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TEA AND COGNITIVE HEALTH IN LATE LIFE: CURRENT EVIDENCE AND FUTURE DIRECTIONS

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Abstract: This review summarizes the literature on the association between tea consumption and cognitive health in late life. Population-based studies reviewed in this article suggest that tea drinking has beneficial effects on cognitive function of elderly persons. However, a cause-effect relationship between tea consumption and cognitive decline and dementia could not be drawn given inconsistent findings from only two longitudinal cohort studies. The neuroprotective effects of tea consumption could be due to catechins, L-theanine and other compounds in tea leaves. More longitudinal observational study is needed. Information on life-time tea consumption and blood concentrations of catechins and L-theanine could be collected in future studies.

Key words: Tea, catechins, elderly, cognitive decline, dementia, prevention.

Introduction

The world faces an emerging dementia epidemic. A group of international experts estimated that the number of people who are affected by dementia worldwide will double every 20 years to 81.1 million by 2040 (1). Dementia prevalence increases rapidly with increasing age, reaching 24.19% among individuals aged 80 to 89 and 37.36% among individuals aged 90 and older (2). This is critical given increasing life-expectancy and fast aging rate of the world population.

There is no curative treatment for dementia, and the importance of prevention is being recognized in the past decade. However, many attempts have been failed (3, 4) and it could be true that a single agent administered in late life is not likely to be effective since multiple factors across the life course influence brain function in old age (5). At the moment, researchers are actively identifying modifiable protective and risk factors that could be the targets of future multifaceted prevention program. Tea is one of the promising candidates that attracted interests only very recently.

In this article, following a brief introduction of the basics of tea, the author critically reviewed findings from population-based studies on tea and cognitive health in late life and discussed possible neurobiological mechanisms underlying the observed association. The directions of future research were pointed out.

Tea: the basics

Tea drinking originated from China around 4000-5000 years ago, and was spread to the rest of the world. Today, tea is frequently consumed by people from all countries. All varieties and cultivars of the tea plant belong to a single species, Camellia sinensis. Depending on the degree of oxidation (commonly known as fermentation) during the manufacturing process, tea can be broadly categorized into three basic types: black tea (fully fermented), oolong tea (semi-fermented), and green tea (non-fermented). Black tea accounts for about 78% of the total tea production worldwide followed by green tea and oolong tea respectively (6).

During the fermentation process, higher molecular weight species such as theaflavins and thearubigins are formed as a result of enzymatic oxidation by polyphenol oxidase of catechins. Therefore, the content of tea polyphenols differs for each tea due to different degrees of fermentation during manufacture, as well as place of origin, plant cultivars and many other factors. For total catechins and epigallocatechin 3-gallate (EGCG, the most abundant catechin in tea), the levels are in the order: green tea > oolong tea > black tea (7). Besides tea itself, the way of making tea also has impact on the physiological effects of tea consumption. For example, the addition of milk to tea could affect the availability of tea polyphenols because of their interaction with milk proteins such as β-casein (8).

Tea leaf also contains L-theanine (an amino acid uniquely found in tea leaf), caffeine and other chemical components. All those constituents could also contribute to various health benefits (6, 9-12) that have been associated with tea drinking, although it is generally believed that catechins, especially EGCG, is the key compound.

Tea and cognitive health in late life: current evidence

The first population-based report on cognitive benefit of tea drinking appeared in 2006. Up to today, empirical evidences are still sparse and the preventive value of tea drinking on cognitive decline and dementia is far from firmly established.

Table1 summarizes findings from previous studies. Four cross-sectional analysis have been conducted based on study samples from Japan (13), Singapore (14, 15), China (16) and Norway (17). The results were generally consistent. Tea consumption was associated with decreased risk of cognitive

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impairment defined by scores on the Mini-Mental State Examination (13, 14), a test that is widely used as a screening tool for dementia and as a measure of global cognitive function (18, 19) . Tea consumption was also associated with better performance as measured by standard neuropsychological tests (15, 17), the relationship is dose-dependent (15, 17) and approximately linear (14, 15, 17).

