Clinical evidence linking coffee and tea intake with Parkinson's disease

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Parkinson's disease is a common neurodegenerative disorder with multifactorial etiology. Although the exact cause remains unknown, various studies have suggested the possibility of genetic and environmental interplay. Among the various environmental factors, chronic exposure to common human habits for example, cigarette smoking and caffeine intake have exhibited an inverse association with risk of developing Parkinson's disease. Coffee and tea, the two most common beverages consumed worldwide, have also been shown to reduce the risk of developing Parkinson's disease. We provide a concise overview of the clinical studies that examine the effect of coffee and tea intake on the risk of Parkinson's disease.

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Introduction

Parkinson's disease (PD) is a common neurodegenerative disease that places an increasing burden on our aging society [1]. It is a debilitating disorder with varying patterns of degeneration in the dopaminergic (mesolimbic and mesocortical) and nondopaminergic (cholinergic, noradrenergic, and serotoninergic) neuronal systems [2]. The cardinal features of PD include bradykinesia, resting tremor, muscular rigidity, gait disturbances, and postural reflex impairment [2]. Apart from these motoric dysfunction, patients with PD also have a wide spectrum of non-motor manifestations which may occur early in the disease but are generally more disabling later on with disease progression. These non-motor symptoms include fatigue, cognitive decline, depression, anxiety, behavioral disturbances, visual dysfunction, dysautonomia, weight loss, sleep abnormalities, abnormal sensations and pain [3].

The prevalence of PD worldwide is known to range from 0.5% to 4% among the elderly aged 65 years or older [1]. And the numbers will likely increase significantly in 20 years time as the global average for life expectancy and elderly population increase. The cause of PD in most patients remains elusive. It is assumed that genetic factors are particularly important in early-onset cases of PD while the environmental factors are probably more relevant in the development of PD at older ages (above 50 years). In the vast majority of patients, complex interaction of genes and environment factors likely contribute to the PD etiology. Even in cases with known cause, the interplay of environment and genes is more likely. For example, the penetrance of the G2019S mutation in the LRRK2 gene is estimated to be 30–80% [4], suggesting a role for other genetic or environmental factors. Likewise, twin studies find low concordance for PD in all but those with young age at onset, indicating the importance of nongenetic factors [5,6].

The potential mechanisms associated with environmental factors may be direct, such as a toxic effect causing cell death, or indirect, such as an effect on DNA expression or repair processes. Some of these environmental factors include cigarette smoking, well-water drinking, herbicide and pesticide exposure as well as heavy metal toxicity [7,8]. Exposures associated with increased risk of PD may indicate a cause of disease, and those inversely associated may indicate a protective effect. For example, cigarette smoking has been inversely associated with the risk of PD in nearly all epidemiological studies worldwide [9–11]. However, direct proof of cause and effect requires controlled investigation. And in most cases, this work can only be conducted in experimental animals because of practical and ethical constraints that limit such experiments in humans.

Tea and coffee are the two most common beverages in the world. Coffee is consumed more commonly in the western countries whereas tea is more popular in the Asian continent. Similar to cigarette smoking, the inverse association of coffee/tea drinking and PD risk have also been observed in the worldwide population [12–16]. However the strength of the evidence for the described inverse associations seems to be weaker for coffee/tea than for smoking. The precise reasons for this are not known although it may in part be due to the fact that there are fewer studies investigating the risk of PD with coffee/tea compared to smoking. Here we provide a concise overview of the clinical studies that examine...
the effects of coffee and tea intakes on the risk of PD. The summary of the literature is based on studies listed in Pubmed in the last two decades.

**Effect of coffee in Parkinson's disease**

The first prospective study was a cohort study of Japanese-American men in Hawaii which demonstrated a significant inverse association between coffee consumption and incident PD [17]. Subsequently, other prospective studies, including the Health Professionals Follow-up Study and the Nurses' Health Study, observed the same inverse association between coffee consumption and the risk of PD among men but no association among women [18]. In the Cancer Prevention Study II Cohort, coffee consumption was inversely associated with PD mortality in men but not in women [19]. This gender difference could be explained if the effect of caffeine on the risk of PD depend on the level of estrogen [18,19]. Coffee consumption was associated with a reduced risk of PD only among women who never used postmenopausal estrogens [19,20]. The use of postmenopausal estrogens seems to modify the effects of caffeine on the risk of PD, although the reasons for this interaction are not yet clear. A similar inverse association of coffee drinking and PD risk has been recently confirmed in two prospective studies from Finland [12,13]. Greater amounts of coffee use were associated with lower risk, and effects were greater in obese persons and those with lower cholesterol levels [13].

