Registered Report

Variations of autonomic arousal mediate the reportability of mind-blanking occurrences

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Abstract

Mind-blanking (MB) is the inability of reporting mental events during unconstraint thinking. Previous work shows that MB is linked to decreased levels of cortical arousal, indicating dominance of cerebral mechanisms when reporting mental states. What remains inconclusive is whether MB can also ensue from autonomic arousal manipulations, pointing to the implication of peripheral physiology to mental events. Using experience-sampling, neural and physiological measurements, we expect that MB reports will be more frequent in low and high autonomic arousal conditions, respectively elicited through sleep deprivation and intense physical exercise. Using classification schemes, we further hypothesize that MB will be predicted by patterns combining brain and physiological markers. If our hypotheses fail, it will imply that cortical and autonomic arousal are distinct pathways for mental state reportability. If our hypotheses get confirmed, the results will indicate an embodied approach to mental events in place of a solely neurocentric that currently prevails.

Introduction

During ongoing mentation, our mind constantly shifts across different mental states. These mental states typically bear some content ("what we think about") and indicate a relationship towards that content (i.e., perceiving, fearing, hoping, remembering) [1]. As we move through the environment, our thoughts fluctuate between the external and internal milieu [2,3], resulting in a fluid stream of consciousness [4]. External content is tightly coupled to the processing of environmental stimuli and task-demanding conditions. Internal content is more associated with self-referential processing and internal dialogue, widely known as Mind-Wandering [4]. Inclusive as this external-internal dipole may seem, it does not capture the full scope of the "aboutness" of mental content. Recent work has highlighted another mental state, where people report that they are "thinking of nothing" or "their mind just went away", a phenomenological experience termed mind-blanking (MB) [5]. As MB is relatively new in the landscape of ongoing cognition, the extent of MB episodes in daily and clinical settings remains widely uncharacterized. For example, a recent study found the MB might be miscategorized as mind wandering in ADHD symptom evaluation [6]. Therefore, the experience of MB occurrences poses a challenge to our everyday functioning and our understanding of the continuous nature of the stream of consciousness.

Currently, there is no clear answer as to how MB reports are generated. So far, behavioral studies show that MB can arise after conscious mental effort to empty our mind [7–9], is usually unintentional [5,10,11] and gets reported less frequently during unconstrainted thinking compared to mind wandering and sensory/perceptual mental states [5,11–13]. At the brain level, the inability to report mental events after the prompt to "empty the mind" has been associated with activation of the anterior cingulate/medial prefrontal cortex, and deactivation of inferior frontal gyrus/Broca's areas and the hippocampus, which the authors interpreted as the inability to verbalize internal mentation (inner speech) [8]. Recently, we found that the functional connectome of fMRI volumes around MB reports was similar to a unique brain pattern of overall positive inter-areal connectivity [12] which was also characterized by increased amplitude of fMRI global signal (i.e. averaged connectivity across all grey matter voxels), an implicit indicator of low

arousal [14–16]. For example, the amplitude of the global signal correlated negatively with EEG vigilance markers (alpha, beta oscillations), while increases in EEG vigilance due to caffeine ingestion were associated with reduced global signal amplitude[14]. Our findings corroborate recent EEG-related evidence supporting the possibility of "local sleeps" during MB reportability [10,17]. "Local sleeps" refer to the scalp distribution of EEG potentials during wakefulness, in the form of high intensity, slow oscillatory activity in the theta/delta band, which could differentiate between MB and mind wandering, with more fronto-central potentials tied to mind wandering and parietal to MB [10]. Together, the presence of slow waves preceding MB reports and the high fMRI global signal hint toward the role of arousal in mental content reportability. Starting from this line of evidence, we generally infer that arousal fluctuations drive MB reportability.

Arousal is a multidimensional term generally referring to the behavioral state of being awake and alert, supporting wakefulness, responsiveness to environmental stimuli, and attentiveness [18,19]. Anatomically, arousal is supported by the ascending arousal system, the autonomic nervous system, and the endocrine system [18]. Early on, Lacey viewed arousal in terms of behavioral arousal (indicated by a responding organism, like restlessness and crying), cortical arousal (evidenced by desynchronized fast oscillatory activity), and autonomic arousal (indicated by changes in bodily functions) [20]. Cortical arousal is self-generated through the reticulate formation and propagated through dorsal thalamic and ventral subthalamic pathways [21], and can be indexed by the alpha, theta, and delta EEG bands during wakefulness [22,23]. Lower levels of cortical arousal in the form of slow waves have been associated with an increased number of missed stimuli in behavioral tasks [11,23] and decreased thought intensity [24]. Also, lower levels of arousal indexed by pupil size have been correlated with a higher probability of MB reports in sustained attention tasks [11,25,26].

