Extinction-resistant attention to long-term conditioned threat is indexed by selective visuocortical alpha suppression in humans

Christian Panitz[a] (christian.panitz@staff.uni-marburg.de),

Andreas Keil[b] (akeil@ufl.edu),

&

Erik M. Mueller[a] (erik.mueller@staff.uni-marburg.de)

[a]University of Marburg, Department of Psychology, Gutenbergstr. 18, 35032 Marburg, Germany

[b]University of Florida, Center for the Study of Emotion and Attention, 3063 Longleaf Road, Gainesville, FL 32608, USA

This study was supported by a grant of the German Research Foundation to Erik M. Mueller [DFG MU3535/2-1]. None of the authors has financial interests or other potential conflicts of interest.

Correspondence concerning this article should be addressed to Christian Panitz, Department of Psychology, University of Marburg, Gutenbergstr. 18, 35032 Marburg, Germany.

E-mail: christian.panitz@staff.uni-marburg.de

22 pages

4 figures

1 table

Abstract: 151 words

Introduction: 649 words

Discussion: 1195 words

Abstract

While ERP studies have shown heightened early visual attention to conditioned threat, it is unknown whether this attentional prioritization is sustained throughout later processing stages and whether it is robust to extinction. To investigate sustained visual attention, we assessed visuocortical alpha suppression in response to conditioned and extinguished threat. N = 87 male participants underwent a two-day threat conditioning paradigm with acquisition and extinction on one day and a critical recall test one day later. EEG time-frequency analyses revealed that, on Day 2, threat-conditioned vs. safety cues evoked stronger occipital alpha power suppression from 600 to 1200 ms. Notably, this suppression was resistant to extinction. The present study showed for the first time that threat conditioning enhances sustained modulation of visuocortical attention to threat in the long term. The long-term stability and extinction resistance of alpha suppression suggests a crucial role of visuocortical attention mechanisms in the maintenance of learned fears.

Keywords: threat; long-term conditioning; long-term extinction; alpha; visual attention

Significance Statement

The present study highlights how selective attentional mechanisms may contribute to the long-term stability of learned fearful behaviors via increased recruitment of early visual cortex areas. Participants were classically conditioned to learn about threat cues predicting an aversive noise and safety cues. As evident in sustained occipital alpha suppression in the EEG – a marker for visuocortical recruitment – individuals showed selectively increased attention to threat cues in a recall test one day after initial conditioning. Importantly, this effect was not affected by intermediate extinction training, where threat cues were not followed aversive noises. Our findings are important for understanding the development and long-term maintenance of fears as well as etiology and therapy of anxiety disorders.

Introduction

Learning to predict threat and safety based on environmental cues is fundamental for adaptive behavior. A well-established paradigm for elucidating mechanisms of associative cue-outcome learning is classical threat conditioning (also fear/aversive conditioning) where conditioned stimuli are threat cues (CS+) when they signal an upcoming aversive event (unconditioned stimulus; US) and safety cues (CS-) when they signal the absence of an aversive event (Rescorla and Wagner, 1972; LeDoux, 2014; Lonsdorf et al., 2017). The acquired conditioned defensive response to the CS+ is expected to diminish again upon extinction training, i.e., repeated presentation of CS+ without US (Myers and Davis, 2007; Quirk and Mueller, 2008).

Importantly, both conditioning and extinction memories need to be consolidated, retained, and recalled in future situations to allow adaptive responding in the long term. Successful short-term learning – i.e., acquisition and extinction of a conditioned response within an experimental session – is considered necessary but not sufficient for successful long-term learning. Such long-term learning effects are indicated by the successful recall of previously acquired and extinguished contingencies in a delayed test session (Myers and Davis, 2007; Quirk and Mueller, 2008). Importantly, acquisition and extinction learning form separate memory traces and individuals may recall previously acquired threat memories without recalling extinction memories. In other words, they may show long-term extinction resistance, which is assumed to be key in the maintenance of fears (Lissek et al., 2005; Milad and Quirk, 2012; Duits et al., 2015). In this case, despite repeated omission of aversive events, individuals keep showing robust conditioned threat responses over time.