In addition, a meta-analysis of five cohort studies and eight case–control studies revealed a strong epidemiological evidence that coffee drinkers have a lower risk of PD [15]. The results indicated that the risk of PD was 30% lower among coffee drinkers than non-coffee drinkers. The PD risk reduction was also noted for non-coffee caffeine sources but not for decaffeinated coffee, thus indicating that caffeine was a likely putative causal agent underpinning the observed coffee–Parkinson's disease association [17,18].

In the Singapore Chinese Health Study, a prospective cohort of 63,257 Chinese men and women were examined from 1993 to 2005 [21]. Coffee intake exhibited a significant, dose-dependent inverse association with Parkinson's disease risk. After adjustment for cigarette smoking the association was attenuated but still remained significant in a dose-dependent manner. However following adjustment for total caffeine exposure the inverse association between coffee intake and Parkinson's disease risk disappeared suggesting that the caffeine content of coffee was primarily responsible for the effect of coffee on Parkinson's disease.

More recently, Costa et al. conducted a systematic review and meta-analysis of published epidemiological studies to better estimate the effect of caffeine/coffee exposure on the incidence of PD [22]. Twenty-six studies were included: 7 cohort, 2 nested case–control, 16 case–control, and 1 cross-sectional study. The meta-analysis confirmed an inverse association between caffeine intake and the risk of PD. A linear relation was observed between levels of exposure to caffeine and the relative risk estimates: RR of 0.76 (95% CI: 0.72–0.80; I² = 35.1%) per 300 mg increase in caffeine intake.

The mechanism by which coffee may exert its effects has been mainly speculated to take place through caffeine. Caffeine as a known central nervous system stimulant has been thought to act through adenosine receptor antagonism mostly by inhibition of adenosine A2A receptors. Studies have shown that the agonist of adenosine receptor produces decreased locomotor activity in rodents, probably through inhibition of dopamine neurotransmission [23–25]. The adenosine A2A receptor appears to be an important target for the treatment of basal ganglia disorders, particularly PD [24]. Controlled clinical trials about the long-term effects of caffeine are difficult to conduct in humans, but the animal models support the hypotheses about the neuroprotective effect of caffeine. It has been reported that caffeine can protect against dopaminergic neuron toxicity in a mouse model of PD [26]. A study by Chen et al. [27] revealed a protective effect of caffeine on the pathophysiological responses of dopaminergic nigrostriatal neurons in a mouse model of PD.

**Effect of tea in Parkinson’s disease**

The most common types of tea include green and black tea. Black tea leaves are fermented and green are not. In green tea, the naturally occurring catechins are minimally oxidized forming four primary polyphenols which are epigallocatechin gallate, epigallocatechin, epicatechin gallate, and epicatechin, the most abundant being epigallocatechin gallate. On the other hand, when black tea is manufactured, the catechins undergo oxidation and polymerization during the fermentation process, resulting in generation of other distinct polyphenols such as thearubigins and theaflavins [28].

Tea has not been investigated in relation to PD risk as extensively or explicitly as coffee has, perhaps because consumption of coffee is far more prevalent in North America and Europe, where most research on PD has been undertaken. There is mixed epidemiologic evidence for the relation of tea with PD. Consumption of at least one cup of tea per day has been associated with reduced PD risks of 30–40% in China [16] and among male health professionals in the United States [18], although no association was found for female nurses in the latter study. In contrast, a nearly twofold increased risk for PD among tea drinkers was reported from a hospital-based case–control study in France [38]. A potentially neuroprotective effect might be inferred from the identification in tea of free-radical scavenging phenolic compounds [39], especially in view of the widely accepted relevance of oxidative stress mechanisms in PD pathogenesis [40].

Like coffee, tea also has caffeine, although in less quantities. An average 5 ounce cup of tea can contain 20–110 mg of caffeine, making it the next highest source of caffeine in beverages after coffee. The amount of caffeine is in a cup of tea will depend upon the type of tea used and how long it was brewed. Green tea contains about one-third the caffeine as black tea and the longer the tea is brewed the higher is the caffeine content.

Three case–control studies (in the United States, Hong Kong, and Singapore) [41,14,16] and a cohort study of male health professionals in the United States [18] have reported an inverse association between tea drinking and Parkinson’s disease risk. The authors attributed the protective effect of tea, at least in part, to its caffeine content. A similar inverse association of tea drinking and PD risk, has been recently confirmed in a prospective study from Finland supporting the proposal that a biologic effect of caffeine may have contributed to this association.

