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Effects of Caffeine on Salivation

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Abstract

Background: Caffeine is a methylxanthine which may decrease salivation through adrenergic mechanisms. Few studies have formally tested whether caffeine actually decreases saliva production.

Methods: Eleven volunteers collected unstimulated 1-minute saliva production (1-MSP) after an overnight fast, followed shortly by a stimulated 1-MSP while chewing a stick of chewing gum. We then asked them to drink a beverage randomly selected to contain either regular or decaffeinated instant coffee. Caffeine content was double-blinded. 1-MSP, both unstimulated and stimulated were then collected 30, 60, 90, and 120 minutes later. The following morning the subject followed the same protocol but drank the other kind of beverage. We used a mixed-effects linear model to analyze our data.

Results: The adjusted mean difference between decaffeinated and caffeinated 1-MSP was -0.14 ml ($p<0.05$). Stimulation with chewing gum caused an unadjusted increase of 2.02 ml ($p<0.001$) and an adjusted increase of 2.01 ml ($p<0.05$). Variation for the unstimulated 1-MSP was much lower (SD 0.4 ml) than the stimulated 1-MSP (SD 1.01 ml), whereas variation for caffeinated 1-MSP (SD 1.29 ml) was similar to decaffeinated 1-MSP (SD 1.25 ml).

Conclusion: Caffeine modestly but significantly decreased both unstimulated and stimulated saliva production. The effect of caffeine was approximately 6.5% that of stimulation. The effect from caffeine was consistent across both stimulated and unstimulated samples. Additionally, caffeine did not increase the variability of saliva production either within or between individuals, in contrast to the effect from stimulation.

Introduction

Saliva has an important homeostatic role in the oral cavity. Hyposalivation can lead to diseases such as caries and mucous membrane candidiasis as well as difficulties in speech, mastication and deglutition. Like all exocrine secretions, salivary production is under the control of the autonomic nervous system, but physical factors such as hypovolemia and dehydration can also play a role. Thus, various systemic conditions, medications, and psychological factors can affect salivary output [1,2].

Caffeine, a natural derivative of coffee beans and tea leaves, is a methylxanthine with proven activity on the central nervous system and the smooth muscle cells of the cardiac, respiratory and digestive organs. Its effects mostly parallel the adrenergic pathway and include increased arterial blood pressure and cardiac output, and decreased gastrointestinal muscle tone [3-5]. Following this teleological path, it would be expected that caffeine had a significant, dose-dependent effect on reducing salivary secretion. This effect has been an accepted tenet of the treatment of hyposalivation [6], yet surprisingly it has not been confirmed scientifically. Further, knowing the size of the effect of caffeine on salivation can inform treatment advice to patients.

We studied the effects of caffeine ingestion on unstimulated and stimulated whole salivary production in a group of healthy adults. We hypothesized that caffeine would significantly decrease salivation in both the stimulated and the unstimulated settings after an overnight fast.

Subjects and Methods

Subjects (n=11) were healthy volunteers on no prescription medications who were regular coffee drinkers. They were informed of the protocol and were asked to sign Informed Consent. The study was approved by the Institutional Review Board at the University.

This was a randomized, controlled, double blinded crossover trial of caffeine effects on whole stimulated and unstimulated salivary production. Subjects were randomly (coin toss) assigned to receive 200 milliliters (ml) of either regular (180 milligrams (mg) caffeine) or decaffeinated (3.6 mg caffeine) instant coffee. Unstimulated and mastication-stimulated saliva were collected before coffee ingestion (baseline) and then at 30, 60, 90 and 120 minutes. The following day, subjects were crossed over to the other group and the process was repeated.

The protocol began on both days at 8 AM, to minimize the influence of circadian variation in salivation. All subjects were required to have had nothing to eat or drink since midnight and no consumption of food or other liquid was permitted during the two-hour protocol. Subjects were also asked to abstain from taking non-prescription drugs (except for birth control pills and vitamins) or consuming alcoholic beverages for the 24 hours preceding the

protocol. We used 15 gm of instant regular or decaffeinated commercial coffee dissolved in 200 ml of heated tap water. Sweetener and non-dairy creamer were restricted to two teaspoons per cup, and no liquid milk was allowed. The 200 ml coffee was consumed in 15 minutes or less and no other food or beverages were allowed during the 2 hour study period.

Saliva was collected in volumetrically marked graduated test tubes (Falcon Blue Max Jr., Becton Dickinson and Co., Franklin Lakes, NJ) with the patient's study number, time of collection and the letters N for unstimulated and S for stimulated secretions printed on the label. Subjects were instructed to swallow before collection began and then spit into the test tube for 60 seconds for one minute saliva production (1-MSP). Stimulation was produced with rhythmic chewing (one chew per second) of a stick of the same commercial brand and flavor of sugar-free chewing gum. Stimulated samples were collected after each unstimulated sample. Tubes were allowed to settle for two hours and the amount of saliva was determined by volumetric reading rounded to the closest tenth ml.

