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## Macronutrient composition of a morning meal and the maintenance of attention throughout the morning

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### Abstract

**Background**—At present, the impact of macronutrient composition and nutrient intake on sustained attention in adults is unclear, although some prior work suggests that nutritive interventions that engender slow, steady glucose availability support sustained attention after consumption. A separate line of evidence suggests that nutrient consumption may alter electroencephalographic markers of neurophysiological activity, including neural oscillations in the alpha-band (8–14 Hz), which are known to be richly interconnected with the allocation of attention. It is here investigated whether morning ingestion of foodstuffs with differing macronutrient compositions might differentially impact the allocation of sustained attention throughout the day as indexed by both behavior and the deployment of attention-related alpha-band activity.

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**Methods**—Twenty-four adult participants were recruited into a three-day study with a cross-over design that employed a previously validated sustained attention task (the Spatial CTET). On each experimental day, subjects consumed one of three breakfasts with differing carbohydrate availabilities (oatmeal, cornflakes, and water) and completed blocks of the Spatial CTET throughout the morning while behavioral performance, subjective metrics of hunger/fullness, and electroencephalographic (EEG) measurements of alpha oscillatory activity were recorded.

**Results**—Although behavior and electrophysiological metrics changed over the course of the day, no differences in their trajectories were observed as a function of breakfast condition. However, subjective metrics of hunger/fullness revealed that caloric interventions (oatmeal and cornflakes) reduced hunger across the experimental day with respect to the non-caloric, volume-matched control (water). Yet, no differences in hunger/fullness were observed between the oatmeal and cornflakes interventions.

**Conclusion**—Observation of a relationship between macronutrient intervention and sustained attention (if one exists) will require further standardization of empirical investigations to aid in the synthesis and replicability of results. In addition, continued implementation of neurophysiological markers in this domain is encouraged, as they often produce nuanced insight into cognition even in the absence of overt behavioral changes.

## Keywords

Attention; Cognition; EEG; Breakfast; Vigilance; Alpha-band; Oscillations

## Introduction

While nutrient intake has been consistently documented to increase cognitive performance in some domains like memory in young/middle-aged adults, its impact on sustained attention and vigilance in this population is less clear.<sup>1,2</sup> However, several interesting findings have emerged to date. For instance, Fischer *et al.*<sup>3</sup> found that pure fat intake during breakfast supported attentional task performance compared to pure protein or carbohydrate intake; in a second study, they observed that protein-rich and balanced (carbohydrate plus protein) breakfasts resulted in increased attentional performance relative to a carbohydrate-rich breakfast, although the latter was associated with a transient increase in performance shortly after consumption.<sup>4</sup> In both cases, the authors attributed their findings to slow, sustained glucose availability following consumption of fat-/protein-rich foodstuffs with low glycemic index, as opposed to rapid glucose availability due to the consumption of carbohydrate-rich foodstuffs with high glycemic index. The effects of post-prandial glycemic availability on attention appear to vary with age<sup>5,6</sup> and individual glucose tolerance.<sup>7</sup> Accordingly, the literature suggests that postprandial glycemic regulation might underlie the relationship between nutrient consumption, macronutrient composition, and sustained attention. But, as many studies also report finding null or inconsistent effects,<sup>8,9</sup> such a connection, while physiologically plausible, is tentative at present.

Likewise, evidence supporting a relationship between nutrient intake and attention-related brain activity has also been mixed, especially when considering nutrient-driven attentional modulations of event-related potentials, which reflect average electrical brain activity

generated in response to stimulation (e.g. auditory or visual stimulation<sup>10</sup>). However, some preliminary investigations suggest that nutrition might play a role in modulating neural oscillations, rhythmic fluctuations in electrical voltage recorded at the scalp. In one study on preadolescents performing a Go/No-Go task, Pivik and Dykman<sup>11</sup> observed significant differences in event-related synchronization in the alpha-band (8-14 Hz) between fed and fasting states, and they suggested that breakfast consumption directly countered the detrimental effects of fasting on brain physiology. However, although alpha oscillatory power and its topographic lateralization across the scalp have been heavily implicated in the deployment of attention in adults,<sup>12,13</sup> it is unclear whether nutritional intake modulates attention-related alpha oscillations in this population as well.

Here, it was tested whether the glycemic availability of foodstuffs modulates the attentional deployment of alpha oscillations in adults. In a cross-over design, EEG, task performance, and metrics of hunger/fullness were simultaneously recorded as adult participants under three breakfast conditions – two calorie-matched, carbohydrate-rich breakfasts with differing carbohydrate availabilities (oatmeal and cornflakes) as well as a volume-matched water condition-performed a demanding continuous performance task (CPT) variant requiring sustained attention across the morning. While CPT variants have been consistently employed to this end and have successfully revealed interactions between nutrition and attention,<sup>1,2</sup> the current CPT variant has an added advantage: it has been validated in the literature to produce reliable attentional deployment of alpha oscillations,<sup>14</sup> suggesting a unique opportunity to probe the nuanced effects of macronutrient composition, as indexed by available carbohydrate load of the two solid breakfast conditions (oatmeal: 39.77 g, cornflakes: 56.66 g), on both behavior and a fundamental neural mechanism of attention. Relative to cornflakes, it was hypothesized that oatmeal, with its reduced available carbohydrate load and glycemic index, would promote steady glycemic availability throughout the experimental session, enabling increased task performance and sustained attentional deployment of alpha oscillations throughout the morning.

## Methods

### Study design

A cross-over study design was employed in which each subject underwent all breakfast conditions (oatmeal, cornflakes, and water) over the course of three consecutive experimental sessions separated by 1–2 weeks. The experimental protocol and time points are shown graphically in Fig. 1a. Subjects were asked to fast overnight starting at 9 p.m. before each study day. At the beginning of each experimental day, subjects completed brief experimental questionnaires to verify that they had fasted overnight; were in good general health; had not taken any new medications between experimental sessions; and were on appropriate contraception. Fasting blood glucose levels were then drawn by finger stick to verify no difference in fasting state between experimental days. Finally, Visual Analog Scales (VASs) for hunger and satiety were recorded, after which subjects were outfitted with a 160-channel EEG cap. After the UDTR (Up-Down Transformation Rule; U) and Baseline (B) blocks (see the section ‘Stimuli, task and experimental protocol’), subjects were provided with one of the breakfast meals described in Fig. 1b. The water intervention (680

ml of water, volume-matched to the oatmeal breakfast) is not explicitly shown as it has no caloric value. Task blocks, foil blocks, and VASs were then administered as indicated for the duration of the day. Per preliminary power analyses, 24 subjects were pseudo-randomly assigned to one of six possible breakfast orderings (1. oatmeal, 2. cornflakes, 3. water; 1. oatmeal, 2. water, 3. cornflakes; etc.), ensuring that, after enrolling all participants, 4 participants had received each breakfast ordering. All subjects were compensated for each day of the study, totaling \$320 in compensation at study completion. Procedures and protocols were approved by the Institutional Review Board of the Albert Einstein College of Medicine. Ethical standards and decisionmaking were in accordance with the principles outlined in the Declaration of Helsinki.

