Temporal contrast enhancement emerges from distinct pain and sound filtering mechanisms

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Abstract

Temporal contrast enhancement (TCE), also termed offset analgesia, describes a temporal filtering mechanism whereby a small contrast in stimulus intensity produces a disproportionately large reduction in perceived pain. Although TCE is considered a robust marker of endogenous pain modulation, its underlying mechanisms remain unresolved. It is unclear whether TCE reflects a nociceptive-specific modulatory process or a supramodal temporal filtering mechanism that generalizes to non-painful but aversive sensory stimulation. In this study, healthy and pain-free participants were enrolled in two experiments: a behavioral study (n=33) or a neurophysiological study (n=29). Continuous pain-ratings, electroencephalography (EEG) and pupillometry data were collected. A conventional TCE paradigm was applied using either noxious heat delivered via a thermal contact stimulator or unpleasant auditory stimulation delivered through over-ear headphones. Both noxious heat and unpleasant sounds induced behavioral TCE-effects ($p<0.01$), indicating a supramodal mechanism with modality-specific temporal dynamics. In the second experiment, noxious heat resulted in decreased power of neural alpha oscillations (~10 Hz, $p<0.05$) and increased pupil size ($p<0.05$) potentially indicating bottom-up modulation of the autonomic nervous system and a release of neural inhibition, respectively. However, subjectively experienced TCE-effects were not represented in neurophysiological correlates. These findings support TCE as a supramodal temporal filtering mechanism characterized by modality-specific temporal dynamics, for which no corresponding signatures are found in EEG or pupillometry.

Keywords: Temporal Filtering, Temporal Contrast Enhancement, Offset Analgesia, Auditory System, Pain, Sensory Processing

Introduction

Human environments contain a plethora of sensory inputs. Sensory integration is a complex process dependent on stimulus intensity, salience and context [75]. Therefore, diverse filtering mechanisms, covering temporal and spatial aspects, are required to selectively enhance specific aspects of stimuli, evaluate their relevance, and modulate perceptual processing [12,50]. Convergences in temporal filtering have been documented across sensory domains. In the context of auditory perception, temporal summation - alternatively referred to as temporal integration [52] or temporal sound summation [7] - describes the perceived increases in loudness when a tone of constant volume is presented for longer durations. Temporal filtering of auditory percepts is of utmost importance, due to its relevance in vocalization and speech recognition [40], as well as in avoiding uncomfortably loud sounds. Temporal summation likewise characterizes nociceptive processing [11], where adaptive temporal filtering is vital for averting tissue injury and protecting the organism. Evidence suggests that temporal filtering processes share similar mechanisms across modalities and sensory systems [8,16,23,56]. However, the extent to which temporal filtering in auditory and nociceptive processing is based on common perceptual and physiological mechanisms remains unclear.

Temporal contrast enhancement (TCE), a putative component of the endogenous pain modulatory system, is conceptualized as a temporal filtering process whose mechanisms remain unclear [47,71,74]. Commonly referred to as offset analgesia, it is characterized by a disproportionally large reduction in perceived pain following a slight decrease in noxious stimulus intensity [22,71,72]. A variety of mechanisms distributed along the neuroaxis have been postulated as potential mediators of TCE. Several brain imaging studies using functional magnetic resonance imaging (fMRI) showed altered activity in cortical [15,47,71] and subcortical structures [6,47,58,71,74].

Interestingly, studies investigating the temporal dynamics of TCE using electroencephalography (EEG) are scarce. Research has been focusing on EEG during applications of tonic or phasic pain, investigating alpha-band oscillations (~10Hz), which consistently showed reduced alpha power during pain [48,49,54]. This might reflect functional inhibition of situational irrelevant information [14,29–31,59], which is already well-established in auditory attention research [57,69,70]. Additional objective measures have been used to characterize neurophysiological correlates of pain and auditory processing. Changes in pupil diameter are closely related to autonomic nervous system activity and have been linked to perceived stimulus intensity and arousal, particularly in response to painful stimuli [10,33]. In auditory research, pupil dilation has been associated with loudness of the stimuli, salience, and aversiveness [37,68,73], highlighting its relevance for tracking perceptual and attentional processes.

Here, it is hypothesized that the effects of TCE on noxious stimuli may not reflect pain-specific processes but rather could be indicative of a general temporal filtering mechanism in response to salient stimuli. To determine whether observed effects in pain are modality specific or merely reflect general arousal, prior studies have employed salience-matched control stimuli; nevertheless the evidence still remains equivocal [27,35,44,54,66]. Therefore, we conducted a multimodal study to test whether TCE is nociceptive-specific by applying painful heat or aversive auditory stimulation within a standard TCE paradigm, measuring behavioral and neurophysiological responses (EEG, pupillometry) to advance understanding of temporal filtering mechanisms.

Materials and methods

Two experiments were conducted: the first investigated behavioral excerpts of TCE alone, while the second additionally incorporated neurophysiological measures.

Experiment 1: Behavioral investigation of the TCE effect in auditory stimulation

The aim of the first experiment was to investigate if it is possible to elicit TCE behaviorally using auditory stimulation. The study was approved by the Ethics Committee of the University of Lübeck (2023-633) and conducted in accordance with the Declaration of Helsinki. The methodology was preregistered on the Open Science Framework (OSF; https://osf.io/643kg).

Participants

Participants (n = 33, 22 females; age = 23.7, SD = 6.0) were included if they subjectively reported being healthy and pain-free on the day of the procedure. Exclusion criteria were chronic pain (> 3 months) within the last two years, diagnosed systemic, neurological, cardiovascular or psychiatric diseases and being with diagnosed hearing loss or tinnitus. All participants were asked not to take any painkillers, consume alcohol or undertake any strenuous physical activity 24 hours before participating in the study. To characterize the study sample age, sex at birth, body mass (kg), stature (cm), handedness and general fear of heat pain and fear of loud noises on a numerical rating scale from 0 (no fear) to 100 (highest possible fear) were recorded for each participant. To measure noise sensitivity the Weinstein Noise Sensitivity Scale (WNSS) was used [76]. In addition, the Pain Vigilance and Awareness Questionnaire (PVAQ) was used to measure attention to pain and assesses awareness, consciousness, vigilance, and observation of pain [41] and the Pain Catastrophizing Scale (PCS) was used to assess the catastrophizing behavior [42].

