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The effects of chewing versus caffeine on alertness, cognitive performance and cardiac autonomic activity during sleep deprivation

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SUMMARY Chewing has been shown to alleviate feelings of sleepiness and improve cognitive performance during the day. This study investigated the effect of chewing on alertness and cognitive performance across one night without sleep as well as the possible mediating role of cardiac autonomic activity. Fourteen adults participated in a randomized, counterbalanced protocol employing a chewing, placebo and caffeine condition. Participants completed tasks assessing psychomotor vigilance, tracking, grammatical reasoning, alertness and sleepiness each hour across the night. All participants received either placebo or caffeine (200 mg), while the chewing condition also chewed on a tasteless and odorless substance for 15 min each hour. Heart rate (HR), root mean square of the successive differences in R-R intervals on the ECG (RMSSD), and preejection period (PEP) were simultaneously recorded. Alertness and cognitive performance amongst the chewing condition did not differ or were in fact worse when compared with placebo. Similarly, measures of HR and RMSSD remained the same between these two conditions; however, PEP was reduced in the later part of the night in the chewing condition compared with a relative increase for placebo. Caffeine led to improved speed and accuracy on cognitive tasks and increased alertness when compared with chewing. Relative increases in RMSSD and reductions in HR were demonstrated following caffeine; however, no change in PEP was seen. Strong associations between cardiac parasympathetic activity and complex cognitive tasks, as well as between subjective alertness and simpler cognitive tasks, suggest a differential process mediating complex versus simple cognitive performance during sleep deprivation.

KEYWORDS caffeine, chewing, cognition, heart rate variability, sleepiness

INTRODUCTION

It has long been claimed that the chewing of gum facilitates concentration, alertness and performance on cognitive tasks. Hollingworth (1939) had described increases in relaxation and improved test performance while chewing. Few studies have since investigated the effectiveness of chewing as an effective and convenient countermeasure to the cognitive impact of a disrupted sleep–wake schedule.

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Hodoba (1999) demonstrated that chewing commercially available gum continuously during one night of total sleep deprivation significantly reduced subjective sleepiness in a controlled environment, and that sleepiness is reduced following 15 min of chewing a similar gum in shift workers during a routine night shift. The potential benefits of chewing in terms of cognitive performance have not been tested under conditions of restricted sleep. Evidence of the influence chewing may have on cognition is only available from a very small number of studies conducted under non-sleep-deprived protocols. Such studies have produced mixed results for varying areas of cognitive performance. On one hand, the effects chewing has on memory performance appear to be in the same general

direction – suggesting enhanced immediate and delayed episodic recall and working memory (Baker *et al*., 2004; Stephens and Tunney, 2004; Wilkinson *et al*., 2002). This effect seems most apparent when information is not presented verbally (Tucha *et al*., 2004). On the other hand, the effect of chewing on other aspects of cognition known to be inhibited by reduced sleep (Dinges and Kribbs, 1991; Wesensten *et al*., 2002), such as attention, vigilance and reasoning ability, have been less studied.

Wilkinson *et al*. (2002) compared measures of attention and concentration between gum-chewing, mimicked chewing and non-chewing control conditions. Simple reaction time measures were improved in the sham chewing condition only, compared with controls. The authors suggest this result may reflect a distraction caused by performing an unfamiliar task, however, related measures including choice reaction time and vigilance measures were unchanged across all conditions. Also, it is unclear from this study as to whether any enhancement of cognitive functioning as a result of chewing is sustained beyond the period of chewing itself or across extended periods of chewing. Results by Tucha *et al*. (2004) suggest chewing differentially impacts specific aspects of attention such that sustained attention is improved by flavored gum while alertness and flexibility are adversely affected by chewing in general. These results point to the effects of gum flavor and fragrance as distinct from chewing itself. Using a wider battery of tests and within-subjects design, Stephens and Tunney (2004) assessed the impact of chewing during assessment of cognitive function following ingestion of a glucose load. They conclude that both chewing and glucose independently enhanced language-based attention and processing speed, however no improvement in non-language-based tests of attention and processing speed were found. The authors propose that their results are consistent with a theory of enhanced glucose delivery to regional brain areas during chewing. However, increases in heart rate (HR) (Wilkinson *et al*., 2002) and either enhancement of sympathetic or suppression of parasympathetic cardiac activity (Shiba *et al*., 2002) by chewing indicate glucose independent increases in arousal may play an important role in any enhancement of cognition.

Indeed, in as much as the cognitive impact of chewing is undefined, the mechanisms underlying any enhancement of cognitive performance by chewing are not known. Farella *et al*. (1999) investigated cardiovascular responses to 20 min of sustained chewing of a commercially available chewing gum. They found that mean blood pressure and HR of resting healthy young adults rose significantly following chewing. Similarly, the low-frequency band to high frequency band spectral power ratio of the R-R intervals in the electrocardiogram (ECG) of healthy adults has been found to be increased by chewing (Shiba *et al*., 2002), suggesting enhancement of cardiac sympathetic nervous activity (SNA) or suppression of cardiac parasympathetic nervous activity (PNA). Wilkinson *et al*. (2002) demonstrated an increase in HR in their chewing condition compared with controls and suggested the enhancement of memory functioning previously described during chewing may be mediated by changes in cranial blood flow. Changes in autonomic activity, such as measured by the analysis of HR variability, provide one target mechanism for the possible enhancement of cognitive functioning due to chewing.

An important limitation to previous studies of the effects of chewing on cognitive function is the widespread use of commercially available flavored chewing gum. There is evidence that the flavors and odors incorporated into chewing gums may themselves alter brain function, and previous studies have indicated that exposure to the fragrances and odors of commercially available chewing gums increase the arousal state of an individual, not the chewing of the gum base itself (Baron and Kalsher, 1998; Masumoto *et al*., 1999; Morinushi *et al*., 2000; Yagyu *et al*., 1998).

