

Underlying Causes and Natural Treatments for Alzheimer's and Dementia

By Michael Edson, MS, LAc

Complete References

1. Alzheimer's Association. 2019 Alzheimer's disease facts and figures. Retrieved August 21, 2019 from <https://www.alz.org/media/Documents/alzheimers-facts-and-figures-2019-r.pdf>
2. Ibid. Alzheimer's Association. (2019).
3. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. (2006). Risk of dementia in diabetes mellitus: a system review. *Lancet Neurol.* Jan;5(1):64-74.
4. Chen JJ, Rosas HD, Salat DH. (2011). Age-associated reductions in cerebral blood flow are independent from regional atrophy. *Neuroimage.* Mar 15;55(2):468-78.
5. Hong CH, Falvey C, Harris TB, Simonsick EM, Satterfield S, et al. (2013). Anemia and risk of dementia in older adults: findings from the Health ABC study. *Neurology.* Aug 6;81(6): 528-33.¹¹; Wang D, Jacobs SA, Tsien JZ. (2014). Targeting the NMDA receptor subunit NR2B for treating or preventing age-related memory decline. *Expert Opin Ther Targets.* 2014;18(10):1121-30.
6. Erickson KI, Voss MW, Prakash RS, Basak C, Szabo A, Chaddock L, et al. (2011). Exercise training increases size of hippocampus and improves memory. *AF Proc Natl Acad Sci U S A.* Feb 15; 108(7):3017-22.
7. Queensland Brain Institute. What is synaptic plasticity? Retrieved Jul 17 2019 from <https://qbi.uq.edu.au/brain-basics/brain/brain-physiology/what-synaptic-plasticity>
8. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. (2013). The hallmarks of aging. *Cell.* Jun 6; 153(6):1194-217.
9. Rao AV, Balachandran B. (2002). Role of oxidative stress and antioxidants in neurodegenerative diseases. *Nutr Neurosci.* Oct; 5(5):291-309.
10. Dhabhar FS. (2009). Enhancing versus suppressive effects of stress on immune function: implications for immunoprotection and immunopathology. *Neuroimmunomodulation.* 16(5):300-17.



11. McEwen BS. (1999). Stress and hippocampal plasticity. *Annu Rev Neurosci.* 22():105-22.
12. Lupien SJ, Lepage M. (2001). Stress, memory, and the hippocampus: can't live with it, can't live without it. *Behav Brain Res.* Dec 14; 127(1-2):137-58.
13. Woolley CS, Gould E, McEwen BS. (1990). Exposure to excess glucocorticoids alters dendritic morphology of adult hippocampal pyramidal neurons. *Brain Res.* Oct 29; 531(1-2):225-31
14. Sapolsky RM, Uno H, Rebert CS, Finch CE. (1990). Hippocampal damage associated with prolonged glucocorticoid exposure in primates. *J Neurosci.* Sep; 10(9):2897-902.
15. Sapolsky RM, Uno H, Rebert CS, Finch CE. (1990). Hippocampal damage associated with prolonged glucocorticoid exposure in primates. *J Neurosci.* Sep; 10(9):2897-902
16. Gould E, Tanapat P, McEwen BS, Flügge G, Fuchs E. (1998). Proliferation of granule cell precursors in the dentate gyrus of adult monkeys is diminished by stress. *Proc Natl Acad Sci U S A.* Mar 17; 95(6):3168-71.
17. Van der Kooij MA, Fantin M, Rejmak E, Grosse J, Zanoletti O, et al. (2014). Role for MMP-9 in stress-induced downregulation of nectin-3 in hippocampal CA1 and associated behavioural alterations. *Nat Comm.* 2014; 5: 4995.
18. Branan N. (2007). Stress Kills Brain Cells Off. *Sci Am.* Jun-Jul.
19. Kang HJ, Voleti B, Hajszan T, Rajkowska G, Stockmeier CA, et al. (2012). Decreased expression of synapse-related genes and loss of synapses in major depressive disorder. *Nat Med.* Sep;18(9):1413-7.
20. Popoli M, Yan Z, McEwen BS, Sanacora G. (2011). The stressed synapse: the impact of stress and glucocorticoids on glutamate transmission. *Nat Rev Neurosci.* Nov 30; 13(1): 22–37.
21. McEwen BS. (1999). Stress and hippocampal plasticity. *Annu Rev Neurosci.* 22():105-22.
22. Dhabhar FS. (2009). Enhancing versus suppressive effects of stress on immune function: implications for immunoprotection and immunopathology. *Neuroimmunomodulation.* 16(5):300-17.
23. Dhabhar FS, Malarkey WB, Neri E, McEwen BS. (2012). Stress-induced redistribution of immune cells--from barracks to boulevards to battlefields: a tale of three hormones--Curt Richter Award winner. *Psychoneuroendocrinology.* Sep; 37(9):1345-68.
24. Roozendaal B, McEwen BS, Chattarji S. (2009) Stress, memory and the amygdala. *Nat Rev Neurosci.* June;10(6):423-33.

