger adult populations.

Future research

Limited research supports a positive relationship between eggs and cognition; however, future clinical and prospective cohort studies assessing egg intake closer to the time of cognitive assessment, as well as those utilizing longer-term cognitive measures that assess multiple cognitive domains over time, are greatly needed among both genders and all stages of life. It is plausible that egg intake may be more critical at certain stages of the life cycle, such as during the first 1000 days from conception, because they contain an array of essential nutrients that may influence cognitive outcomes. Another important gap in the current state of knowledge is the effect of eggs versus other dietary sources or supplemental intakes on the bioavailability of nutrients like choline. The unique amino acid profile of eggs may be another interesting area of research in regard to cognition, as suggested by La Rue and others (39).

Choline intake and cognition

Studies assessing choline intake or status in relation to cognition during several periods throughout the life cycle are summarized in Table 1. Those examining effects during the fetal period and early childhood are largely longitudinal, case-controlled, and/or cross-sectional in design, whereas clinical intervention studies are predominant among adult populations.

Exposure during pregnancy: Neurological birth defects

Three studies have assessed choline intake or status during pregnancy and the risk of neurological birth defects (40–42). Shaw and others showed that higher choline intake resulted in an inverse relationship with the incidence of spina bifida (OR, 0.45; 95% CI, 0.22–0.93) in a case-controlled study of 424 neural tube defect cases as compared to 440 nonmalformed controls using a retrospective 100-item maternal food frequency questionnaire (FFQ) (40). A similar study found borderline but insignificant decreases in rates of spina bifida in a longitudinal study of 955 infants after 1 year's follow-up (41). The only study to examine maternal plasma total choline concentrations at the first prenatal visit found no associations with development of spina bifida among 769 infants at birth (42). None of the three studies found significant effects on anencephaly (40–42). Limitations of these studies include the use of self-reported FFQs as well as potential specific susceptible critical window(s) in fetal development. In the absence of clinical interventions, animal studies are quite compelling and suggest a causal relationship between pregnancy and cognitive function in offspring, as it has a critical role in central nervous system development (43).

Exposure during pregnancy: Cognition

Six studies have assessed choline intake or status during pregnancy on child cognition (44–49). Two randomized double-blind trials are currently present in the peer-reviewed literature (44,45). Caudill and others most recently examined the effects of maternal choline supplementation (480 mg/d or 930 mg/d) during the third trimester on infant processing speed and visuospatial memory at 4, 7, 10, and 13 months of age ($n = 24$). This controlled feeding study found that maternal consumption of approximately twice the recommended amount of choline during the first trimester (i.e., 930 vs 480 mg/d) improved infant information and processing speed. In the lower-intake group (i.e., 480 mg/d), there was a linear effect of exposure duration (i.e., infants exposed longer showed faster reaction times), suggesting that even modest increases in maternal choline intake during pregnancy may produce cognitive benefits for offspring (44). The second intervention study assessed the effects of 750 mg/d choline supplementation (administered as ~5 g phosphatidylcholine/d) versus placebo in women whose baseline diets delivered ~80% of the recommended intake at 18 weeks of gestation. All participants agreed to continue the supplement regimen and breastfeed through 90 days postpartum. At 10 and 12 months of age, infants receiving choline did not show any difference from those receiving the placebo on tests for global development, language development, short-term visuospatial memory, or long-term episodic memory (45). It is unclear why this study did not observe similar cognitive effects of increased maternal choline to the more recent study by Caudill and others; however, poor participant adherence and/or uncontrolled variations in the intake of choline and other nutrients has been suggested to play a role (44). Maternal dietary intake of choline during the first and second trimesters of pregnancy was not associated with cognitive performance in offspring at age 3 years in a longitudinal study (46). However, a more recent longer-term analysis of 895 mothers in Project Viva by the same group found that offspring with mothers in the highest quartile of maternal choline intake during the second trimester scored higher on tests for nonverbal intelligence and visuospatial memory. Similar but weaker trends were shown in offspring with mothers in the highest quartile of maternal choline intake during the first trimester (47).

Data from a prospective study of 404 maternal–child pairs showed that serum and umbilical cord blood concentrations of free and total choline at 16 to 18 weeks, 24 to 26 weeks, 30 to 32 weeks, and 36 to 38 weeks were not related to Full Scale Child IQ or selected scales related to visuospatial processing

Table 1. Choline Intake or Status in Relation to Cognitive Function Across the Life-Span.

