Can South Asian Diet Leads to Healthy Brain Ageing

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Introduction

Traditional South Asian diet is rich in pulses, cereals, fruits and vegetables. To the best of our knowledge this is the first brain autopsy study that has investigated the possible protective effect of South Asian diet on ageing cytoskeletal pathologies.

Materials & Methods

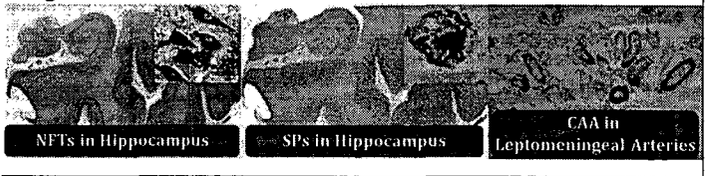
- Human brain samples from 76 elderly subjects aged ≥50yrs (mean age 67·3yrs ± 10.0, mean ± S.D., male: female = 52:24, mean post mortem interval 17·3hours ± 14·2, mean ± S.D.) were used for this study.
- Atherosclerosis of the circle of Willis (CW) was graded in all samples based on degree of stenosis of the each component arteries and gross visual inspection as none, mild, moderate & severe (WHO, 1958).
- Among them, 50 brains aged ≥60yrs (mean age 72·1yrs ± 7·8, male: female = 29:21) were subjected to neuropathological diagnosis using histopathological / immunohistochemical techniques with three antibodies namely;
  - β amyloid– monoclonal antibody (1:200 dilution) from Novacastra™
  - Ubiquitin– monoclonal antibody (1:150 dilution) from Novacastra™ &
  - Phosphorylated tau– PHF–1 monoclonal antibody (1:50 dilution), a gift from Prof. Shankar.
- Based on NIA-AA criteria (2012), Alzheimer's disease (AD) related neuropathological changes [neurofibrillary tangles (NFTs), neuritic plaques (NPs) and senile plaques (SPs)] were identified, and counted in specific neuroanatomical regions; hippocampus, entorhinal cortex, superior frontal gyrus and midbrain at superior colliculus level using medium high power fields (200X magnification, Olympus U-CTR30-2 Trinocular objective tubes and 10X eye piece producing a visual field of 0.785mm²) (Purohit et al., 2011).
- Cerebral amyloid angiopathy (CAA) in leptomeningeal and cortical arteries of the specific neuroanatomical regions was graded semi quantitatively based on Greenberg and Vonsattel (1997) specifications and the average CAA grade was reported for each case.
- Other cerebrovascular changes such as white matter hyper intensities, spongiform cortex, dilated perivascular spaces & hippocampal cell loss in CA1 region stained with H & E were noted semi quantitatively as absent (none/rare) or present (minimum involvement at least in one region).
- An antimortem questionnaire was administrated to obtain the consumption pattern of the deceased via kin
- Pure black tea consumption as never, <1cup/week, 1cup/week, 2-3cups/week, 4-6cups/week, 1cup/day, 2-3cups/day & >2-3cups/day;
  [Ceylon black tea demonstrated greatest antioxidant activity and highest total content of antioxidants (186·6 mg/g) compared to other world black tea products, Yashin et al., 2011]
- Green-yellow vegetable consumption as <1time/week, 1-6times/week & ≥1time/day; and
- Fish consumption as no, <1time/week, 1-6times/week & ≥1time/day).

Statistical Analysis

- The relationship between black tea consumption pattern (≤2–3cups/day referred as "light tea drinkers" and >2–3cups/day referred as "heavy tea drinkers") and AD related lesions including square root values of NFTs count, SPs count and total CAA score was determined using two sample independent t–test.
- Binary logistic regression was used to find the relationship between cerebrovascular pathologies and consumption pattern (pure black tea, green-yellow vegetables and fish) of the deceased in addition to other risk factors such as genetic factors [apolipoprotein E *(ApoE)*, angiotensin converting enzyme *(ACE)*, methylenetetrahydrofolate reductase (*MTHFR)* and factor V Leiden *(FVL)*], past medical history (diabetes, high blood pressure or hypertension, high cholesterol, ischemic heart disease and stroke), and health habits (smoking and alcohol consumption). Due to the small sample size, each factor was individually tested controlling for age and sex.

