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Research Article

Quantification of Superficial Cerebral Veins with AI After Tea via Susceptibility-Weighted Imaging and Exploration of Possible Neuroprotective Mechanisms from Tea

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Abstract

Aim: The vein serves as the downstream outflow channel of the artery and is also a component of the perivascular space (PVS) around the vein of the glymphatic system (GS). The acute effect of tea on superficial cerebral veins (SCVs) in the human cerebral cortex was evaluated with susceptibility-weighted imaging (SWI) *in vivo* to explore the possible mechanism of tea neuroprotection.

Methods: 35 participants aged 22-71 with normal cognition were prospective recruited. About one hour after drinking purified water, Pu-erh tea, oolong tea and green tea separately, Magnetic Resonance (MR)-SWI data of the subject's brain were collected and imported into a deep learning algorithm model based on SWI. SCVs in cerebral hemispheres were automatically recognized and the quantitative data were collected for statistical analysis.

Results: All subjects exhibited no adverse reactions following tea consumption. Compared with drinking purified water, after drinking Pu-erh tea, or oolong tea, or green tea, the subjects' SCVs were significantly dilated with a significant increase in the number of visible SCVs ($p = 0.000 \sim 0.026$, $t = -5.871 \sim -2.385$, $df = 16\text{-}24$, t test). Whether drinking tea or not, males had significantly more visible SCVs than females ($p = 0.001\text{-}0.007$, nonnormal distribution, Mann–Whitney U test). People who eat fish regularly, after drinking oolong tea, showed significantly more SCVs in the left cerebral hemisphere compared to those who did not eat fish ($p = 0.011$, Kruskal–Wallis test). Regular moderate drinkers, after drinking oolong tea, showed significantly more SCVs in the right cerebral hemisphere compared to non-drinkers ($p = 0.015$, Kruskal–Wallis test). might serve as an effective method

Conclusions: Drinking tea might increase volume flow of SCVs in the cortex, indicating that the active substances in tea might increase the reflux of SCVs. Tea consumption might serve as an effective method to clean the microcirculation system of the human brain. The effects of tea intake might be relevant to mechanisms of CNS protection.

Keywords: Magnetic Resonance Imaging (MRI); Susceptibility-weighted Imaging (SWI); Tea; Superficial Cerebral Veins (SCVs); Image Segmentation Algorithm; Neuroprotection

Abbreviations

AD: Alzheimer's Disease; PD: Parkinson's Disease; GS: Glymphatic System; CSF: Cerebrospinal Fluid; IPAD: Intramural Periarterial Drainage; ISF: Interstitial Fluid; PVS: Perivascular Space; Aβ: Amyloid Beta; P-tau: Phospho-Tau Proteins; MRI: Magnetic Resonance Imaging; SWI: Susceptibility-weighted Imaging; SCVs: Superficial Cerebral Veins; MMSE: Mini-mental State Examination; MinIP: Minimum Intensity Projection; ANOVA: One-Way Analysis of Variance; CNS: Central Nervous System

Introduction

Aging is accompanied by a reduction in the cerebral microvascular network, oxidative stress, mitochondrial dysfunction and the accumulation of toxic proteins, leading to the gradual loss of neurons and deterioration of brain function [1-3]. Therefore, aging is the most significant risk factor for neurodegenerative diseases (such as Alzheimer's disease (AD)), with cognitive impairment as the main symptom [3]. Increasing evidence has suggested that certain diets, such as the currently recognized Mediterranean diet, could reduce the risk of dementia [4,5]. In addition, research on the potential reduction in dementia risk caused by tea has attracted widespread attention [6-10]. Currently, there is no research on whether drinking tea aids in the elimination of toxic waste from the brain.

To determine whether tea plays a role in reducing the accumulation of toxic proteins in the brain, researchers need to observe whether tea causes changes in the structure and function of the brain waste excretion system.

In 2012, Iliff., *et al*. first confirmed the metabolic waste clearance system in the brain, the glymphatic system (GS): cerebrospinal fluid (CSF) enters the brain through intramural periarterial drainage (IPAD), then converges into the brain parenchyma interstitial fluid (ISF) and ultimately transfers to the perivascular space (PVS) around the vein, transferring solutes and brain waste to the meningeal lymphatic system [11]. The impairment of GS function may lead to the accumulation of toxic proteins in the brain, such as amyloid beta (Aβ) and phospho-tau (P-tau) proteins, which are among the pathophysiological mechanisms that mediate neurodegenerative diseases and accelerate their progression [12,13]. These toxic proteins are closely related to advanced functions such as cognition, execution, and memory in patients [12,13]. The arterial branches and venous network in brain tissue are important communication channels upstream and downstream of the GS, theoretically providing kinetic energy for clearing the system. Therefore, observing the changes in cerebral arterial perfusion and veins caused by drinking tea *in vivo* may provide important information for explaining the pathological and physiological mechanisms underlying the impact of tea on cognitive function.

A magnetic resonance imaging (MRI) study revealed that the intake of tea polyphenols increased cerebral blood flow, supporting the cerebral vascular mechanism of tea from an arterial perspective [8].

MR susceptibility-weighted imaging (SWI) breaks down the barrier of *in vivo* visualization of the brain venous network [14], which is closely related to the GS. In our previous research, we established a deep learning neural network image segmentation model for automatic recognition of the superficial cerebral veins (SCVs) on the basis of SWI images [15,16]. The model was used to obtain the quantitative value of the cerebral hemisphere SCVs of 144 volunteers in axial sections at the level of the corpus callosum [15]. The analysis revealed sex differences in the quantitative value of the SCVs in the brain in the observed slices, and the quantitative value of the SCVs in men was greater than that in women. The cognition of males is greater than that of females. The quantitative value of SCVs is positively correlated with cognition [15]. Daily tea consumption may have a positive impact on the quantitative features of SCVs in the young group [16]. Therefore, we speculate that evaluating the blood circulation mechanism of the neuroprotective effects of tea via the use of the quantitative value of the SCVs via SWI is possible. Moreover, observing the acute effects of tea on SCVs may provide valuable information for dietary choices that delay human cognitive decline.