## Participants

Participants were required to be: 18–44 years of age; healthy and taking no regular medications beyond hormonal contraception/hormone replacement therapy; and willing to use effective contraception during the study if sexually active and capable of bearing children. Additionally, they were to have: normal or corrected-to-normal hearing and vision; no history of neurological or psychiatric illness in the prior year; no history of nicotine, alcohol or substance dependence; and BMI less than 35 kg/m<sup>2</sup>. Exclusion criteria included: women who were pregnant or nursing; weight gain or loss of more than 4 kg in the past 3 months; current use of supplements/medications for weight loss and/or neurological/psychiatric illness; history of diabetes mellitus or fasting glucose greater than 126mg/dl; Three Factor Eating Questionnaire (TFEQ) score greater than or equal to 14; allergy to any food employed in the study; history of gastrointestinal and/or eating disorder or gastrointestinal procedures for weight loss; and daily caffeine consumption of more than 400 mg. In total, 27 participants were recruited to participate in experimental testing. Three subjects did not complete the full protocol (two withdrew voluntarily; one was unable to maintain eye-fixation during the task), leaving 24 adults (age: 26.5 ± 3.9, 11 females, 3 left-handed). Three of the 24 subjects had previously participated in a one-day study with an identical task.

## Stimuli, task, and experimental protocol

The primary task employed in the present experiment was the Spatial Continuous Temporal Expectancy Task (Spatial CTET<sup>14</sup>). As a variant of a Continuous Performance Task (CPT), the Spatial CTET requires sustained visuospatial attention to a stream of visual information over a time-scale of several minutes. Such tasks requiring extended vigilance to an incoming stimulus stream, possibly in the presence of a distractor, have been consistently employed in the study of nutritive effects on attention and have occasionally yielded positive results,<sup>1,2</sup> indicating that CPT variants can be sensitive to macronutrient manipulation. In addition to being a CPT variant, the Spatial CTET is also a visuospatial attention task, again a type of task that has previously shown sensitivity to nutrient intervention.<sup>15,16</sup> Finally, the Spatial CTET has been previously demonstrated to reliably elicit attentional deployment of alpha oscillatory activity. For these reasons, the Spatial CTET is particularly well suited for the current aim. The task is here described briefly, but the reader is encouraged to review Gray *et al.*<sup>14</sup> for another thorough description of the task and characterization of associated neurophysiological findings.

As shown in Fig. 2a, the stimulus consisted of a black fixation dot and two checkerboards presented against a gray background. In each block (3–4 minutes), one of the checkerboards rotated every 766.66 ms (1.3 Hz) and the other rotated every 666.66 ms (1.5 Hz), resulting in two simultaneously presented streams of predictable, rhythmic visual information. Participants were instructed to: maintain central fixation on the fixation dot; attend the prompted checkerboard stream covertly for an entire block; and respond via mouse click with their right index finger whenever they detected a target – a brief pause (break) in the attended checkerboard’s rotation rhythm. All participants, including left-handed participants, were asked to respond with a right-handed mouse. Targets occurred in each checkerboard stream every 8–12 seconds with the number of standards (normal-duration checkerboards) between targets drawn from a uniform distribution over this time interval. Targets occurred independently in each checkerboard stream. No information was given to participants about responding to targets in the unattended stream, and no participant reported noticing targets in the unattended stream. The number of standards between targets in each block was determined before data collection and held constant across participants.

At the beginning of the first day of experimentation, participants were presented with a practice block of the task, during which the task was verbally explained. Task difficulty was then adjusted over the course of two titration blocks by adjusting the duration of the target using a 3-up, 1-down Up-Down Transformation Rule (UDTR), wherein a single miss increased the duration of the target by 33 ms and three hits in a row decreased its duration by the same amount. Hits were defined as responses (mouse clicks) that occurred within 1500 ms after the point at which the duration of the target exceeded that of the standards. Across subjects, titration produced target durations that exceeded standard durations by 610 ms ( $\sigma = \pm 190$  ms) on average and resulted in an average detection rate of 62% ( $\sigma = \pm 17\%$ ) across all participants and experimental days.

Subjects began each experimental day with two task blocks (together dubbed the Baseline block), after which a short break for breakfast was given; thereafter, a break was given after every five blocks (every 15–20 minutes). Additionally, between these larger five-block experimental segments, participants performed two blocks of a foil task similar to the Spatial CTET (results not discussed here). Stimulus configuration (which checkerboard rotated at which frequency) and attended checkerboard were counterbalanced over the course of 27 blocks on each day for a total time on-task between 80 and 110 minutes. A total of 437 targets and 6821 standards were presented per day; thus, the 24 subjects who completed the entire experimental protocol were each presented with 1311 targets and 20 463 standards. For additional technical details on the design of the Spatial CTET, see the section ‘Supplementary methods’.

## Data acquisition

EEG data were acquired from 168 sintered Ag-AgCl active electrodes (160 scalp electrodes; 8 external electrodes) in conjunction with the BioSemi ActiveTwo system. Each active electrode integrates the first amplifier stage locally on the electrode, enabling electrode output impedances of less than 1  $\Omega$ . Recordings were digitized at a sampling rate of 512 Hz and referenced during acquisition to the active, two-electrode (CMS-DRL; Common Mode

Sense-Driven Right Leg) referencing system. In this system, two electrodes (CMS and DRL) near the midline on posterior-parietal scalp are used to create a feedback loop that actively drives the subject's average potential (the Common Mode Voltage) to the reference voltage of the ADC (analog-to-digital converter). As recorded potentials are referenced to the driven CMS electrode and not the potential measured from another recording electrode (or a group of them), potentials recorded with this referencing system are often labeled 'reference-free'. Alternative referencing conventions (any electrode or combination of them) can then be chosen freely offline without loss of information. During online acquisition, signals were bandpass filtered between 0.16 and 100 Hz.

To ensure central fixation during the task, eye-tracking data were acquired during mini-blocks with an infrared eye-tracking system (EyeLink 1000 Remote/Head Free Upgrade; SR Research). With a highspeed camera, the EyeLink 1000 system captures the infrared light reflected from a subject's cornea and the darkness of the pupil, enabling calculation of fixation position. In Remote/Head Free mode, fixation measurements have a maximum resolution and accuracy of 0.05° and 0.5° visual angle, respectively. Eye-tracker data were digitized at 500 Hz. Calibration of the system was performed at the start of the day and after each scheduled break with a nine-point grid. Triggers denoting checkerboard presentation were sent from the stimulus-presentation computer to each of the eye-tracking and EEG acquisition systems to allow for synchronization of these records during offline data processing. For a full technical description of EEG and eye-tracking data preprocessing steps, see the section 'Supplementary methods'.

