HHS Public Access

Author manuscript

Int J Cancer. Author manuscript; available in PMC 2021 May 01.

Published in final edited form as:

Int J Cancer. 2020 May 01; 146(9): 2442–2449. doi:10.1002/ijc.32574.

A prospective study of tea and coffee intake and risk of glioma

David J. Cote[1,2,3], **Alaina M. Bever**[1], **Kathryn M. Wilson**[1,2], **Timothy R. Smith**[3], **Stephanie A. Smith-Warner**[2,4], **Meir J. Stampfer**[1,2,4]

[1]Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

[2]Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA

[3]Computational Neuroscience Outcomes Center (CNOC), Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

[4]Department of Nutrition, Harvard T. H. Chan School of Public Health, Boston, MA

Abstract

Tea and coffee have antioxidant and neuroprotective effects. Observational studies suggest that tea and coffee intake may reduce cancer risk, but data on glioma risk are inconclusive. We evaluated the association between tea, coffee and caffeine intake and glioma risk in the female Nurses' Health Study (NHS) and Nurses' Health Study II (NHSII) and the male Health Professionals Follow-Up Study (HPFS). Cumulative intake was derived from validated quadrennial food frequency questionnaires. Glioma cases were confirmed by medical record review. Multivariable-adjusted hazard ratios of glioma by beverage intake category were estimated using Cox proportional hazards models. We documented 554 incident cases of glioma (256 in NHS, 87 in NHSII and 211 in HPFS). Compared to <1 cup/week, higher tea consumption was borderline inversely associated with glioma risk in pooled cohorts (hazard ratio [HR] = 0.73, 95% confidence interval [CI]: 0.49–1.10 for >2 cups/day, p-trend = 0.05), but not in women (HR = 0.74, 95% CI: 0.47–1.18 for >2 cups/day, p-trend = 0.11) or men (HR = 0.70, 95% CI: 0.30–1.60 for >2 cups/day, p-trend = 0.30) separately. Overall, we observed no significant associations between caffeinated, decaffeinated or total coffee intake and glioma risk. There were no material differences in the results with baseline values, 8-year lagged responses, or when limited to glioblastoma (n = 362). In three large prospective cohort studies, tea intake was borderline inversely associated with glioma risk. No significant associations were observed for coffee intake and glioma risk. These results merit further exploration in prospective studies.

Keywords

glioma; glioblastoma; tea; coffee; epidemiology

Correspondence to: David J. Cote, Department of Epidemiology, Channing Division of Network Medicine, Harvard T.H. Chan School of Public Health, Brigham and Women's Hospital, 181 Longwood Avenue, Boston, MA 02115, USA, Tel.: 617-525-2749, Fax: 617-525-2008, david_cote@hms.harvard.edu.

Conflict of interests: The authors have no potential conflicts of interest.

Additional Supporting Information may be found in the online version of this article.

Introduction

Increased consumption of tea and coffee, two of the most popular beverages worldwide, has been associated with decreased risk of cancers of several sites in human studies.[1–10] Less is known about the association between tea or coffee consumption and risk of glioma, a cancer for which few lifestyle factors have been identified.[11,12] Coffee is a rich source of caffeine, and both tea and coffee contain additional biologically active compounds. Animal models and *in vitro* studies demonstrate neuroprotective, antioxidant and anti-inflammatory effects of compounds found in coffee and tea, which may have implications for the prevention of glioma development in humans.[13–17]

Prior findings from human studies on tea or coffee intake and glioma risk are inconclusive.[12,18–20] Several of the largest studies have utilized a case–control study design, due to the relative infrequency of glioma. Case–control studies are susceptible to selection bias and potential recall bias. A previous report from the prospective Nurses' Health Study (NHS), Nurses' Health Study II (NHSII) and Health Professionals Follow-Up Study (HPFS) found an inverse association of combined tea and coffee intake with glioma risk, but no significant association for individual beverages.[21] The present study adds an additional 219 glioma cases (a 60% increase in number of cases) and 1,917,825 more person-years of follow-up.

The objective of the present study was to analyze the relation of tea and coffee intake with glioma risk in three large prospective cohort studies, the NHS, NHSII and HPFS. Analyses were performed separately for each cohort and pooled by meta-analysis. We also evaluated intake of total caffeine consumption in relation to glioma risk.

Materials and Methods

Study participants

The methods of the NHS, NHSII and HPFS have been described in detail elsewhere.[22–24] NHS began in 1976 with 121,701 female nurses aged 30–55 years. NHSII began in 1989 with 116,686 female nurses aged 25–42 years. HPFS began in 1986, with 51,529 male health professionals aged 40–75 years. In each cohort, participants completed a baseline questionnaire and subsequent biennial follow-up questionnaires with updated information. Follow-up rates in the cohorts have exceeded 90%.[25] The Institutional Review Boards at the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health approved this study.

Dietary and covariate assessment

To assess dietary intake in each cohort, food frequency questionnaires (FFQs) were initially collected in 1980 for 92,468 women in NHS, in 1991 for 95,391 women in NHSII and in 1986 for 49,935 men in HPFS. For the NHS, a 61-item semiquantitative FFQ was used at baseline,[26] which was expanded to approximately 130 food and beverage items in 1984, 1986 and every 4 years thereafter. For the NHSII and HPFS cohorts, baseline dietary intake was assessed using a 131-item FFQ that was also used for updates generally every 4 years subsequently.[27] For each item, FFQs prompted participants to report their average intake over the preceding year for a specified serving size of each food and beverage from nine

possible responses, ranging from never or almost never to six or more times per day. Intakes of various nutrients, including caffeine, were calculated by multiplying the frequency of each food or beverage consumed by the nutrient content of the specified portion size, and then summing the contributions from all foods and beverages in the FFQ.