Results

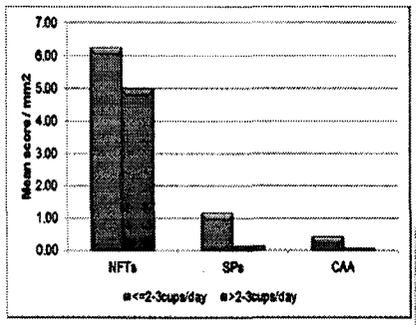
(i) Effects of frequent black tea consumption on AD related neuropathological changes



Regions	Lesion	Light tea drinkers mean counts/mm² (S.E.) (≤2-3cups/day)	Frequent tea drinkers mean counts/mm² (S.E.) (>2-3cups/day)	Two sample independent t test (P value)
Hippocampus	NFTs	4·69 (0·85)	3·22 (0·75)	0.279
	SPs	0·44 (0·18)	0·10 (0·10)	0.119
Entorhinal cortex	NFTs	2·78 (0·45)	2.66 (0·81)	0.887
	SPs	0·64 (0·21)	0·04 (0·04)	0.009*
Superior frontal gyrus	NFTs	0·24 (0·08)	0·10 (0·07)	0.303
	SPs	0·60 (0·20)	0·11 (0·11)	0.041*
Midbrain	NFTs	1·71 (0·31)	1·30 (0·36)	0.431
	SPs	0·14 (0·12)	0·05 (0·05)	0.588
All regions	NFTs	6·27 (0·88)	5·02 (0·92)	0.383
	SPs	1·17 (0·35)	0·16 (0·16)	0.014*
Cortical and leptomeningeal arteries	CAA	0·45 (0·15)	0·08 (0·08)	0.037*

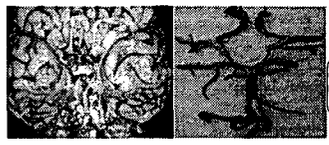
1st Neuropathological evidence possibly from Asia

- Mean age at death between light and heavy tea drinkers was also tested with Mann Whitney U test as these pathologies are age–dependent and the p value was not significant (>0·05).



Frequent Pure Black Tea consumption → Reduced Aβ accumulations/ depositions → Opens new avenue to investigate the anti plaque effect/ neuroprotective effect of Ceylon black tea on AD

(ii) Effects of moderate consumption of green-yellow vegetables on cerebral atherosclerosis

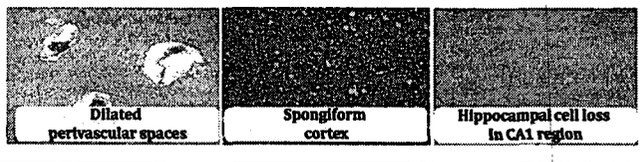


Atherosclerosis of the CW

Dichotomized variables	Sample size	Factors	P value	Odds Ratio	95% CI
Atherosclerosis of the CW					
None Vs. Mild, Moderate & Severe	76	Age	0·046*	1·10	1·00–1·22
		Apoe E3/E2 Genotype	0·028*	0·03	0·00–0·68
None & Mild Vs. Moderate &Severe		Age	0·057	1·05	1·00–1·10
		Hypertension	0·000**	15·06	3·27–69·31
		Diabetes	0·176	2·31	0·69–7·75
		High Cholesterol	0·172	3·55	0·58–21·93
		Ischemic Heart Disease	0·190	2·25	0·70–7·58
		Green-yellow Vegetables (1-6 Times/Week)	0·011*	0·17	0·04–0·67
None, Mild & Moderate Vs. Severe		Apoe E3/E4 Genotype	0·038*	4·48	1·09–18·44
		Hypertension	0·050*	5·68	1·00–32·18
		Sex (Male)	0·143	0·39	0·11–1·38
		Green-yellow Vegetables (1-6 Times/Week)	0·148	0·24	0·03–1·66

Binary logistic regression controlled for age and sex. P values <0.2 are only presented.