Reference	Study Design	Participants	Age	Exposure Assessment	Variables	Outcomes
Caudill et al., 2017 (44)	Intervention (6 mo) with 430 vs 930 mg/d choline as PPTC given from third trimester until 90 d postpartum	26 pregnant females in the third trimester and their offspring	13 mo	ND	Infant information processing speed and visuospatial memory taken at 4, 7, 10, and 13 mo of age	Maternal consumption of approximately twice the recommended amount of choline during the first trimester (i.e., 930 vs 480 mg/d) improved infant information and processing speed. In the lower-intake group (i.e., 480 mg/d), there was a linear effect of exposure duration (i.e., infants exposed longer showed faster reaction times), suggesting that even modest increases in maternal choline intake during pregnancy may produce cognitive benefits for offspring.
Lippelt et al., 2016 (61)	Intervention (2 hr) with 2–2.5 g choline bitartrate vs placebo	28 healthy persons (23 female)	18–28 y	ND	Visuospatial working memory, declarative memory, verbal working memory	No significant effects were reported.
Nguyen et al., 2016 (52)	Intervention (6 wk) with 625 mg/d choline vs placebo	55 children with fetal alcohol spectrum disorders (28 female)	5–10 y	ND	Neuropsychological measures of learning and memory, executive function, planning, attention, and motor	No significant effects were reported.
Knott et al., 2015 (57)	Intervention (4 hr) with 500 or 1000 mg C5DC vs placebo	24 healthy right-handed males stratified for auditory gating level	21 y	ND	Auditory gating as indexed by suppression of P50 event-related potential in a paired-stimulus paradigm and executive function	Both C5DC treatments improved gating and suppression of the P50 response, with effects being selective for individuals with low gating (suppression) levels.
Knott et al., 2015 (58)	Intervention (4 hr) with 500 or 1000 mg C5DC vs placebo	24 healthy right-handed males stratified for auditory gating level	21 y	ND	Processing speed, working memory, verbal learning, verbal memory, and executive function	Both treatments improved processing speed, working memory, verbal learning, verbal memory, and executive function in low baseline performers while exerting no effects in medium baseline performers and diminishing cognition in high baseline performers.
Knott et al., 2015 (59)	Intervention (4 hr) with 500 or 1000 mg C5DC vs placebo	24 healthy right-handed males stratified for auditory gating level	21 y	ND	P50 response, processing speed, working memory, verbal learning, verbal memory, and executive function	Both treatments improved gating and suppression of the S_2 P50 response, with the effects being selective for individuals with low suppression levels. Tentative support was also shown for improvement in executive function in low suppressors.
Naber et al., 2015 (60)	Intervention (70 min) with 2 g choline bitartrate vs placebo	28 healthy persons (24 female)	19 y	ND	Visuomotor aiming task and pupil size	Treatment group increased precision of rapidly hitting centers of targets. Pupil size (a cognition-sensitive biomarker) decreased, suggesting that choline intake alters cholinergic functions in the nervous system.
Mapstone et al., 2014 (72)	Case-controlled (5 y)	525 community-dwelling persons who were healthy at baseline	$\geq$ 70 y	Blood level	Metabolic and lipidomic profiling of 2700 positive-mode features and 1900 negative-mode features	10 metabolites comprising PPTC were depleted in the plasma of individuals who phenoconverted from nonimpaired memory status at baseline to MCI or AD during the 5-y period. These depleted levels were similar to the levels found in individuals who had MCI/AD at baseline.
Mills et al., 2014 (42)	Case-controlled (NR)	769 pregnant women who had an NTD-affected pregnancy vs unaffected controls	Birth	Blood level at first prenatal visit	Betaine and total choline concentrations, as well as single-nucleotide polymorphisms related to choline metabolism were measured as predictors.	Mean choline and betaine concentrations did not differ significantly from the controls. NTD cases were significantly more likely to have the G allele of PEMT.
Boeke et al., 2013 (47)	Longitudinal (7 y)	895 mothers and their offspring	7 y	Dietary intake in second and third trimesters	Offspring visual memory and intelligence at age 7	No significant effects were reported.
Strain et al., 2013 (51)	Cross-sectional	210 preschool-aged children (104 females)	5 y	Blood level	Finger tapping, total language, auditory comprehension, verbal knowledge, applied problems, letter-word recognition, and verbal reasoning	No significant effects were reported.

Cheatham et al., 2012 (45)	Intervention (18 wk gestation through 90 d postpartum) with 750 mg/d PPTC vs placebo	140 pregnant women and their offspring	1 y	ND	Short-term visuospatial memory, long-term episodic memory, language development, and global development of infants at 12 mo	No significant effects were reported.
Nurk et al., 2012 (68)	Cross-sectional	2195 persons (55% female)	70–74 y	Blood level	Sensorimotor speed, perceptual speed, executive function, global cognition, episodic memory, visuospatial skills, and semantic memory	Higher choline levels improved scores on tests for sensorimotor speed, perceptual speed, executive function, and global cognition, but there were no effects on episodic memory, visuospatial skills, or semantic memory.
Ross et al., 2012 (50)	Intervention (second trimester to 3 mo) with 6300 mg/d PPTC until birth, then 100 mg PPTC vs placebo	100 pregnant women and their offspring	6 mo	ND	P50 inhibition ratio and electrophysiological assessment of infant's inhibitory brain function	The PPTC-supplemented group showed a decrease in P450 response. By approximately 5 wk postnatal infants treated with PPTC were significantly more likely to have normal cerebral inhibition.
Villamor et al., 2012 (46)	Longitudinal (4 y)	1210 pregnant women and their offspring	3 y	Dietary intake in first and second trimesters	Cognition and visuomotor skills	No significant effects were reported.
Wu et al., 2012 (49)	Longitudinal (2 y)	154 mother–infant pairs	18 mo	Blood level in mothers at 16 and 32 wk gestation	Infant development across 5 domains: receptive language, expressive language, cognitive skills, and fine motor and gross motor skills	Positive associations were found between infant cognitive test scores and maternal plasma free choline at 16 wk of gestation.
Poly et al., 2011 (69)	Longitudinal (3–10 y)	1391 persons (744 female)	36–83 y	Dietary intake	Neuropsychological evaluation for verbal memory, visual memory, verbal learning, and executive function, as well as brain MRI	Performance on verbal memory and visual memory was better with higher concurrent choline intake. Remote choline intake was inversely related to log-transferred white-matter hyperintensity volume.
Carmichael et al., 2010 (41)	Case-controlled (1 y; RD)	955 infants with spina bifida or anencephaly or nonmalformed	Birth	Dietary intake	Differences in infants with spina bifida or anencephaly and those who were nonmalformed	Choline intake was modestly associated with a decreased risk of spina bifida, but there was no effect on anencephaly.
Signore et al., 2008 (48)	Longitudinal (6 y)	404 mother–infant pairs	Birth	Blood level measured at 4 gestational age intervals	Child IQ, visuospatial processing, and memory	No significant effects were reported.
Shaw et al., 2004 (40)	Case-controlled	864 infants with and without NTDs	Birth	Dietary intake of mother	Differences in infants with NTDs vs healthy controls	Choline intakes in the 75th percentile vs the 25th percentile were associated with a reduced risk of NTDs.
Deuster et al., 2002 (55)	Intervention (3 hr) with 50 mg/kg choline citrate vs placebo	13 males	28 y	ND	Reaction time, logistical reasoning, visual vigilance, serial addition and subtraction, working memory, spatial memory, or repeated acquisition	No significant effects were reported.