## Behavioral analyses

In addition to recording electrophysiological signals, the EEG datasets also recorded experimental timing of stimulus presentation and participant responses. By examining each trial individually, including those that may have been rejected because of eye-movements, task performance in each block was analyzed. For each block, the following were computed: hit rate, false alarm rate, perceptual sensitivity ( $d'$ ), and average reaction time. Reaction times were recorded relative to the time point at which the duration of the target exceed that of the stimulus.

## Subjective ratings of hunger and fullness

To track subjective feelings of hunger, each participant was given a series of Visual Analog Scales (VASs) over the course of each experimental day. The VAS designed for the current experiment was composed of four questions:

Q1. How hungry are you?

Q2. How full are you?

Q3. How strong is your desire to eat?

Q4. How much food do you think you could eat?

For each question, subjects were presented with a 10 cm line (see Fig. 2b). On either end of the line were two extremum answers. For example, in response to question 1 (above), one end of the line was labeled 'Not at all hungry', and the other was labeled 'Extremely



hungry'. For each question, subjects were asked to indicate their reply on the (10 cm) spectrum between these two extremum values with a thin, small mark that crossed the 10 cm line at only one point.

VAS scales were administered eight times over the course of each experimental day (as indicated in Fig. 1a). After all data collection, the VAS scales were manually measured to the nearest millimeter from the left extremum value.

## EEG data analyses

To measure changes in the deployment of attention-related alpha oscillations over the course of the day as a function of breakfast intervention, scalar indices of alpha deployment were created, and their trajectories over experimental blocks were recorded. Their trajectories were then subjected to statistical testing to detect a main effect of breakfast condition.

**Tonic alpha activity**—One simple measure of alpha activity is its average power within a trial. Since alpha oscillations can be found over the posterior scalp, two symmetric sets of posterior sensor pools were defined (Fig. 2c). The signal from each sensor was subjected to the Fast Fourier Transform. By averaging across the alpha range (8–14 Hz), an average alpha power at each electrode for each trial ( $\alpha_{i,j}$ ) was calculated. Tonic posterior alpha for a trial was then defined as

$$LTA = \ln \left( \frac{1}{NS} \sum_{j=1}^N \sum_{i=1}^S \alpha_{i,j} \right)$$

where  $i$  runs across *all* sensors highlighted in Fig. 2c and  $j$  runs across all trials, resulting in a measurement of tonic alpha activity for each block across the experimental day. As shown in the formula above, the natural logarithm of this value was taken for plotting and statistical testing by convention.

**Alpha lateralization index**—Alpha activity is also known to lateralize as a function of spatial attention. A metric of alpha lateralization similar to that used elsewhere in the literature was therefore employed.<sup>17,18</sup> For each trial, EEG data were averaged *within* each sensor pool (Fig. 2c). The average time courses of each pool were then subjected to the Fast Fourier Transform as before. After the frequency transform, the mean of the power data at each sensor group was taken across the alpha-band.

As in Fig. 1a, each large block of experimental presentation consisted of either two or five individual blocks of the Spatial CTET. As each individual block alternated which checkerboard was to be attended (left or right), each large block contained trials with both of these conditions. Alpha power values described above for the two sensor pools were then averaged separately for attend left and attend right conditions. As a result, for each large block, four values were obtained: one for each of two sensor pools across two attentional conditions.

An alpha lateralization index (ALI) was then defined as

$$ALI = \frac{1}{2} \left[ \left( \frac{\alpha_{l,l} - \alpha_{l,r}}{\hat{\alpha}_l} \right) + \left( \frac{\alpha_{r,r} - \alpha_{r,l}}{\hat{\alpha}_r} \right) \right]$$

Here, the first subscript describes the attended direction (left vs. right) and the second describes the sensor pool at which alpha is measured (left vs. right). The notation  $\hat{\alpha}_l$  is taken to be the arithmetic mean of alpha powers detected at left and right sensor groups during the attend left condition (the generalization to  $\hat{\alpha}_r$  is the same). The ALI was, therefore, the mean lateralization value across attend left and attend right conditions, and a positive ALI indicated that alpha was lateralized ipsilateral to the attended target. The expression above resulted in one scalar value for each large block that described the magnitude of the detected lateralization effect.

### Statistical testing

As depicted in Fig. 1a, fasting blood glucose measurements were taken by finger stick to verify equivalence of initial fasting states across experimental days. For statistical testing, a two-way, repeated-measures ANOVA was conducted on the fasting glucose data with factors Breakfast and Breakfast Order (see the section ‘Study design’). Two subjects, each of whom were missing one fasting glucose measurement from one study day, were not included in the analysis as the ANOVA design does not accommodate missing or incomplete data.

All scalar metrics collected from behavioral data (hit rate, false alarm rate, perceptual sensitivity, and average reaction time), VAS data (measurements for questions 1–4), and EEG data (LTA and ALI) were computed at multiple time points throughout the day for each breakfast condition. To detect any main effect of Breakfast (or any Time  $\times$  Breakfast interaction) on any of these scalar metrics, a mixed linear model was employed in SPSS Version 24 (IBM Corp.). Each scalar metric (Y) was modeled as

$$Y = \text{Time} + \text{Breakfast} + (\text{Time} \times \text{Breakfast}) + \text{Breakfast Order} + \text{Subject} + \varepsilon$$

where the effects of Breakfast, Time, their interaction (Time  $\times$  Breakfast) and Breakfast Order were treated as fixed. Subject was treated as a random effect, and its intercept was allowed to vary randomly (covariance type: *Scaled Identity*). Finally, as measurements were repeated within subjects across times and breakfasts, Time and Breakfast were modeled as repeated measurements with a heterogeneous, first-order autoregressive covariance matrix (*AR(1): Heterogeneous*). Additionally, *post hoc* statistical testing was employed as appropriate (see the section ‘Results’ for a full enumeration of these tests).

## Results

The initial fasting glucose concentration averaged across all experimental sessions was  $87 \pm 2$  mg/dl (95% CI [82, 91]; by Breakfast condition: oatmeal:  $85 \pm 2$  mg/dl, 95% CI [80, 91]; cornflakes:  $88 \pm 3$  mg/dl, 95% CI [82, 94]; water:  $86 \pm 3$  mg/dl, 95% CI [81, 91]). Regarding statistical testing of this data (see the section ‘Statistical testing’), neither the main effects (Breakfast, Breakfast Order) nor the interaction term (Breakfast  $\times$  Breakfast



Order) was found to be significant (all  $P > 0.45$ ), indicating that fasting glucose measurements did not significantly vary across experimental days.