Most (72%) of the study participants in the Japan study consumed at least 2 cups green tea daily (13) while there were only 10 (0.40%) pure green tea drinker and 6.28% subject who consumed >= 1 cup green tea/day in the Singapore sample (14). Different tea consumption habits of the study subjects could explain the inconsistent findings on tea types from the two studies. Although the Norway study didn't collect information on types of tea, since black tea comprised 96% of the total tea imported in to Norway (17), we would expect that most of their participants only consumed black tea. In general, current evidences suggest that both green tea and black/oolong tea have beneficial cognitive effects, but no cause-effect conclusion could be drawn given cross-sectional nature of those analyses.

Only two studies examined the association between tea consumption and cognitive decline or dementia prospectively. As shown in Table 1, Ng et al reported that tea consumption was associated with reduced risk of cognitive decline (14) while mid-life tea consumption was not associated with the risk of dementia or Alzheimer disease in the analysis by Eskelinen et al (20). It should be pointed out that tea drinking was relatively uncommon among participants of the latter study, and this could have influenced the results significantly (note that only 61 dementia cases and 48 Alzheimer disease cases were identified in the follow-up assessment).

From another angle, tea drinking also could be viewed as a leisure time activity: people often drink tea with peers and chat with each other, especially in Asian countries. Since increased leisure activity has been shown to be associated with lower risk of cognitive decline and dementia (21-23), it is plausible to speculate that tea drinking behavior itself could contribute to the neuroprotective effects in addition to chemical compounds that tea contains (15).

Neurobiological mechanisms

The underlying mechanisms of the neuroprotective effect of tea are complex. Possible mechanisms regarding tea catechins, especially EGCG, may involve their antioxidant and iron chelating activity and the modulation of signal transduction pathways, cell survival/death genes, and mitochondrial function (24). Cognitive impairment has diverse etiologies and findings from recent animal studies suggest that tea polyphenols may exert neuroprotective effect through different mechanisms. Tea polyphenols inhibit cognitive impairment induced by chronic cerebral hypoperfusion via modulating oxidative stress (25). They improve cognitive impairments caused by psychological stress through the secretion of stress hormones, production of catecholamines and regulation of cytokines in addition to their antioxidant activities (26). As for age-related spatial learning and memory decline, main mechanism of the protective effect could be the regulation of hippocampal cAMP-response element binding protein (CREB) signaling cascade (27).

Table 1
Studies on the association between tea consumption and cognitive health in late life

Author, year	Study design	Study sample	Main findings	Level of evidence[1]
Kuriyama et al, 2006 (13)	Cross-sectional	1003 Japanese aged 70 and above	Higher consumption of green tea but not black/oolong tea was associated with a lower prevalence of cognitive impairment defined as Mini-Mental State Examination test scores <26.	2c
Nurk et al, 2009 (17)	Cross-sectional	2031 elderly persons aged 70-74 years old	Compared with non-consumers, tea consumers had better performance on modified-Mini-Mental State Examination, Trail Making Test-A, modified- Digit Symbol Test, and modified Block Design test.	2c
Huang et al, 2009 (16)	Cross-sectional	681 Chinese nonagenarians/ centenarians	Cognitive impairment was associated with lower prevalence of tea consumption habit in men but not women.	2c
Feng et al, 2010 (15)	Cross-sectional	716 Chinese aged 55 years and above	Total tea consumption was associated with better performances on global cognition, memory, executive function, and information processing speed. Both black/oolong tea and green tea were associated with better cognitive function.	2c
Ng et al, 2008 (14)	Cross-sectional and longitudinal	2501 Chinese aged 55 years and above. For longitudinal analysis, the subjects were 1438 cognitively intact participants followed up for 1-2 years.	Total tea consumption was significantly associated with a lower risk of cognitive impairment (defined as Mini-Mental State Examination score < or =23) and cognitive decline (defined as drop in Mini-Mental State Examination score of > or = 1 point). The effects were more evident for black and oolong tea.	2b
Eskelinen et al, 2009 (20)	Longitudinal	1409 elderly persons aged 65 to 79 who were reassessed after an average follow-up of 21 years	Mid-life tea drinking was not associated with the risk of dementia and Alzheimer disease in late life.	2b