Much as it may have been done in terms of cortical arousal, the present study will focus on how autonomic arousal influences MB reportability, which is widely understudied. Our choice is justified by the theoretical assumption that mental function is tightly linked to peripheral body functions, explicitly

expressed by the embodied cognition stance [27]. Briefly, embodiment holds that cognition is bound to a living body interacting with a dynamic environment and conceptualizes cognition as the result of brain-body interactions during dynamic contexts. From that perspective, modifications in autonomic arousal are expected to lead to differential reportability of mental states. Autonomic arousal links the body and the brain through spinal-cord projections from peripheral organs to the brainstem and can be indexed by physiological signals reflecting sympathetic/parasympathetic balance, such as heart rate, galvanic skin response, and fluctuations in pupil size [28]. Converging evidence suggests that afferent physiological signals and biological rhythms, such as the cardiac or the respiratory phase, play a modulatory role in conscious perception [29,30], metacognition [31], affective salience of information[32], and perceptual confidence of sensory sampling [33], both during task performance and in-silico simulations [34]. Alterations in autonomic arousal were also found to influence brain activity in that fMRI volumes characterized by lower arousal levels (indexed by decreased pupil size), showed reduced in-between network integration and inter-subject variability in comparison to scans characterized by high arousal levels (indexed by increased pupil size) [35].

Taken together, we here propose a direct link between autonomic arousal and content reportability. Firstly, we will examine how MB report distribution shifts across different autonomic arousal stages. To this end, we will use experience-sampling under differently elicited arousal conditions. Experience-sampling is a though-sampling methodology, where people are probed to report their mental content at random intervals, probed by an external cue [4,36]. We will employ this task at three distinct arousal levels: baseline, high (post-workout), and low (post-sleep deprivation). Our operational hypothesis is that optimal levels of arousal (fixed variable) are necessary for optimal mental content reportability (dependent variable). We expect that deviations from optimal levels, such as after sleep deprivation or intense physical exercise, will alter our stream of consciousness, therefore promoting more frequent MB reports (See Table 1 for the full scope of our hypothesis). Secondly, we will opt to identify specific brain-body interaction patterns that promote MB reportability. To this end, we will utilize multimodal

neurophysiological recordings and a machine learning approach to decode reports from arousal measurements. If our hypotheses fail, it will suggest that cortical and autonomic excitability contribute differentially to the reportability of mental absences. If our hypotheses get confirmed, a new path will open toward an embodied approach of reporting content-less events, whereby bodily influences will be among the key determinants of the MB phenomenology.

Methods

Ethics Information

The experimental procedure has been approved by the CHU Liège local ethics committee and conforms with the Declaration of Helsinki and the European General Data Protection Regulation (GDPR). Before the onset of the protocol, participants will provide informed consent of their participation in the study. Participants will receive monetary compensation for their participation in the study.

Design

The study will include healthy volunteers recruited after campus poster advertisements, intranet electronic invitations, and through the ULiège "petites annonces" e-campus platform. Inclusion criteria are: a) right-handedness, b) age>18 years, c) minimal exercise background (<2h per week), d) good subjective sleep quality (Pittsburgh Sleep Quality Index [PSQI] ≤ 5 [37]), e) habitual sleep duration of 8 ± 1 hours. Exclusion criteria are: a) history of developmental, psychiatric, or neurological illness resulting in documented functional disability, b) severe anomalies in pupil shape or inability to open both eyes preventing pupil measurement [38], c) analgesic medication which may affect physiological arousal, d) history of psychiatric illness pertaining to anxiety disorders or scores < 9 in the General Anxiety Disorder-7 (GAD-7 scale) [39] as anxious participants experience biased perceptions of their bodily states [40], e) extreme chronotypes, f) shift work or traveling over time zones in the past 3 months.

Experience-sampling will be utilized in a within-participants repeated-measures design. During the experience-sampling session, participants will lay restfully and will be directed to let their minds wander,

without any specific instructions towards internal (daydreaming, memories, prospective events) or external thoughts (body sensations, sensory stimuli in their immediate environment). Auditory probes (total n=40, 500Hz simple tones) will invite participants to report what they were thinking at the moment just preceding the probe. The inter-probe interval will be sampled from a uniform distribution between 110 and 120 seconds. Report times will be monitored online to examine if participants miss the probe or fell asleep due to our experimental manipulation. In case of a report time > 6s, participants will be reminded to report their mental state as soon as they hear the probe, and indicate they are awake via button press. In case of unresponsiveness, the experimenters will manually awaken the participant. Depending on the probes' trigger times and participants' reaction times, we anticipate that each recording session will vary between 70-90 minutes. We chose to present 40 probes, as to keep the overall length of our experience-sampling paradigm approximately one hour and fifteen minutes, avoiding fatigue/drowsiness and participants returning to baseline conditions after our experimental manipulation. The relatively large experience-sampling interval, compared to previous studies, is used to record enough samples to accurately estimate physiological markers from slow oscillatory signals, such as the heart rate variability. Upon the probe, participants will have to choose among distinct choices describing their mental content: MB, mind wandering, and perceptual sensations or sleep. These response options were chosen to minimize assumptions about what the actual partitions of mental content might be. For example, debates about what can be classified as mind wandering[41] refer to whether mind wandering is a coherent cluster of events [1,42] and how it is separated from awareness and processing of environmental stimuli [41,43]. We believe that our divisions respect the literature on internal/external thinking networks [3,44,45] while introducing minimum assumptions as to the actual content of each state. The introduction of the sleep option facilities the identification of trials where participants fell asleep due to our experimental manipulation. Participants will indicate their response via button press from a response keyboard placed under their dominant hand.

