

**Brain**  
**Plasma/Serum Lycopene and Disease Risk**

Disease type	First Author	Study Title and Complete Citation	Date	Abstract	Study Type	G.Tom +, N, -	P.Tom +, N, -	F.Tom +, N, -	Lyco +, N, -	Other +, N, -
Brain	Foy CJ	Plasma chain-breaking antioxidants in Alzheimer's disease, vascular dementia and Parkinson's disease.  Foy CJ, Passmore AP, Vahidassr MD, Young IS, Lawson JT.  QJM. 1999 Jan;92(1):39-45	1999	We studied the plasma chain-breaking antioxidants alpha carotene, beta carotene, lycopene, Vitamin A, Vitamin C, Vitamin E and a measure of total antioxidant capacity, TAC, in 79 patients with Alzheimer's disease (AD), 37 patients with vascular dementia (VaD), 18 patients with Parkinson's disease and dementia (PDem), and 58 matching controls, together with 41 patients with Parkinson's disease (PD) and 41 matching controls. Significant reductions in individual antioxidants were observed in all dementia groups. When compared to controls, the following were reduced: Vitamin A in AD (p < 0.01) and VaD (p < 0.001); Vitamin C in AD (p < 0.001), VaD (p < 0.001) and PDem (p < 0.01); Vitamin E in AD (p < 0.01) and VaD (p < 0.001); beta carotene in VaD (p = 0.01); lycopene in PDem (p < 0.001). Lycopene was also reduced in PDem compared to AD (p < 0.001) and VaD (p < 0.001). Antioxidant levels in PD were not depleted. No significant change in TAC was seen in any group. The reduction in plasma chain-breaking antioxidants in patients with dementia may reflect an increased free-radical activity, and a common role in cognitive impairment in these conditions. Increased free-radical activity in VaD and PDem could be associated with concomitant AD pathology. Individual antioxidant changes are not reflected in TAC.	CC				(-)	(-) [lyco] significantly lower in PDem vs controls, AD and VaD.
Brain	Mecocci P	Lymphocyte oxidative DNA damage and plasma antioxidants in Alzheimer disease.  Mecocci P, Polidori MC, Cherubini A, Ingegneri T, Mattioli P, Catani M, Rinaldi P,	2002	CONTEXT: A large body of experimental evidence suggests that in Alzheimer disease (AD) pathogenesis an important role is played by oxidative stress, but there is still a lack of data on in vivo markers of free radical-induced damage.  OBJECTIVES: To evaluate levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG), a marker of oxidative damage to DNA, in peripheral lymphocytes; to measure plasma concentrations of several	CC				(-)	plasma lyco ↑ in control vs AD  found ↑ 8-OHdG is

		<p>Cecchetti R, Stahl W, Senin U, Beal MF.</p> <p>Arch Neurol. 2002 May;59(5):794-8.</p>		<p>nonenzymatic antioxidants; and to assess the relationships between any observed changes in lymphocyte DNA 8-OHdG content and plasma antioxidant levels in patients with AD and healthy aged control subjects. SUBJECTS: Forty elderly outpatients with AD and 39 healthy age- and sex-matched controls were studied.</p> <p>MAIN OUTCOME MEASURES: The level of 8-OHdG was determined in DNA extracted from lymphocytes and plasma levels of vitamin C, vitamin A, vitamin E, and carotenoids (zeaxanthin, beta-cryptoxanthin, lycopene, lutein, and alpha- and beta-carotene) were measured by high-performance liquid chromatography.</p> <p>RESULTS: Lymphocyte DNA 8-OHdG content was significantly higher and plasma levels of antioxidants (with the exception of lutein) were significantly lower in patients with AD compared with controls. In patients with AD, a significant inverse relationship between lymphocyte DNA 8-OHdG content and plasma levels of lycopene, lutein, alpha-carotene, and beta-carotene, respectively, was observed.</p> <p>CONCLUSIONS: Markers of oxidative damage are increased in AD and correlate with decreased levels of plasma antioxidants. These findings suggest that lymphocyte DNA 8-OHdG content in patients with AD reflects a condition of increased oxidative stress related to a poor antioxidant status.</p>						<p>significantly correlated with a ↓ plasma carotenoids in patients with AD</p>
Brain	Polidori MC	<p>Plasma susceptibility to free radical-induced antioxidant consumption and lipid peroxidation is increased in very old subjects with Alzheimer disease.</p> <p>Polidori MC, Mecocci P.</p> <p>J Alzheimers Dis.</p>	2002	<p>Oxidative stress is believed to play a major role in the pathogenesis of Alzheimer disease (AD). Plasma concentrations of vitamins C, A and E, of uric acid, thiols and carotenoids were lower and of malondialdehyde (MDA) higher in 35 AD patients (85.9 +/- 5.5 y) compared to 40 controls 85.5 +/- 4.4 y). Differences were significant for vitamin C, vitamin E, lutein, lycopene, alpha-carotene and MDA (p &lt; 0.001). Plasma exposed to peroxy radicals showed a rate of antioxidant consumption and of MDA production higher in AD patients than in controls. AD in advanced age is accompanied by a poor plasma antioxidant status and increased</p>	CC					(-)

