Received: 24 July 2023 | Revised: 11 February 2024 | Accepted: 12 February 2024

DOI: 10.1111/psyp.14550

PSYCHOPHYSIOLOGY SPR WILEY

ORIGINAL ARTICLE

Correlated P300b and phasic pupil-dilation responses to motivationally significant stimuli

Danilo Menicucci[1] | **Silvia Animali**[1] | **Eleonora Malloggi**[2] | **Angelo Gemignani**[1] | **Enrica Bonanni**[3] | **Francesco Fornai**[2] | **Filippo Sean Giorgi**[2] | **Paola Binda**[2]

[1]Department of Surgical, Medical and Molecular Pathology and Critical Care Medicine, University of Pisa, Pisa, Italy

[2]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

[3]Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

Correspondence
Paola Binda, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy.
Email: paola.binda@unipi.it

Funding information
Italian Ministry of University and Research, Grant/Award Number: program FARE-2 - grant SMILY and program PRIN2017 - grant MISMATCH; European Union's Horizon 2020, Grant/Award Number: grant n. 801715 (PUPILTRAITS)

Abstract

Motivationally significant events like oddball stimuli elicit both a characteristic event-related potential (ERPs) known as P300 and a set of autonomic responses including a phasic pupil dilation. Although co-occurring, P300 and pupil-dilation responses to oddball events have been repeatedly found to be uncorrelated, suggesting separate origins. We re-examined their relationship in the context of a three-stimulus version of the auditory oddball task, independently manipulating the frequency (rare vs. repeated) and motivational significance (relevance for the participant's task) of the stimuli. We used independent component analysis to derive a P300b component from EEG traces and linear modeling to separate a stimulus-related pupil-dilation response from a potentially confounding action-related response. These steps revealed that, once the complexity of ERP and pupil-dilation responses to oddball targets is accounted for, the amplitude of phasic pupil dilations and P300b are tightly and positively correlated (across participants: $r = .69$ $p = .002$), supporting their coordinated generation.

KEYWORDS

attention, independent component analysis of ERPs, linear modeling of pupil responses, locus coeruleus, oddball, p300, pupil dilation

1 | INTRODUCTION

Unexpected and motivationally significant events evoke a stereotypical complex of physiological responses, which involve the central and the autonomic nervous systems.

The central component of the response has been thoroughly studied with electroencephalography (EEG), where it emerges as a positive late deflection of event-related potentials (ERP) termed P300 (Sutton et al., 1965). This is accompanied by a coordinated orienting response, presumably aimed at turning processing resources toward salient and/or behaviorally relevant stimuli; it includes an autonomic component consisting of variations of the heart and respiratory rate, skin conductance, and a phasic pupil dilation (Lynn, 1966). All these responses have similar antecedent conditions: failure of expectations (an unexpected stimulus occurs or an expected one does not) and motivational significance (the stimulus is task-relevant or it has intrinsic valence, e.g., fearfulness), with little impact

of the sensory properties of the stimulus (e.g., auditory and visual stimuli elicit similar P300 and pupil dilation responses). These conditions are recapitulated in the laboratory with the oddball paradigm (Comerchero & Polich, 1999), which has been repeatedly used to reveal a concomitant P300 and autonomic response, the latter often indexed through pupil dilation.

There is a long-standing interest in establishing whether the co-occurrence of these central and autonomic responses is explained by shared neural generators. Addressing this question is challenging because both the P300 and the autonomic response are probably linked with large multi-component circuits, still incompletely characterized. Based on the critical review of a vast literature, Nieuwenhuis et al. (2005) introduced the idea that the locus coeruleus (LC) plays a pivotal role in the coordination of these responses, both linked with the outcome of an internal decision-making process. The LC is a small nucleus of the pons with a critical role in neuromodulation, it being the main source of norepinephrine (NE) for the entire brain. By measuring LC activity, multiple experiments revealed a phasic response under much the same conditions that elicit P300 and pupil-dilation responses. Consideration of the pattern of LC connectivity with the brain cortex, and of the effects of NE release on cortical responses, led to the notion that LC phasic activation could trigger the P300 component, which in turn might index the mobilization of cortical processing responses to prepare an appropriate behavioral response (Aston-Jones & Cohen, 2005). Recent evidence supported this position showing that optogenetic activation of the LC elicits a wave of activity across the brain cortex, compatible for latency and distribution with the P300 (Vazey et al., 2018).

By assigning a critical role to the LC for P300 generation, this theory naturally generated a hypothesis that may account for the co-occurrence of P300 and autonomic responses, based on the close connections between the LC and the subcortical nuclei that orchestrate activity of the sympathetic system (Nieuwenhuis et al., 2011). This is receiving increasing support from experiments showing a link between phasic pupil dilations and LC activations, both in animal models (Joshi et al., 2016; Reimer et al., 2016) and humans (de Gee et al., 2017; Murphy et al., 2014)—although the relation is weak (Megemont et al., 2022), it may be easily confounded by the many other determinants of pupil size, which include light, even just perceived or imaged (Binda & Murray, 2015; Mathot, 2018), and it may be obscured by the activation of other subcortical areas that also influence pupil diameter (Joshi & Gold, 2020).

While there is no question that the antecedent conditions leading up to the P300 and pupil-dilation responses coincide, there is surprising little evidence that the amplitudes of these responses correlate—across or within individuals. Since the 2011 review paper, several experiments have addressed this issue. To our knowledge, there is only one recent study reporting correlated P300 and pupil dilation responses in the context of a Stroop paradigm (Chang et al., 2023). However, all previous studies using the oddball paradigm failed to detect a significant association between the phasic pupil-dilation response elicited by an oddball stimulus and the amplitude of the P300 (Hong et al., 2014; Kamp & Donchin, 2015; LoTemplio et al., 2021; Murphy et al., 2011). The same applies to more subtle manipulations of subjective probability, which also yielded uncorrelated P300 and phasic pupil dilations (de Gee et al., 2021).

One way to interpret this lack of correlation is by assuming that P300 and autonomic (pupil dilation) responses index separate phenomena, which would run against the unifying attempt of the P3-LC theory. For example, a classic theory interprets the P300 as an index of context-updating, that is, a process of revising one's cognitive scheme of the task settings (Donchin & Coles, 1988; Polich, 2007). As a purely cognitive process, this is harder to relate to sympathetic activity, which is tightly linked with action preparation as in "fight or flight." In this view, the P300 and autonomic responses may be fundamentally distinct processes, of cognitive and motor nature, that merely happen to be elicited under similar conditions.

An alternative possibility is that P300 and pupil-dilation responses really are coordinated, perhaps through LC activation, and their correlation is often missed due to independent factors and noise sources affecting the two responses. In the present study, we tested this concept, re-evaluating the correlation between pupil dilation and P300 responses in the oddball paradigm, after discounting the effect of two potentially confounding factors, presented next.

We started by considering the notion that the P300 is a composite response, as it may be elicited by two categories of stimuli: with or without behavioral relevance. Stimuli with motivational significance, like any stimulus that requires a behavioral response, typically elicit the P300b characterized by centro-posterior scalp distribution. In contrast, unexpected salient stimuli that do not require action are typically related with the P300a, which has shorter latency, more frontal distribution, and rapid habituation. Thus, the typical oddball stimulus that is both rare (unexpected) and task-relevant (motivationally significant), generates a complex P300 encompassing multiple independent components, only one of which (P300b) may be related to the preparation of a behavioral response (Nieuwenhuis et al., 2005)—but note that the interpretation of the P300b is also debated

(Donchin & Coles, 1988; Polich, 2007; Verleger, 2020). If the autonomic component of the orienting response is an expression of this behavioral preparation process, it follows that autonomic responses like pupil dilations should be selectively associated with the P300b component; if the ERP waveform includes other components, like the P300a, these could obscure the association with pupil dilations. To test this hypothesis, we aimed to isolate the P300b component from oddball ERPs. To this end, we employed a three-stimulus oddball paradigm that dissociates stimulus frequency from task relevance (Comerchero & Polich, 1999) by testing responses to two rare events: a distracter and a target stimulus, only the latter requiring a behavioral response. Combined with independent component analysis (Makeig, Debener, et al., 2004; Makeig, Delorme, et al., 2004; Onton et al., 2006), this allowed us to isolate a P300b component, selectively related to task-relevant stimuli and separated from other components including a P300a response.