We will repeat the experience-sampling task on three distinct days, over the span of two weeks under three conditions: a) experience-sampling under spontaneous thinking without arousal modulations, b) experience-sampling elicited through short, high-intensity interval training (high autonomic arousal), c) experience-sampling after total sleep deprivation (low autonomic arousal) (See Figure 1). The goal of both arousal manipulations is to promote distinct changes in physiological and cortical markers associated with arousal mechanisms (see Table 2). Monitoring of arousal changes will be done with physiological and cortical measurements. In case participants do not show distinct changes in cortical and physiological changes after our arousal manipulations, they will be excluded from further analysis. Effect monitoring will be done by examining the heart rate in the high arousal condition and the pupil size in the low arousal condition, as well as the EEG spectra in both conditions.

In the high autonomic arousal condition, participants will first perform high-intensity interval activity in the form of cycling. They will start with a warm-up training session of 3 minutes to avoid potential muscle trauma and then will cycle for 45 seconds as fast as possible. A resting period of 15 seconds will follow. A total number of 10 workout cycles will be administered. The choice of this timing protocol rests on previous studies indicating that similar exercise routines produce distinct and sustained sympathetic activity [46,47] and cortical excitation [47], which can last between 30-90 minutes after exercise cessation[48].

In the low autonomic arousal condition, participants will perform the experience-sampling task after one night of total sleep deprivation. Sleep deprivation leads to an arousal state that is behaviorally distinct from typical wakefulness[49,50], promotes specific neuronal signatures ("local sleeps" in the delta bands)[11], and has a distinct physiological expression. Critically, we do wish to claim that sleep states are identical to "local sleeps", nor do we suggest an overlap between low arousal due to sleep deprivation and unconsciousness during sleep.To acquire estimates of their mean sleep schedule, participants will be required to wear an actimeter for one week before the total sleep deprivation protocol. The total sleep deprivation protocol will be as follows: A week prior to sleep deprivation, participants will be provided with an actimetry device, to track wake-sleep schedule, and will be instructed to follow a consistent 8-

hour sleep schedule. On the deprivation day, participants will arrive at the lab one hour before their normal sleep time to extract their actimetry baseline data, estimate the optimal sleep deprivation window and provide baseline vigilance, drowsiness, and sleepiness measurements. After a total sleep deprivation of 26h (16h of typical wakefulness, 8h of sleep deprivation, and a 2h post-sleep deprivation period) participants begin their post sleep-deprivation, experience-sampling session. As an example, a participant who typically sleeps at 12 am will arrive at the lab at 11 am, start sleep deprivation at 12 am, finish sleep deprivation at 8 am, and perform the experience-sampling task at 10 am. Should slow-wave activity during wakefulness follow the same circadian modulation it follows during sleep [51], a potential confound that might lower the power of our analysis is the time-window of the experience-sampling task. However, as suggested in [51], the relative time-window we have selected does not fall under a critical point of large reductions in the amplitude of the slow-waves. The 2-hour, post-deprivation waiting window will allow us to match the time of the experience-sampling across the 3 conditions, avoiding potential circadian confounds on experience-sampling, as we can easier match sleep-wake cycles and the time of the experience-sampling within each participant. We have chosen this sleep manipulation as similar manipulations have been previously used to examine the effects of sleep pressure [52,53], and have been shown to elicit distinct low-arousal cortical profiles [54,55], as well as changes in the sympathetic/parasympathetic balance [56].

Sleep deprivation will be controlled with regard to light influence (illuminance = 15 lux during wakefulness and 0 lux during sleep), caloric intake (standardized meals every 4 h), and body posture (semirecumbent position during scheduled wakefulness) to minimize potential masking effects on the sleep-wake regulatory system. Participants will not be allowed to stand up except for regularly scheduled bathroom visits and will not have any indications of the time of the day. The experimenters will continually monitor participants to keep them awake. In case of a sleep event, the experimenters will first try to awaken the participant through an intercom, and in case of failure, they will manually awaken the participant. We will also be monitoring for sleep lapses through the experience-sampling tasks. In case

participants close their eyes for time-period < 30 seconds, they will be probed by a tone to wake up. If they do not, the experimenter in the room will awaken the participant.

A one-week interval will take place between sleep deprivation and further recordings in order to minimize potential carry-over effects of sleep deprivation on our follow-up conditions. In that way, the participants' sleep schedules will also reset to their respective normal cycles. The order of the three arousal conditions will also be randomized.