(*Continued on next page*)

Table 1. (*Continued*)

Reference	Study Design	Participants	Age	Exposure Assessment	Variables	Outcomes
Spiers et al., 1996 (70)	Intervention (3 mo) with 1 g/d citicoline vs placebo, followed by an additional crossover intervention (2 mo) of 2000 mg/d vs placebo in the subgroup with relatively inefficient memories	Original study: 95 persons (47 female)	50–85 y	Blood levels at 0, 30, 60, and 90 d in original study	Verbal memory using logistical memory passage	In the original study citicoline improved delayed recall on logical memory only for patients with relatively inefficient memories.
		Crossover study: 32 persons (16 female)		Blood levels at 60 d in crossover study		In the crossover study, the higher dose of citicoline was associated with improved immediate and delayed logical memory.
Ladd et al., 1993 (64)	Intervention (90 min) with 10 and 25 g PPTC	80 healthy persons	20 y	ND	Explicit memory measured by a serial learning task	PPTC intake improved explicit memory observed 90 min postingestion, with slight improvements observed at 60 min.
Sorgatz et al., 1988 (62)	Intervention (6 wk) with 5.4 g/d lecithin vs placebo	65 healthy persons	44 y	ND	Concentration and attention	Choline treatment improved scores on tests for concentration and attention.
Sanchez et al., 1984 (65)	Cross-sectional	258 healthy persons	72 y	Dietary intake and blood level	Nonverbal abstract thinking, short-term memory, and long-term memory	No significant effects were reported.
Harris et al., 1983 (56)	Intervention (5 hr) with 20 g PPTC vs placebo	9	22–55 y	Blood level	Word list memorization, retrieval paired associates, and word recognition	No significant effects were reported.
Drachman et al., 1982 (66)	Intervention (5 wk) with 26 g/d PPTC vs placebo	16	70 y	ND	Memory, digit span, word span, supraspan, learning, or subjective memory	No significant effects were reported.
Benton & Donahoe, 1980 (53)	Intervention (3 d) with 1.6 g/d PPTC vs placebo	400 females	22 y	ND	Reaction time, vigilance, mood, and memory	PPTC treatment improved vigilance but no other measures.
Davis et al., 1980 (54)	Intervention (3 d) with 16 g/d choline chloride vs placebo	15 healthy persons	18–34 y	ND	Short-term and long-term memory function	No significant effects were reported.
Mohs et al., 1980 (67)	Intervention (21 d) with 2 g/d choline chloride vs placebo	10 healthy persons	> 60 y	ND	Memory retrieval and storage	No significant effects were reported.
Sitaram et al., 1978 (63)	Intervention (90 min) with 10 g choline chloride	10 healthy persons	24 y	ND	Serial learning and selective reminding	Choline-treated participants showed improved scores on tests for serial learning and selective reminding.

AD = Alzheimer's disease; C5DC = cytidine-5-diphosphocholine; MCI = mild cognitive impairment; MRI = magnetic resonance imaging; ND = no data; ND = ; NTD = neural tube defect; P450 = cytochrome; P450 = ; PEMT = phosphatidylethanolamine N-methyltransferase; PPTC = phosphatidylcholine; RD = retrospective data collection.

and memory (48). Contrary to these findings, maternal free plasma choline and betaine status at 16 weeks but not 32 weeks of gestation was positively associated with infant cognitive test scores, but not motor skills or receptive and expressive language, at 18 months in a more recent prospective analysis of 154 maternal–child pairs (49).

Limitations of many of these studies include timing of the maternal intervention or assessment, which mostly occurred during the second and third trimesters. Brain development has been largely shown to occur during the first trimester of pregnancy and exposure to choline at earlier gestational stages might be more relevant to cognitive outcomes in the offspring. Replication of the study by Caudill and others (44) during the third trimester of pregnancy is also needed, as the sample size was somewhat small.