The second element we considered is that pupil dilation responses are likely to be composite too. Given the slow dynamics of pupil-size variations, the pupil diameter observed at any one time-point is inevitably affected by a multitude of factors. Besides visual factors (which we controlled by using an auditory oddball task so that visual stimulation remained always constant throughout the experiments), pupil diameter is also systematically affected by the execution of actions, including manual responses like keypresses (Einhauser et al., 2010; Hupe et al., 2009). In the context of our paradigm, this implies that an oddball stimulus might elicit pupil dilation not only because of its task relevance, but also following the keypress that it prompts. This action-related component is likely to be completely independent of the processing of the stimulus, merely reflecting its final motor outcome. For example, it may scale with the range of the motor act or the strength it requires (Voudouris et al., 2023), which are clearly unrelated to stimulus processing. The presence of this action-related dilation could therefore obscure the relation between the stimulus-related pupil dilations and the P300b component. To test this hypothesis, we aimed to break down the pupil-dilation response to our oddball stimuli into a stimulus- and an action-related component, which we achieved through linear modeling of the pupil traces (Denison et al., 2020).

To summarize, the general aim of our study was to provide evidence in support of a coordinated central and autonomic response to motivationally significant stimuli. We approached this by re-evaluating the correlation between P300b and pupil-dilation responses to motivationally salient events (presented in the auditory modality), after discounting the effect of stimulus- and action-related variables that could act as confounds.

2 | MATERIALS AND METHODS

2.1 | Participants

We recruited 26 young adults (14 cisgender males and 12 cisgender females; age range: 21–29). Eight participants were excluded due to a clear deterioration of the EEG signal-to-noise ratio over the course of the experiment. As a result, the analyzed dataset included 18 participants (10 males, and 8 females, all cisgender, age range: 21–29). This numerosity is within the range of previous studies that tested the relationship between P300b and pupil dilation responses and failed to reveal a correlation (de Gee et al., 2021; Hong et al., 2014; Kamp & Donchin, 2015; LoTemplio et al., 2021; Murphy et al., 2011).

Participants gave written informed consent to their participation in the study, which was conducted according to a protocol approved by the local medical ethics committee (Comitato Bioetico dell'Università di Pisa, Prot: 0062475/2019). Upon recruitment, they were administered a general health and drug questionnaire, and the Symptom Checklist 90—Revised (SCL-90-R) (Sarno et al., 2011), through which we excluded psychopathological conditions. We also checked that no participant suffered from any neurological disorder (self-reported).

2.2 | Experimental protocol

The experiment was performed in a dark and quiet room. Participants sat in front of a computer monitor (Acer V206HQL) placed at 53 cm from their eyes, with their head stabilized with a chin rest. They were instructed to minimize body and head movements and to maintain their gaze on a fixation target (0.5 deg red dot) presented over a homogeneous gray background (24 cd/m^2). Auditory stimuli for the oddball task were 60 ms long sinusoidal tones of one of three frequencies: 1940 Hz (standards), 2000 Hz (targets), and 500 Hz (distracters). The very close frequencies of targets and standards created the conditions for an evaluation under uncertainty. Interstimulus intervals varied randomly between 1.1 and 1.9 sec. Target and distractors were interspersed pseudo-randomly among standards, each representing approximately 10% of the 500 trials (365 standards, 66 distractors, and 69 targets). Stimuli were delivered through the Psychophysics toolbox (Brainard, 1997), housed in a MacBook Pro computer

running macOS Mojave (version 10.14.2) and presented through two speakers (CREATIVE SBS250, Creative Technology Ltd.) placed bilaterally at 50 cm from the participant. Participants were instructed to respond to target tones with a right-index finger mouse click as fast and accurately as possible, while ignoring the presentation of the distracters and standards. All participants used their right (dominant) hand; the lack of counterbalancing of the hand across participants represents a methodological limitation of the present study. Before the experiment, participants completed a practice run with about 40 trials. These were followed by the 500 trials of the experiment, which lasted approximately 12 min.

2.3 | Quantification of behavioral performance

Behavioral performance was recorded in terms of correct responses (keypresses made after a target stimulus and before the following stimulus occurred) and reaction times (measured as delay of keypresses from the target stimulus presentation). Reaction times were indexed by taking their median across correct responses. The proportion of correct and incorrect responses was transformed using signal detection theory into d-prime (sensitivity) and criterion (liberal/conservative criterion), according to the following definitions: d-prime = H − F and criterion = −1/2(H + F), where H = hits (keypresses made after a target stimulus) and FA = False alarms (keypresses made after a standard or distracter stimulus). We used the log-linear approach (Hautus, 1995) to correct for the biasing effect of extremely high or low proportions (e.g., H = 1 or FA = 0). The main advantage of using d-prime over percent correct is that it generally allows for assuming a normal distribution, permitting the use of parametric tests.

2.4 | Electrophysiological and pupil recording

EEG signals were collected along with electro-oculograms (EOG) and cardiac activity (EKG). For the EEG, a 64-electrode 10–20 system cap (EB-Neuro, IT) was used with the reference electrode placed between AFz and Fz electrodes; during recordings, the electrode impedance was below 10 KΩ. For EOG, disposable electrodes were placed at 1 cm distance from the outer canthus of each eye and above and underneath the right eye. For EKG, disposable electrodes were applied underneath each collarbone. All signals were acquired with the same polygraph (BE Plus LTM–EB Neuro, IT, with lowpass limit of 0.001 Hz), thus using the same ground, and recorded at 256 Hz using GALILEO software (EB-Neuro, IT). At the same time, continuous pupil-diameter variations were recorded monocularly at 1000 Hz through a remote video-based eye-tracking system (Eyelink1000 Plus, SR Research), with the infra-red camera positioned below the monitor screen. Pupil diameter measures were transformed from pixels to millimeters after calibrating the tracker with an artificial 4 mm pupil, positioned at the location of each participant's left eye. The two systems recorded signals continuously and in parallel; they both received a digital signal from the stimulus delivery computer that was used to synchronize the recordings.

2.5 | EEG data preprocessing and analyses

EEG pre-processing and analyses were performed with the EEGLAB toolbox (Delorme & Makeig, 2004) and custom MATLAB 2022a scripts. Recordings were band-pass filtered (band pass: 0.5–45 Hz, band stop: 0.1–45.5 Hz, two-way least-squares FIR filtering) and visually inspected by expert examiners (EM and DM) to reject segments affected by artifacts such as swallowing, electrode or subject movements, or other sources of noise. Visual inspection was supported by the artifact subspace reconstruction (ASR) method, as implemented in EEGLAB. The ARS indicates signal bursts related to movement or muscular artifacts, as well as temporary declines in signal quality related to instability or loss of contact with the skull, based on sudden increases in RMS and changes in signal statistics. After confirmatory visual inspection, we permanently discarded these EEG epochs. Although partly subjective, the visual inspection and removal of small signal fractions containing occasional (rare) and strong artifacts remains an important step to avoid polarization effects, which could bias the convergence of the independent component analysis (described next). In addition, individual channels showing quality decline (due to instability or loss of contact with the scalp during recordings) were visually identified and replaced with signals obtained via spline-interpolation (Fletcher et al., 1996).

Retained EEG signals were re-referenced to the average potential of the two mastoids and, along with concurrent EOG e EKG, they were segmented into 900 ms long epochs (henceforth "trials"), from 100 ms before to 800 after each stimulus onset. In order to eliminate residual eye movement artifacts, we further discarded all trials where frontal channels (AFz, AF3, AF4, AF7, AF8, Fpz, Fp1, and Fp2) signals exceeded the 50 μV range, a stricter criterion compared to previous work (Menicucci et al., 2014).

