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Differential neural processing of spontaneous blinking under visual and auditory sensory environments: An EEG investigation of blink-related oscillations

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ABSTRACT

Blink-related oscillations (BROs) are a recently discovered neurophysiological response associated with spontaneous blinking, distinct from the well-known oculomotor and visual suppression effects. BROs strongly activate the bilateral precuneus along with other cortical regions involved in visuospatial processing and associative episodic memory, and are believed to represent environmental monitoring processes that occur following blink-induced visual interruptions. Although these responses have been reported across multiple imaging modalities under both resting and cognitive loading conditions, it is yet unknown whether these responses also exist under external sensory stimulation conditions. To address this, we investigated BRO responses in healthy adults using 64-channel electroencephalography (EEG), while participants underwent passive external auditory and visual stimulation. Our results showed that BRO responses are present under both auditory and visual stimulation conditions ($p < 0.05$), with similar temporal and spectral features compared to rest. However, visual stimulation did result in decreased BRO amplitude compared to auditory and resting conditions ($p < 0.05$), suggesting decreased neuronal resources for processing blink-related information in the visual but not auditory environment. There were also additional pre-blink spectral changes in the visual condition compared to rest ($p < 0.05$), which suggest that passive visual stimulation induces neural preparatory processes occurring in anticipation of the upcoming blink event. Together, these findings provide new and compelling evidence that blink-related neural processes are modulated not only by the internal cognitive loading due to simultaneous task demands, but also by competing external sensory requirements. This highlights the link between blinking and cognition, and further demonstrates the importance of BROs as a new window into brain function.

1. Introduction

We blink spontaneously 15–20 times every minute, producing about 110 ms of pupil occlusion each time (Tsubota et al., 1999; Volkmann et al., 1980). Although most of us rarely give blinking a second thought, studies are increasingly pointing towards a link between blinking and cognitive processing. Blinking has been shown to occur preferentially at moments of low attentional demand, such as punctuation marks when reading (Orchard and Stern, 1991) and speaker pauses when listening to speech (Nakano and Kitazawa, 2010); it activates frontal and parietal cortical regions associated with attentional switching mechanisms in the brain (Nakano et al., 2013); and blinking also induces visual suppression, a reduction of visual sensitivity that mitigates the impact of blink-induced vision loss and helps to maintain continuity in the subjective visual experience (Volkmann, 1986). There is strong evidence that, in addition to lubricating the cornea, blinking also has important cognitive implications.

Abbreviations: BROs, blink-related oscillations; VAN, ventral attention network; ERS, event-related synchronization; ERD, event-related desynchronization; ICA, independent component analysis; vEOG, vertical electrooculogram; OCI, ocular contamination index; CWT, continuous wavelet transform.

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Blink-related oscillations (BROs) are a recently discovered neurophysiological phenomenon which is thought to represent the brain's environmental monitoring and information processing mechanisms associated with blinking (Bonfiglio et al., 2013, 2014; Liu et al., 2017, 2019a, 2019b). These responses occur on a millisecond scale following each blink event, and are distinct from the well-known oculomotor and visual suppression effects (Fig. 1a). In the temporal domain, the BRO response is characterized by increased activity in the delta frequency band (0.5–4 Hz), peaking at approximately 250–300 ms post-blink (Fig. 1a) (Bonfiglio et al., 2013; Liu et al., 2017). Its cortical activations have been shown to engage the bilateral precuneus along with other temporal, parietal, and occipital brain regions associated with visuospatial processing and associative episodic memory (Bonfiglio et al., 2013, 2014; Liu et al., 2017, 2019b). Blink-related spectral effects within the precuneus have been shown to encompass an early event-related synchronization (ERS) in both delta and beta/low-gamma (12–35 Hz) bands, followed by a later and more prolonged event-related desynchronization (ERD) in the theta (4–8 Hz) and alpha (8–10 Hz) bands (Fig. 1b) (Liu et al., 2019b). These have been postulated to represent an early sensory response to visual information produced by blink events, followed by a later and more prolonged response related to information processing and episodic memory (Liu et al., 2019b). To date, BROs have been demonstrated across different imaging modalities including both electroencephalography (EEG) (Bonfiglio et al., 2013; Liu et al., 2019a) and magnetoencephalography (MEG) (Liu et al., 2017, 2019b), and studies have shown these responses to be endogenous neural processes occurring in the absence of dynamic external sensory stimulation (Liu et al., 2017, 2019a, 2019b).

Importantly, a previous MEG study from our group demonstrated that BRO responses are also modulated by cognitive loading, with reduced cortical activations when spontaneous blinking occurs during a challenging mental arithmetic task compared to blinking during rest – while controlling for the external sensory environment (Liu et al., 2019b). Decreased BRO-induced cortical activations were especially prominent in the precuneus region known to be involved in environmental monitoring and awareness (Cavanna and Trimble, 2006) and is also a key cortical source of the BRO response (Liu et al., 2017, 2019a, 2019b;). The observed reduction in BRO-induced precuneus activation during mental arithmetic was thought to be the result of competing cognitive demands between BROs and the simultaneous mental arithmetic task, which both engaged the precuneus region. Interestingly, the same study also showed that BRO responses activated regions of the ventral attention network (VAN) (i.e. right inferior frontal gyrus and supramarginal gyrus) during mental arithmetic, but did not do so during rest. As the VAN is known to be involved in stimulus-driven attention for the detection of unexpected but potentially salient events (Corbetta and Shulman, 2002), BRO-induced activation of VAN during mental arithmetic was postulated to represent the brain's recruitment of additional attentional resources for processing blink-related information when attention was already engaged in the ongoing cognitive task (Liu et al., 2019b).

Although BROs are known to be endogenous neural responses which are modulated by cognitive loading, little is known about BRO effects under passive external sensory stimulation. Given the ubiquity of spontaneous blinking behavior, the elucidation of this response under sensory stimulation conditions is crucial to demonstrating the cognitive role of this response. Indeed, if BROs do represent a neurocognitive phenomenon associated with information processing following blink events, the effects should be observable both with and without sensory stimulation. Moreover, as this response is related to processing of *visual* information that appears following the interruption of visual input due to blinking, its effects should be differentially modulated when comparing between visual and auditory environments.