### Behavioral analyses

Figure 3 presents behavioral data gathered in the study. Hit Rate and Perceptual Sensitivity ( $d'$ ) were observed to decline significantly over the course of the experimental day (Hit Rate:  $F_{(1,221.632)} = 48.390$ ,  $P < 1 \times 10^{-10}$ , Effect Size Estimate:  $-0.032 \pm 0.007$ , 95% CI  $[-0.045, -0.018]$ ; Perceptual Sensitivity:  $F_{(1,164.036)} = 25.841$ ,  $P < 1 \times 10^{-6}$ , Effect Size Estimate:  $-0.09 \pm 0.03$ , 95% CI  $[-0.14, -0.036]$ ). No such effects were found for False Alarm Rate nor Reaction Time. Thus, across each experimental session, selective reductions in target detection (errors of omission) were observed, as opposed to increases in false alarms (errors of commission) or reaction times. Surprisingly, an unexpected significant main effect of Breakfast Order on False Alarm Rate was also observed ( $F_{(1,22.729)} = 2.839$ ,  $P < 0.04$ ), suggesting that at least one of the breakfast orderings might have impacted the commission of false alarms. However, a *post hoc*, repeated-measures ANOVA indicated that, across all time points and breakfast conditions, no significant differences in aggregate False Alarm Rates were observed between subjects in each breakfast ordering group. Furthermore, explorative analysis suggested that the observed effect was likely driven by increased False Alarm Rates for one of the six groups during the whole of their first (cornflakes) and last (water) study sessions. As this increase was also observed during the Baseline blocks (i.e. pre-breakfast) on those days, it was unlikely to be related to nutrient intake and will not be discussed further. Finally, no main effects of Breakfast nor Time  $\times$  Breakfast interactions reached significance for any behavioral metric. Consequently, no relationship between task performance on the Spatial CTET and nutritional intervention was identified.

### Subjective ratings of hunger and fullness

Visual Analog Scale data are shown in Fig. 4. Main effects of Time were significant for all four VAS prompts, indicating that responses to all questions changed significantly over the course of the experimental sessions (see the section 'Subjective ratings of hunger and fullness'; Q1:  $F_{(1,171.612)} = 53.231$ ,  $P < 1 \times 10^{-10}$ ; Q2:  $F_{(1,73.144)} = 5.070$ ,  $P < 0.03$ ; Q3:  $F_{(1,345.138)} = 57.469$ ,  $P < 4 \times 10^{-13}$ ; Q4:  $F_{(1,156.982)} = 37.027$ ,  $P < 9 \times 10^{-9}$ ). Significant main effects of Breakfast were found for two prompts (Q1:  $F_{(2,76.940)} = 3.841$ ,  $P = 0.03$ ; Q4:  $F_{(2,66.149)} = 6.107$ ,  $P = 0.004$ ) and a third approached significance (Q3:  $F_{(2,176.425)} = 2.699$ ,  $P = 0.07$ ). In each case, visual inspection reveals that oatmeal/cornflakes responses diverged from water responses directly after breakfast. Statistical analysis confirmed this effect, as significant Time  $\times$  Breakfast interactions were observed for three of the four VAS prompts (see the section 'Subjective ratings of hunger and fullness'; Q1:  $F_{(2,174.080)} = 9.280$ ,  $P < 2 \times 10^{-4}$ ; Q3:  $F_{(2,248.153)} = 10.220$ ,  $P < 6 \times 10^{-5}$ ; Q4:  $F_{(2,172.909)} = 19.062$ ,  $P < 4 \times 10^{-8}$ ). A Time  $\times$  Breakfast interaction also approached significance for the fourth prompt (Q2:  $F_{(2,185.017)} = 3.016$ ,  $P = 0.051$ ). The data, therefore, suggest that VAS trajectory across the day depended on breakfast. In sum, breakfasts with caloric content (oatmeal and cornflakes) had direct effects on hunger and fullness that were not observed in the volume-matched, non-caloric water condition.

However, it was not immediately clear whether metrics of hunger and fullness differed between the two caloric interventions. To rigorously detect any significant differences in subjective responses between oatmeal and cornflakes, traditional area-under-the-curve (AUC) analyses were employed.<sup>19</sup> To this end, AUC data for each VAS prompt were calculated and four separate two-way, repeated-measures ANOVAs were conducted with factors Breakfast and Breakfast Order. As before, since the ANOVA design does not accommodate missing or incomplete records, data from two subjects (each of which were missing one VAS measurement) were excluded from AUC analyses. For each VAS prompt, significant main effects of Breakfast were observed (all  $P$  values  $< 2 \times 10^{-4}$ ), while no significant main effects of Breakfast Order nor significant Breakfast  $\times$  Breakfast Order interactions were found. *Post hoc* pairwise *t*-Testing confirmed significant differences in AUC for the oatmeal/water and cornflakes/water comparisons ( $P$  values for all VAS prompts  $< 0.002$ , Bonferroni corrected); however, *post hoc t*-Testing for the oatmeal/cornflakes comparison revealed no significant differences in AUC between the two ( $P$  values for all VAS prompts  $> 0.96$ , Bonferroni corrected). The subjective data collected with the VAS instrument, therefore, suggested that calorie-containing breakfasts (oatmeal and cornflakes) reduced hunger and increased fullness with respect to the volume-matched, non-caloric control (water). Yet, no differences in AUC between oatmeal and cornflakes were confirmed, suggesting that the macronutrient differences between these two foodstuffs did not lead to differing levels or time-courses of post-prandial hunger/fullness.

## EEG data analyses

Recorded EEG metrics are shown in Fig. 5. LTA increased over the course of the experimental day for all breakfast conditions, as evidenced by a significant main effect of Time ( $F_{(1,206.158)} = 44.171$ ,  $P < 3 \times 10^{-10}$ , Effect Size Estimate:  $0.05 \pm 0.02$ , 95% CI [0.02, 0.09]). However, neither the main effect of Breakfast ( $F_{(2,170.732)} = 2.693$ ,  $P = 0.07$ ) nor the Time  $\times$  Breakfast interaction ( $F_{(2,210.914)} = 2.443$ ,  $P = 0.09$ ) reached significance, although they admittedly approached it. The ALI metric revealed a similar trend. A significant main effect of Time on ALI was detected ( $F_{(1,181.504)} = 4.601$ ,  $P = 0.03$ ). However, with an estimated effect size of  $-0.003 \pm 0.005$  (95% CI [-0.013, 0.008]), it was not immediately clear whether ALI rose or fell over the course of the day. As with the LTA metric above, neither the main effect of Breakfast ( $F_{(2,71.678)} = 0.741$ ,  $P = 0.48$ ) nor the Time  $\times$  Breakfast interaction ( $F_{(2,92.319)} = 0.312$ ,  $P = 0.73$ ) was significant. Consequently, the EEG data suggested that, although tonic alpha power (LTA) rose over the course of the day, neither tonic alpha power nor alpha lateralization was significantly impacted by caloric intake or the macronutrient composition of breakfast.