		2002 Dec;4(6):517-22.		plasma lipid peroxidation, as well as by a low resistance to peroxy radical exposure.						
Brain	Polidori MC	<p>Plasma antioxidant status, immunoglobulin G oxidation and lipid peroxidation in demented patients: relevance to Alzheimer disease and vascular dementia.</p> <p>Polidori MC, Mattioli P, Aldred S, Cecchetti R, Stahl W, Griffiths H, Senin U, Sies H, Mecocci P.</p> <p>Dement Geriatr Cogn Disord. 2004;18(3-4):265-70. Epub 2004 Jul 29.</p>	2004	<p>A large body of evidence supports a role of oxidative stress in Alzheimer disease (AD) and in cerebrovascular disease. A vascular component might be critical in the pathophysiology of AD, but there is a substantial lack of data regarding the simultaneous behavior of peripheral antioxidants and biomarkers of oxidative stress in AD and vascular dementia (VaD). Sixty-three AD patients, 23 VaD patients and 55 controls were included in the study. We measured plasma levels of water-soluble (vitamin C and uric acid) and lipophilic (vitamin E, vitamin A, carotenoids including lutein, zeaxanthin, beta-cryptoxanthin, lycopene, alpha- and beta-carotene) antioxidant micronutrients as well as levels of biomarkers of lipid peroxidation [malondialdehyde (MDA)] and of protein oxidation [immunoglobulin G (IgG) levels of protein carbonyls and dityrosine] in patients and controls. With the exception of beta-carotene, all antioxidants were lower in demented patients as compared to controls. Furthermore, AD patients showed a significantly higher IgG dityrosine content as compared to controls. AD and VaD patients showed similar plasma levels of plasma antioxidants and MDA as well as a similar IgG content of protein carbonyls and dityrosine. We conclude that, independent of its nature-vascular or degenerative-dementia is associated with the depletion of a large spectrum of antioxidant micronutrients and with increased protein oxidative modification. This might be relevant to the pathophysiology of dementing disorders, particularly in light of the recently suggested importance of the vascular component in AD development.</p>	CC				(-)	<p>~ [Lyc] in AD, VaD vs Ctrl</p> <p>Prot Ox prod</p>
Brain	Rinaldi P	<p>Plasma antioxidants are similarly depleted in mild cognitive impairment and in Alzheimer's disease.</p> <p>Rinaldi P, Polidori MC, Metastasio A, Mariani E, Mattioli P,</p>	2003	<p>In order to assess peripheral levels and activities of a broad spectrum of non-enzymatic and enzymatic antioxidants in elderly subjects with mild cognitive impairment (MCI) and Alzheimer's disease (AD), plasma levels of water-soluble (Vitamin C and uric acid) and of lipophilic (Vitamin A, Vitamin E and carotenoids including lutein, zeaxanthin, beta-cryptoxanthin, lycopene, alpha- and beta-carotene) antioxidant micronutrients as well as activities of plasma and red blood cell (RBC)</p>	CC				(-)	<p>~ [Lyc] in MCI vs AD vs Ctrl</p>

