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Caffeine Ingested Under Natural Conditions Does Not Alter Taste Intensity

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MELA, D. J. *Caffeine ingested under natural conditions does not alter taste intensity*. PHARMACOL BIOCHEM BEHAV **34**(3) 483–485, 1989.—It has been reported that prolonged application of 10 micromolar (μM) caffeine (CAF) to the dorsal surface of the tongue may markedly enhance the perceived intensity of many taste stimuli, including NaCl and several noncarbohydrate sweeteners. The present study investigated the effect of oral CAF vs. placebo ingestion on perceived taste intensity. Ingestion of CAF (5.5 mg/kg) raised median salivary CAF levels to 19.8 μM at 50 minutes post-dose, when subjects evaluated the intensity of solutions of 5 noncarbohydrate sweeteners, 2 carbohydrate sweeteners, 2 bitter tastants, NaCl, citric acid, 2 odors, and a tone. Taste solutions were prepared using either 1) deionized water or 2) 10 μM CAF as the medium, and all stimuli were rated for intensity on a 9-point category scale. There was no effect of condition (CAF or placebo) or tastant medium on any response measure. The results suggest that perceptions of taste intensity are not appreciably altered under natural conditions of CAF ingestion and subsequent lingual adaptation to μM levels of CAF in saliva.

Caffeine Taste Sweeteners Saliva

SCHIFFMAN *et al.* (3) reported that prolonged exposure of the lingual surface to micromolar (μM) concentrations of caffeine (CAF) and other methylxanthines markedly enhanced the perceived taste intensities of the nonnutritive sweetener acesulfam-K, as well as NaCl (salty) and quinine HCl (bitter). In a later publication (4), they found that CAF enhances the taste intensities of a number of noncarbohydrate sweeteners, including saccharin. In both studies, exposure to CAF was achieved by covering the halves of each subject's tongue for 4 minutes with 2 pieces of filter paper, one of which had been soaked in a CAF solution, and the other in a deionized water control. Immediately after removal of adapting solutions, small disks of filter paper which had been soaked in taste solutions (prepared in the same concentration of CAF) were placed on the CAF-adapted side, and the concentration of taste stimulus (prepared in deionized water alone) having equivalent intensity was determined on the other. Using a 10 μM CAF adaptation solution, they reported significantly enhanced intensities for quinine HCl (85% increase in intensity), NaCl (20–26% increase), and the noncarbohydrate sweeteners acesulfam-K (100% increase), neohesperidin dihydrochalcone (60% increase), d-tryptophan (50% increase), thaumatin (50% increase), stevioside (50% increase), and saccharin (40% increase) (3,4). Taste intensities were unaffected for urea, aspartame, sucrose, fructose, and calcium cyclamate.

Given such marked effects on taste perception, it seemed appropriate to examine whether CAF might exert similar influences under more natural conditions of consumption, with lingual exposure occurring through the presence of CAF in saliva. In previous studies from this laboratory, we found that following a CAF dose of 5.5 mg/kg, salivary CAF concentration is commonly in the range of 10–20 μM from 45–180 minutes post-dose (2). Thus, the present investigation was intended to test the findings of Schiffman *et al.* (3,4), using a variety of selected sweeteners and other taste compounds under naturalistic conditions of caffeine ingestion.

METHOD

Subjects were 11 males and 13 females, mean age 24 years, recruited by public advertisement. Criteria for exclusion included use of any form of tobacco, and current health disorders or use of medications either reported to alter taste or smell or contraindicative of caffeine ingestion.

Two test sessions of about 90 minutes duration each were conducted two days apart. Participants were requested to abstain from use of caffeinated foods, beverages, and medications beginning at least 24 hours prior to testing and continuing until the last session was completed. Subjects ingested a gelatin capsule containing 5.5 mg/kg body weight CAF (equivalent to about 3–4 cups of coffee for a 70 kg subject) at the start of one test session and a placebo (a similar weight of cornstarch) in the other. The order of CAF vs. placebo was randomized and the study was of a double-blind design. Subjects were told that they might get CAF in one, both, or neither of the test sessions. In later debriefing, and despite the anticipated pharmacological effects of caffeine, subjects were often incorrect in guessing which session had involved CAF ingestion.