In this study, MR-SWI and anatomical imaging data were obtained approximately 1 hour after the participants consumed warm purified water and three types of tea, respectively, from subjects without cognitive impairment aged 22--71 years. The acute effects of tea on SCVs in the entire cerebral hemisphere of the human brain were observed via MR-SWI *in vivo* to explore the possible mechanisms and evaluate the markers underlying the impact of tea on brain GS and neuroprotection.

Methods

This study adopted a prospective within-subjects design and was approved by the Ethics Committee of the hospital responsible for the project: Guangzhou First People's Hospital (K-2019-166-01). The medical examinations related to this study were conducted with the written informed consent of the participants in accordance with the Helsinki Declaration (revised in 2013).

Participants

Participants in this study were recruited from the community population.

The inclusion criteria were as follows: (1) Participants agreed to the MR examination and had no contraindications to the MR examination. (2) Population without cognitive impairment: Mini-mental State Examination (MMSE) neuropsychological scale examination score≥ 27 points. (3) Regular tea drinkers should avoid drinking coffee and non-tea soft drinks containing caffeine. (4) The subject's native language was Chinese, and the subject agreed to long-term follow-up without visual or auditory impairments. They are generally in good condition. (5) Female subjects who were not pregnant or lactating.

The exclusion criteria were as follows: (1) Neurological disorders that can lead to cognitive decline, such as AD, PD, vascular dementia, Huntington's disease, positive pressure hydrocephalus, brain tumors, progressive supranuclear palsy, epilepsy, subdural hematoma, multiple sclerosis, brain trauma or other structural abnormalities that cause neurological damage. Other systemic diseases that can cause cognitive decline, such as Hashimoto's encephalopathy, metabolic encephalopathy, paralytic dementia, anemia, hepatic encephalopathy, renal encephalopathy, etc. (2) A history of severe depression, bipolar disorder, schizophrenia, and other mental illnesses. (3) Patients who had a history of alcohol or drug abuse/addiction in the past two years. (4) Any other systemic disease or uncertain condition that prevents the completion of the project. (5) The magnetic resonance sequence is incomplete, or the image quality does not meet the standard.

With α set at 0.05, power at 0.95, and effect size at 0.5, the total sample size calculated by G*Power3.1.9.7 (https://stats.oarc.ucla.edu/other/gpower/) was 34. After confirming that the score of the subject was within the normal range through the MMSE test, basic information was collected, including sex, age, years of education, occupation, dietary habits (drinking tea, coffee, smoking, drinking alcohol, eating fish, etc.), history of chronic diseases, history of trauma, history of poisoning, etc. Finally, 35 subjects were included, including 18 males and 17 females aged 22-71 (49.51 ± 14.613) years, with a duration of school education of 7-20 years and an average of 12.57 years.

Selection of tea types and tea beverage preparation

On the basis of the degree of tea fermentation and domestic tea consumption, 10 g of Pu-erh tea (Ripe Pu, fully fermented), oolong tea (semifermented), and green tea (unfermented) produced in Yunnan were selected and packaged separately. Ten grams of each of the abovementioned types of tea were soaked in 300 ml of naturally pure water at 100 °C for 15 minutes, and then the tea water was separated from the tea leaf and naturally cooled for 30 minutes (approximately 40 °C) for later use.

MR data acquisition

The subjects underwent four MR examinations, with each examination consisting of drinking pure water, Pu-erh tea, oolong tea, and green tea respectively in sequence, followed by a 30--minute rest period. After eliminating urination and defecation, they changed into examination gowns and underwent MR examination. The interval between two MR examinations should be at least 48 hours. Subjects only drank pure water and did not consume nerve-stimulating drinks, foods, or medications for 24 hours prior to the examination. They refrained from eating or drinking water for at least 4 hours before the examination.

After separately drinking 200 ml of approximately 40 °C purified water (control group), Pu-erh tea, oolong tea, or green tea water prepared as described above, the subjects sat quietly for 30 minutes and underwent four separate MR examinations of the following sequences. A Siemens Skyra 3.0T superconducting magnetic resonance instrument and a 32-channel head coil (Siemens Healthineers, Erlangen, Germany) were used to perform subsequent sequential scanning in the supine position.

- T1_mprage_3D_sag_p2: Repetition time/echo time/inversion time/flipping angle = 2530 ms/2.97 ms/1100 ms/7°, field of view = 250 mm × 250 mm, matrix = 256 × 256, thickness = 1.0 mm, slice oversampling = 33.3%, orientation in the sagittal position, slices = 176, final voxel size = 1 × 1 × 1 mm^3. Scan time = 4 minutes and 30 seconds.

- SWI_3D_tra_p2: Repetition time = 28 ms, echo time = 20 ms, flipping angle = 15°, field of view = 220 mm × 220 mm, matrix = 352 × 352, thickness = 1.0 mm, sliceoversampling = 11.1%, and orientation in the axis position. The final voxel size = 0.8 × 0.8 × 1 mm^3. Minimum intensity projection (MinIP) images were reconstructed with a thickness of 12 mm and a slice gap of 1 mm. Scan time = 6 minutes and 56 seconds.

The time for initiating SWI_3D_tra_p2 sequence in 35 subjects was 50–58 minutes after drinking the beverage.

Analysis of MR data

The steps for obtaining the SCVs values from the SWI data were the same as those used in previous research by the project team [15,16]. For further details, refer to the supplementary materials of the Manuscript, as shown in the flowchart in Figure 1.