As a result of these pre-processing step, the median number of included trials (and interquartile range across participants) were 246 (63), 39 (16), and 51 (17) for standard, distracter, and target stimuli, respectively.

2.6 | Event-related potentials analyses

Trials were baseline corrected by subtracting the average in the pre-stimulus interval (from 100 to 0 ms before stimulus onset).

As a first quantification of the P300 amplitude, we averaged ERPs across trials of the same type, measuring responses to oddball target and distracter stimuli and to the repeating standard stimulus. We selected ERPs from the Pz electrode (where the responses to target stimuli typically exhibit the highest voltage) and took its maximum in the time window from 250 to 500 ms post-stimulus onset, where the P300 is typically reported (Polich, 2007; van Dinteren et al., 2014).

Next, we submitted ERPs (concatenated across participants and stimulus types) to a group-level independent component analysis (ICA)-based decomposition (Himberg et al., 2004; Menicucci et al., 2014; Sebastiani et al., 2015) using the Infomax algorithm (Bell & Sejnowski, 1995; Makeig, Debener, et al., 2004). This models ERPs as the sum of temporally independent components arising from distinct brain processes, shared among subjects. The inclusion of EKG and EOG signals facilitates the ICA-based decomposition, by separating any residual and small artifact into specific components. The ICA was set to identify five independent components; by taking the trimmed average of each component timecourse over the relevant trials (excluding the 5% most extreme observations), we derived the component activity template for each stimulus type and participant. Visual examination of the resulting components identified one that had the spatial distribution, temporal dynamic, and antecedent conditions characteristics of the P300b: a late deflection preferentially evoked by oddball-target stimuli with a posterior localization. We dubbed this component P300b and focused further analyses on its amplitude, which we computed as the absolute peak of the component timecourse.

2.7 | Pupil data analyses

Pupil data were analyzed with custom MATLAB scripts (MATLAB_2019a). Timepoints with unrealistically small pupil size (<0.1 mm) or with unrealistically fast pupil changes (>2 mm/s) were eliminated; data were then down-sampled at 20 Hz to attenuate high-frequency variations (non-physiological noise). Pupil traces were parsed into 1500 ms long epochs (henceforth "trials") from 0 to 1500 ms following the onset of each stimulus. Each was baseline corrected by subtracting the average pupil diameter between −100 and +100 ms from stimulus onset. Baseline correction is a crucial step to highlight the pupil deflections that consistently followed stimulus presentation, attenuating the low-frequency variations that occur across trials. Pupil traces were finally averaged across trials of the same type, yielding the pupil-dilation responses to the three stimulus types: oddball target and distracter and standard stimuli.

As a first estimate of the pupil response magnitude, we took the maximum of this pupil-dilation responses (per stimulus type and per participant).

Next, we applied a linear model to the average pupil-dilation responses, concatenated across stimulus types so as to fit them simultaneously. We assumed that pupil dilations mainly result from the combination of two processes: one related to the stimulus and one related to the keypress actions. Each was modeled by convolving a predictor representing the temporal distribution of stimuli or keypresses with a canonical impulse response function (IRF). All predictors were histograms representing the distribution of events across the trials from which the average pupil traces were extracted (at the individual trial level, each event was represented as a Dirac function). Following previous work (Hoeks & Levelt, 1993), we modeled the IRF with an Erlang gamma function:

$$\mathrm{IRF}(t) = t^n \, e^{\frac{-nt}{tmax}}$$

This has two parameters: n controls the shape of the function, and it was set to 10.1 following (Denison et al., 2020); *tmax* controls the temporal scale of the function, and it coincides with its time-to-peak, which we varied to fit the individual participants' responses. We chose this approach (Denison et al., 2020), instead of a more powerful alternative (Burlingham et al., 2022), because it allowed us to explicitly separate the two components of interest, action- and stimulus-related, and ultimately assess the correlation between the stimulus-related component of the pupil dilation and the P300b response.

For each participant, we chose the IRF *tmax* that optimized the match between predicted and observed traces (measured as the percent of explained variance) across time and across stimulus types. We used the best-fitting impulse-response function to estimate the beta-weights assigned to each predictor, which quantifies the magnitude of each component (stimulus and keypress related) of the observed pupil-dilation response. Note that this beta-weight summarizes the amplitude of the entire waveform of the related component, waiving the need for

extracting a single value (e.g., the peak) or an average over an arbitrary temporal window.

2.8 | Statistical analysis

Statistical analyses were performed in MATLAB (MATLAB_R2019a). We used parametric tests (ANOVAs or Pearson's correlations) after confirming that all analyzed variables were normally distributed (Lilliefors test) or that the correlating variables conformed to pairwise normality (Shapiro test). When the latter assumption failed, we quantified correlations using the Spearman's rank coefficient. We focused on correlations across participants, to maximize the signal-to-noise ratio afforded by the limited number of trials available.

One-way ANOVAs were used to test for a significant effect of stimulus type over the variable of interest (indexing the P300 or pupil-dilation responses), applying the Greenhouse–Geisser correction when the sphericity assumption was rejected based on Mauchly's test. ANOVAs were followed up with a *t*-test comparing responses to the two infrequent stimuli: distracter and target; these tested the hypothesis that the target response would be larger than the distracter one, as expected for the P300b.

Correlations were mainly used to test the association between our indices of P300 and pupil-dilation responses, which we expected to covary – implying that participants with a larger P300 would also show a larger pupil dilation. In addition, we ran exploratory correlation analyses between each of these indices and summary indices of behavioral performance (d-prime and median reaction times).

3 | RESULTS

We applied a three-stimulus version of the oddball paradigm, with a recurrent standard stimulus and two rare oddball stimuli; all were pure tones of different acoustic frequencies. One of these (the distracter) was clearly distinguishable from the standard but participants were asked to ignore it; the other (the target) had a very similar frequency as the standard and participants were required to signal its occurrence via keypress. The error rate (Figure 1a) was low, both for false alarms (keypress responses following a non-target stimulus) and misses (target stimuli not followed by a keypress), resulting in very high d-prime values. Reaction times were within the range reported in previous oddball studies (e.g., LoTemplio et al., 2021) and no speed-accuracy trade-off emerged across participants (Figure 1b, Pearson's $r = -.34$, $p = .169$).

Due to the auditory nature of the stimuli, their presentation did not elicit the pupil constriction that often accompanies visual stimulation. As Figure 1c illustrates, there was little if any pupil-size variation following the standard stimulus, while the distracter stimulus elicited a small and transient dilation. The target stimulus elicited a much larger dilation, starting at about the same time as the distracter response but perduring well after it; given the timing of keypresses that followed the target stimulus (Figure 1d), the later portion of the pupil-dilation response to the target could be in part related to these keypress actions.

Simultaneous measurement of EEG revealed the classic P300 response to infrequent stimuli (Figure 1e shows the waveform for the a-priori selected parietal electrode Pz), with shorter latency and smaller amplitude for the distracter relative to the target.

To quantify these pupillary and EEG responses, we started with standard methodology and simply took their peak within predefined temporal windows, after averaging across trials to attenuate noise. Clearly, the choice of the relevant temporal window (and of the electrode for ERP measures) represents an element of arbitrariness, which we mitigated by setting our parameters based on previous studies. Coherently, we found the expected stimulus-dependance of these responses, as revealed by one-way ANOVAs for repeated measures (pupil dilation: $F(2,17) = 64.69$, $p < .001$ after Greenhouse–Geisser correction; P300: $F(2,17) = 53.62$, $p < .001$) and post hoc *t*-tests that revealed stronger responses to the target compared to the distractor (pupil dilation: $t(17) = 6.42$, $p < .001$; P300: $t(17) = 3.98$, $p = .001$). In line with previous studies, we failed to find any relationship between the P300 and pupil dilation responses quantified this way (Figure 4a, Pearson's $r = -.34$, $p = .163$).

