# Exploring the relationships of gamma-hydroxybutyrate and sleep on metabolism, physiology, and behavior in humans

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# CHAPTER 9

## Eating Decisions Based on Alertness Levels after a Single Night of Sleep Manipulation: A Randomized Clinical Trial

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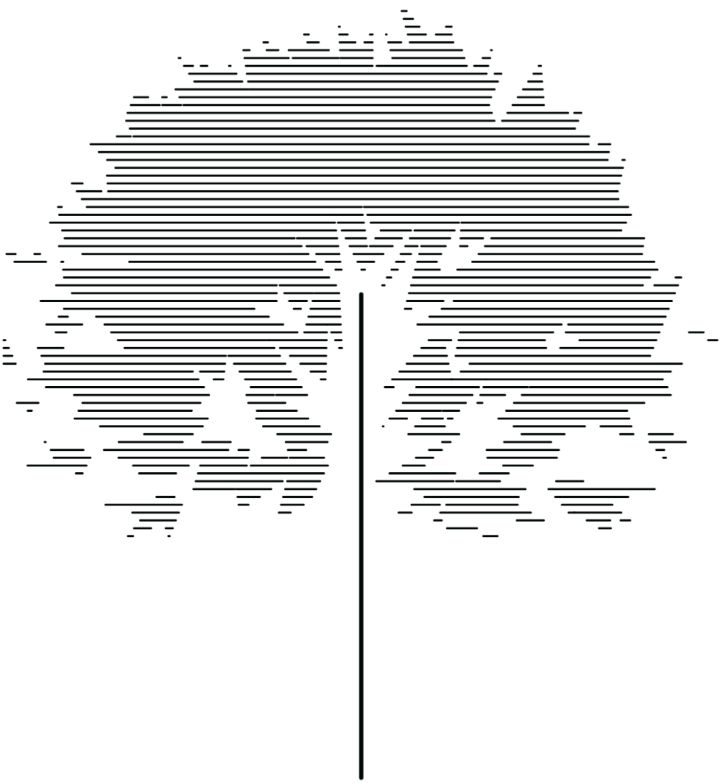

## Abstract

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| **Study Objective** | To determine the relationship between an ecologically-relevant change in sleep behavior and its subsequent effects on daytime alertness and feeding behavior. |
| **Methods** | Fifty healthy, young participants (10 male, 40 female) completed two 3-hour study sessions that were at least five days apart. The first session was a baseline evaluation. On the night prior to Session 2, the amount of time in bed was manipulated to be 60-130% of the individual's habitual sleep time. Within both sessions, subjective (Stanford Sleepiness Scale) and objective (Psychomotor Vigilance Test) alertness were measured. During the middle of each session, a 40-minute ad libitum meal opportunity allowed participants to eat from eight different food items. Food healthfulness, caloric density, distribution and number of calories were measured and compared to alertness levels. |
| **Results** | The induced variation in time in bed resulted in induced variation in both subjective and objective ($p<0.05$) measures of alertness. Decreased subjective alertness was associated with increased total caloric consumption ($p<0.05$), and a greater number of calories consumed from less healthy food ($p<0.05$), as rated by both the investigators and by the participant. Decreased objective alertness was associated with less healthy food choices ($p<0.05$), and the consumption of more food from the calorically-dense items ($p<0.05$). |
| **Conclusion** | Ecologically-relevant impairments in subjective and objective alertness are associated with increased caloric intake and dysfunctional eating decisions. People experiencing reduced alertness after modest sleep loss may be more willing to eat food they recognize as less healthful and appear to prefer more calorically dense foods. |
| **Statement of Significance** | Both laboratory-based and epidemiologic research demonstrate a relationship between reduced sleep and increased body weight. The laboratory-based studies, however, have relied on fairly extreme models of sleep loss in order to observe substantive changes in metabolic measures. Our research demonstrates that even small, ecologically-relevant changes in daytime alertness are associated with changes in food choices and eating behaviors. |

## Introduction

Substantial epidemiological evidence shows significant association between reduced sleep and increased body weight and a multitude of energy-regulation mechanisms have been explored to better understand this association[1-3]. Cross-sectional and prospective data show that short-duration sleepers have modified eating behaviors, including altered within-day eating timing,[4, 5] increased snacking behavior,[4, 6] and increased calories from beverages[4]. Controlled, prospective research demonstrates an increase in caloric intake on the day following one[7] to several nights[5, 8, 9] of partial sleep restriction in normal weight adults. While it is common for self-reported hunger to increase after sleep deprivation,[10, 11] some studies show no difference in hunger between the sleep-rested and sleep-deprived conditions, despite difference in food selection behavior[12]. The increase in caloric intake may in part be explained by reduced satiety[13].

