Experimental increase of blood glucose alters resting state EEG measures of excitation–inhibition balance

Christopher P. Walker¹,² | John B. Buse³ | Flavio Frohlich¹,²,4,5,6,7

¹ Department of Psychiatry, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
² Carolina Center for Neurostimulation, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
³ Department of Medicine, Division of Endocrinology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
⁴ Department of Cell Biology and Physiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
⁵ Department of Biomedical Engineering, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
⁶ Department of Neurology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
⁷ Neuroscience Center, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

Correspondence
Flavio Frohlich, Department of Psychiatry, 6018A Mary Ellen Jones Building, 116 Manning Drive, University of North Carolina at Chapel Hill, Chapel Hill, NC 27514, USA.
Email: flavio_frohlich@med.unc.edu

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Abstract
Brain network oscillations can be divided broadly into periodic and aperiodic signal components, which are sensitive to state-dependent changes in network coordination and excitation–inhibition (E:I) balance. We sought to address whether the dominant energy source of the brain, glucose, is implicated in the regulation of network activity and excitability. We conducted an experimenter-blind, crossover study of the effect of blood glucose level (BGL) on the resting EEG frequency spectrum. Participants consumed a glucose drink (75 g glucose) or an equivalent volume of water on two separate visits. EEG data were sampled before and ≤3 h after the drink. We found that the experimentally induced changes in BGL exhibited an inverted U-shaped relationship, with changes in the individual α frequency peak, whereas the slope of the aperiodic signal component of the frequency spectrum showed a positive linear association suggestive of greater excitation. In contrast, peak α power, which is typically associated with top-down inhibitory processes, was negatively associated with changes in BGL. Collectively, these results suggest that high BGL alters brain network coordination in the form of α oscillations and measures associated with E:I balance.

KEYWORDS
blood glucose, electroencephalography, excitation–inhibition balance

1 | INTRODUCTION

The organization of large-scale brain network activity often exhibits rhythmic structure; state-dependent changes in these brain oscillations are ubiquitously reported as outcomes in both basic (Canolty et al., 2006; Cho et al., 2015; Haegens et al., 2011; Roux & Uhlhaas, 2014) and clinical neuroscience studies (Ahn et al., 2019; Cho et al., 2006; Kömek et al., 2012; Uhlhaas et al., 2008). Traditionally, oscillatory network activity is described by spectral analysis of neurophysiology time series (such as EEG; local field potential) that uses...
predefined canonical frequency bands to determine the oscillation amplitude. However, recent insights into the interpretation of the aperiodic component of the spectrum (operationalized as the slope of the log-transformed power spectrum) have provided a non-invasive measure of neural excitability: the aperiodic signal has been proposed as a holistic measure of excitatory–inhibitory (E:I) balance. A shallow negative slope is associated with an E:I balance weighted toward excitatory drive, whereas a steep negative slope corresponds to greater inhibition (Gao et al., 2017). Given that α oscillation power is inversely related to neuronal activity (Haegens et al., 2011; Klimesch, 2012; Klimesch et al., 2007), a combined consideration of both the slope (aperiodic) and the α frequency peak (periodic) provides the most comprehensive assessment of neuronal inhibitory processes at the network level.

However, it remains unknown how even basic physiological processes modulate these indices of functional inhibition in cortical networks. Such an understanding will: (i) provide experimental manipulations for modulating inhibitory drive by physiological perturbations; (ii) motivate the incorporation of non-neural physiological measurements to explain variance in neurophysiology studies; and (iii) broaden the applicability of neurophysiological signals to other areas of physiology. One such physiological process that has been largely ignored despite its broad implications is glucose metabolism. Recent studies have suggested spatially unspecific and non-linear effects of blood glucose level (BGL) on resting EEG (An et al., 2015; Rachmiel et al., 2016). Given the lack of published reports on how blood glucose modulates excitability in terms of aperiodic and periodic signal analysis, we sought to address this fundamental question in an experimenter-blind study that combined repeated EEG during an adapted glucose tolerance test. We hypothesized that elevated blood glucose would transiently increase measures associated with E:I balance owing to a greater availability of energy compared with the fasting state.