Sampling Plan

We used a Neyman-Pearson frequentist approach to balance false-negative and false-positive rates by setting power to 95% and establishing a Type I error rate (alpha) of 5%. To estimate the desired sample size, a simulation approach was utilized: data were generated consistent with a latent binomial regression model, in which one categorical predictor with 3 levels (Base, High, Low) predicted a binary outcome Y (presence of MB or not). An original probability p_{MB} = .1 was specified as the underlying generative probability in the baseline model based on previous research [5,11,12]. We allowed the random intercepts and slopes to freely vary around a normal distribution with a standard deviation of s.d. = .1. Given that no previous study to our knowledge has provided evidence for the distribution of the effect sizes of arousal on mental reports, and to account for possible reverse effects (such as decreased MB report probability), we reasoned that a meaningful yet conservative effect for the "Low" arousal condition would be an odds ratio of 1.6, and an odds ratio of 0.55 for the "High" arousal condition. Since our initial hypothesized distribution is expected to yield ~3-5 MB reports per session [11,12], this effectively translates to a small effect size of interest of at least 3 more reports across conditions.

Considering these parameters, for each population sample, ranging from 5 to 50 participants, we sampled 500 datasets, and fit a binomial model with the participant ID as random factors, keeping the regression coefficients for the levels of the predictor constant. Based on the simulation analysis, using a

false positive threshold of .05, we calculated a sample size of 26 participants to achieve a power of .95 (See Figure 2).

Given our sample size, and the estimated 3-week recording period for each participant, we expect that data collection will be completed within 4 months. Subsequent data analysis and discussion preparation will take an additional 3-4 months. Therefore, we anticipate submitting our manuscript within 8 months.

Analysis Plan

Behavioral data

Statistical analysis will be performed using generalized linear mixed-effects models. To address whether arousal affects MB occurrence, we will use a binomial, linear model with arousal as a categorical independent variable, and the proportion of mental reports across a sampling period (40 trials) as our dependent variable. The data will be binary coded (presence or not of MB report) and fit into the model using a logit link. Given that the underlying distribution is unknown, a Bernoulli generative process minimizes the assumptions about the model. In order to examine whether the multinomial distribution of mental reports itself changes across different arousal conditions, we will use the generalized estimating equations (GEE) approach (Liang & Zeger, 1986), an extension of generalized mixed-effects models that can account for correlated, repeated-measures count data from multinomial distributions [58]. Mental reports will be aggregated as counts across participants and conditions, and we will examine shifts in distribution using the three experimental arousal conditions as predictors. We will consider as response time the interval between the response probe and the participant's response. To examine reaction times as a function of mental states, we will specify a generalized linear mixed effect model with mental reports and arousal conditions as categorical variables and use a gamma distribution with an inverse link function. As reaction-times are usually an indicator of arousal effects on the task-performance, an effect of arousal state as a covariate might be informative about a potential shift of the overall slower mental report times distribution and about the arousal state of the subject itself. The choice of the distribution and the link

minimizes assumptions about the model, respects the positive, skewed distribution of reaction times, and was previously found to provide a better fit compared to other link functions [59]. To examine whether arousal shifts the dynamics of mental reports, i.e one state might be more likely to be followed by MB in one of the arousal states compared to baseline, we will estimate dynamical transition probabilities across different mental states using Markov models. The transition probabilities for MB will be then compared using a linear model with an identity link, with the transition probabilities as the dependent variable and the arousal condition as the categorical, independent variable.

All specified models will be compared against null models using likelihood ratio tests. We will introduce the participant's ID as a priori random factor, i.e., we will allow the model's intercept to vary. In case of multiple models compared, p values will be corrected using Bonferroni correction. In case of significance of a fixed predictor, we will use corrected pairwise comparisons to examine the marginal means of the predictors.

Brain-based measures

Physiological and cortical timeseries will be segmented based on the response probe time. We will consider the 120-second period before the response probe as a meaningful analysis epoch, representing the neuronal and physiological dynamics that result in a specific mental state. This period will be used in subsequent analysis.

We plan to record EEG with an EasyCap (64 active electrodes) connected to a BrainAmp system (Brain Products GmbH) using the 10-20 standard configuration. A ground electrode will be placed frontally (Fpz in the 10–20 system). Online, we will reference the electrodes to a frontal electrode. Impedance will be kept below 10 kOhm. To minimize impedance, we will use conductive gel. Data will be sampled at a sampling frequency of 500 Hz. Preprocessing will encompass band-pass filtering (>.1Hz, <45Hz), notch filtering (50Hz), and epoch definition (t_start = 120s preceding the probe, t_max= probe). By visual inspection, we will check and remove noisy electrodes and epochs. Should we discard more

than 50% of the total epochs for a single participant, that participant will be discarded from future analysis. We will use ICA decomposition to remove non-neuronal components such as blinks, heartbeats, muscle artifacts, etc. Finally, channels removed due to rejection will be interpolated using neighboring channels, and all channels will be re-referenced to the average.