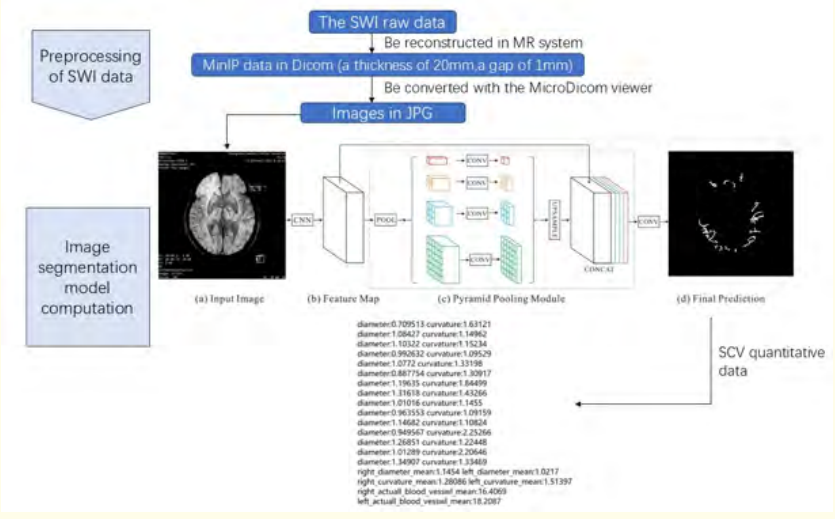

Figure 1: The steps for obtaining SCV quantification values in the flowchart.

MinIP images in JPG format, including all levels of the bilateral cerebral hemispheres of 35 subjects, were imported into the above image segmentation model. SCVs in the bilateral cerebral hemispheres were automatically recognized, and the vessel diameter, curvature, length, and number of SCVs were obtained. The quantitative data of detectable SCVs from each subject were collected for statistical analysis. The process of the image segmentation algorithm model for identifying the SCVs in the bilateral cerebral hemispheres after drinking pure water or tea is shown in Figure 2.

Statistical analysis

The collected data were input into the SPSS 25.0 statistical software package (version 25.0; IBM Corp., Armonk, NY, USA) for statistical analysis. Paired samples t tests (quantitative data) and nonparametric tests (nonnormal distribution or small sample size)

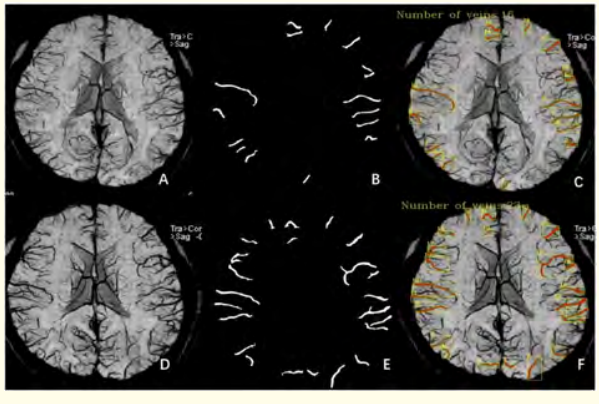

Figure 2: Segmentation and recognition steps of superficial cerebral vein images.

Figure A-C are images after drinking water, and figure D-F are images after drinking Pu-erh tea. Figure A,D: Original MinIP image. Figure B,E: Identified bilateral superficial cerebral veins. Figure C,F: Superimpose the recognition of superficial cerebral veins on the MinIP map, and automatically generate various quantified indexes of superficial cerebral veins.

were used to compare the differences in short-term detectable SCVs in the bilateral cerebral hemispheres caused by different beverages, as well as the effects of physiological and external factors on human detectable SCVs in the bilateral cerebral hemispheres. If the data followed a normal distribution with uniform variance, one-way analysis of variance (ANOVA) was used to compare the differences in the SCVs values among the different tea groups and age groups. Otherwise, the Kruskal–Wallis test was used. $P < 0.05$ was considered to indicate statistical significance with 95% Confidence Interval of the Difference.

Results

Basic clinical data of the studied population

The age groups of the subjects were a youth group (≤ 44 years old) with 13 cases (7 males and 6 females), a middle-aged group (45-59 years old) with 12 cases (6 males and 6 females), and an elderly group (≥ 60 years old) with 10 cases (5 males and 5 females). The distribution of subjects who consumed different beverages according to physiological factors (gender, age), occupation, diet, lifestyle habits, etc., is shown in Figure 3.

Thirty-five subjects consumed purified water and Pu-erh tea.

Acute changes in the SCV after drinking purified water or three types of tea

All participants reported no adverse symptoms before or after drinking water or tea.

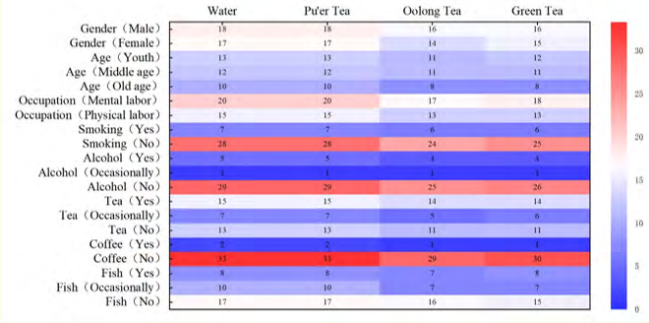

Figure 3: The distribution of subjects drinking different beverages in the experiment.

The quantitative SCVs data analysis indicated that 39 out of 54 pairs were normally distributed (Shapiro-Wilk test, p = 0.052-0.974, see Supplementary Materials) with homogeneity of variance (Levene's Test, F = 0.001-3.471, p = 0.067-0.977), thus paired t-tests were employed. Statistical results demonstrated that, compared to pure water, three types of tea significantly increased bilateral SCVs quantification values (p = 0.000-0.011, t = -2.677 -11.358, df = 34; Table 1). The Pu-erh tea group exhibited higher SCVs count, right curvature, and left length than the oolong tea group (p = 0.004-0.041, t = 2.120-3.106, df = 34; Table 1).