2 METHODS

2.1 Ethical approval

All participants provided written informed consent in accordance with the Institutional Review Board at the University of North Carolina at Chapel Hill (reference number: 19-1451; approval date: 9 August 2019) and with the principles of the Declaration of Helsinki except for registration in a database.

2.2 Participants

We recruited nine participants who reported good mental and physical health, with a body mass index <30 kg m\(^{-2}\) and a fasting BGL <95 mg dl\(^{-1}\) at an initial screening visit. Most participants were female (n = 7); they were relatively young (mean = 26.93 years, SD = 13.85), had a normal body mass index (mean = 21.21 kg m\(^{-2}\), SD = 4.09) and relatively low fasting BGL (mean = 85.11 mg dl\(^{-1}\), SD = 7.03).

2.3 Study design

Participants returned for two study visits, during which they received either a water drink or a glucose drink containing 75 g of glucose (296 ml; Azer Scientific, Morgantown, PA, USA), which is roughly equivalent to two 355 ml cans of a typical soft drink. Participants abstained from alcohol for 24 h and completed 12 h fasts before the screening and study visits. Participants were allowed water during the testing sessions but not any caloric food or drink items. After the baseline data collection, which included a resting-state EEG, participants consumed one of the two study drinks, which were prepared in opaque bottles. The experimenter left the room during consumption to ensure experimenter blinding. The blood glucose sampling and the EEG measurements were repeated at 0, 30, 60, 120 and 180 min after the drink (Figure 1a,b). The study included other measurements unrelated to this report, such as behavioural questionnaires and investigation of motor cortex function, which have been presented elsewhere (Walker et al., 2021). Nevertheless, an analysis of positive and negative affect schedule (PANAS) composite scores, which were collected at each time point, has been included here for context. The PANAS is a 20-item survey assessing a range of mood-related symptoms on a five-point Likert scale (Watson et al., 1988). The composite PANAS positive affect and negative affect scores (10 items each) were submitted for final analysis.
2.4 Blood glucose sampling

Capillary blood glucose samples were collected by finger prick using a safety lancet. Approximately 5 μl of blood was collected with a microcuvette, and BGLs were determined using a Hemocue Glucose 201 Analyzer (HemoCue America, Brea, CA, USA), which provides an estimate of BGL within 3 min. The device was tested for proper calibration before each study visit using a low- and high-level control liquid (Glucotrol-AQ; EuroTrol, Elizabethtown, KY, USA).

2.5 Electroencephalography

Resting state EEG (3 min eyes open; 2 min eyes closed) data were collected using a 128-channel system at 1000 Hz sampling rate (Microcel-128, Geodesic EEG system 410, Electrical Geodesics, Eugene, OR, USA). Before the experiment, an electrolyte gel was applied to reduce electrode impedances to $<50 \, \Omega$. Continuous EEG data were preprocessed in Matlab (Mathworks, Natick, MA, USA) using the EEGLAB toolbox (Delorme & Makeig, 2004). Data were submitted to a standard preprocessing pipeline, which included bandpass filtering (0.1–100 Hz) and automatic subspace reconstruction (ASR; burst criterion $k = 10$) (Chang et al., 2019) before removal of blink, ECG, EMG and line noise artefacts via Infomax independent component analysis (ICA) (Delorme & Makeig, 2004; Jung et al., 2000; Lee & Sejnowski, 1997) and a final visual inspection to remove segments with residual artefacts. Given that ASR can reduce the rank of the data, the ICA was computed with the number of output components set to the rank of the covariance matrix of the continuous data (Mean (M) number of components removed $= 54.47$, Standard deviation (SD) of components removed $= 17.02$). Power spectra were computed on a subset of 90 scalp electrodes using Welch’s method of averaging the Fourier transform of the clean data windows (window length $= 2000$ ms, no overlap, 0.25 Hz frequency resolution; pWelch.m in Matlab).