MycoPul™ Exceptionally pure, vigorous mycotoxin binder



25. Bennur S, et al. (2007) Stress-induced spine loss in the medial amygdala is mediated by tissue-plasminogen activator. *Neuroscience*. Jan 5; 144(1):8-16.
26. Lau T, et al. (2017) Stress-induced structural plasticity of medial amygdala stellate neurons and rapid prevention by a candidate antidepressant. *Mol Psychiatry*. Feb; 22(2):227-234.
27. Joëls M, Fernandez G, Roozendaal B. (2011). Stress and emotional memory: a matter of timing. *Trends Cogn Sci*. Jun; 15(6):280-8.
28. McEwen BS, Nasca C, Gray JD. (2016). Stress Effects on Neuronal Structure: Hippocampus, Amygdala, and Prefrontal Cortex. *Neuropsychopharmacology*. Jan; 41(1): 3–23.
29. Fietta P, Fietta P. (2007). Glucocorticoids and brain functions. *Riv Biol*. Sep-Dec;100(3):403-18.
30. Dhabhar FS, Malarkey WB, Neri E, McEwen BS. (2012). Stress-induced redistribution of immune cells--from barracks to boulevards to battlefields: a tale of three hormones--Curt Richter Award winner. *Psychoneuroendocrinology*. Sep; 37(9):1345-68.
31. Fietta P, Fietta P. (2007). Glucocorticoids and brain functions. *Riv Biol*. Sep-Dec;100(3):403-18.
32. De Felice FG, Lourenco MV, Ferreira ST. (2014). How does brain insulin resistance develop in Alzheimer's disease? *Alzheimers Dement*. Feb; 10(1 Suppl):S26-32.
33. Montaron MF, Drapeau E, Dupret D, Kitchener P, Aurousseau C, Le Moal M, et al. (2006 White Matter versus Gray Matter. *Neurobiol Aging*. Apr; 27(4):645-54.
34. Ibid. Bonda. (2010). *Neuropharmacology*.
35. Chauhan V, Chauhan A. (2006). Oxidative stress in Alzheimer's disease. *Pathophysiology*. Aug; 13(3):195-208.
36. Gibson GE, Huang HM. (2002). Oxidative processes in the brain and non-neuronal tissues as biomarkers of Alzheimer's disease. *Front Biosci*. Apr 1; 7():d1007-15
37. Montine TJ, Neely MD, Quinn JF, Beal MF, Markesbery WR, et al. (2002). Lipid peroxidation in aging brain and Alzheimer's disease. *Free Radic Biol Med*. Sep 1; 33(5):620-6.
38. Arlt S, Beisiegel U, Kontush A. (2002). Lipid peroxidation in neurodegeneration: new insights into Alzheimer's disease. *Curr Opin Lipidol*. Jun; 13(3):289-94.
39. Lovell MA, Gabbita SP, Markesbery WR. (1999). Increased DNA oxidation and decreased levels of repair products in Alzheimer's disease ventricular CSF. *J Neurochem*. Feb; 72(2):771-6.

40. Harris ME, Hensley K, Butterfield DA, Leedle RA, Carney JM. (1995). Direct evidence of oxidative injury produced by the Alzheimer's beta-amyloid peptide (1-40) in cultured hippocampal neurons. *Exp Neurol*. Feb; 131(2):193-202
41. Sponne I, Fifre A, Drouet B, Klein C, Koziel V, et al. (2003). Apoptotic neuronal cell death induced by the non-fibrillar amyloid-beta peptide proceeds through an early reactive oxygen species-dependent cytoskeleton perturbation. *J Biol Chem*. Jan 31; 278(5):3437-45.
42. Stampfer MJ. (2006). Cardiovascular disease and Alzheimer's disease: common links. *J Intern Med*. 2006 Sep; 260(3):211-23.
43. Akiyama H, Barger S, Barnum S, Bradt B, Bauer J, et al. (2000). Inflammation and Alzheimer's disease. *Neurobiol Aging*. May-Jun; 21(3):383-421.
44. Rogers J, Mastroeni D, Leonard B, Joyce J, Grover A. (2007). Neuroinflammation in Alzheimer's disease and Parkinson's disease: are microglia pathogenic in either disorder? *Int Rev Neurobiol*. 2007; 82():235-46.
45. Landreth GE, Reed-Geaghan EG. (2009). Toll-like receptors in Alzheimer's disease. *Curr Top Microbiol Immunol*. 2009;336():137-53.
46. Zonis S, Pechnick RN, Ljubimov VA, Mahgerefteh M, Wawrowsky K, et al. (2015). Chronic intestinal inflammation alters hippocampal neurogenesis. *J Neuroinflammation*. Apr 3;12:65.
47. Engelborghs S, De Brabander M, De Créé J, D'Hooge R, Geerts H, et al. (1999). Unchanged levels of interleukins, neopterin, interferon-gamma and tumor necrosis factor-alpha in cerebrospinal fluid of patients with dementia of the Alzheimer type. *Neurochem Int*. Jun; 34(6):523-30.
48. Yaffe K, Lindquist K, Penninx BW, Simonsick EM, Pahor M, et al. (2003). Inflammatory markers and cognition in well-functioning African-American and white elders. *Neurology*. Jul 8; 61(1):76-80.
49. Harris TB, Benjamin EJ, Au R, Kiel DP, Wolf PA, et al. (2007). Inflammatory markers and the risk of Alzheimer's disease: the Framingham Study. *Neurology*. May 29; 68(22):1902-8.
50. Zuliani G, Ranzini M, Guerra G, Rossi L, Munari MR, et al. (2007). Plasma cytokines profile in older subjects with late onset Alzheimer's disease or vascular dementia. *J Psychiatr Res*. Oct; 41(8):686-93.
51. Aisen PS, Davis KL. (1994). Inflammatory mechanisms in Alzheimer's disease: implications for therapy. *Am J Psychiatry*. Aug; 151(8):1105-13.
52. Galasko D, Montine T. (2010). Biomarkers of oxidative damage and inflammation in Alzheimer's disease. *J Biomark Med*. Feb; 4(1):27-36