Equipment

All heat stimuli were applied with a thermal contact stimulator (TCS; André Dufour, University of Strasbourg, France). The probe of the TCS has a total stimulation zone of 9 cm^2 (five equal stimulation zones, each $0.74 \times 2.4cm = 8.88cm^2$) and was applied to the left forearm. The probe weighs 440g and the TCS has a temperature range of 0°C to 60°C, adjustable at 0.1°C intervals. The maximum temperature rise and fall rate is 100°C/second. For auditory stimulation, a 1000-Hz sine wave tone sampled at 44.100Hz, generated using Adobe Audition (Adobe Systems Software, Dublin, Republic of Ireland), was applied. The sound was presented using over-ear headphones (PXC 550-II, Sennheiser, Wedemark, Germany). Probing pain intensity was conducted with a Python-based eVAS [20,43]. The eVAS was displayed using a computer and ranged from 0 "no sensation" to 200 "worst heat pain imaginable", while a value of 100 represented the “pain threshold” for thermal stimulation. For auditory stimulation, the same eVAS was used but it displayed different anchors, 0 representing “no sound audible”, 200 being “maximum discomfort imaginable” and 100 representing the “discomfort threshold”.

Familiarization and calibration procedure

Before attending the main part of the experiment, participants were familiarized to the rating procedure and stimulus intensities. For this, they received three different stimulus intensities, a high (48°C, 100dB), low (33°C, 49dB) and an intermediate (40°C, 82dB) level of intensity for thermal and auditory stimulation, respectively. Afterwards, the stimulation intensities for each modality were calibrated, using a staircase procedure (S1 Fig. in the Supporting Information). Participants were asked to continuously rate their sensory experience using the eVAS scale. The calibration consisted of ascending stimulation intensities, where each stimulation was applied for ten seconds, followed by ten seconds of either no stimulation (0dB) or baseline temperature (32°C) depending on the applied modality. The stimulation started at

either 33°C or 49dB and increased in 1°C or 3dB steps up until the highest stimulation intensity of 48°C or 100dB was reached. This procedure was repeated for each modality with the modalities being alternated. The stimulation intensities were then derived from the second iteration of each modality by using stimulation intensities that produced perceived pain intensities of 150/200 and 175/200 on the eVAS. These values were used for the initial stimulation intensity (T1) and increase in stimulation intensity (T2) in offset trials (see Experimental paradigm). Mean heat pain that corresponded to 150 points on the 0- to 200-point eVAS was 46.4°C (SD 0.8°C) and 47.4°C (SD 0.8°C) for 175/200 points respectively. Mean sound stimulation parameters for 150/200 and 175/200 eVAS ratings were 90.8dB (SD 8.0dB) and 95.0dB (SD 7.5dB), respectively.

Experimental paradigm

A TCE paradigm with three successive periods (T1-T2-T3) consisting of an OT and a CT was performed [62]. CTs were administered for a duration of 35 seconds, during which continuous heat or sound stimulation was applied at a calibrated intensity corresponding to 150/200 on the eVAS. The OTs consisted of an intensity corresponding to 150/200 (T1), followed by ten seconds of 175/200 (T2) and then decreased back to the stimulation intensity of T1 for 15 seconds (T3). Rise and fall rates were kept constant (100°C/s). Each trial was performed four times (4× OT, 4× CT) with a break of 2 min in between the trials. The order of trials was pseudorandomized in a counterbalanced manner.

Participants continuously rated the experienced pain intensity throughout each trial and were instructed to attend carefully and indicate even very subtle sensations or changes. This procedure was repeated once for each modality, resulting in a total of 16 trials per participant. All trials were completed for one modality before the other modality was tested. This transition was preceded by a 5-min interval of no stimulation to reduce possible carry-over effects.

Statistical analysis

Sample size calculation was based on the previously described OA effect size [62]. With an estimated effect size of $d_z = 0.76$ [22], an estimated group size of n = 25 participants for paired comparisons (two-sided t-test, $\alpha = 5\%$) was required to reach statistical power of 95% (G*Power, University of Düsseldorf) [18]. To preserve planned power, improve precision, and mitigate sex imbalance, the sample size was prospectively increased to n=33 [2].

Statistical analyses were performed using R Studio (RStudio version 2024.04.11 with R version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria) [55] and MATLAB (The Mathworks Inc., 2024) [65]. Parametric data is presented in means ($\bar{x}$) with standard deviations (SD) and nonparametric data in median (M) with ranges (R) or absolute and relative frequencies. The average eVAS ratings were obtained for each time interval (T1, T2 and T3). The first 5s of T1, T2 and T3 and the last 5s of T3 were not considered in our analysis. This approach was oriented on prior studies to consider the delay in pain response and extract stable pain ratings [38,64]. A 2x3 repeated measures ANOVA with the factors ‘trial’ (CT, OT) and ‘time’ (T1, T2, T3) was calculated per modality. If there were significant findings, FDR corrected [3,4] t-tests were performed. The level of significance was set at $p < 0.05$. The initial preregistered analysis plan (dependent t-tests) was modified to ensure greater coherence with the analytical approach of the second study. Additionally, a Pearson’s correlational analysis was used to examine a possible association of TCE effects between the modalities.

Experiment 2: Neurophysiological expression of TCE in auditory and thermal stimulation

The aim of this experiment was to investigate neural and autonomic nervous system responses using a similar stimulation paradigm and the same modalities as explained above. For this, EEG data, pupillometry data and behavioral ratings were collected. The study was approved by the Ethics Committee of the University of Lübeck (2023-633) and conducted in accordance

with the Declaration of Helsinki. Again, the methodology was preregistered on the Open Science Framework (OSF; https://osf.io/v37mp).

Participants

A total of 29 healthy participants (sex = 19 females; age = 24.6, SD = 5.7) were used for analysis. In- and Exclusion criteria were similar for both experiments. None of the volunteers that participated in the behaviorally focused experiment were recruited for the second experiment.