If chewing does induce increased alertness and improved cognitive performance in sleep-deprived individuals, it is valuable to know the extent to which it does so compared with products already widely used to achieve this same end. Caffeine is considered the most widely used and readily available countermeasure to the effects of sleep deprivation, most commonly taken in products such as coffee, tea, cola drinks, confectionaries and over-the-counter formulations (Nehlig, 1999). Caffeine is an established psychostimulant that has been shown to effectively increase alertness and cognitive performance (Penetar *et al*., 1993; Rees *et al*., 1999; Van Dongen *et al*., 2001; Wesensten *et al*., 2001). When compared with chewing alone, chewing combined with bi-hourly administration of 200 mg caffeine has significantly increased vigilance and maintained performance at baseline levels across one night without sleep. Subjective measures of sleepiness however, were not different between groups in the same study (Kamimori *et al*., 2005). As with many pharmacological fatigue countermeasures however, caffeine has been associated with a number of side effects including agitation, anxiety, insomnia, and transient hypertension (Boutrel and Koob, 2004).

The limited research available, combined with the discrepancy in results, highlights the need for assessment of the effect of chewing on various cognitive functions. To date, no study has investigated the effect of chewing alone on cognition, either compared with control data or a known psychostimulant, during a period of sleep deprivation. The present study aimed to determine whether intermittent chewing was able to alleviate the typical decrement in cognitive performance and alertness that is experienced during periods of sleep deprivation, and to establish whether such effects were mediated by changes in cardiac autonomic activity. Further, the results are compared with the effects of caffeine, commonly used in the workplace and known to have alerting effects in sleep-deprived individuals.

METHOD

Participants

Fifteen participants were initially recruited for this study from respondents to advertisements posted at local universities,

however one withdrew before completing all test conditions. Of the remaining 14, seven participants were male and seven were female, aged 18–36 years (M = 24.7, SD = 6.6). All participants completed a general health questionnaire and a 7-day sleep/wake diary prior to the study to confirm that they had no current health problems, psychiatric and/or sleep disorders and that none used medications known to effect sleep or psychomotor performance or had undertaken transmeridian travel in the past three months. No subjects were smokers, shift workers, or had a body mass index (kg m^{-2}) >30. All consumed caffeine at doses of <400 mg day^{-1}. Participants were required to abstain from caffeine and alcohol and maintain their normal sleep/wake patterns 24 h prior to the commencement of the study. All subjects received compensation of $225 on completion of the study for any inconvenience associated with their participation. The study was approved by the relevant institutes' ethics and human research committees.

Materials

Chewing substance

Participants were given a new 2 cm × 5 cm piece of Parafilm (American National Can, Greenwich, CT, USA) for each chewing period. Parafilm is an odorless, tasteless sheet-form of paraffin wax with no nutritional value. Parafilm has been used in previous studies to stimulate salivation via chewing (Rogers *et al*., 1998; Voultsios *et al*., 1997).

Caffeine and placebo

Capsules, each containing 100 mg of anhydrous caffeine from a commercially available non-prescription product (No-Doz; Key Pharmaceuticals, Rhodes, NSW, Australia), and identical lactose containing placebo capsules were prepared by The Queen Elizabeth Hospital Pharmacy Production group.

Cognitive performance

Grammatical reasoning. Grammatical reasoning was assessed using one task from a computerized cognitive test battery (Worksafe Australia, Sydney, NSW, Australia), the design of which is based on a test previously developed by Baddeley (1968). The task involves presentation of 32 statements in random order on a standard computer monitor. Participants were required to hold the index finger of their dominant hand on a 'home' button of a response box until they had decided whether the statement was true or false, at which time they were to use the same index finger to press one of two other buttons corresponding to a 'true' or 'false' response. The grammatical reasoning task provides a measure of accuracy (% correct) and response time (the time between statement appearance and the participant pressing the true or false response button in seconds).

Psychomotor vigilance. The ability to maintain vigilance was measured using the psychomotor vigilance task (PVT) developed by Dinges and Powell (1985). This computerized task required subjects to watch a blank time display. Subjects were instructed to press a response button as soon as numbers appeared in the time display. The numbers, beginning at '000', would increment as soon as they appeared and a response by the subject would stop the time display and initiate the next trial which was randomly delayed by 2, 4, 6, 8, or 10 s. Subjects were also instructed to use their dominant hand to press the response button and to use the same finger for each trial. Data from the PVT were used to assess number of lapses (reaction time >500 ms) and increases in duration of response rate, as measured by the reciprocal of reaction time (ms) for a given trial. Task duration was 10 min.

Tracking. Participants also completed a compensatory tracking task (Occupational Safety Performance Assessment Technology; OSPAT version 4, Romtech, Perth, Australia). Participants were required to use a large tracking ball to manipulate a cross appearing on a standard computer monitor, maintaining the cross as close as possible to the center of a target for the 30 s duration of the test. The cross moved independently of the participant's manipulations, forcing the participant to compensate for these independent, random deviations. The OSPAT generates one score for each administration of the task, which is an index of performance based on arbitrary units algorithmically. Scores typically fall between 10 and 20 with higher scores indicating better performance.

No feedback was provided to participants in regard to their performance on any task throughout the duration of the study.