Based on EEG recordings, we will estimate three classes of measures: 1) measures estimating spectral power - raw and normalized power spectra, Median Spectral Frequency (MSF), spectral edge 90 (SEF90), and spectral edge 95 (SEF95), 2) measures estimating information content – spectral entropy, Kolmogorov-Chaitin complexity (K) and Permutation Entropy, and 3) measures estimating functional connectivity – Symbolic Mutual Information and weighted Symbolic Mutual Information. Power spectrum density (PSD) will be computed over the delta (1-4 Hz), theta (4-8Hz) alpha (8-12Hz), beta (12-30Hz), gamma (30-60Hz) spectral bands, using the Welch spectrum approximation (segments = 512 ms, overlap = 400ms). Segments will be windowed using a Hanning window and zero-padded to 4096 samples. Kolmogorov-Chaitin complexity will be computed by compressing a discretization of the signal using a histogram approach with 32 bins. Permutation Entropy will be obtained by computing the entropy of a symbolic transformation of the signals, within the alpha, delta, and theta bands. SMI and wSMI are then computed from the same symbolic transformation, but data was first filtered using Current Source Density estimates to diminish the volume conduction. SMI and wSMI will be computed in theta, delta, and alpha bands [60]. From the available connectivity metrics, we chose to use only wSMI as it is the only one that can detect purely nonlinear interaction dynamics and can be computed for each epoch [61].

Physiological measures

Electrocardiogram (ECG) data will be acquired using the BIOPAC MP160 system (BIOPAC SYSTEMS inc.), amplified through the BIOPAC ECG100C amplifier. The data will be sampled at a sampling frequency of 2kHz and recorded using the AcqKnowledge v4.4 software. ECG disposable adhesive skin electrodes will be used in a bipolar arrangement of two electrodes and ground. The positive

electrode will be at the non-dominant wrist of the participant and the negative on the contralateral ankle. The ground electrode will be placed on the ipsilateral ankle.

ECG data will be filtered with a notch filter (.05Hz) to remove baseline wander artifacts. A Butterworth high-pass filter will be applied (<.5Hz) to attenuate linear drifts and physiological artifacts. Powerline interference will be attenuated with a notch filter (50Hz). Finally, the data will be smooth with a 3rd-order polynomial Savitzky-Golay filter. Peaks will be detected using the Pan-Tompkins algorithm [62]. Finally, data will be epoched based on the partition scheme in the EEG preprocessing section.

ECG metrics can be grouped into three domains: time, spectral power, and information content. Time-domain metrics are a) the Heart Rate (HR), b) the standard deviation of the RR-intervals (SDNN), and c) the Root Mean Square of Successive Differences (RMSSD). Spectral power features are a) Low Frequency of the Heart Rate Variability (LF-HRV), b) High Frequency of the Heart Rate Variability (HF-HRV) and c) the LF/HF HRV ratio. Information content metrics are : a) Approximate Entropy (AE), b) Sample Entropy (SE), c) Multiscale Entropy (MSE). Initially, we will use the Pan-Tompkins algorithm [62] to extract the peaks of the QRS complex. RR intervals will be estimated as the sequential difference of the peak times. We will estimate the time domain features based on the RR timeseries. For the spectral power metrics, the RR will be evenly resampled at 4 Hz. Power spectra will be computed over the LF-HRV (0.04–0.15 Hz) and the HF-HRV (0.15-0.4) bands. The power spectrums will be estimated using the Welch procedure.

Respiration. Respiratory data will be acquired using a respiratory belt and amplified through the BIOPAC amplifier. Data will be sampled at a sampling frequency of 50 Hz and recorded using the AcqKnowledge v4.4 software.

Respiratory metrics can be grouped in the time and information content domain. Time-domain metrics are the: a) respiration rate and b) respiration rate variability. Information content will be estimated based on multiscale entropy.

Pupillometry. Eye movements and pupil size in both eyes will be recorded using oculometric glasses (Phasya recording system) with a sampling frequency of 1000 Hz. The eye tracker will be calibrated at the start of each recording. Data will be epoched based on the epoching scheme in the EEG preprocessing section. Initially, pupil data will be downsampled to 120Hz. We will identify 100ms blink periods around blinks and remove the whole segment, as pre- and post-blink periods can introduce pupil dilation artifacts while the eye is recovering to its standard size. We will interpolate segments using 3rd-degree cubic interpolation. Dilation speed outliers will be calculated by estimating the median absolute deviation (MAD) of each value. Samples exceeding the deviation threshold will be removed. Pupil dilation will be smoothed using a moving average filter and baseline corrected with a 100ms period 2s after the probe.

Pupil metrics can be grouped in the same three domains: time, spectral power, and information content. Time-domain metrics are: 1) Blink rate, 2) Pupil size, 3) Pupil size variability. Spectral power metrics are: 1) Low Frequency Pupil Component (LFC), 2) High Frequency Pupil Component (HFC). The information content metric is MSE. The power spectrums will be estimated using the Welch procedure.