Item	Cerebral Hemisphere	Water (n = 35)	Pu-erh Tea (n = 35)	Oolong Tea (n = 35)	Green Tea (n = 35)
The number of SCV	Bilateral	868 ± 37	1221 ± 37**^{dd}	1126 ± 27**^{dd}	1184 ± 35**
	Right	432 ± 18	614 ± 18**^{dd}	562 ± 15**^{dd}	594 ± 18**
	Left	436 ± 19	607 ± 21**^{d}	564 ± 15**^{d}	589 ± 18**
The width of SCV	Right	1.10 ± 0.02	1.17 ± .0.01**	1.15 ± 0.01	1.16 ± 0.01**
	Left	1.12 ± 0.15		1.16 ± 0.01*	1.17 ± 0.01**
The curvature of SCV	Right	1.25 ± 0.02$^{\#\#}$	1.39 ± 0.02**^{d}	1.35 ± 0.02**$^{\#\#\#d}$	1.36 ± 0.02**$^{\#\#\#}$
	Left	1.15 ± 0.02$^{\#\#}$		1.21 ± 0.01**$^{\#\#\#}$	1.23 ± 0.02**$^{\#\#\#}$
The long of SCV	Right	15.14 ± 0.34	16.92 ± 0.32**	16.68 ± 0.28**	16.68 ± 0.25**
	Left	15.55 ± 0.32	17.08 ± 0.31**^{d}	16.33 ± 0.19*^{d}	16.72 ± 0.32**

Table 1: Intra-group differences of quantitative parameters of SCV in related factors (± SD) SEM.
SCV: superficial cerebral veins.

*P < 0.05,**P < 0.01（Compared to natural purified water group）; #P < 0.05, ##P < 0.01 (Comparison of left and right cerebral hemispheres); dP < 0.05, ddP < 0.01 (Comparison between different types of tea).

Kruskal-Wallis non-parametric tests were used in Non-Normally Distributed Groups (15/54 pairs, see Supplementary Materials). Results indicated no significant changes in left SCVs width after Pu-erh tea or right SCVs width after oolong tea, while other metrics showed significant increases. There was no significant difference in the quantitative values of SCVs between different tea groups (Table 2).

Sample 1-Sample 2	Test parameter	Std. Error	Cohens_d	Sig.	Adj. Sig.[a]
water-Pu-erh	The number of SCV- Bilateral	9.074	-0.6733	0.000	0.000
water-Pu-erh	The number of SCV- Right	9.074	-2.1215	0.000	0.000
water- Pu-erh	The width of SCV-Left	9.074	-0.5077	0.063	1.000
water-Pu-erh	The curvature of SCV-Right	9.074	-1.1524	0.000	0.000
water- Pu-erh	The curvature of SCV-Left	9.074	-1.0847	0.000	0.000
water- Pu-erh	The long of SCV-Right	9.074	-0.853	0.001	0.003
water-oolong	The width of SCV-Right	9.445	-0.6542	0.018	0.111
water-green	The long of SCV-Right	9.362	-0.6543	0.005	0.029
green- Pu-erh	The number of SCV- Bilateral	9.362	0.208	0.529	1.000
green- Pu-erh	The number of SCV- Right	9.362	0.2225	0.474	1.000
green- Pu-erh	The curvature of SCV-Left	9.362	0.2003	0.456	1.000
green- Pu-erh	The width of SCV-Left	9.362	-0.011	0.314	1.000
Oolong-Pu-erh	The curvature of SCV-Right	9.445	0.4112	0.101	.605
oolong- Pu-erh	The width of SCV-Left	9.445	0.0537	0.035	.209
oolong-green	The long of SCV-Left	9.722	-0.2306	0.252	1.000
Each row tests the null hypothesis that the Sample 1 and Sample 2 distributions are the same. Degree Of Freedom is 3. Asymptotic significances (2-sided tests) are displayed. The significance level is .05. a. Significance values have been adjusted by the Bonferroni correction for multiple tests.					

Table 2: Differences in quantitative parameters of SCV between non normal distribution groups.

The sample size of subjects with physiological factors and regular external factors was small, and only exploratory statistical analysis was performed as following. Significance values have been adjusted by the Bonferroni correction for multiple tests for Kruskal–Wallis test.

Observation of the effects of physiological factors on the SCV after tea consumption

The number of detectable SCVs was closely related to their diameter and length. When the effects of physiological and external factors were analyzed, the number of detectable SCVs in cerebral hemispheres was selected as the observation indicator. The results are shown in Tables 3 and Figures 4-5.

As age increased, the number of detectable SCVs in the purified water group decreased, but the difference was not significant (p = 0.187-0.314, Kruskal–Wallis test, df = 2, Table 3, Figure 4). Compared with drinking purified water, drinking tea significantly increased the number of detectable SCVs in the brain hemispheres for different age groups (p = 0.000-0.048, Kruskal–Wallis test, df = 3, Table 3, Figure 4) or sex groups (p = 0.000-0.046, Kruskal–Wallis test, df = 3, Table 3, Figure 5). Within the same age group, there was no significant difference in the detectable number of SCVs in the cerebral hemispheres caused by the three types of tea (p = 0.258-1 , Kruskal–Wallis test, df = 3, Table 3, Figure 4). There was no significant difference in the number of detectable SCVs of cerebral hemispheres of the same type of tea across the different age groups (p = 0.430-1, Kruskal–Wallis test, df = 3, Table 3, Figure 4).