Some increase in caloric intake after sleep loss would be expected to accommodate for increased energy expenditure from additional wake time[5]. Several studies show that, indeed, homeostatic factors contribute to increased caloric intake after sleep loss;[5, 11] although, this increased caloric intake seems to exceed the level expected to accommodate for energy expenditure associated with the additional time awake[14]. It has been argued that altered hedonic-valuation factors increase portion size and alter food selection after sleep loss[15].

A well-described and consistent response to sleep loss is impaired alertness, which can be observed in multiple ways, including decreases in both subjective and objective alertness measurements[16]. Moreover, it has been hypothesized that sleep deprivation-induced cognitive impairments, such as reduced alertness and attention, result from instability in the wake state[17] and that such an increase in moment-to-moment variability of attention impairs a wide variety of cognitive tasks, including goal-directed activities[17]. Eating is one such goal-directed activity with food decisions being made 200 times or more each day[18]. Eating is influenced by a wide variety of factors. Internal factors include metabolic state, health beliefs and objectives, emotional state, and the behavioral and metabolic consequences of dietary habits[19-21]. External influences include food presentation and environmental conditions[22-29]. External factors can shift awareness away from internal drivers of food intake, potentially causing diminished accordance with health goals and internal signals of satiety[30]. Thus, the act of self-monitoring food intake volume and food type, as well as satiety requires awareness, which is influenced by alertness, which is influenced by sleep.

We hypothesized that lowered alertness would lead to less surveillance in both total caloric intake and decisions about the types of food one eats. In the current study, we examined whether experimentally induced changes in subjective or objective alertness were associated with changes in total calorie consumption, and calorie consumption based on several categorizations, including the healthfulness, the tempting nature, and the caloric density of the offered foods.

## Methods

### Design

Using a within-participant design, we examined whether, compared to baseline, changes in alertness are related to changes in food consumption. To induce changes in alertness, participants were randomized to receive more, less, or the same duration of time in bed relative to their habitual sleep time for a single night immediately prior to their second visit. The first visit served as a baseline assessment. The study described in this manuscript was approved by the Stanford University Institutional Review Board (IRB) on May $15^{th}$, 2011 and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki. Each participant provided written informed consent prior to enrollment. The trial was registered with ClinicalTrials.gov (registration number NCT02484846). The authors confirm that all ongoing and related trials for this intervention are registered.

### Recruitment

A group of healthy adult men (n = 10) and women (n = 40) were recruited via Facebook Ads for a research study of sleep and decision making, cognition, and mood (Figure 1). Participants needed to be aged 18-45 years, with a BMI between 20-29 $kg/m^2$, eat breakfast at least five days per week, have a wake time between 5 and 10 AM at least 5 days per week and a time in bed allocated for sleep of 5-10 hours at least 5 days per week. Potential participants were excluded from the study if they had dietary restrictions that prohibited them from selecting any of the food options offered in the study (e.g., gluten allergies, diabetes, vegan diet, dairy avoidance, allergies to the respective food choices available), were currently on a calorie-restricted diet, or were currently at a weight that was less than 20% of their highest weight within the last three years. Other exclusion criteria included participation in shift work within seven nights of the experiment, being diagnosed as having a sleep disorder (including moderate or severe sleep apnea syndrome, narcolepsy, chronic insomnia) or an eating disorder, having an active serious health condition, regularly taking CNS-acting medication (e.g., methylphenidate), or typically consuming more than 600 mg of caffeine or smoking more than 10 cigarettes per day. Four females, one obese and three underweight, were included in the study despite being outside the range of our inclusion criterion for BMI. The study staff determined these individuals to be appropriate candidates based on their stable weight and positive health status. *Post hoc* examination of caloric intake (during both sessions as well as the difference between the two sessions) of these four participants indicated that it was within the 95% confidence interval of the remaining subjects. We also ran a parallel analysis in which we examined caloric intake normalized for subject bodyweight and found that caloric intake in these four subjects was statistically indistinguishable from the remaining subjects.