## Discussion

### Study design, considerations, and caveats

At present, sustained attention and vigilance in young adults share an uncertain relationship with nutrient intake and macronutrient composition.<sup>1,2</sup> However, as previous work in preadolescents suggests that nutrient intake before an attention task may alter biological markers of neurophysiology,<sup>11</sup> it was hypothesized that neurophysiological phenomena may be more sensitive for the observation of nutritive impacts on attention in young adults than

behavior. To this end, alpha oscillations, which are richly interconnected with the deployment of attention and track attentional allocation even in the absence of behavioral output,<sup>12,13</sup> were recorded as subjects participated in a demanding, sustained visuospatial attention task, the Spatial CTET, which is a variant of the Continuous Performance Tasks (CPTs) used commonly in this setting. Since previous CPT variants have shown sensitivity to macronutrient interventions, it is reasonable to expect that, given their shared structure, the Spatial CTET will also be sensitive to such manipulations. Additionally, lateralized spatial attention tasks like the Spatial CTET have previously shown differential sensitivity to nutritive conditions in young adults.<sup>15,16</sup> Finally, the Spatial CTET is known to produce reliable deployment of alpha activity.<sup>14</sup> It is, therefore, particularly well suited to the current investigation.

Task in hand, a cross-over design was employed across three experimental days to study the longitudinal effects of macronutrient breakfast composition on three categories of dependent measures: behavioral performance, subjective hunger/fullness, and alpha oscillations. Given its low carbohydrate availability with respect to cornflakes, it was expected that oatmeal should provide for a sustained release of glucose across the morning, supporting improved behavioral performance, increased fullness, and optimized alpha deployment with respect to the other interventions. Behavioral performance (i.e. Hit Rate and Perceptual Sensitivity) fell over the course of the experimental day as expected, although no difference in this decline due to breakfast intervention was detected. Measurement of subjective hunger/fullness data revealed that breakfasts with equal caloric value (cornflakes and oatmeal) increased ratings of fullness relative to the non-caloric, volume-matched water control, but significant differences in hunger/fullness between the caloric interventions were not found. Finally, electrophysiological data showed no significant effects of breakfast intervention on alpha oscillations, although tonic alpha power was observed to increase over the experimental session in all conditions.

Before contextualizing these results in the broader literature, it is worth noting a few important caveats of the present study design. First, glucose measurements were only recorded at the start of each experimental day. Although initial glucose values suggested no differences in initial fasting state between breakfast conditions as intended, blood glucose levels throughout the morning in response to breakfast were not measured. While glycemic indices and available carbohydrate loads are proxy measures for this effect, it is possible that individual differences in glucose tolerance and/or other metabolic variables confounded the impact of nutrient intake on glycemic availability. For instance, although fasting glucose levels were equivalent at the start of the day, subjects were only asked to fast starting at 9 p.m. on the night before testing. This is not atypical: of the 25 works here cited with nutritional manipulations, 15 of them implemented a similar overnight fast. However, as it is known that the glycemic index of an evening meal impacts the glycemic response to nutrient intake the next morning (i.e. the second meal effect<sup>20,21</sup>), it is possible that nutrient intake before the start of the evening fast altered the glycemic impact of our breakfast intervention. It is, therefore, possible that such an effect confounded the relationship between nutrient intake and subsequent dependent measures. However, given the study design and randomization of breakfast orderings, there is no reason to expect that such a confounder would have preferentially impacted one breakfast condition over another. That is, this

potential pre-fasting exposure was expected to be independent of the breakfast condition on the following morning. Nonetheless, it remains an important caveat, and to this end, serial glucose measurements throughout the day would have been helpful to confirm the glycemic impact of our primary nutrient interventions. Second, although one exclusion criterion for the study was daily caffeine consumption of more than 400 mg, effects of caffeine withdrawal cannot be ruled out entirely, since caffeine withdrawal can occur with daily intake as low as 100 mg.<sup>22</sup> However, no subjects in the present study reported symptoms indicative of caffeine withdrawal, consistent with the assertion that such an effect did not play a significant role in our results. Additionally, as with consideration of the second meal effect, there is again no reason to expect that caffeine withdrawal would have affected the outcome of one breakfast condition preferentially. Thus, even if it were present, it is unlikely to have altered the primary conclusions of the study.

### Nutrient intake, macronutrient composition, and attention

Although much of the work conducted in children and adolescents indicates a positive impact of nutrient intake on cognition (for a review, see Hoyland *et al.*<sup>23</sup>), investigations with adult populations are less conclusive. Concerning behavioral metrics of attention in adults, although several studies have identified positive effects of nutrient intake,<sup>24–26</sup> multiple others have found no such effect.<sup>8,27–29</sup> While each of these studies employed CPT variants designed to probe sustained attention and vigilance, they varied in both their designs and their nutrient interventions, suggesting one possible explanation for their inconsistent conclusions: they cannot be directly compared because of differing methodologies. Another possibility is that the effects of nutrient intake on attention are simply inconsistent. In such a situation, underlying metabolic physiology – like that underlying the second meal effect, for instance – might intercede to confound the relationship between nutrient intake and its effects on behavior. In either case, the present results add to the collection of empirical data on this topic. On the one hand, they do not appear to support the notion that nutrient intake in adults affects behavioral performance on general attention tasks; on the other, it is possible that the Spatial CTET, despite a reasonable expectation otherwise, is simply not sensitive to this effect. However, as before, observation of a nutritive effect on attention is inconsistent even with tasks that have established sensitivity. It cannot, therefore, be generally concluded that nutritive input does not affect attention nor that the present CPT variant is insensitive. Instead, continued standardization of such investigations (i.e. standardization of study design, nutrient intervention, and behavioral probes of attention) is encouraged, as it will be helpful to verify (or refute) consistent effects.

More to the point, to account for the effects of metabolic intermediaries that may confound the relationship between nutrient intake and effects on behavioral performance in attention tasks, it is recommended that blood glucose responses to nutrient interventions be recorded throughout experimental sessions. If, as is typically argued,<sup>30,31</sup> the pharmacokinetic profile of blood glucose after a meal (as suggested by glycemic index) is an underlying variable of interest with a causal relationship to behavior, it might be expected that blood glucose levels themselves should show a relationship to attentional performance, regardless of what foodstuff was consumed to alter glycemic homeostasis.<sup>6</sup> However, previous investigation on this topic has also produced conflicting results. For instance, although Reay *et al.*<sup>32</sup> observed

a benefit to attentional performance following a direct glucose load, Green *et al.*<sup>33</sup> observed this effect only when subjects were aware that they would be consuming glucose instead of a placebo (and not in response to the glucose load alone). It, therefore, appears that, in addition to the complicated relationship between nutrient intake and blood glucose concentration, the relationship between blood glucose concentration and attentional performance itself is not straightforward and merits further study.