Intake of tea, caffeinated coffee, decaffeinated coffee and total coffee (caffeinated and decaffeinated combined) was assessed using quadrennial FFQs. To assess tea intake, FFQs in NHS inquired about the amount of tea consumed, without reference to type of tea or brewing method. Beginning with the 1998 questionnaire in NHS, participants reported tea and herbal or decaffeinated tea separately. In NHSII, all questionnaires inquired about tea, with herbal tea specifically assessed as a separate variable starting with the second FFQ in 1995. Similarly, in HPFS, participants reported tea and herbal tea consumption as two separate variables starting in 1998. For this analysis, herbal or decaffeinated tea was excluded; we could not distinguish black *vs.* green tea. Categorization of each exposure for analysis was based on the distribution of responses observed in the cohorts, in 8 oz cups, before data analysis. For caffeinated coffee, more participants reported heavy use, so this variable was categorized as <1/week, 1/week–1.5/day, 1.5/day–2.5/day, 2.5–4/day and >4/day. This categorization was also used for total coffee and total coffee and tea combined. For decaffeinated coffee and tea, fewer participants were heavy users, so these variables were categorized as <1/week, 1/week-1.5/day, 1.5–3/day or >3/day. For analyses using baseline values, the categorization used in the initial questionnaire was used with the highest categories collapsed to ensure adequate cases in each category (<1/month, 1/month to 1–3/month, 1–3/month to 1/week, 1/week to 2–4/week, 2–4/week to 5–6/week, 5–6/week to 1/day, 1/day to 2–3/day, 2–3/day to 4–5/day, >4–5/day). Caffeine intake was assessed in quintiles within each cohort. For both cohorts, total caffeine was calculated by summing the amount of caffeine in coffee, tea, soda, decaffeinated coffee, chocolate and candies consumed by participants.

The validity of the FFQs for assessing food and beverage intake has been described previously for the NHS[26,28,29] and HPFS cohorts.[27,30] Pearson correlations between the average intake assessed by two 1-week diet records completed 6 months apart and the baseline FFQ were 0.93 and 0.78 for tea and coffee, respectively, in NHS,[29] and 0.77 and 0.93 for tea and coffee, respectively, in HPFS.[30]

We also collected data on smoking (never *vs.* former *vs.* current), height and weight. At each follow-up questionnaire, participants reported updated smoking behavior and updated weight. Body mass index (BMI) was computed using the height reported on the baseline questionnaire in each cohort. In the case of missing values, smoking behavior and BMI were carried forward up to 4 years (two cycles), and considered missing.

Identification of cases

Primary brain malignancy cases were self-reported on biennial questionnaires and then confirmed by medical record review. Deaths were identified through the National Death Index, next-of-kin and postal authorities. For all deaths that may have been due to primary brain cancer, we sought medical records to confirm the diagnosis. Data on tumor subtype, including diagnosis of glioblastoma, was extracted from medical records. Follow-up for

mortality through these methods assured nearly complete ascertainment of deaths and their causes.[31] Only cases with confirmed ICD-9-CM diagnoses of 191.x, indicating primary malignant neoplasm of the brain, were included in this analysis.

Statistical analyses

We began follow-up time at the date of return of the initial questionnaire and continued to the date of diagnosis, death or the end of follow-up (December 31, 2013 for NHS and NHSII; December 31, 2016 for HPFS), whichever came first. Total person-years of follow-up were 2,821,489 for NHS, 2,169,203 for NHSII and 1,032,049 for HPFS. For all measures of beverage and nutrient intake, our primary analyses were based on the cumulative average of all of the available dietary questionnaires up to that point in time, to best represent long-term intake and to reduce random within-person measurement error. For example, in HPFS, intake for the period 2006–2010 was represented by the average of the intake reported in 1986, 1990, 1994, 1998, 2002 and 2006. We excluded from the analyses participants who did not report on their coffee or tea intake at baseline. If dietary data were missing on a non-baseline questionnaire, responses from the prior FFQ were carried forward up to two cycles (8 years), then set to missing.

All analyses were performed for glioma overall and glioblastoma specifically. We used Cox proportional hazards models to calculate multivariable-adjusted hazard ratios (HRs) of glioma and 95% confidence intervals (CIs) by category of beverage intake. We used age as the underlying time scale and stratified by calendar time, with additional adjustment by total caloric intake (categorized in quintiles), BMI (categorized as <25 kg/m^2, 25–29.9 kg/m^2, ≥30 kg/m^2 or missing) and smoking status (categorized as never, former, current or missing). Adjustment for total caloric intake minimizes extraneous variation due to underreporting or overreporting in the FFQ.[32] Additionally, we constructed mutually adjusted models in each cohort, which adjusted tea for the three coffee variables individually (caffeinated coffee, decaffeinated coffee and total coffee, each separately), and total coffee for tea. We also constructed models which adjusted for caffeine intake for tea, and *vice versa*. We further performed lagged analyses that excluded the first 8 years of follow-up, to assess the possibility of changes in behavior due to preclinical tumor and to explore potential timing of associations. For NHS and HPFS, we performed analyses of baseline reported values of coffee, tea and caffeine intake using the categories included in the questionnaire; this was not performed for NHSII due to the small number of cases in some strata.