Conditioned threat responses have different functions and manifest at various levels of central and autonomic physiology. Among these, increased attentive processing promotes capture of threat-relevant information, improving chances of successful defensive responding (Bradley, 2009; Lang and Bradley, 2010). Supporting this notion, studies using visual evoked brain potentials in humans have found selectively heightened visual attention when viewing threat cues (Bublatzky and Schupp, 2012; Michalowski et al., 2015; Gruss et al., 2016; Muench et al., 2016; Wieser et al., 2016; Kastner-Dorn et al., 2018). However, because visual evoked potentials to threat generally reflect early brain activity (i.e. < 500 ms; Miskovic and Keil, 2012), it is unknown, whether enhanced visual attention is

sustained throughout later visual processing stages. Moreover, it is unclear, if heightened attention displays long-term resistance to extinction. These are clinically relevant questions given that enduring prioritization of threat processing may interfere with fear reduction through extinction and exposure therapy. The present study addresses these questions using a robust electrophysiological marker of sustained visual attention, suppression of visuocortical oscillatory activity in the alpha range.

Alpha oscillations (e.g., 8-12 Hz; de Cesarei and Codispoti, 2011; Bartsch et al., 2015) indicate inhibition processes in neural populations (Pfurtscheller, 2001; Klimesch et al., 2007). Visually evoked posterior alpha suppression has been associated with increased excitability of early visual areas in the occipital cortex (Klimesch et al., 2011; Scheeringa et al., 2016; Green et al., 2017; Iemi et al., 2017; Iemi and Busch, 2018) in response to increased attentional demands (Foxe and Snyder, 2011; Klimesch, 2012; Ben-Simon et al., 2013; Frey et al., 2015). Moreover, posterior alpha power suppression has been found stronger in response to aversive vs. neutral/appetitive pictures (Huster et al., 2009; de Cesarei and Codispoti, 2011; Vagnoni et al., 2015; but also see Uusberg et al., 2013), taken to reflect prioritized visual processing of threat information (Bradley, 2009; Lang and Bradley, 2010).

In the present study, we estimated current source density of alpha-band activity at scalp sites consistent with visuocortical sources, to investigate (a) whether heightened visuocortical alpha suppression indexes selective visual attention to threat cues one day after conditioning, and (b) if conditioned alpha suppression is extinguished in the long term. We employed a two-day differential threat conditioning paradigm with threat acquisition and extinction on one day and a critical recall test one day later, comparing alpha power changes in response to previously extinguished vs. non-extinguished CS.

Materials and Methods

Sample

We analyzed data of a sample of N = 87 healthy, male participants (mean age: 23.7, SD: 3.85, range: 18-34), described in more detail elsewhere (Panitz et al., 2018). Participants were compensated 65 € (ca. 75 US$) for two experimental sessions (total 7 hours on two subsequent days). The study was conducted in accordance to the Declaration of Helsinki and was approved by the ethics committee of the German Psychological Association (DGPs).

Experimental Design

Conditioning and Extinction paradigm. We employed a two-day differential threat conditioning and extinction paradigm (Mueller et al., 2014; Panitz et al., 2018; also see Figure 1). Briefly, on Day 1, participants underwent CS habituation, followed by an acquisition phase. Two CS (CS+E, CS+N) were paired with a US in 21 out of 45 trials (46.6 %), the other two CS (CS-E, CS-N) were never paired with the US (also 45 trials per CS). The extinction phase started exactly three hours after the end of acquisition and consisted of 40 CS+E and CS-E presentations ('E' standing for *presented during extinction phase)*. CS+N, CS-N, and US were not presented during the extinction phase ('N' standing for *not presented during extinction phase)*. Approximately 24 h after the extinction, participants returned for a Day 2 recall test which included 60 trials of each CS. No US were presented on Day 2.

Stimuli and trial structure. We used four different male faces with neutral expression from the Karolinska Directed Emotional Faces set (Lundqvist et al., 1998) as CS (pictures: AM10NES, AM13NES, AM31NES, BM08NES; also see Figure 1). Assignment of face stimuli to the different CS types was permutated and balanced across participants. The US was a 1 s white noise burst at 95 dB(A) delivered by a room speaker as we had previously shown that noise bursts are particularly well suited for threat conditioning with many trials (Sperl et al., 2016). In every trial, a fixation cross (1 s duration) was presented before participants saw the CS for 4 s. In paired trials the CS co-terminated with the US for 1 s. A black screen (jittered duration, 6-8 s) was presented between trials.