Exposure during pregnancy and infancy: Schizophrenia risk

One randomized placebo-controlled trial examined the effects of dietary phosphatidylcholine supplementation (~900 mg/d choline) on pathophysiology related to later schizophrenia risk during the second trimester and through the third postnatal month (100 mg q/d or same treatment as in utero). No adverse effects of choline were observed in maternal health and delivery, birth, or infant development. At the fifth postnatal week, the P50 (i.e., an event-related potential occurring approximately 50 milliseconds after the presentation of a stimulus) response was suppressed in more choline-treated infants (76%) compared with placebo-treated infants (43%; effect size, 0.7). A CHRNA7 genotype associated with schizophrenia diminished P50 inhibition in the placebo-treated infants, but not the choline-treated infants (50). These data suggest that perinatal choline activates timely development of cerebral inhibition, even in the presence of gene mutations that otherwise delay it.

Exposure during childhood

One cross-sectional analysis investigated the association between plasma concentrations of free choline and its metabolites and neurodevelopment in 210 children aged 5 years enrolled in the Seychelles Child Development Nutrition Study. There was no indication that free plasma choline concentration (or choline metabolites) within the normal physiological range was associated with neurodevelopmental outcomes (51). Additional intervention and observational studies are needed across all age groups of children.

Exposure during childhood: Effects on fetal alcohol spectrum disorders

One 6-week intervention study investigated supplemental intake of 625 mg/d choline in children aged 5 to 10 years with diagnosed fetal alcohol spectrum disorders but failed to find any effect on cognitive outcomes (52).

Exposure during young adulthood

Ten studies (12 articles) have assessed choline intake or status on cognition during early adulthood (53–64); however, their duration was short, ranging from 90 minutes to 3 days and one 6-week intervention. The 6-week interventional study of 65 individuals found that the lecithin-supplemented group had higher scores on tests for concentration and attention (59). Other shorter-duration studies had mixed results and utilized several heterogeneous cognitive batteries. The most compelling short-term data showed pupil size, a known biomarker of cholinergic function in the nervous system, to be beneficially affected within 70 minutes of supplementation with choline bitartrate. Decreased pupil size enabled individuals in the treatment group to have greater precision in rapidly hitting centers of targets (60). Other more recent short-duration studies by Knott and others have measured and shown benefits of choline bitartrate supplementation on multiple cognitive measures among young males with low baseline performance, as well as those with an increased P50 expression (57–59), once again suggesting that choline requirements may vary among individuals even within the same subpopulation.

Exposure during mid and older adulthood

Six studies have assessed choline intake or status on cognition during mid to late adulthood (65–70). Five studies showed no effects on any of the measured cognitive outcomes (65–67,69,70); however, one study found that higher blood choline levels were associated with better scores on tests for sensorimotor speed, perceptual speed, and executive function (68). To date, the most powerful functional evidence that current recommendations for choline intake may not be sufficient or optimal for lifelong cognitive function is derived from animal models. Numerous animal models demonstrate lasting beneficial effects of increased maternal choline intake that becomes more pronounced with aging (71).

The only data among individuals with diagnosed cognitive decline found that patients with Alzheimer's disease had lower levels of eight choline-containing phospholipid species (and two non-choline-containing species) as compared to healthy controls using a case-controlled design. These 10 lipids derived from peripheral blood have been validated to predict mild cognitive impairment or Alzheimer's disease within a 2- to 3-year time frame with greater than 90% accuracy (72). These data, while weak and inconsistent, might suggest that sufficiency and/or treatment during the latter part of life may not be as crucial in regard to cognition as they are during the beginning stages of life.

Future research

Nutrient needs are a population-wide distribution and current DRIs for choline established by the National Academies of Medicine are grouped to account for recognized unique needs associated with age, gender, and reproductive status (16). "Consistent and strong" evidence supports that genetic factors, such as common variants in choline and folate pathway enzymes, impact the metabolic handling of the nutrient and the risk of nutrient inadequacy, as recently reviewed by Ganz and others (73). For instance, common variants in the PEMT gene may increase dependence on dietary choline to meet phosphatidylcholine requirements. A randomized controlled trial of postmenopausal women found that those who received estrogen versus placebo were 4 times less likely to experience signs of organ dysfunction while consuming choline-deficient diets (74). Results from older interventions yield a variety of inconsistent results, which may be due to the lack of more recent technologies with the ability to identify these types of nutrient

interactions and inaccuracies in calculating actual choline intakes. Additional nutrigenetics-based research is needed and should be considered when revising new dietary requirements for choline. Along the same lines, more reliable and standardized biomarkers of choline status need to be identified since blood levels often fluctuate, especially in short-term challenge studies. In humans, choline bitartrate increases plasma levels within 1 hour after ingestion (75,76), with brain concentrations peaking around 2 to 3 hours postingestion. Choline's effect on the cholinergic peripheral system seems to peak between 1 and 2 hours after ingestion (77,78).