We aimed to give a more complete account of the ERP responses by breaking it down into independent components with distinct scalp topology and timecourses. Figure 2 shows that the independent component analysis approach isolated two (out of five) components that fit well with the two main P300 sub-types: the P300b (with centro-posterior distribution) and the P300a (with more anterior distribution and shorter latency compared to the P300b, especially for the distracter stimulus). The amplitude of the P300b component, computed as the absolute peak of the template, showed the expected stimulus dependance, as revealed by the one-way ANOVA ($F(2,17) = 50.21$, $p < .001$) and the post hoc *t*-test comparing the target and distractor responses ($t(17) = 2.80$, $p = .012$). This motivated us to test the relationship between this more specific index of the P300b amplitude with pupil dilation (quantified with the same index used for Figure 4a). Figure 4b shows that a positive trend emerged mainly for the target response ($r = .40$, $p = .096$), but it was not statistically reliable.

Finally, we aimed to give a better account of the pupil-dilation responses using a linear modeling approach

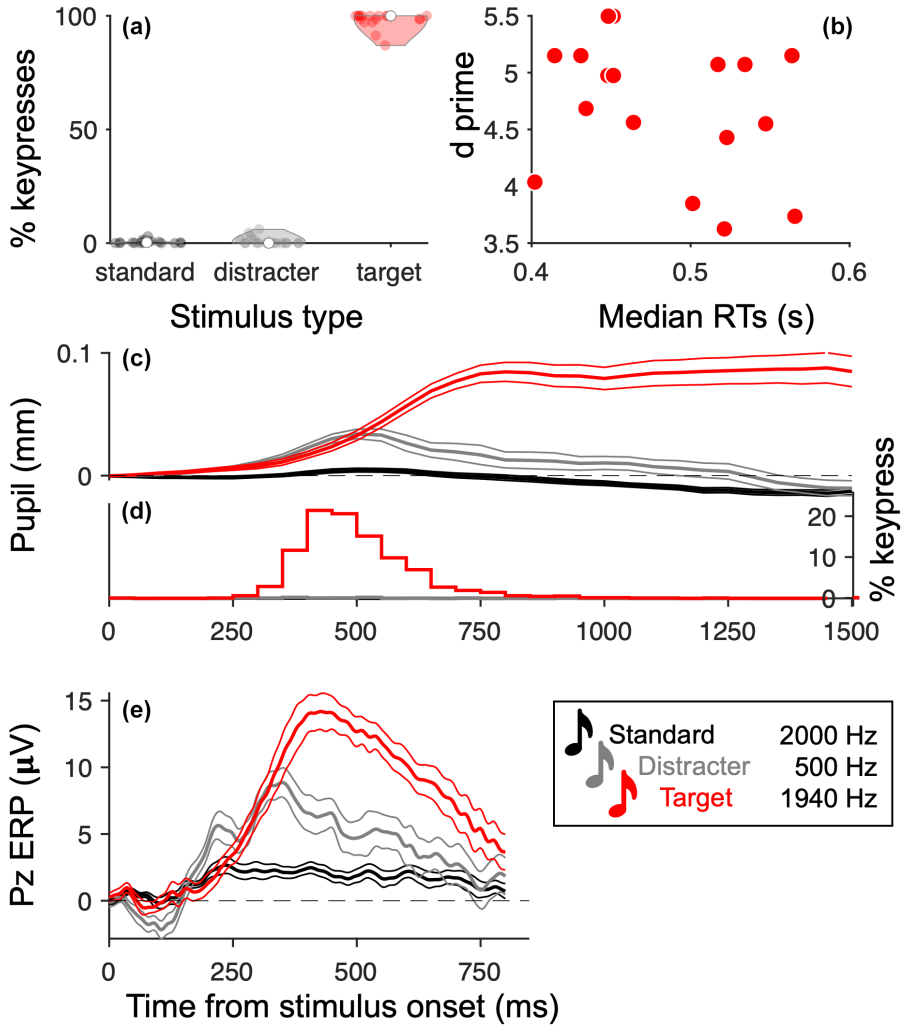

FIGURE 1 Behavioral, phasic pupil-dilation and ERP responses in a three-stimulus oddball paradigm. (a) Percent of keypresses in response to each stimulus type; individual dots are single participants; the white dot and line give the median and interquartile range. (b) Sensitivity (quantified as d-prime with signal detection theory, see methods) and speed (median reaction times) across participants. (c) Timecourses of pupil dilation for each stimulus type; thick and thin lines show the grand-average ± one standard error of the mean. (d) Average temporal distribution of keypresses (almost exclusively observed after the target stimuli). (e) Timecourses of the ERP recorded at the Pz electrode for each stimulus type; thick and thin lines show the grand-average ± one standard error of the mean.

(outlined in Figure 3 using data from one example participant). This assumes that the average pupil-dilation traces in each condition is the sum of two components: one representing the stimulus (modeled separately for the standard, distracter, and target) and the other representing the keypress actions (captured by the distribution of reaction times across trials). Each component (dashed curves in Figure 3b) is modeled by convolving the corresponding predictor (shown in Figure 3a) with an impulse response function (IRF), then scaling it by an appropriate beta-weight. The IRF was assumed to be a fixed characteristic of each participant, describing the dynamics of their pupil-dilation response to any event—stimulus or keypress-action alike. We varied its time-to-peak to achieve the best fit of each participant's pupil traces; Figure 3c shows the best-fitting IRF parameter and the corresponding variance explained, which averaged 88 ± 3%.

The beta-weight assigned to each component provides an overall index of its relative importance in the pupil-dilation trace. Because keypress-actions mostly occurred after an oddball-target stimulus, the main effect of the model was to decompose the pupil-dilation response to the target into an earlier component related to the stimulus presentation (with the same latency as the standard and distracter responses, set by the IRF parameters) and a later component related to the keypress action (resulting from the convolution of the reaction-time distribution with the same IRF). After separating out this second action-related component, the stimulus-related component remained systematically dependent on stimulus type, as supported

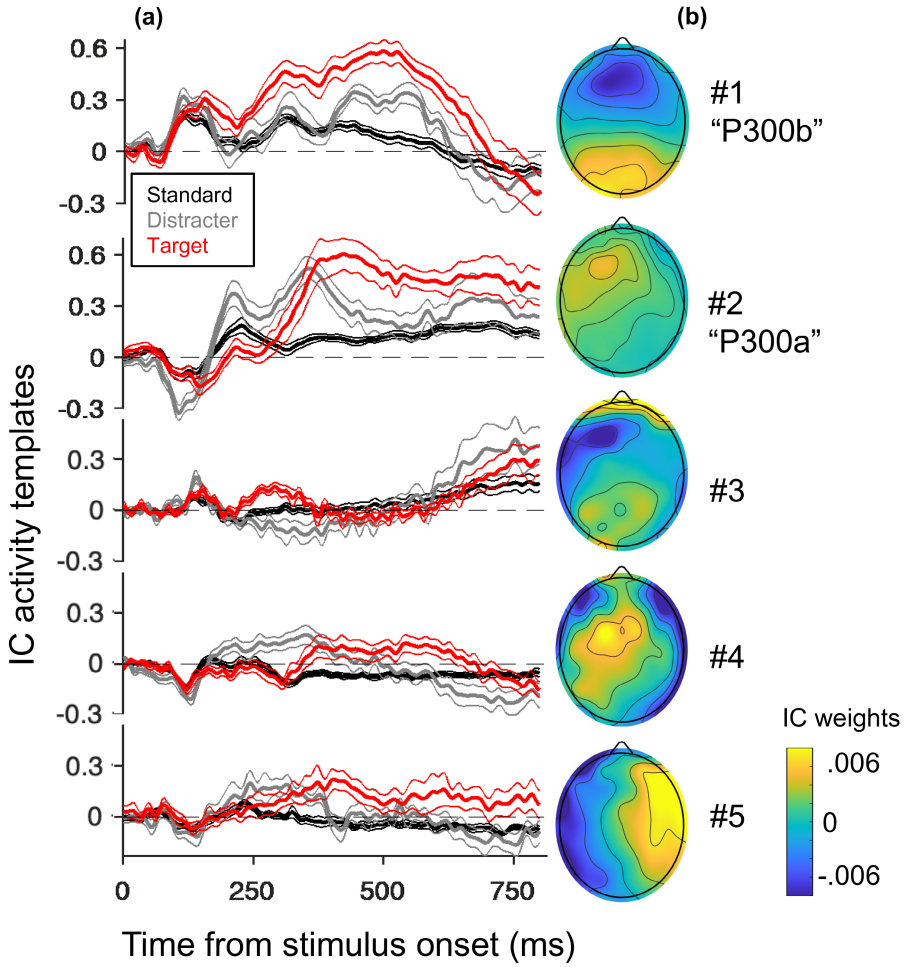

FIGURE 2 ERP components resulted from independent component analysis. (a) Activity templates of the five components extracted from ICA. Thick and thin lines show the grand-average ± one standard error of the mean. (b) Spatial distribution of the same components.