Tests of linear trend in glioma risk for increasing categories of coffee, tea and caffeine were evaluated by assigning the median values for each beverage intake category and treating those as a single continuous variable, using Cox proportional hazards regression. Analyses of the female NHS and NHSII cohorts were combined by meta-analysis using the fixed-effect model because of the relatively small number of cases in the NHSII cohort. Analyses of all three cohorts were then combined by meta-analysis using the fixed-effect model, and *p*-heterogeneity was calculated for each measure. All statistical analyses were performed using the SAS 9.3 statistical package (SAS Institute, Cary, NC), and all *p*-values were derived from two-sided tests.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Results

Cases and baseline characteristics

We documented 554 cases of glioma during 6,022,741 person-years of follow-up, including 256 cases of glioma in the NHS, 87 cases in the NHSII and 211 cases in the HPFS (Table 1). Of these, 362 were glioblastoma (NHS: 159, NHSII: 52, HPFS: 151). In general, cases were older than each respective cohort overall.

Coffee consumption and glioma risk

Caffeinated coffee intake, decaffeinated coffee intake and total coffee intake were not significantly associated with glioma risk in women (HR for >4 cups/day compared to <1 cup/week = 1.31, 95% CI: 0.81–2.13 for caffeinated coffee, *p*-trend = 0.40) or men (HR for >4 cups/day compared to <1 cup/week = 0.80, 95% CI: 0.37–1.69 for caffeinated coffee, *p*-trend = 0.87) when using cumulative average intake (corresponding HR for pooled cohorts = 1.13, 95% CI: 0.75–1.70, *p*-trend = 0.56) (Table 2). Using 8-year lagged values to account for possible changes in use due to subclinical tumor effects did not materially change these results (Table 3). Use of baseline values also showed no significant association between coffee intake of any type and glioma risk (Supplementary Table S1). Results were not materially changed when adjusted for tea intake (Table S2), or when limited to glioblastoma only (Table S3). There was no significant heterogeneity when pooling results from the three cohorts (all *p*-heterogeneity >0.09).

Tea consumption and glioma risk

Cumulative average tea intake was borderline significantly inversely associated with glioma risk in pooled cohorts (HR for >2 cups/day compared to <1 cup/week = 0.73, 95% CI: 0.49–1.10, *p*-trend = 0.05), but not in women (HR = 0.74, 95% CI: 0.47–1.18, *p*-trend = 0.11) or in men (HR = 0.70, 95% CI: 0.30–1.60, *p*-trend = 0.30) separately (Table 2). These findings were fairly robust to different classifications, although there was slight attenuation with the use of 8-year lagged values (*p*-trend = 0.12 for women, 0.43 for men, 0.12 in the pooled analysis; Table 3). Baseline tea intake was also borderline significantly inversely associated with glioma risk in women (*p*-trend = 0.05) and was significantly inversely associated with glioma in the pooled analysis (*p*-trend = 0.02) but not in men (*p*-trend = 0.22) (Table S1). Results were not materially changed when adjusted for coffee intake or total caffeine intake, or when limited to glioblastoma only (Table S3). There was no significant heterogeneity when pooling results from the three cohorts (all *p*-heterogeneity >0.35).

Combined coffee and tea consumption and glioma risk

To directly update the prior analysis reported by Holick *et al.*, we also examined the association between combined coffee and tea intake and glioma risk in both age-adjusted and multivariable-adjusted models. In age-adjusted models, a similar trend to that reported

in the paper by Holick *et al.* was found, with a significant inverse association in pooled cohorts (p-trend = 0.03). Compared to those who drank <1 cup of tea or coffee per week, those who drank >4 cups of tea or coffee per week had significantly reduced risk of glioma in pooled cohorts (HR = 0.62, 95% CI: 0.41–0.93). In multivariable-adjusted models, however, we found no significant inverse association in pooled cohorts (p-trend = 0.56), or in women (p-trend = 0.83) or men (p-trend = 0.21) separately.

Caffeine consumption and glioma risk

Using cumulative average intake, caffeine intake had a suggestive but not statistically significant trend toward reduced risk of glioma with higher intake (HR for highest compared to lowest quintile = 0.82, 95% CI: 0.58–1.15, p-trend = 0.18 for women, HR = 0.66, 95% CI: 0.41–1.06, p-trend = 0.16 for men, HR = 0.76, 95% CI: 0.58–1.00, p-trend = 0.06 in pooled cohorts; Table 2). When 8-year lagged values and baseline values were used, these findings were attenuated (p-trend = 0.77 for pooled with 8-year lag, p-trend = 0.38 for pooled with baseline values). There was no significant heterogeneity when pooling results from the three cohorts (all p-heterogeneity >0.33).

Discussion

In three large prospective cohort studies, we observed a borderline statistically significant inverse association between tea consumption and glioma risk for women and men combined, but not among women or men separately. No significant relationship between coffee consumption and glioma risk was observed for women, men or in the pooled analysis.

The strengths of this study include its prospective design, repeated assessment of coffee and tea intake during adulthood and a large number of participants. Additionally, these food items have been shown to have high validity as assessed by FFQ, despite the data being generated by self-report.[29,30] The large number of participants allowed us to analyze a relatively large number of glioma cases. Our findings were also fairly robust to various statistical analyses. For example, we used 8-year lagged values of the various beverages analyzed and caffeine in order to determine if changes in behavior in the years immediately prior to diagnosis may have biased our findings. We also used intake of each beverage reported at baseline. Although in lagged analyses there was some attenuation of the inverse association between tea and glioma risk, in baseline analyses there was a significant inverse association (p-trend = 0.02). The results were also unchanged when mutually adjusted for the other beverage (tea, in the case of coffee intake; total coffee, in the case of tea intake). Although the data do not allow for meaningful adjustment by race/ethnicity or social class, given that the cohorts are largely white and have similar incomes, this restriction also precludes confounding by these factors. A major limitation of our study is the lack of information on types of tea (e.g., black *vs.* green tea) and brewing methods. Because some participants may have reported herbal or other noncaffeinated teas as tea, in the early years of assessment before separate questions were introduced, there may be some exposure misclassification that would not be expected to be differential by glioma status.