The current study aimed to investigate BRO responses in healthy adults using 64-channel EEG to elucidate these responses during passive

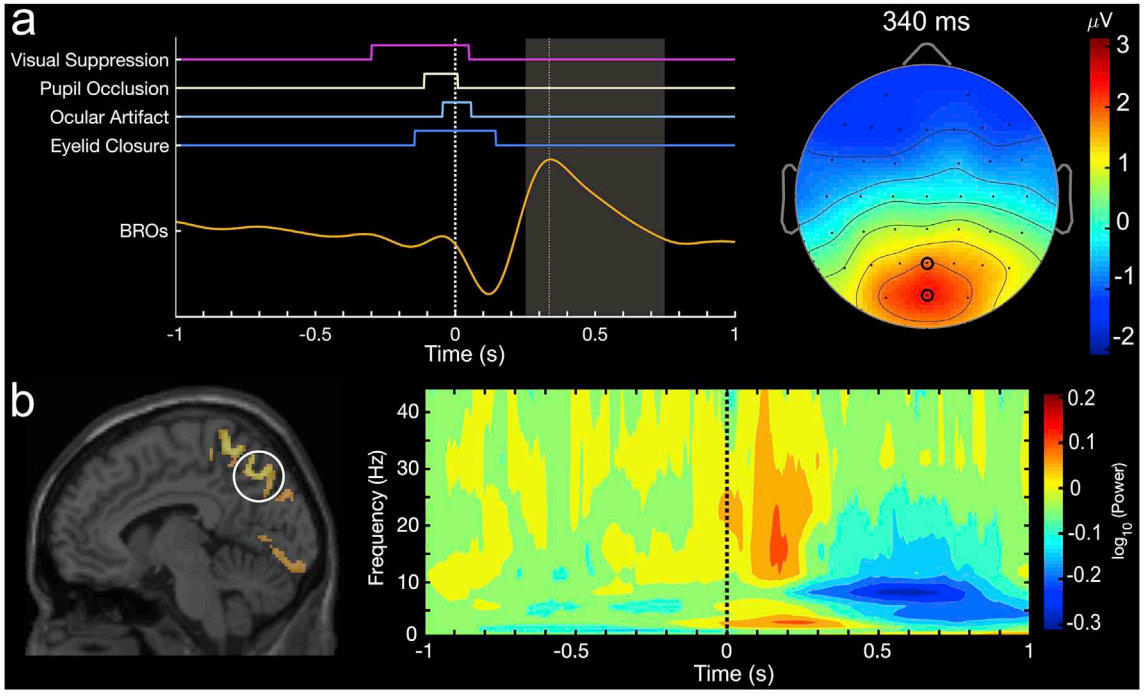

Fig. 1. BRO characteristics under resting conditions. a) Left: BRO time course compared to other known effects of blinking, including visual suppression, pupil occlusion, ocular artifact, and eyelid closure. Response normalized to arbitrary units. Peak BRO response occurs during a 500-ms interval (shaded region) after blinking has already ended. Grey dotted line denotes latency of maximum BRO response. Right: Topography of scalp signal distribution at peak latency, with locations of Pz and POz electrodes closest to the precuneus shown in black circles. b) Left: BROs strongly activate the precuneus (white circle), which is associated with environmental monitoring and awareness (Cavanna and Trimble, 2006; Kjaer et al., 2001). Right: Blink-induced spectral effects within the precuneus show sequential changes in signal power consistent with an early sensory processing (beta/gamma increase, 12–40 Hz) followed by later information processing and episodic memory-related effects (theta/alpha decrease, 4–12 Hz). Data obtained from prior studies by Volkmann et al. (Volkmann et al., 1980) and (Liu et al., 2017; 2019a, 2019b).

visual and auditory stimulation. We hypothesized that BRO responses should: 1) be present across different sensory environments with consistent morphological features relative to that during rest, and 2) be modulated by different sensory demands between the visual and auditory environments.

2. Methods

2.1. Participants

Twenty-eight healthy adults (age 33.25 ± 13.30, 17 female) volunteered for this study. This research was approved by the Research Ethics Boards of Simon Fraser University and Fraser Health Authority. Participants all had normal or corrected-to-normal vision, and each provided written informed consent prior to data acquisition.

2.2. Experimental design

The experimental design consisted of three tasks: *resting*, *visual*, and *auditory* (Fig. 2a). The visual and auditory tasks utilized stimulus paradigms from the 'brain vital signs' framework, which has been described in detail elsewhere (Ghosh Hajra et al., 2018a, 2018b, 2016; Pawlowski et al., 2019). These stimulus sequences have been designed to elicit a multitude of brain responses corresponding to sensation, attention, and language processing, and their use in the current study enabled comparisons of BRO responses while participants underwent wholistic stimulation that was closely mirrored between the visual and auditory domains. In summary, the visual task involved passive viewing of a visual sequence comprising repeating blocks of written words, in which each block contained one word followed by a word pair (Fig. 2a). No environmental sounds were present during the visual task. In the auditory