Equipment

The same stimulation equipment as in the previous experiment was used for all procedures. Behavioral data were collected using an eVAS similar in style and anchors, but the visual presentation, data collection and stimulus control was achieved using MATLAB (The Mathworks Inc., 2024). For visual presentation purposes, the psychophysics toolbox [5] was used. The EEG was recorded at 24 passive scalp electrodes (SMARTING, mBrainTrain, Belgrade, Serbia) at a sampling rate of 500 Hz (DC to 250 Hz bandwidth), referenced against electrode FCz. Electrode impedances were kept below 10 kΩ. The amplifier was attached to the EEG cap (Easycap, Herrsching, Germany) and the EEG data were transmitted via Bluetooth to a nearby computer, which recorded the data using the Smarting Streamer (Version 3.4.2). For pupillometry, a Tobii X3-120 Eye Tracker (Tobii Technology Inc., Stockholm, Sweden) was used with sampling rate of 120Hz. Pupillometry data were directly recorded via MATLAB.

Familiarization and calibration procedure

Contrary to the first experiment, stimulus intensity was not individually calibrated. This approach was chosen due to the robust effects seen in the first experiment. Furthermore, the application of constant stimulation intensities ensures uniform stimulus input across all

participants, a feature that assumes greater significance in the context of neurophysiological investigations [1]. The stimulus intensities were derived from mean values of the stimulation parameters of the behavioral experiment. The initially derived stimulation parameters from the first experiment that were used for thermal stimulation led to major pain habituation effects resulting in close to zero pain felt by the participants after a few trials. Due to this, the temperature was increased by 1.5°C (initially 46°C and 47°C) to reduce the observed habituation effects. The participants (n = 11) that received the stimulation protocol prior to this change were excluded from the analysis. In order to account for the missing practice using the eVAS, the participants underwent a brief familiarization procedure. This procedure comprised five stimuli in ascending order, either starting from 44.5°C for thermal stimulation and increasing in 1°C steps or starting from 80dB and increasing in 5dB steps. Each stimulus was presented for 10 seconds and then followed by a 10-second pause (matching the calibration procedure from the first experiment).

Experimental paradigm

The TCE paradigm matched the behavioral protocol but used fixed stimulation intensities of 47.5°C or 95dB for T1, 48.5°C or 100dB for T2 and 47.5°C or 95dB for T3, respectively. Each modality was tested twice, and each stimulation block consisted of ten trials. The first two trials per block were designated as an OT or CT, with the objective of collecting behavioral data. Participants were tasked with continuously rating their perceived stimulus intensity. For the remaining eight trials, participants were instructed to maintain their gaze on a fixation cross, focusing on their sensory experience without moving. The order of trials was pseudorandomized to a matching number of trials per block. Each “modality block” was followed by a 5-min break and then alternated to the other modality. For an overview of the procedure, consult Figure 1.

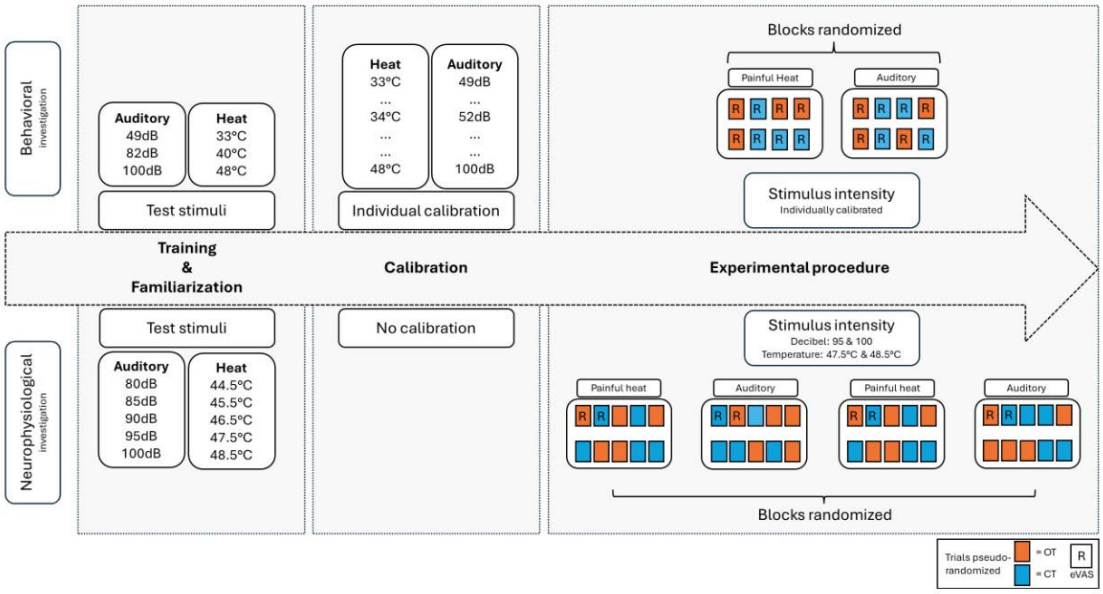

Figure 1. Study design. *Schematic representation of the study design of both experiments. After preparation, participants underwent a training & familiarization phase to accustom to stimuli and the operation of the electronic visual analogue scale (eVAS). In Experiment 1 (top of the figure), stimulus intensities were individually calibrated. The experimental procedure was split into two blocks (1 per modality) consisting of 8 trials with offset (OT) or constant (CT) trials in pseudorandomized sequence. In each trial, participants rated their sensory experience using the eVAS. A two-minute pause was conducted after each trial and a five-minute break was conducted after switching to the other modality. In Experiment 2 (bottom of the figure) fixed stimulus intensities were used. The experimental procedure was split into four blocks (2 per modality) consisting of 10 trials with offset (OT) or constant (CT) trials in pseudorandomized sequence. Each trial was followed by a two-minute break, and after each modality block participants had a five-minute break. The first two trials of each block were fixed to include an OT and CT (being randomized in order) and were used to collect the behavioral response. The remaining 8 trials did not include any eVAS ratings, only collecting neurophysiological responses.*

Statistical analysis

The determination of sample size was based on the effect sizes derived from the first experiment. For the auditory modality, an effect size of d_z = 0.64 (thermal d_z = 1.09), with statistical thresholds set at alpha = 0.05 and beta = 0.1 (90% power), indicated an estimated sample size of 28 participants. Due to the mentioned changes in temperature (see Familiarization and calibration procedure) and the exclusion of 11 participants that were previously recorded the final sample size for analysis was n = 29.