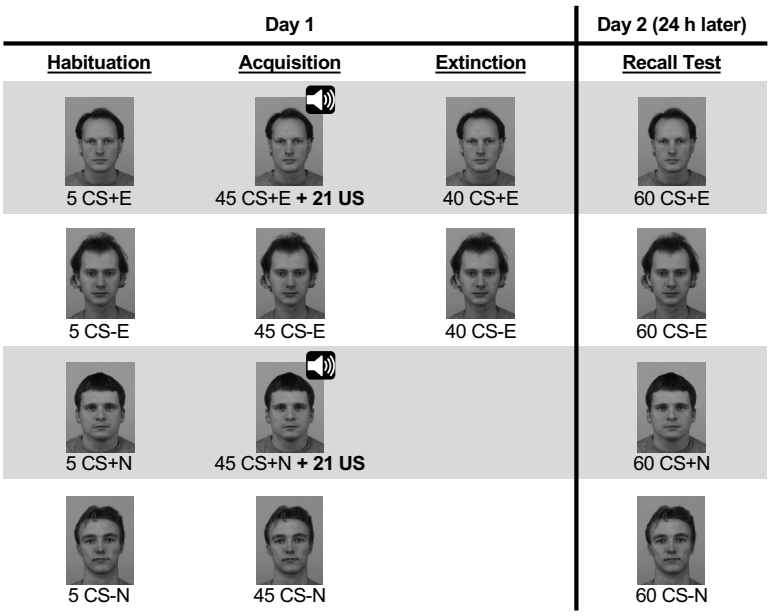

Figure 1. **Conditioning and extinction paradigm**. Face stimuli and number of presentations in the two-day differential threat conditioning and extinction paradigm. The US was only presented during acquisition, indicated by the speaker symbol. Assignment of different faces to CS type was permutated across participants. CS+E = extinguished CS+, CS+N = non-extinguished CS+, CS-E = CS- presented during extinction phase, CS-N = CS- not presented during extinction phase. Stimuli were presented in color. KDEF stimuli IDs from top to bottom: AM10NES, AM13NES, AM31NES, BM08NES. Figure from Panitz et al. (2018).

EEG recording and preprocessing

64-channel EEG was recorded with a QuickAmp72 amplifier and actiCAP active electrodes (Brain Products, Gilching, Germany) at 1000 Hz, with a 200 Hz online lowpass-filter and referenced against the average. EEG processing was performed in BrainVision Analyzer 2 (Brain Products, Gilching, Germany). The EEG was downsampled to 500 Hz, highpass-filtered (-3 dB at 0.1 Hz, 24 dB/oct., zero-phase IIR Butterworth filter) and notch-filtered (50 Hz, 5 Hz bandwidth, 16th order). Extended Infomax ICA (Lee et al., 1999) was applied to the continuous data. Critical independent components reflective of horizontal and vertical eye movements, blinks, and cardiac artifacts were identified and removed by an experienced rater. To increase signal stationarity required for ICA, large EEG artifacts were removed manually, the signal was 0.5 Hz highpass-filtered for ICA only and the resulting weights were subsequently applied to the 0.1 Hz filtered data (Winkler et al., 2015). Segments with remaining artifacts were removed manually and channels with excessive amounts of bad data were interpolated (spline interpolation). Continuous EEG data were lowpass-filtered (30 Hz,

filter specifications identical to highpass filter). After correcting marker latencies for monitor delay (33 ms), data were segmented relative to CS onset (-600 to 2000 ms).

To estimate current source density and improve the spatial specificity of the voltage map, the surface Laplacian was computed using the algorithm of Perrin, Pernier, Bertrand, and Echallier (1989) as implemented in BrainVision Analyzer 2 (spline order: 4, Legendre polynomial: 10, lambda: 1e-5). In order to facilitate comparison with previous studies, we also analyzed the average-referenced scalp data. The results converged with the present results in the surface Laplacian data and are available on OSF (Panitz et al., 2019).

Wavelet analyses

Wavelet analyses were conducted in MATLAB 2013a (MathWorks, Natick, MA, USA) using established custom scripts (Keil et al., 2007). First, EEG segments in the time domain were baseline-corrected (subtraction of the mean from -600 to -500 ms) and tapered with a cosine square window (20 samples rise/fall). Complex Morlet wavelets were applied with variable bandwidths (Morlet parameter $= f/\sigma_f = 12$) to compute power for frequency bands from 3.8 to 30.4 Hz in linear steps of 0.38 Hz. Power in each frequency band was baseline-corrected by dividing the signal by the mean amplitude between -400 ms and -200 ms relative to CS onset. Mean power of all discrete frequencies from 8.1 Hz to 11.9 Hz (e.g., de Cesarei and Codispoti, 2011; Bartsch et al., 2015) was used for statistical analyses on alpha.