The findings presented in this article provide encouragement that maternal–infant choline intake may hold significant promise for lifelong effects on cognition. Microarray or RNA-sequencing studies may prove to be useful in determining the effect of maternal choline supplementation on cell survival and neuroplasticity in offspring. Identification of specific genes that exhibit epigenetic marks (DNA and histone methylation) as well as transcripts that display lasting changes in gene expression following choline supplementation and their association with cognitive measures and end points is pivotal. Intervention studies must be designed using new novel technologies from the time of conception through early childhood so that critical windows may be identified for which choline supplementation is most impactful. Tracer studies similar to those published by the Caudill's lab (78) are needed not only to determine choline requirements across subpopulations but to better understand the biological influences of this essential nutrient across the life-span.

In the absence of consistent and prospective observational data, it is important that investigators continue to assess potential relationships between choline intake and levels and multiple cognitive domains over time, among a wide age range, and using well-designed prospective cohort studies. Continuous updates to the U.S. Department of Agriculture's (USDA) National Nutrient Database for Standard Reference to comprise more detailed information on the choline content of foods, particularly in regard to choline derived from food additives, and further development of validated FFQs will be essential to developing a more robust understanding of the role choline plays in cognition. Currently, there is no way to accurately estimate choline intakes from food additives (e.g., lecithin) within the USDA food composition databases; one may speculate that a significant amount of dietary intake may be derived from processed foods, thus underrepresenting current population status. Choline intake data from whole foods are limited, and again actual intakes may be underestimated because only a small number of foods have been assessed for their content.

Lutein intake and cognition

Studies assessing lutein intake or status in relation to cognition during several periods throughout the life cycle can be found in Table 2. MPOD has been found to be a reliable biomarker of brain concentrations of lutein as well as smaller concentrations of zeaxanthin and meso-zeaxanthin, which can be easily measured noninvasively using heterochromatic flicker photometry (79,80). MPOD, unlike serum lutein and zeaxanthin concentrations, is a direct reflection of lutein and zeaxanthin in the neural tissue (81). Many trials coadminister lutein and zeaxanthin in supplemental form. Apart from cognitive function relationships with macular pigment, there seems to be less evidence for a relationship between zeaxanthin and cognitive outcomes (82).

Exposure during pregnancy: Cognition and neurological birth defects

No studies have identified lutein intake or status or MPOD during pregnancy and effects on cognition or neurological birth defects. One cross-sectional study found lutein concentrations in infant brain tissue to be strongly related to steroidogenic acute regulatory domain 3 (StARD3), a lutein-binding protein, suggesting that it has a role in neural development (83). To elucidate potential mechanisms by which lutein may influence infant cognition, a similar study assessed and found lutein concentrations in brain tissues to be correlated with several metabolic brain-region-specific pathways thought to be involved with infant brain development (84). The infant retina and brain need antioxidants because of their high metabolic rates and relative deficiencies in endogenous antioxidant enzymes (85). In children's brains, the concentration of lutein relative to total carotenoids is twice that found in adults. Lutein accounts for more than half of infant brain carotenoids, suggesting that the antioxidant may play a major role in neuronal development (31).

Exposure during childhood

Three studies have assessed lutein intake or status or MPOD during early childhood (86–88). A 6-month intervention study of 56 children aged 8 to 9 years found MPOD to be related to overall academic achievement and mathematics and written language composite standard scores (86). A similar cross-sectional analysis investigated the relationship of MPOD with behavioral and neuroelectric indices elicited during a cognitive control task in preadolescent children aged ~8 years and found it to be associated with both measures. The data suggested that children with higher MPOD may respond to cognitive tasks more efficiently, maintaining high performance while displaying neural indices indicative of lower cognitive load (87). Similar findings were not found in a cross-sectional study that examined dietary intake and plasma levels of lutein with measures of cognition (88). Data on the effect of lutein during early childhood are currently scarce.

Exposure during young adulthood

Two studies have assessed lutein intake or status or MPOD during young adulthood (89,90). Similar to their study in children, Walk et al. found that cognitive control was increased during cognitive control tasks designed to assess different aspects of attentional control. They found a relationship between MPOD and neuroelectric indices underlying cognitive control, suggesting that lutein may have a protective role in the central nervous system prior to the onset of disease (89). MPOD was also related to reaction time and coincidence anticipation errors at high speed in younger adults, suggesting that it plays a critical role in visuomotor behavior (90). It is possible that lutein may enhance cognition due to some type of local interaction with neural cells (the neural efficiency hypothesis) (91) and is likely due to, at least in part, its antioxidant functions (31).

Table 2. Lutein Intake or Status in Relation to Cognitive Function Across the Life-Span.