Fewer studies still have examined the impact of macronutrient manipulations on attention in adults, and of those that have, they have predominantly contrasted carbohydrate-rich interventions with protein-/fat-enriched alternative(s). Although some studies have shown positive effects of fat or protein intake on attention relative to carbohydrate intake,<sup>3,4</sup> the thrust of evidence is again inconsistent<sup>8,9,34</sup> likely due to varying methodologies and interventions. Interestingly, the effect of macronutrient intervention on metrics of attentional performance may also be related to age. For instance, Kaplan *et al.*<sup>35</sup> and Nilsson *et al.*<sup>5,6</sup> observed that interventions that engender low, sustained post-prandial glucose availability (e.g. fat intake, low glycemic index interventions) improved metrics of attention in older and middle-aged adults, whereas Benton and Nabb<sup>25</sup> observed no such effects for younger adults. One interesting albeit speculative possibility is rooted in compensation. Although younger adults might be able to compensate and maintain equivocal attentional task performance across differing post-prandial glucose responses secondary to macronutrient manipulations, the aging process may lead to a decline in this compensatory ability. Consequently, attentive functioning in older adults may be more susceptible to macronutrient intervention. The results presented here certainly do not contradict such an hypothesis. In earnest, they merely show that young-adult subjects performed equivalently on the same task during all nutrient conditions, despite that the trajectories of subjective hunger/fullness were significantly different during the non-caloric (water) condition with respect to the caloric conditions. Nonetheless, the extent to which behavioral output is maintained across a range of blood glucose levels and subjective states of hunger/fullness – and the extent to which behavior may fail at the extrema of these compensatory domains – deserves further study, as such investigation will likely uncover fundamental homeostatic mechanisms for regulating neural output across a diversity of metabolic states.

### Neurophysiological metrics in the context of nutrient intervention

Finally, it is worthwhile to emphasize briefly the importance of neurophysiological markers to investigations relating nutrient consumption to cognitive and behavioral performance. As evident from the above discussion, one major mechanistic hypothesis linking nutrient intake to cognition involves regulation of post-prandial glycemia. Implicit in this mechanism is the notion that neural glucose availability goes on to affect behavior by directly altering glucose utilization by the brain and, consequently, brain physiology. In this case, it should be expected that markers of neurophysiological activity will themselves be affected by nutritive intervention as an intermediary to behavior.<sup>11,36,37</sup> Furthermore, it is important to note that such markers often give nuanced insight into cognitive processing even in the absence of overt changes in behavior. For instance, alpha oscillations reflect the retinotopic allocation of covert spatial attention even without any overt changes in eye position;<sup>12,14</sup> moreover, they are predictive of lapses in behavioral performance up to 20 seconds before such lapses

occur.<sup>38</sup> That is, despite that the present results showed no divergence between neural and behavioral markers of attentional allocation, it remains highly likely that neurophysiology itself possesses greater sensitivity to nutritive intervention than behavior alone, as neurophysiological markers are commonly more revealing than gross behavioral metrics. To this end, continued investigations of macronutrient effects on neurophysiological markers are strongly encouraged, as they will likely be critical to untangle the complex relationship between nutrient consumption and behavior.

## Supplementary methods

Refer to Web version on PubMed Central for supplementary material.

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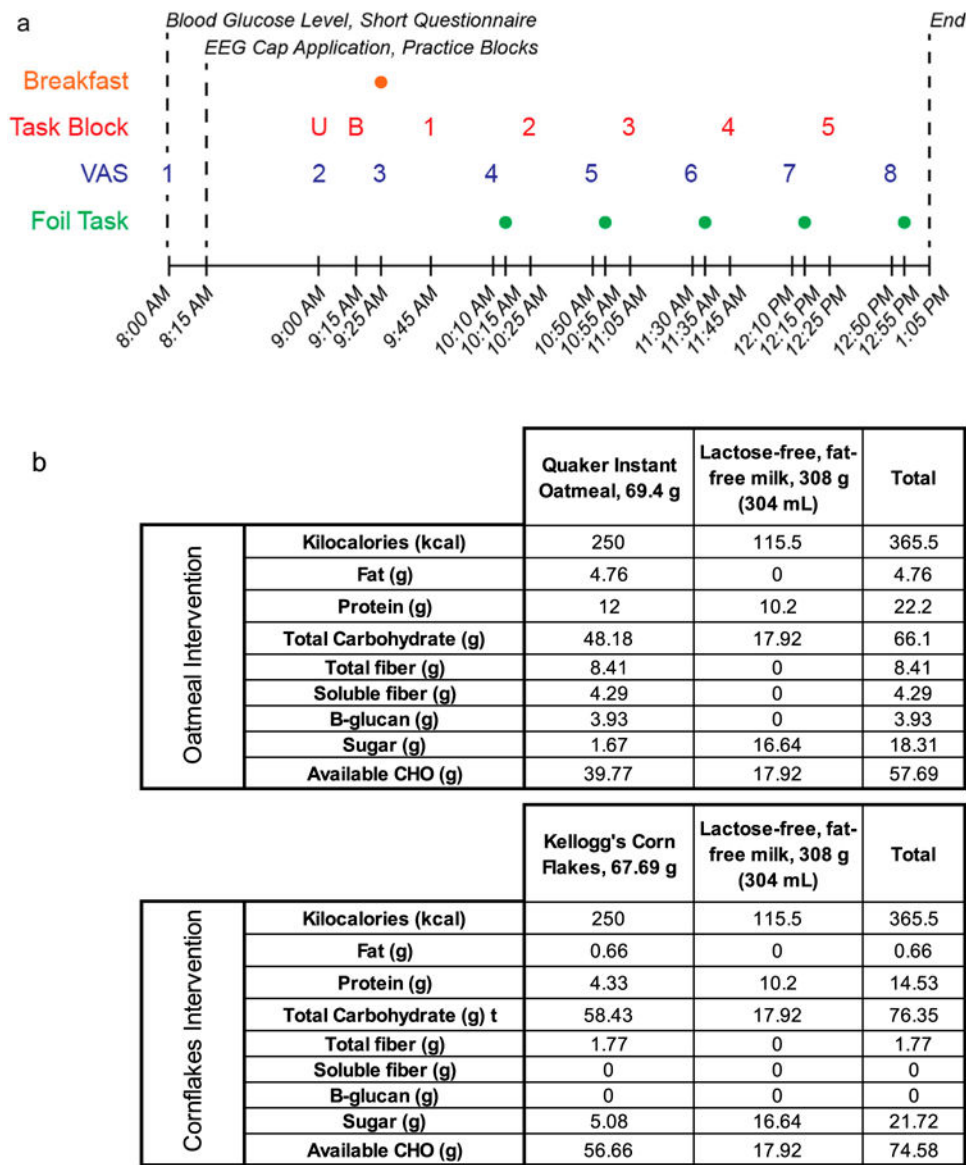
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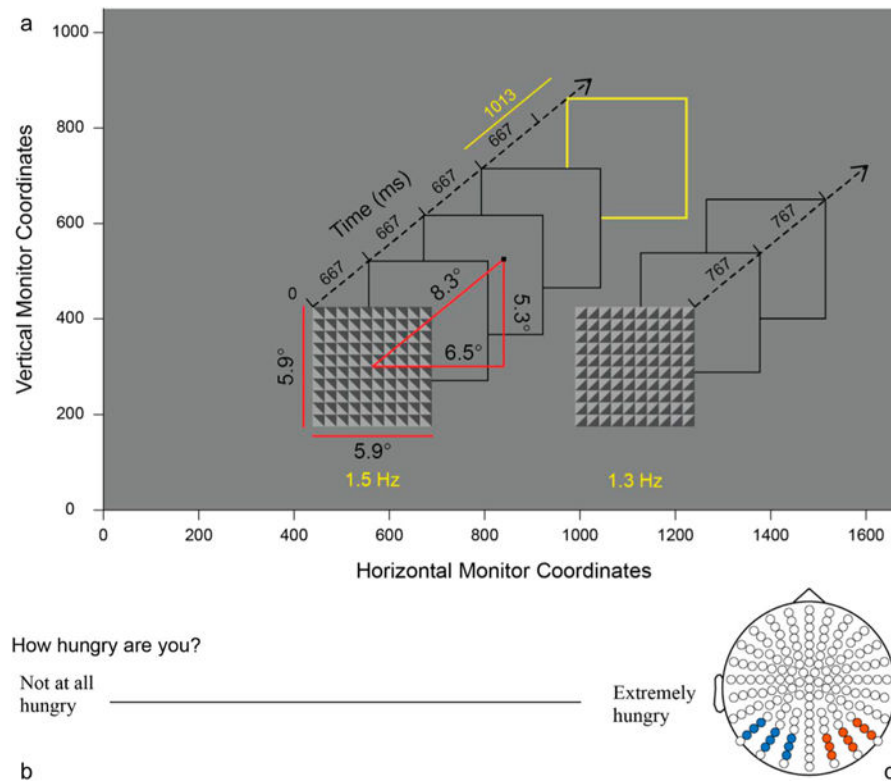