Electrodermal activity (EDA) data will be acquired through skin electrodes on the index and middle finger and amplified through the BIOPAC amplifier. Data will be sampled at a sampling frequency of 250 Hz and recorded using the AcqKnowledge v4.4 software. All EDA metrics will originate from the time domain: a) Galvanic Skin Response (GSR), b) tonic GSR, and c) phasic GSR. Extraction of the phasic and tonic components of the GSR will be conducted with deconvolution of the GSR signal with a biologically plausibly impulse response function with initially fixed parameters that are iteratively optimized per participant [63].

Pattern recognition

To examine the physiological counterpart of the behavioral shifts in MB reports, we will employ a supervised decoding approach. Using the multimodal neurophysiological measurements during the three

experience-sampling sessions, we will train classifiers to discriminate across MB, mind wandering and Perceptual Sensations, to identify whether MB is supported by a unique brain-body interaction pattern. This approach will allow us to extract meaningful brain-body interactions from the proposed arousal metrics without being conservative about the nature of the multiple comparisons between the various body metrics.

As features, we will use every measurement we opted to collect meaningful data in the time, frequency, information, and connectivity domain, unless such measurements could not be reliably estimated within our selected time window. The goal of the multiple selected metrics is to capture potential diverse spatiotemporal relationships (low-high frequency interactions, phase-amplitude interactions) that might extend across different recording modalities. Overall, we will compute 47 features.

As targets, we will use the participants' reports (MB, mind wandering, and perceptual sensations). Since this creates a multiclass classification problem, we will focus on the binary classification of MB vs other reports. We expect to acquire 40 samples per participant and condition (i.e. baseline and arousal states), giving a total of 1040 (26*40) samples per condition. We expect that 5% of the samples correspond to the target report (MB), yielding an imbalanced problem with only 52 target samples.

As learning algorithms, we will first test parametric and non-parametric models such as Support Vector Machines, Random Forests, and Extremely Randomized Trees. Support vector machines are a nonlinear classification technique that aims to separate labeled inputs by creating a hyperplane that maximizes the distance of their features. Given a set of n-labeled inputs, SVM will provide a hyperplane in an n-dimensional space that maximally separates the differently labeled groups. A random forest classifier is a meta-estimator. Various classifiers ("decision trees") are trained in different parts of the input dataset, and each classifier uses only that part of the dataset to predict the label of the input. Then, the predictions of each classifier are pooled ("bagged") together, and an optimal decision is chosen based on the label with the most predictions ("votes"). Finally, an extremely randomized tree classifier is a

meta-estimator that employs a similar voting scheme. However, in the case of extremely randomized trees, trees are trained on all the features and the cutoff point of the trees (how the various metric nodes are arranged to reach a decision) is randomized. Since our problem is highly imbalanced, we will also test outlier detection algorithms (i.e. one-class classifiers), aiming to isolate MB from the other reports by considering MB as either an inlier or outlier. We will test the one-class counterparts of the SVM (One-class SVM) and Random Forests (i.e. isolation forests) algorithms.

For model selection and performance estimation, we will employ two different cross-validation approaches. First, we will use a 5-fold stratified cross-validation scheme trained with all the samples. This will provide us with performance estimates of classifiers aimed at obtaining patterns of brain and body function that can predict the report of MB in known participants. As a second approach, we will use a 5-fold group stratified cross-validation scheme, using participants as groups. In this scenario, each participant can be either on the train or the test set. Thus, it aims to learn general patterns of brain and body function that can predict the report of MB in unseen participants. In other terms, the first approach aims to learn patterns that can discriminate MB from other reports while accounting for each participant's variance, while the second strengthens the claim, aiming to learn general patterns that can be found in unseen participants.

As performance metrics, we will report a) recall, b) precision, c) F1-score, d) area under the ROC curve (AUC), and e) balanced accuracy. Recall is the ratio of how often an item was classified correctly as a positive (True Positive / True Positive + False Negative). Similarly, precision is the ratio of actual correct positive classifications among positive classifications (True Positive / True Positive + Positive). F1-score is the harmonic mean of precision and recall. The AUC curve is another evaluation metric that summarizes how well the classifier predicts a class based on different thresholds of true positive and false positive ratios. Finally, balanced accuracy is an evaluation metric suitable for imbalanced datasets, where one class appears at significantly different frequencies than the others. Balanced accuracy is useful because it is estimated as the average of precision and recall, simultaneously controlling for very high

precision due to classifying nothing as the infrequent class and very high recall due to classifying everything as the infrequent class.

We will also select each model's hyperparameters using nested cross-validation (same scheme as the outer cross-validation), using the F1-score as our optimization metric.

To evaluate the variance in the classifier performance and compare it to chance level, we will do repeated cross-validation (10 times), while training also a "dummy" classifier to obtain the empirical chance level of the training samples distribution. This type of classifier generates predictions based on the distribution of training samples for each class without accounting for the features.