Statistical analyses were performed using R Studio (RStudio version 2024.04.11 with R version 4.5.0, R Foundation for Statistical Computing, Vienna, Austria) [55] and MATLAB [65]. Parametric data is presented in means ($\bar{x}$) with standard deviations (SD) and nonparametric data in median (M) with ranges (R) or absolute and relative frequencies. A 2x3 repeated-measures ANOVA with the factors 'trial' (CT, OT) and 'time' (T1, T2, T3) was calculated per modality. If there were significant effects, FDR corrected [3,4] post-hoc t-tests were performed. The level of significance was set at $p < 0.05$. For behavioral data analysis, the extracted time intervals matched the ones chosen in the first study. To analyze the EEG and pupillometry data, the extracted time intervals were shifted to right after onset of the stimulus, since we did not expect any delay in response compared to the behavioral data, resulting in T1 being 0-5s, T2 being 10-15s and T3 being 20-25s.

EEG preprocessing and analysis

The continuous EEG data were high-pass (1 Hz) and low-pass filtered (100 Hz), re-referenced to the average reference across all electrodes, and epoched from –5 to +40s relative to the onset of auditory/thermal stimulation. An independent component analysis (ICA) was used to remove components related to eye-blinks, eye-movements and muscle activity. Remaining artefactual epochs were removed afterwards by visual inspection. All data analyses were carried out in Matlab (R2024b), using custom scripts and the Fieldtrip toolbox [51]. Time-frequency oscillatory power representations of single-trial EEG data were obtained using Fast Fourier Transform (FFT) with multi-tapering (DPSS, discrete prolate spheroidal sequences) for a moving time window (length: 2s; moving in steps of 0.1s through the trial) for frequencies 1–80Hz in steps of 1 Hz with 2Hz spectral smoothing.

Pupillometry preprocessing

Similarly to EEG analysis, Fieldtrip [51] was used to conduct the necessary preprocessing steps for the pupillometry data. First, samples reflecting physiologically implausible pupil changes were identified using a velocity-based criterion: data points whose dilation speed exceeded three standard deviations above the mean velocity within each trial were marked as invalid. Next, short gaps of missing data (< 500 ms) were interpolated using a cubic spline method to reconstruct brief blink-related signal loss, following the recommendations of Sebastiaan Mathôt and Kret and Sjak-Shie [32,39]. Longer gaps were left unaltered to avoid introducing artificial signal. Finally, pupil size data from the left and right eye were averaged to obtain a single mean for subsequent analyses.

Results

A total of 62 healthy volunteers were recruited in this study (behavioral investigation: n = 33, behavioral + neurophysiological investigation: n = 29). All participants tolerated the selected stimulus intensities without difficulty and exhibited no signs of adverse events (see S2 and S3 Tables for details). An overview of stimulation parameters, as well as additional analyses for each individual experiment can be accessed in the Materials and Methods Section and the Supporting Information (S4 – S7 Tables).

Experiment 1

Temporal contrast enhancement is robust in heat-induced pain and aversive auditory stimulation

ANOVAs revealed interactions of time interval x trial type for auditory ($F(2, 64) = 43.77$, $p < 0.001$, $\eta_p^2 = 0.58$) and thermal ($F(2, 64) = 84.37$, $p < 0.001$, $\eta_p^2 = 0.73$) stimulation. Comparing trials using false discovery rate (FDR) -corrected post-hoc testing for auditory stimulation revealed no difference between OT and CT during T1 ($p = 0.65$). However,

significantly higher discomfort ratings for OT vs. CT in T2 ($p < 0.001$) and a reversal of this difference in T3 ($p < 0.001$) were observed, indicating that a return to the stimulus intensity of T1 induced a significant TCE effect in the interval of interest (T3). Similarly, post hoc testing for thermal stimulation showed no difference between OT and CT during T1($p = 0.49$), but significantly higher pain ratings for OT vs. CT in T2 ($p < 0.001$) and a reversal of this difference in T3 ($p < 0.001$). These findings demonstrate that TCE – a significant and disproportionate reduction in perceived intensity following a brief decrease in stimulus intensity – occurs for both, painful heat and aversive auditory stimulation.

Across participants, TCE effects (i.e. the OT - CT difference in T3) were not significantly correlated between auditory and thermal stimulation ($r = 0.26$, $p = 0.14$, $BF = 0.99$), indicating that the data were approximately equally likely under the null hypothesis and the alternative hypothesis. Additionally, to test temporal filtering within each modality, dependent-samples t-tests were calculated comparing T1 and T3 within each trial type. Auditory stimulation displayed significantly lower discomfort ratings in T1 compared to T3 despite constant stimulation (CT; $t(32) = -3.82$, $p < 0.001$, $d_z = 0.54$, $M_{DIFF} = -16.14$), indicating temporal loudness summation. However, no difference between T1 and T3 was found for offset trials (OT; $t(32) = 0.27$, $p = 0.79$, $d_z = 0.04$, $M_{DIFF} = 1.11$). To the contrary, for thermal stimulation, pain ratings decreased from T1 to T3 despite constant stimulation (CT, $t(32) = 4.28$, $p < 0.001$, $d_z = 0.60$, $M_{DIFF} = 17.81$), indicating temporal adaptation. Furthermore, a pronounced decrease in pain ratings from T1 to T3 was observed for offset trials (OT, $t(32) = 7.62$, $p < 0.001$, $d_z = 1.72$, $M_{DIFF} = 55.50$), resulting in a strong TCE effect. Figure 2 provides an Overview of the behavioral results.

