

Role of lutein and zeaxanthin in visual and cognitive function throughout the lifespan

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The relationship between lutein and zeaxanthin and visual and cognitive health throughout the lifespan is compelling. There is a variety of evidence to support a role for lutein and zeaxanthin in vision. Lutein's role in cognition has only recently been considered. Lutein and its isomer, zeaxanthin, are taken up selectively into eye tissue. Lutein is the predominant carotenoid in human brain tissue. Lutein and zeaxanthin in neural tissue may have biological effects that include antioxidation, anti-inflammation, and structural actions. In addition, lutein and zeaxanthin may be protective against eye disease because they absorb damaging blue light that enters the eye. In pediatric brains, the relative contribution of lutein to the total carotenoids is twice that found in adults, accounting for more than half the concentration of total carotenoids. The greater proportion of lutein in the pediatric brain suggests a need for lutein during neural development as well. In adults, higher lutein status is related to better cognitive performance, and lutein supplementation improves cognition. The evidence to date warrants further investigation into the role of lutein and zeaxanthin in visual and cognitive health throughout the lifespan.

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INTRODUCTION

Extensive epidemiological observation indicates that fruits and vegetables rich in carotenoids provide a variety of health benefits.¹⁻³ The relationship between lutein, a dietary xanthophyll carotenoid, and visual and cognitive health is particularly compelling because lutein is taken up selectively into eye and brain tissue.⁴⁻⁶ In part, the beneficial effects of lutein are thought to be attributable to its antioxidant and anti-inflammatory properties. In addition, lutein may be protective in the eye because it absorbs damaging blue light that enters the eye.⁷

The purpose of this review is to describe the current evidence that supports a role for lutein in visual and cognitive function. To date, the majority of the evidence supports a role for lutein in the visual health of adults; however, data are accumulating in support of a role for

lutein in early visual development as well as in cognitive function throughout the lifespan.

A ROLE FOR LUTEIN IN VISUAL HEALTH

Compared with other carotenoids, lutein and its isomer zeaxanthin are taken up preferentially into many areas of the eye^{8,9} but are particularly concentrated in the central region of the retina, referred to as the macula.⁴ Bone et al.⁴ have studied the retinal distribution of lutein and zeaxanthin in human retina. The lutein-to-zeaxanthin ratio increased from an average of 1:2.4 in the central macula (0–0.25 mm eccentricity) to 2:1 in the periphery (8.7–12.2 mm eccentricity). These investigators have shown the components of human macular pigment to be lutein, zeaxanthin, and *meso*-zeaxanthin. *Meso*-zeaxanthin is located primarily in the center of the

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macula, where it is found in an approximate ratio of 1:1 with zeaxanthin. *Meso-zeaxanthin* is not generally present in the diet.¹⁰ Its presence in the macula is due to conversion from lutein alone.¹¹ In the macula, lutein, zeaxanthin, and *meso-zeaxanthin* are referred to as macular pigment and are believed to prevent damage that leads to age-related macular degeneration,¹² a leading cause of visual impairment and blindness in the United States.^{13,14} Recently, it has been suggested that lutein may also play a role in early visual development.¹⁵

The measurement of macular pigment can be performed noninvasively and has been validated in adults.¹⁶ Therefore, macular pigment density can potentially serve as a biomarker not only for protecting against the risk of certain eye diseases but also for visual function (see “Visual function in healthy adults” section below). Augmented macular pigment levels may improve visual performance and visual comfort throughout the lifespan. It should be noted that macular pigment is composed of lutein, zeaxanthin, and *meso-zeaxanthin*. Therefore, investigations on macular pigment and visual function cannot determine effects due to lutein specifically. However, the source of two of the three pigments is dietary lutein,¹¹ and dietary intake of lutein is 5–7 times that of zeaxanthin.¹⁷