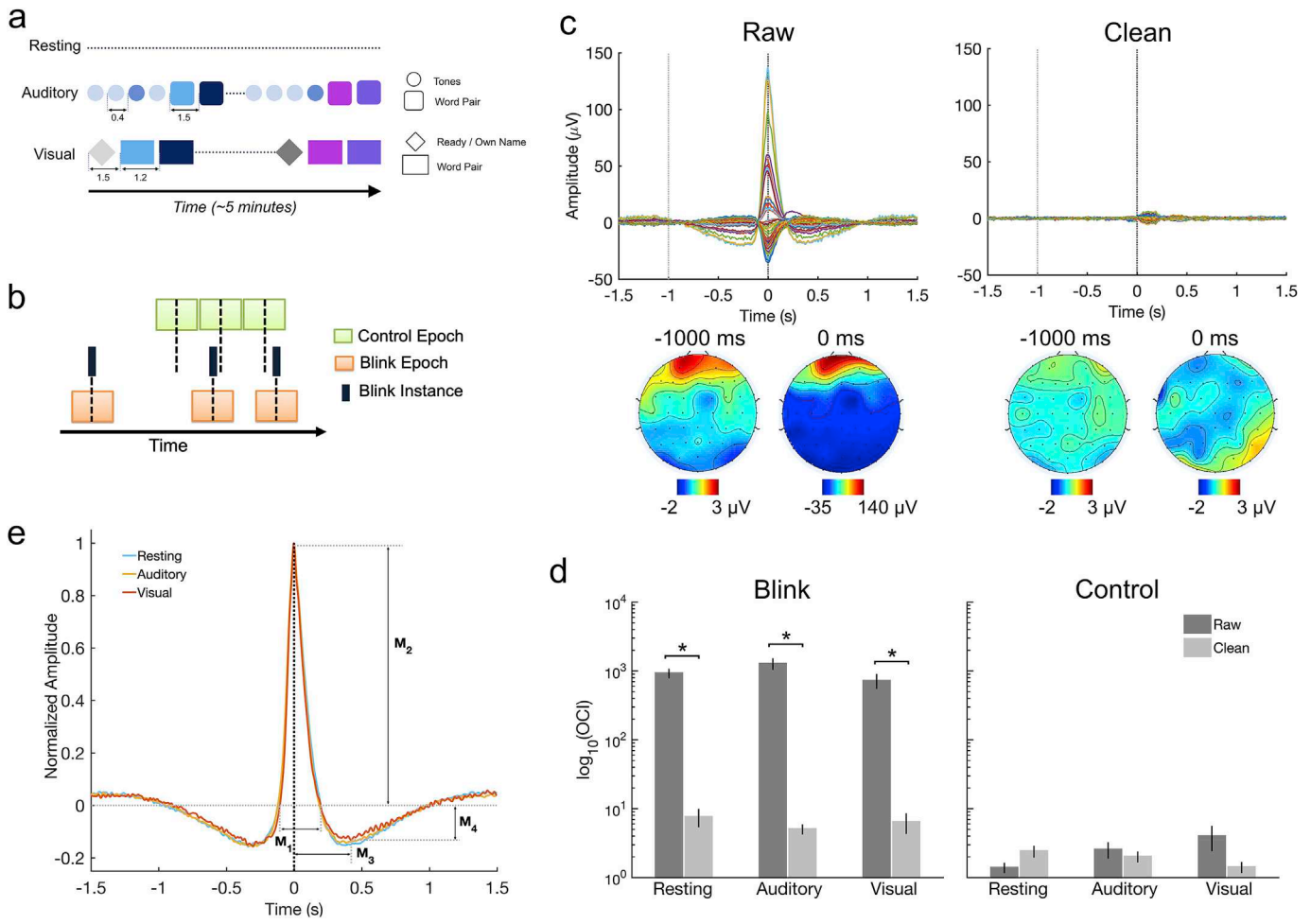

Fig. 2. Study methodology. a) Stimulus paradigms. Resting task did not utilize any dynamic stimuli. Auditory task involved repeating blocks of four tones followed by a spoken word pair (e.g. 'bread' 'butter'). Visual task involved repeating blocks of a single written word (i.e. either 'ready' or participant's own name) followed by a written word pair. Both auditory and visual sequences used identical word pairs. Duration labels are in seconds. b) Schematic illustration of data segmentation technique. *Blink* epochs were centred at time zero (T_0) corresponding to the moment of complete eye closure for each blink event, and were used to assess BRO effects. *Control* epochs were pseudo-random in timing with respect to blink instances, and helped ensure that observed blink-related effects were not due to background brain activity in each of the sensory stimulation environments. All epochs were 3 s in duration, and the number of trials was matched between *control* and *blink* conditions for each task and subject. Black dotted line represents time zero for each condition. c) Representative subject data before and after artifact removal. Top panel shows all-channel trial-averaged BRO waveforms, while bottom panel shows corresponding spatial topographies. Dotted lines denote latencies of maximum blink amplitude at time T_0 (black, 0 ms) and pre-blink baseline (grey, −1000 ms). d) OCI results showing >99% reduction in blink signal contribution relative to baseline following artifact removal. *p < 0.001 e) Grand-average of normalized 3-s blink epochs in vEOG data showing the quantitative morphological features used to evaluate behavioral characteristics across individuals and tasks. M_1 = positive peak width; M_2 = positive peak amplitude; M_3 = negative peak time; M_4 = negative peak amplitude. Black dotted line at 0 ms denotes the moment of complete eye closure or T_0.

task, participants listened passively to an auditory sequence comprising repeating blocks of four tones followed by a word pair, while maintaining visual fixation on an unchanging crosshair. Identical word pairs were used between the visual and auditory stimulus sequences, and both sequences had durations of approximately 5 min.

The resting condition utilized passive fixation on an unchanging crosshair, without dynamic sensory stimuli. To provide equal quantities of data for comparison, the 5-min visual and auditory paradigms were each repeated twice per participant, while the 10-min resting condition was collected once. The order of task performance was counter-balanced across individuals. Participants were instructed to passively attend to the visual and auditory sequences, and to remain alert during the resting task. Volunteers were not informed of the purpose of the study in order to obtain natural blink behaviors.

2.3. Data acquisition

EEG data were collected using a 64-channel system with active electrodes (BrainAmp actiCAP) and BrainVision Recorder software (Version 1.20.0801, Brain Products GmbH). Acquisition took place in a designated experimental suite, with consistent brightness across participants. Volunteers were seated at the centre of the room, and were instructed to minimize movement at all times. Electrode impedances were kept below 20 kΩ. Data were sampled at 1000 Hz, and EEG traces were monitored online throughout the recording session.

2.4. Preprocessing and artifact rejection

Analyses were performed using a combination of EEGLAB (Delorme and Makeig, 2004) and custom processing software in MATLAB (The Mathworks Inc.). Data were first visually inspected, and signals from artifactual channels were removed. The remaining data were down-sampled to 500 Hz, re-referenced to the average of all sensors, and filtered to 0.1–45 Hz frequency using a zero-phase 4th order butterworth filter along with a 60 Hz notch filter (5 Hz bandwidth) to remove power line noise. Independent component analysis (ICA) was performed using the InfoMax algorithm in accordance with prior published procedures (Delorme and Makeig, 2004; Ghosh Hajra et al., 2018a, 2018b; Liu et al., 2017; Makeig et al., 1997), and components corresponding to artifact (e.g. blinks, saccades, muscle contractions, cardiac activity, breathing) were removed.