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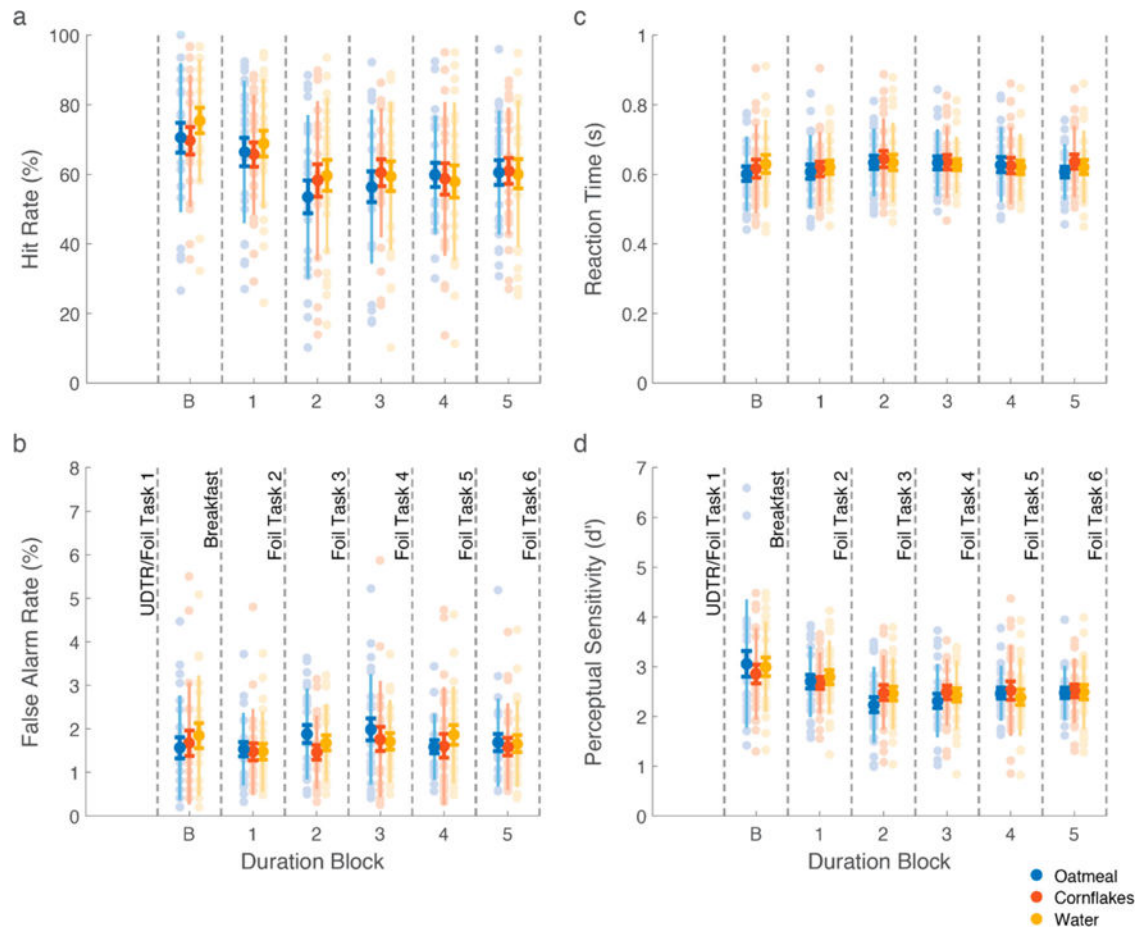


**Figure 1.** Experimental layout of the study. (a) shows the key experimental time points across the experimental day, color-coded by the type of event. Task Block refers to a large block composed of several smaller blocks of the Spatial CTET (described in the section ‘Methods’). Except for the UDTR (U) and Baseline (b) Task Blocks, each Task Block was composed of five smaller Spatial CTET blocks. The Baseline block was composed of two Spatial CTET blocks; the UDTR block was also composed of 2, but as it is the task titration block, it was only run on the first day of the study (on the second and third days of the study, it was replaced with the Foil Task). VAS refers to the Visual Analog Scales collected across the course of the day. Practice blocks were administered only on the first day. (b) shows the caloric values of the breakfast interventions employed in the current study. The water intervention (680 ml of water, volume-matched to the oatmeal breakfast) is not shown as it has no caloric value.