1. Based on the Oxford Centre for Evidence-based Medicine levels of evidence rating scheme (http://www.cebm.net/index.aspx?o=1025)

Tea may also have neuroprotective effects through the modification of Alzheimer's pathology. In-vitro and in-vivo studies have shown that EGCG reduce β-amyloid generation by promoting α-secretase cleavage of amyloid precursor protein (28, 29), and markedly reduce sarkosyl-soluble phosphorylated tau isoforms (29). EGCG also efficiently inhibits the fibrillogenesis of amyloid-beta by directly binding to the natively unfolded polypeptides and preventing their conversion into toxic, on-pathway aggregation intermediates (30). Furthermore, both black tea and green tea inhibit human acetylcholinesterase activity (31) and display protective action against -amyloid–induced toxicity (32).

Although the 'amyloid hypothesis' of Alzheimer disease (AD) has been dominating for decades, it is clear now that amyloid and tau are far more not enough to explain the entire pathogenesis. Vascular hypothesis of AD has been advocated by some researchers. The hypothesis assumes a causal relation between vascular mechanisms and the development of AD and proposes that neurodegeneration is a downstream event of neuroglial energy crisis secondary to cerebral hypoperfusion (33, 34). In addition to AD, there are larger number of individuals who are affected by vascular cognitive impairment (VCI), which comprises a range of cognitive disorders related to cerebral vessel disease (35). Interestingly, there is strong evidence that support cerebrovascular protective effects of tea drinking: in a meta-analysis that pooled data from 9 studies involving 4,378 strokes among 194, 965 individuals, it was shown that individuals consuming 3 cups of tea per day had a 21% lower risk of stroke than those consuming <1 cup per day (12). Hence, it is highly possible that vascular benefits of tea drinking could contribute to the observed neuroprotective effects significantly.

In addition to tea polyphenols, L-theanine, a free amino acid naturally found in tea, also possess neuroprotective effect (36-38). Tea contains caffeine and caffeine can improve attention (36, 39, 40). In population-based study, coffee consumption has been related to reduced dementia risk (20) . Hence both L-theanine and caffeine could contribute to the cognitive benefits of tea consumption.

Because tea leaf contains various other phytochemicals, it is possible that the cognitive protective effect of tea is not due to a single compound, but rather the synergistic effect of several or many of its chemical components. The combined effects of those compounds could be more than just the sum of the effects from each of the compounds. At the same time, antagonistic effects of complex compounds cannot be ruled out.

Directions for future research

As reviewed, currently evidence on the value of tea as a preventive measure of cognitive decline and dementia is still sparse and inconclusive. There is no doubt that more research is needed.

Longitudinal studies with large sample size, long follow-up period, sensitive cognitive outcome measures, and accurate identification of all dementia (Alzheimer disease, vascular dementia, mixed dementia, and others) cases should be conducted to establish a firm cause-effect relationship. In such study, detailed information on lifelong tea intake (frequency × duration) and information on the changing of tea drinking habit should be collected. Duration of tea consumption could be different among individuals who report the same level of current tea intake, and elderly persons with longer tea consumption duration would have better cognitive outcomes than those who have shorter duration. With the collection of detailed duration data, a clear dose-effect relationship could be established. Furthermore, objective blood measure of certain compounds such as catechins and L-theanine would help to identify (confirm) the constituents that are responsible for the observed beneficial effects of tea consumption on cognitive function.