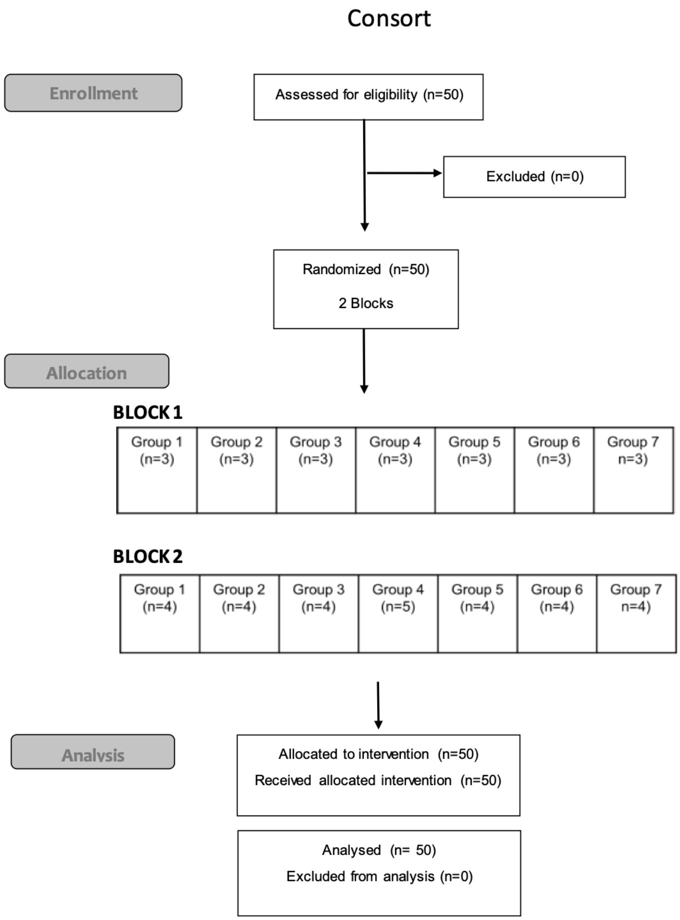


**FIGURE 1.** Consort diagram.

As participants were recruited for a study on sleep and cognitive function, the recruited participants were not made aware that the study would measure eating behaviors. As much as possible, the study was designed to not draw attention to the fact that their eating behavior would be evaluated as a part of the study. For that reason, there was no randomization for the order of the sessions and subjects were only asked to complete the Food Health and Liking Assessment Battery (FH-LAB) at the end of the second session. All participants completed the study within a six-month time frame between September 2011 and March 2012 in the San Francisco Bay Area. The research was conducted at two different study locations (Palo Alto and San Francisco, California); the configuration was identical at both sites and set-up by the same person (DP).

**Study Outline**

The study evaluated participants across two sessions that occurred at least five days apart: a baseline session after an unmodified night of sleep (Session 1) and a second session that immediately followed a night of sleep during which the time in bed was experimentally manipulated (Session 2). Given the experimentally-induced sleep restriction in some of the participants prior to Session 2 (see below), we requested that all participants be driven to or take public transportation to the laboratory on Session 2. On the morning of both study sessions, participants were asked to rise at their self-reported average wake time and arrive at the testing center 1.5 hours later. Between waking and arrival, participants were instructed not to exercise or consume food, beverages or cigarettes. Participants were allowed access to water throughout the duration of the study (approximately three hours) and to a restroom between study sections. Testing took place in a dimly lit room. The conditions between the two sessions were identical except that participants were consented during Session 1 and experienced an alteration of their time in bed on the night immediately prior to Session 2.

**Randomization**

To induce variability in the independent variable, participants were randomly assigned (by S. Pardi) to one of seven sleep intervention groups: 60% (Group 1, n=7), 70% (Group 2, n=7), 80% (Group 3, n=7), 90% (Group 4, n=8), 100% (Group 5, n=7), 115% (Group 6, n=7), and 130% (Group 7, n=7) of average habitual time in bed, as captured from self-report from the five nights immediately prior to Session 1. We used a 2-block randomization procedure to assign half of the participants in each block. Three subjects were assigned to each group in block 1. Four to five subjects were allocated to each group in block 2. We did the allocation procedure in this manner to ensure that the distribution of participants was spread out more evenly across the entirety of the enrollment period. All investigators were blind to participant allocation until all study procedures were completed, and all data were entered, and the database was locked.

**At-Home Sleep Monitoring**

At-home sleep patterns were recorded by participants using the Consensus Sleep Diary[31] for 5-7 days prior to Session 1 and the night prior to Session 2. The data collected prior to Session 1 were used to establish an average amount of time in bed for each participant. Target time in bed duration on the intervention night prior to Session 2 was calculated as the self-reported average nightly time in bed duration from the five nights prior to Session 1, multiplied by the randomization Group percentage. For example, a participant randomized to Group 3 (80%) who normally spent 7 hours in bed would be scheduled to be in bed for 5 hours 36 minutes for the night prior to Session 2. Sleep data collected prior to Session 2 were used to examine compliance with the randomization procedure. The wake time documented for morning of Session 1 was prescribed as the wake time for Session 2. The bedtime for the intervention night of sleep was calculated by subtracting the prescribed sleep time from established wake time. This way, between sessions, wake times were fixed and time-to-bed times and total time in bed were adjusted.