Subjective alertness

Sleepiness and subjective alertness was assessed using the Stanford Sleepiness Scale (SSS; Hoddes *et al*., 1972, 1973) and via a Visual Analogue Scale (VAS; Bond and Lader, 1974; Folstein and Luria, 1973). The SSS is a pencil and paper form including seven points ranging from 1 ('feeling active and vital; alert; wide awake') to 7 ('almost in reverie; sleep onset soon; lost struggle to remain awake'). Participants write the number best describing their current state on the form. The SSS is a commonly used (Curcio *et al*., 2001) and sensitive measure of sleepiness (Babkoff *et al*., 1991). Also a pen and paper questionnaire, the VAS contained a linear 100 mm blank line which represented a continuum of alertness ranging from 'alert and wide awake' at one pole or 'struggling to remain awake' at the other pole. Participants marked on the line the extent to which they perceive themselves as closer to or further away from one or the other pole statements. A score of alertness was made by measuring the distance at which a mark was made in millimeters from the 'struggling to remain awake' pole.

Cardiac autonomic activity

Root mean square of the successive differences in R-R intervals (RMSSD) in normal inter-beat intervals is a measure of the rapid fluctuations in autonomic activity that accompany respiration and has been recommended by the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology (1996) as a reliable measure of cardiac PNA. This validation has largely come about from the repeated observation that RMSSD almost perfectly correlates with another well-validated cardiac PNA measure, respiratory sinus arrhythmia (Bigger *et al.*, 1992; Vrijkotte *et al.*, 2001). Assessment of ECG to determine HR and RMSSD was obtained using pregelled Ag-AgCl ECG spot electrodes (Meditrace; 3M, St Paul, MN, USA) that were placed in three positions on each subject: the jugular notch of the sternum, 4 cm below the left nipple, and at the right lateral side between the lower two ribs. All electrodes were connected to a Vrije Universiteit ambulatory monitoring system (VU-AMS, version 4.6, TD-FPP, Vrije Universiteit, Amsterdam, The Netherlands). The VU-AMS recorded ECG by using an amplifier with a time constant of 0.3 s, 1 MΩ impedance, and a low-pass software filter of 17 Hz. Each R peak was detected and from the R-peak time series, an average value for HR was obtained for each 30-s period. The VU-AMS device from the raw beat-to-beat intervals calculated RMSSD automatically. An average value for RMSSD was also obtained for each 30-s period.

One of the most widely validated non-invasive measures of SNA is preejection period (PEP) (Berntson *et al.*, 1994; Cacioppo *et al.*, 1994). PEP is a reflection of ventricular contraction and, as such, is considered a relatively '*pure*' measure of SNA (Sherwood, 1993). PEP is inversely related to cardiac SNA such that as cardiac SNA increases, contraction of the heart is faster and PEP shortens. Assessment of impedance cardiogram, to determine PEP was obtained with the attachment of three similar spot electrodes. One electrode was placed on the base of the neck over vertebrae C3–C4, a second on the xiphoid process of the sternum, and the third over the vertebrae below the line connecting the tips of the shoulder blades, and with regard to the front, at least 3 cm below the electrode over the xiphoid. To obtain measures of PEP a constant current of 350-μA at 50 kHz was applied through the electrodes on the neck and back and the resulting impedance was recorded via the electrodes on the jugular notch and xiphoid. The change in impedance with time (dZ/dt) signal was time locked to the R wave on the ECG signal and 30 s ensemble averages of the dZ/dt derived. PEP was later determined as the time period between the R wave on the ECG signal and the upstroke on the ensemble-averaged dZ/dt signal.

Procedure

Each participant undertook training in each of the cognitive tests within 7–14 days prior to commencing the study. Training occurred on a single day from 14:00 until 20:00 hours and involved 10 trials of the OSPAT and grammatical reasoning tasks beyond reaching a performance asymptote and a minimum of five PVT trials. Each participant completed one night of assessments for each of the conditions (chewing, caffeine, and control) in a randomized crossover fashion, with 7 days between trials in groups of three people. Participants were blinded to the status of their pharmacological condition (caffeine versus placebo) for the duration of the study.

On the day of each test condition subjects were instructed to awake and rise between 06:30 and 08:00 hours. Subjects attended the testing location from 19:30 hours. From this time until the beginning of data collection participants completed a practice trial of each of the cognitive tests. Electrodes were then attached to subjects and connected to a VU-AMS. ECG and ICG signals were confirmed before measurements began at 21:30 hours. All subjects remained awake for the entire testing procedure, which concluded at 06:30 hours the following morning.

During each condition participants completed a VAS and SSS immediately prior to completing the three computer-based cognitive tests at the beginning of each hour across the testing period. Participants completed each of the three cognitive tests in a crossover fashion under the supervision of one examiner such that each completed a different test at a given time. The order of test administration was balanced within an individual and across conditions over the entire study. Cognitive tests were conducted in an adjacent room and results were digitally stored in an automated fashion until after completing each study night. Participants remained seated when not moving to the assessment room and were allowed to engage in quiet activities, including listening to quiet music, watching non-arousing videos or television programs, talking, or reading. Visits to the toilet were allowed *ad libitum*. No vigorous movement, exercise, or napping was permitted. All participants were administered two capsules at 24:00 hours containing a total 200 mg dose of caffeine (Caffeine condition) or placebo (Control and Chewing condition). In the Chewing condition, participants were required to chew Parafilm continuously for 15 min each hour prior to completing the VAS, SSS, and cognitive tests. Participants were told to chew steadily and constantly, but the rate was not otherwise controlled. All participants were given a light snack at 24:35 and 03:35 hours and water was freely accessible. The ambient temperature for the testing location was set at 25 $\pm$ 1 °C and light was kept below 50 lux at the angle of subjects' gaze.