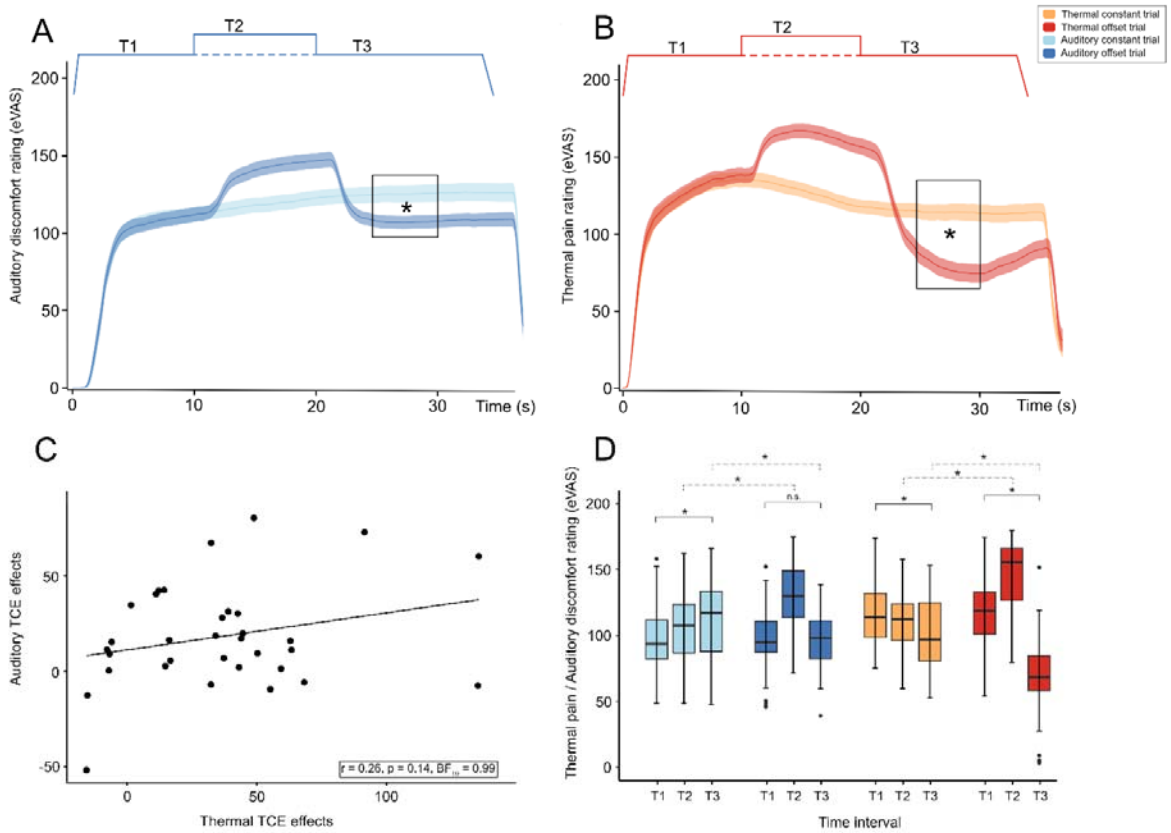

Figure 2: Behavioral Temporal Contrast Enhancement (TCE) response in two modalities (Experiment 1)*. Means and standard errors of the mean (SEM) for behavioral responses are displayed as obtained by an electronic visual analogue scale (eVAS). Thermal stimulation (A) and auditory stimulation (B) both induced significant (*, p < .05) TCE effects in T3 when comparing offset (OT) (darker colors) and constant (CT) (lighter colors) trials. The correlation of TCE effects (C) (CT-OT at T3 between both modalities was not significant. Boxplots of eVAS ratings (D) for each of the four conditions split into three relevant time intervals (T1: 5-10s, T2: 15-20s, T3: 25-30s). Significant (p < .05) within-modality comparisons indicated by solid lines, between-modality comparisons indicated by dashed lines.*

Experiment 2

The behavioral results were replicated in the second experiment, again indicating a significant interaction between time interval and trial type for auditory ($F(2, 56) = 62.10$, $p < 0.001$, $\eta_p^2 = 0.69$) and thermal ($F(2, 56) = 115.22$, $p < 0.001$, $\eta_p^2 = 0.80$) stimulation, respectively.

Pupil size reflects perception of pain but not auditory discomfort

When investigating the event-related pupil dilation to determine whether TCE is accompanied by modality-dependent autonomic modulation, auditory stimulation displayed a significant main effect of 'time' ($F(2, 56) = 32.67$, $p < 0.001$, $\eta_p^2 = 0.54$). FDR corrected post hoc testing revealed significant reduction in the pupil size for T3 vs. T2 ($p < 0.001$), T3 vs. T1 ($p < 0.001$) but not for T2 vs. T1 ($p = 0.74$). This indicates a gradual decrease in pupil size during the trial. For thermal stimulation, there was a significant interaction effect of 'trial type' and 'time' ($F(2, 56) = 64.35$, $p < 0.001$, $\eta_p^2 = 0.70$). Comparing trial types at different time intervals, resulted in significantly enhanced pupil size for OT vs. CT in T2 ($p < 0.001$) but not in T1 ($p = 0.88$) and T3 ($p = 0.08$). In addition to these planned statistical analyses, a exploratory cluster based permutation test [19] was performed, comparing OT and CT during the entire trial time course (see Figure 3).

