The effects of tea and caffeine on cerebral blood flow measured using Arterial Spin Labelling

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Introduction: Black tea contains moderate doses of caffeine (30 mg per cup), a neurostimulant that has been shown to reduce cerebral blood flow by acting as an adenosine receptor antagonist (1). Consumption of black tea and one of its major constituents, flavonoids have also been shown to improve dilatory responses of conduit arteries (2), and are associated with reduced cardiovascular disease, including stroke (3). Different tea components thus seem to exert different vascular effects. The overall effect of tea and caffeine on cerebral blood flow (CBF) remains to be elucidated in healthy humans. Thus the aim of this study was to observe any effects on global and regional CBF that may be driven by the presence of caffeine or other components in tea.

Methods: This study was approved by the University of Liverpool ethics committee. Twenty healthy males (mean age: 24.2 ± 4.0 years) took part after screening to ensure that their alcohol, tea and coffee consumption and BMI were within a predefined limit. This was a double blinded crossover study involving 4 single dose interventions: caffeine (184 mg), placebo (microcrystalline cellulose), tea (2820 mg black tea solids, equivalent to 6 cups of tea and containing approximately 184 mg of caffeine) and decaffeinated tea, each administered on a separate day. Subjects arrived fasted and were given a standardised breakfast prior to the first scan (pre-intervention scan). The intervention was then administered in capsule form and 1.5 hours later they were re-scanned with the same scan protocol (post-intervention scan). Scans included high resolution T1 weighted structural scans, and Arterial Spin Labelling using QUIPSS acquisition and PICORE labelling. Key ASL acquisition parameters were: 8 slices – repeated twice to cover the top half and bottom half of the brain with resolution of 3.5 x 3.5 x 6 mm, label delay time of 1400 ms, TE 19ms, TR 2000 ms and 75 control-label pairs. ASL images were analysed using in-house MATLAB routines assuming a single blood compartment model (4) to produce quantitative CBF maps. SPM8 was used to extract whole brain grey matter CBF and also to perform voxel based analyses comparing CBF maps pre and post each intervention. Analysis of variance (ANOVA) was used to determine the least square mean difference in grey matter CBF between each intervention and placebo, using MATLAB's statistical toolbox.

Results:

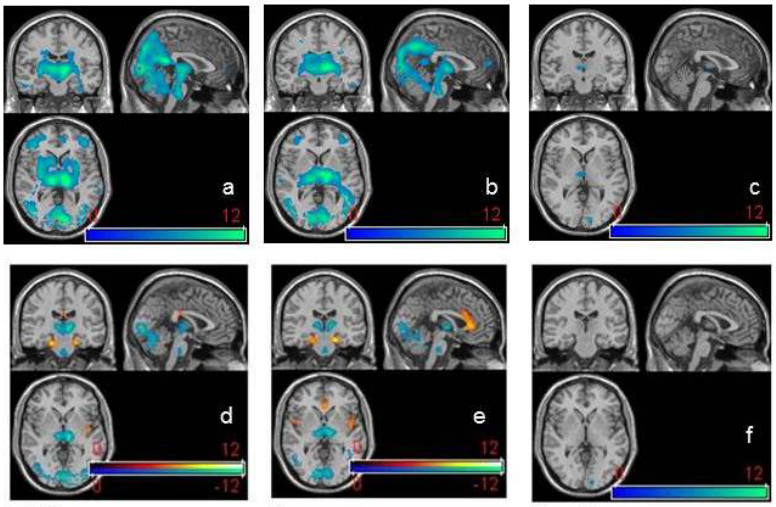

Figure 1 Row 1: Regions of significant CBF reduction following caffeine (a) tea (b) and decaffeinated tea (c). No regions of CBF increase were seen and no change was seen following placebo. Both caffeine and tea showed similar patterns of CBF response, whilst decaff tea showed minimal response. T-statistic maps are shown, thresholded to p<0.00001 uncorrected.

Figure 1 Row 2: Patterns of CBF response following global normalisation of each CBF image to 50ml/min/100ml. Specific bilateral regions of response become apparent in both caffeine (d) and tea (e). T-statistic maps, thresholded to p<0.00001 uncorrected.

Caffeine Tea Decaff

Comparisons	Lower 95% CI	Difference	Upper 95% CI
Tea-Placebo	-10.2	-8.1	-6.0
Caffeine-Placebo	-9.6	-7.5	-5.4
Decaff-Placebo	-3.7	-1.6	0.5

Table 1a: Least squares difference outputs between comparisons of the different interventions with placebo.

Intervention	Before	After
Tea	3.78±5.2 *	29.2±3.0 *
Caffeine	38.3±5.0 *	30.0±3.6 *
Decaff	37.5±4.2	35.8±3.8
Placebo	37.0±5.2	36.9±4.8

Table 1b: Descriptive statistics showing the mean +- SD CBF (ml/min/100ml) for each intervention in grey matter. (p<0.0001*).

Conclusions: We find highly significant global reduction in grey matter CBF following both caffeine and tea of 22 and 23% respectively (Table 1). However, decaffeinated tea did not show any significant change in CBF, suggesting that tea components other than caffeine do not influence CBF acutely. The effect of tea on CBF can be entirely accounted for by the presence of the high dose caffeine. This notion is supported by the similar regional effects on CBF for caffeine (Figure 1a) and tea (Figure 1b). Further analysis using global normalisation of the CBF maps (to remove the effect of global reductions in CBF) showed tighter bilateral regions of CBF response within the thalamic, parahippocampal and occipital regions. To our knowledge, regional CBF effects of caffeine have not previously been measured. These regional changes are in close agreement with findings of a previous study (5) that suggests the existence of adenosine receptors and other caffeine sensitive receptors (such as dopamine) in these areas. The bilateral nature of these changes suggest that we are sensitive to neuronal mechanisms. While tea has been shown to improve dilatory responses in large peripheral arteries, this study shows that there is no effect of tea on resting CBF. It can therefore be concluded that the effects of caffeine on CBF are not affected by other components in tea. This study does, however, not exclude different effects of tea and caffeine chronically consumed in moderate doses.

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