Data analysis

Experimenters were blinded to the group status of participants during the entire study and analysis. Cardiac data recorded during the 15-min period prior to completing the VAS, SSS, and cognitive assessments each hour were used for analysis and an average score for each hour was derived from these data. Measures of HR, RMSSD, and PEP were automatically calculated for every 30-s period during recording using the

AMS software. Because baseline cardiac activity can demonstrate large inter-individual variation, measures of HR, RMSSD, and PEP were recalculated for each participant relative to their individual baseline values. The cardiac data from two participants were not included in analysis, one due to signal loss and the second due to a large variation from the group mean beyond 2 standard deviations.

Statistical analysis

Statistical analysis was conducted using SPSS version 12.0 for Windows (Chicago, IL, USA). Because of the categorical nature of questionnaires used and a failure of the majority of measures to fit a normal distribution, non-parametric procedures were used for between condition analyses. All between condition analyses were conducted separately for precaffeine/placebo administration and postcaffeine/placebo administration, as caffeine and placebo conditions are effectively equivalent before capsule administration. The Friedman test for repeated measures was used to assess changes in variables between conditions across the night. *Post hoc* pair-wise analysis was conducted using the Wilcoxon signed-ranks test for paired samples. Linear regression was performed to assess the association of subjective alertness and cognitive performance measures on each of the cardiac variables as well as to determine the predictive value of subjective measures in estimating cognitive performance during sleep deprivation. Statistical significance was determined at $\alpha = 0.05$. Data are presented as mean ± standard deviation unless otherwise stated.

RESULTS

Precapsule administration

Precapsule administration, the Friedman test for repeated measures showed no effect of condition for any of the measures obtained during the study except for the tracking task (see Table 1). *Post hoc* Wilcoxon tests showed that when in the chewing condition, participants tended to perform better on the tracking task prior to capsule administration when compared with either of the other two conditions ($P < 0.05$).

Postcapsule administration

Across the night following administration of the capsules at midnight an overall effect of condition was seen on the Friedman test for all cardiac autonomic variables (HR, RMSSD, and PEP), for both measures of subjective alertness (SSS and VAS), and for response time and number of lapses as measured on the PVT (see Table 2). In contrast to results of precapsule administration, no effect of condition was seen for tracking performance. While effects of condition on accuracy and response speed as measured on the Grammatical Reasoning tasks were not significant overall, chi-square values demonstrated a trend with $P = 0.08$ and 0.05, respectively.

Post hoc analyses using the Wilcoxon test demonstrated a significant reduction in HR and rise in RMSSD (increase in PNA) compared with baseline in the caffeine condition compared with both chewing and placebo conditions. No difference was seen between chewing and placebo conditions for these measures. PEP significantly increased relative to baseline (reduction in SNA) in the placebo condition compared with both chewing and caffeine conditions, with caffeine showing almost no change to baseline and chewing showing a significant reduction in PEP relative to baseline (increase in SNA) and compared with both other conditions. Fig. 1 displays mean cardiac activity for each hour across the night in the three conditions.

Post hoc analyses of performance on the PVT demonstrated that response speed significantly slowed and lapses were more frequent in the chewing condition compared with both caffeine and placebo conditions across the night postcapsule administration; however, no difference was seen between performances in the caffeine versus placebo conditions for either measure (Table 2). Despite there being only a trend for overall differences between conditions on the Grammatical Reasoning task, *post hoc* tests were conducted and revealed that performances in the caffeine condition were both faster and more accurate than the chewing condition, and faster when compared with the placebo condition. No differences were

Table 1 Condition effects precapsule administration

Test	*Condition (mean ± SD)*			*Overall effect (χ^2)*
	Chewing	*Caffeine*	*Placebo*	
Delta HR	−2.1 ± 2.7	−2.5 ± 4.7	−1.8 ± 3.8	2.4
Delta RMSSD	2.9 ± 5.2	4.4 ± 8.1	2.9 ± 5.9	0.6
Delta PEP	−2.3 ± 12.0	−0.4 ± 4.1	1.3 ± 5.2	2.8
PVT (response speed, ms)	4.3 ± 0.5	4.2 ± 0.7	4.4 ± 0.6	0.3
PVT (lapses, no.)	1.5 ± 1.7	2.9 ± 5.4	1.5 ± 2.1	0.4
GR (accuracy, %)	97.3 ± 3.6	97.7 ± 3.1	97.0 ± 3.1	0.5
GR (response time, s)	2.3 ±0.9	2.4 ±0.7	2.4 ± 0.8	1.4
Tracking	16.1 ± 1.3	15.0 ± 1.3	15.4 ± 1.2	7.6*
SSS	2.1 ± 0.7	2.3 ± 0.6	2.3 ± 0.9	1.7
VAS	76.2 ± 10.9	74.0 ± 11.3	75.0 ± 14.6	1.4

*$P < 0.05$.