2.6 Aperiodic and periodic EEG signal components

In electrophysiological recordings, the aperiodic signal component, also known as the 1-over-1 component, refers to the characteristic decrease in signal power with increasing frequency. Recent work has argued that there is an association between the slope of the log-transformed spectrum in animal and human neurophysiological recordings and the E/I balance of the cortex (Gao et al., 2017; Voytek & Knight, 2015). Thus, to estimate the aperiodic signal slope, individual channel power spectra and frequencies (excluding 6–30 Hz to remove $\alpha$ and $\beta$ peaks) were log-transformed and fitted with a straight line (Figure 1c). Slope coefficients for each channel were taken as estimates of the aperiodic signal slope. Periodic signal components that represent oscillations in the EEG are peaks that extend above the aperiodic component. To capture the periodic $\alpha$ oscillation, we derived measures of the individual $\alpha$ frequency (IAF) and $\alpha$ power at IAF. The IAF was
identified automatically (findpeaks.m in Matlab) as the frequency of peak power between 7 and 14 Hz in the spectrum with the aperiodic component subtracted. A search space wider than the typical α band was used to ensure that peaks at the edges of the typical band (e.g., 8 Hz) could be identified properly as peaks. To ensure a robust estimate, IAF was determined using the mean spectra across a cluster of posterior electrodes (Figure 1c inset), where the α peak is most prominent. Finally, peak α power was determined per channel as the mean power at IAF ± 1 Hz in the detrended spectrum. All EEG spectral measures were derived from the recordings with eyes closed.

2.7 Data analysis and statistics

For two participants, the last time point was missing for their glucose visit, and for one participant a blood glucose value for the 0 min time point was missing. Therefore, BGLs, aperiodic slopes and IAFs were submitted to a linear mixed effect analysis (fitlme.m in Matlab), which is robust to missing data points. For the blood glucose measurements, time point, drink and the time point-by-drink interaction were treated as fixed factors (dummy coded). Participant was treated as a random factor. Individual time point differences between the glucose and control visit curves were evaluated using the drink-by-time point parameter estimate t tests.

For IAF, peak α power and aperiodic signal slope, baseline measures were subtracted from the 0–180 min time points to isolate within-session changes from baseline. For these measures, the corresponding difference in blood glucose from baseline and study visit order were included as fixed factors, with participant as a random factor. Kolmogorov–Smirnov (KS) tests were used to determine the normality of residuals, and Breusch–Pagan tests were used to detect heteroscedasticity. Violations of these assumptions do not bias parameter estimates but can influence variance estimates, which, in turn, affect statistical inference. No models demonstrated significant heteroscedasticity; however, several channels had non-normal residuals for peak α power. Therefore, channels that violated either assumption were masked from final analysis. Significance was determined with a false discovery rate (FDR) adjusted α = 0.05 for the scalp-wide slope and with power analyses and an uncorrected α = 0.05 for IAF and blood glucose changes. Lastly, between-session measurement reliability was assessed using Pearson correlations and Student’s paired t tests between the baseline measurements from the glucose and control visits to ensure that our findings were not simply attributable to baseline differences.

As a final review of potential affective changes that occurred during the session, two final models predicting PANAS-positive affect and PANAS-negative affect scores from BGL, IAF, peak α power and aperiodic signal slope were computed controlling for session order. Study measures were included as fixed linear predictors, with participant as a random factor. Model assumptions were tested as above.

Unless otherwise specified, model statistics are summarized with parameter slope estimates (B); standard errors of parameter estimates (SE), and 95% confidence intervals (95% CI). Null hypothesis significance tests for model parameter estimates and mean group comparisons are reported as t-scores with the degrees of freedom in subscript (e.g., $t_6$). Pearson correlation coefficients are reported in the same fashion with the letter, r. Associated NHST probabilities (i.e., p-values) are reported as P.