53. Bonda DJ, Wang X, Perry G, Nunomura A, Tabaton M, et al. (2010). Oxidative stress in Alzheimer disease: a possibility for prevention. *Neuropharmacology*. Sep-Oct; 59(4-5):290-4.
54. Ibid. Steele. (2007). *Exp Gerontol*.
55. Alzheimer's Association. (2017). Alzheimer's Disease Facts and Figures. Retrieved Jun 29 2019 from [https://www.alzheimersanddementia.com/article/S1552-5260\(17\)30051-1/fulltext](https://www.alzheimersanddementia.com/article/S1552-5260(17)30051-1/fulltext).
56. Di Benedetto S, Muller L, Wenger E, Duzel S, Pawelec G. (2017). Contribution of neuroinflammation and immunity to brain aging and the mitigating effects of physical and cognitive interventions. *Neurosci Biobehav Rev*. Apr;75:114-128.
57. Heneka MT, Carson MJ, El Khoury J, Landreth GE, Brosseron F, et al. (2015). Neuroinflammation in Alzheimer's Disease. *Lancet Neurol*. Apr;14(4):388-405.
58. Sperling RA, Aisen PS, Beckett LA, Bennett DA, Craft S, et al. (2011). Toward defining the preclinical stages of Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. May; 7(3):280-92.
59. Wirth M, Madison CM, Rabinovici GD, Oh H, Landau SM, et al. (2013). Alzheimer's disease neurodegenerative biomarkers are associated with decreased cognitive function but not β -amyloid in cognitively normal older individuals. *J Neurosci*. Mar 27; 33(13):5553-63.
60. Najjar S, Pearlman DM, Alper K, Najjar A, Devinsky O. (2013). Neuroinflammation and psychiatric illness. *J Neuroinflammation*. Apr 1; 10():43.
61. Onore C, Careaga M, Ashwood P. (2012). The role of immune dysfunction in the pathophysiology of autism. *Brain Behav Immun*. Mar; 26(3):383-92.
62. Theoharides TC, Zhang B. (2011). Neuro-inflammation, blood-brain barrier, seizures and autism. *J Neuroinflammation*. Nov 30; 8():168.
63. Kuhn HG, Dickinson-Anson H, Gage FH. (1996). Neurogenesis in the dentate gyrus of the adult rat: age-related decrease of neuronal progenitor proliferation. *J Neurosci*. Mar 15; 16(6):2027-33.
64. Hattiangady B, Shetty AK. (2008). Aging does not alter the number or phenotype of putative stem/progenitor cells in the neurogenic region of the hippocampus. *Neurobiol Aging*. Jan; 29(1):129-47.
65. Li Y, Luikart BW, Birnbaum S, Chen J, Kwon CH, et al. (2008). TrkB regulates hippocampal neurogenesis and governs sensitivity to antidepressive treatment. *Neuron*. Aug 14; 59(3):399-412.
66. Palmer TD, Takahashi J, Gage FH. (1997). The adult rat hippocampus contains primordial neural stem cells. *Mol Cell Neurosci*. 1997; 8(6):389-404.

67. Huang EJ, Reichardt LF. (2001). Neurotrophins: roles in neuronal development and function *Annu Rev Neurosci.* 2001; 24():677-736.
68. Schwartz PM, Borghesani PR, Levy RL, Pomeroy SL, Segal RA. (1997). Abnormal cerebellar development and foliation in BDNF^{-/-} mice reveals a role for neurotrophins in CNS patterning. *Neuron.* Aug; 19(2):269-81.
69. Lindsay RM. (1988). Nerve growth factors (NGF, BDNF) enhance axonal regeneration but are not required for survival of adult sensory neurons. *J Neurosci.* Jul; 8(7):2394-405.
70. Muramatsu R, Yamashita T. (2014). Concept and molecular basis of axonal regeneration after central nervous system injury. *Neurosci Res.* 2014 Jan; 78():45-9.
71. Ichim G, Tauszig-Delamasure S, Mehlen P. (2012). Neurotrophins and cell death. *Exp Cell Res.* Jul 1; 318(11):1221-8.
72. Nagahara AH, Tuszynski MH. (2011). Potential therapeutic uses of BDNF in neurological and psychiatric disorders. *Nat Rev Drug Discov.* Mar; 10(3):209-19.
73. Heese K, Low JW, Inoue N. (2007). Nerve growth factor, neural stem cells and Alzheimer's disease. *Neurosignals.* 2006-2007; 15(1):1-12.
74. De Munter JP, Melamed E, Wolters E. (2014). Stem cell grafting in parkinsonism--why, how, and when. *Parkinsonism Relat Disord.* Jan; 20 Suppl 1():S150-3.
75. Rosser A, Svendsen CN. (2014). Stem cells for cell replacement therapy: a therapeutic strategy for HD? *Mov Disord.* Sep 15; 29(11):1446-54.
76. NIH. What Happens to the Brain in Alzheimer's Disease. Retrieved Aug 2 2019 from <https://www.nia.nih.gov/health/what-happens-brain-alzheimers-disease>.
77. Blackburn D, Sargsyan S, Monk PN, Shaw PJ. (2009). Astrocyte function and role in motor neuron disease: a future therapeutic target? *Glia.* Sep;57(12):1251-64.
78. Blackburn D, Sargsyan S, Monk PN, Shaw PJ. (2009). Astrocyte function and role in motor neuron disease: a future therapeutic target? *Glia.* 2009 Sep;57(12):1251-64.
79. Jones PA, Baylin SB. *Nat Rev Genet.* 2002 Jun; 3(6):415-28
80. Santos-Rebouças CB, Pimentel MM. *Eur J Hum Genet.* 2007 Jan; 15(1):10-7.
81. Feng J, Fan G. *Int Rev Neurobiol.* 2009; 89():67-84.
82. Lattal KM, Wood MA. (2013). Epigenetics and persistent memory: implications for reconsolidation and silent extinction beyond the zero. *Nat Neurosci.* Feb; 16(2):124-9.
83. Pembrey M, Saffery R, Bygren LO; Network in Epigenetic Epidemiology. (2014). Human transgenerational responses to early-life experience: potential impact on development, health and biomedical research. *J Med Genet.* Sep; 51(9): 563–572.