Forty-five minutes after ingesting the CAF or placebo, subjects rinsed thoroughly with deionized water, and provided a 3-minute

TABLE 1

TEST STIMULI

Stimulus	Concentration*	Predominant Sensory Quality
Aspartyl-Phenylalanine Methyl Ester (Aspartame)	0.008 M	Sweet
Calcium Cyclamate	0.02 M	Sweet
Fructose	0.6 M	Sweet
Neohesperidin Dihydrochalcone	3.0×10^{-4} M	Sweet
Saccharin	0.00187 M	Sweet
Sucrose	0.8 M	Sweet
D-Tryptophan	0.0147 M	Sweet
NaCl	0.2 M	Salty
Citric Acid	0.02 M	Sour
Caffeine	0.0125 M	Bitter
Denatonium Benzoate	2.5×10^{-8} M	Bitter
Phenyl Ethyl Alcohol	0.25%†	Rose aroma
Benzaldehyde	0.15%†	Bitter Almond aroma
1000 Hz Tone	60 dB	

*All taste solutions except caffeine and denatonium benzoate were prepared in both deionized water and 10^{-5} M CAF.

†Aromas were prepared in 20 ml mineral oil in 250 ml polypropylene sniff bottles.

TABLE 2

EFFECT OF CAFFEINE (VS. PLACEBO) ON INTENSITY RATINGS

Stimulus	Median Number of Units Difference in Rating	p
Aspartame	0.0	ns*
Aspartame in 10 μM Caffeine	−0.5	ns
Ca Cyclamate	−0.6	ns
Ca Cyclamate in 10 μM Caffeine	+0.5	ns
Fructose	0.0	ns
Fructose in 10 μM Caffeine	−0.25	ns
Neohesperidin	0.0	ns
Neohesperidin in 10 μM Caffeine	0.0	ns
Saccharin	−0.5	0.03
Saccharin in 10 μM Caffeine	0.0	ns
Sucrose	+0.5	ns
Sucrose in 10 μM Caffeine	0.0	ns
D-Tryptophan	0.0	ns
D-Tryptophan in 10 μM Caffeine	0.0	ns
NaCl	+0.25	ns
NaCl in 10 μM Caffeine	0.0	ns
Citric Acid	0.0	ns
Citric Acid in 10 μM Caffeine	0.0	ns
Caffeine	0.0	ns
Denatonium Benzoate	−0.5	ns
Phenyl Ethyl Alcohol	0.0	ns
Benzaldehyde	0.0	ns
1000 Hz Tone	+0.2	ns

*ns = not significant ($p>0.05$) vs. placebo condition.

stimulated saliva sample for CAF analysis. Saliva secretion was stimulated by use of an unflavored gum base and paced by a metronome at 80 chews/min. Saliva was collected and discarded at the end of the first minute, and then collected into a funnel and test tube at the end of each of the next three minutes.

Sensory testing began immediately after saliva collection, at 50 minutes post-dose. The taste stimuli listed in Table 1 were each presented 2 times in random order. Stimulus concentrations were selected in two ways: For those stimuli which had been tested by Schiffman *et al.* the same concentrations were used in the present work. For other stimuli, concentrations were selected which represented the midrange of suprathreshold series used in other experiments in this laboratory, or which were generally judged to be moderately strong. Taste solutions were sipped and expectorated as 10 ml in a 30 ml medicine cup, with a single deionized water rinse between each sample. Two odorants and a tone were included to control for a possible general effect of CAF on scale usage and nongustatory sensory perception. Odor samples consisted of 20 ml of odorant solution in 250 ml opaque polypropylene squeeze bottle, which subjects squeezed and sniffed. The 60 dB 1000 Hz tone was generated binaurally through an audiometer equipped with earphones. All intensity ratings were made verbally using a 9-point category rating scale ("No Taste" to "Extremely Strong"). The means of the two ratings of each stimulus under the different conditions (CAF or placebo) were computed, and the effect of condition compared using the Wilcoxon matched-pairs signed-rank test, employing a probability level of $p<0.05$ as the criterion for statistical significance.

Caffeine was extracted from saliva and analyzed by HPLC, by the method of Hartley *et al.* (1). Extractions were achieved with reverse-phase silica gel columns (Bond-Elut C-18, 3 ml size; Analytichem International, Harbor City, CA) conditioned by washing with 2 ml methanol followed by 2 ml water. A 200 μl saliva sample was applied to each column and drawn through by vacuum; caffeine was retained, while other polar substances passed through the column. The column was then washed with 2 ml water, and caffeine eluted by washing with 400 μl methanol. Recovery of caffeine from Bond-Elut columns was found to average 99.4% over the range of salivary caffeine concentrations. A measured amount of β-hydroxytheophylline was added to the sample as an internal standard and a 10 μl aliquot was analyzed using a reverse-phase HPLC column (5 micron, 4.6 × 150 mm Pecosphere; Perkin-Elmer, Norwalk, CT), with 1% acetic acid in methanol (83:17, v/v) as the eluting solvent and a 1 ml/min flow rate. Caffeine was detected by ultraviolet absorption at 273 nm.