Reference	Study Design (Follow-Up)	Participants	Age	Exposure Assessment	Variables	Outcomes
Lindbergh et al., 2017 (91)	Intervention (1 y) with 10 and 2 mg/d lutein and zeaxanthin vs placebo	44 community-dwelling persons (26 female)	64–86 y	MPOD	Neurocognitive performance via an fMRI-adapted task involving learning and recalling word pairs; image contrasts of BOLD signal	Lutein and zeaxanthin treatment appeared to buffer cognitive decline on the verbal learning task. Interactions during learning were observed in the left dorsolateral prefrontal cortex and anterior cingulate cortex. Supplementation appeared to benefit neurocognitive function by enhancing cerebral perfusion, even if consumed for a discrete period of time in late life.
Walk et al., 2017 (89)	Cross-sectional	60 healthy persons (31 female)	25–45 y	MPOD	Cognitive control using event-related potentials during performance of cognitive control tasks designed to measure aspects of attentional control	MPOD was related to both age and the P3 component of participants' neuroelectric profile (P3 amplitude) for attentional but not response inhibition. Older participants with higher MPOD displayed P3 indices similar to their younger counterparts in amplitude, suggesting that the protective role of carotenoids within the central nervous system may be evident during early and middle adulthood, decades prior to the onset of older age.
Barnett et al., 2017 (86)	Intervention (9 mo)	56 healthy persons	8–9 y	MPOD	Academic achievement scores	MPOD was correlated with increased overall academic achievement, mathematics, and written language composite standard scores.
Walk et al., 2017 (87)	Cross-sectional	49 healthy persons (31 female)	8 y	MPOD	Neuroelectric indices elicited during a cognitive control task	MPOD was associated with both behavioral performance and P3 amplitude such that children with higher MPOD had more accurate performance and lower P3 amplitudes. The relationships were more pronounced for tasks requiring greater cognitive control.
Feeney et al., 2017 (92)	Cross-sectional	4076 community-dwelling persons (53.6% female)	50+ y	Blood levels	Global cognition, memory, and executive function scores	Higher plasma lutein was associated with better composite scores across the domains of global cognition, memory, and executive function.
Lindbergh et al., 2017 (93)	Cross-sectional	43 community-dwelling persons (25 female)	72 y	Blood levels and MPOD	Learn and recall pairs of unrelated worlds in an fMRI-adapted paradigm (BOLD signal measured)	Lutein and zeaxanthin were found to negatively relate to BOLD signal in many areas of the brain, suggesting that the carotenoids may enhance neural efficiency in older individuals.

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Table 2. (*Continued*)

Reference	Study Design (Follow-Up)	Participants	Age	Exposure Assessment	Variables	Outcomes
Zamroziewicz et al., 2016 (94)	Cross-sectional	76 healthy persons (51 female)	65–75 y	Blood levels	Crystalized intelligence measured by acquired knowledge, verbal reasoning, and attention to verbal information; volumetric brain fMRI analyses focused on gray matter volume in the temporal cortex	The mediation analysis revealed that gray thickness of one region within the temporal cortex, the right parahippocampal cortex (Brodmann area 34), partially mediates the relationship between serum lutein and crystallized intelligence.
Feart et al., 2016 (95)	Longitudinal (9.5 y)	1092 persons without dementia at baseline (687 female)	74 y	Blood levels	Diagnosed cases of dementia and AD by committee of neurologists	Higher plasma lutein moderately decreased the risk of all-cause dementia and AD.
Tanprasertsuk et al., 2016 (96)	Cross-sectional	10 decedents 8 decedents 10 decedents	1–4 mo 55–86 y 98–105 y	Brain tissue levels	StARD3 (identified by its binding protein in retinal tissue)	The strong relationship of brain lutein and StARD3 in infants suggests that lutein has a role in neural development. The relationship remained significant but weak in older adults and insignificant in centenarians.
Chew et al., 2015 (98)	Intervention (5 y) with 10 and 2 mg/d lutein and zeaxanthin vs placebo	3501 persons at risk for late AMD (57.5% female)	72.7 y	ND	Cognitive tests for attention, memory, executive function, current events, serial subtraction, counting, language, letter fluency, alternating fluency, and other domains	No significant effects were reported.
Kelly et al., 2015 (99)	Cross-sectional	105 healthy persons with low MPOD at baseline (53 female) 121 persons with AMD (81 female)	47 y 65 y	Blood levels and MPOD	Cognitive tests for phonemic fluency, semantic fluency, and attention switching as well as visual and verbal memory and learning	Significant correlations were evident between MPOD and measures of cognitive function in healthy individuals and those with AMD. Serum lutein concentrations correlated significantly with semantic fluency cognitive scores and Verbal Recognition Memory learning slope scores in those with AMD. Most of the correlations with MPOD, but not serum lutein, remained significant after controlling for age, gender, diet, and education level.
Lieblein-Boff et al., 2015 (97)	Cross-sectional	30 decedent infants (9 female)	1–488 d	Brain tissue levels	Metabolomic profiles	Lutein concentrations correlated with lipid pathway metabolites, energy pathway metabolites, brain osmolytes, amino acid neurotransmitters, and the antioxidant homocarnosine. These correlations were often brain region–specific.