3 RESULTS

3.1 Blood glucose levels

As expected, BGLs increased significantly after consumption of the glucose drink (drink × time interaction: $F_{5,93} = 10.6, P = 4.48 \times 10^{-8}$, uncorrected), with the largest glucose versus water differences observed at the 30, 60 and 120 min time points ($P < 6.36 \times 10^{-5}$; Figure 1b).

3.2 Periodic signal: α oscillations

To test our hypothesis, we first asked whether increased blood glucose impacted the α oscillation (Figure 1c). The scalp topography of eyes-closed α power followed the typical distribution, with expected peaks at posterior electrode sites (Figure 1c inset) that were used to identify IAFs. Pre-drink baseline IAF measurements were generally stable between the experimental sessions, with high between-visit correlations ($r = 0.88, P = 0.002$; Figure 2a) and no mean differences (Glucose Visit: $M = 9.36, SD = 0.80$; Control Visit: $M = 9.44, SD = 0.69$; $t_{9} = -0.67, P = 0.524, 95\% CI = -0.37, 0.20$; Figure 2b). Visual inspection of the scatter plot for change in posterior IAF to the change in BGL suggested a potential quadratic relationship. Therefore, we added a quadratic term for change in blood glucose as a fixed effect. The IAF demonstrated both a significant positive linear (Linear effect of BGL: $B = 8.74 \times 10^{-3}, SE = 2.88 \times 10^{-3}, t_{93} = 3.03, P = 0.003$, uncorrected, 95% CI 2.99 × 10⁻³, 1.45 × 10⁻²) and a significant negative quadratic relationship (Quadratic effect of BGL (BGL²): $B = -6.64 \times 10^{-5}, SE = 3.12 \times 10^{-5}, t_{93} = -2.13, P = 0.037$, uncorrected, 95% CI −1.28 × 10⁻⁴, −4.25 × 10⁻⁶) with change in BGL when controlling for session order (Figure 2c). For each unit increase in BGL, IAF increased by 8.74 × 10⁻³ Hz, but at a decreasing rate. The IAF began to decrease above 60 mg dl⁻¹ over fasting levels.

In contrast, peak α power did not show the same reliability from session to session. Only five electrode sites were significantly correlated between the visits at an uncorrected $P < 0.05$ threshold ($r$ range = 0.67–0.74, $P$ range = 0.049–0.023, uncorrected) (Figure 2d). As with IAF, no significant mean differences between the visit baselines were observed for peak α power (maximum $t_6 = 1.17, P = 0.28$, uncorrected, 95% CI −1.18, 3.59; Figure 2e). The KS tests revealed that the residuals from 58 electrodes were non-normal, which indicated that the model was inadequate to capture patterns in α power fully. These electrodes were masked from further analysis, and the remaining 32-electrode models were interpreted. Changes in BGL showed significant negative associations with peak α power over bilateral centroparietal scalp regions when controlling for session order.
**FIGURE 2** Individual α frequency (IAF) and peak α power changes as a function of blood glucose level (BGL). (a,b) Baseline estimates of IAFs for each visit demonstrated a high level of reproducibility, with no discernable between-visit differences. Dotted lines indicate 95% confidence intervals. Error bars indicate mean ± SD. (c) The IAFs were found to show both linear and quadratic relationships with BGL, whereby higher blood glucose corresponded to increases in IAF, but the increases reduced at peak BGLs. The estimated linear mixed effects trend line is depicted in black, with the dotted lines indicating the 99% confidence bounds. Colours indicate individual participants. (d,e) Same as (a,b) except for peak α power. Given that power was calculated at all electrodes, the scalp plot represents the distribution of \(D_r\) and \(E_t\)-values. White markers indicate electrodes showing significant \(r/t\)-values at \(P < 0.05\), uncorrected. (f) The scalp-wide linear mixed effects analysis demonstrated a negative linear relationship between change in peak α power and change in BGL in electrodes over central and posterior scalp regions. Colours indicate the magnitude of the related \(t\)-score for the BGL effect at each electrode. Black dots indicate \(P < 0.05\), uncorrected. White dots indicate \(P < 0.05\), false discovery rate adjusted. (g) Same as (c), but for change in peak α power as a function of change in BGL. Note that the power values shown represent the mean across the cluster of significant electrodes and are intended for demonstration of trend only (i.e., no significance testing).