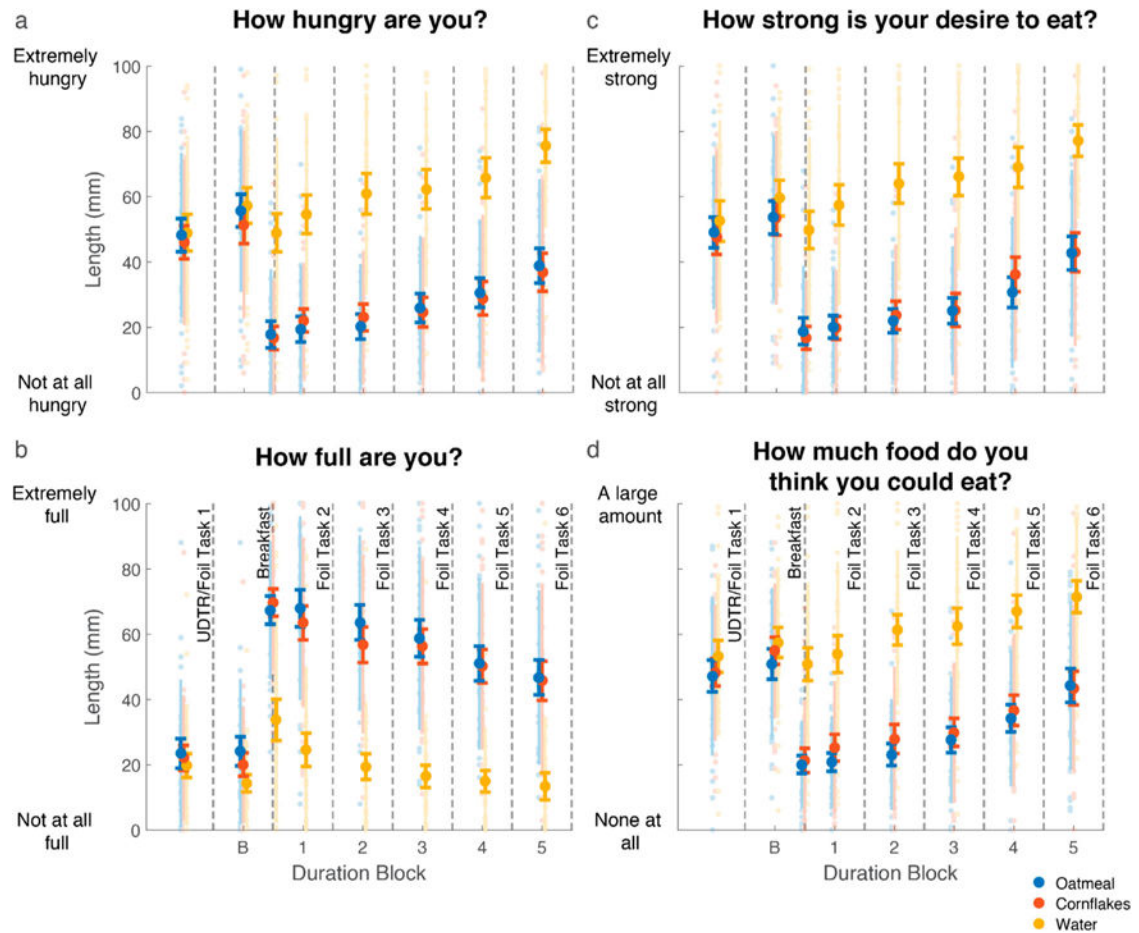
**Figure 2.**

Instruments and conventions used for the study. (a) is a depiction of the Spatial CTET presented in monitor coordinates. Two checkerboards were presented along with a central, black fixation point. All other items (axes, boxes, angular measurements, etc.) are presented to the reader to illustrate task structure but are not presented during the task. Only one stimulus configuration (left checkerboard stream at 1.5 Hz; right at 1.3 Hz) is shown. Subjects covertly attended one checkerboard stream (left or right) for the duration of a block (~3 minutes) and reported the appearance of infrequent duration deviants (shown in yellow) via mouse click. Gray and yellow boxes denote the moments at which new orientations of each checkerboard were presented. (b) shows a sample VAS prompt (not to scale). Subjects responded by making a solid vertical line through the spectrum between the two extremum values. (c) shows the electrode pools used to construct measurements on the electrophysiological data. Nine sensors were selected for both left and right posterior scalp where alpha oscillations are known to be detected.



**Figure 3.**

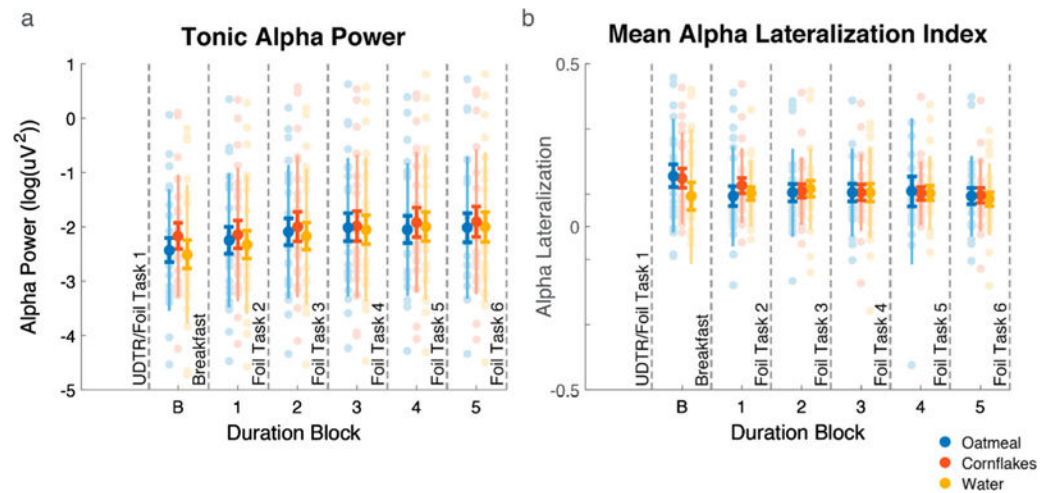
Behavioral analyses by breakfast condition. Sample means  $\pm$  standard errors are marked by opaque dots with error bars. Transparent lines behind the error bars indicate standard deviations. Raw data are shown in light, colored dots in the background. (a) (Hit Rate) and (b) (False Alarm Rate) are shown as a percentage of total targets/standards presented, respectively. Note the change in y-axis between these two metrics. (c) shows average Reaction Time in seconds over the course of the day, while (d) shows Perceptual Sensitivity (d').



**Figure 4.**

Subjective reports by breakfast condition. Values from 0 to 100 mm are plotted as a function of experimental block. For each panel, the relevant survey question is printed above the graph, and the two extremum answers are plotted along the side. As before, sample means  $\pm$  standard errors are marked by opaque dots with error bars. Transparent lines behind the error bars indicate standard deviations. Raw data are shown in light, colored dots in the background. (a)–(d) each correspond to one of the subjective questions asked of participants.





**Figure 5.**

Metrics of alpha oscillations by breakfast condition. As before, sample means  $\pm$  standard errors are marked by opaque dots with error bars. Transparent lines behind the error bars indicate standard deviations. Raw data are shown in light, colored dots in the background. (a) shows the LTA metric (Logarithm of the Tonic Alpha power) over the experimental day as a function of breakfast condition; (b) shows the ALI metric (Alpha Lateralization Index) in the same fashion.