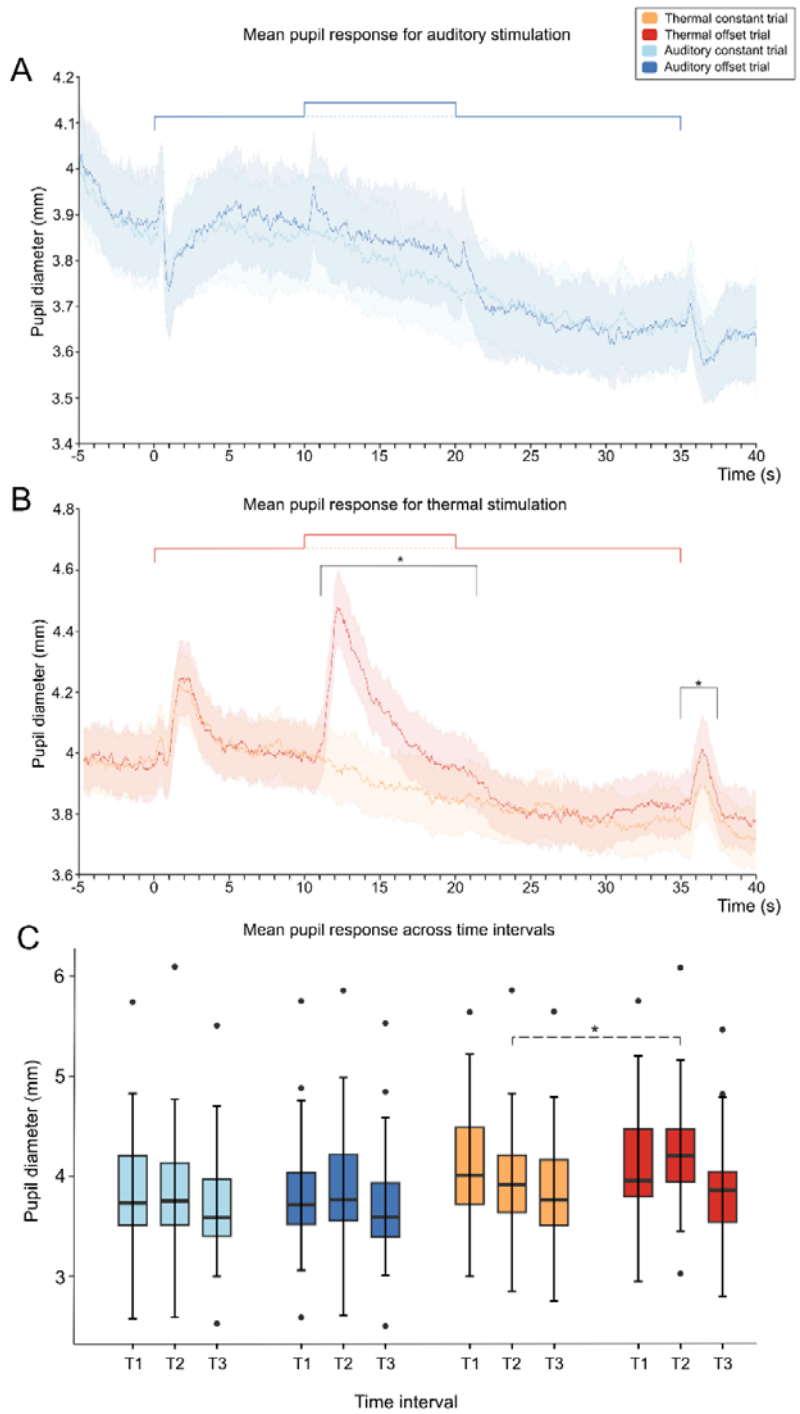

Figure 3 Mean pupil response over time. *Mean pupil diameter (mm) over time was measured for auditory (A) and thermal (B) stimulation. Thermal stimulation induced significant changes (*, $p < .05$; cluster-based permutation test) in the pupil diameter when comparing offset trials (OT, darker colors) with constant trials (CT, lighter colors). No significant clusters could be identified for auditory stimulation, despite visually observable changes to stimulus onset and offset. The timing of the stimulation intensity is displayed as a solid (OT) and dashed (CT) line at the top of the figure and was similar for both modalities. Mean pupil diameter (mm) for each condition (C) split into three time intervals (T1: 0-5s, T2: 15-20s, T3: 20-25s). Significant ($p < .05$) between-modality comparisons indicated by dashed lines.*

Neural alpha power reflects pain sensation and expectation

Conducting a modality-specific 2 (trial type) x 3 (time interval) ANOVA, revealed a significant main effect of 'time' ($F(2, 56) = 9.92$, $p < 0.001$, $\eta_p^2 = 0.26$) for auditory stimulation, while thermal stimulation displayed a significant interaction effect of 'trial' and 'time' ($F(2, 56) = 5.91$, $p = 0.005$, $\eta_p^2 = 0.17$). Comparing the different time intervals in auditory simulation with FDR corrected post-hoc tests resulted in a significant difference in alpha power between T1 and T2 ($p = 0.033$), T2 and T3 ($p = 0.004$), and T3 and T1 ($p = 0.004$), indicating an overall alpha power increase over time. The interaction effect in thermal stimulation was driven by a significant difference between OT and CT only for T2 ($p = 0.002$) but not for T1 ($p > 0.05$) and T3 ($p > 0.05$). See Figure 4, for a visual representation of alpha power over time.

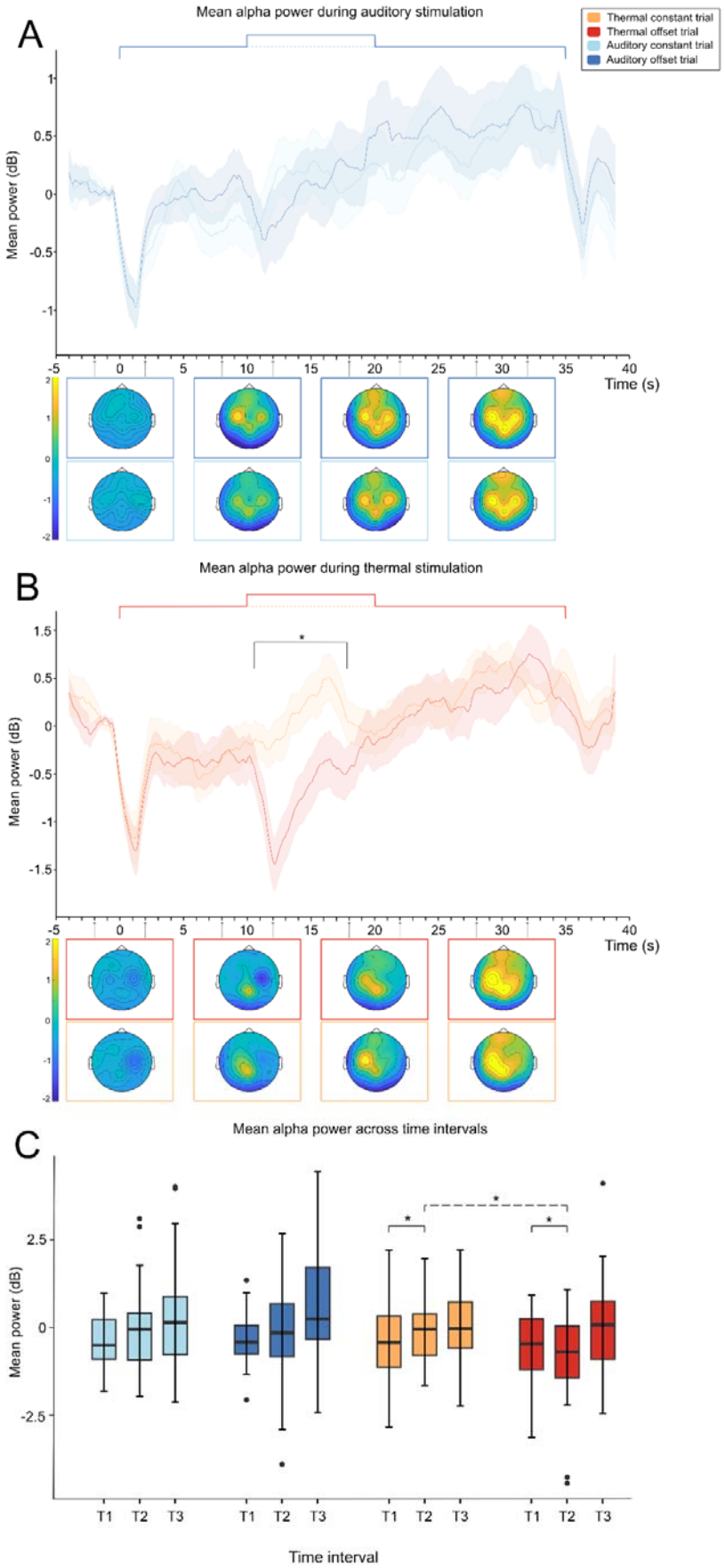
A
Mean alpha power during auditory stimulation
Thermal constant trial
Thermal offset trial
Auditory constant trial
Auditory offset trial
Mean power (dB)
Time (s)
B
Mean alpha power during thermal stimulation
Mean power (dB)
Time (s)
C
Mean alpha power across time intervals
Mean power (dB)
T1
T2
T3
Time interval