Physiological Factor	Cerebral Hemisphere	Water (n = 35)	Pu-erh Tea (n = 35)	Oolong Tea (n = 30)	Green Tea (n = 31)
Youth	Bilateral	947 ± 57	1322 ± 54**	1172 ± 50 *	1233 ± 51**
	Right	470 ± 26	663 ± 21**	579 ± 35 *	615 ± 26**
	Left	477 ± 34	659 ± 30**	593 ± 35 *	618 ± 30**
Middle-aged	Bilateral	829 ± 67	1176 ± 69**	1047 ± 39*	1133 ± 80**
	Right	414 ± 35	595 ± 31**	513 ± 18*	567 ± 40**
	Left	414 ± 34	582 ± 43**	534 ± 27*	566 ± 42*
Old Age	Bilateral	811 ± 64	1143 ± 70**	1116 ± 44**	1165 ± 79**
	Right	403 ± 35	573 ± 40**	577 ± 29**	596 ± 47**
	Left	409 ± 31	570 ± 34**	539 ± 20**	570 ± 34**
Male	Bilateral	981 ± 43$^{\#\#}$	1310 ± 54$^{**\#\#}$	1177 ± 39$^{**\#\#}$	1276 ± 46$^{**\#}$
	Right	490 ± 22$^{\#\#}$	655 ± 26$^{**\#\#}$	576 ± 25*	632 ± 26**
	Left	491 ± 24$^{\#\#}$	655 ± 33$^{**\#\#}$	601 ± 20$^{**\#\#}$	644 ± 24$^{**\#\#}$
Female	Bilateral	747 ± 45$^{\#\#}$	1127 ± 39$^{**\#\#}$	1037 ± 42$^{**\#\#}$	1078 ± 56$^{**\#}$
	Right	370 ± 22$^{\#\#}$	570 ± 21$^{**\#\#}$	530 ± 21**	551 ± 30**
	Left	377 ± 24$^{\#\#}$	556 ± 21$^{**\#\#}$	506 ± 22$^{**\#\#}$	527 ± 27$^{**\#\#}$

Table 3: Number of cerebral hemispheres detectable SCV under different physiological factors (± SD).

SCV: superficial cerebral veins.

*P < 0.05,**P < 0.01 (Compared to natural purified water group); $^{\#}$P < 0.05,$^{\#\#}$P < 0.01 (Comparison of male and female).

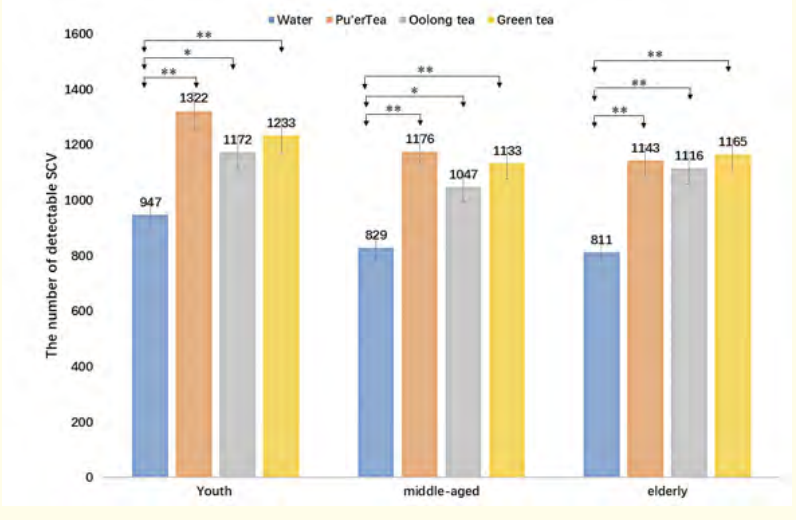

Figure 4: Changes in the number of detectable SCV in bilateral cerebral hemispheres after drinking purified water or tea at different age groups. *P < 0.05, **P < 0.01. For further details, refer to Table 3.

Drinking purified water or Pu-erh tea resulted in a greater detectable SCV in males than in females in the bilateral, right and left cerebral hemispheres (p = 0.001-0.007, Mann–WhitneyU test, Table 3, Figure 5). Drinking oolong tea or green tea resulted in a greater detectable SCV in males than in females in the bilateral and left cerebral hemispheres (p = 0.001-0.014, Mann–Whitney U test, Table 3). There was no significant difference in the number of detectable SCVs between the left and right cerebral hemispheres between the male and female groups (p = 0.078-0.224, Mann–Whitney U test). Compared with drinking purified water, after drinking three types of tea, both males and females presented a significant increase in the detectable SCVs (p = 0.47-0.000 , Kruskal–Wallis test, df = 3, Table 3, Figure 5). Within the same sex group, there was no significant difference in the number of detectable SCVs caused by the three types of tea (p = 0.178-1 , Kruskal–Wallis test, df = 3, Table 3, Figure 5).

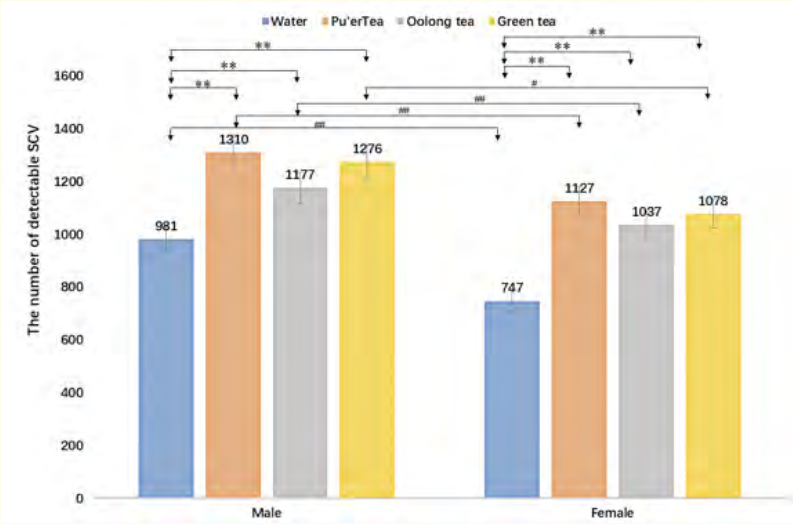

Figure 5: Changes in the number of SCVs displayed in bilateral cerebral hemispheres after drinking purified water or tea of different genders. *P < 0.05, **P < 0.01 (Compared to natural purified water group). #P < 0.05, ##P < 0.01 (Comparison of male and female). For further details, refer to Table 3.