Visual development

The evidence to date indicates that lutein may influence early maturation of the retina.¹⁵ Lutein is concentrated in the area of the retina that is most immature at birth.¹⁸ Studies in nonhuman primates suggest this is important. In a study involving rhesus monkeys raised on a standard laboratory diet or xanthophyll-free diets, the xanthophyll-free monkeys were found to have no macular pigment. Compared with the monkeys on the standard laboratory diet, these animals had more drusen-like bodies in the retinal pigment epithelial cells (cells that are crucial for nourishment of the retina), increased macular hyperfluorescence, and more retinal abnormalities.^{19,20} It was later noted that the xanthophyll-free diets also were high-fat diets designed for cardiovascular disease studies.¹² Therefore, additional dietary factors may have contributed to the abnormalities observed. However, in subsequent studies designed to examine the effects of diets devoid of xanthophylls more specifically, rhesus monkeys on a lifelong diet devoid of lutein or zeaxanthin had distinct morphological changes in the eye compared with control monkeys raised on diets containing lutein or zeaxanthin.²¹ The structural changes involved the retinal pigment epithelium. Xanthophyll-free monkeys showed a dip in the retinal pigment epithelial cell-density profile at the foveal center (center of the macula, which contains the largest concentration of cone cells and is responsible

for central, high-resolution vision), rather than the normal peak. After supplementation with lutein or zeaxanthin, the retinal pigment epithelium profile of animals with a low intake of n-3 fatty acids no longer had a dip at the foveal center but became asymmetric, with higher densities observed in the inferior retina. Therefore, retinal pigment epithelial cells are sensitive to the absence of macular pigment. These studies suggest that xanthophylls and n-3 fatty acids are essential for the development and/or maintenance of a normal distribution of retinal pigment epithelial cells. In this regard, adequate lutein and zeaxanthin intakes during early visual development may of particular importance. The findings showing a preferential uptake of lutein in breast milk lend support to this role.^{22,23}

Visual function in healthy adults

It has been suggested that macular pigment can improve visual function by means of its light-filtering properties.²⁴ Studies in young and older adults strongly suggest that an increased lutein intake improves visual performance. Lutein supplementation alone or in combination with zeaxanthin for 12 months was found to improve contrast acuity thresholds at high mesopic levels. That is, there was better visual performance when ambient illumination was low.²⁵ This was not evident in the placebo group. These results suggest that xanthophyll supplementation may improve visual performance during activities such as driving at night. Six months of supplementation with 12 mg of lutein per day was shown to increase macular pigment density in healthy subjects and to improve visual performance in glare function tests.²⁶

Lutein has also been reported to protect against the detrimental effects of long-term computer display light exposure in healthy, young adult subjects.²⁷ In this study, 12 weeks of supplementation with 12 mg of lutein per day also improved contrast sensitivity. Lutein supplementation (5 mg) in combination with zeaxanthin (1 mg) and black currant extract (200 mg) was also shown to reduce symptoms of visual fatigue associated with visual proof-reading tasks in healthy subjects aged 22 to 45 years.²⁸ Macular pigment may improve glare disability and photostress recovery through its light-filtering properties. It has also been suggested that lutein may improve visual function through certain biological mechanisms, such as, for example, increased neuronal signaling efficiency in the eye.²⁹

Visual function in eye disease

Increased intake of lutein is related to a decreased risk of age-related macular degeneration.³⁰ Similarly, the dietary information from the Age-Related Eye Disease Study 1

(AREDS1) pointed to lutein and zeaxanthin as being protective against the development of age-related macular degeneration.³¹ AREDS2,³² a multicenter phase III randomized clinical trial, assessed the effects of oral supplementation with lutein plus zeaxanthin (10 mg and 2 mg, respectively) and/or eicosapentaenoic acid plus docosahexaenoic acid (650 mg and 350 mg, respectively) as a treatment for age-related macular degeneration. In secondary analysis, lutein and zeaxanthin supplements in addition to the AREDS supplement (500 mg of vitamin C, 400 IU of vitamin E, 15 mg of β -carotene, 80 mg of zinc, and 2 mg of copper) slowed the progression to advanced age-related macular degeneration in persons with low dietary lutein and zeaxanthin.³²