Table 2 Condition effects postcapsule administration with *post hoc* analysis

	Group (mean ± SD)				*Group comparisons (z)*		
Test	*Chewing*	*Caffeine*	*Placebo*	*Overall effect (χ^2)*	*Chewing–placebo*	*Chewing–caffeine*	*Caffeine–placebo*
Delta HR	−6.6 ± 4.3	−8.0 ± 7.2	−5.5 ± 4.7	6.2*	−1.3	−2.0*	−2.3*
Delta RMSSD	7.2 ± 10.9	21.4 ± 21.6	5.7 ± 11.3	22.5***	−0.8	−3.1**	−4.5***
Delta PEP	−6.9 ± 17.6	0.1 ± 10.0	6.9 ± 15.9	12.1**	−3.6***	−3.6***	−2.5*
PVT (response speed, ms)	3.8 ± 0.6	4.1 ± 0.7	4.1 ± 0.8	19.4***	−4.0***	−3.9***	−1.0
PVT (lapses, no.)	5.0 ± 5.5	3.2 ± 5.1	3.6 ± 6.7	22.9***	−3.3**	−2.9**	−0.67
GR (accuracy, %)	96.7 ± 3.5	97.8 ± 3.0	96.9 ± 4.0	5.0	−0.5	−2.5*	−1.6
GR (response time, s)	2.5 ± 0.8	2.2 ± 0.6	2.4 ± 0.7	5.9	−0.5	−4.00***	−3.02**
Tracking	15.2 ± 1.3	15.2 ± 1.5	15.3 ± 1.5	2.0	−0.8	−0.36	−0.19
SSS	4.2 ± 1.4	3.5 ± 1.2	4.1 ± 1.4	37.8***	−1.7	−5.21***	−4.30***
VAS	48.6 ± 20.2	60.7 ± 18.1	51.2 ± 21.1	32.5***	−1.9	−5.59***	−4.84***

*$P < 0.05$; **$P < 0.005$; ***$P < 0.001$.

found between chewing and placebo conditions for Grammatical Reasoning task performances (Table 2).

When comparing differences in scores between conditions on both the SSS and VAS, results from Wilcoxon tests show that following capsule administration ratings of alertness were greater and ratings of sleepiness less for the caffeine condition compared with both chewing and placebo conditions. No differences in subjective ratings were found between chewing and placebo conditions (Table 2). The change in subjective alertness and sleepiness across the night for each group is illustrated in Fig. 2.

In general cardiac autonomic activity did not appear to make a significant contribution to either cognitive performance or alertness during one night of total sleep deprivation. The exception to this pattern was for performance on the grammatical reasoning tasks. RMSSD and HR response time were shown to be significant predictors of both response time and accuracy for this task (Table 3).

While scores from the VAS and SSS were closely associated ($R = 0.89$, $P < 0.001$), the SSS appeared to be a more sensitive measure of cognitive performance decrements because of the decline in alertness during acute sleep deprivation. Linear regression analysis to assess the contribution of alertness on cognitive performance revealed that alertness assessed by the VAS only trended toward making a significant contribution to response speed on the PVT. The SSS on the other hand was shown to be predictive of both reaction time and number of lapses on the PVT as well as tracking performance (Table 4).

DISCUSSION

The typical decline in alertness and cognitive performance during acute sleep deprivation was observed in the current study. While chewing appeared to improve performance on a simple motor tracking task early during the period of sleep deprivation, this performance trend was not sustained. In contrast, performance of speed and accuracy amongst the chewing condition on a simple and more complex cognitive task appeared either unchanged or worse than the placebo condition across the period of sleep deprivation. Further, 200 mg of caffeine administered during this period improved cognitive performance on both simple and complex tasks and improved subjective feelings of alertness when compared with chewing conditions. Similarly, cardiac autonomic activity remained unchanged between chewing and placebo conditions early in the night, however, increases in PNA (increased RMSSD) and reductions in HR were observed in the caffeine condition after capsule administration. SNA activity (PEP) remained relatively unchanged in the caffeine group but showed significant reductions in the placebo group and increases in the chewing group postcapsule administration. While a change in RMSSD and HR were predictive of speed and accuracy on the more complex cognitive tasks during sleep deprivation (Grammatical Reasoning), subjective alertness was better able to predict performance on a simpler task (PVT). As no association between cardiac autonomic measures and subjective ratings were found, this suggests that physiological autonomic processes may modulate more complex reasoning performance during sleep deprivation and psychological influences such as perceived tiredness are differentially important for performance on simple tasks. Caffeine appears to achieve both increases in alertness and increases to cardiac PNA and therefore benefited both simple and complex tasks. Chewing on the other hand did not alter either process and consequently no improvements in cognitive measures were found. The increase in performance on the tracking task amongst the chewing condition early in the night is thought to be the result of one of two processes – either an initial response to a novel activity or due to participant bias or expectations of what is an obvious treatment condition. In the later case this bias was relatively short lived and chewing may have caused a stress response later in the night as evidenced by increased SNA activity and generally lower cognitive performance and alertness compared with the placebo condition.

A previous study by Hodoba (1999) reports decreased sleepiness between 01:00 and 05:00 hours amongst subjects chewing a gum compared with controls and medical