84. Waterland RA, Jirtle RL. (2004). Early nutrition, epigenetic changes at transposons and imprinted genes, and enhanced susceptibility to adult chronic diseases. *Nutrition*. Jan; 20(1):63-8.
85. Den Heijer T, Launer LJ, Prins ND, van Dijk EJ, Vermeer SE, et al. (2005). Association between blood pressure, white matter lesions, and atrophy of the medial temporal lobe. *Neurology*. Jan 25; 64(2):263-7.
86. Seshadri S, Beiser A, Selhub J, Jacques PF, Rosenberg IH, et al. (2002). Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *N Engl J Med*. Feb 14; 346(7):476-83.
87. Calderon-Garciduenas L, Azzarelli B, Acuna H, Garcia R, Gambling TM, Osnaya N, et al. (2002). Air pollution and brain damage. *Toxicol Pathol*. 2002 May-Jun;30(3):373-89.
88. Calderon-Garciduenas L, Reynoso-Robles R, Vargas-Martinez J, Gomez-Maqueo-Chew A, Perez-Guille B. (2016). Prefrontal white matter pathology in air pollution exposed Mexico City young urbanites and their potential impact on neurovascular unit dysfunction and the development of Alzheimer's disease. *Environ Res*. 2016 Apr;146:404-17.
89. Calderon-Garciduenas L, Leray F, Heydarpour P, Torres-Jardon R, Reis J. (2016). Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. *Rev Neurol (Paris)*. 2016 Jan;172(1):69-80.
90. Payton M, Riggs KM, Spiro A 3rd, Weiss ST, Hu H. (1998). Relations of bone and blood lead to cognitive function: the VA Normative Aging Study. *Neurotoxicol Teratol*. Jan-Feb; 20(1):19-27.
91. Dobbs MR. *Clinical Neurotoxicology: Syndromes, Substances, Environments*. Saunders; 2009
92. Schwartz BS, Stewart WF, Bolla KI, Simon PD, Bandeen-Roche K, et al. (2000). Past adult lead exposure is associated with longitudinal decline in cognitive function. *Neurology*. Oct 24; 55(8):1144-50.
93. Kamel F, Umbach DM, Hu H, Munsat TL, Shefner JM, et al. (2005). Lead exposure as a risk factor for amyotrophic lateral sclerosis. *Neurodegener Dis*. 2005; 2(3-4):195-201.
94. Kamel F, Umbach DM, Lehman TA, Park LP, Munsat TL, et al. (2003). Amyotrophic lateral sclerosis, lead, and genetic susceptibility: polymorphisms in the delta-aminolevulinic acid dehydratase and vitamin D receptor genes. *Environ Health Perspect*. Aug; 111(10):1335-9.
95. Weisskopf MG, Weuve J, Nie H, Saint-Hilaire MH, Sudarsky L, et al. (2010). Association of cumulative lead exposure with Parkinson's disease. *Environ Health Perspect*. Nov;118(11):1609-13.

96. Calderon-Garciduenas L, Azzarelli B, Acuna H, Garcia R, Gambling TM, Osnaya N, et al. (2002). Air pollution and brain damage. *Toxicol Pathol.* 2002 May-Jun;30(3):373-89.
97. Calderon-Garciduenas L, Reynoso-Robles R, Vargas-Martinez J, Gomez-Maqueo-Chew A, Perez-Guille B. (2016). Prefrontal white matter pathology in air pollution exposed Mexico City young urbanites and their potential impact on neurovascular unit dysfunction and the development of Alzheimer's disease. *Environ Res.* 2016 Apr;146:404-17.
98. Calderon-Garciduenas L, Leray F, Heydarpour P, Torres-Jardon R, Reis J. (2016). Air pollution, a rising environmental risk factor for cognition, neuroinflammation and neurodegeneration: The clinical impact on children and beyond. *Rev Neurol (Paris).* 2016 Jan;172(1):69-80.
99. Calderon-Garciduenas L, Reynoso-Robles R, Gonzalez-Maciell A. (2019). Combustion and friction-derived nanoparticles and industrial-sourced nanoparticles: The culprit of Alzheimer and Parkinson's diseases. *Environ Res.* 2019 Jul 5;176:108574.
100. Tata AM, Velluto L, D'Angelo C, Reale M. (2014). Cholinergic system dysfunction and neurodegenerative diseases: cause or effect? *CNS Neurol Disord Drug Targets.* 2014;13(7):1294-303.
101. Bergmann C, Sano M. (2006). Cardiac risk factors and potential treatments in Alzheimer's disease. *Neurol Res.* Sep; 28(6):595-604.
102. Andreoulakis E, Hyphantis T, Kandylis D, Iacovides A. (2012). Depression in diabetes mellitus: a comprehensive review. *Hippokratia.* Jul;16(3):205-14.
103. Huang C, Chung C, Leu H, et al. (2014). Diabetes mellitus and the risk of Alzheimer's disease: a nationwide population-based study. *PloS One.* 2014;9(1):e87095.
104. Chew BH, Sherina MS, Hassan NH. (2015). Association of diabetes-related distress, depression, medication adherence, and health-related quality of life with glycated hemoglobin, blood pressure, and lipids in adult patients with type 2 diabetes: a cross-sectional study. *Ther Clin Risk Manag.* 2015;11:669-81
105. K. Talbot. (2013). Brain insulin resistance in Alzheimer's disease and its potential treatment with a Mediterranean diet and GLP-1 analogues. *Psychiatric Times.* Aug 20:18-21.
106. Kivipelto M, Helkala EL, Laakso MP, Hänninen T, Hallikainen M, et al. (2002). Apolipoprotein E epsilon4 allele, elevated midlife total cholesterol level, and high midlife systolic blood pressure are independent risk factors for late-life Alzheimer disease. *Ann Intern Med.* Aug 6; 137(3):149-55.
107. Velaquez R, Ferreria E, Winslow W, Dave N, Piras IS, et al. (2019). Maternal choline supplementation ameliorates Alzheimer's disease pathology by reducing brain homocysteine levels across multiple generations. *Mol Psychiatry.* Jan 8.