by the one-way ANOVA on the beta-weights of the three stimulus-predictors (F (2,17) = 46.43, $p < .001$) and the post hoc t-test comparing the beta-weights assigned to the target and distracter predictors (t (17) = 6.34, $p < .001$). We therefore tested the correlation between this stimulus-related component of the pupil-dilation response and the P300b component of the ERPs. Figure 4c shows that a strong positive correlation emerged selectively for the target responses (Pearson's $r = .69$, $p = .002$), supporting the notion of coordinated ERP and pupil responses to the behaviorally relevant target stimulus. In contrast, no correlation was observed for either standard or distracter stimuli (both $|r| < .3$, $p > .2$), or for the beta-weights of the keypress predictors (all $|r| < .2$, all $p > .4$, not shown).

As a final step, we checked whether the observed correlation is mediated by behavioral performance, which could potentially influence both P300b and target-related pupil-dilation responses. We found no evidence in support of this hypothesis, given that neither of our parameters (the stimulus-related component of pupil dilation in Figure 5a,b or the P300b component in Figure 5c,d) was systematically correlated with either speed (measured with the median RTs) or sensitivity (measured with d-prime; we verified that similar results are obtained when substituting percent correct for d-prime). For completeness, we also examined the correlation between these behavioral indices and the more standard indices of the pupil-dilation (peak dilation, Figure 5e,f) and P300 amplitude (measured within a pre-set window at the Pz electrode, Figure 5g,h). The amplitude of the P300 showed a positive relation with d-prime, meaning that participants with more accurate behavior tended to show a larger deflection of the Pz signal within the time-window of interest. Instead, the peak pupil dilation showed no association with either index of behavioral performance.

4 | DISCUSSION

Using a three-stimulus version of the oddball paradigm and auditory stimuli, we confirmed the emergence of a pupil-dilation response with the same antecedent conditions of the P300; relative to a salient but task-irrelevant

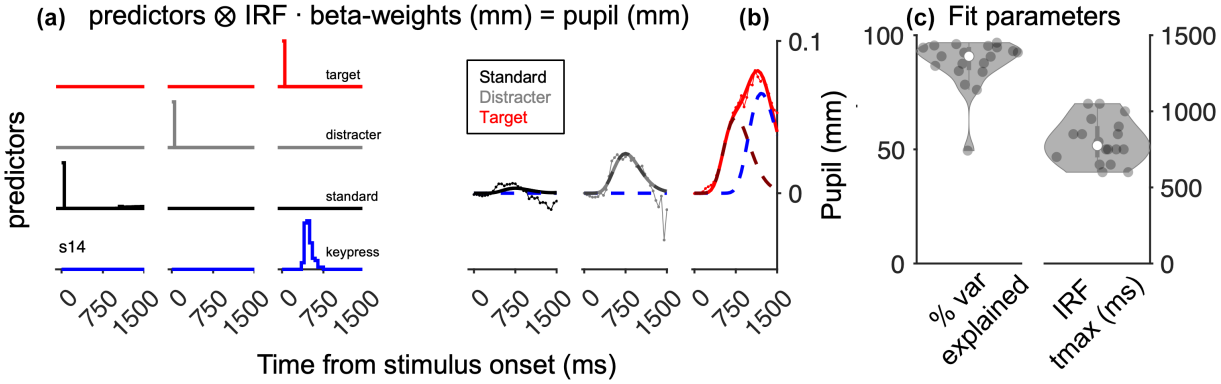

FIGURE 3 Linear modeling of the phasic pupil-dilation responses. (a–b) Linear modeling procedure for pupil-dilation responses, presented for one example participant whose results are highlighted with a blue cross in Figure 4. Panel a shows the temporal distribution of the stimuli and keypress events. These were convolved with an impulse response function (IRF) yielding predictors of the pupil-dilation responses to each factor and ultimately setting the shape of the dashed curves in panel b. The amplitude of these curves is set by a linear regression of the observed pupil-dilation responses against the predictors, yielding a set of beta-weights. In panel b, the dashed curves show the individual predictors scaled by the corresponding beta-weights, and the continuous lines show their sum, which closely approximates the observed datapoints (dots connected with thin lines). (c) Violin plots of the parameters of the fit: percent variance explained (left) and time-to-peak of the best fitting *IRF* (right). Individual dots are single participants; the white dot and line give the median and interquartile range.

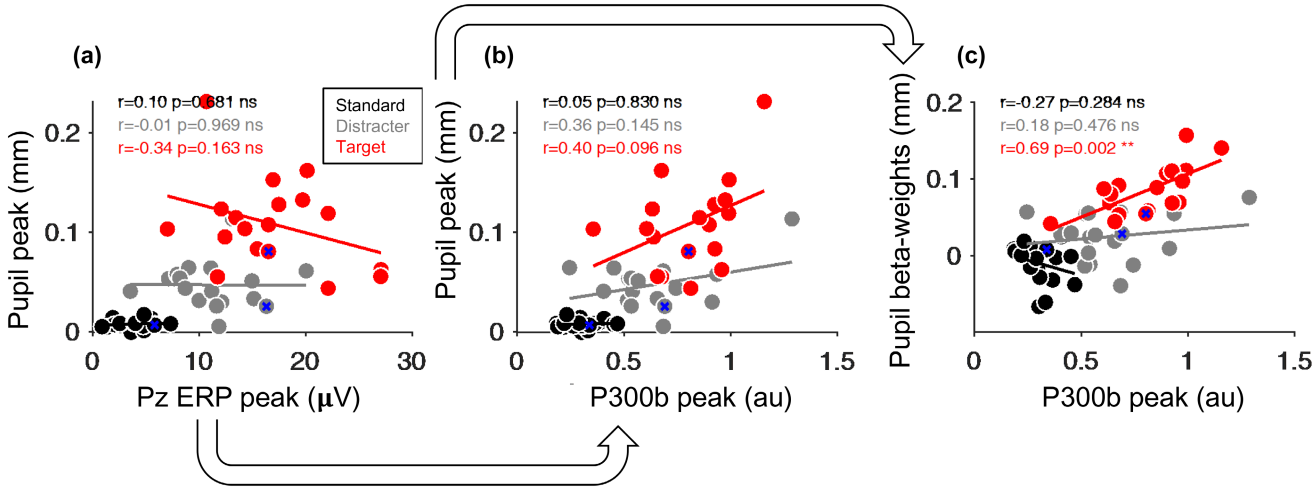

FIGURE 4 Analysis of the association between the phasic pupil-dilation responses and the P300. (a) Lack of correlation between the pupil-dilation and P300 responses, when indexed with standard methodology, that is, quantifying them by the peak of the mean pupil-dilation time courses and peak of the average ERP waveform extracted from the electrode Pz between 250 and 500 ms post-stimulus onset. (b) A non-significant positive trend emerges for responses to the oddball targets, when the phasic pupil dilation is indexed with the same methodology as in A but the P300 is characterized by the peak of the P300b component extracted by the independent component analysis of ERPs. (c) A strong positive correlation emerges for responses to the oddball targets when a stimulus-related component of pupil-dilation responses is extracted via the linear modeling presented in Figure 3, and it is correlated with the amplitude of the P300b component extracted by ICA. In all panels, the continuous line shows the best-fitting linear function and text insets report the Pearson's r correlation coefficients with associated *p*-values (ns for non-significant, * for $p < .5$, ** for $p < .01$, *** for $p < .001$).