(iii) Effects of no fish consumption on cerebrovascular changes



Dichotomized variables	Sample size	Factors	P value	Odds Ratio	95% CI
Spongiform Cortex					
Present Vs. Absent	50	No Fish Consumption	0·012*	0·10	0·01–0·60
		Hypertension	0·188	2·89	0·59–13·99
Dilated Perivascular Spaces					
Present Vs. Absent	50	No Fish Consumption	0·019*	0·08	0·01–0·66
Hippocampal Cell Loss in CA1 Region					
Present Vs. Absent	50	Age	0·002**	1·18	1·06–1·31
		Sex (Male)	0·072	0·23	0·04–1·14
		MTHFR CT/ TT Genotype	0·141	0·12	0·01–2·03
		No Fish Consumption	0·038*	0·05	0·00–0·85
		Black Tea (<=2-3cups/day)	0·121	3·77	0·70–20·20

Binary logistic regression controlled for age and sex. P values <0.2 are only presented.

Conclusion

Despite methodological limitations, our findings revealed a possible protective effect between diet Ceylon Tea, Green-yellow vegetables; and both Alzheimer and cerebrovascular pathologies in aging brains that warrants future studies to ascertain healthy eating habits among the South Asian population.

References

1) Classification of Atherosclerotic lesions; a report of a study group. World Health Organ Tech Rep Ser 1958;57:1-20.
2) Montine TJ, Phelps CH, Beach TG, Bigio EH, Cairns NJ, Dickson DW, Duyckaerts C, Frosch MP, Masliah E, Mirra SS, Nelson PT, Schneider JA, Thal DR,
3) Trojanowski JQ, Vinters HV, Hyman BT; National Institute of Aging; Alzheimer's Association. (2012) National Institute on Aging-Alzheimer's Association guidelines for the neuropathological assessment of Alzheimer's disease: practical approach. Acta Neuropathol 123(1):1-11.
4) Purohit DP, Batheja NO, Sano M, Jashnani KD, Kalaria RN, Karumanuthy A, Kaur S, Shenoy AS, Van Dyk K, Schmeidler J, Perl DP (2011) Profile of Alzheimer's disease-related pathology in an aging urban population sample in India. J Alzheimers Dis 24(1):187–196.
5) Greenberg SM, Vonsattel JP (1997) Diagnosis of cerebral amyloid angiopathy: Sensitivity and specificity of cortical biopsy. Stroke 28(7):1418–1422.
6) Yashin A, Yashin Y, Nemzer B (2011) Determination of antioxidant activity in tea extracts, and their total antioxidant content. Am J Biomed Sci 3(4):322-335.

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Introduction: Traditional South Asian diet is rich in pulses, cereals, fruits and vegetables. To the best of our knowledge this is the first brain autopsy study that has investigated the possible protective effect of South Asian diet on ageing cytoskeletal pathologies.

Methods: Human brain samples from 76 subjects aged ≥50yrs were used to assess atherosclerosis of the circle of Willis (CW), and out of that 50 brains aged ≥60yrs were subjected to neuropathological diagnosis using histopathological/ immunohistochemical techniques. Alzheimer's disease (AD) related neuropathological changes were counted in specific neuroanatomical regions. Antimortem questionnaire was administrated to obtain the consumption pattern of pure black tea, green-yellow vegetable, and fish, of the deceased via kin.

Results: Frequent consumption of pure black tea ≥4cups/day showed a significant reduction in β-amyloid (Aβ) accumulations- senile plaque counts in the region of entorhinal cortex (p=0.009), superior frontal gyrus (p=0.041) and in all region (p=0.04) and the average cerebral amyloid angiopathy_ grades in cortical and leptomeningeal region (p=0.037) compared to decedents who had consumed lightly (≤2-3cups/day) with 2 sample independent t-test. Moderate consumption of green-yellow vegetables (1-6times/week) showed a significant negative association with moderate and severe atherosclerosis of CW with the odds of 0·17 [p=0·011, 95% confident level (CI) = 0·04–0·67] adjusted for age and sex. Cerebrovascular lesions: spongiform changes of neuropil [odds ratio (OR) =0·09; 95% CI 0·13–0·63; p=0·016)], dilated perivascular spaces (OR=0·05; 95% CI 0·00–0·65; p=0·022) and hippocampal CA1 cell loss (OR=0·05, 95% CI 0·00–0·85, p=0·038) were also found significantly low in cases who had not consumed fish adjusted for age and sex.

Conclusions Despite methodological limitations, our findings revealed a possible protective effect between diet and both Alzheimer and cerebrovascular pathologies in aging brains that warrants future studies to ascertain healthy eating habits among the South Asian population.

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