3.3 Aperiodic signal component

Baseline estimates of the aperiodic signal slope were highly correlated between visits (\(r_r = 0.41 - 0.97\), \(P = 0.021\), FDR adjusted, 95% CI \(1.06 \times 10^{-3}, 2.79 \times 10^{-3}\); Figure 3a). The \(\alpha\) power in these regions decreased below baseline with higher BGLs. Collectively, these results suggest that \(\alpha\) power might change with circulating glucose, but for our model the estimates of \(\alpha\) power are too inconsistent for more than a preliminary assessment.

3.4 Behavioural questionnaires

Finally, changes in PANAS-positive and PANAS-negative affect scores were submitted to a linear mixed effects analysis to determine whether
changes in BGL, IAF, peak $\alpha$ power or aperiodic signal slope significantly predicted affect scores. Positive affect scores showed a high test–retest correlation ($r = 0.94$, $P = 6.25 \times 10^{-5}$) and no significant baseline differences ($t_{65} = 0.47$, $P = 0.65$, 95% CI $1.70, 2.59$). Negative affect scores were also reliable, albeit to a lesser degree ($r = 0.75$, $P = 0.019$; $t_{65} = 1.13$, $P = 0.290$, 95% CI $1.03, 3.03$). Neither model showed significant violations of normality or heterogeneity of variances. Peak $\alpha$ power demonstrated a negative linear trend-level relationship with positive affect at the $P < 0.1$ level when controlling for session order and the other variables of interest, but no other predictor of interest was found to be significantly different from zero. In contrast, changes in BGL ($B = -1.98 \times 10^{-2}$, $SE = 4.79 \times 10^{-3}$, $t_{65} = -4.14$, $P = 8.51 \times 10^{-5}$, uncorrected, 95% CI $2.93 \times 10^{-2}, -1.02 \times 10^{-2}$) and peak $\alpha$ power ($B = -0.11$, $SE = 0.04$, $t_{65} = -2.38$, $P = 0.019$, uncorrected, 95% CI $-0.19, -0.017$) were negatively associated with negative affect scores (for additional effect estimates, see Table 1). Thus, negative affect decreased as BGL or peak $\alpha$ power increased.

### 4 DISCUSSION

The data we present here highlight a potential impact of the metabolic state of a participant on measures of brain function. Previous studies have shown that resting EEG power exhibits a non-linear relationship with BGL in patients with type 1 diabetes (Rachmiel et al., 2016). In healthy control subjects, a small amount of ingested glucose (17 g) has been shown to increase $\alpha$- and $\delta$-band power 30 min after consumption (An et al., 2015). Our data expand upon these earlier studies by suggesting that such effects might reflect dynamic shifts in E1 balance rather than oscillatory power per se. Here, we modulated BGL experimentally with a glucose drink containing 75 g of glucose. The resulting increases in BGL were positively associated with changes in IAF and aperiodic signal slope and negatively associated with peak $\alpha$ power. Although affect scores covaried with BGL, no other relationship between the EEG measures and affect was observed.

Our findings carry two key messages. On a practical level, a participant who consumes a beverage or snack with a high sugar content might experience shifts in their baseline state that can unintentionally interact with target measures during study visits. Our experiments took place over a 3 h window, but the greatest increases in blood glucose occurred 30–60 min after ingestions, which is on the order of the duration of a typical human neurophysiology experiment. For example, a shift upward or downward in IAF would change the mean power within the $\alpha$ band (i.e., 8–12 Hz) by moving the ‘centre of mass’ into or out of this canonical band. In addition, a change in aperiodic signal slope could be misconstrued as a change in $\gamma$-band power (>30 Hz). These findings emphasize the importance of recommending that participants consume foods/drinks that provide consistent and stable glucose levels before and during experimental sessions.