Nolan et al., 2015 (100)	Intervention (6 mo) with 10 mg meso-zeaxanthin, 10 mg lutein, 2 mg zeaxanthin, or placebo	31 healthy persons 31 persons with AMD	76 y 80 y	MPOD	Semantic fluency, phonemic fluency, visual learning and memory, verbal learning and memory, and motor speed and accuracy	Participants in the treatment group exhibited four significant results (from five spatial frequencies tested) in the AD group and two in the non-AD group.
Noogens et al., 2015 (101)	Longitudinal (5 y)	2613 persons with low or high cognitive function at baseline	43–70 y	Dietary intake	Global cognitive function, memory, processing speed, and cognitive flexibility	Global cognitive decline in the highest lutein intake quintile was greater than in the lowest intake quintile. No other significant effects were reported.
Dias et al., 2014 (102)	Cross-sectional	33 healthy persons 27 persons with AD 16 persons with AD + CVDc	73 y 80 y 79 y	Blood levels	Plasma HDL	Plasma HDL and lutein concentrations were lower in the AD + CVDc group compared to those in the control or AD-only groups.
Kesse-Guyot et al., 2014 (103)	Longitudinal (13 y)	2983 healthy persons	65.5 y	Blood intake and dietary intake	Episodic memory, semantic memory, semantic fluency, phonemic fluency, short-term working memory, and mental flexibility	A carotenoid-rich dietary pattern was found to be associated with a higher composite cognitive score after adjustment for
Mulder et al., 2014 (113)	Cross-sectional	160 healthy children (84 female)	5 y	Dietary intake and blood levels	Mental process, sequential process, simultaneous process, and learning ability	No significant effects were reported.
Renzi et al., 2014 (104)	Cross-sectional	29 healthy persons 24 persons with MCI(60% total population female)	74 y 75 y	MPOD	Time and place, attention, language ability, visual construction ability, calculation skills, and immediate and delayed recall of short word list	In healthy older adults, MPOD was only related to visuospatial and constructional abilities. In persons with MCI, MPOD was broadly related to cognition, including the composite score on the MMSE, visuospatial and constructional abilities, language ability, attention, and the total scale on the Repeatable Battery for the Assessment of Neuropsychological Status.
Vishwanathan et al., 2014 (105)	Cross-sectional	108 healthy persons (55 female)	78 y	MPOD and blood levels	Global cognition, verbal learning and fluency, recall, processing speed, and perceptual speed	MPOD levels were significantly associated with better global cognition, verbal learning and fluency, recall, processing speed and perceptual speed, whereas serum lutein and zeaxanthin were only related to verbal fluency.
Feeney et al., 2013 (106)	Cross-sectional	4453 healthy persons	$\geq$ 50 y	MPOD	Global cognition, memory, executive function, processing speed, and sustained attention	Lower MPOD was associated with poorer performance on the MMSE and the Montreal Cognitive Assessment. Individuals with lower MPOD also had poorer prospective memory, took longer to complete a trail-making task, and had slower and more variable reaction times on a choice reaction time task. There was no significant association between MPOD and verbal fluency, word recall, visual reasoning, or picture memory.

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Table 2. (*Continued*)

Reference	Study Design (Follow-Up)	Participants	Age	Exposure Assessment	Variables	Outcomes
Johnson et al., 2013 (30)	Cross-sectional	220 centenarians (184 female) 78 octogenarians (51 female)	100 y 84 y	Blood levels Brain tissue levels	Global cognitive function, dementia, and depression as well as cognitive domains including memory, processing speed, or attention and executive functioning	Serum lutein concentrations were most consistently related to better cognition in octogenarians and centenarians. In brain tissues, a significant positive correlation was observed for lutein concentrations in the cortex and global cognitive function as well as language, and a negative association was observed with depression.
Renzi et al., 2013 (107)	Cross-sectional	49 older persons (25 female) 106 younger persons (73 female)	55 y 23 y	MPOD MPOD	Balance ability and simple reaction time Fixed and variable reaction time and coincidence anticipation ability	MPOD was associated with increased reaction time and balance ability in older participants. MPOD was associated with fixed and variable position reaction time and coincidence anticipation errors at high speed in younger individuals.
Johnson et al., 2008 (108)	Intervention (4 mo) with 12 mg/d lutein, 800 mg/d DHA and 12 mg lutein, or placebo	49 healthy women	60–80 y	ND	Verbal fluency, memory, processing speed and accuracy, and self-reports of mood	The lutein and lutein + DHA groups showed improvement in verbal fluency scores compared to placebo. Memory scores and rate of learning improved significantly in the lutein + DHA group, who also displayed a trend toward efficient learning. No other significant effects were reported.
Wang et al., 2008 (109)	Cross-sectional	10 healthy persons (5 female) 36 persons with AD (20 female)	70 y 75 y	Blood levels	MMSE from moderately severe to mild AD	Patients with moderately severe AD had much lower plasma lutein concentrations as compared to those with mild AD or healthy patients.
Akbaraly et al., 2007 (110)	Cross-sectional	589 healthy persons (361 female)	73.5 y	Blood levels	Cognitive impairment measured by MMSE, Trail-Making Test Part B, Digit Symbol Substitution Test, finger-tapping test, and Word Fluency Test.	No significant effects were reported.
Rinaldi et al., 2003 (111)	Cross-sectional	53 healthy persons (36 female) 25 persons with MCI (14 female) 63 persons with AD (46 female)	76 y 76 y 77 y	Blood levels	Clinical, neurological, and neuropsychological evaluation as well as cerebral computed tomography or fMRI	Plasma lutein was lower in patients with MCI as compared to healthy controls. Plasma levels were also lower in those with AD compared to those with MCI and healthy controls.
Schmidt et al., 1998 (112)	Cross-sectional	1769 healthy persons	50–75 y	Blood levels	Mattis Dementia Rating Scale scores	No significant effects were reported.