Lutein supplementation has also been shown to improve visual function in patients with eye disease. In a double-blind, placebo-controlled study in cataract patients ($n = 17$), supplementation with 15 mg of lutein 3 times a week resulted in improved visual acuity and glare sensitivity.³³ In patients with retinal degeneration, lutein supplementation (20–40 mg/d for 26 weeks) improved both visual acuity and mean visual-field area; improvement began 2–4 weeks after the intervention but plateaued at 6–14 weeks.³⁴ To determine whether lutein supplementation would slow visual function decline in patients with retinitis pigmentosa receiving vitamin A, a randomized, controlled, double-blind trial was conducted in 225 non-smoking patients over a 4-year period.³⁵ Patients received 12 mg/d lutein or placebo. Lutein supplementation significantly slowed the loss of midperipheral visual field in these subjects. Randomized control trials involving patients with age-related macular degeneration have shown that lutein supplementation, at doses ranging from 8 mg to 20 mg,^{36–39} improved dark adaptation, visual acuity, foveal sensitivity, contrast sensitivity, and glare recovery. Therefore, increased lutein intake appears to improve visual function in both healthy individuals and patients with eye disease.

The mechanism by which lutein improves certain aspects of visual function may involve its ability to absorb short-wave light, which is easily scattered and poorly focused. The observed improvement in visual acuity with lutein supplementation is more difficult to understand. Decreased visual acuity is a refractive error in an area where lutein (as macular pigment) is minimal. Therefore, it seems unlikely that macular pigment can change the refractive state. Furthermore, in contrast to the lutein intervention studies, a cross-sectional study reported that macular pigment density was not correlated with visual acuity.⁴⁰ Therefore, it is uncertain whether lutein affects visual acuity.

The relationships observed between lutein and vision may not simply be due to antioxidative, blue light filtering, or structural effects but also to postphotoreceptor

processes involving cognitive processing. Temporal measures, which are sensitive measures of visual processing, are useful for quantifying photoreceptor processes. Critical flicker fusion threshold, a postphotoreceptor process,⁴¹ is the frequency at which an intermittent light stimulus appears to be steady to the individual. This is often measured by 1) exposing the individual to a low-frequency flicker and increasing the frequency to the point at which the subject has the sensation that the flickering stops, and 2) exposing the individual to a high-frequency flicker that decreases to the point at which the flicker is detected. The critical flicker fusion threshold is the average of the two. Macular pigment density has been reported to be positively related to the critical flicker fusion threshold, which is independent of age.⁴² This suggests that lutein and zeaxanthin may be involved in visual processing. Renzi and Hammond⁴³ measured the more complete temporal contrast sensitivity function to fully characterize temporal vision and reported that macular pigment density was positively related to this measure. These observations support direct effects of lutein and zeaxanthin in neural function that would be important in both vision and cognition.

A ROLE FOR LUTEIN IN COGNITIVE HEALTH

Given that the eye is an extension of the neural system, lutein is increasingly recognized as having a role in cognitive function.⁴⁴ Apart from cognitive function relationships with macular pigment (see “Role of lutein in cognitive function in adults” section), there is less evidence for a relationship between zeaxanthin and cognition. The omega-3 fatty acids are an example of a dietary intervention, and their addition to infant formulas supports both visual and cognitive development in early life.⁴⁵ Furthermore, several studies have shown cognitive impairment to be related to age-related eye diseases,^{46–49} suggesting that similar factors may be involved. These observations are in line with the view that vision and cognition are not easily separable.

The rationale supporting a role for lutein in cognitive function is based on the following observations: 1) lutein is the predominant carotenoid in human brain tissue in early as well as late life^{5,6}; 2) primate retinal lutein concentrations, i.e., macular pigment density, are related to brain lutein concentrations⁵⁰; 3) macular pigment density is related to cognitive function in adults^{51,52}; and 4) lutein supplementation in adults improves cognitive function.⁵³

Role of lutein in early life

Optimal visual performance in early life could influence brain development, which is rapid in the first year.⁵⁴

Environmental enrichment, as would occur with visual cues, has long been investigated as an influence on brain structure and function. Morphological and functional effects elicited by environmental enrichment at the neuronal level have been reported to be accompanied by improvements in cognitive performance.⁵⁵ Lutein's role in early neural development is a relatively new concept supported by a limited amount of research. The first step in investigating such a role is to assess concentrations of lutein in infant brain.