The decoding analysis will be implemented in Python using Julearn and Scikit-Learn[64]. Metrics will be estimated from existing Python libraries: MNE[65], NICE[66], Systole[67], Neurokit[68], and custom in-lab Python functions.

Code Availability

All codes to replicate the power analysis, and the experience-sampling paradigm can be found at https://gitlab.uliege.be/Paradeisios.Boulakis/mind_blanking_arousal. The data and the preprint will be made available at https://osf.io/wm29x/.

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Author Contributions

P.A.B and A.D took part in the conceptualization. P.A.B, A.D, and C.S took part in the design formulation. P.A.B, A.D, and F.R took part in the methodology. P.A.B will conduct the analysis. F.R. will supervise the analysis. P.A.B visualized the data. P.A.B and A.D took part in the original draft writing. All authors took part in the review and editing of the manuscript.

Competing Interests

The authors declare no competing interests

Table 1. Design Table

Question	Hypothesis	Sampling Plan	Analysis Plan	Alternative Explanation
Is automimic arousal implicated in mental state reportability?	Low and high arousal promote more frequent MB reports.	500 Simulations for datasets ranging from 5 to 50 participants. For each dataset, we fit a binomial model with an odds ratio of .1 for MB occurrence N=26 participants	MB ~ Arousal Mental Report ~ Arousal RT ~ Mental Report Transitions ~ Mental Report	Low arousal manipulation was not effective in modifying autonomic signals. High arousal manipulation did not last throughout the experience-sampling procedure. Higher arousal levels might facilitate monitoring, reducing MB reports.
Can mental absences be attributed to cerebral mechanisms only, or to brain-body interactions?	We can decode MB from other mental reports based on a brain-body profile characterized by lower overall complexity.	NA	Train 4 classifiers: 1.Support Vector Machine 2.One class SVM 3.Random Forest 4. Random Trees Optimize for F1-score Nested CV hyperparameter tuning	Given the unbalanced nature of our dataset, our classifiers might not converge properly to accurate prediction parameters. Physiological timeseries might be too slow (few oscillations) to contribute to short events, such as a mental state.

Table 2. A brief overview of the effects of sleep deprivation and exercise on arousal metrics

Modality	Metric	Previous Studies
Electrocardiogram (EEG)	Alpha oscillations Delta oscillations Theta oscillations	Borbély et al , (1981). Gutmann, B. *et al.* (2015). Posada-Quintero, et al (2019).
Electroencephalogram (ECG)	Heart Rate Heart Rate Variability	Gourine, et al (2019). Glos et al. (2013)
Pupillometry	Pupil Size	Ishikagi (1991) Franzen et al (2009)
Electrodermal activity (EDA)	Galvanic Skin response (GSR)	Posada-Quintero, Het al (2018). Posada-Quintero, et al (2017).