2.5. Blink detection and behavioral assessments

The dual runs for each of the visual and auditory tasks were first concatenated and matched in length to achieve 10 min of data for each task. Blink detection and behavioral assessments were then performed prior to ICA-based denoising. Blink events were identified using a semi-automated, convolution-based, template matching procedure as described previously (Liu et al., 2017, 2019a, 2019b). Briefly, data from the vertical electrooculogram (vEOG) channel (Fp2 electrode) were band-pass filtered to 0.5–30 Hz, and a blink instance that best represents stereotypical blink morphology was manually selected as 'template'. This template was then convolved with the entire vEOG signal, and candidate blink instances were identified via amplitude thresholding. Thereafter, temporal thresholding was used to exclude blink instances that were less than 3 s apart in order to minimize contamination from adjacent blinks. This procedure was performed separately for each dataset and participant. Datasets in which no candidate blink instances passed temporal thresholding (due to volunteers' frequent blinking) were excluded from further analyses. Blink rates were measured prior to temporal thresholding to enable behavioral evaluation. Additionally, to ensure consistency across tasks, only participants for whom data from all three tasks survived temporal thresholding were retained for further analyses. The final results were thus based on data from 23 out of the 28 participants.

Behavioral assessments were undertaken using both qualitative and quantitative measures in line with prior works (Liu et al., 2017, 2019b). Qualitative comparisons across tasks were based on grand-averaged blink waveforms, which were derived after first normalizing individual waveforms by their respective maximum amplitudes in order to minimize potential bias due to differential voltages in the raw blink signal. Quantitative assessment involved extracting morphological features corresponding to the height and width of various portions of the blink waveform. Features were derived from un-normalized, individual-level vEOG traces after averaging together all identified blink events (Fig. 2b,e), then compared at the group level using repeated-measures analysis of variance (ANOVA) to examine within-subject differences across tasks, with Bonferroni correction for post-hoc multiple comparisons.

2.6. Data epoching

Denoised continuous data were segmented into 3-s epochs according to two conditions (Liu et al., 2017, 2019b): a *blink* condition centered on the latency of maximum blink amplitude or T_0, and an analytical *control* condition corresponding to consecutive non-overlapping epochs which were pseudo-random in timing with respect to blink events (Fig. 2b). The *blink* condition was used to elucidate the BRO response, while the *control* condition helped to account for inherent brain activity in each of the three sensory environments that were not time-locked to blinking.

2.7. Effectiveness of artifact removal

To ensure complete artifact removal prior to extracting BROs, the effectiveness of the ICA-based denoising procedure was critically evaluated using both qualitative and quantitative approaches (Liu et al., 2017, 2019a, 2019b). Qualitative assessments were performed by examining individual-level, trial-averaged *blink* condition data before and after denoising to ensure the elimination of known temporal and topographical features of the ocular artifact (Fig. 2d). Quantitative assessments utilized the ocular contamination index (OCI), which measures the contribution of maximum blink amplitudes at T_0 relative to baseline levels according to the following:

$$OCI = \frac{\sum_{i=1}^{n}(y_i - \bar{y})^2}{\sum_{i=1}^{n}(x_i - \bar{x})^2}$$

where n is the number of channels, and y_i and x_i are the event-related potential signal amplitudes at 0 ms and −1000 ms latencies, respectively. Statistical comparisons were made using two-tailed, paired t-test between raw and cleaned data for each analytical condition and task.

2.8. Time domain analysis

Analyses focused on the Pz and POz electrodes chosen for their proximity to the precuneus region known to be a key source of the BRO response (Liu et al., 2017, 2019a, 2019b) (Fig. 1a and b). Data from these channels were pooled to provide information about the regional response surrounding the medial posterior parietal cortices. To derive delta-band BRO waveforms, denoised continuous data were first band-pass filtered to the 0.5–4 Hz frequency range using a zero-phase, 4th order butterworth filter, then segmented into the *blink* and *control* conditions before averaging across trials for each dataset and participant. Windows of interest were identified corresponding to the prominent temporal features of the waveform (80–170 ms and 280–420 ms for the P1 and P2 peaks, respectively). An additional interval was also selected corresponding to the pre-blink baseline (−1300 ms to −1100 ms), in line with previous studies (Liu et al., 2017, 2019b). Mean amplitudes were computed within these windows of interest at the individual level. Peak latencies were identified as the location of the most negative and positive peaks within the 80–170 ms and 280–420 ms windows, respectively. Overall effects in amplitude were assessed using an omnibus test of two-way repeated

measures analysis of variance (ANOVA), with 'time' and 'task' as within-subject factors. This was carried out separately for the *blink* and *control* conditions. Only the *blink* condition exceeded omnibus statistical threshold and was subjected to further analyses. Thereafter, blink-related changes in amplitude were assessed using one-way repeated-measures ANOVA, with 'time' as the within-subject factor. Task-related differences in both amplitude and peak latency were assessed using one-way repeated-measures ANOVA, with 'task' as the within-subject factor. Bonferroni correction was utilized for all post-hoc multiple comparisons examining both blink-related and task-related effects.

Additional analyses were conducted using Pearson correlation to examine individual-level amplitude relationships in the *blink* condition between pairs of tasks, with Bonferroni correction for multiple comparisons.

To ensure that potential differences in BRO amplitude were not due to other experimental factors, multiple regression analysis was performed to predict the response amplitudes in each task using a variety of behavioral and analytical factors, including the number of trials, the extent of OCI reduction following data denoising, and blink morphological features. All factors were examined in the *blink* condition; the *control* condition analysis only utilized the number of trials as a regression factor since the other factors were related to blinking.

2.9. Frequency domain analysis

Spectral analysis was performed using continuous wavelet transform (CWT) with Morlet function and 6 cycles in line with previous literature (Liu et al., 2017, 2019b). CWT was first computed for each channel and trial, and the log spectral power was calculated as the logarithm of the squared absolute values of the wavelet coefficients. To examine blink-related effects, baseline correction was carried out by subtracting from each trial the mean log spectral power during a pre-blink baseline interval, chosen as −1500 ms to −500 ms to be consistent with prior studies (Liu et al., 2017, 2019b). Results were trial-averaged at the individual level for each of the *blink* and *control* conditions, then averaged across participants. Analysis was undertaken separately for each of the three experimental tasks.