		<p>Cherubini A, Catani M, Cecchetti R, Senin U, Mecocci P.</p> <p>Neurobiol Aging. 2003 Nov;24(7):915-9.</p>		<p>superoxide dismutase (SOD) and of plasma glutathione peroxidase (GPx) were measured in 25 patients with MCI, 63 AD patients and 53 controls. Peripheral levels and activities of antioxidants were similarly lower in MCI and AD patients as compared to controls. As MCI may represent a prodromal stage of AD, and oxidative damage appears to occur as one of the earliest pathophysiological events in AD, an increased intake of antioxidants in patients with MCI could be helpful in lowering the risk of conversion to dementia.</p>						
Brain	Schmidt R	<p>Plasma antioxidants and cognitive performance in middle-aged and older adults: results of the Austrian Stroke Prevention Study.</p> <p>Schmidt R, Hayn M, Reinhart B, Roob G, Schmidt H, Schumacher M, Watzinger N, Launer LJ.</p> <p>J Am Geriatr Soc. 1998 Nov;46(11):1407-10.</p>	1998	<p>OBJECTIVES: To study the association between cognitive status and plasma concentrations of various antioxidants in middle-aged and older individuals without neuropsychiatric disease. DESIGN: Evaluation of cross-sectional data from a cohort study.</p> <p>SETTING: The Austrian Stroke Prevention Study. PARTICIPANTS: A total of 1769 subjects aged 50 to 75 years, with no history or signs of neuropsychiatric disease, selected randomly from the community register.</p> <p>MEASUREMENTS: The score on the Mattis Dementia Rating Scale (MDRS) was dichotomized according to age-and education-specific lowest quartile cut-off points. Reversed-phase high performance liquid chromatography measurements of the plasma concentrations of lutein/zeaxanthin, cryptoxanthin, canthaxanthin, lycopene, alpha-carotene, beta-carotene, retinol, gamma-tocopherol, alpha-tocopherol, and ascorbate were measured.</p> <p>RESULTS: Individuals with MDRS results below the lowest quartile cut-off point had lower levels of beta-carotene and alpha-tocopherol than their counterparts with test performance above this limit (0.44+/-0.33 micromol/L vs 0.51+/-0.48 micromol/L, P &lt; .001; and 29.50+/-7.98 micromol/L vs 30.93+/-11.10 micromol/L, P &lt; .001, respectively). Only alphatocopherol remained significantly associated with cognitive functioning when logistic regression analysis was used to adjust for possible confounders including age, sex, month of blood sampling, years</p>	CS				N	

				of education, smoking, lipid status, and major risk factors for stroke (P = .019). CONCLUSION: These observations are compatible with the view that some dietary antioxidants may protect against cognitive impairment in older people.						
Brain	Akbaraly NT	Plasma carotenoid levels and cognitive performance in an elderly population: results of the EVA Study. Akbaraly NT, Faure H, Gourlet V, Favier A, Berr C.  J Gerontol A Biol Sci Med Sci. 2007 Mar;62(3):308-16.	2007	BACKGROUND: The hypothesis of carotenoids having a preventive role in cognitive impairment is suggested by their antioxidant properties.  METHODS: We examined, in a cross-sectional analysis, the relationship between cognitive performance (assessed by the Mini-Mental State Examination, Trail Making Test Part B, Digit Symbol Substitution, Finger Tapping Test, and Word Fluency Test) and different plasma carotenoids (lutein, zeaxanthin, beta-cryptoxanthin, lycopene, alpha-carotene, and trans-beta-carotene and cis-beta-carotene) in a healthy elderly population (the EVA, "Etude du Vieillissement Artériel," study; n = 589, age = 73.5 +/- 3 years).  RESULTS: Logistic regression showed that participants with the lowest cognitive functioning (<25th percentile) had a higher probability of having low levels of specific plasma carotenoids (<1st quartile): lycopene and zeaxanthin. For zeaxanthin, odds ratios (ORs) were as follows: OR(DSS) = 1.97 (95% confidence interval [CI] = 1.21-3.20), OR(FTT) = 1.70 (CI = 1.05-2.74), and OR(WFT) = 1.82 (CI = 1.08-3.07); for lycopene, OR(DSS) = 1.93 (CI = 1.20-3.12) and OR(TMTB) = 1.64 (CI = 1.04-2.59).  CONCLUSION: Even if it is not possible to affirm if these low levels of carotenoids precede or are the consequence of cognitive impairment, our results suggest that low carotenoid levels could play a role in cognitive impairment. The biological significance of our findings needs further research	CS				(-)  Cognitive impairment	
Brain	Polidori MC	High fruit and vegetable intake is positively correlated with antioxidant status and cognitive performance in	2009	A higher daily intake of fruits and vegetables in healthy elderly is associated with an improved antioxidant status in comparison to subjects consuming diets poor in fruits and vegetables, but the impact on cognitive performance is unclear. Healthy community dwellers (45 to 102 years old,	CS				(-)  Cognitive endpoints and Ox stress	