distractor stimulus, the target stimulus (prompting a keypress action) elicited a stronger and more sustained pupil dilation, coherent with the stronger deflection of the late positive ERP observed in the parietal area. Despite their similar dependence on stimulus type, however, the P300 and pupil-dilation responses did not show correlated amplitudes across participants, like in previous studies (de Gee et al., 2021; Hong et al., 2014; Kamp & Donchin, 2015; LoTemplio et al., 2021; Murphy et al., 2011). We hypothesized that this seeming lack of correlation resulted from confounding factors independently affecting the P300 and the pupil-dilation responses. We obtained evidence in support of this view, as a strong positive correlation emerged after isolating a component of the responses that was specifically related to stimulus processing and linked with motivational significance. The application of

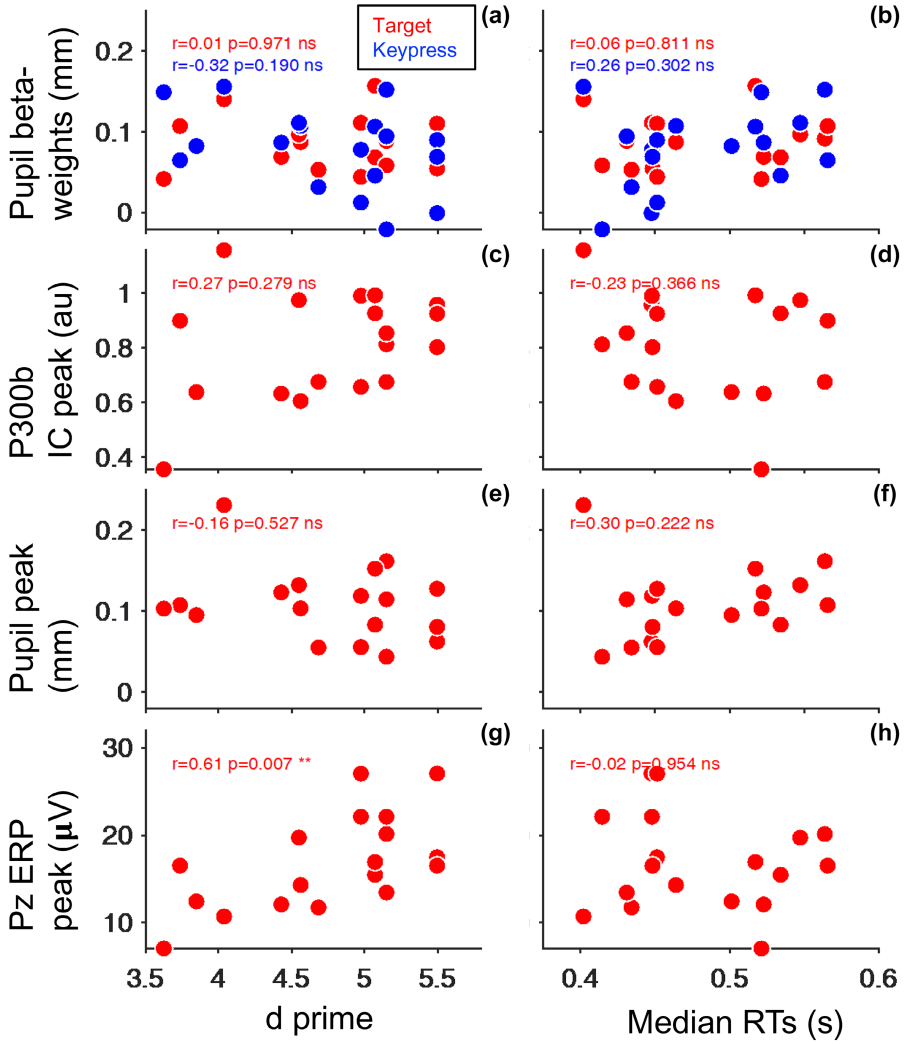

FIGURE 5 Exploration of the associations between the accuracy/speed of behavioral responses and either the phasic pupil-dilation or the P300 responses. The *x*-axis of panels a, c, e, and g (left column) reports participants' accuracy in the oddball task, expressed as d-prime values (signal detection theory); the *x*-axis of panels b, d, f, and h (right column) reports participants' speed, expressed as median reaction times. The y-axis shows (a, b) beta-weight of the stimulus-related component of pupil-dilation responses to the target stimulus (red) and of the action-related component (blue); (c, d) peak of the P300b component for the target stimulus; (e, f) peak of the pupil-dilation response to the target stimulus; and (g, h) peak of the ERP at Pz for the target stimulus. In all panels, text insets report the Spearman's rank correlation coefficients with associated *p*-values (ns for non-significant, * for $p < .5$, ** for $p < .01$, *** for $p < .001$).

independent component analysis to the ERP spatiotemporal profiles allowed us to break down the P300 into a P300a and a P300b component with a minimum a-priori assumptions (Makeig, Debener, et al., 2004; Makeig, Delorme, et al., 2004; Onton et al., 2006), both substantially contributing to the response to the target stimulus. This suggests that the P300 elicited by our oddball target stimulus was a composite response that combined a phasic arousal response to infrequent stimuli (indexed by the P300a) with a process of response selection and/or stimulus evaluation relative to its context (indexed by the P300b). Interestingly, the composite P300 correlated with participants' sensitivity, in line with the concept that a stronger P300 response is conducive to more accurate behavior (Hillyard et al., 1971). However, this was not the case for its P300b component; this suggests that the association between the composite P300 and behavioral performance is explained by components other than the P300b, which could include motor or sensory aspects of the keypress action (especially since, in our experiment, sensitivity was largely determined by the number of keypress responses correctly made after the target stimulus).

We found that also pupil dilations could be decomposed into simpler waveforms: a stimulus-related component, modeled by the same function for all stimuli (target, distracter, and standard, merely scaled by different

beta-weights), and a subsequent broader dilation observed following target stimuli and related to the temporal distribution of the keypress actions that they prompted. Even after discounting this action-related component, the stimulus-related dilation retained a preference for the target stimulus. The amplitude of this component was tightly and selectively correlated with the P300b component. These observations support the notion that at least part of the autonomic response to motivationally significant stimuli, as indexed by pupil dilations, is coordinated with their central processing, as indexed by the P300 (Nieuwenhuis et al., 2011).

The autonomic response to motivationally significant stimuli is classically interpreted as contributing to the appropriate behavioral response (as in "fight or flight"), and thereby fundamentally linked with action. This may seem incompatible with the possibility of discarding an action-related component from the autonomic (pupillary) response, leaving a component that still meaningfully relates to the different stimulus types. However, this is in line with accumulating evidence that pupil dilations are not only linked with actions but also reliably index aspects of stimulus processing, particularly linked with their match to expectations and prior beliefs (de Gee et al., 2017; Eldar et al., 2021; Murphy et al., 2021). In turn, these observations are coherent with the proposal that phasic pupil dilations are often (Joshi et al., 2016; Reimer et al., 2016) though not always (Megemont et al., 2022) linked with activity in the locus coeruleus and the consequent diffuse release of NE in many cortical regions. The effect of this NE release may be a generalized increase of response gain, leading to a multiplicative enhancement of cortical responses that could be responsible for the wave of activity captured by EEG as the P300 (Nieuwenhuis et al., 2005; Swick et al., 1994) and might implement an optimal strategy for allocating cortical responses (Aston-Jones & Cohen, 2005).