Statistical analysis was undertaken to evaluate both blink-related and task-related spectral changes using a nonparametric, bootstrapping approach adapted from Monte Carlo estimates in accordance with prior established procedures (Liu et al., 2017, 2019b; Maris and Oostenveld, 2007). To examine blink-related changes, a group-level T-statistic value was first computed between log spectral power in the pre-blink and post-blink intervals at each time point and frequency. The data for each frequency were then randomly permuted between the two intervals, and new T-statistic values derived. The permutation was repeated 1000 times, and a distribution of permuted T values was generated. Thereafter, the actual T statistic was compared to this distribution to determine probabilities. Results were deemed significant if $p < 0.05$. This process was carried out separately for the *blink* and *control* conditions in each task.

Task-related changes were assessed in a similar manner, but comparisons were made between whole-epoch data across pairs of tasks. The probability thresholds were also Bonferroni-corrected for task-related comparisons.

3. Results

3.1. Behavioral

Behavioral assessments showed that blink rates were comparable across tasks (Table 1). Given that blink rates are known to be a behavioral indicator of cognitive load (Bentivoglio et al., 1997; Oh et al., 2012), this suggests that the passive sensory stimulation in the visual and auditory environments did not produce significant changes in cognitive load compared to rest. Additionally, quantitative measures of blink morphology were also largely similar across tasks; only negative peak amplitude (M_4) showed lower magnitude in the visual compared to resting condition. This may be due to potential differences in blink kinematics as a result of the visual sensory environment, although more studies are needed to further investigate these effects. No other morphological differences were found in any of the tasks (Table 1).

3.2. Artifact removal

Qualitative examination of individual-level time-domain BRO signals showed that signal features consistent with ocular artifact (e.g. spike at 0 ms latency, frontally concentrated scalp topography) disappeared following the artifact rejection procedure (Fig. 2c). Quantitative assessments using OCI revealed that the ratio of maximum blink amplitude at T_0 relative to baseline levels was reduced by more than 99% following artifact removal in the *blink* condition ($p < 0.001$), indicating the dramatic reduction of blink signal contribution (Fig. 2d). On the other hand, the *control* condition OCI were close to unity both before and after artifact rejection, which was expected given that the *control* condition was pseudo-random in timing relative to blink instances, and thus did not reflect much blink-related activity. Together, these results suggest that ICA-based artifact rejection effectively removed ocular contamination due to blinking.

3.3. Temporal effects

Time-domain results showed that BRO responses were present in both visual and auditory environments, with similar morphological features compared to those during rest (Fig. 3a). In particular, the BRO waveforms exhibited an early negative peak occurring at approximately 120–130 ms latency (P1), followed by a later positive peak occurring at approximately 330 ms latency (P2). This P1-P2 complex was observed in all three tasks with narrow 95% confidence intervals across participants, indicating that the responses were highly consistent across individuals (Fig. 3a). No such morphologies were seen in the *control* condition for any task, suggesting the responses were specific to blink

Table 1

		Measure Name	Resting	Auditory	Visual	*Within-Subject* $F_{2,44}$
Behavioral Characteristics		Blink Rate (#/min)	16.65 ± 2.92	15.11 ± 2.67	14.57 ± 2.49	0.757
	M_1	Positive Peak Width (s)	0.318 ± 0.012	0.307 ± 0.012	0.297 ± 0.01	2.398
	M_2	Positive Peak Amplitude (μV)	116.47 ± 11.60	118.57 ± 12.42	115.15 ± 13.72	0.099
	M_3	Negative Peak Time (s)	0.381 ± 0.015	0.404 ± 0.018	0.380 ± 0.019	1.277
	M_4	Negative Peak Amplitude (μV)	−20.84 ± 2.31	−20.67 ± 2.75	−17.15 ± 2.03	3.763*
Response Latency	P1	Peak Latency (ms)	132.8 ± 6.7	128.7 ± 6.6	123.5 ± 7.0	1.283
	P2	Peak Latency (ms)	330.8 ± 8.8	333.5 ± 8.5	331.5 ± 8.6	0.05

Measurements of blink behavioral characteristics and the BRO peak latencies. Behavioral characteristics delineate morphological features of vEOG waveform; BRO response measures denote latencies of P1 and P2 peaks. All results were computed at the individual level and reported as mean ± SE across subjects. *$p < 0.05$ between visual and resting conditions with Bonferroni correction for post-hoc multiple comparisons.