RESULTS

The median (interquartile range) salivary CAF concentration just prior to initiating taste testing in the placebo condition was 0.0 (0.0 to 2.1) μM, indicating that subjects had largely complied with the 24-hour pretest abstention from caffeinated foods and beverages. At 45 minutes post-caffeine dose, salivary caffeine was the expected range, with a median value of 19.8 (7.1 to 26.9) μM.

Changes in intensity ratings following caffeine ingestion (as compared to the placebo condition) are presented in Table 2. With a single exception, none of these differences were statistically significant, and they generally show only minor and inconsistent deviations from zero. While saccharin was rated as having significantly greater intensity in the placebo condition, the actual magnitude of the difference was small and, in light of the large number of comparisons conducted, little importance can be assigned to this one result. The overall findings were similar even when analyses were conducted using only that half of the subjects showing the largest placebo vs. caffeine change in salivary caffeine concentration. Lastly, there was no consistent relationship between salivary caffeine levels and either the absolute intensity ratings or relative change in intensity ratings following caffeine ingestion.

DISCUSSION

Under realistic conditions of ingestion and peripheral and systemic exposure to caffeine, there were negligible changes in the perceived intensity of a battery of sensory stimuli. Addition of caffeine to taste solutions also did not alter their rated intensity under either the placebo or caffeine conditions. It appears doubtful that taste potentiation from caffeine would have any noticeable influence in common experience. No effects were seen in the present study where the amount of caffeine consumed was about 2–3 times greater than what might be considered typical in a natural setting. In addition, sensory testing was timed to coincide with the peak levels of salivary caffeine, and subjects were specifically instructed to attend to the intensity of sensations. In earlier work from this laboratory (2), we found no effect of acute CAF exposure on detection thresholds for CAF itself or NaCl.

The difference between the present findings and those of Schiffman *et al.* (3,4) with regard to NaCl, neohesperidin dihydrochalcone, d-tryptophan, and saccharin may be attributable to a number of methodological considerations. In the present investigation, salivary CAF levels at the time of testing were approximately double the 10 μM used by Schiffman *et al.* with sweeteners (4); however, they reported similar effects with concentrations up to 10 mM (3). Their sensory testing method, a simultaneous side-by-side comparison on each half of the tongue, is probably more sensitive than the temporally separated comparisons used in the present study. This seems unlikely to account for such large discrepancies in the results, as a computation of statistical power shows that the present study had a 95% probability of detecting at least a 1 unit change in category scale ratings. One major difference between this work and that of Schiffman *et al.* (3,4) is that their adapting solutions and tastants were contained in filter paper applied to, and presumably largely restricted to, the dorsal surface of the tongue. However, it is not clear how this method alone might have contributed to their discrepant results for selected stimuli. Their human studies with peripheral caffeine and adenosine exposure are consistent with their animal work and proposed role for the A_1 adenosine receptor in taste perception (3). The present study involved both peripheral and central exposure to caffeine and it is possible, though unlikely, that some counterbalancing effect may exist.

There is little other support for an effect of caffeine on taste in everyday experience. In a specific test of the effect of whole-mouth stimulation with caffeine on perceived NaCl intensity, Sheperd *et al.* (5) had subjects rate the intensity of NaCl solutions prepared in either water or 0.1 molar caffeine, preceded by mouth rinses with the solvent alone. They found essentially no effect of caffeine using this procedure, and concluded that "the application of caffeine as a taste potentiator in real drinking and eating situations is limited." Schiffman *et al.* themselves note that they have not observed any alteration in taste recognition thresholds following ingestion of tea (3) and, in a simple test of a commonly consumed caffeine-sweetener combination, we have observed that subjects do not distinguish between the intensity of similarly sweetened (using sucrose, saccharin, or aspartame) regular and decaffeinated coffee solutions (Mela, unpublished observations). Overall, it may be concluded that, under natural conditions of ingestion, caffeine appears to have negligible effects on perceptions of intensity of common chemosensory stimuli.

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