One question that remains relatively open concerns the functional significance of this LC-NE activation. On the one hand, there is evidence that LC activation is triggered only after a stimulus is fully processed and categorized as motivationally significant (e.g., its latency is best predicted by reaction times, rather than stimulus timing). This implies that NE release may primarily contribute to the selection of an appropriate behavioral response (Aston-Jones & Cohen, 2005; Nieuwenhuis et al., 2005). On the other hand, recent work implicated the LC-NE system with the process of "belief updating," which involves adjusting the probability of one's a priori hypotheses or beliefs in the light of new evidence. This is usually tested in relatively complex task settings, where participants are implicitly called to guess a latent variable based on noisy samples of information. The efficiency of this process is reliably indexed by both P300 amplitude and phasic pupil dilations (Jepma et al., 2016, 2018; Murphy et al., 2021; Nassar et al., 2012), and it is interfered with by pharmacological manipulation of catecholamine activity (Jepma et al., 2016, 2018). In the simplified context of an oddball task, an a priori belief could be envisaged as the expectation that stimuli tend to repeat themselves, which is built over the repeated occurrence of the standard stimulus and needs revising when a different (oddball) sound occurs—a concept that is inevitably linked with the context updating model of P300 (Donchin & Coles, 1988). There is a longstanding debate whether a process of context updating is best suited for explaining the occurrence of the P300b responses (and related autonomic components), or whether these are primarily related to the outcome of decisions (Verleger, 2020). Although our results do not speak directly to this issue, they do indicate the existence of a component of the pupil-dilation response that is tied to the stimulus and independent of reaction times. The tight positive association observed between the amplitude of this component and our estimate of the P300b amplitude suggests that it is this stimulus-related aspect of the autonomic response, not the action-related one, that best reflects the central processing of motivationally significant stimuli.

Previous studies examining the relation between pupil dilations and P300 in the context of the oddball task did not attempt to separate action- and stimulus-related components. It is interesting to note that the one study that reported correlated pupil-dilation and P300 responses (Chang et al., 2023) used a task that equated the action components across stimulus categories; for their inter-individual correlation analyses, they estimated pupil responses by subtracting traces for incongruent and congruent trials, which effectively factored out the action-related component from pupil-dilation responses.

5 | LIMITATIONS AND FURTHER DIRECTIONS

Our analysis approach removed many aspects of arbitrariness that are often found in standard methodology. For example, the estimation of P300 components generally relies on the definition of one or more electrodes of interest, from which the signal is extracted and averaged; instead, our ICA approach yielded a single waveform with associated scalp distribution. Similarly, estimating the amplitude of a pupil-dilation response typically

requires choosing a window where the mean or maximum is defined; instead, our linear modeling allowed us to capture the amplitude of responses by considering the entire waveform. This methodological advantage, however, came with a strong limitation, as it forced us to average pupil dilations across trials to achieve sufficient signal-to-noise ratio for the linear modeling. This prevented us from examining the co-variation of pupil diameter and ERPs intra-individually, which many previous studies did (de Gee et al., 2021; Hong et al., 2014; Kamp & Donchin, 2015; LoTemplio et al., 2021; Murphy et al., 2011). For the same reason, we were also unable to examine the relevance of spontaneous oscillation of pupil diameter (measured before stimulus onset), which the same previous studies generally found to be better predictors of the P300 and behavioral responses than the phasic pupil dilations following the stimuli. Future studies may employ our methodology to address intra-individual variability, by increasing the amount of data collected per participant and analyzing variations over blocks of trials. Finally, it is important to note that our analysis of inter-individual variability was based on a sample of 18 participants; this small sample size represents another limitation of our study.

6 | CONCLUSIONS

Our observations are consistent with multiple factors participating in the generation of the central and autonomic response to motivationally significant stimuli.

They suggest the existence of at least one factor that affects both responses, resulting in a positive correlation between P300b ERPs and a component of the pupil dilations that is tied to the presentation of an oddball-target stimulus.

This correlation supports the notion that phasic pupil-dilation responses provide a sensitive index of central stimulus processing. It also provides evidence in favor of the hypothesis that phasic pupil-dilation and P300 responses may be coordinated (Nieuwenhuis et al., 2011).

AUTHOR CONTRIBUTIONS

Danilo Menicucci: Conceptualization; data curation; investigation; methodology; supervision; visualization; writing – original draft; writing – review and editing. **Silvia Animali:** Data curation; investigation; writing – original draft. **Eleonora Malloggi:** Data curation; investigation; writing – original draft. **Angelo Gemignani:** Supervision; writing – review and editing. **Enrica Bonanni:** Resources; supervision. **Francesco Fornai:** Resources; supervision. **Filippo Giorgi:** Conceptualization; supervision; writing – review and editing. **Paola Binda:** Conceptualization; data curation; funding acquisition; methodology; supervision; visualization; writing – original draft; writing – review and editing.

FUNDING INFORMATION

This research was funded by the European Union—Next Generation EU, in the context of The National Recovery and Resilience Plan, Investment 1.5 Ecosystems of Innovation, Project Tuscany Health Ecosystem (THE, CUP I35C22000780001), and of the grant PRIN 2022 (Project "RIGHTSTRESS—Tuning arousal for optimal perception," Grant no. 2022CCPJ3J, CUP I53D23003960006); by the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program grant no. 801715 (PUPILTRAITS); and by the Italian Ministry of University and Research under the program FARE-2 (grant SMILY).

CONFLICT OF INTEREST STATEMENT

The authors declare no competing interests.

DATA AVAILABILITY STATEMENT

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

ORCID

Danilo Menicucci https://orcid.org/0000-0002-5521-4108

REFERENCES

Aston-Jones, G., & Cohen, J. D. (2005). An integrative theory of locus coeruleus-norepinephrine function: Adaptive gain and optimal performance. *Annual Review of Neuroscience*, *28*, 403–450.

Bell, A. J., & Sejnowski, T. J. (1995). An information-maximization approach to blind separation and blind deconvolution. *Neural Computation*, *7*, 1129–1159.

Binda, P., & Murray, S. O. (2015). Keeping a large-pupilled eye on high-level visual processing. *Trends in Cognitive Sciences*, *19*, 1–3.

Brainard, D. H. (1997). The psychophysics toolbox. *Spatial Vision*, *10*, 433–436.

Burlingham, C. S., Mirbagheri, S., & Heeger, D. J. (2022). A unified model of the task-evoked pupil response. *Science Advances*, *8*, eabi9979.

Chang, Y. H., Chen, H. J., Barquero, C., Tsai, H. J., Liang, W. K., Hsu, C. H., Muggleton, N. G., & Wang, C. A. (2023). Linking tonic and phasic pupil responses to P300 amplitude in an emotional face-word Stroop task. *Psychophysiology*, e14479.

Comerchero, M. D., & Polich, J. (1999). P3a and P3b from typical auditory and visual stimuli. *Clinical Neurophysiology*, *110*, 24–30.

de Gee, J. W., Colizoli, O., Kloosterman, N. A., Knapen, T., Nieuwenhuis, S., & Donner, T. H. (2017). Dynamic modulation of decision biases by brainstem arousal systems. *eLife*, *6*, e23232.

de Gee, J. W., Correa, C. M. C., Weaver, M., Donner, T. H., & van Gaal, S. (2021). Pupil dilation and the slow wave ERP reflect surprise about choice outcome resulting from intrinsic variability in decision confidence. *Cerebral Cortex*, *31*, 3565–3578.

Delorme, A., & Makeig, S. (2004). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. *Journal of Neuroscience Methods*, *134*, 9–21.

Denison, R. N., Parker, J. A., & Carrasco, M. (2020). Modeling pupil responses to rapid sequential events. *Behavior Research Methods*, *52*, 1991–2007.

Donchin, E., & Coles, M. G. H. (1988). Is the P300 component a manifestation of context updating. *Behavioral and Brain Sciences*, *11*, 357–374.

Einhauser, W., Koch, C., & Carter, O. L. (2010). Pupil dilation betrays the timing of decisions. *Frontiers in Human Neuroscience*, *4*, 18.

Eldar, E., Felso, V., Cohen, J. D., & Niv, Y. (2021). A pupillary index of susceptibility to decision biases. *Nature Human Behaviour*, *5*, 653–662.