## Alertness Testing

*Psychomotor Vigilance Test (PVT)*

Performance on a sustained vigilance test was assessed using the PVT-192 (Ambulatory Monitoring, Ardsley, NY). The PVT is a commonly used objective measure of alertness[32] in which users are asked to hit a button as soon as they see a light (LED millisecond timer) appear on the device. This is followed by a variable delay between 2,000 and 10,000 milliseconds and a subsequent light stimulus. The PVT has been shown to be sensitive in testing sessions lasting up to 20 minutes[33]. In this iteration of the PVT, we had participants continue for 15 minutes. The median reaction time (mRT) on the PVT was used as the main measure of objective alertness, with an increase in mRT indicating a decrease in alertness.

*Stanford Sleepiness Scale*

Current subjective alertness was measured using the Stanford Sleepiness Scale (SSS). The SSS is a 7-point scale in which each point has a descriptive label, ranging from 1 — 'feeling active and vital; alert or wide awake,' to 7 —' No longer fighting sleep, sleep onset soon; having dream-like thoughts'[34]. The SSS has been found to be sensitive to changes in alertness due to both circadian variations and sleep loss[35]. Additionally, it has been shown that performance scores for the SSS are more sensitive when taken after, instead of before, a PVT[35].

## Food, Eating, and Nutrition Quantitation

During the approximately 40-minute eating opportunity, eight food items were placed between the participant and a video screen. While the participant ate, two different videos from TED.com (TED Conferences LLC, New York, NY), both approximately 20 minutes in length, played back to back. The two videos from Session 1 ('Seth Berkley on HIV and Flu – The Vaccine Strategy' and 'Hans Rosling Shows the Best Stats You've Ever Seen') differed from the two videos played during Session 2 ('Dan Dennett on The Illusion of Consciousness' and 'William McDonough on Cradle to Cradle Design') but the total video time for both sessions was identical (41 minutes 53 seconds). The purpose of these videos was to distract the participants while they ate, in an attempt to engender less mindfulness about their eating.

To eliminate possible inter-brand bias in food selection, all food items provided were from the Whole Foods Market brand (Whole Foods Market, Inc., Austin, TX). Each item was provided in large enough quantities so that item availability was not a limiting factor in consumption volume. Available items were: Butter Toffee Peanuts, Whole Almonds (raw, unsalted), Apple Rings (dried apple slices), Cinnamon and Sugar Glazed Walnuts, Fig Bars, Turkish Apricots, Chocolate Cherry Trail Mix, and Agave Gummy Bears. We aimed to provide participants with food items that ranged in perceived healthfulness. Food containers were weighed before and after the meal sections and measured in grams to the nearest 0.1 g. Participants were not informed that their choice of food was part of the experimental protocol. The foods were placed as a "snack" between cognitive testing periods and all participants, who had fasted since the previous evening, were told that it was important that they eat before the last cognitive testing section. At the start of the eating opportunity, the exact phrase "*it is better to be closer to full then still hungry*" was used with each participant and during each session. Consumed gram totals were multiplied by individual calorie-per-gram amounts provided on the back of the food packaging to yield total calories consumed per food item.

**Food Health and Liking Assessment Battery**

The Food Health and Liking Assessment Battery (FH-LAB) was created by our research group for this study. This questionnaire assesses two areas related to food consumption recall and assessment. The first part measures subjective liking of each of the eight food items provided. Two questions are asked per item: (1) Do you like this food item? (2) Do you regularly eat this food item? Responses are collected on a bipolar visual analog scale (100 mm, with 1 mm segmenting). For the former, the ends are anchored by "dislike strongly" (0) and "enjoy maximally" (100). For the latter, the ends are anchored by "never eat it" (0) and "eat this everyday" (100). The second part measures a subjective assessment of the healthfulness of each individual food item on a bipolar visual analog scale (100 mm, with 1 mm segmenting), anchored by "unhealthy" (0) and "most healthy" (100).