108. K. Talbot. (2013). Brain insulin resistance in Alzheimer's disease and its potential treatment with a Mediterranean diet and GLP-1 analogues. *Psychiatric Times*. Aug 20:18-21.
109. Seshadri S, Beiser A, Selhub J, Jacques PF, Rosenberg IH, et al. (2002). Plasma homocysteine as a risk factor for dementia and Alzheimer's disease. *N Engl J Med*. Feb 14; 346(7):476-83.
110. Swerdlow RH, Burns JM, Khan SM. (2014). The Alzheimer's disease mitochondrial cascade hypothesis: progress and perspectives. *Biochim Biophys Acta*. Aug; 1842(8):1219-31.
111. Picone P, Nuzzo D, Caruana L, Scafidi V, Di Carlo M. (2014). Mitochondrial dysfunction: different routes to Alzheimer's disease therapy. *Oxid Med Cell Longev*. 2014():780179.
112. Asgari N, Berg CT, Morch MT, Khorooshi R, Owens T. (2015). Cerebrospinal fluid aquaporin-4-immunoglobulin G disrupts blood brain barrier. *Ann Clin Transl Neurol*. Aug;2(8):857-863.
113. Abbot NJ. (2000). Inflammatory mediators and modulation of blood-brain permeability. *Cell Mol Neurobiol*. 2000 Apr;20(2):131-47.
114. Sofroniew MV. (2015). Astrocyte barriers to neurotoxic inflammation. *Nat Rev Neurosci*. May;16(5):249-263
115. Visser J, Rozing J, Sapone A, Lammers K, Fasano A. (2009). Tight junctions, intestinal permeability, and autoimmunity: celiac disease and type 1 diabetes paradigms. *Ann N Y Acad Sci*. May;1165:195-205.
116. Grenham S, Clarke G, Cryan JF, Dinan TG. (2011). Brain-gut-microbe communication in health and disease. *Front Physiol*. 2011; 2():94.
117. Wade PR, Cowen T. Neurodegeneration: a key factor in the ageing gut. *Neurogastroenterol Motil*. 2004 Apr;16 Suppl 1:19-23
118. Alkadir R, Li J, Li X, Jin M, Zhu B. (2017). Human gut microbiota: the links with dementia development. *Protein Cell*. Feb;8(2):90-102.
119. Parker JC, McCloskey JJ, Lee RS. (1981). Human cerebral candidosis—a postmortem evaluation of 19 patients. *Hum Pathol*. Jan;12(1):23-8.
120. Hill JM, Clement C, Pogue AI, Bhattacharjee S, Zhao Y, et al. (2014). Pathogenic microbes, the microbiome, and Alzheimer's disease (AD). *Jn Front Aging Neurosci*. 2014 6():127.
121. Hadjivassiliou M, Williamson CA, Woodroffe N. (2004). The immunology of gluten sensitivity: beyond the gut. *Trends Immunol*. Nov; 25(11):578-82.

122. Fasano A, Catassi C. (2001). Current approaches to diagnosis and treatment of celiac disease: an evolving spectrum. *Gastroenterology*. Feb; 120(3):636-51.
123. Hadjivassiliou M, Grünewald RA, Davies-Jones GA. (2002). Gluten sensitivity as a neurological illness. *J Neurol Neurosurg Psychiatry*. May; 72(5):560-3.
124. Briani C, Zara G, Alaedini A, Grassivaro F, Ruggero S, et al. (2008). Neurological complications of celiac disease and autoimmune mechanisms: a prospective study. *J Neuroimmunol*. Mar; 195(1-2):171-5.
125. Hu WT, Murray JA, Greenaway MC, Parisi JE, Josephs KA. (2006). Cognitive Impairment and Celiac Disease. *Arch Neurol*. 2006;63(10):1440-1446.
126. Borhani Haghghi A, Ansari N, Mokhtari M, Geramizadeh B, Lankarani KB. (2007). Multiple sclerosis and gluten sensitivity. *Clin Neurol Neurosurg*. Oct;109(8):651-3.
127. Konishi T. (2004). Dementia due to celiac disease. [in Japanese]. *Nihon Rinsho*. Jan;62 Suppl:450-5.
128. Daulatzai MA. (2015). Non-celiac gluten sensitivity triggers gut dysbiosis, neuroinflammation, gut-brain axis dysfunction, and vulnerability for dementia. *CNS Neurol Disord Drug Targets*. 2015;14(1):110-31.
129. Dahele A, Ghosh S. (2001). Vitamin B12 deficiency in untreated celiac disease. *Am J Gastroenterol*. Mar;96(3):745-50.
130. Hinks LJ, Inwards KD, Lloyd B, Clayton BE. (1984). Body content of selenium in coeliac disease. *Br Med J (Clin Res Ed)*. Jun 23; 288(6434):1862-3.
131. Richardson K, Fox C, Maidment I, Steel N, Loke YK, et al. (2018). Anticholinergic drugs and risk of dementia: case-control study. *BMJ*. Apr 25;361:k1315.
132. Perry EK, Kilford L, Lees AJ, Burn DJ, Perry RH. (2003). Increased Alzheimer pathology in Parkinson's disease related to antimuscarinic drugs. *Ann Neurol*. Aug; 54(2):235-8.
133. Ray PG, Meador KJ, Loring DW, Zamrini EW, Yang XH, et al. (1992). Central anticholinergic hypersensitivity in aging. *J Geriatr Psychiatry Neurol*. Apr-Jun; 5(2):72-7.
134. Fox C, Richardson K, Maidment ID, Savva GM, Matthews FE, et al. Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study. *J Am Geriatr Soc*. Aug; 59(8):1477-83.
135. Ibid. Fox. (2011).
136. Ibid. Erickson. (2011). *AF Proc Natl Acad Sci U S A*.