Tea intake was borderline inversely associated with glioma risk in overall and in analyses using baseline values only. In men and women separately, glioma risk decreased with

increasing tea consumption, but the CIs for each category were wide, most likely due to the overall smaller number of cases and the relatively low levels of intake. The observed inverse association between tea intake and glioma risk is consistent with two prior studies, one from the American NIH-AARP cohort and one in Iranian adults, which both found a decreased risk of glioma with increasing tea consumption.[18,19] One prospective cohort study found no association between tea consumption and glioma risk (HR = 1.07 for ≥3 cups/day compared to ≤4/days per week, 95% CI: 0.70–1.62), although the analysis was limited to green tea intake in a Japanese population and included only 157 cases of glioma.[33] Additionally, that study used tea consumption of <4 cups/week as the reference group, rather than nearly zero tea consumption as used as the reference category in the current study.

The previously published study from our cohorts[21] observed a nonsignificant inverse association between extreme categories of tea intake and glioma risk (RR = 0.71 for >8 cups/week compared to 0–1 cup/week, 95% CI: 0.45–1.12, *p*-trend = 0.24) and a significant inverse association across categories of combined tea and coffee intake and glioma risk (RR = 0.60 for ≥5 cups/day compared to 0–1 cup/day, 95% CI: 0.41–0.87, *p*-trend = 0.04). The current analysis demonstrated a similar finding, with significant reductions in glioma risk with higher consumption of combined coffee and tea in age-adjusted models in combined cohorts (*p*-trend = 0.03). In multivariable-adjusted models, however, there was no significant reduction in glioma risk with higher consumption of combined coffee and tea in the combined cohorts (*p*-trend = 0.56), or in women (*p*-trend = 0.83) or men (*p*-trend = 0.21) separately. Therefore, while the age-adjusted results are similar to the prior study, the results adjusted for BMI and smoking behavior were attenuated. The additional glioma cases and years of follow-up in the present study suggest that the previous observations may have lacked power to detect an association between tea and glioma, and that tea is driving the previously reported inverse association between combined tea and coffee intake and glioma risk.

The association of tea consumption with decreased glioma risk is biologically plausible. Tea contains polyphenols including epigallocatechin (EGC) gallate and EGC, flavonoids found in tea which have been linked to the prevention of cancers of various sites.[17] *In vitro*, EGC gallate and EGC can suppress breast cancer cell growth *via* induction of apoptosis.[34] Human and animal studies have observed markers of decreased oxidative stress in response to EGC gallate and EGC supplementation, and several studies have demonstrated that EGC and its derivatives can penetrate the blood brain barrier and enter the brain parenchyma.[35–38] Taken together, this evidence suggests that EGC gallate may possibly play a role in reducing the burden of neurodegenerative diseases.[38] These mechanisms could also explain the decreased glioma risk associated with tea consumption observed in this study. It is unclear whether the divergent results observed in men and women are due to biologic factors or lack of power in the HPFS; in most populations, age-adjusted rates of glioma are about 1.4-fold higher in men than women.[11]

On the other hand, we observed a null association between coffee intake and glioma risk in women and men, consistent with previous prospective cohort studies.[18,21] In 8-year lagged analyses, those who consumed >4 cups of caffeinated coffee per day had a statistically significantly increased risk of glioma compared to those who drank <1 cup per week (HR =

1.70, 95% CI: 1.17–2.47). The linear trend across categories was not statistically significant ($p = 0.16$), however, and no such finding was observed in nonlagged analyses, where the corresponding hazard ratio was 1.13 (95% CI: 0.75–1.70) and the linear trend across categories was also nonsignificant ($p = 0.56$). Taken together, the data suggest little or no association between coffee intake of any type and glioma risk. The largest prospective studies that suggested an inverse relationship between coffee consumption and glioma risk used combined coffee and tea intake.[21] The null association between coffee consumption and glioma is somewhat surprising given the previously observed inverse associations between coffee intake and other cancers and beneficial effects on cardiometabolic health; however, other studies have revealed that glioma risk factors appear to differ from those for other cancers, such as smoking.[1,3,6,7,10,11,39]

Conclusion

In three large prospective studies, we observed a borderline inverse association between cumulative tea consumption and risk of glioma in pooled cohorts, but not in women and men separately. No association was observed between coffee consumption and glioma risk. Additional analyses in prospective studies, including pooled analyses across cohorts in order to increase sample sizes, would be useful to further evaluate the association between tea consumption and glioma risk and especially whether the association is generalizable to both men and women and among diverse populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

The authors would like to thank the participants and staff of the Nurses' Health Study, Nurses' Health Study II and Health Professionals Follow-Up Study for their valuable contributions as well as the following state cancer registries for their help: AL, AZ, AR, CA, CO, CT, DE, FL, GA, ID, IL, IN, IA, KY, LA, ME, MD, MA, MI, NE, NH, NJ, NY, NC, ND, OH, OK, OR, PA, RI, SC, TN, TX, VA, WA, WY. The authors assume full responsibility for analyses and interpretation of these data. This research was supported by the following grants from the National Institutes of Health: T32 CA009001 (D.J.C.), UM1 CA186107, P01 CA87969 and UM1 CA167552.