Figure 4: Mean alpha power over time for both modalities. *Auditory (**A**) and thermal (**B**) stimulation-induced mean alpha power (7–13 Hz) averaged across centro-occipital electrodes (P7, P3, O1, C3, POz, Pz, CPz, P8, P4, O2, C4). Topographic maps show spatial distributions of alpha power at time points 0, 10, 20 and 30 seconds (color limits: yellow = +2dB, blue = –2dB). Comparing alpha oscillatory power during Offset (OT) (darker colors) and Constant (CT) (lighter colors) trials using cluster-based permutation tests resulted in significant (*, p < .05) differences only during thermal stimulation. Mean (alpha) power for each condition (C) split into the three time intervals of interest (T1: 0-5s, T2: 10-15s, T3: 20-25s). Significant (p < .05) within-modality comparisons indicated by solid lines, between-modality comparisons indicated by dashed lines.*

Notably, significant alpha modulation in the T2 interval for thermal stimulation was attributable to two distinct underlying mechanisms reflecting the occurrence and expectation of the stimulus (Figure 5). Post-hoc tests comparing a baseline interval during T1 (5–10 s) to the time interval wherein a cluster-based permutation test indicated a significant difference for OT vs. CT (10.6 - 17.8 s; see Figure 4) revealed the following: First, the increase in thermal stimulation intensity induced an alpha power decrease in OT trials, resulting in significantly lower alpha power compared to T1 ($t(28) = -2.61$, $p = 0.015$, $d_z = 0.48$, $M_{DIFF} = -0.40$). Second, an omission of the expected increase in thermal stimulation intensity induced an alpha power increase in CT trials compared to the baseline interval during T1 ($t(28) = 3.34$, $p = 0.002$, $d_z = 0.62$, $M_{DIFF} = 0.49$). Additionally, a visual representation of the event-related potential can be accessed in the Supporting Information (S8 Fig. and S9 Fig.).

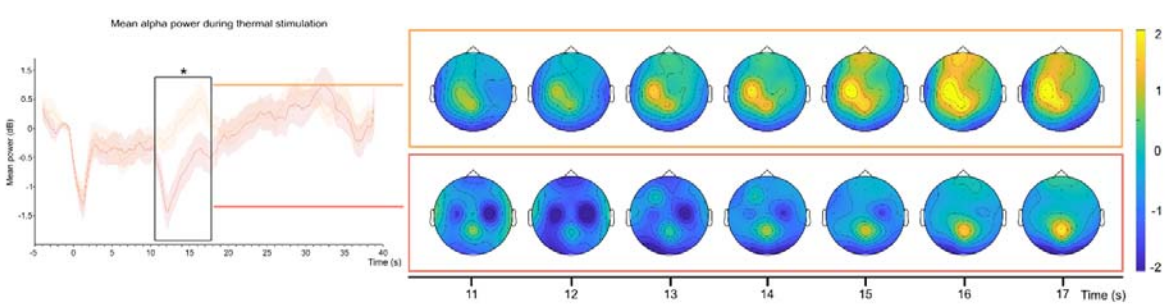

Figure 5: Topographic distribution of alpha power. *Stimulation-induced mean alpha power (7–13 Hz) averaged across centro-occipital electrodes (P7, P3, O1, C3, POz, Pz, CPz, P8, P4, O2, C4). Topographic maps show spatial distributions of alpha power at the significant time point (11 sec – 17 sec, one topography per second) of a cluster-based permutation test (* p < .05) comparing offset (OT) and constant (CT) trials (color limits: yellow = +2dB, blue = –2dB).*

Discussion

Temporal filtering operates across sensory modalities, including vision, audition, and pain perception [16,23]. Here, we aimed to delineate behavioral and (neuro-)physiological substrates of temporal filtering and to assess its specificity to pain and unpleasantness. To this end, we employed the phenomenon of TCE, a temporal filtering mechanism thought to underlie offset analgesia [72]. TCE was elicited by pain-inducing heat and aversive sound, indicating a supramodal temporal filtering process with distinct temporal dynamics across modalities. Pupil dilation, indexing autonomic nervous system activation, and alpha-band oscillations, reflecting cortical inhibition, were both modulated by temporal increases in noxious heat but not by auditory stimulation. However, these observations did not match the disproportionally large decrease in pain perception, that we observed in behavioral TCE ratings. Nonetheless, these findings suggest pain-specific temporal filtering acting on both the processing of painful input and its temporal expectation.