Statistical analyses

Statistical analyses were performed with R (R Core Team, 2018) in the RStudio environment (Team, 2016). In order to assess the influence of Day 1 learning on occipital alpha during Day 2, we computed mean alpha power across Oz and adjacent electrodes (Oz, POz, O1, and O2) in the time window of 500 – 1200 ms after the CS. The resulting values were entered into an ANOVA with the within-subject factors Contingency (CS+ vs. CS-) and Extinction (extinguished vs. non-extinguished) using the *aov* function in R. In addition to null-hypothesis testing, we conducted Bayesian analyses as implemented in the *anovaBF* function in the BayesFactor package (Morey and Rouder, 2018) for R.

We computed Bayes factors (100,000 iterations) for four different models (main effect Contingency only, main effect Extinction only, additive model of Contingency + Extinction main effects, complete model including both main effects and the interaction term; cf. Rouder et al., 2016) compared to the null model (BF_{10}). All models had equal prior probabilities and included a random effect term to account for between-subject variance. In a second step, we computed Bayesian inclusion factors (BF_{Incl}) for each effect (i.e., Contingency, Extinction, and Contingency x Extinction) that indicate whether models including this effect are more likely to explain the data than matched models without this effect. More precisely, all models containing the effect of interest – but no higher-order interactions of this effect – were compared to matched models stripped of the effect (BAWS factor suggested by Sebastiaan Mathôt; also implemented in JASP 0.9, JASP Team, 2018). As an example, for the Contingency effect, the models *Contingency only* and *Contingency + Extinction* were compared to the null model and the *Extinction only* model.

After using a predefined time window (500 to 1200 ms; Vagnoni et al., 2015; Chien et al., 2018) for hypothesis testing, we conducted follow-up analyses on the exact time window of the Contingency effect based on the present data. We used permutation-controlled *t*-tests (adapted from the t_{max} approach from Blair and Karniski, 1993), comparing alpha power (averaged across Oz, POz, O1, O2) at each time sample between both CS+ and both CS- (i.e., Contingency contrast). First, we randomly permutated the CS+ and CS- condition in each participant 1,000 times and computed *t*-values for each of the 1,300 time samples. Then, the tails of each permutation's *t*-value distribution were determined and stored in a t_{min} and t_{max} distribution, respectively, each having 1,000 values corresponding to the 1,000 permutations. Finally, 2.5^{th} and 97.5^{th} percentiles from the resulting distribution of t_{min} and t_{max} values were used as critical *t*-values to compare empirical *t*-values against (i.e., $\alpha = .05$, two-sided; t_{crit}: CS+ < CS-: -2.59; CS+ > CS-: 2.64).

Open Data and Materials

Scripts for stimulus presentation and response logging in Presentation (Neurobehavioral Systems, Inc., Berkeley, CA) as well as single-participant data (.txt files) and R scripts for statistical analyses are available on OSF (Panitz et al., 2019).

Results

Conditioning and extinction effects during Day 2 recall test

The ANOVA showed a significant main effect of Contingency ($F(1, 86) = 9.85$, $p = .002$, $\eta_p^2 = .103$) as CS+ were followed by a stronger suppression of alpha power compared to CS- (also see Figure 2). Meanwhile, the main effect Extinction ($F(1, 86) = 0.18$, $p = .669$, $\eta_p^2 = .002$) and the Contingency x Extinction interaction ($F(1, 86) = 1.29$, $p = .259$, $\eta_p^2 = .015$) were not significant.

In line with the frequentist ANOVA, Bayesian ANOVA provided strongest evidence for a main effect of Contingency in the absence of other effects ($BF_{10} = 26.0$, all other models: $BF_{10} < 3.3$). In line with this pattern, Bayesian inclusion factors provided support for the inclusion of the main effect of Contingency ($BF_{Incl} = 25.9$) and against the inclusion of the main effect of Extinction ($BF_{Incl} = 1 / 8.1$) or the Contingency x Extinction interaction ($BF_{Incl} = 1 / 4.0$). Figure 3 shows time-frequency plots and topographic mapping of the Contingency effect on alpha power.