Grant sponsor: National Institutes of Health; Grant numbers: P01 CA87969, T32 CA009001, UM1 CA167552, UM1 CA186107

Abbreviations:

BMI	body mass index
CI	confidence interval
EGC	epigallocatechin
FFQ	food frequency questionnaire
HPFS	Health Professionals Follow-Up Study
HR	hazard ratio

NHS	Nurses' Health Study
NHSII	Nurses' Health Study II

References

1. Cao S, Liu L, Yin X, et al. Coffee consumption and risk of prostate cancer: a meta-analysis of prospective cohort studies. Carcinogenesis 2014; 35:256–61. [PubMed: 24343360]
2. Bravi F, Tavani A, Bosetti C, et al. Coffee and the risk of hepatocellular carcinoma and chronic liver disease: a systematic review and meta-analysis of prospective studies. Eur J Cancer Prev 2017;26: 368–77. [PubMed: 27111112]
3. Zhou Q, Luo ML, Li H, et al. Coffee consumption and risk of endometrial cancer: a dose-response meta-analysis of prospective cohort studies. Sci Rep 2015;5:13410. [PubMed: 26302813]
4. Liu J, Shen B, Shi M, et al. Higher caffeinated coffee intake is associated with reduced malignant melanoma risk: a meta-analysis study. PLoS One 2016;11:e0147056. [PubMed: 26816289]
5. Wilson KM, Kasperzyk JL, Rider JR, et al. Coffee consumption and prostate cancer risk and progression in the Health Professionals Follow-up Study. J Natl Cancer Inst 2011;103:876–84. [PubMed: 21586702]
6. Schmit SL, Rennert HS, Rennert G, et al. Coffee consumption and the risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 2016;25:634–9. [PubMed: 27196095]
7. Salazar-Martinez E, Willett WC, Ascherio A, et al. Coffee consumption and risk for type 2 diabetes mellitus. Ann Intern Med 2004;140:1–8. [PubMed: 14706966]
8. Galeone C, Tavani A, Pelucchi C, et al. Coffee and tea intake and risk of head and neck cancer: pooled analysis in the international head and neck cancer epidemiology consortium. Cancer Epidemiol Biomarkers Prev 2010;19:1723–36. [PubMed: 20570908]
9. Sun CL, Yuan JM, Koh WP, et al. Green tea, black tea and breast cancer risk: a meta-analysis of epidemiological studies. Carcinogenesis 2006;27: 1310–5. [PubMed: 16311246]
10. Hashibe M, Galeone C, Buys SS, et al. Coffee, tea, caffeine intake, and the risk of cancer in the PLCO cohort. Br J Cancer 2015;113:809–16. [PubMed: 26291054]
11. Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults: a "state of the science" review. Neuro Oncol 2014;16:896–913. [PubMed: 24842956]
12. Hochberg F, Toniolo P, Cole P. Nonoccupational risk indicators of glioblastoma in adults. J Neurooncol 1990;8:55–60. [PubMed: 2319291]
13. Trinh K, Andrews L, Krause J, et al. Decaffeinated coffee and nicotine-free tobacco provide neuroprotection in Drosophila models of Parkinson's disease through an NRF2-dependent mechanism. J Neurosci 2010;30:5525–32. [PubMed: 20410106]
14. Kang SS, Han KS, Ku BM, et al. Caffeine-mediated inhibition of calcium release channel inositol 1,4,5-trisphosphate receptor subtype 3 blocks glioblastoma invasion and extends survival. Cancer Res 2010;70:1173–83. [PubMed: 20103623]
15. Lee KW, Im JY, Woo JM, et al. Neuroprotective and anti-inflammatory properties of a coffee component in the MPTP model of Parkinson's disease. Neurotherapeutics 2013;10:143–53. [PubMed: 23296837]
16. Lambert JD, Elias RJ. The antioxidant and pro-oxidant activities of green tea polyphenols: a role in cancer prevention. Arch Biochem Biophys 2010; 501:65–72. [PubMed: 20558130]
17. Yang CS, Wang H, Li GX, et al. Cancer prevention by tea: evidence from laboratory studies. Pharmacol Res 2011;64:113–22. [PubMed: 21397027]
18. Dubrow R, Darefsky AS, Freedman ND, et al. Coffee, tea, soda, and caffeine intake in relation to risk of adult glioma in the NIH-AARP Diet and Health Study. Cancer Causes Control 2012;23: 757–68. [PubMed: 22457000]
19. Malmir H, Shayanfar M, Mohammad-Shirazi M, et al. Tea and coffee consumption in relation to glioma: a case-control study. Eur J Nutr 2019;58: 103–11. [PubMed: 29124385]
20. Burch JD, Craib KJ, Choi BCK, et al. An exploratory case-control study of brain tumors in adults. J Natl Cancer Inst 1987;78:601–9. [PubMed: 3104645]