Observation of the effects of regular external factors on the SCV in the cerebral hemisphere after tea intake

In this study, occupational information (mental and physical work) and lifestyle habits, such as smoking, drinking alcohol, drinking tea, drinking coffee, and eating fish, were collected from participants. Eating fish more than once a week was defined as regularly eating the fish. Smoking, drinking small alcohol, drinking tea, and drinking coffee every day were defined as regular lifestyle habits. Only two participants drank coffee according to the regular pattern, so drinking coffee was not included in the analysis. In addition, subjects who smoked or drank alcohol, tea or coffee but did not have daily habits were defined as having occasional habits; these subjects were not included in the analysis.

Compared with physical workers, mental workers who drank purified water or tea had a greater number of SCVs, but the difference was not significant (p = 0.066-0.842, Kruskal–Wallis test, Table 4).

A comparative analysis was conducted between subjects with regular lifestyle habits and those without the aforementioned lifestyle habits. The results are shown in Table 4. After drinking oolong tea, regular fish eaters presented more SCV in the left cerebral hemisphere than did those who did not eat fish (p = 0.011, Kruskal–Wallis test, Table 4, Figure 6). After drinking oolong tea, regular small drinkers presented a more number of SCVs in

External Factor (n)	Cerebral Hemisphere	Water	Pu-erh Tea	Oolong tea	Green Tea
Mental worker (20)	Bilateral	893 ± 49	1224 ± 54	1152 ± 50	1202 ± 51
	Right	452 ± 24	626 ± 26	589 ± 27	613 ± 28
	Left	441 ± 27	597 ± 30	563 ± 27	589 ± 26
physical worker (15)	Bilateral	821 ± 59	1207 ± 53	1060 ± 32	1139 ± 67
	Right	395 ± 28	590 ± 24	514 ± 15	559 ± 32
	Left	426 ± 31	617 ± 32	546 ± 22	580 ± 37
No smoking(28)	Bilateral	851 ± 42	1198 ± 42	1099 ± 37	1165 ± 45
	Right	420 ± 20	604 ± 21	551 ± 20	588 ± 24
	Left	431 ± 22	594 ± 23	547 ± 19	577 ± 23
Smoking(7)	Bilateral	935 ± 78	1312 ± 71	1161 ± 43	1242 ± 90
	Right	479 ± 43	653 ± 31	567 ± 26	614 ± 44
	Left	456 ± 40	659 ± 50	591 ± 36	628 ± 51
No alcohol (29)	Bilateral	856 ± 41	1229 ± 39	1086 ± 32	1174 ± 44
	Right	420 ± 20	613 ± 19	537 ± 17*	587 ± 23
	Left	435 ± 22	616 ± 23	549 ± 19	587 ± 23
Alcohol(5)	Bilateral	925 ± 85	1184 ± 11	1238 ± 77	1213 ± 96
	Right	485 ± 44	618 ± 57	642 ± 36*	625 ± 48
	Left	440 ± 44	566 ± 56	597 ± 43	589 ± 49
No tea(13)	Bilateral	850 ± 53	1194 ± 79	1101 ± 52	1230 ± 70
	Right	432 ± 27	604 ± 37	555 ± 28	620 ± 40
	Left	418 ± 28	590 ± 46	546 ± 29	610 ± 33
Tea(15)	Bilateral	856 ± 54	1217 ± 41	1137 ± 46	1182 ± 53
	Right	419 ± 27	608 ± 20	565 ± 25	591 ± 24
	Left	437 ± 28	608 ± 23	572 ± 25	591 ± 32
No fish(17)	Bilateral	842 ± 43	1157 ± 59	1087 ± 39	1151 ± 58
	Right	428 ± 22	584 ± 27	552 ± 23	580 ± 31
	Left	415 ± 22	573 ± 36	535 ± 20*	571 ± 28
Fish(8)	Bilateral	956 ± 60	1294 ± 66	1245 ± 74	1219 ± 70
	Right	479 ± 37	661 ± 38	597 ± 47	607 ± 36
	Left	477 ± 29	632 ± 36	648 ± 35*	611 ± 41

Table 4: Number of detectable SCV in the cerebral hemispheres under different external factors (± SD)

SCV: superficial cerebral veins.

*P < 0.05 (Comparison of fish and no fish, and comparison of alcohol and no alcohol).

the right cerebral hemisphere than non-drinkers did (p = 0.015, Kruskal–Wallis test; Table 4, Figure 7).

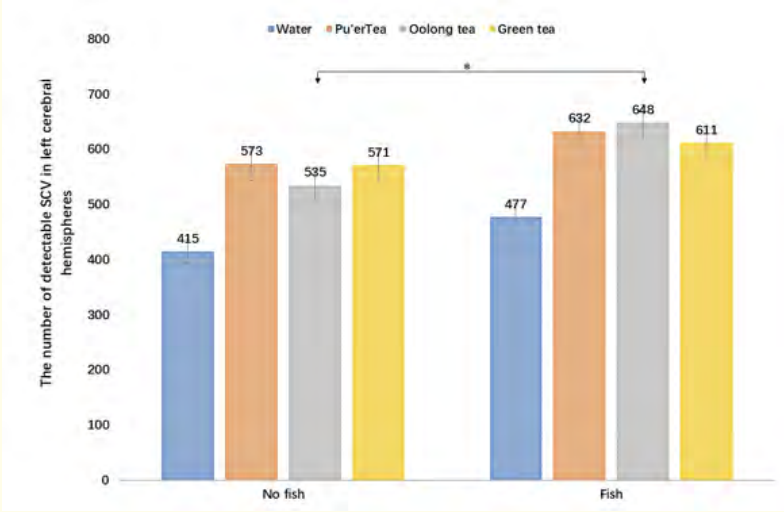

Figure 6: Changes in the number of detectable SCV in left cerebral hemispheres of individuals who regularly eat fish or not after drinking purified water or tea. *P < 0.05, **P < 0.01. For further details, refer to Table 4.