In order to assess brain concentrations of carotenoids, brain tissues from 30 decedents who died during the first year of life were assessed for carotenoids⁶ using standard methods.⁵⁶ Brain tissues (hippocampus, frontal, auditory, occipital cortices) were obtained from a federally funded tissue bank. It is noteworthy that these regions of the brain are associated with memory (hippocampus), executive function (frontal cortex), hearing (auditory cortex), and vision (occipital cortex). The cause of death was either sudden infant death syndrome (50%) or other conditions (50%). Lutein was found to be the major carotenoid in infant brains. There was significantly greater accumulation of xanthophylls (lutein, zeaxanthin, and cryptoxanthin) than of carotenes (β -carotene and lycopene) in all four regions of the brain. Lycopene was detected in only 2 decedents. No α -carotene was detected in any tissues. The average concentration of lutein in all four brain regions was significantly greater than that of the other dietary carotenoids (zeaxanthin, cryptoxanthin, β -carotene, and lycopene).

There were no dietary data for these specific decedents; however, data for NHANES III (1988–1994)⁵⁷ was collected during a timeframe that most closely matched that in which the decedent tissue samples became available. Evaluation of the NHANES III data for dietary carotenoids in infants, 2–11 months, shows a much different pattern from the decedents, with β -carotene being the major dietary carotenoid (43% total), followed by lycopene (28%), α -carotene (13%), and lutein (12%); the respective values in the decedent infant brain tissue were 16%, 2%, 0%, and 59%. This strongly suggests a preferential uptake of lutein into infant neural tissue. Further substantiating a preferential uptake of lutein is the observation that there were 2 decedents for whom lutein and its isomer zeaxanthin were the only carotenoids in brain tissue. There were no decedent tissues that contained other carotenoids but no lutein. The relative contribution of lutein to total carotenoids was approximately twice that found in adults (59% vs 31%, respectively),^{5,6} indicating a possible additional role of lutein in early neural development. Of further interest was the finding that preterm infants ($n = 8$) had significantly lower concentrations of lutein, zeaxanthin, and cryptoxanthin in their brain compared with full-term infants ($n = 22$), despite

similarity in postmenstrual age. Among formula-fed infants, preterm infants ($n = 3$) had lower concentrations of lutein and zeaxanthin compared with full-term infants ($n = 5$). Concentrations of brain lutein did not differ between breast-milk-fed ($n = 3$) and formula-fed ($n = 5$) term decedents. In contrast, term decedents with measurable brain cryptoxanthin, a carotenoid that is inherently low in formula, had higher brain lutein levels, suggesting that mode of feeding is an important determinant of brain lutein concentrations.

Role of lutein in cognitive function in adults

Epidemiological studies indicate that dietary lutein may be of benefit in maintaining cognitive health. As stated above, among the carotenoids, lutein and zeaxanthin are the only two that cross the blood-retina barrier to form macular pigment in the eye,¹² and lutein is the dominant carotenoid in human brain tissue.^{5,6,58} The finding that lutein is the major carotenoid in brain tissue despite not being the major carotenoid in matched serum (an indicator of dietary intake) strongly suggests preferential uptake into brain tissue.⁵ Lutein and zeaxanthin in macula were found to be significantly correlated with their levels in matched brain tissue.⁵⁰ Therefore, macular pigment can be used as a biomarker in brain tissue. This is of interest, given that a significant correlation was found between macular pigment density and global cognitive function in healthy older adults.^{51,52} Examination of a relationship between cognition and lutein levels in brain tissue of decedents from a population-based study of adults found that, among the carotenoids, only lutein was consistently associated with a wide range of cognitive measures that included executive function, language, learning, and memory, which are all associated with specific brain regions.⁵ The association of lutein with more than one cognitive function, the higher lutein concentrations in all areas of the brain evaluated, and the fact that these associations remained statistically significant after controlling for potential confounding factors all support a role for lutein in age-related cognitive health.