Fletcher, E. M., Kussmaul, C. L., & Mangun, G. R. (1996). Estimation of interpolation errors in scalp topographic mapping. *Electroencephalography and Clinical Neurophysiology*, *98*, 422–434.

Hautus, M. J. (1995). Corrections for extreme proportions and their biasing effects on estimated values of D. *Behavior Research Methods, Instruments, & Computers*, *27*, 46–51.

Hillyard, S. A., Squires, K. C., Bauer, J. W., & Lindsay, P. H. (1971). Evoked potential correlates of auditory signal detection. *Science*, *172*, 1357–1360.

Himberg, J., Hyvarinen, A., & Esposito, F. (2004). Validating the independent components of neuroimaging time series via clustering and visualization. *NeuroImage*, *22*, 1214–1222.

Hoeks, B., & Levelt, W. J. M. (1993). Pupillary dilation as a measure of attention—a quantitative system-analysis. *Behavior Research Methods, Instruments, & Computers*, *25*, 16–26.

Hong, L. B., Walz, J. M., & Sajda, P. (2014). Your eyes give you away: Prestimulus changes in pupil diameter correlate with poststimulus task-related EEG dynamics. *PLoS One*, *9*, e91321.

Hupe, J. M., Lamirel, C., & Lorenceau, J. (2009). Pupil dynamics during bistable motion perception. *Journal of Vision*, *9*, 10.

Jepma, M., Brown, S., Murphy, P. R., Koelewijn, S. C., de Vries, B., van den Maagdenberg, A. M., & Nieuwenhuis, S. (2018). Noradrenergic and cholinergic modulation of belief updating. *Journal of Cognitive Neuroscience*, *30*, 1803–1820.

Jepma, M., Murphy, P. R., Nassar, M. R., Rangel-Gomez, M., Meeter, M., & Nieuwenhuis, S. (2016). Catecholaminergic regulation of learning rate in a dynamic environment. *PLoS Computational Biology*, *12*, e1005171.

Joshi, S., & Gold, J. I. (2020). Pupil size as a window on neural substrates of cognition. *Trends in Cognitive Sciences*, *24*, 466–480.

Joshi, S., Li, Y., Kalwani, R. M., & Gold, J. I. (2016). Relationships between pupil diameter and neuronal activity in the locus coeruleus, colliculi, and cingulate cortex. *Neuron*, *89*, 221–234.

Kamp, S. M., & Donchin, E. (2015). ERP and pupil responses to deviance in an oddball paradigm. *Psychophysiology*, *52*, 460–471.

LoTemplio, S., Silcox, J., Federmeier, K. D., & Payne, B. R. (2021). Inter- and intra-individual coupling between pupillary, electrophysiological, and behavioral responses in a visual oddball task. *Psychophysiology*, *58*, e13758.

Lynn, R. (1966). *Attention, Arousal, and the Orientation Reaction*. Pergamon Press.

Makeig, S., Debener, S., Onton, J., & Delorme, A. (2004). Mining event-related brain dynamics. *Trends in Cognitive Sciences*, *8*, 204–210.

Makeig, S., Delorme, A., Westerfield, M., Jung, T. P., Townsend, J., Courchesne, E., & Sejnowski, T. J. (2004). Electroencephalographic brain dynamics following manually responded visual targets. *PLoS Biology*, *2*, e176.

Mathot, S. (2018). Pupillometry: Psychology, physiology, and function. *Journal of Cognition*, *1*, 16.

Megemont, M., McBurney-Lin, J., & Yang, H. (2022). Pupil diameter is not an accurate real-time readout of locus coeruleus activity. *eLife*, *11*, e70510.

Menicucci, D., Artoni, F., Bedini, R., Pingitore, A., Passera, M., Landi, A., L'Abbate, A., Sebastiani, L., & Gemignani, A. (2014). Brain responses to emotional stimuli during breath holding and hypoxia: An approach based on the independent component analysis. *Brain Topography*, *27*, 771–785.

Murphy, P. R., O'Connell, R. G., O'Sullivan, M., Robertson, I. H., & Balsters, J. H. (2014). Pupil diameter covaries with BOLD activity in human locus coeruleus. *Human Brain Mapping*, *35*, 4140–4154.

Murphy, P. R., Robertson, I. H., Balsters, J. H., & O'connell, R. G. (2011). Pupillometry and P3 index the locus coeruleus-noradrenergic arousal function in humans. *Psychophysiology*, *48*, 1531–1542.

Murphy, P. R., Wilming, N., Hernandez-Bocanegra, D. C., Prat-Ortega, G., & Donner, T. H. (2021). Adaptive circuit dynamics across human cortex during evidence accumulation in changing environments. *Nature Neuroscience*, *24*, 987–997.

Nassar, M. R., Rumsey, K. M., Wilson, R. C., Parikh, K., Heasly, B., & Gold, J. I. (2012). Rational regulation of learning dynamics by pupil-linked arousal systems. *Nature Neuroscience*, *15*, 1040–1046.

Nieuwenhuis, S., Aston-Jones, G., & Cohen, J. D. (2005). Decision making, the P3, and the locus coeruleus-norepinephrine system. *Psychological Bulletin*, *131*, 510–532.

Nieuwenhuis, S., De Geus, E. J., & Aston-Jones, G. (2011). The anatomical and functional relationship between the P3 and autonomic components of the orienting response. *Psychophysiology*, *48*, 162–175.

Onton, J., Westerfield, M., Townsend, J., & Makeig, S. (2006). Imaging human EEG dynamics using independent component analysis. *Neuroscience and Biobehavioral Reviews*, *30*, 808–822.

Polich, J. (2007). Updating p300: An integrative theory of P3a and P3b. *Clinical Neurophysiology*, *118*, 2128–2148.

Reimer, J., McGinley, M. J., Liu, Y., Rodenkirch, C., Wang, Q., McCormick, D. A., & Tolias, A. S. (2016). Pupil fluctuations track rapid changes in adrenergic and cholinergic activity in cortex. *Nature Communications*, *7*, 13289.

Sarno, I., Preti, E., Prunas, A., & Madeddu, F. (2011). *SCL-90-R symptom checklist-90-R* Adattamento italiano. Giunti, Organizzazioni Speciali.

Sebastiani, L., Castellani, E., Gemignani, A., Artoni, F., & Menicucci, D. (2015). Inefficient stimulus processing at encoding affects formation of high-order general representation: A study on cross-modal word-stem completion task. *Brain Research*, *1622*, 386–396.

Sutton, S., Braren, M., Zubin, J., & John, E. R. (1965). Evoked-potential correlates of stimulus uncertainty. *Science*, *150*, 1187–1188.

Swick, D., Pineda, J. A., Schacher, S., & Foote, S. L. (1994). Locus-coeruleus neuronal-activity in awake monkeys—relationship to auditory P300-like potentials and spontaneous Eeg. *Experimental Brain Research*, *101*, 86–92.

van Dinteren, R., Arns, M., Jongsma, M. L., & Kessels, R. P. (2014). P300 development across the lifespan: A systematic review and meta-analysis. *PLoS One*, *9*, e87347.

Vazey, E. M., Moorman, D. E., & Aston-Jones, G. (2018). Phasic locus coeruleus activity regulates cortical encoding of salience information. *Proceedings of the National Academy of Sciences of the United States of America*, *115*, E9439–E9448.

Verleger, R. (2020). Effects of relevance and response frequency on P3b amplitudes: Review of findings and comparison of hypotheses about the process reflected by P3b. *Psychophysiology*, *57*, e13542.

Voudouris, D., Schuetz, I., Schinke, T., & Fiehler, K. (2023). Pupil dilation scales with movement distance of real but not of imagined reaching movements. *Journal of Neurophysiology*, *130*, 104–116.

How to cite this article: Menicucci, D., Animali, S., Malloggi, E., Gemignani, A., Bonanni, E., Fornai, F.S., Giorgi, F., & Binda, P. (2024). Correlated P300b and phasic pupil-dilation responses to motivationally significant stimuli. *Psychophysiology*, *61*, e14550. https://doi.org/10.1111/psyp.14550