We evaluated consumption in several ways. *Experimenter rating.* We divided the eight food options into two categories: 'good' and 'bad.' The 'good' category included the four foods that the experimenters considered more healthful on the 8-item list (apple rings, apricot, almonds, and fig bars). The 'bad' category included the four foods that the experimenters estimated less healthful on the 8-item food list (gummy bears, cinnamon-sugar walnut, toffee peanuts, and sweetened trail mix). *Participant rating.* Scores of participant-rated food healthiness were obtained from the FH-LAB. To obtain a healthfulness session value, we took the fraction of calories eaten per item multiplied by the participant's healthiness rating of that item and summed these per-item values across each of the eight items to get a session health score.

**Calories consumed based on four distinct decision types**

Food decisions were also evaluated by combining the participants rating of two components of the FH-LAB: liking of each food item and healthfulness of each food item. Participants faced four possible decision types:

1. Low like, low health (lowest temptation)
2. Low like, high health (characteristic of some health decisions)
3. High like, high health (easiest choice)
4. High like, low health (tempting, hedonic-driven choice)

The ratio of liking to health (L:H) was calculated for each food in each participant. We evaluated the relationship between objective and subjective alertness on the various decision types, with highest interest in how alertness influenced decisions in category 4: high like, low health (food choices characterized by a polarization of low health and high liking, thus a more hedonically-driven choice). On a per participant basis, we determined this by taking the fraction of calories eaten per food option multiplied by the participant's L:H ratio per food.

### Calories consumed based on caloric density per food item

To assess caloric consumption based on the caloric density of each food item, we first divided number of grams per serving by calories per serving to yield a caloric density score per item. Each food item was assigned a percentage of total grams consumed within a session. This was multiplied by the caloric density and the sum of each of these (for each of the eight food items) generated a caloric density score for the session.

### Neurocognitive and Psychological Testing

We captured information on delayed discounting (Kirby Monetary Choice Questionnaire), mood (Profile of Mood States), and working memory (N-Back Working Memory test). The results of these measures are not reported in this paper.

### Data Analyses

We used linear regression, Spearman correlation, t-test, and $\chi^2$ test to test the relationship between alertness and food. Linear regression and Spearman correlations were calculated using OriginPro (v.8.0891, OriginLab Corporation, Northampton MA), t-tests were calculated using Microsoft Excel (v.12.0.6683.5002, Microsoft Corporation, Redmond WA), and $\chi^2$ tests were calculated using the java script found on www.physics.csbsju.edu/stats/contingency.html (accessed 09-15-14). Outlier detection was done using the Extreme Studentized Deviate, calculated using the java script found on graphpad.com/quickcalcs/Grubbs1.cfm (accessed 03-23-15).

### Results

All 50 of the individuals who were recruited completed this study, though there are instances of missing data. Of the 50, 10 were men (aged 23-43, 30 ± 6.3 years), 40 were women (aged 21-40, 27 ± 4.2 years), and 10 were smokers, all of whom reported smoking four cigarettes per day or fewer. Among the men, 5 were healthy weight (BMI = 18.5-24.9 kg/$m^2$) and 5 were overweight (BMI = 25-29.9 kg/$m^2$). Among the women, 29 were healthy weight, 7 were overweight, 1 was obese (BMI>30 kg/$m^2$), and 3 were underweight (BMI<18.5 kg/$m^2$). There was no difference between the BMI of male (24.3 ± 2.69) and female (22.4 ± 3.52) participants ($p = 0.12$, t-test), nor was there a sex difference in the categorical BMI distribution ($p = 0.16$, $\chi^2$ test). At baseline, participants had time in bed (TIB) of 7.73 ± 0.875 hrs (7.33-8.50 hrs, Q1-Q3).

### Randomization and Sleep Intervention

On the night immediately prior to Session 2, participants had a TIB of 6.78 ± 2.00 hrs (5.25-8 hrs, Q1-Q3). In comparing the targeted change in TIB to the self-reported TIB preceding Session 2, participants were generally compliant, having an actual TIB within 0.4% ± 12.6% of the assigned TIB. This change in TIB had a concurrent evoked change in both objective and subjective measures of alertness. For objective alertness, mRT during Session 1 was 260 ms ± 35.2 (range 192 – 406 ms) and for Session 2 it was 259 ms ± 35.0 ms (range 196 – 371 ms) with a change between session of -2.6 ms ± 21 ms (range -61 – 72 ms). For subjective alertness, SSS for Session 1 was 3 ± 0 IQR (range 2 –6) and for Session 2 it was 3 ± 2 IQR (range 1 – 6) with a change between session of 0 + 2 IQR (range -4 - 3). Change in TIB was linearly associated with change in scores on the SSS, such that individuals who got less than their usual TIB were less subjectively alert during Session 2 ($r = -0.45$, $p < 0.01$, Spearman correlation). Change in TIB was also linearly associated with change in mRT on the PVT such that individuals who got less than their usual TIB had greater mRT (less objectively alert) during Session 2 ($r = -0.38$, $p < 0.05$, linear regression).