137. hitman H. (2017). Sedentary behavior raises Alzheimer's risk as much as genetic factors. Retrieved Jun 20 2019 from <https://www.medicalnewstoday.com/articles/315173.php>.
138. Tari AR, Nauman J, Zisko N, Skjellegrind HK, Bosnes I, et al. (2019). Temporal changes in cardiorespiratory fitness and risk of dementia incidence and mortality: a population-based prospective cohort study. *Lancet Public Health*. Nov;4(11):e565-e574.
139. Abrous DN, Adriani W, Montaron MF, Aurousseau A, Rougon G, Le Moal M, et al. (2002). Nicotine Self-Administration Impairs Hippocampal Plasticity. *J Neurosci*. May 22 (9) 3656-3662.
140. Couey JJ, Meredith RM, Spijker S, Poorthuis RB, Smit AB, Brussaard AB, et al. (2007). Distributed network actions by nicotine increase the threshold for spike-timing-dependent plasticity in prefrontal cortex. *Neuron*. Apr 5; 54(1):73-87.
141. Guillem K, Bloem B, Poorthuis RB, Loos M, Smit AB, Maskos U, et al. (2011). Nicotinic acetylcholine receptor $\beta 2$ subunits in the medial prefrontal cortex control attention. *Science*. Aug 12; 333(6044):888-91.
142. Vaynman S, Ying Z, Gomez-Pinilla F. (2004). Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *Eur J Neurosci*. Nov; 20(10):2580-90.
143. Vaynman S, Ying Z, Gomez-Pinilla F. (2004). Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. *Eur J Neurosci*. Nov; 20(10):2580-90.
144. HM, Glass AL, Shors TJ. (2007). Neurogenesis and the spacing effect: Learning over time enhances memory and the survival of new neurons. *Learn Mem*. 14:368-375.
145. Poulouse SM, Miller MG, Scott T, Shukitt-Hale B. (2017). Nutritional Factors Affecting Adult Neurogenesis and Cognitive Function. *Adv Nutr*. Nov 15;8(6):804-811.
146. Fidaleo M, Cavallucci V, Pani G. (2017). Nutrients, neurogenesis and brain aging: From disease mechanisms to therapeutic opportunities. *Biochem Pharmacol*. Oct 1;141:63-76.
147. Molteni R, Barnard RJ, Ying Z, Roberts CK, Gómez-Pinilla F. (2002). A high-fat, refined sugar diet reduces hippocampal brain-derived neurotrophic factor, neuronal plasticity, and learning. *Neuroscience*. 2002; 112(4):803-14.
148. Bensalem J, Dudonne S, Gaudout D, Servant L, Calon F, et al. (2018). Polyphenol-rich extract from grape and blueberry attenuates cognitive decline and improves neuronal function in aged mice. *J Nutr Sci*. May 21;7:e19.
149. Shukitt-Hale B, Bielinski DF, Lau FC, Willis LM, Carey AN, et al. (2015). The beneficial effects of berries on cognition, motor behavior and neuronal function in aging. *Br J Nutr*. Nov 28;114(10):1542-9.

150. Devore EE, Kangs JH, Breteler MM, Grodstein FA. (2012). Dietary intakes of berries and flavonoids in relation to cognitive decline. *Neurology*. 72(1):135-43
151. Joseph JA, Shukitt-Hale B, Willis LM. (2009). Grape juice, berries, and walnuts affect brain aging and behavior. *J Med*. 139(9):1813S-7S.
152. Tiwari SK, Agarwal S, Seth B, Yadav A, Nair S, et al. (2014). Curcumin-loaded nanoparticles potently induce adult neurogenesis and reverse cognitive deficits in Alzheimer's disease model via canonical Wnt/B-catenin pathway. *ACS Nano*. Jan 28;8(1):76-103.
153. Ibid. Poulouse. (2017). *Adv Nutr*.
154. Shehzad A, Rehman G, Lee YS (2013). Curcumin in inflammatory diseases. *Biofactors*. Jan-Feb; 39(1):69-77.
155. Kim GY, Kim KH, Lee SH, Yoon MS, Lee HJ, et al. (2005). Curcumin inhibits immunostimulatory function of dendritic cells: MAPKs and translocation of NF-kappa B as potential targets. *J Immunol*. Jun 15; 174(12):8116-24.
156. Cheng J, Zhou ZW, Sheng HP, He LJ, Fan XW, et al. (2014). An evidence-based update on the pharmacological activities and possible molecular targets of Lycium barbarum polysaccharides. *Drug Des Devel Ther*. Dec 17;9:33-78.
157. Po KK, Leung JW, Chan JN, Fung TK, Sanchez-Vidana DI, et al. (2017). Protective effect of Lycium Barbarum polysaccharides on dextromethorphan-induced mood impairment and neurogenesis suppression. *Brain Res Bull*. Sep;134:10-17.
158. Ibid. Poulouse. (2017).
159. Calon F, Cole G. (2007). Neuroprotective action of omega-3 polyunsaturated fatty acids against neurodegenerative diseases: evidence from animal studies. *Prostaglandins Leukot Essent Fatty Acids*. Nov-Dec; 77(5-6):287-93.
160. Ibid. Calon. (2007).
161. Bousquet M, Calon F, Cicchetti F. (2011). Impact of ω -3 fatty acids in Parkinson's disease. *Ageing Res Rev*. Sep; 10(4):453-63.
162. Ibid. Wysoczanski. (2016).
163. Rathod R, Kale A, Joshi S. (2016). Novel insights into the effect of vitamin B12 and omega-3 fatty acids on brain function. *J Biomed Sci*. Jan 25;23:17.
164. Szwajgier D, Baranowska-Wojcik E, Borowiec K. (2018). Phenolic Acids Exert Anticholinesterase and Cognition-Improving Effects. *Curr Alzheimer Res*. 15(6):531-543.
165. Moore K, Hughes CF, Ward M, Hoey L, McNulty H. (2018). Diet, nutrition and the aging brain: current evidence and directions. *Proc Nutr Soc*. May;77(2):152-163.