Statistical analysis

Since observations on the same individual over time were correlated, we used a mixed effects linear model approach to evaluate the effects of caffeine on saliva production. Observations from stimulated collections were significantly more variable than those from the unstimulated collections. Thus, we included random effects for the intercept, the slope as well as a stimulation factor, and also allowed for different error variances for the stimulated and unstimulated responses.

Results

Eleven subjects (two males, nine females, average age 39.9 years) completed the study and were eligible for analyses. Two additional subjects were enrolled but failed to show for the second day and were removed from the study. No deviation from the study protocol was noted and no adverse effects were reported.

Subset	Mean (ml/min)	Standard Deviation
All Data	1.81	1.27
Caffeinated	1.74	1.29
Decaffeinated	1.88	1.25
Stimulated	2.82	1.01
Unstimulated	0.8	0.4
Caf/Stim	2.74	1.08
Caf/Unstim	0.74	0.38
Decaf/Stim	2.9	0.94
Decaf/Unstim	0.85	0.41

Table 1: Saliva production in response to caffeine and stimulation.

Table 1 presents a summary of the differences in salivary production for unstimulated and stimulated samples, with and without caffeine. As expected, stimulated secretions were considerably larger than unstimulated saliva production, but the differences in salivation following caffeinated vs. decaffeinated drinks was far more modest.

We encountered great variability in saliva production between subjects in the effects of stimulation for both caffeinated and decaffeinated beverages (Figure 1). While stimulated saliva production increased over unstimulated saliva as a whole, individual subjects were likely to produce consistently larger or smaller amounts of stimulated saliva over time, regardless of the caffeine content of the beverage. This is reflected in the wide "between subject" scatter of the stimulated saliva production plots vs. time.

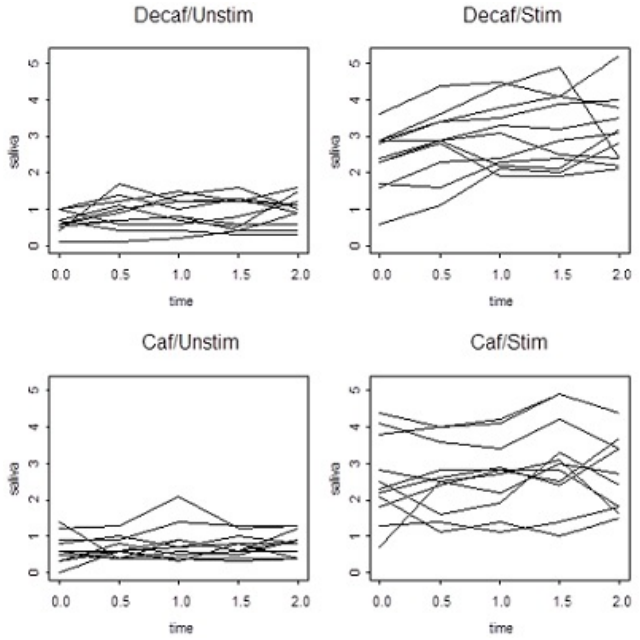

Figure 1: Graphs of one-minute saliva production (Ml) by time (Hours) for all combinations: note the high variation in stimulated saliva production for the 11 subjects.

A random effect for stimulation was included to account for this between subject variability in the effect of stimulation. Additionally, because the "within-subject" variation increased for the stimulated samples, the error variances were allowed to differ between stimulated and unstimulated samples. Furthermore, the responses differed between subjects, both initially and over time, with some individuals displaying increases in saliva production over time, others displaying decreases, and others displaying initial decreases followed by increases. To reflect this variation in response, random effects were added for the individual subject initial value (intercept) and change over time (slope) of saliva production. Finally, an interaction term between stimulation and time was entered into the adjustment model to account for differences in the change of saliva production over time between stimulated and unstimulated samples. Saliva production adjusted for these variations is presented in (Table 2).

Fixed Effect	Estimate	Standard Error	z-value
Intercept	0.86	0.09	9.80*
t (time)	0.1	0.04	2.51*
s (stimulated)	2.02	0.23	8.97*
c (caffeine)	-0.12	0.05	-2.59*
s*t (interaction)	0.13	0.06	2.22*
*significant at alpha=0.05 level			

Table 2: Saliva production adjusting for variation (fixed effect estimates).