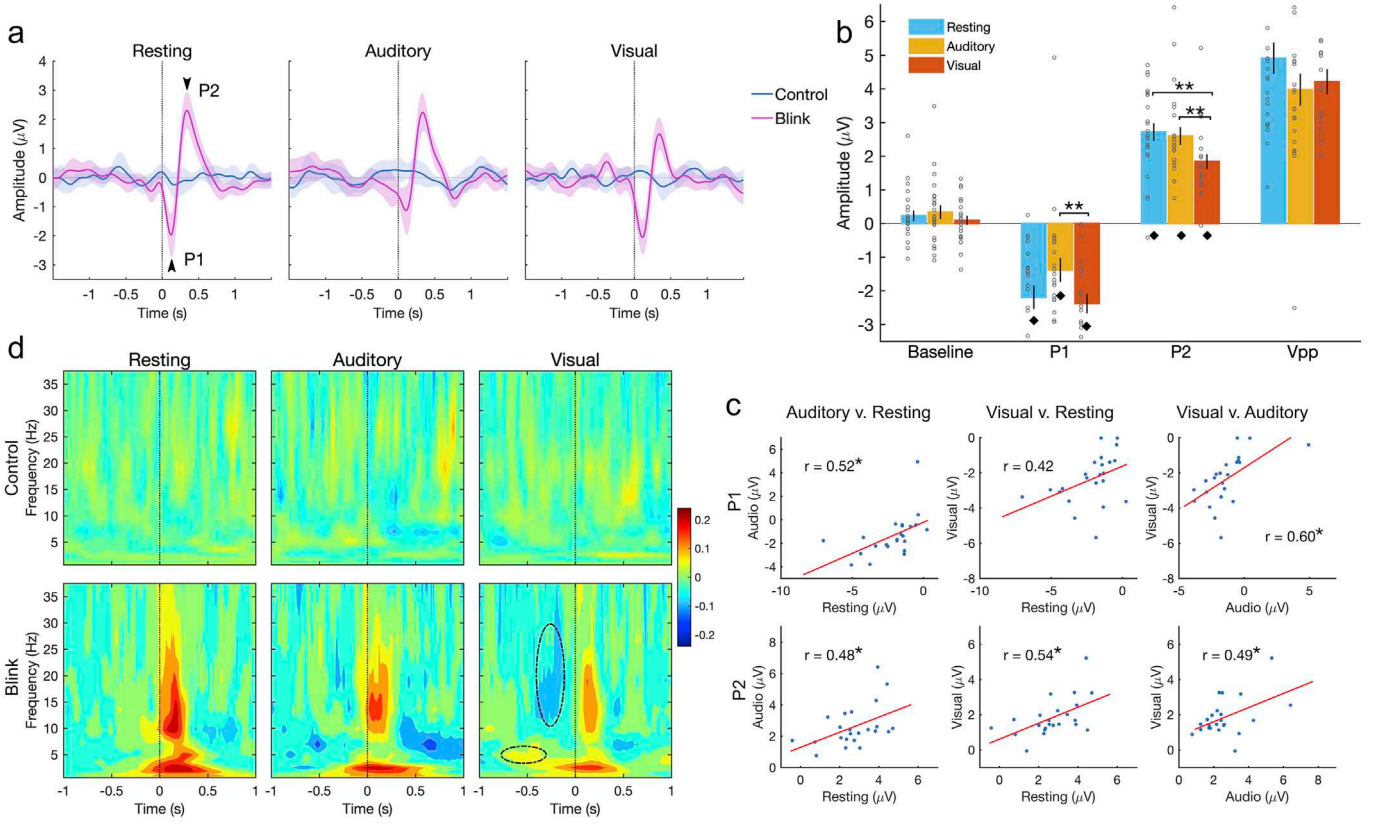

Fig. 3. Results. a) Grand-averaged time course activity in the delta (0.5–4 Hz) frequency band. BRO responses are present in all three tasks with similar morphological features (P1-P2 complex), which are only observed in the *blink* condition. Shading denotes 95% confidence intervals across participants. b) Amplitudes of the P1-P2 complex in the *blink* condition only, presented as mean ± SE across subjects and overlaid with scatter plot of individual subject amplitudes. Vpp denotes peak-to-peak voltage. ◆$p < 0.001$ compared to baseline; **$p < 0.05$ as indicated. c) Scatter plots of individual-level peak amplitudes across task pairs, with least squares regression line and associated correlation coefficients overlaid. *$p < 0.025$ d) Time evolution of spectral content. Blink-induced spectral features are observable in the *blink* condition across all tasks, and are absent in *control*. Visual task leads to decreased beta (12–30 Hz) and increased theta (4–7 Hz) power immediately before blink onset (black ellipses, $p < 0.05$ compared to resting). Color bar denotes log power values.

instances and were not due to background brain activity. Additionally, the *control* condition waveforms were relatively flat across all three tasks, indicating that the BRO-related signal features were not a consequence of differences in the perceptual environments across the visual and auditory task states.

Comparison of response amplitudes across tasks revealed that the P1-P2 complexes in all three tasks were statistically significant compared to the pre-blink baseline, indicating that changing sensory stimulation in the environment did not obscure blink-related processing effects (Fig. 3b). Additionally, response latencies were not different between tasks (Table 1), suggesting that blink-related processing speed was not impacted by changes in the external sensory environment. However, visual stimulation did reduce P2 amplitude compared to the other two conditions, while auditory stimulation only reduced P1 amplitude compared to the visual condition (Fig. 3b). These results suggest that the visual and auditory stimulation environments differentially modified various components of the P1-P2 complex, such that only visual stimulation led to reduced BRO amplitude for either peak compared to rest. Nonetheless, the peak-to-peak amplitude was not significantly different across any of the tasks (Vpp, Fig. 3b), indicating that the overall dynamics of the P1-P2 complex were not impacted by differences in passive external sensory loading.

To further compare individual-level differences between modalities, Pearson correlation was performed between the various task pairs. Both P1 and P2 amplitude measures were found to be significantly correlated across most task pairs at the individual level (Fig. 3c), suggesting that the observed task-related amplitude differences were likely due to systematic shifts between the visual, auditory, and resting conditions. The only exception was P1, which was not different in amplitude between the visual and resting conditions, nor correlated at the individual level. This suggest that the P1 response feature did not reflect any task-related differences between resting and visual conditions.

3.4. Spectral effects

Time-frequency analysis revealed that blinking during both visual and auditory stimulation led to post-blink spectral changes consistent with those during rest, with spectral features comprising an early momentary increase in beta/gamma (12–40 Hz) band power occurring during the first ~300 ms latency, followed by later and more prolonged reduction in theta (4–8 Hz) and alpha (8–12 Hz) band power (Fig. 3d). There was also a prolonged delta band power increase observed in all three tasks. These characteristics are in agreement with previously reported spectral features for this response (Liu et al., 2017, 2019a, 2019b), and suggest that passive external visual and auditory stimulation did not obscure BRO effects in the spectral domain. Crucially, none of these spectral features were present in the *control* condition, indicating they were due to blink events and were not caused by background brain activity. Moreover, the *control* condition did not exhibit spectral features that were significantly different between the *pre*-0ms and *post*-0ms intervals for any of the tasks, and were also not significantly different between tasks. This suggests that the observed spectral effects in the *blink* condition were not induced by differences in the sensory and perceptual environments across task states.