166. Hablemariam S. (2018). Molecular Pharmacology of Rosmarinic and Salvianolic Acids: Potential Seeds for Alzheimer's and Vascular Dementia. *Int J Mol Sci.* Feb 3;19(2):E458.
167. Szwajgier D, Borowiec K, Pustelniak K. (2017). The Neuroprotective Effects of Phenolic Acids: Molecular Mechanism of Action. *Nutrients.* May 10;9(5):E477.
168. Gomes BAQ, Silva JPB, Romeiro CFR, Dos Santos SM, Rodrigues CA, et al. (2018). Neuroprotective Mechanisms of Resveratrol in Alzheimer's Disease: Role of SIRT1. *Oxid Med Cell Longev.* Oct 30;2018:8152373.
169. Rao AV, Balachandran B. (2002). Role of oxidative stress and antioxidants in neurodegenerative diseases. *Nutr Neurosci.* Oct; 5(5):291-309.
170. Greenwood CE, Winocur G. (2005). High-fat diets, insulin resistance and declining cognitive function. *Neurobiol Aging.* Dec; 26 Suppl 1():42-
171. Francis H, Stevenson R. (2013). The longer-term impacts of Western diet on human cognition and the brain. *Appetite.* Apr;63(1):119-128.
172. Kanoski SE, Davidson TL. (2011). Western diet consumption and cognitive impairment: Links to hippocampal dysfunction and obesity. *Physiol Behav.* Apr 18;103(1):59-68.
173. Landau SM, Marks SM, Mormino EC, Rabinovici GD, Oh H, et al. (2012). Association of lifetime cognitive engagement and low B-amyloid deposition. *Arch Neurol.* May;69:623-29.
174. Muller S, Preische O, Sohrabi HR, Graber S, Jucker M, et al. (2018). Relationship between physical activity, cognition, and pathology in autosomal dominant Alzheimer's disease. *Alzheimers Dement.* Nov;14(11):1427-1437.
175. Head D, Bugg JM, Goate AM, Fagan AM, Mintun MA, et al. (2012). Exercise engagement as a moderator of the effect of ApoE genotype on amyloid deposition. *Arch Neurol.* May;69(5):636-43.
176. Wu L, Sun D, He Y. (2017). Coffee intake and the incident risk of cognitive disorders: A dose-response meta-analysis of nine prospective cohort studies. *Clin Nutr.* 2017;36(3):730-6.
177. Vaynman S, Ying Z, Wu A, Gomez-Pinilla F. (2006). Coupling energy metabolism with a mechanism to support brain-derived neurotrophic factor-mediated synaptic plasticity. *Neuroscience.* 139(4):1221-34.
178. Mattson MP. (2005). Energy intake, meal frequency, and health: a neurobiological perspective. *Annu Rev Nutr.* 2005; 25():237-60.
179. Pearson KE, Wadley VG, McClure LA, Shikany JM, Unverzagt FW, et al. (2016). Dietary patterns are associated with cognitive function in the REasons for

Geographic and Racial Differences in Stroke (REGARDS) cohort. *J Nutr Sci.* Sep 28;5:e38.

180. Ozawa M, Shipley M, Kivimaki M, Singh-Manoux A, Brunner EJ. (2017). Dietary pattern, inflammation and cognitive decline: The Whitehall II prospective cohort study. *Clin Nutr.* Apr;36(2):506-512.
181. Cortright B. (2015). The Neurogenesis Diet & Lifestyle. Psyche Media.
182. Crane PK, Walker R, Hubbard RA, Li G, Nathan DM, et al. (2013). Glucose levels and risk of dementia. *N Engl J Med.* Aug 8;369(6):540-548.
183. Pass MP, Himali JJ, Beiser AS, Aparicio HJ, Satizabal CL, et al. (2017). Sugar- and Artificially Sweetened Beverages and the Risks of Incident Stroke and Dementia: A Prospective Cohort Study. *Stroke.* May;48(5):1139–1146.
184. Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, et al. (2011). Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the american heart association/american stroke association. *Stroke.* Sep; 42(9):2672-713.
185. Romano M, Diomede L, Guiso G, Caccia S, Perego C, et al. (1990). Plasma and brain kinetics of large neutral amino acids and striatum monoamines in rats given aspartame. *Food Chem Toxicol.* May;28(5):317-321.
186. Wang YY, Zheng W, Ng CH, Ungvari GS, Wei W, et al. (2017). Meta-analysis of randomized, double-blind, placebo-controlled trials of melatonin in Alzheimer's disease. *Int J Geriatr Psychiatry.* Jan;32(1):50-57.
187. Gupta YK, Gupta M, Kohli K. (2003). Neuroprotective role of melatonin in oxidative stress vulnerable brain. *Indian J Physiol Pharmacol.* Oct;47(4):373-86.
188. Bondy SC, Lahiri DK, Perreau VM, Sharman KZ, Campbell A, et al. (2004). Retardation of brain aging by chronic treatment with melatonin. *Ann N Y Acad Sci.* Dec;1035:197-215.
189. West KE, Jablonski MR, Warfield B, Cecil KS, James M, et al. (2011). Blue light from light-emitting diodes elicits a dose-dependent suppression of melatonin in humans. *J Appl Physiol.* Mar;110(3):619-26.
190. Bradbury J. (2011). Docosahexaenoic acid (DHA): an ancient nutrient for the modern human brain. *Nutrients.* May;3(5):529-54.
191. Bazan NG. (2005). Neuroprotectin D1 (NPD1): a DHA-derived mediator that protects brain and retina against cell injury-induced oxidative stress. *Brain Pathol.* Apr;15(2):159-66.
192. Pauwels EK, Volterrani D, Mariani G, Kairemo K. (2009). Fatty acid facts, Part IV: docosahexaenoic acid and Alzheimer's disease. A story of mice, men and fish. *Drug News Perspect.* May;22(4):205-13.