Modality-specific processes underlie temporal contrast enhancement

Consistent with prior evidence [26,62], we were able to successfully induce TCE using thermal stimulation. Noxious heat is known to produce robust TCE effects, indicated by statistically significant decreases in pain sensation following a brief heat offset [26] that far exceed natural adaptation to heat induced pain. To our knowledge, this is the first experiment investigating TCE using non-painful yet aversive auditory stimuli, demonstrating that TCE reflects a modality-general (i.e., supramodal) mechanism of afferent contrast filtering rather than a nociception-specific process. In addition to domain-general effects, we observed modality-specific patterns in subjective ratings, suggesting processing differences between modalities during the stimulation paradigm. When comparing different time intervals (T1 vs. T3) during constant stimulation, we found pain ratings decreasing over time while the opposite was observed for subjective auditory discomfort ratings. We argue that these novel observations

represent two different temporal filtering mechanisms. First, adaptation to pain, which is well-known to be induced by tonic heat [21,24]. Second, temporal sound summation, reflecting neural integration of auditory energy over time [7,52].

Comparing ratings between time windows of interest for offset trials, we found a typical decrease in perceived pain following heat offset (T3) compared to baseline (T1). In the auditory modality, however, the same contrast was not significant, suggesting a differently constituted TCE effect. Here, TCE was driven by a gradual increase in temporal sound summation during constant stimulation, which was absent during offset trials, thereby yielding a comparable overall TCE magnitude. Taken together, these results indicate temporal pain inhibition but an absence of such an effect for auditory stimulation. Importantly, the dissociation of underlying generators of TCE effects for pain and auditory stimulation receives further support from the absence of a correlation between TCE effects, suggesting partly independent mechanisms.

Neurophysiological signatures of filtering perception of pain and auditory discomfort

Alongside subjective behavioral responses, we collected objective neuro(physiological) measures (pupillometry and EEG) in a second experiment aiming to better understand the differences between the observed TCE effects for auditory vs. thermal stimulation. Thermal stimulation induced significant differences in pupil size between OT and CT in T2, the interval with the highest stimulus intensity. Reactive increases in pupil diameter to pain-inducing stimuli may reflect autonomic nervous system (ANS) activation, specifically sympathetic arousal associated with heightened awareness and the fight-or-flight response, as observed in previous studies on pupillary responses to pain [9,10,13,17,60]. Our observed phasic increases in pupil diameter likely reflect bottom-up processes induced by increases in stimulus temperature and are in line with previous research [10]. However, auditory stimulation did not display such trial type-specific differences, only eliciting significant decreases of pupil diameter over time. This

suggests that auditory discomfort did not elicit sizeable modulation of activity in the ANS. Possible explanations for this difference could be factors such as stimulus intensity or salience, with painful stimulation arguably resulting in a higher perceived threat level compared to auditory stimulation, hence inducing greater changes in pupil diameter.

Consistent with the pupillary dynamics, time–frequency EEG analyses revealed a similar modality-specific pattern: thermal stimulation elicited a significant alpha power reduction during offset trials in T2, which was not observed for auditory stimulation. A reduction of alpha power in response to painful stimulation is in line with previous reports of alpha decreases accompanying increased pain perception [25,48,54]. Moreover, when comparing T1 and T2 in OTs, we observed a significant alpha desynchronization, reflecting bottom-up processes associated with increased stimulus intensity. In contrast, CTs exhibited significant alpha synchronization (i.e., an alpha power increase) that may reflect top-down processes, possibly induced by expectation of an increase in painful stimulation. This is in line with prior research observing top-down processes influencing alpha oscillations [53]. For auditory stimulation, we hypothesized similar spatial and temporal patterns of oscillatory activity. However, no significant changes in alpha power were observed for either stimulation pattern. Given the comparable stimulation paradigm employed in both modalities, one could expect that participants would manifest a comparable increase in alpha power, driven by the anticipation of a change in stimulus intensity. However, no such effects were observed, which lends further support to the view that the neural modulation and representation of auditory discomfort differ from that of painful stimulation.

Interestingly, we did not observe any neurophysiological changes mirroring the TCE effect that we observed in behavior. Neither pupillometry, nor EEG displayed any significant modulations by trial type (OT vs. CT) during T3. Based on literature showing a robust link

between tonic pain and reduced alpha oscillatory power, we hypothesized that the TCE effect would elicit measurable changes in alpha activity—potentially an alpha increase reflecting the experienced relief - as it has been reported for placebo analgesia [28,36]. Contrary, we did not observe any representation of the behavioral TCE effects in neural recordings. One plausible explanation could be that the brain regions responsible for processing or mediating TCE are mainly located subcortically, which would be less accessible to surface EEG. Previous fMRI studies have reported changes to activity in the insula [47,71], structures of the brainstem [15,71], putamen and nucleus accumbens [74] or the spinal cord [58]. It might thus be that these structures are more relevant to TCE compared to the more superficially located ones. Furthermore, one should be cautious expecting identical findings when comparing fMRI to EEG, since both imaging techniques show distinct sensitivities to neural and hemodynamic processes, temporal and spatial resolution, and often can display different correlations depending on measured frequencies [34,45]. Additionally, subjective experiences such as changes in pain perception may not always align with objective indices, which could be the case for TCE. Our pupillometry findings provide partial support for this hypothesis, since both modalities displayed temporal filtering as evidenced by decreases in pupil diameter over time. However, these temporal patterns did not correspond with the observed patterns in the subjective domain, where only pain decreased over time, but auditory discomfort increased. However, to our knowledge, studies investigating TCE employing objective measures besides fMRI are scarce [46,63,67] making it difficult to assess the extent to which subjective and physiological responses to TCE diverge and whether our findings reflect such an incongruence.

We observed modality-specific patterns of temporal dynamics, particularly represented in the behavior of participants. An identical stimulation paradigm was employed for all trials, enabling direct comparison between modalities and providing a common framework for interpreting differences in temporal filtering dynamics. As demonstrated in previous research,

TCE has been consistently identified as a highly robust filtering mechanism in pain. TCE effects can be induced with a variety of stimulus intervals, temperature changes and even repeated instead of tonic stimuli [26,61,62]. However, future research could benefit from the use of variable stimulus sequences to further improve our understanding of these supramodal temporal filtering dynamics, driving TCE across modalities. Additionally, the aim should be to characterize the temporal dynamics of TCE in different sensory modalities without compromising spatial resolution, ideally incorporating approaches that target subcortical regions potentially underlying the effect. Further exploration of pain-specific paradigms, and of potential shared filtering mechanisms across sensory modalities, may provide deeper insight into how such processes shape perceptual experience in our multisensory environment.

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