AD = Alzheimer's disease; AMD = Age-related macular degeneration; BOLD = blood-oxygen-level-dependent; CVDc = cardiovascular disease comorbitities; DHA = docosahexaenoic acid; fMRI = fuctional magnetic resonance imaging; HDL = high-density lipoproteins; MCI = mild cognitive impairment; MPOD = macular pigment optical density; MMSE = Mini Mental State Examination; ND = no data; StARD3 = steroidogenic acute regulatory domain 3 (a lutein-binding protein).

Exposure during mid and older adulthood

The majority of studies identified assessed the role of lutein intake or status or MPOD during mid to older adulthood (30,91–115). Five studies assessed patients with Alzheimer's disease and found significant beneficial effects of higher lutein intake or blood or tissue levels (95,100,102,109,111). The only intervention study in patients with Alzheimer's disease found significant effects of supplementation among five spatial frequencies tested in those with Alzheimer's disease as compared to two spatial frequencies in the healthy control group. MPOD increased in both groups after supplementation (100). An investigation into the Irish Longitudinal Study on Aging found that older adults with higher MPOD had better results on various indices of cognitive function as compared to those with lower MPOD (106). Using functional magnetic resonance imaging (fMRI), Terry and others found that among community-dwelling older adults, higher levels of MPOD were associated with increased blood-oxygen-level-dependent activation in the left frontal and inferior frontal gyri, left middle temporal gyrus, and other areas associated with verbal memory during learning and recall (poster abstract; not included in Table 2) (114). Primate and human retinal lutein concentrations (i.e., MPOD) are also related to brain concentrations (33,34).

Consistent with MPOD data, evidence from the Three-City Bordeaux prospective cohort showed plasma lutein concentrations to decrease the risk of all-cause dementia and Alzheimer's disease by 19% and 24%, respectively (HR, 0.81; 95% CI, 0.67–0.97; HR, 0.76; 95% CI, 0.60–0.96) (94). Elevated serum cholesterol concentrations in midlife seem to increase risk of Alzheimer's disease. Lower concentrations of high-density lipoproteins (HDLs) and their principal apolipoprotein A1 also correlate with increased risk of this disease. One role of HDL is to efficiently transport oxocarotenoids, which are scavengers of peroxynitrite. Lower levels of oxocarotenoid concentrations during Alzheimer's disease may render HDLs susceptible to nitration and oxidation and in turn reduce their efficiency to reverse cholesterol transport from lipid-laden cells (102).

Two studies assessing individuals with mild cognitive impairment also found similar effects as compared to healthy controls, but to a lesser extent (102,110). A recent study failed to show a relationship between brain lutein and the StARD3 lutein-binding protein among 10 centenarians (96); however, an older assessment of 220 centenarians enrolled in the Georgia Centenarian Study found that both serum and brain tissue levels were related to better cognition using a wide range of measures (30). Dietary intake of lutein as well as blood measures have frequently, but not always, consistently correlated with better cognitive performance in general among middle-aged to older adults. MPOD has been consistently correlated with better cognition in this group (91,93,99,104–107) and has been shown across studies to be a more reliable biomarker of both brain concentrations of lutein and cognitive status in older adults. How lutein enhances cognition is relatively unknown. It has been suggested that lutein may help protect brain tissues from the accumulated effects of oxidative and inflammatory stress (5), and certainly the data correlating MPOD to cognitive impairment are consistent with this notion.

Future research

Studies show that lutein peaks in the plasma around 14 to 16 hours after consumption (115). The half-life of plasma lutein was shown to be 76 days in one study (116) and only 22 days in another study (117). Greater clarity is needed on the half-life of lutein and how it is eliminated so that dose ranges and regimens can be better developed for clinical use. Additional intervention studies examining cognitive effects of lutein intake and MPOD across all age ranges and cognitive states using more novel measures of brain health (e.g., fMRI) are greatly needed. Baseline MPOD should be taken into consideration when designing intervention studies and assessing data from populations/cohorts. Future studies evaluating the association between differences in carotenoid-related gene expression profiles and lutein-related function in brain tissue may help to determine its impact on cognition. Utilizing baseline MPOD measures as inclusion/exclusion criteria for clinical trials and longitudinal analyses is critical for measuring cognitive outcomes, as many foods contain either lutein and/or zeaxanthin. MPOD measures may prove to better represent lutein/zeaxanthin status versus cross-referencing food intake data with the USDA food composition databases, which again are limited by the number of foods assessed for these two carotenoids. It is also important to consider potential interactions between nutrients within a food matrix, as higher choline with higher lutein levels have been shown to be related to better recognition memory in 6-month-olds (118).

Conclusions

Eggs are a primary source of both choline and lutein in the western diet. There is clear scientific evidence to suggest that both choline and lutein play a vital role in brain and neurological development during the first 1000 days postconception. The extent to which higher intakes of choline have the potential to enhance or influence cognition during childhood, adulthood, and/or age-related cognitive decline needs further investigation. Prospective cohort studies that accurately assess choline intakes from food are greatly needed, as are randomized clinical interventions. Emerging but consistent research suggests that lutein has the potential to influence cognition across the life-span and that sufficient intakes during mid to late adulthood may help to ward off age-related cognitive decline. MPOD has been reported to be a reliable and consistent biomarker of brain lutein concentrations across the life-span and may have potential for clinically assessing cognitive status.

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