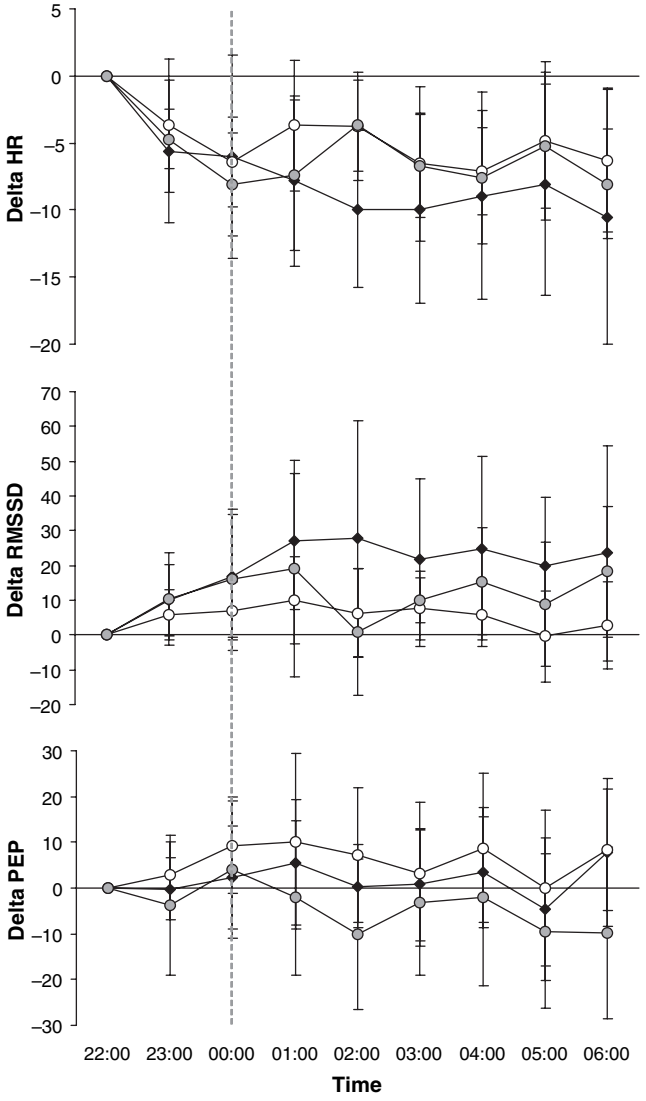

Figure 1. Change in cardiac variables compared with baseline during one night of sleep deprivation for the chewing group (gray circle), caffeine group (black diamond), and placebo group (white circle). Heart rate (HR, in beats per minute), preejection period (PEP, in ms), and root mean square of the successive differences in R-R intervals (RMSSD, in ms) are averaged over 12, 12 and 11 subjects, respectively, across the night. Dashed line indicates the time of caffeine or placebo administration.

Table 3 Linear regression analysis with response time and accuracy on the grammatical reasoning task as dependent variables and cardiac autonomic variables as predictors

Dependent ariable	*Predictors*	β	*Partial* R^2	*t*
Response time	HR	−0.15	−0.21	−1.61**
	RMSSD	−0.30	−0.27	−4.61**
	PEP	0.10	0.10	1.76 ($P = 0.09$)
Accuracy	HR	0.17	0.14	2.30*
	RMSSD	0.14	0.12	1.99*
	PEP	0.01	0.01	0.10

*$P < 0.05$; **$P < 0.001$.

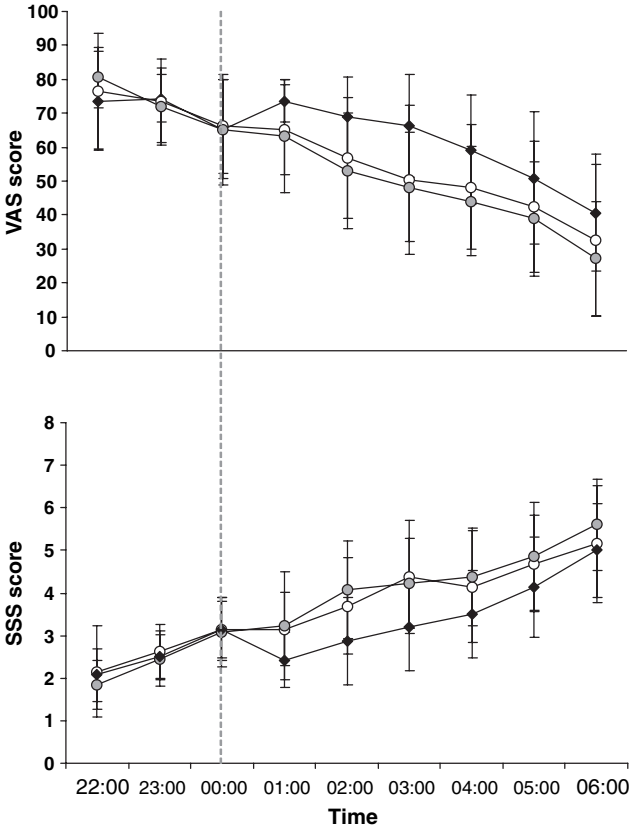

Figure 2. Ratings of alertness and sleepiness during one night of sleep deprivation for the chewing group (gray circle), caffeine group (black diamond), and placebo group (white circle). Visual analogue scale (VAS) and Stanford Sleepiness Scale (SSS) score are averaged over all 14 subjects for each scale across the night.

Table 4 Linear regression analysis with cognitive performance measures as dependent variables and measures of self-reported alertness (VAS) and sleepiness (SSS) as predictors

Dependent variable	*Predictors*	β	*Partial* R^2	*t*
Response speed (PVT)	VAS	−0.21	−0.10	−1.95 ($P = 0.05$)
	SSS	−0.57	−0.27	−5.34***
Lapses (PVT)	VAS	0.10	0.05	0.90
	SSS	0.32	0.15	2.83**
Accuracy (reasoning)	VAS	0.06	0.03	0.44
	SSS	−0.03	−0.01	−0.24
Response time (reasoning)	VAS	0.07	0.03	0.63
	SSS	0.05	0.02	0.45
Tracking	VAS	−0.19	−0.09	−1.65
	SSS	−0.28	−0.13	−2.45*

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$.