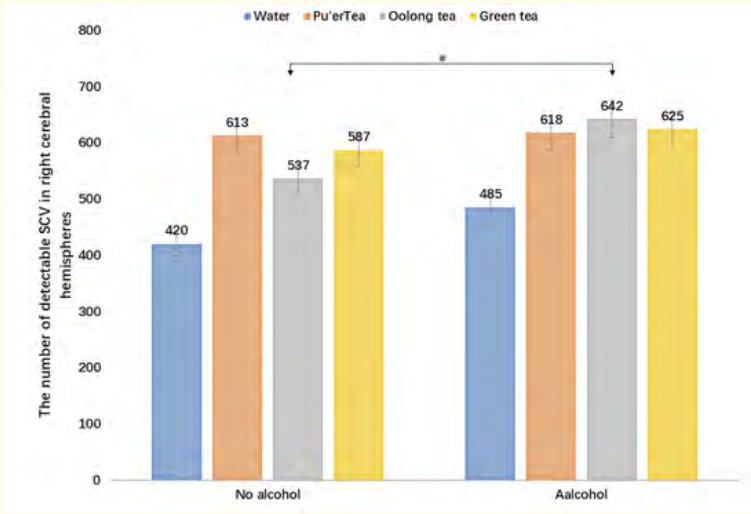

Figure 7: Changes in the number of detectable SCV in right cerebral hemispheres of moderate and regular drinkers or non-drinkers after drinking purified water or tea. *P < 0.05, **P < 0.01. For further details, refer to Table 4.

Discussion

A study showed that after caffeine was consumed for approximately 30 minutes, the plasma concentration reached its peak, with a half-life of approximately 2.5–5 hours [9]. On the basis of the above results, we speculate that the concentration of tea components in the plasma may approach the peak approximately one hour after tea is consumed. Therefore, magnetic resonance MR SWI_3D_tra_p2 sequence data collection was initiated 50 to 58 minutes after the subjects drank purified water or tea to observe changes in the SCVs in their cerebral hemispheres in this study. Compared with drinking purified water, drinking Pu-erh tea, oolong tea, or green tea significantly expanded the SCVs in both hemispheres of the subjects' brains, with significant increases in the diameter, curvature, and length of the SCVs, resulting in a

significant increase in the number of detectable SCVs. The SCVs curvature of the brain in the purified water group, oolong and green tea groups was greater in the right hemisphere than in the left hemisphere. The quantitative SCVs values were higher in the Pu-erh tea group compared to the oolong tea group.

Tea is produced via simple kneading and drying processes via the use of camellia sprouts and tender leaves as raw materials, where natural antioxidants are rarely destroyed or converted [17-20]. Tea is divided into six categories according to its degree of processing and fermentation, namely, green tea (unfermented), white tea (lightly fermented), yellow tea (lightly softened), oolong tea (semifermented), black tea (fully fermented), and dark tea (post fermented) [8]. Tea contains various bioactive compounds, including polyphenols, vitamins, minerals, lipids, proteins, and various metabolites from yeast and bacteria. These bioactive compounds, especially polyphenols, endow tea with various biological activities [7,18-21].

Over the past decade, numerous studies have demonstrated the neuroprotective effects of tea [7-10,18,19,22-24]. The bioactive substances in tea, such as catechins, which account for approximately 70–80% of tea polyphenols, exert anti-inflammatory effects by regulating the levels of inflammatory markers such as tumor necrosis factor alpha, nuclear factor kappa-B, interleukin 6, interleukin 1, nuclear factor B, and nitric oxide, blocking the excessive production of cytokines and inflammatory pathways [7-9]. Catechin increases the levels of antioxidants such as glutathione, superoxide dismutase, and catalase [6,7] and reduces lipid peroxidation, which may inhibit tau protein phosphorylation, Aβ aggregation, and the release of apoptotic proteins, as well as the ability to chelate metal ions and scavenge free radicals, demonstrating antioxidant effects [22,23]. They can also lower the levels of alpha synaptic nucleoprotein and increase dopamine levels [24]. All of these factors may delay the progression of neurodegeneration. In addition, the ability of catechins to cross the blood–brain barrier makes tea a neuroprotective candidate against neurodegenerative diseases [7].

At present, it is not possible to observe *in vivo* the pathways involved in antioxidant, anti-inflammatory, antiapoptotic, neuronal activation, and neuroprotective effects in humans after they consume tea. Some studies using MR arterial spin labelling imaging have revealed an increase in cerebral blood flow within a few hours after polyphenol intake, suggesting an immediate effect of polyphenols [8]. The visualization of veins in SWI is influenced by multiple factors, including technical parameters, changes in venous blood flow due to local hemo-dynamics, the content of deoxyhemoglobin in veins, artifact interference, and post-processing strategies [14]. In this study, data from all participants were acquired using the same MR imaging system with identical parameters and analyzed by the same AI model, ensuring stable image quality. The quantitative values of SCVs in the brain were compared within the same participant after consuming different beverages. Therefore, the primary factor affecting venous visualization changes in this study is attributed to variations in venous blood flow. Our research results indicated a significant increase in venous blood in the SCVs. This result validated the immediate effect of tea on increasing cerebral arterial blood flow perfusion from the perspective of tea-induced increases in venous blood flow.