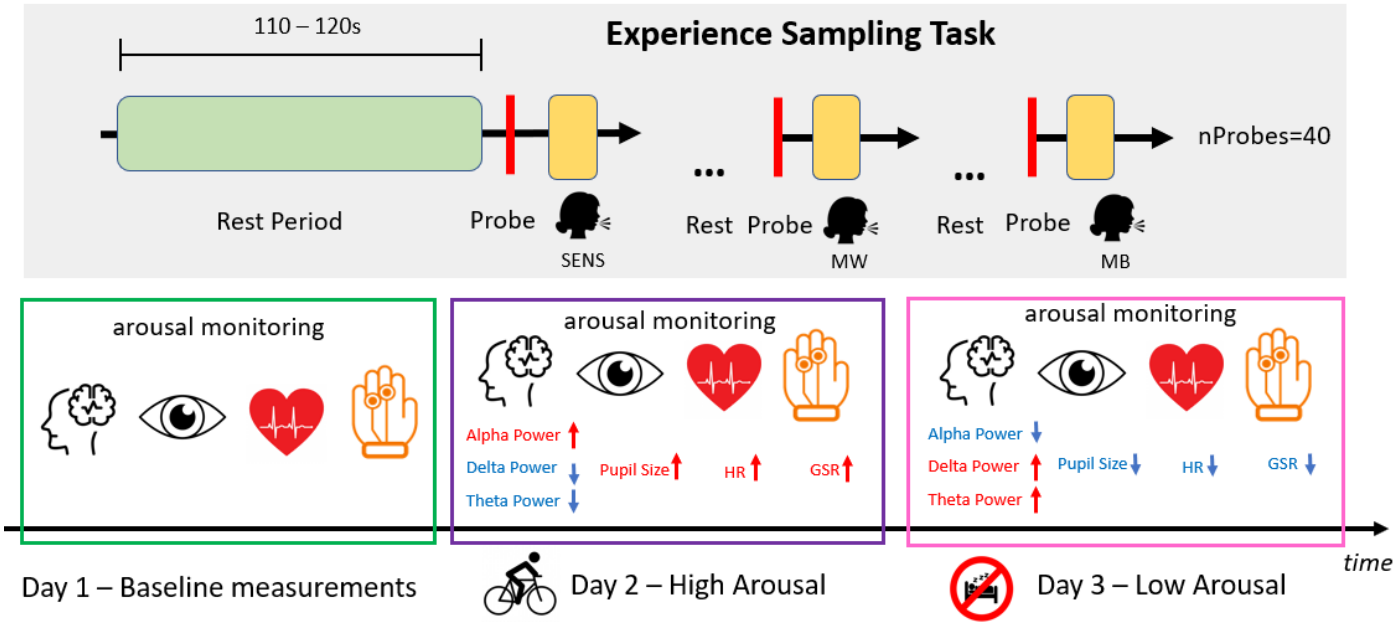

Figure 1. Experimental protocol. *Top* The experience-sampling task will invite participants to sit idly and relax, letting their minds wander. Every 110-120s, a 500 Hz auditory cue will probe participants to report what they were thinking at that moment. Participants will be able to choose from 3 presented responses: Mind Blanking, Mind-wandering, Perceptual Sensations and Sleep. *Bottom* Repeated measures autonomic arousal recordings. To test how spontaneous thoughts unfoldμθ over time across different arousal profiles, we will invite people for a follow-up experience-sampling session, following a 15-minute high-intensity exercise routine and total sleep deprivation. To monitor whether arousal manipulations affected the participants, we will examine their current arousal levels using multimodal physiological recordings. The dataset will be constituted of EEG, pupillometry, ECG, EDA, and respiratory data.

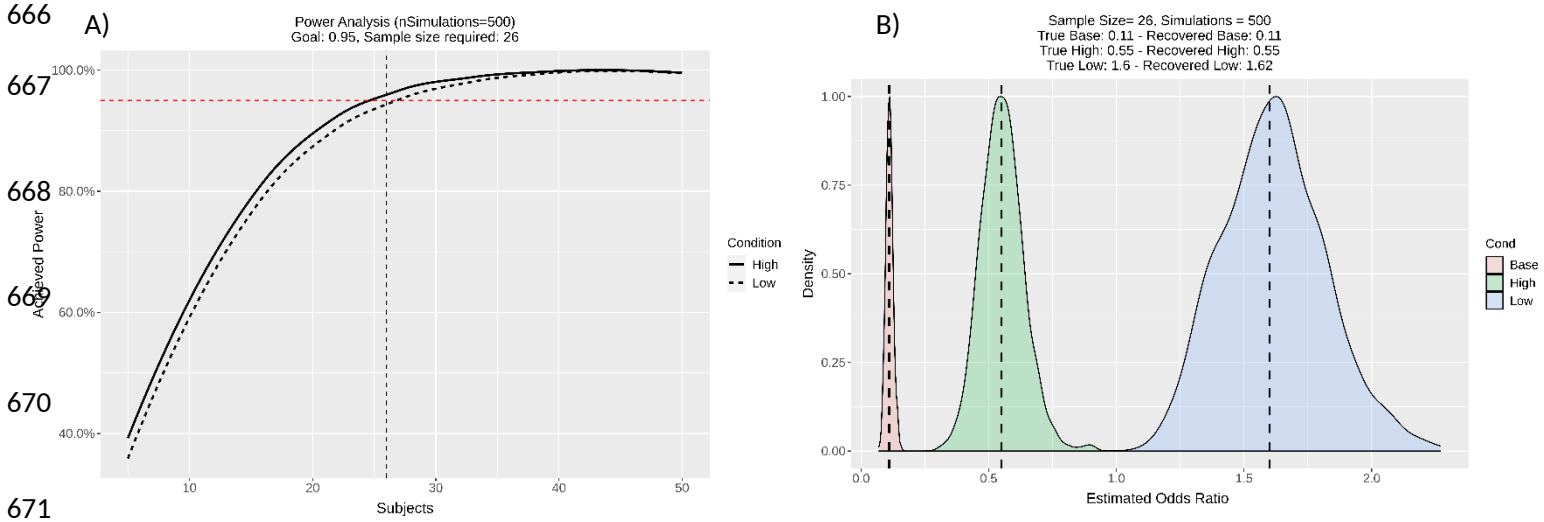

Figure 2. Simulation analysis for sample size calculation. A) We ran 500 simulations for sample sizes ranging from 5 to 50 participants to estimate the optimal sample size to achieve 95% power. Using a base odds ratio of .11 to report MB during free thinking, an odds ratio of 1.6 when arousal decreases (low arousal condition, dotted line), and .55 when arousal increases (high arousal condition, solid line), we estimated that a sample of 26 participants is sufficient to achieve significant power in both arousal conditions. B) To validate whether our model can recover the true parameters, we ran additional 500 simulations using a sample size of 26 participants. Our results show that our model can indeed estimate the true parameters. *Notes*: dashed line = true parameters.