### Subjective but not objective alertness associated with calories consumed

There was a linear relationship between change in subjective alertness and change in total number of calories consumed ($r = 0.29$, $p < 0.05$, linear regression) and total number of calories consumed relative to body weight ($r = 0.31$, $p < 0.05$, linear regression), such that when subjects were less subjectively alert than during Session 1, they ate more calories (Figure 2). There was, however, no relationship between change in mRT on the PVT and change in the total number of calories consumed ($p = 0.93$, linear regression) or mRT and change in total number of calories consumed relative to body weight ($p = 0.80$, linear regression).

### Alertness associated with calories from investigator- or participant- determined 'bad' foods

We found a positive association between change in subjective alertness and caloric intake from 'bad' choices as defined by the investigators ($p < 0.05$, linear regression), such that when individuals were less subjectively alert than during Session 1, they ate more calories from 'bad' choices (Figure 2). We, however, found no linear association between subjective alertness and calories from 'good' choices ($p = 0.78$, linear regression), indicating that as subjective alertness changed between Session 1 and Session 2, there was no associated change in the amount of 'good' calories eaten (Figure 2). There was no association between objective alertness (mRT) and either 'bad' ($p = 0.27$, linear regression) or 'good' ($p = 0.26$, linear regression) choices.

We also found a negative association between subjective alertness and self-rated food healthiness such that when participants rated themselves less alert they chose to eat foods that they rated less healthy ($p < 0.05$, linear regression). In addition, we also found a negative association between objective alertness and self-rated food healthiness such that when participants had higher mRT (less alert), they chose to eat foods that they rated less healthy ($p < 0.05$, linear regression).

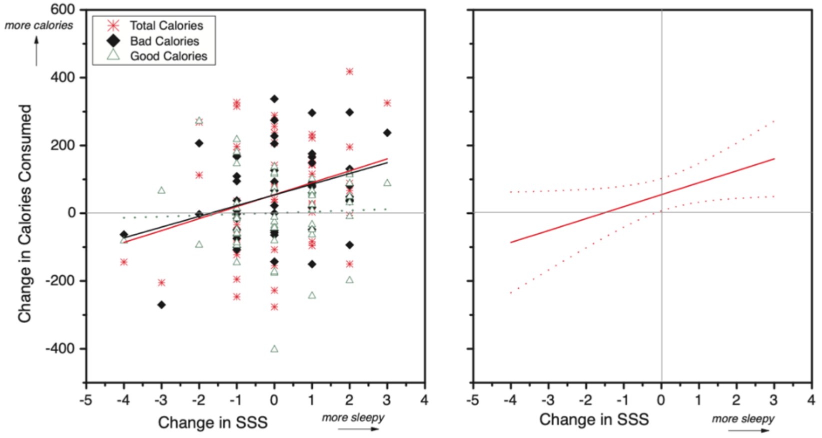


**FIGURE 2**. [Left] Change in total (red), investigator-rated 'bad' (black), and investigator-rated 'good' (green) calories as compared with change in subjective alertness (SSS, Stanford Sleepiness Scale). There was a significant linear relationship between the change in subjective sleepiness and change in both total and bad calories consumed, but no such relationship with good calories consumed. Significant linear fits are indicated by the appropriately colored solid line; the non-significant linear fit is indicated by the dotted colored line. [Right] The relationship between change in total calories and change in objective alertness is re-plotted with 95% confidence intervals (dotted lines). The 95% confidence interval crosses y=0 (no change in calories) for all negative changes in SSS score (i.e., increased alertness) indicating that increased calories are associated with decreased alertness but the converse is not true.

## Calories consumed based on four distinct decision types

The absolute level of subjective alertness correlated with greater number of calories consumed from ‘tempting, hedonic foods’ ($r = -0.23$, $p < 0.05$, Spearman). We did not see a within-participant difference between sessions.

## Calories consumed based on caloric density per food item

While changes in caloric density were not associated with changes in subjective alertness ($r = 0.14$, $p = 0.19$, linear regression), they were associated with changes in objective alertness such that when subjects had decreases in objective alertness (i.e., higher mRT), they were more likely to eat more calorically-dense foods ($r = 0.32$, $p < 0.05$) (Figure 3).