193. Xiao Y, Wang L, Xu RJ, Chen ZY. (2006). DHA depletion in rat brain is associated with impairment on spatial learning and memory. *Biomed Environ Sci.* Dec;19(6):474-80.
194. Morris MC, Evans DA, Tangney CC, Bienias JL, Wilson RS. (2005). Fish consumption and cognitive decline with age in a large community study. *Arch Neurol.* Dec;62(12):1849-53.
195. Levi FY, Vedin I, Cederholm T, Basun H, Faxen Irving G, et al. (2014). Transfer of omega-3 fatty acids across the blood-brain barrier after dietary supplementation with a docosahexaenoic acid-rich omega-3 fatty preparation in patients with Alzheimer's disease: The OmegAD study. *J Intern Med.* Apr;275(4):428-36.
196. Shukla D, Mandal PK, Ersland L, Gruner ER, Tripathi M, et al. (2018). Multi-Center Study on Human Brain Glutathione Conformation using Magnetic Resonance Spectroscopy. *J Alzheimers Dis.* 2018;66(2):517-532.
197. Baer RA. (2003). Mindfulness training as a clinical intervention: A conceptual and empirical review. *Clinical Psychology: Science & Practice.* 2003;10:125–143.
198. Kuyken W, Byford S, Taylor RS, Watkins E, Holden E, White K, Barrett B, Byng R, Evans A, Mullan E, Teasdale JDet al. (2008). Mindfulness-based cognitive therapy to prevent relapse in recurrent depression. *J Consult Clin Psychol.* 2008 Dec; 76(6):966-78.
199. Carlson LE, Garland SN. (2005). Impact of mindfulness-based stress reduction (MBSR) on sleep, mood, stress, and fatigue symptoms in cancer outpatients. *Int J Behav Med.* 12(4):278-85.
200. Ong JC, Shapiro SL, Manber R. (2009). Mindfulness meditation and cognitive behavioral therapy for insomnia: a naturalistic 12-month follow-up. *Explore (NY).* Jan-Feb; 5(1):30-6.
201. Jha AP, Krompinger J, Baime MJ. (2007). Mindfulness training modified subsystems of attention. *Cogn Affect Behav Neurosci.* Jun; 7(2):109-19.
202. Mantle F. (2002). The role of alternative medicine in treating postnatal depression. *Complement Ther Nurs Midwifery.* Nov; 8(4):197-203.
203. Ballard CG, Gauthier S, Cummings JL, Brodaty H, Grossberg GT, et al. (2009). Management of agitation and aggression associated with Alzheimer disease. *Nat Rev Neurol.* May; 5(5):245-55.
204. Pinweha S, Wanikiat P, Sanvarinda Y, Supavilai P (2008).The signaling cascades of Ganoderma Lucidum extracts in stimulating non-amyloidegenic protein secretion in human neuroblastoma SH-SY5Y cell lines. *Neurosci Lett,* 448: 62-6.
205. Jimbo D, Kimura Y, Taniguchi M, Inoue M, Urakami K. (2009). Effect of aromatherapy on patients with Alzheimer's disease. *Psychogeriatrics.* Dec;9(4):173-9.

206. Rai KS, Murthy KD, Karanth KS, Nalini K, Rao MS, et al. (2002). Clitoria ternatea root extract enhances acetylcholine content in rat hippocampus. *Fitoterapia*. Dec; 73(7-8):685-9.
207. Kako H, Fukumoto S, Kobayashi Y, Yokogoshi H. (2008). Effects of direct exposure of green odour components on dopamine release from rat brain striatal slices and PC12 cells. *Brain Res Bull*. Mar 28; 75(5):706-12.
208. Smallwood J, Brown R, Coulter F, Irvine E, Copland. (2001). Aromatherapy and behavior disturbances in dementia: A randomized controlled trial. *Int J Geriatr Psychiatry*. Oct;15(10):1010-3.
209. Holmes C, Hopkins V, Hensford C, MacLaughlin V, Wilkinson D, et al. (2002). Lavender oil as a treatment for agitated behaviour in severe dementia: a placebo controlled study. *Int J Geriatric Psychiatry*. 17(4):305–308.
210. Burns A, Byrne J, Ballard C, and Holmes C. (2002). Sensory stimulation in dementia. *Brit Med J*. 325(7376):1312–1313, 2002.
211. Han X, Gibson J, Eggett DL, Parker TL. (2017). Bergamot (Citrus bergamia) Essential Oil Inhalation Improves Positive Feelings in the Waiting Room of a Mental Health Treatment Center: A Pilot Study. *Phytother Res*. May;31(5):812-816.
212. McDonnell B, Newcomb P. (2019). Trial of Essential Oils to Improve Sleep for Patients in Cardiac Rehabilitation. *J Altern Complement Med*. Sep 26.
213. Al-Yasiry AR, Kiczorowsha B. (2016). Frankincense—therapeutic properties. *Postepy Hig Med Dosw* (Online). Jan 4;70:380-91.
214. Raman R. (2019). 11 Impressive Health Benefits of Saffron. Retrieved Dec 12 2019 from <https://www.healthline.com/nutrition/saffron>.
215. Ballard CG, O'Brien JT, Reichelt K, Perry EK. (2002). Aromatherapy as a safe and effective treatment for the management of agitation in severe dementia: *J Clin Psychiatry*. 2002 Jul;63(7):553-8.
216. Harris ML, Titler MG, Struble LM. (2019). Acupuncture and Acupressure for Demential Behavioral and Psychological Symptoms: A Scoping Review. *West J Nurs Res*. Dec 5:193945919890552.
217. Zeng BY. (2017). Effect and Mechanism of Chinese Herbal Medicine on Parkinson's Disease. *Int Rev Neurobiol*. 2017;135:57-76.
218. Han L, Xie YH, Wu R, Chen C, Zhang Y, et al. (2017). Traditional Chinese medicine for modern treatment of Parkinson's disease. *Chin J Integr Med*. Aug;23(8):635-640.