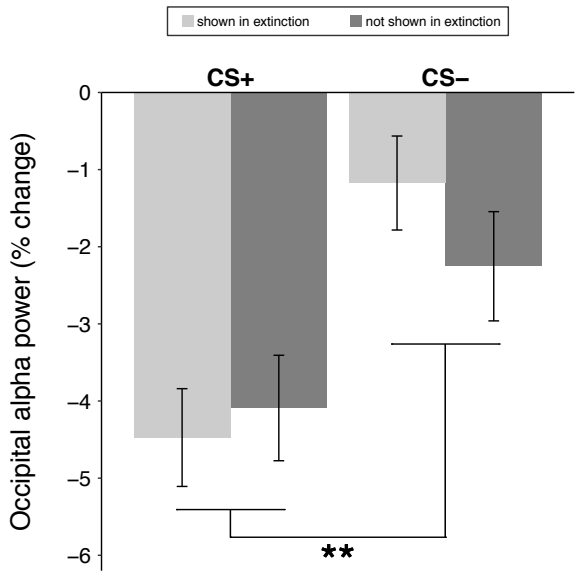

Figure 2. **Conditioning effects on Day 2 alpha power.** Mean alpha power (relative to baseline) at occipital sites in the time window of 500 – 1200 ms. Light bars represent CS presented during Day 1 extinction, dark bars represent CS not presented during Day 1 extinction. Error bars indicate SEM based on within-subject variance. **p < .01 for the main effect of Contingency.

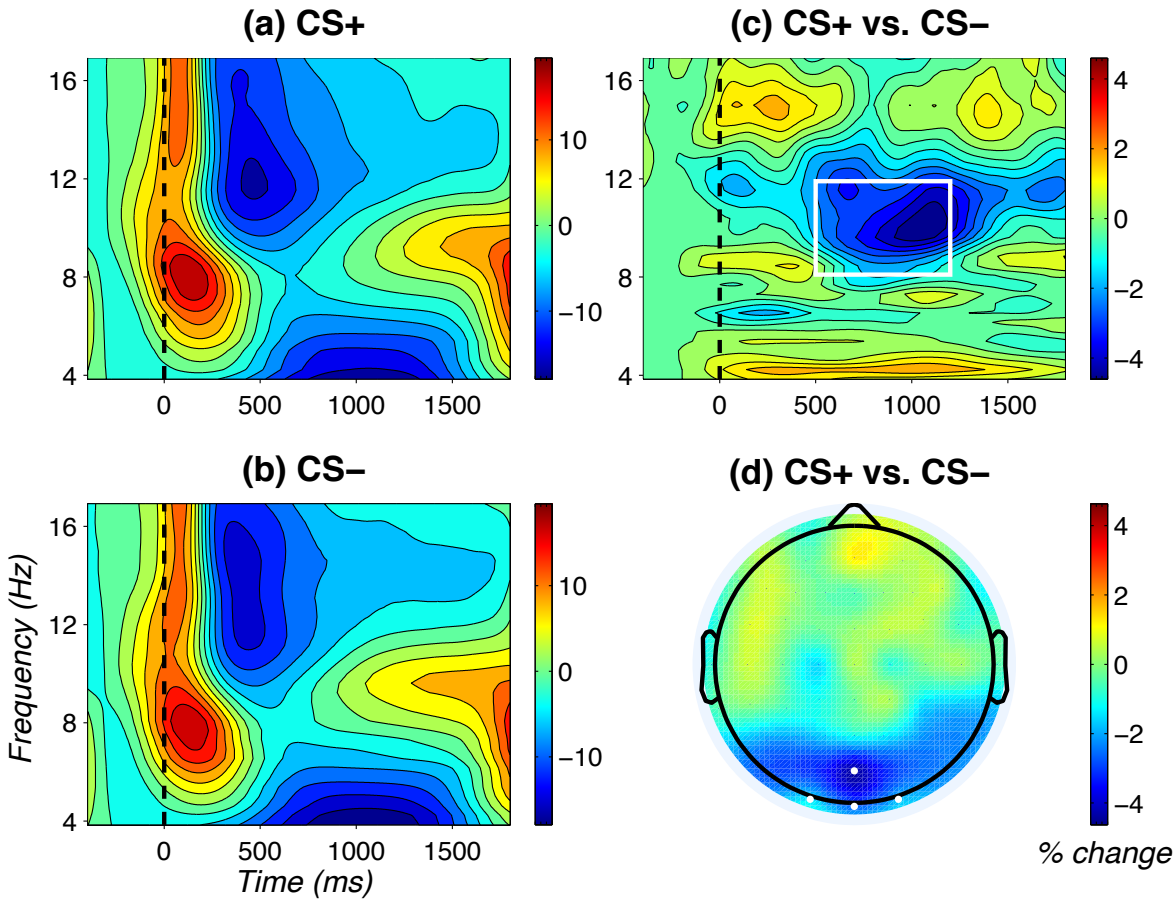

***Figure 3*. Main effect of Contingency on occipital alpha power. (a)** and **(b)** Time-frequency plots for CS+ and CS-, respectively. Power values are % change relative to baseline (-400 to -200 ms) and averaged across Oz, POz, O1, and O2. **(c)** Time-frequency plot of the difference between CS+ and CS-, across Oz, POz, O1, and O2; the white rectangle indicates time (500 to 1200 ms) and frequency (8.1 to 11.9 Hz) windows for statistical analyses. **(d)** Topography of the difference between CS+ and CS- in the a priori defined time window (500 to 1200 ms). White dots depict the electrodes used for statistical analyses.