professionals permitted to stand or walk in an attempt to alleviate their sleepiness. While the environments in which these investigations took place were relatively uncontrolled the results are purported to represent a real-life night work environment. Two fundamental differences between this

previous study and ours were that in the previous study (1) chewing was continuous throughout the study, and (2) the chewing substance was a commercially available gum containing added flavor and aroma. A second study (Wilkinson *et al.*, 2002) demonstrated little improvement on measures of reaction time and vigilance during periods of chewing. Again, chewing was of a commercially available gum and chewing was continuous during task assessment. This study was conducted during the day using, presumably, non-sleep-deprived individuals. This final point is an important consideration as there may have been little room for improvement of performance on measures of simple cognitive tasks such as reaction time and vigilance tests. More recently Tucha *et al.* (2004), incorporating a repeated measures design similar to our own, found sustained chewing of a flavored chewing gum, neutral gum or mimicked chewing did not change performance in tasks assessing short-term attention or vigilance when compared with controls, and that all chewing groups demonstrated longer reaction times and reduced alertness and mental flexibility when compared with controls. The one exception amongst the chewing groups of this study was that the flavored gum group demonstrated improved sustained attention compared with controls. This study was performed during the day and performance assessed during a period of sustained chewing. Stephens and Tunney's (2004) assessment of cognitive function during chewing following ingestion of a glucose load indicates chewing may enhance language-based attention and processing speed. Such a result would be consistent with our own if cardiac autonomic changes were evident during periods of chewing itself, unfortunately however, these data are not available for comparison. Again, Stephens and Tunney's study was conducted during the day in non-sleep-deprived individuals.

Previous studies provide some concordance as to the potential ability of chewing to improve alertness and speed and accuracy on cognitive tasks and suggest little enhancement is probably achieved. The presumption that chewing benefits cognition in general may possibly be due to a generalization of reported effects on simple memory tasks. As to the ability of chewing to counter the alerting and cognitive decrements seen during sleep restriction, this study indicates, as for Tucha *et al.*, that chewing on its own does not alleviate any decrement in alertness and 'non-memory' cognitive tasks. The strength of the current study in its applicability to real life situations is that the testing environment involved a location and activity not dissimilar to those undertaken by night office staff, such as administrative positions, call-center customer service employees or security staff monitoring surveillance video images, while controlling for other factors such as light, movement, noise, food intake, and ambient temperature. Also, chewing was carried out intermittently, for 15 min every hour, much like someone would self-administer standard flavored chewing gum. Herein also lays a possible reason for the discrepancy between our results and others. All previous studies assessed performance during periods of sustained chewing while tasks in the present study were completed immediately after a period of chewing. It may be that chewing activates processes of cognitive enhancement and alertness only while the act of mastication is occurring, and that any effects are extremely short lived. Given the very short period of time between cessation of chewing and completion of an individual task we believe such effects are unlikely but need to be investigated.

As expected, caffeine delayed the decline in alertness commonly seen during sleep deprivation (Dinges *et al.*, 1997; Dorrian *et al.*, 2000). Ratings of alertness and sleepiness were improved in the caffeine group compared with chewing and placebo conditions during a single night without sleep. These results are consistent with previous studies. Penetar *et al.* (1993) administered caffeine doses of around 150, 300 and 600 mg, and placebo to 50 adults after 49 h of total sleep deprivation. Irrespective of dose, caffeine reduced ratings of sleepiness on the SSS and increased feelings of alertness as measured on a VAS for 2 h following administration. The shorter duration of effect in this previous study may be due to the fact that caffeine was administered at a time of greater reported sleepiness and following a longer period of sleep deprivation than in the present study. Alternatively, the fact that caffeine was administered at around 08:00 hours in this previous study may have left little time before circadian driven increases in alertness were apparent in the placebo group. Wesensten *et al.* (2001) report a significant decrease in sleepiness as reported on the SSS for 2 h following a 600 mg dose of caffeine at midnight (as in the present study) amongst 10 subjects compared with 10 subjects receiving a placebo. Caffeine was administered after 41.5 h of total sleep deprivation in this study, suggesting the increased sleep debt in both previous studies may be the factor shortening the drugs effectiveness. The study by Wesensten *et al.* also included bihourly PVT recordings. Unlike in the present study, response speed was maintained at predrug, presleep deprivation levels from 2 h postcaffeine administration for up to 9 h postcaffeine. This compared with a decline in performance amongst the placebo group consistent with typical circadian rythmicity. Subjects in the study were informed they would receive a substantial bonus monetary reward if performance was maintained above a set (but undisclosed) of criteria. It is possible that the effects of caffeine were attenuated and extended by motivational forces acting as a mediator to PVT performance. Further, the caffeine dose was three times that in the present study, and while dose affects do not seem to occur for ratings of sleepiness (Penetar *et al.*, 1993) the same may not hold true for cognitive performance during periods of sleep deprivation.

Strong associations were found between HR and RMSSD with response time and accuracy on the grammatical reasoning task. This may suggest that tasks requiring higher cognitive processing are sensitive to increases in PNA across the night. The subjective reports of alertness and sleepiness from the VAS and SSS were found to be predictive of psychomotor vigilance and tracking performance. Such 'simpler' cognitive tasks are perhaps sensitive to subjective states of arousal. Previous studies have found similar results in that tasks requiring higher cognitive skills are relatively unaffected by

sleep deprivation compared with tasks requiring less cognitive demand (Harrison and Horne, 2000; Horne, 1985). Borbély (1986) stated that 'it is amazing to see how well sleep-deprived persons perform tasks needing only brief concentration' (p. 158). This is an important consideration given that the grammatical reasoning tasks lasted for only 3 min compared with the 10 min of a PVT trial. However, associations between sleepiness and tracking were also found while each trial of the tracking task only lasted 30 s.