21. Holick CN, Smith SG, Giovannucci E, et al. Coffee, tea, caffeine intake, and risk of adult glioma in three prospective cohort studies. Cancer Epidemiol Biomarkers Prev 2010;19:39–47. [PubMed: 20056621]
22. Wolpin BM, Chan AT, Hartge P, et al. ABO blood group and the risk of pancreatic cancer. J Natl Cancer Inst 2009;101:424–31. [PubMed: 19276450]
23. Khalili H, Wolpin BM, Huang ES, et al. ABO blood group and risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 2011;20:1017–20. [PubMed: 21415359]
24. Belanger CF, Hennekens CH, Rosner B, et al. The nurses' health study. Am J Nurs 1978;78:1039–40. [PubMed: 248266]
25. Smith-Warner SA, Spiegelman D, Ritz J, et al. Methods for pooling results of epidemiologic studies: the pooling project of prospective studies of diet and cancer. Am J Epidemiol 2006;163:1053–64. [PubMed: 16624970]
26. Willett WC, Sampson L, Stampfer MJ, et al. Reproducibility and validity of a semiquantitative food frequency questionnaire. Am J Epidemiol 1985;122:51–65. [PubMed: 4014201]
27. Rimm EB, Giovannucci EL, Stampfer MJ, et al. Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. Am J Epidemiol 1992;135:1114–26. discussion 27–36. [PubMed: 1632423]
28. Willett WC, Sampson L, Browne ML, et al. The use of a self-administered questionnaire to assess diet four years in the past. Am J Epidemiol 1988; 127:188–99. [PubMed: 3337073]
29. Salvini S, Hunter DJ, Sampson L, et al. Food-based validation of a dietary questionnaire: the effects of week-to-week variation in food consumption. Int J Epidemiol 1989;18:858–67. [PubMed: 2621022]
30. Feskanich D, Rimm EB, Giovannucci EL, et al. Reproducibility and validity of food intake measurements from a semiquantitative food frequency questionnaire. J Am Diet Assoc 1993;93: 790–6. [PubMed: 8320406]
31. Stampfer MJ, Willett WC, Speizer FE, et al. Test of the National Death Index. Am J Epidemiol 1984;119:837–9. [PubMed: 6720679]
32. Willett WC. Nutritional epidemiologyed. New York: Oxford University Press, 1998.
33. Ogawa T, Sawada N, Iwasaki M, et al. Coffee and green tea consumption in relation to brain tumor risk in a Japanese population. Int J Cancer 2016; 139:2714–21. [PubMed: 27560973]
34. Vergote D, Cren-Olive C, Chopin V, et al. (−)-Epigallocatechin (EGC) of green tea induces apoptosis of human breast cancer cells but not of their normal counterparts. Breast Cancer Res Treat 2002;76:195–201. [PubMed: 12462380]
35. Yang CS, Wang X, Lu G, et al. Cancer prevention by tea: animal studies, molecular mechanisms and human relevance. Nat Rev Cancer 2009;9: 429–39. [PubMed: 19472429]
36. Unno K, Pervin M, Nakagawa A, et al. Blood-brain barrier permeability of green tea catechin metabolites and their neuritogenic activity in human neuroblastoma SH-SY5Y cells. Mol Nutr Food Res 2017;61:28891114.
37. Pervin M, Unno K, Nakagawa A, et al. Blood brain barrier permeability of (−)-epigallocatechin gallate, its proliferation-enhancing activity of human neuroblastoma SH-SY5Y cells, and its preventive effect on age-related cognitive dysfunction in mice. Biochem Biophys Rep 2017;9: 180–6. [PubMed: 28956003]
38. Pogacnik L, Pirc K, Palmela I, et al. Potential for brain accessibility and analysis of stability of selected flavonoids in relation to neuroprotection in vitro. Brain Res 2016;1651:17–26. [PubMed: 27639810]
39. Cote DJ, Downer MK, Smith TR, et al. Height, waist circumference, body mass index, and body somatotype across the life course and risk of glioma. Cancer causes & control : CCC 2018;29: 707–19. [PubMed: 29943102]

What's new?

Few lifestyle factors have been associated with glioma risk. Nonetheless, intake of coffee and tea, owing to potential neuroprotective and antioxidant effects, are of particular interest as lifestyle factors that defend against glioma. Here, the authors analyzed data from food frequency questionnaires and medical records from three large prospective cohort studies in the United States to assess the relationship between tea and coffee intake and glioma risk. Analyses show that tea intake has a marginal inverse association with glioma risk. Meanwhile, caffeinated or decaffeinated coffee intake and total coffee consumption had no impact on risk.

Table 1.

Age-adjusted demographics of study participants by cohort at baseline, 1980 for NHS, 1991 for NHSII and 1986 for HPFS[1]

	NHS (*n* = 92,389)		NHSII (*n* = 95,242)		HPFS (*n* = 49,885)	
	Incident glioma cases (*n* = 256)	**Overall cohort**	**Incident glioma cases (*n* = 87)**	**Overall cohort**	**Incident glioma cases (*n* = 211)**	**Overall cohort**
Age, years (mean ± SD)	49.0 (6.7)	46.8 (7.2)	37.9 (4.8)	36.6 (4.7)	55.7 (8.9)	54.7 (9.8)
BMI, kg/m^2 (mean ± SD)	24.7 (3.4)	24.4 (4.5)	24.7 (2.7)	24.6 (5.3)	25.8 (2.6)	25.5 (3.4)
Smoking status (%)						
Never smoker	47	43	62	65	46	44
Former smoker	31	28	28	22	41	42
Current smoker	22	29	9	12	7	10
Unknown	0	0	2	0	6	4
Coffee intake, cups/day (mean ± SD)	2.2 (1.4)	2.2 (1.9)	1.3 (1.0)	1.2 (1.5)	1.4 (1.1)	1.3 (1.6)
Decaffeinated coffee intake, cups/day (mean ± SD)	0.5 (0.7)	0.5 (1.1)	0.2 (0.3)	0.3 (0.8)	0.6 (0.7)	0.6 (1.1)
Total coffee intake, cups/day (mean ± SD)	2.7 (1.6)	2.7 (2.2)	1.5 (1.0)	1.5 (1.7)	1.9 (1.2)	1.9 (1.8)
Tea intake, cups/day (mean ± SD)	0.8 (0.9)	0.9 (1.3)	0.5 (0.6)	0.7 (1.1)	0.4 (0.5)	0.4 (0.8)
Caffeine intake, mg/day (mean ± SD)	387 (198)	397 (275)	234 (139)	244 (224)	248 (174)	239 (250)

[1]All values apart from age are age-adjusted to the distribution of the cohort.