References

1. Ferri CP, Prince M, Brayne C, et al. Global prevalence of dementia: a Delphi consensus study. Lancet 2005;366:2112-7.
2. Plassman BL, Langa KM, Fisher GG, et al. Prevalence of dementia in the United States: the aging, demographics, and memory study. Neuroepidemiology 2007;29:125-32.
3. Schneider LS. Ginkgo biloba Extract and Preventing Alzheimer Disease. JAMA 2008;300:2306-2308.
4. Kaye J. Ginkgo biloba Prevention Trials: More Than an Ounce of Prevention Learned. Arch Neurol 2009;66:652-654.
5. Feng L. Ginkgo biloba and Cognitive Decline. JAMA 2010;303:1477-.
6. Cheng TO. All teas are not created equal: the Chinese green tea and cardiovascular health. Int J Cardiol 2006;108:301-8.
7. Lin Y-S, Tsai Y-J, Tsay J-S, Lin J-K. Factors Affecting the Levels of Tea Polyphenols and Caffeine in Tea Leaves. Journal of Agricultural and Food Chemistry 2003;51:1864-1873.
8. Jöbstl E, Howse JR, Fairclough JPA, Williamson MP. Noncovalent Cross-Linking of Casein by Epigallocatechin Gallate Characterized by Single Molecule Force Microscopy. Journal of Agricultural and Food Chemistry 2006;54:4077-4081.
9. Niu K, Hozawa A, Kuriyama S, et al. Green tea consumption is associated with depressive symptoms in the elderly. Am J Clin Nutr 2009;90:1615-1622.
10. Khan N, Mukhtar H. Tea polyphenols for health promotion. Life Sci 2007;81:519-33.
11. Nakachi K, Eguchi H, Imai K. Can teatime increase one's lifetime? Ageing Res Rev 2003;2:1-10.
12. Arab L, Liu W, Elashoff D. Green and Black Tea Consumption and Risk of Stroke: A Meta-Analysis. Stroke 2009;40:1786-1792.
13. Kuriyama S, Hozawa A, Ohmori K, et al. Green tea consumption and cognitive function: a cross-sectional study from the Tsurugaya Project 1. Am J Clin Nutr 2006;83:355-61.
14. Ng TP, Feng L, Niti M, Kua EH, Yap KB. Tea consumption and cognitive impairment and decline in older Chinese adults. Am J Clin Nutr 2008;88:224-31.
15. Feng L, Gwee X, Kua EH, Ng TP. Cognitive function and tea consumption in community dwelling older Chinese in Singapore. J Nutr Health Aging 2010;14:433-8.
16. Huang C-Q, Dong B-R, Zhang Y-L, Wu H-M, Liu Q-X. Association of Cognitive Impairment With Smoking, Alcohol Consumption, Tea Consumption, and Exercise Among Chinese Nonagenarians/Centenarians. Cognitive and Behavioral Neurology 2009;22:190-196 10.1097/WNN.0b013e3181b2790b.
17. Nurk E, Refsum H, Drevon CA, et al. Intake of Flavonoid-Rich Wine, Tea, and Chocolate by Elderly Men and Women Is Associated with Better Cognitive Test Performance. J. Nutr. 2009;139:120-127.
18. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-98.
19. Ng T-P, Niti M, Chiam P-C, Kua E-H. Ethnic and Educational Differences in Cognitive Test Performance on Mini-Mental State Examination in Asians. Am. J. Geriatr. Psychiatry 2007;15:130-139.
20. Eskelinen MH, Ngandu T, Tuomilehto J, Soininen H, Kivipelto M. Midlife Coffee and Tea Drinking and the Risk of Late-Life Dementia: A Population-Based CAIDE Study. Journal of Alzheimer's Disease 2009;16:85-91.
21. Qiu C, Xu W, Fratiglioni L. Vascular and psychosocial factors in Alzheimer's