Although the evidence for a role of lutein in cognitive function is accumulating, the studies discussed thus far are correlative and do not demonstrate cause and effect. However, in a double-blinded, placebo-controlled trial of women who received lutein supplementation (12 mg/d), docosahexaenoic acid supplementation (800 mg/d), or a combination of the two for 4 months, verbal fluency scores improved significantly in all 3 treatment groups. Memory scores and rates of learning improved significantly in the combined treatment group, who also displayed a trend toward more efficient learning.⁵³ Taken together, these observations suggest that lutein could influence cognitive function.

LUTEIN'S MECHANISM OF ACTION IN EYE AND BRAIN TISSUE

Lutein protects the neural tissue during particularly vulnerable periods (such as in infancy, when the retina and brain are changing dramatically after birth) and conditions (such as aging). However, examination of the mechanistic effect of lutein on aspects of neural function is sparse. Neural lutein is likely protective in nature and may also influence interneuronal communication and function through multiple mechanisms. The eye and brain are especially vulnerable to free radical attacks because of their high polyunsaturated fatty acid concentrations and their high metabolic activity.⁵⁹ Although the molecular basis of these neuroprotective effects of lutein remains unknown, several mechanisms have been proposed, such as decreased oxidative stress and activation of anti-inflammatory pathways.

Antioxidant and anti-inflammatory functions

Lutein can inhibit the formation of damaging free radicals by physical or chemical quenching singlet oxygen. Indeed, increased measures of oxidative stress and inflammation are found early in age-related macular degeneration, Alzheimer's disease, and mild cognitive impairment.^{60–63} Furthermore, in a double-blind, placebo-controlled trial of lutein supplementation conducted in healthy nonsmokers randomly assigned to receive 10 or 20 mg/d lutein or placebo for 12 weeks, plasma lutein and antioxidant capacity significantly increased in both treatment groups. Oxidative stress was significantly reduced in the 20-mg lutein group. C-reactive protein (CRP) concentration decreased with lutein supplementation. Serum CRP was directly related to the changes in plasma lutein and antioxidant capacity for both active treatment groups.⁶⁴

Neuroinflammation is also one of the factors that contribute to the pathogenesis of age-related macular degeneration,⁶¹ mild cognitive impairment, and Alzheimer's disease, as increased levels of inflammatory markers are correlated with cognitive impairment.^{60,62,63} The ability of lutein to induce changes in expression of inflammation-related genes has been demonstrated in retinal pigment epithelium.⁶⁵ In addition, studies examining retinal neural damage caused by inflammation using a mouse endotoxin-induced uveitis model reported that downstream inflammatory signals and reactive oxygen species, which are upregulated in this model, were reduced with lutein treatment.⁶⁶ The effect of lutein on Müller cells, which play a role in retinal inflammation, was examined in a murine model of ischemia/reperfusion injury.⁶⁷ Lutein treatment increased cell viability and decreased nuclear factor- κ B, interleukin-1, and cyclooxygenase 2. The decreased production of

proinflammatory factors from Müller cells suggests an anti-inflammatory role of lutein in retinal injury.

Evidence of lutein's anti-inflammatory function in early life comes from a randomized controlled multicenter trial that compared plasma carotenoid levels in preterm infants ($n = 203$, gestational age <33 weeks) fed diets with and without added lutein, lycopene, and β -carotene with levels in human-milk-fed term infants.⁶⁸ Plasma carotenoid levels were significantly higher in the supplemented group at all time points and were similar to those in term human-milk-fed infants. Supplemented infants had significantly lower plasma CRP levels. Plasma lutein levels significantly correlated with the full-field electroretinogram-saturated response amplitude in rod photoreceptors. The supplemented group also showed greater rod photoreceptor sensitivity. These results suggest that lutein has a protective effect on preterm retinal health and maturation through an anti-inflammatory role, demonstrating that lutein may improve neuroretinal health in neonates, especially in preterm infants who are at risk for retinopathy and vision loss. This suggests that interventions using a dietary antioxidant and anti-inflammatory agent, such as lutein, may delay the extent of oxidative damage to neural tissues and, therefore, may have an enormous impact on early neural development as well as the delay of age-related cognitive decline.