Quintana et al. reviewed all observational studies that evaluated the association between PD risk and tea consumption [42]. Of the 12 studies which were identified, 11 were case–control and 1 was a cohort study. These studies were carried out between 1981 and 2003 and they represented different populations from three continents; North America, Europe and Asia. There was a
clear protective effect of tea consumption in the pooled risk estimate; however, the homogeneity test was significant, denoting heterogeneity across the pooled studies. Pooling the seven case-control studies with population-based control showed a clear protective effect of tea consumption against PD risk with homogeneity between the pooled studies. However, pooling the remaining four case-control studies, with hospital-based control and had significant homogeneity between the studies, did not show any protective effect. This observation suggests that the case-control studies that evaluated the possible protective effect of tea against PD could be attributed to the study design (population-based versus hospital-based). Meanwhile, analyzing the three studies from Asia which consisted of case-control studies of Chinese populations, tea consumers had significantly reduced risk of PD compared to non-consumers with clear homogeneity across the pooled three studies. This observation suggests that tea has clear protective effect in the Chinese population.

PD prevalence was found to be low in Asian countries, like China, meanwhile it was much higher in Europe and North America [43]. This could be attributed to genetic variations, environmental factors including dietary habits like tea consumption or both [44,45]. Another explanation is the type of tea consumed by the Chinese populations. Unlike in most Caucasian communities, green tea is by far the most common type of tea used in China. The green tea is not fermented and has more polyphenols than other types of tea. Although the scientific evidence is not sufficient, the polyphenols could protect against PD and other neurodegenerative diseases [34] as recently demonstrated in cellular cultures and animal models [29,46]. According to Ahmed [47], the polyphenols in the green tea have antioxidants effects equal or more than vitamins C and E. He reported that epigallocatechin gallate, the principal polyphenol in the tea has more than 100 times antioxidant effect than vitamin C and 25 times than vitamin E [48-54].

In a another study, black tea showed an inverse association with Parkinson’s disease risk that was not confounded by total caffeine intake or tobacco smoking [21]. However, green tea drinking, after adjustment for cigarette smoking and total caffeine consumption, was unrelated to PD risk. The authors speculated that the protective effect of black tea may be mediated via an estrogen-related pathway. This was based on what they had reported earlier that among the women in their study cohort, levels of circulating estrogen were highest in regular black tea drinkers, intermediate in non-tea drinkers, and lowest in regular green tea drinkers; these differences were dose dependent and significant [55].

In terms of a dose-response relationship, only few studies have stratified their results according to the number of cups of tea daily consumed. Fall et al. [56] showed a dose-dependent protective effect of PD in tea consumers; OR of 0.48 for daily consumption of a cup of tea versus OR of 0.27 for daily consumption of 2 or more cups of tea.

Similarly, Tan et al. [14] have reported a dose-dependent protective effect of PD in coffee and tea consumers in an ethnic Chinese population. They had demonstrated that one unit of coffee and tea (3 cups/day for 10 years) would lead to a 22% and 28% risk reduction of PD. In contrary, Paganini-Hill [57] could not demonstrate such dose-dependent protective effect in their hospital-based case-control study. The results of Ascherio [43], reported a clear dose dependent effect has been demonstrated in males but not in females. Recently, Sumpio et al. [58] suggested that the average 1.2 l of green tea consumed daily by many people in Asia offers sufficient anti-oxidants of the polyphenolic epigallocatechin gallate, and in turn reduces or cures diseases with an inflammatory component, together with improving neurologic and psychological health.

Conclusion

In conclusion, both tea and coffee exhibit an inverse effect on the risk of PD. The exact mechanism of these effects is not clear but is likely due to caffeine effect on adenosine A2A receptor. Apart from caffeine effect, tea may also have the antioxidant effect from the various polyphenols it contains. The observed protective effect (from mostly case-control studies) of these two common beverages should be further investigated in large prospective cohort studies to better understand the interplay of various (environmental and genetic) factors that may be important for future therapies and preventive measures.

References


Dong ZG, Ma WY, Huang ZS, Yang ZS. Inhibition of tumor promoter-induced activator protein 1 activation and cell transformation by tea polyphenols, epigallocatechin gallate and theaflavins. Cancer Res 1997;57:4414–9.