The second message is that cortical oscillations are modulated by low-level changes in individual physiology. In particular, our results suggest that consuming high levels of sugar can transiently alter proximal metrics of cortical E1 balance. The aperiodic signal slope has been hypothesized to index the balance of excitatory to inhibitory drive at various neurophysiological levels (Gao et al., 2017; Voytek & Knight, 2015). According to this interpretation, the increased slope with higher BGLs indicates that either increased excitation or decreased inhibition follows elevation in blood glucose. This notion is supported further by the pattern of increased IAF for elevated BGLs and decreased IAF for BGLs below fasting baseline. The $\alpha$ oscillations are thought to serve as an inhibitory signal that suppresses neuronal firing in a given region (Klimesch, 2012; Klimesch et al., 2007). Typically, amplitude is used to describe the $\alpha$ oscillation, but more recent evidence suggests that $\alpha$ oscillations might behave as an attentional and perceptual gating mechanism where the peak frequency is adjusted endogenously depending on the optimal sampling regimen for the task at hand (Samaha & Postle, 2015). The individual $\alpha$ frequency has been shown to be correlated with a wide array of perceptual and cognitive functions, including working memory, where IAF has been shown to increase dynamically with higher cognitive demands (Grandy et al., 2013; Gray & Emmanouil, 2020; Haegens et al., 2014; Klimesch et al., 1993). In...
the context of increases in aperiodic slope and decreases in peak $\alpha$ power, our finding of an increase in $\alpha$ oscillation frequency might also represent a marker of increased excitation.

As with all studies, our work presented here is not without limitations. Of note, the present investigation was not capable of identifying the precise mechanism of the observed effects, but instead focused on characterizing the influence of glucose ingestion on the brain in healthy participants. Given that a linear increase in circulating blood glucose can result in a proportional increase in brain glucose (Shestov et al., 2011), we infer that our results reflect altered glucose availability in cortical tissues. However, we cannot rule out the the interactions of glucose consumption with metabolic state, homeostatic regulation or other perceptual processes that might alter brain state on the same time scale as blood glucose clearance. Indeed, glucose clearance rates have been shown to be modulated by consumption of a non-caloric sweetened beverage, suggesting that hormone release is signalled, at least in part, by perceptual processes (Nichol et al., 2016). Further replication of our findingsshould takethesecomplications into consideration when planning the study design.

Additionally, all participants were fasting at the start of the experimental session to mimic an oral glucose tolerance test procedure that might be conducted in a clinical environment. Ingestion of large volumes of glucose in this state might differ fundamentally from more naturalistic settings where glucose is consumed with or after a meal with other macronutrients. The metabolic response to dietary glucose is dynamic and involves large increases in circulating hormones, including insulin and the incretin hormones, which covary on the same or similar time scales as blood glucose (Drucker & Nauck, 2006). Lastly, our study sample was predominantly female. Our study was underpowered to address such sex differences with our sample; therefore, our findings might not generalize equally to males and females. Metabolic hormones and the response to oral glucose tolerance test have been found to differ between males and females (Faerch et al., 2010; Tramunt et al., 2020). Females tend to show greater insulin secretion after an oral glucose tolerance test and are generally more sensitive to insulin levels (Tramunt et al., 2020), which, in hippocampal slice preparations, can activate extrasynaptic GABA$_A$ channels that regulate inhibitory tone (Jin et al., 2011). Future studies using more nuanced clamp techniques will be needed to disentangle the relative contributions of these hormones to the regulation of neuronal network activity.