Abbreviations: BMI, body mass index; HPFS, Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; SD, standard deviation.

Table 2.

Multivariable-adjusted risk of glioma in women (NHS, NHSII) and men (HPFS) by coffee, tea and caffeine, using Cox proportional hazard modeling, cumulative average consumption

			Women (n = 343)[1]			Men (n = 211)			Total (n = 554)[2]		
		Daily median intake[3]	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI
Caffeinated coffee cups[4]	<1/w	0, 0, 0	80	Ref.		70	Ref.		150	Ref.	
	≥1/w to ≤1.5/d	0.9, 0.8, 0.8	104	0.92	0.68–1.25	75	0.93	0.67–1.31	179	0.93	0.74–1.16
	>1.5 to ≤2.5/d	2.2, 2.5, 2.3	97	1.13	0.83–1.53	36	0.80	0.53–1.20	133	0.99	0.78–1.27
	>2.5 to ≤4/d	3.2, 3.2, 3.2	36	0.93	0.61–1.40	22	1.36	0.82–2.24	58	1.08	0.79–1.49
	>4/d	4.5, 4.5, 4.5	26	1.31	0.81–2.13	8	0.80	0.37–1.69	34	1.13	0.75–1.70
	p-trend				0.40			0.87			0.56
Decaffeinated coffee cups[4]	<1/w	0, 0, 0	195	Ref.		103	Ref.		298	Ref.	
	≥1/w to ≤1.5/d	0.6, 0.5, 0.6	113	1.14	0.90–1.46	80	0.96	0.72–1.30	193	1.07	0.88–1.29
	>1.5 to ≤3/d	2.3, 2.3, 2.3	31	1.25	0.84–1.86	25	1.13	0.72–1.76	56	1.19	0.89–1.61
	>3/d	4.1, 4.1, 4.3	4	0.86	0.32–2.35	3	0.60	0.19–1.91	7	0.74	0.35–1.57
	p-trend				0.60			0.84			0.79
Total coffee cups, caffeinated and decaffeinated[4]	<1/w	0, 0, 0	59	Ref.		41	Ref.		100	Ref.	
	≥1/w to ≤1.5/d	1.0, 0.9, 0.9	75	0.84	0.59–1.19	63	0.81	0.54–1.22	138	0.83	0.63–1.08
	>1.5 to ≤2.5/d	2.1, 2.1, 2.1	90	1.06	0.75–1.50	50	0.91	0.60–1.40	140	1.00	0.77–1.31
	>2.5 to ≤4/d	3.1, 3.0, 3.0	80	1.15	0.80–1.67	42	1.01	0.64–1.57	122	1.09	0.82–1.45
	>4/d	4.9, 4.6, 4.8	39	1.11	0.71–1.75	15	0.72	0.39–1.33	54	0.96	0.66–1.37
	p-trend				0.18			0.74			0.38
Tea cups[4]	<1/w	0, 0, 0	153	Ref.		118	Ref.		271	Ref.	
	≥1/w to ≤1.5/d	0.4, 0.4, 0.4	134	0.86	0.68–1.08	75	0.96	0.71–1.28	209	0.89	0.74–1.07
	>1.5 to ≤2/d	1.4, 1.5, 1.5	34	0.78	0.53–1.13	12	0.82	0.45–1.50	46	0.79	0.57–1.09
	>2/d	2.5, 2.5, 2.5	22	0.74	0.47–1.18	6	0.70	0.30–1.60	28	0.73	0.49–1.10
	p-trend				0.11			0.30			0.05
Caffeine quintiles[4]	1	66, 27, 16 mg	84	Ref.		50	Ref.		134	Ref.	
	2	175, 99, 77 mg	80	0.97	0.71–1.32	41	0.76	0.50–1.16	121	0.89	0.69–1.14
	3	287, 183, 168 mg	48	0.59	0.41–0.84	33	0.64	0.41–1.00	81	0.61	0.46–0.80
	4	396, 313, 300 mg	66	0.78	0.56–1.09	37	0.75	0.48–1.16	103	0.77	0.59–1.00

			Women (n = 343)[1]			Men (n = 211)			Total (n = 554)[2]		
		Daily median intake[3]	**Cases**	**Hazard ratio**	**95% CI**	**Cases**	**Hazard ratio**	**95% CI**	**Cases**	**Hazard ratio**	**95% CI**
	5	643, 485, 522 mg	65	0.82	0.58–1.15	31	0.66	0.41–1.06	96	0.76	0.58–1.00
	p-trend				0.18			0.16			0.06

[1]Obtained *via* meta-analysis of NHS and NHSII cohorts using the fixed effect model.

[2]Obtained *via* meta-analysis of NHS, NHSII and HPFS cohorts using the fixed effect model.