Other functions

A neuroprotective effect of lutein may not be limited to its antioxidative or anti-inflammatory functions. Nor would a protective effect be limited to certain cognitive domains, given that its status is associated with a range of cognitive functions and that lutein concentrations do not vary widely between brain regions.^{5,6} Lutein has also been suggested to modulate functional properties of synaptic membranes along with certain changes in the physiochemical and structural features of these membranes.⁶⁹ Lutein has also been shown to enhance gap junctional communication,⁷⁰ which, in the retina, is important for light processing and may be important for the development of neural circuitry in the visual system.

DIETARY SOURCES OF LUTEIN

Lutein is commonly found in green, leafy vegetables and brightly colored fruits. Additionally, egg yolk is a highly bioavailable source of lutein and zeaxanthin.⁷¹ In general, lutein and zeaxanthin are found in many of the same foods, and most dietary databases include them together. Because there has been discussion on their individual roles in eye health, Perry et al.⁷² have analyzed lutein and zeaxanthin separately in food. Table 1 shows examples

Table 1 Lutein/zeaxanthin content of foods.^{a,b}

Food	Serving	Milligrams
Avocado	1/2 fruit	0.3
Broccoli, cooked	1/2 cup (78 g)	1.7
Brussels sprouts, cooked	1/2 cup (78 g)	1.0
Corn, sweet, cooked	1/2 cup (75 g)	1.4
Egg, hard-boiled	1 large	0.2
Kale, cooked	1/2 cup (65 g)	10.3
Lettuce, raw, romaine	1/2 cup (38 g)	1.1
Peas, green, cooked	1/2 cup (80 g)	1.1
Spinach, cooked	1/2 cup (95)	6.7
Spinach, raw	1/2 cup (38 g)	4.5

^a Edible portion.^b Data from previous reports.^{73,74}

of lutein/zeaxanthin-rich foods, along with suggested serving sizes.^{73,74}

Evidence from human studies suggests that dietary intake of lutein can lead to the accumulation of lutein in retinal neural tissue and may, therefore, promote eye and brain health. In a recent prospective study, 11 subjects modified their usual daily diets by adding 60 g of spinach (containing 11 mg of lutein and 0.3 mg of zeaxanthin) per day for 15 weeks.⁷⁵ Eight subjects had increases in serum lutein and macular pigment density, 2 subjects showed substantial increases in serum lutein but not macular pigment, and 1 subject showed no changes in serum lutein or macular pigment density. Although the results were varied, augmentation of macular pigment through dietary modification appears to be possible for many people. Finding similar results, Landrum et al.⁷⁶ found that supplementation with lutein (30 mg/d for 140 days) resulted in increased serum levels of lutein as well as corresponding increases in the concentration of lutein in the macula in the human eye.

DIETARY INTAKES OF LUTEIN

Given that the major dietary sources of lutein are fruits and vegetables,⁷² low intakes of these foods reflect low dietary intakes of lutein. Low dietary intake of lutein is related to low macular pigment density.⁷⁷ Macular pigment density and brain concentrations of lutein are highly variable in the infant and adult.^{5,6,51,78} One probable cause for this is variability in intakes of dietary lutein. Breast milk typically contains higher concentrations of lutein than other carotenoids and higher levels of lutein than formula.^{22,79} Moreover, the bioavailability of lutein is higher in breast milk than in infant formula.⁷⁹ It has been reported that breast-milk-fed infants and formula-fed infants had the same levels of plasma lutein at birth, but after 1 month, plasma concentrations increased significantly in the breast-milk-fed infants and decreased in the formula-fed infants.⁷⁹ This suggests that macular pigment

and brain levels of lutein are low in infants fed formula that does not contain lutein. Possible implications of low lutein status early in life include an influence on early neural development, an effect on maturation of retinal pigment epithelium, and an increased exposure of the neural tissue to damage from oxidative stress.