Despite genetic predisposition, the degeneration of the central nervous system (CNS) is a slow process [25]. Therefore, enhancing the antioxidant capacity and maintaining redox balance in the brain microenvironment through daily dietary interventions should be one of the key strategies to delay neurodegenerative disorders. Additionally, efficient transport and clearance of harmful metabolic waste in the brain are critical for ensuring homeostasis and preserving normal CNS function.

Since 2012, interdisciplinary research has revealed that the GS is a perivascular network that connects cerebrospinal fluid with lymphatic fluid in the meninges through the interstitium and is a key foundation for controlling solute transport and waste clearance processes in the brain [11,12]. The GS consists of three key structures include the inflow pathway of the PVS around the arteries to the deeper brain regions, the brain parenchyma ISF, the outflow pathway of the PVS around the veins, and the aquaporin-4 channels between the ISF and perivascular spaces in the astrocytic end feet [11,12]. The GS is one of the main pathways for clearing extracellular metabolites of neurons, including Aβ [11], p-tau protein [26], and lactate [27]. In addition, the GS contributes to the global distribution of several important molecules in the brain, such as glucose, amino acids, lipids, growth factors, and neuromodulators [28].

In recent years, studies have proposed an integrated concept of central nervous system (CNS) hydrodynamic regulation [29-31]. The "neuro-fluids" – comprising arterial blood, venous blood, cerebrospinal fluid (CSF), and interstitial fluid (ISF) – form four interconnected extracellular fluid compartments. Structural or functional alterations in any of these compartments may disrupt cerebral hydrodynamics, potentially elevating intracranial pressure, impairing neuronal respiration, and hindering metabolic waste clearance [29-31].

This study may suggest that tea consumption increases SCVs blood volume. We hypothesize that the elevated venous blood volume simultaneously enhances the kinetic energy of "neuro-fluid" outflow in the perivenous spaces and local regions, thereby facilitating the efficient transport and clearance of harmful metabolic waste in the brain. This mechanism helps maintain homeostasis and supports normal CNS function. With repeated long-term tea intake, the CNS hydrodynamic regulatory mechanisms may become more efficient due to the sustained increase in "neuro-fluid" outflow kinetic energy, and the chronic vascular activation induced by tea could also yield long-term positive effects.

This study explored the influence of physiological factors on the effects of tea consumption on SCVs. The results may suggest that aging is also accompanied by a reduction in the cerebral venous network. After tea consumption, SCVs blood flow significantly increased across different age groups, with Pu-erh tea exhibiting a greater effect than oolong tea. These findings may indicate that Pu-erh tea contains a higher quantity of bioactive substances leading to increased venous blood content compared to oolong tea, which warrants further nutritional research for confirmation.

In this study, following results were also observed. Whether drinking tea or pure water, the number of visible SCVs in males was significantly higher than in females. After drinking tea, a significant increase in the number of SCVs was found in male and female individuals. Our previous research on natural populations revealed that men had better cognition than women, and men had more SCVs than women [15,16]. The number of SCVs was positively correlated with the human cognitive level [15,16]. For daily tea drinkers in the youth group, the number of SCVs in both hemispheres were negatively correlated with total tau protein (T-tau), and the curvature of SCVs in the right hemisphere was negatively correlated with phospho-tau181(P-tau181) and T-tau concentrations in venous blood [16]. There was a negative correlation between the T-tau concentration in venous blood and daily tea consumption [16].

On the basis of the above results, we further hypothesize that the increase in venous blood may facilitate fluid extravasation from the venous lumen into to the PVS around the veins, which is beneficial for toxin clearance via lymphatic outflow pathway, reducing toxin levels in the blood, and providing certain protection for neurocognitive function.

This study conducted an exploratory analysis of the influence of non-physiological factors on the effects of tea on SCVs. The results indicated that, compared to non-fish consumers, oolong tea consumption might significantly increase the number of SCVs in the left cerebral hemisphere of regular fish consumers. Similarly, regular low-level alcohol drinkers showed a significant increase in SCVs in the right cerebral hemisphere after drinking oolong tea compared to non-drinkers. However, due to the small sample size, the impact of different types of fish could not be analyzed. Further studies with larger sample sizes and long-term follow-up are warranted.

Limitations

This study is the first to use an artificial intelligence image segmentation model to observe changes in the SCVs in vivo and explore the possible mechanisms of the neuroprotective effects of tea on the CNS. However, the following limitations exist. First, on the basis of the increase in the number of detectable SCVs, it was speculated that an increase in SCVs blood may increase the efficiency of the exclusion pathway in GS. This inference is based on the existing understanding of the GS and requires microscopic physiological observation and verification. Second, the research results cannot be used to determine the tea ingredients that cause an increase in venous blood flow, which needs further observation and research by joint nutritionists. Third, owing to limitations in detection technology, this study cannot simultaneously monitor the IPAD pathway and ISF. Therefore, it is not possible to evaluate the relative contribution of increased SCVs blood flow to brain fluid drainage. It is necessary to develop better exploration tools to comprehensively study these lymphatic drainage systems and their interactions. Fourth, the sample size of this study was small,

and the observed phenomena still need to be further validated by expanding the sample size. Fifth, the neuroprotective mechanism of tea on veins still requires further longitudinal research and confirmation in a large sample of long-term tea drinkers and non-tea drinkers, as well as their relationship with cognition.

Summary and Conclusions

The findings of this study, along with our project team's previous research [15,16], suggest that there may be gender differences in the cerebral SCVs system, with males exhibiting greater SCVs blood flow than females, which is positively correlated with cognition. With aging, SCVs blood flow decreases. Tea consumption might increase SCVs blood flow. Drinking tea might serve as an effective method to cleanse the brain's microcirculatory system, thereby potentially improving the efficiency of waste clearance by the GS. Thus, the effects of tea intake might be relevant to mechanisms of CNS protection.

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