In additional to confirming the presence of BRO responses under different sensory environments, our findings also showed that ongoing external visual stimulation also modulated BRO responses compared to rest, especially during the pre-blink interval. In particular, blinking in the visual environment produced an earlier theta-band ERS occurring during the −750 ms to −300 ms interval prior to blink onset, followed by a beta-band ERD occurring during the −400 ms to −100 ms interval ($p < 0.05$, Fig. 3d). Although the auditory condition also showed some apparent spectral differences compared to rest (i.e. pre-blink theta-band ERD occurring at approximately −500 ms latency, greater theta/alpha ERD occurring at approximately 500–600 ms latency), these differences were not statistically significant.

4. Discussion

This study investigated BRO responses during passive auditory and visual stimulation to determine BRO effects across different sensory environments. Whereas previous studies only examined BRO responses without dynamic external sensory input, our findings now demonstrate that BRO responses are also present during ongoing auditory and visual stimulation. Moreover, BROs are also differentially modulated between the auditory and visual environments, further confirming the active processing of blink-related information across multiple sensory conditions.

We examined BROs by extracting neural responses following spontaneous blink events while participants underwent ongoing external passive stimulation in either visual-only or auditory-only paradigms compared to silent resting fixation. Our analysis focused on the Pz and POz electrodes with close proximity to the precuneus region, which is known to be a key cortical source of BRO processes and is also crucial to consciousness and cognition (Boly et al., 2013; Cavanna and Trimble, 2006; Liu et al., 2017, 2019a, 2019b).

Our results showed that BRO responses were present across all three tasks, with similar post-blink morphological features in both time and frequency domains. These features included a P1-P2 complex in the time-domain waveform (Fig. 3a), as well as event-related spectral changes comprising an early beta/gamma ERS followed by a later theta/alpha ERD, along with an early and more prolonged delta ERS (Fig. 3d). These effects are in agreement with previous studies examining BRO responses without sensory inputs (Bonfiglio et al., 2013, 2011; Liu et al., 2017, 2019a, 2019b), with the spectral effects having been postulated to represent early visual sensory processing (beta/gamma ERS), followed by later information processing (alpha ERD) and episodic memory-related responses (theta ERD) (Liu et al., 2017, 2019b). The delta ERS following blinking is believed to represent long-range cortical communication processes (He and Raichle, 2009; Liu et al., 2019b). Importantly, BRO response characteristics were highly robust across individuals with narrow 95% confidence intervals (Fig. 3a). These characteristics were not observed in the analytical *control* condition designed to measure background brain activity within each participant and task, further confirming that the effects were not due to any inherent brain activations or to differences in perceptual processing across sensory environments (Fig. 3a,d).

BROs are thought to index environmental monitoring and awareness processes occurring with each blink, as the brain evaluates new information after the eyes re-open (Bonfiglio et al., 2013, 2014; Liu et al., 2017, 2019a, 2019b). The presence of consistent BRO features across all three tasks confirmed our hypothesis that BRO responses would be observable across different environments with dynamic sensory inputs, providing further evidence that BROs represent neural responses associated with blink-related environmental and information processing. Moreover, our results also demonstrated the differential modulation of BRO responses across the visual and auditory environments, with visual stimulation leading to reduced P2 amplitude compared to both auditory and resting conditions, but without impacting the overall dynamics of the P1-P2 complex (Fig. 3a,b). Since BROs are believed to represent processing of blink-related *visual* information, the simultaneous presence of external visual stimulation would be expected to create competing sensory demands relative to blinking. As such, the decreased amplitudes of BRO responses in the visual stimulation environment are consistent with reduced availability of neuronal resources for processing blink-related information when the brain was already engaged in an ongoing visual task. This was not the case in the auditory condition, as ongoing auditory stimuli did not present competing sensory requirements for processing blink-related visual information. However, the reduction of P1 amplitude in the auditory modality compared to visual suggests potential differences in sensory processing of blink-related information when under an external auditory environment. Nonetheless, the lack of task-related differences in peak-to-peak amplitude suggests that the overall dynamics of the P1-P2 complex were not significantly impacted by differences in external sensory loading.

In addition to validating the presence of blink-related spectral features in multiple sensory environments, our findings also revealed important differences which suggest that the brain dynamically modulates its blink-related processes *in anticipation of* upcoming blink events when there are competing sensory requirements. In particular, our results showed that visual, but not auditory, stimulation led to significant pre-blink spectral changes compared to rest, comprising an earlier theta ERS followed by a beta ERD, both preceding blink onset (Fig. 3d). Interestingly, the pre-blink theta ERS is consistent with pre-stimulus effects in viewing of visual stimuli that are later successfully recalled in episodic memory as part of the subsequent memory effect (Addante et al., 2011). Our results therefore suggest that the brain may be making additional efforts to "study" the visual environment in anticipation of the upcoming blink-induced blackout, such that the current surroundings may be recalled later for comparison with new environmental information after the blink. This interpretation is also in line with the previously postulated mechanism for blink processing that involves episodic memory responses in comparing the new image with the previous image stored in memory (Bonfiglio et al., 2014; Liu et al., 2017, 2019b). Similarly, since post-blink beta/gamma ERS is associated with processing of blink-related visual information, the beta ERD prior to blink onset suggests that the brain may be suppressing ongoing visual processes in preparation for evaluating incoming blink-related visual information.

The fact that pre-blink spectral changes were only observed in the visual condition suggests that the recruitment of these additional environmental encoding processes are dependent on underlying sensory loading requirements. For instance, when blinking occurs during rest, there are ample neuronal resources for processing blink-related information without invoking additional cortical processes. Similarly, when blinking occurs during auditory stimulation, the ongoing auditory stimuli and the incoming visual information are processed separately without much adaptation. However, when blinking occurs during visual stimulation, the competing sensory loading between the ongoing visual input and the incoming blink-related visual information results in conflicting processing requirements which necessitate dynamic adaption. Nonetheless, this adaptation for blink-related environmental encoding seems to occur in response to competing sensory processing rather than cognitive loading conditions, as a previous study in our group examined BROs under cognitive loading conditions without extraneous sensory stimuli, and no pre-blink spectral differences were found relative to rest (Liu et al., 2019b). In contrast, the current study employed sensory stimulation paradigms that were closely mirrored between the auditory and visual modalities while maintaining similar levels of overall cognitive loading between the two modalities, but results revealed pre-blink spectral differences in the visual modality only.