Of note, the sample presented here is relatively small; thus, we emphasize caution in interpreting our results. Data collection was halted prematurely owing to COVID-19 restrictions, and we have presented an analysis of our data so far. As such, we recognize that our effect sizes are likely to be inflated compared with the true population effect. Assuming a true effect that is half the magnitude of our observed effects, a priori power simulations using the simr package in R (https://cran.r-project.org/web/packages/simr/index.html) estimate that 35 participants will be needed to achieve 84.1% power for the linear effect of BGL on IAF, 40 participants to achieve 85.1% power for peak $\alpha$ power and 25 participants to achieve 88.0% power for aperiodic slope (Green & MacLeod, 2016). Further replication of our findings should take these estimates into consideration when planning the study design.

In conclusion, BGLs influence neurophysiological measures of resting brain activity in subjects with healthy glucose metabolism.

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Positive affect scores $B$ (SE [95% CI])</th>
<th>Negative affect scores $B$ (SE [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.42 (0.71) [-1.00, 1.84]</td>
<td>-0.97 (0.49) [-1.94, -4.18 x 10^{-2}]*</td>
</tr>
<tr>
<td>$\Delta$BGL</td>
<td>$-8.26 \times 10^{-2}$ (7.80 x 10^{-3}) [2.37 x 10^{-2}, 7.25 x 10^{-3}]</td>
<td>$-1.98 \times 10^{-2}$ (4.79 x 10^{-3}) [2.93 x 10^{-2}, 1.03 x 10^{-2}]</td>
</tr>
<tr>
<td>$\Delta$I$\alpha$ power</td>
<td>-0.76 (0.62) [-2.00, 0.48]</td>
<td>0.17 (0.38) [-0.59, 0.93]</td>
</tr>
<tr>
<td>$\Delta$Aperiodic slope</td>
<td>1.30 (2.09) [-2.87, 5.46]</td>
<td>0.72 (1.29) [-1.85, 3.30]</td>
</tr>
<tr>
<td>Session order</td>
<td>-2.11 (0.51) [-3.12, -1.10]</td>
<td>0.85 (0.31) [0.23, 1.47]</td>
</tr>
<tr>
<td>$R^2$</td>
<td>0.49</td>
<td>0.54</td>
</tr>
<tr>
<td>Adjusted $R^2$</td>
<td>0.46</td>
<td>0.52</td>
</tr>
</tbody>
</table>

Note: Model parameter estimates ($B$) are given above with appropriate standard errors (SE) in parentheses, and 95% confidence intervals (95% CI) in brackets. Abbreviations: BGL, blood glucose level; IAF, individual $\alpha$ frequency; PANAS, positive and negative affect schedule. P < 0.05. **P < 0.001.
It is estimated that 34.5% of adults in the USA exhibit signs of prediabetes and an additional 10.5% have diabetes (Centers for Disease Control and Prevention, 2020), and abnormalities in glucose metabolism have been observed in several mental illnesses, including major depression (Graham et al., 2020) and schizophrenia (Bushe & Holt, 2004). Expanding our understanding of how glucose metabolism modulates brain network dynamics will be crucial for determining how such abnormalities interact with diet in various clinical contexts.

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COMPETING INTERESTS
F.F. is the lead inventor of intellectual property filed on the topics of non-invasive brain stimulation by the University of North Carolina. F.F. is the founder, chief science officer and majority owner of Pulvinar Neuro LLC, which played no role in this research. The other authors declare no competing interests.

AUTHOR CONTRIBUTIONS
F.F. and J.B. conceived the work and designed the experiments. The experimental work was completed at the University of North Carolina at Chapel Hill by C.P.W. and overseen by F.F. and J.B. C.P.W. oversaw acquisition of the data and generation of the results. All authors reviewed, analysed and interpreted the results. The manuscript was prepared by C.P.W. and overseen by F.F. and J.B. All authors approved the final version of the manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID
Christopher P. Walker https://orcid.org/0000-0002-1042-075X
Flavio Frohlich https://orcid.org/0000-0002-3724-5621

REFERENCES


Psychophysiology, 57, 1114–1121.


Psychophysiology, 57, 1114–1121.


Psychophysiology, 57, 1114–1121.