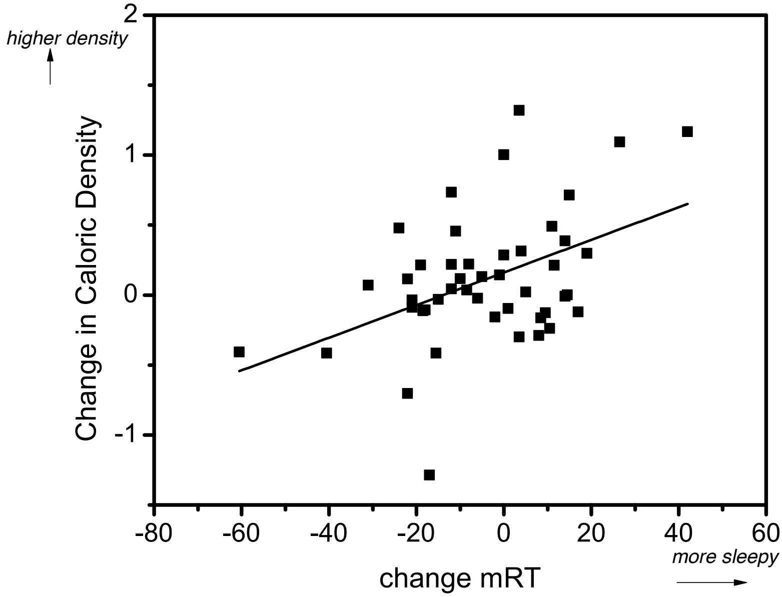


**FIGURE 3**. Change in caloric density as a function of change in median reaction time (mRT) on the PVT. There was a linear relationship between an increase in mRT, indicating slower responses commensurate with increased sleepiness, and an increase in the caloric density of foods elected to be consumed ($r = 0.32$, $p < 0.05$). A point in the lower right of the graph ($x = 72$, $y = -0.24$) was found to be an outlier (Extreme Studentized Deviate test, $p < 0.05$), but the correlation was stronger ($p < 0.01$, $r = 0.45$) when removed.

**Discussion**

This study suggests that reductions in alertness that follow a single night of modest sleep loss have an impact on eating behaviors, and that some of these altered behaviors depend on whether alertness is changed subjectively (i.e., feeling sleepier) or objectively (i.e., reacting more slowly). The subjective feeling of sleepiness correlated with total calories consumed and the caloric intake from foods categorized as 'bad' by the investigators and 'less healthy' by the participants. Additionally, the absolute level of subjective sleepiness positively correlated with the intake of calories from 'tempting, hedonic foods.'

These findings suggest several things. First, when a person feels less alert, the hedonic processing of tempting foods may be intensified. Previous work using functional magnetic resonance imaging (fMRI) has observed that one night of total sleep deprivation induced an amplification of subcortical areas that code salience for food decisions, and that these neural changes are associated with a greater desire for caloric density[12]. Similar to our findings, Greer et al.,[12] showed that after sleep deprivation, subjective sleepiness positively correlated with the percentage of overall calories wanted by participants classified as high-calorie foods. Interestingly, a recent study simulating one night of shift work under experimental conditions demonstrated a similar response: compared to the control condition, shift work participants ate significantly more high-fat breakfast items[36].

Another possibility is that when people feel less alert, they may relax personal standards resulting in the consumption of foods that they ordinarily may try to avoid or limit. It's been shown that sleep loss promotes effort discounting, which is when a person is less likely to make an effort to gain something he or she values as important or desirable. In our study, this could mean that participants with impaired alertness might have eaten foods they would otherwise avoided if they were more alert[23]. We did not, however, capture information about the participant's eating standards, so we were unable to assess whether choosing 'high like, low health' foods constituted a defection from a person's typical health pattern. This should be studied in future research as it is an important component to the multiplex relationship of sleep, eating, and weight control.

Similar to the effects of decreased subjective alertness, we found a negative association between reaction time and caloric intake related to self-rated food healthiness, such that when participants were less alert, a greater fraction of their caloric intake came from foods they rated as less healthy. While it is possible that the mild sleep deprivation may have altered the *post hoc* assessment of food-option healthiness by participants who had shorter time in bed, such a mild sleep loss is unlikely to reverse a person's characterization of an item[37]. For example, it is unlikely that a person who typically perceives cookies as unhealthy will view them as healthy when mildly sleep deprived. It should be noted, however, that during sleep loss, economic preferences can be altered to produce an 'optimism bias' where individuals become increasingly focused on potential gains and decreasingly focused on potential losses[38]. Translating this finding to health choices and food consumption, a sleep-deprived individual might be more focused on taste and less focused on health consequences of a 'high like, low health' food. Additionally, because mood and optimism can change after sleep loss, it is possible that the food ratings themselves were altered by state to be more or less generous in perceived healthfulness[38]. Future research should evaluate this question directly.