The idea that BROs represent a neural process by which the brain actively monitors the environment following blink-induced blackouts is intriguing and somewhat surprising given that blinking has traditionally not been associated with neurocognitive processing. Nonetheless, given that this response exhibits its most prominent features long *after* blinking

has ended and does not have much temporal overlap with other known processes (Fig. 1a), it is likely that blinking also induces other, more prolonged responses in the brain. Evidence for the cognitive implications of blink-related processing has been reported in prior studies showing that BROs strongly activate the precuneus cortical region which is crucial to brain health (Cavanna and Trimble, 2006; Liu et al., 2017), with precuneus roles including environmental monitoring and awareness (Cavanna and Trimble, 2006; Kjaer et al., 2001; Liu et al., 2017, 2019b), supporting consciousness (Boly et al., 2013; Laureys et al., 1999, 2004; Vanhaudenhuyse et al., 2010; Voss et al., 2006), and serving as a key hub within the default mode network (Gusnard and Raichle, 2001; Hagmann et al., 2008). The BRO-induced activation of the precuneus has been postulated to represent environmental monitoring processes occurring with each blink, as the brain examines new visual images that appear following eye re-opening (Bonfiglio et al., 2013, 2014; Liu et al., 2017, 2019b, Raichle et al., 2001). Moreover, this interpretation has also been supported by studies showing that BROs also engage other cortical areas including the occipital, fusiform, and lingual regions involved in assessment of visual sensory information (Bar et al., 2001; Liu et al., 2019b; Machielsen et al., 2000), along with the parahippocampal gyri involved in processing of environmental contexts and associative episodic memory (Aminoff et al., 2013; Liu et al., 2019b). Its spectral characteristics are consistent with visual sensory processing, episodic memory, and information processing effects (Liu et al., 2019b). In fact, when blinking occurs while the brain is already engaged in a challenging cognitive task that involves many of the same cortical areas, the BRO response has also been shown to recruit additional brain regions that subserve attentional mechanisms for detecting unexpected but salient objects or events (Liu et al., 2019b). It is as though the brain attempts to compensate for the decreased availability of neural resources when required to process blink-related information during cognitively demanding tasks (Liu et al., 2019b).

Most importantly, the current study provides compelling new evidence that these blink-related processes are dynamically modulated not only to accommodate internal cognitive loading demands, but also to address specific sensory processing requirements as a result of differences in external environment. Indeed, when blinking occurs during ongoing visual stimulation, the conflicting sensory requirements are managed even prior to blink onset by dynamically adjusting internal neurocognitive mechanisms *in anticipation* of the upcoming blink-related information processing. Finally, these mechanisms of blink-related environmental monitoring may have conferred evolutionary advantages by enabling environmental scanning for threat detection following momentary vision loss induced by blinking, and may also be related to vigilance in animals as studies have reported a relationship between blink behavior and the level of anti-predator vigilance in wild primates (Beauchamp, 2015; Matsumoto-Oda et al., 2018).

Although the current study employed auditory and visual experimental paradigms that did not require active responses from the participants besides listening to or visually fixating on the external stimuli being presented, it should be noted that these paradigms were not entirely *passive*. The stimulation was expected to elicit internal neural processes within the participants; indeed, previous research using the same paradigms have shown that these stimuli elicit numerous event-related potential (ERP) brain responses spanning the sensory (N100 ERP), attentional (P300 ERP), and language processing (N400 ERP) domains in both auditory (Ghosh Hajra et al., 2018a, 2018b, 2016) and visual modalities (Pawlowski et al., 2019). To ensure that the blink-induced BRO responses were distinct from those elicited by the external stimuli in the current study, further analyses were conducted to evaluate the timing of external stimulation relative to blinking in the visual and auditory tasks. Results showed that there was no consistent timing between stimulation and spontaneous blinks; blinking occurred throughout the recording sessions, and blink timing was not related to stimulus onsets (Supplementary Materials Figure S1). These results indicate that blinking was not time-locked to or induced by external stimulation, and the observed differences in BRO effects were not caused by the external stimuli themselves, but rather due to the modulation of endogenous blink processing by changes in the external sensory environment.

Our findings on the visual modulation of blink processing in particular are also in line with a previous study using functional magnetic resonance imaging (fMRI) to examine cortical effects when participants blinked spontaneously while viewing videos (Nakano et al., 2013). In that study, the authors reported increased activation of the precuneus along with other regions of the default mode network which is engaged in the absence of attention-demanding tasks (Raichle et al., 2001), with concomitant reduction in regions of the dorsal attention network which is involved in top-down control of attention (Corbetta and Shulman, 2002). The authors concluded that spontaneous blinking must be involved in mediating attentional disengagement during the processing of dynamic external visual inputs (Nakano et al., 2013). These prior findings help to reinforce our observations in the current study that dynamic external visual input actively modulates neural processes related to spontaneous blinking. Moreover, the blink-related precuneus activation reported by Nakano et al. also provides important support for the involvement of the precuneus in blink processing, as these effects have now been reported across numerous complementary modalities including MEG, EEG, and fMRI (Bonfiglio et al., 2013, 2014, 2011; Liu et al., 2017, 2019a, 2019b).

5. Conclusion

This is the first study to investigate BRO responses under external visual and auditory sensory stimulation, and our results showed that the brain dynamically modulates blink-related processing to accommodate differences in external sensory environment, particularly when under competing sensory processing requirements. Our findings support the hypothesis that blink-related processing represents monitoring of environmental information before and after spontaneous blinking, and significantly advance our understanding of brain function.

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Declaration of competing interest

The authors have no competing interests to declare.

CRediT authorship contribution statement

Careesa C. Liu: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization, Funding acquisition, Writing - review & editing. **Sujoy Ghosh Hajra:** Conceptualization, Methodology, Investigation, Writing - review & editing. **Gabriela Pawlowski:** Investigation, Writing - review & editing. **Shaun D. Fickling:** Investigation, Writing - review & editing. **Xiaowei Song:** Supervision, Project administration, Funding acquisition, Writing - review & editing. **Ryan C.N. D'Arcy:** Supervision, Project administration, Funding acquisition, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2020.116879.

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