Lutein’s Influence on Neural Processing Speed
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The macular carotenoids lutein and zeaxanthin influence many aspects of central nervous system function. These effects extend from optical filtering within the eye to physiological activity of neurons within the brain. Postreceptortorally, they have been linked to faster visual processing speeds as assessed by numerous tasks. Macular pigment optical density (MPOD), for instance, is significantly \( P<0.05 \) related to fixed and variable reaction time, coincidence anticipation errors (estimating the arrival of a stimulus at a target location moving at varying velocity), and balance ability. Reduced processing speed is a central feature of cognitive decline, and current data suggest that higher MPOD (likely a biomarker for more central levels of lutein and zeaxanthin) is related to preservation of cognitive function. Taken together, the multiple effects of lutein on nervous system function manifest throughout life and address vulnerabilities that also appear to change with age, eg, increased actinic stress to the retina in infants and the elderly.

Overview
A growing body of evidence suggests that lutein and the zeaxanthins can enhance neural processing speed. This is particularly important for the elderly since slowing appears to be a central feature of cognitive decline and impairment. This summary focuses on the mechanisms by which lutein could produce such effects.

Sensory Decline Is the Gateway to Cognitive Decline
Numerous executive functions, especially those based on processing speed, decline with age. Salthouse et al originally argued that this decline is due to inefficient utilization of cognitive resources at the earliest stage of input, ie, sensory processing. For example, older people with hearing loss have a rate of cognitive decline that is up to 40% faster than the rate in those with normal hearing. This finding can be explained by the observation that such subjects both receive less information (eg, they periodically hear fewer words) and have a higher cognitive load (meaning they focus on trying to hear such that fewer resources are available for other cognitive processes). This suggests that preventing sensory loss would help reduce cognitive decline.
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Lutein has been linked to preservation of sensory function with age⁵ and may reduce the probability of age-related visual disease such as macular degeneration. In addition to preventing sensory loss, lutein appears to be palliative. Lutein levels in the retina (termed macular pigment) have been shown to be related to chromatic contrast enhancement, glare disability and discomfort, faster photostress recovery, and increases in visual range.⁶ Preliminary unpublished data from our laboratory suggest that lutein may be related to improvements in audition and hearing measured under noise conditions in young healthy adults. Hence, lutein may be linked to reducing cognitive decline by improving sensory functions associated with vision and hearing.

Lutein May Prevent Cognitive Decline by Reducing Oxidative and Inflammatory Stress

A large confluence of data exists, derived from both laboratory and epidemiological research, showing that damage due to reactive oxygen species (ROS) and chronic inflammation promotes cognitive decline. Since neurons in the brain do not undergo mitosis, much of this damage is cumulative over time. Lutein might help prevent this process by reducing oxidative and inflammatory stress.

Carotenoids are efficient lipid-based antioxidants. They function in this capacity due to their stable electron-rich chemical structure—carbon ring compounds linked to chains that possess alternating single and double bonds. This extended conjugated double-bond system allows these compounds to form extremely stable peroxyl radicals. Consequently, carotenoids can tolerate the loss of an electron since this loss is distributed throughout the polyisoprenyl chain. The “excited” carotenoid easily can relax into its ground state by dissipating the excess energy as heat. Empirical data have shown that carotenoids do, in fact, markedly lower overall oxidative stress (Fig 1).⁷
Fig 1. The antioxidant effects of lutein.

Serum carotenoids also have been related to lower levels of markers of inflammatory stress, including the inflammatory cytokine interleukin-6. Quasim et al showed that circulating carotenoid levels are low in critically ill patients with high indices of inflammatory stress such as C-reactive protein. An inverse relationship between markers of inflammatory stress and serum carotenoid levels—namely, α-carotene and β-carotene, zeaxanthin/lutein, and β-cryptoxanthin—also was shown in the Coronary Artery Risk Development in Young Adults (CARDIA) study. This is a large prospective (0-7 years) multicenter epidemiological study of young black and white men and women (N=4580).

Both oxidative and inflammatory stress tend to increase with age and neurodegenerative disease, creating a cascade that increases the need for antioxidant/anti-inflammatory protection. Lutein, a major food component that enters neural tissues, appears to be optimal for addressing this increased need of the elder brain.
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Lutein May Directly Influence Neural Activity

The idea that lutein may directly improve neural function within the brain was formally stated as the Neural Efficiency Hypothesis. The hypothesis is based on several observations: 1) lutein and zeaxanthin are found throughout the visual pathway (e.g., brain areas such as occipital and frontal lobes) in amounts that vary significantly across subjects; 2) ex vivo data show that lutein and zeaxanthin directly influence cell-to-cell communication (e.g., enhancing gap junction communication, as has been shown in somatic cells); and 3) empirical results indicate that macular pigment is related to temporal processing speeds, a visual measure known to be largely determined postreceptorially and cognitive function.

Fig 2. Diffusion tensor imaging. Reduced processing speed is a central feature of cognitive decline.

How might lutein improve neural efficiency? One possibility is based on improving collective processing. One reason that processing speed is slowed in older adults is that more neural areas (e.g., more cortical volume) must be recruited to achieve the same result—an increasing lack of functional differentiation. Distributing processing in this manner takes more time and hence slows processing speeds. Less neural real estate is necessary to solve a given problem in younger brains, probably because of the higher density of cells in any given neural region. If carotenoids induce neurons to connect laterally, as they presumably do through effects on connexin and gap junctions, they may facilitate the recruitment of adjoining areas during a processing task.

Another possibility is based on the preservation of white matter within the brain. One hypothesis explaining cognitive decline and loss of executive skills with age is
the selective age-related loss of fiber tracts within white matter causing, essentially, a cortical disconnection.20 These white-matter tracts form the essential pathways for much of the higher order reasoning that is facilitated by the neocortex. White matter (and myelin) has a much higher lipid content than gray matter,19 and carotenoids in the brain associate more highly with white matter.13 It is possible that lutein and zeaxanthin promote the preservation of white matter and the stabilization of informational tracts. This interpretation is consistent with the fact that lutein and zeaxanthin are known to stabilize membranes (the xanthophylls are sometimes described as transmembrane rivets spanning lipid bilayers) and bind to microtubules21 in the cytoskeleton.

Lutein likely serves multiple functions within the central nervous system. In biology, a single molecular component often serves multiple purposes—eg, the actions of dopamine within the basal ganglia (motor) and limbic (emotional) system. These many functions seem optimally suited to the preservation and perhaps even enhancement of cognitive performance.

References


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