Time course of Contingency effect

As suggested by permutation *t*-tests, viewing CS+ compared to CS- prompted significantly lower alpha power in the time window from 630 to 1230 ms post-CS (Figure 4), largely converging with our a priori window (500 to 1200 ms).

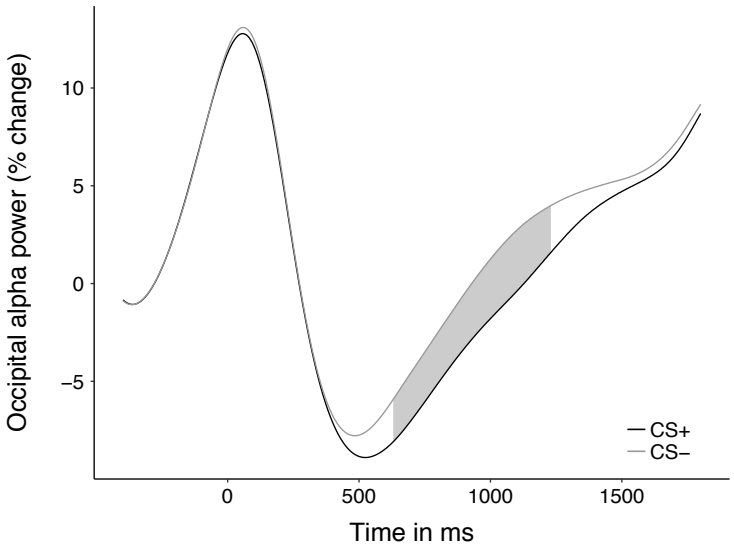

Figure 4. **Time course of Contingency effect on mean occipital alpha power.** Alpha power (relative to baseline) for collapsed CS+ and CS-, respectively, averaged across occipital sites. The gray-shaded area indicates significant differences between CS+ and CS- as determined by permutation testing ($p < .05$, two-sided).

Discussion (max 1500 words)

In the present study, we investigated the role of heightened selective attention to threat cues in long-term threat conditioning and extinction. For this purpose, participants underwent a differential threat conditioning paradigm with acquisition and extinction on Day 1 and a test phase on Day 2 that allowed to assess long-term recall of extinguished and non-extinguished threat-conditioned responses. We found that, one day after threat conditioning, CS evoked a suppression of alpha power at occipital sites between 600 and 1200 ms, which was more pronounced for threat cues (i.e., CS+) compared to safety cues (i.e., CS-). Importantly, this conditioning effect was unaffected by Day 1 extinction training.

In the present sample, we observed robust alpha power suppression at occipital electrodes that was stronger for threat-conditioned CS+ than for CS-. This is the first time that occipital alpha power suppression is shown in response to conditioned threat cues. The present effects converge with previously shown alpha suppression to naturally threatening stimuli (Huster et al., 2009; de Cesarei and Codispoti, 2011; Vagnoni et al., 2015) and can be interpreted as stronger disinhibition of early visuocortical areas facilitating attentional prioritization of behaviorally more relevant (i.e., threat) cues (Foxe and Snyder, 2011; Frey et al., 2015). They are also consistent with previous ERP research showing threat-related prioritization of visuocortical processing (Bublatzky and Schupp, 2012; Michalowski et al., 2015; Gruss et al., 2016; Mueller and Pizzagalli, 2016; Muench et al., 2016; Wieser et al., 2016; Thigpen et al., 2017; Kastner-Dorn et al., 2018). Prioritization of threat is highly important for the successful choice of adaptive responding (Bradley, 2009; Lang and Bradley, 2010; Bradley et al., 2012), given limited capacities for information processing in the brain (Broadbent, 1965; Lavie, 2005; Chun et al., 2011).

Threat-potentiated alpha suppression was found in the time window from about 600 to 1200 ms post-CS. Therefore, this alpha suppression likely indicates *sustained* attention allocation to the threat cue via recruitment of visuocortical resources (de Cesarei and Codispoti, 2011). This process may be initiated after initial stimulus recognition and affective stimulus categorization as presumably indicated by early event-related potential (Schupp et al., 2006; Miskovic and Keil, 2012) and may reflect a more thorough analysis of threat cues. Taken together, the present results suggest occipital

alpha as a promising new marker of sustained visuocortical attention modulation in response to conditioned threat cues.