Both stimulated and unstimulated saliva production were modestly but signi icantly reduced by consumption of regular coffee as compared to its decaffeinated counterpart (1-MSP difference= -0.12 ml/min, p<0.05). This effect was approximately the same size in both stimulated and unstimulated samples. The effect of caffeine was 6.5% of the effect of gum stimulation. Figure 2 demonstrates that saliva production was consistently and signi icantly albeit modestly lower with caffeinated coffee. Three of 11 subjects produced slightly more stimulated saliva with caffeinated coffee, but that difference was not signi icant.

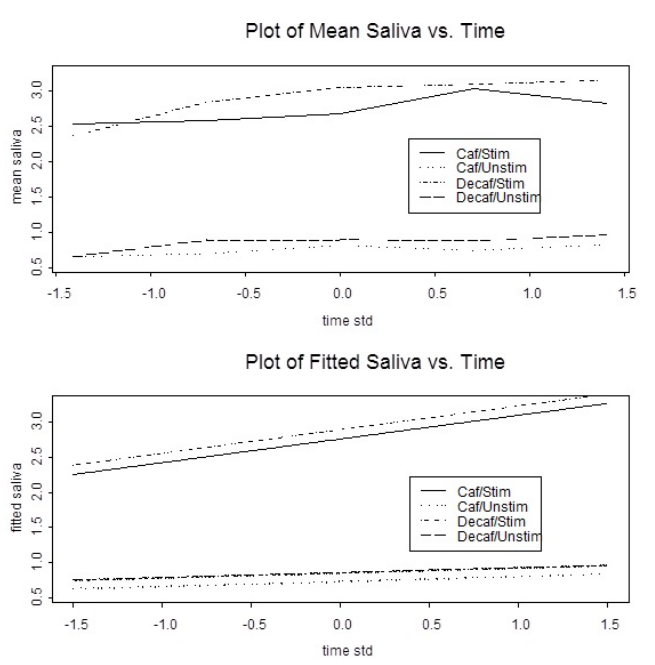

Figure 2 Plots of mean one minute saliva production vs. time and one minute saliva production adjusted for variability vs time

Discussion

Caffeine, a popular member of the methylxanthine drug class, is a very commonly ingested substance the world over, mostly due to its perceived stimulation of the central nervous system through antagonism of the adenosine receptors A1 and A2 [3,4,7-11]. Other possible mechanisms of clinical effects of caffeine have been postulated and include calcium ion mobilization and increased epinephrine production.12,13 However, the complete mechanism of caffeine's effects is still elusive.5,12

Among documented clinical effects of caffeine are increased heart rate, systolic blood pressure and left ventricular output [7,8,11] stimulation of autonomic responses [12,13] decreased tone of the gastrointestinal smooth muscles increased ocular pressure in glaucoma patients [14] central nervous system excitation and increased alertness [2,5,9] However, the only study we were able to find documenting the response of salivation to ingestion of any methylxanthine was a retrospective analysis of Pavlovian date [15]. Nevertheless, in the dental community, the belief that caffeine consumption decreases salivary production is widely held [6].

Results of our study support this assumption. Caffeine consumption significantly decreased salivary secretions for two hours after ingestion. However, the reduction was modest in healthy volunteers and its clinical significance in this population is unclear. Stimulation from chewing gum readily made up this loss multiplied by a factor of five. This is consistent with the results of an animal study evaluating carcinogenicity of caffeine, which showed no differences between the caffeine and control groups [16]. Future studies will have to determine the clinical significance of caffeine's modest inhibition of salivation in humans, particularly among those with high risk for oral diseases. Furthermore, the effects of caffeine on salivation in subjects with impaired function remain a subject worthy of further study.

An additional interesting finding of the current study is the high variability of salivation response to chewing gum stimulation (SD 1.01 ml/min). Few reports in the literature address inter-individual variations in saliva production, but significant differences between individuals have been described for salivary glucose clearance over time [17], for the secretion of various substances in saliva [18-20] as well as salivary response to stimulation by glucocorticoids [21]. Another possible explanation could rest with the patient's caffeine ingestion history, which was not included as a variable in this study. Although all participants had been exposed regularly to coffee, current drinking patterns were not obtained. Developments of metabolic tolerance to caffeine as well as withdrawal symptoms have been documented, but remain controversial [13]. This subject too should be explored in further studies.

Conclusions

In this study, caffeine modestly but significantly reduced salivation in the tested population. Since the decrease in saliva production was just over one-tenth cubic centimeter per minute, caffeine's effects may not be clinically important in most routine situations, and widespread advice to refrain from caffeine ingestion to improve salivation may not be warranted. Further study in diseased individuals with impaired salivary production should be carried out. We also described high variability among individuals in the quantity of saliva produced in response to stimulation. We did not observe similar high variability for salivary production without stimulation. Caffeine did not influence this pattern of variability. The clinical implications of these findings are unclear and should be explored in further studies.

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