No association between indices of cardiac autonomic activity and alertness or cognitive performance was found in the present study. However, the typical rise in PNA during the night and concurrent decline in HR, as seen during a normal sleep/wake cycle (Furlan *et al*., 1990; Huikuri *et al*., 1994), was observed across the night. In general such results suggest a circadian influence on cardiac PNA activity and similar results have been previously reported (Burgess *et al*., 1997). The comparative increase in RMSSD, reduction in HR, and inferred increase in overall PNA amongst the caffeine group following ingestion is also consistent with previous studies (Richardson *et al*., 2004; Yeragani *et al*., 2005), however contrary results have been reported (Sondermeijer *et al*., 2002). Barry *et al*. (2005) have demonstrated that caffeine is associated with increased skin conductivity, EEG alpha frequency and reduced EEG alpha power, despite no effect on measures of cardiovascular function including HR, blood pressure and respiration. The authors suggest caffeine induces a state of arousal, and such results may explain the reported increase in subjective alertness following caffeine ingestion in the present study. Cardiac SNA, inferred from PEP, remained relatively stable across the night. This is in contrast to the typical decline in activity from a daytime peak across the normal sleep/wake cycle (Furlan *et al*., 1990; Huikuri *et al*., 1994). Holmes *et al*. (2002) observed a similar plateau of PEP as wakefulness was extended beyond subjects' normal sleep onset time; however, other studies have argued for a circadian dependency on cardiac SNA (Shiels *et al*., 2002; Trinder *et al*., 2000) and this discrepancy in results remains unresolved. The relative decrease in PEP amongst the chewing condition compared with placebo condition increased cardiac sympathetic activity during the early morning period around 02:00 hours. This increase in PEP may suggest induction of a mild state of stress and/or fatigue due to chewing across the night. In support of this, Farella *et al*. (1999) have demonstrated increases in HR and blood pressure during chewing gums of differing hardness. Cardiovascular and masticatory muscle activity were found to be proportional to gum hardness and perceived fatigue proportional to the level of muscle activity. It is not unreasonable to expect that chewing intermittently across an entire night while deprived of sleep would lead to similar fatigue. Anecdotally, this is consistent with our observations of subjects' displeasure in chewing the Parafilm during the later part of the night and this in itself may present a possible limitation to the study if the chewing of this unfamiliar substance impacted on mood. Future studies should endeavor to either obtain as soft as possible gum-base for chewing or take measures of mood across any extended period, particularly if participants are sleep deprived and therefore possibly less resistant to the cognitive impact of a potentially unpleasant stimuli.

While Wilkinson *et al*. (2002) observed increases in HR in their chewing condition and subsequent improvement in various aspects of short-term memory function, we are unsure whether any association between the two was apparent. Their results were explained in terms of possible increased cerebral blood flow (Momose *et al*., 1997) and insulin release. In support of their findings it has been shown that spectral analysis of HR during chewing of a gum-base increased the low-frequency band and decreased the high-frequency band relative to baseline. The ratio of high- to low-frequency power was markedly increased during chewing, indicating either enhancement of cardiac SNA or suppression of cardiac PNA (Shiba *et al*., 2002). While Tucha *et al*. (2004) did not observe differences in pulse rate between chewing groups and control no differences in measures of memory and attention were similarly found, still allowing the proposal by Wilkinson *et al*. to hold true. The present study is unique in that comprehensive cardiovascular measures were taken, differences between conditions were observed, yet no corresponding change in cognitive performance was found. The decrease in PEP, a marker of cardiac SNA, is consistent with previous results however our interpretation differs. Indeed, both interpretations may still hold true given the differences in time of day of testing.

Using a 19-channel EEG recording to determine the change in strength of five frequency bands from prechewing to chewing, Yagyu *et al*. (1998) demonstrated that chewing of a commercially available gum containing flavor and aroma led to increased power of high-frequency alpha and low-frequency beta bands with trends for higher delta and theta power when compared with chewing of unflavored gum base. VAS measures made during chewing indicated subjects chewing the commercial gum felt more refreshed and comfortable compared with their gum-base chewing counter-parts. Such results have been replicated and extended to show that significant increases in brain-state arousal is primarily due to the aromas and/or flavors which are constituents in commercially available gums, and not the chewing of the gum *per se* (Masumoto *et al*., 1999; Morinushi *et al*., 2000). These results are consistent with the results of the present study and suggest chewing on its own does not improve alertness or cognitive performance during periods of acute sleep deprivation. However, chewing-gum containing added flavors and aromas may increase alertness and cognitive performance. Such hypotheses are yet to be thoroughly tested and no conclusions can be drawn from the present study as constituents of commercial chewing gum were not included for comparison and no measures of brain activation were made.

The smaller sample size and fact that caffeine consumption was not adjusted for body weight of individuals was in part addressed by the counterbalanced design of this study and within-subjects analyses. The group *n* was not unlike previous

studies which range from 14 to 30 and generally incorporate an independent sample design (Baker *et al*., 2004; Stephens and Tunney, 2004; Tucha *et al*., 2004; Wilkinson *et al*., 2002). Such samples would be sufficient to detect a 'medium' effect with moderate power (Rosenthal and Rosnow, 1991). Of interest, a measure of memory performance would have provided valuable information and acted as a type of positive control for chewing effects. Unfortunately, this study was conducted before the majority of research on memory and chewing was published and therefore these effects not considered. Further, the schedule of activities each hour across the night did not allow for addition testing. Despite such limitations the present results are very informative given the paucity of research investigating the cognitive impact of chewing during sleep deprivation.

The present study is only the second attempt in the literature to determine the efficacy of chewing in alleviating the increase in feelings of sleepiness experienced during periods of sleep deprivation. It is also the first study published which attempts to look at the efficacy of chewing in countering cognitive decrements during sleep deprivation while comparing such effects to another countermeasure for sleepiness, and exploring possible mechanisms which mediate any effects. This study suggests chewing *per se* does not increase alertness or improve cognitive performance during such periods of sleep loss, and may in fact induce a state of mild stress or fatigue if continued over extended periods. Future studies need to address the influence that flavors and aromas of commercially available chewing gum may have on measures of alertness and cognition during sleep deprivation, as such factors may still provide an effective short-term counter-fatigue alternative.

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