Importantly, the stronger alpha suppression in response to CS+ was evident one day after initial learning, indicating successful long-term recall of selectively increased attention allocation to threat cues. To our knowledge, this is the first study to show such long-term threat conditioning effects on selective visual attention, stable across timely spaced situations. The long-term stability of the present alpha suppression suggests selective attention modulation in threat as a central feature of stable fear. While there is some evidence that selective attention to threatening information contributes to the long-term maintenance of fear (Richards et al., 2014; Van Bockstaele et al., 2014), the neural underpinnings of this link are not well understood. The present study suggests a mechanism in which differential activation of visuocortical areas is a temporally stable threat-conditioned response and underlies increased attentional processing of threat cues across time. Increased attentional threat processing may consolidate fearful behavior via increased levels of state fear (and other negative affects; MacLeod et al., 2002; Van Bockstaele et al., 2014) and by a reduced ability to disengage from threat cues at the cost of other potentially relevant stimuli (Fox et al., 2002; Georgiou et al., 2005; Rinck et al., 2005) – e.g., concurrent safety cues or cues for successful coping. Moreover, attentional biases may interact with negative expectancy, memory, and interpretation biases related to threat (Aue and Okon-Singer, 2015). Future studies may use occipital alpha to investigate these and other potential mechanisms in order to elucidate attentional mechanisms of long-term fear maintenance.

In addition to long-term threat recall, we observed long-term extinction resistance of threat-conditioned alpha suppression. In other words, the initially threat-conditioned CS+ continued to evoke conditioned threat responses on Day 2, regardless of Day 1 fear extinction. The conclusion of extinction resistance was backed by Bayesian analyses, which favored models excluding the extinction factor. Note that the present result pattern of extinction-resistant alpha suppression mirrors the pattern of long-term extinction-resistance of (a) rapid processing enhancements of threat-conditioned faces (Mueller and Pizzagalli, 2016) and (b) cardiac deceleration in the present sample (Panitz et al., 2018) as well as in previous studies (Panitz et al., 2015; Sperl et al., 2016). Threat-evoked cardiac deceleration has been suggested to also reflect attentional processes, namely orienting in the face of

imminent harm (Löw et al., 2015; Bastos et al., 2016; Roelofs, 2017; Wendt et al., 2017). On the other hand, the present sample showed reduced differential skin conductance responses for extinguished (CS+E vs. CS-E) compared to non-extinguished (CS+N vs. CS-N) threat cues (Panitz et al., 2018), which indicates successful extinction recall of CS-US contingency awareness (Hamm and Vaitl, 1996). This suggests that attention-related processes in general, and occipital alpha suppression in particular, could be more extinction-resistant than other conditioned responses and may occur in a better-safe-than-sorry fashion. In other words, the cost of increased attentional engagement to invalid threat cues (i.e., false alarms) may be judged as significantly smaller than the cost for overlooking valid threat cues – even after repeated omission of harmful events.

As discussed earlier, alpha-related attentional processes may be crucial in the long-term maintenance of fears. The observed extinction resistance in the present study suggests that former threat cues continue drawing on attentional resources even in the absence of contingent reinforcement by harmful outcomes, i.e., even when cues are not followed by negative consequences anymore after initial learning. Moreover, occipital alpha suppression may prove useful for investigating the influence of threat-focused attention and attentional biases on the effectiveness of exposure therapy (Barry et al., 2015; Mogg and Bradley, 2018) .

The limitations of the current study should be addressed. First, using the current paradigm, it cannot be ruled out that CS+ evoked stronger alpha suppression than CS- due to partial reinforcement and changing contingencies across phases, making predictions of US occurrence more difficult in CS+ vs. CS- and motivating participants to process CS+ more thoroughly. This, however, is unlikely to explain the present effects given that threat-depicting pictures, with no learning history, also evoked stronger alpha suppression in previous studies (Güntekin and Basar, 2007; Huster et al., 2009; de Cesarei and Codispoti, 2011; Vagnoni et al., 2015). Second, we only used male participants in order to investigate conditioning and extinction without the influence of known sex differences (Lebron-Milad et al., 2012; Merz et al., 2012). As there also may be gender differences in visuocortical threat processing (Sass et al., 2010; Pintzinger et al., 2017), the present results should be replicated in females.