Lutein intake in adults also varies, with average intakes being 1–2 mg/day.⁸⁰ Intakes of lutein and zeaxanthin in the United States are generally lower than intakes of the other major dietary carotenoids, β -carotene and lycopene, although levels of 3 mg/d can be easily achieved with a diet high in fruits and vegetables.⁸¹ Lutein and zeaxanthin are generally found together in many of the same foods, although the lutein content is roughly 5–7 times greater than that of zeaxanthin.⁷² In fact, this was the basis for the selection of the lutein and zeaxanthin doses (10 mg and 2 mg, respectively) in the AREDS2 trial (see above). Although lutein is considered one of major carotenoids in the US diet, few Americans consume foods rich in this carotenoid. Fewer than 1 in 10 Americans meet their calorie-specific MyPyramid fruit or vegetable recommendations.⁸² Dark green vegetables accounted for only a small portion of vegetable intake, and few people met the recommendations.

While there is no recommended dietary intake for lutein, intakes of approximately 6 mg/d have been associated with a decreased risk of age-related macular degeneration.³⁰ The current intakes of lutein among adults fall well below this level, with average intakes of <2 mg/d for both men and women. Only men in the 99th percentile of lutein/zeaxanthin intake and women in the 95th percentile meet the dietary intakes that have been related to decreased risk of age-related macular degeneration.⁸⁰ Therefore, there is a dietary gap between the intakes believed to be of benefit and the intakes being consumed. Increasing dietary lutein intake through healthy food choices could be an important public health strategy for reducing the risk of visual or cognitive impairment.

CONCLUSION

Lutein may be uniquely important for visual and cognitive health at all stages of life. Certainly, the most cost-effective approach to neural health is through prevention. Thus, adequate intakes of lutein-rich foods may be important throughout the lifespan. The current evidence supports a role for lutein in neural health (visual and cognitive function) in the adult. There is less information available for a role in earlier life. However, the preferential uptake of lutein into breast milk and pediatric eye and brain tissues lends support for its role in early life. While it is not known whether lutein's role in neural health is specific to the adult, the proposed mechanisms by which lutein may exert its effect (antioxidant,

anti-inflammatory, structural) would apply to the infant as well. In fact, in a randomized, double-blind, placebo-controlled study of healthy term newborns, supplemental lutein was found to significantly increase serum measures of antioxidant activity.⁸³ This is particularly important in the early neonatal period, when oxidative stress plays a crucial role in pathological conditions. The retina and brain are especially in need of antioxidants because of their high metabolic rates, and the human newborn brain has a relative deficiency of endogenous antioxidant enzymes.⁸⁴ In addition, neuronal membranes are rich in polyunsaturated fatty acids, which are highly oxidizable. Thus, the pairing of an antioxidant in a highly oxidizable environment would be of benefit.

Lutein is the predominant carotenoid in pediatric and adult brain tissue. In infant brains, the relative contribution of lutein to the total carotenoids is twice that found in adults, accounting for more than half of the concentration of total carotenoids. Therefore, the greater proportion of lutein in the pediatric brain suggests a need for lutein during neural development. Infant formula is not routinely supplemented with lutein, whereas breast milk is a highly bioavailable source of lutein.⁷⁹ Given the meta-analysis of 11 studies that showed breastfeeding to be associated with significantly higher scores for cognitive development than formula feeding, further investigation of the impact of lutein intake on neural development is warranted. Further support is provided by the results of a prospective, randomized, controlled, double-blind study of healthy term infants fed either lutein-free control formula or experimental formula containing 200 µg/L lutein for 16 weeks.⁸⁵ Both study formulas were well tolerated, and no differences between treatment groups were found in any of the measures of growth. Based on the evidence to date, infants who are deprived of lutein could be at risk of impaired or suboptimal neural development. Given that the first year of life is a time of rapid neural growth and development that can be significantly affected by nutrition, optimal lutein status during this time could be an important strategy for achieving optimal long-term health outcomes.

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