While there was some overlap between the effects of subjective and objective alertness on food intake, there were also differences. When reaction time slowed, participants ate more calories per session from denser food options; an observation unique to objective alertness. This finding is consistent with a recent study by Fang et al.,[39] that showed that compared to the day following baseline sleep, after a night of total sleep deprivation, participants consumed a greater percentage of calories from the more calorically-dense macronutrient (fat) compared to the less calorically-dense macronutrient (carbohydrate). Evaluation by fMRI revealed that after sleep deprivation, brain regions core to the food-salience network positively correlated with the percentage of calories consumed from fat and negatively correlated with the percentage of calories consumed from carbohydrates. These findings also align with the previously-mentioned Greer et al.,[12] study that showed that the highest calorie foods accrued the largest increase in desirability ratings following sleep loss.

The changes in subjective and objective alertness observed in this study occurred after degrees of sleep loss commonly experienced in modern society[40, 41]. Most previous studies examining the relationship between sleep deprivation and food intake, or appetitive processing, utilized much greater degrees of sleep loss, evoking larger impairments in alertness, but perhaps yielding findings that are not as ecologically relevant. While losing an entire night of sleep, or experiencing sleep curtailment closer to a common sleep-restriction protocol (e.g., only 4-6 hrs of sleep per night for five continuous nights[42]), undoubtedly occurs with unfortunate regularity in modern life, typical sleep curtailment is much less severe[41]. As such, our data are directly relevant to types of changes in food-intake patterns that occur under conditions of modern society and are therefore notably germane to the consistent epidemiological findings inversely connecting sleep loss to weight gain.

It must be noted that while we manipulated the amount of time people spent in bed, we did not objectively record sleep with polysomnography or actigraphy or use the amount of self-reported sleep as the main predictor in our analyses. Rather, we examined the *consequence* of the change in sleep, that is, a change in daytime alertness - and its variability - as our main predicting variable. By not having participants endure an extended, significant curtailment of sleep we limited the change in daytime alertness to a more restricted - likely more typical - range. This probably diminished the statistical power in our correlation analyses, but while previous work has explored the capacity of sleep loss to modify eating behaviors and metabolism, we aimed to probe sensitivity of the system. In other words, by not having dichotomous groups on two ends of the alertness spectrum (i.e., normally alert vs. very tired), we limited our ability to detect correlations between alertness and our food-intake outcomes. Despite this imposed restriction, we did detect significant and meaningful correlations between small changes in alertness - changes typically experienced by normal people day-by-day - and changes in food choices. It should be noted, however, that only worsening of alertness between sessions correlated with the changes in eating behaviors observed as improvements in alertness did not yield changes (Figure 2). Because sleep restricted participants were asked to stay awake past their normal bedtimes on the night prior to Session 2, it is possible that light at night, during the wake extension period, could have caused a small shift in circadian phase. Such a shift could modify eating behavior independent of changes in alertness. It is also important to point out that 80% of our participants are female. Future research should look to confirm these findings in males. Additionally, it would be useful for subsequent investigations into this topic to include objective measurements of sleep so as to further explore the relationship between sleep loss *per se* and eating behaviors.

In Western societies, many people regularly experience varying degrees of sleep-deprivation, and it is common to be surrounded by palatable, energy-dense foods. Regardless of accuracy, people have opinions on the healthfulness of foods, and may be more likely to consume foods recognized as unhealthy after mild sleep curtailment. Because alertness is a measure of the functionality of attentional networks in the central nervous system - and because attention is a requirement of many goal-directed activities - reduced alertness, therefore, could impair health-goal directed behavior related to food choice. The ability to purposefully avoid foods perceived as unhealthy is likely an important factor in maintaining a consistent level of adiposity. Reduced alertness, therefore, is possibly an important contributor to weight gain in our society. Future research should examine whether variability in alertness leads to meaningful net-differences in eating behaviors over extended periods of time.

**Acknowledgements**

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**Competing Interests**

DP is the founder of humanOS.me, a commercial health technology organization that supports healthy lifestyle practices. He is the majority shareholder of the organization but does not receive a salary from it. The other authors have declared that no competing interests exist.

**Conflicts of Interest**

The authors report no conflicts of interest.

**Author Contributions**

Conceived and designed the experiments: DP, JB, GJ, JZ. Performed the experiments: DP. Analyzed the data: DP, JZ, MB. Wrote the paper: DP, JZ, MB, GJL.

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