disease: epidemiological evidence toward intervention. J Alzheimers Dis 2010;20:689-97.
22. Yaffe K, Fiocco AJ, Lindquist K, et al. Predictors of maintaining cognitive function in older adults: The Health ABC Study. Neurology 2009;72:2029-2035.
23. Scarmeas N, Luchsinger JA, Schupf N, et al. Physical Activity, Diet, and Risk of Alzheimer Disease. JAMA 2009;302:627-637.
24. Mandel SA, Amit T, Kalfon L, Reznichenko L, Youdim MBH. Targeting Multiple Neurodegenerative Diseases Etiologies with Multimodal-Acting Green Tea Catechins. J. Nutr. 2008;138:1578S-1583.
25. Yan X, Zhang J-j, Li X, Lei Z, Dong S, Hui L. Green tea polyphenols inhibit cognitive impairment induced by chronic cerebral hypoperfusion via modulating oxidative stress. The Journal of Nutritional Biochemistry 2010;21:741-748.
26. Chen W-Q, Zhao X-L, Hou Y, et al. Protective effects of green tea polyphenols on cognitive impairments induced by psychological stress in rats. Behavioural Brain Research 2009;202:71-76.
27. Li Q, Zhao HF, Zhang ZF, et al. Long-term administration of green tea catechins prevents age-related spatial learning and memory decline in C57BL/6 J mice by regulating hippocampal cyclic amp-response element binding protein signaling cascade. Neuroscience 2009;159:1208-1215.
28. Rezai-Zadeh K, Shytle D, Sun N, et al. Green Tea Epigallocatechin-3-Gallate (EGCG) Modulates Amyloid Precursor Protein Cleavage and Reduces Cerebral Amyloidosis in Alzheimer Transgenic Mice. J. Neurosci. 2005;25:8807-8814.
29. Rezai-Zadeh K, Arendash GW, Hou H, et al. Green tea epigallocatechin-3-gallate (EGCG) reduces [beta]-amyloid mediated cognitive impairment and modulates tau pathology in Alzheimer transgenic mice. Brain Research 2008;1214:177-187.
30. Ehrnhoefer DE, Bieschke J, Boeddrich A, et al. EGCG redirects amyloidogenic polypeptides into unstructured, off-pathway oligomers. Nat Struct Mol Biol 2008;15:558-566.
31. Okello EJ, Savelev SU, Perry EK. In vitro anti-beta-secretase and dual anti-cholinesterase activities of Camellia sinensis L. (tea) relevant to treatment of dementia. Phytother Res 2004;18:624-7.
32. Bastianetto S, Yao ZX, Papadopoulos V, Quirion R. Neuroprotective effects of green and black teas and their catechin gallate esters against beta-amyloid-induced toxicity. Eur J Neurosci 2006;23:55-64.
33. de la Torre JC. The Vascular Hypothesis of Alzheimer's Disease: Bench to Bedside and Beyond. Neurodegenerative Diseases 2010;7:116-121.
34. de la Torre JC. Is Alzheimer's disease a neurodegenerative or a vascular disorder? Data, dogma, and dialectics. The Lancet Neurology 2004;3:184-190.
35. Moorhouse P, Rockwood K. Vascular cognitive impairment: current concepts and clinical developments. The Lancet Neurology 2008;7:246-255.
36. Nathan PJ, Lu K, Gray M, Oliver C. The neuropharmacology of L-theanine(N-ethyl-L-glutamine): a possible neuroprotective and cognitive enhancing agent. J Herb Pharmacother 2006;6:21-30.
37. Kakuda T. Neuroprotective effects of the green tea components theanine and catechins. Biol Pharm Bull 2002;25:1513-8.
38. Kim TI, Lee YK, Park SG, et al. l-Theanine, an amino acid in green tea, attenuates [beta]-amyloid-induced cognitive dysfunction and neurotoxicity: Reduction in oxidative damage and inactivation of ERK/p38 kinase and NF-[kappa]B pathways. Free Radical Biology and Medicine 2009;47:1601-1610.
39. Haskell CF, Kennedy DO, Milne AL, Wesnes KA, Scholey AB. The effects of L-theanine, caffeine and their combination on cognition and mood. Biol Psychol 2008;77:113-22.
40. Owen GN, Parnell H, De Bruin EA, Rycroft JA. The combined effects of L-theanine and caffeine on cognitive performance and mood. Nutr Neurosci 2008;11:193-8.