		<p>healthy subjects.</p> <p>Polidori MC, Praticó D, Mangialasche F, Mariani E, Aust O, Anlasik T, Mang N, Pientka L, Stahl W, Sies H, Mecocci P, Nelles G.</p> <p>J Alzheimers Dis. 2009;17(4):921-7.</p>		<p>n=193) underwent cognitive testing and blood withdrawal for the measurement of antioxidant micronutrients and biomarkers of oxidative stress as well as administration of a food frequency questionnaire to assess the daily intake of fruits and vegetables (high intake HI, low intake LI). Ninety-four subjects of the HI group had significantly higher cognitive test scores, higher levels of carotenoids, alpha- and gamma-tocopherol as well as lower levels of F2 alpha isoprostanes than the 99 subjects of the LI group. Cognitive scores were directly correlated with blood levels of alpha-tocopherol and lycopene and negatively correlated with F2 alpha isoprostanes and protein carbonyls. The results were independent of age, gender, body mass index, education, total cholesterol, LDL- and HDL-cholesterol, triglycerides, and albumin. Healthy subjects of any age with a high daily intake of fruits and vegetables have higher antioxidant levels, lower levels of biomarkers of oxidative stress, and better cognitive performance than healthy subjects of any age consuming low amounts of fruits and vegetables. Modification of nutritional habits aimed at increasing intake of fruits and vegetables should be encouraged to lower prevalence of cognitive impairment in later life.</p>						
Brain	Rao AV	<p>Role of oxidative stress and antioxidants in neurodegenerative diseases.</p> <p>Rao AV, Balachandran B.</p> <p>Nutr Neurosci. 2002 Oct;5(5):291-309.</p>	2002	<p>Neurodegenerative diseases (NDD) are a group of illness with diverse clinical importance and etiologies. NDD include motor neuron disease such as amyotrophic lateral sclerosis (ALS), cerebellar disorders, Parkinson's disease (PD), Huntington's disease (HD), cortical destructive Alzheimer's disease (AD) and Schizophrenia. Numerous epidemiological and experimental studies provide many risk factors such as advanced age, genetic defects, abnormalities of antioxidant enzymes, excitotoxicity, cytoskeletal abnormalities, autoimmunity, mineral deficiencies, oxidative stress, metabolic toxicity, hypertension and other vascular disorders. Growing body of evidence implicates free radical toxicity, radical induced mutations and oxidative enzyme impairment and mitochondrial dysfunction due to congenital genetic defects in clinical manifestations of NDD. Accumulation of oxidative damage in neurons either primarily or secondarily may account for the increased incidence of NDD such as AD, ALS and stroke in</p>	Review					

				<p>aged populations. The molecular mechanisms of neuronal degeneration remain largely unknown and effective therapies are not currently available. Recent interest has focused on antioxidants such as carotenoids and in particular lycopene, a potent antioxidant in tomatoes and tomato products, flavonoids and vitamins as potentially useful agents in the management of human NDD. The pathobiology of neurodegenerative disorders with emphasis on genetic origin and its correlation with oxidative stress of neurodegenerative disorders will be reviewed and the reasons as to why brain constitutes a vulnerable site of oxidative damage will be discussed. The article will also discuss the potential free radical scavenger, mechanism of antioxidant action of lycopene and the need for the use of antioxidants in the prevention of NDD.</p>						
Brain	Harrington M.	<p>Edible tools to fight Alzheimer's.</p> <p>Harrington M.</p> <p>Lab Anim (NY). 2008 Aug;37(8):340.</p>	2008	<p>NO ABSTRACT (excerpts from paper) Two separate groups of researchers are now pursuing edible options for the treatment or prevention of Alzheimer's disease. One study carried out by HyunSoon Kim (Korea Research Institute of Bioscience and Biotechnology) and colleagues showed that tomatoes may serve as effective carriers for an oral vaccine against <math>\beta</math>-amyloid in mice. Accumulation of <math>\beta</math>-amyloid protein in the brain leads to neuronal death, which is thought to underlie the neurodegeneration characteristic of Alzheimer's disease. The other group, led by Richard Wurtman at Massachusetts Institute of Technology (Cambridge, MA), found that dietary supplements of docosahexaenoic acid (DHA), uridine and choline improved learning and memory in gerbils. Kim's group used bacteria-mediated transformation to generate tomato plants that expressed human <math>\beta</math>-amyloid protein. They then made a soluble extract and administered it orally to mice once a week for 3 weeks, with a booster 7 weeks after the initial administration. The mice had a strong immune response to the booster and produced antibodies to the foreign human <math>\beta</math>-amyloid protein</p>	Review					