[3]Daily median intake by category for NHS, NHSII and HPFS, respectively.

[4]Adjusted for age, total caloric intake (quintiles), BMI (<25 kg/m^2 *vs.* 25–29.9 kg/m^2 *vs.* ≥30 kg/m^2 *vs.* missing) and smoking status (never *vs.* past *vs.* current *vs.* missing).

Abbreviations: d, day; HPFS, Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; w, week.

Int J Cancer. Author manuscript; available in PMC 2021 May 01.

Table 3.

Multivariable-adjusted risk of glioma in women (NHS, NHSII), and men (HPFS) by coffee, tea and caffeine consumption, using Cox proportional hazard modeling, 8-year lagged values

			Women (n = 267)[1]			Men (n = 156)			Total (n = 423)[2]		
		Daily median intake[3]	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI
Caffeinated coffee cups[4]	<1/w	0, 0, 0	59	Ref.		45	Ref.		104	Ref.	
	≥1/w to ≤1.5/d	0.9, 0.8, 0.8	77	1.09	0.76–1.58	57	1.28	0.86–1.91	134	1.17	0.90–1.54
	>1.5 to ≤2.5/d	2.3, 2.5, 2.5	69	1.07	0.74–1.55	26	0.94	0.57–1.54	95	1.02	0.76–1.38
	>2.5 to ≤4/d	3.2, 3.4, 3.3	29	1.20	0.74–1.95	15	2.00	1.08–3.69	44	1.46	1.00–2.14
	>4/d	4.5, 4.5, 4.5	33	1.65	1.04–2.61	13	1.80	0.94–3.43	46	1.70	1.17–2.47
	p-trend				0.16			0.13			0.16
Decaffeinated coffee cups[4]	<1/w	0, 0, 0	156	Ref.		89	Ref.		245	Ref.	
	≥1/w to ≤1.5/d	0.6, 0.5, 0.6	77	1.08	0.81–1.44	45	0.71	0.49–1.02	122	0.92	0.74–1.16
	>1.5 to ≤3/d	2.5, 2.5, 2.5	28	1.24	0.82–1.88	20	1.00	0.61–1.65	48	1.14	0.83–1.56
	>3/d	4.5, 4.5, 4.5	6	1.21	0.53–2.78	2	0.42	0.10–1.73	8	0.92	0.45–1.89
	p-trend				0.39			0.42			0.39
Total coffee cups,caffeinated and decaffeinated[4]	<1/w	0, 0, 0	40	Ref.		29	Ref.		69	Ref.	
	≥1/w to ≤1.5/d	1.0, 0.9, 0.9	58	1.13	0.74–1.74	47	0.99	0.61–1.59	105	1.07	0.77–1.46
	>1.5 to ≤2.5/d	2.2, 2.3, 2.2	64	1.21	0.78–1.87	29	0.86	0.51–1.46	93	1.05	0.75–1.47
	>2.5 to ≤4/d	3.1, 3.0, 3.0	59	1.34	0.85–2.11	33	1.25	0.75–2.10	92	1.30	0.92–1.83
	>4/d	4.9, 4.6, 4.8	46	1.65	1.03–2.64	18	1.16	0.62–2.15	64	1.45	1.00–2.11
	p-trend				0.08			0.45			0.08
Tea cups[4]	<1/w	0, 0, 0	122	Ref.		104	Ref.		226	Ref.	
	≥1/w to ≤1.5/d	0.5, 0.4, 0.4	100	0.82	0.62–1.07	42	0.96	0.65–1.42	142	0.86	0.69–1.07
	>1.5 to ≤2/d	1.5, 1.5, 1.5	20	0.60	0.37–0.97	6	1.04	0.44–2.42	26	0.68	0.45–1.04
	>2/d	2.5, 2.5, 2.5	25	0.83	0.53–1.28	4	0.61	0.22–1.69	29	0.79	0.53–1.18
	p-trend				0.12			0.43			0.12
Caffeine quintiles[4]	1	68, 24, 14 mg	59	Ref.		27	Ref.		86	Ref.	
	2	184, 96, 76 mg	56	0.98	0.68–1.42	36	1.29	0.77–2.14	92	1.08	0.80–1.45
	3	309, 182, 171 mg	46	0.82	0.55–1.21	31	1.23	0.73–2.07	77	0.94	0.69–1.29
	4	415, 331, 314 mg	52	0.91	0.62–1.33	30	1.20	0.70–2.04	82	1.00	0.73–1.36

			Women (n = 267)[1]			Men (n = 156)			Total (n = 423)[2]		
		Daily median intake[3]	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI	Cases	Hazard ratio	95% CI
	5	681, 513, 545 mg	54	0.96	0.66–1.42	32	1.37	0.81–2.34	86	1.09	0.80–1.48
	p-trend				0.81			0.40			0.77

[1]Obtained *via* meta-analysis of NHS and NHSII cohorts using the fixed effect model

[2]Obtained *via* meta-analysis of NHS, NHSII and HPFS cohorts using the fixed effect model.

[3]Daily median intake by category for NHS, NHSII and HPFS, respectively.

[4]Adjusted for age, total caloric intake (quintiles), BMI (<25 kg/m^2 *vs.* 25–29.9 kg/m^2 *vs.* ≥30 kg/m^2 *vs.* missing) and smoking status (never *vs.* past *vs.* current *vs.* missing).

Abbreviations: d, day; HPFS, Health Professionals Follow-Up Study; NHS, Nurses' Health Study; NHSII, Nurses' Health Study II; w, week.