In the present study, we could show that conditioned visual threat cues evoke enhanced alpha suppression at occipital sites. Moreover, we showed for the first time that increased attention allocation to conditioned threat cues via sustained recruitment of early visuocortical areas is long-term stable and resistant to extinction. Future studies may use occipital alpha power to further elucidate mechanisms of visual attention in the development, maintenance, and extinction of fears.

References

Aue T, Okon-Singer H (2015) Expectancy biases in fear and anxiety and their link to biases in attention. Clin Psychol Rev 42:83–95.

Barry TJ, Vervliet B, Hermans D (2015) An integrative review of attention biases and their contribution to treatment for anxiety disorders. Front Psychol 6:968.

Bartsch F, Hamuni G, Miskovic V, Lang PJ, Keil A (2015) Oscillatory brain activity in the alpha range is modulated by the content of word-prompted mental imagery. Psychophysiology 52:727–735.

Bastos AF, Vieira AS, Oliveira JM, Oliveira L, Pereira MG, Figueira I, Erthal FS, Volchan E (2016) Stop or move: Defensive strategies in humans. Behav Brain Res 302:252–262.

Ben-Simon E, Podlipsky I, Okon-Singer H, Gruberger M, Cvetkovic D, Intrator N, Hendler T (2013) The dark side of the alpha rhythm: FMRI evidence for induced alpha modulation during complete darkness. Eur J Neurosci 37:795–803.

Blair RC, Karniski W (1993) An alternative method for significance testing of waveform difference potentials. Psychophysiology 30:518–524.

Bradley MM (2009) Natural selective attention: Orienting and emotion. Psychophysiology 46:1–11.

Bradley MM, Keil A, Lang PJ (2012) Orienting and emotional perception: facilitation, attenuation, and interference. Forntiers Psychol 3:493.

Broadbent DE (1965) Information Processing in the Nervous System. Science (80-) 150:457–462.

Bublatzky F, Schupp HT (2012) Pictures cueing threat: Brain dynamics in viewing explicitly instructed danger cues. Soc Cogn Affect Neurosci 7:611–622.

Chien JH, Colloca L, Korzeniewska A, Cheng JJ, Campbell CM, Hillis AE, Lenz FA (2018) Oscillatory EEG Activity Induced by Conditioning Stimuli During Fear Conditioning Reflects Salience and Valence of these Stimuli More than Expectancy. Neuroscience 346:81–93.

Chun MM, Golomb JD, Turk-Browne NB (2011) A Taxonomy of External and Internal Attention. Annu Rev Psychol 62:73–101.

de Cesarei A, Codispoti M (2011) Affective modulation of the LPP and α-ERD during picture viewing. Psychophysiology 48:1397–1404.

Duits P, Cath DC, Lissek S, Hox JJ, Hamm AO, Engelhard IM, Van Den Hout MA, Baas JMP (2015) Updated meta-analysis of classical fear conditioning in the anxiety disorders. Depress Anxiety 32:239–253.

Fox E, Russo R, Dutton K, Fox E, Russo R, Dutton K (2002) Attentional bias for threat: Evidence for delayed disengagement from emotional faces. Cogn Emot 16:355–379.

Foxe JJ, Snyder AC (2011) The role of alpha-band brain oscillations as a sensory suppression mechanism during selective attention. Front Psychol 2:154.

Frey JN, Ruhnau P, Weisz N (2015) Not so different after all: The same oscillatory processes support different types of attention. Brain Res 1626:183–197.

Georgiou GA, Bleakley C, Hayward J, Russo R, Dutton K, Eltiti S, Fox E (2005) Focusing on fear: Attentional disengagement from emotional faces. Vis cogn 12:145–158.

Green JJ, Boehler CN, Roberts KC, Chen L-C, Krebs RM, Song AW, Woldorff MG (2017) Cortical and Subcortical Coordination of Visual Spatial Attention Revealed by Simultaneous EEG–fMRI Recording. J Neurosci 37:7803–7810.

Gruss LF, Langaee T, Keil A (2016) The role of the COMT val158met polymorphism in mediating aversive learning in visual cortex. Neuroimage 125:633–642.

Güntekin B, Basar E (2007) Emotional face expressions are differentiated with brain oscillations. Int J Psychophysiol 64:91–100.

Hamm AO, Vaitl D (1996) Affective learning: Awareness and aversion. Psychophysiology 33:698–710.

Huster RJ, Stevens S, Gerlach AL, Rist F (2009) A spectralanalytic approach to emotional responses evoked through picture presentation. Int J Psychophysiol 72:212–216.

Iemi L, Busch NA (2018) Moment-to-Moment Fluctuations in Neuronal Excitability Bias Subjective Perception Rather than Strategic Decision-Making. eNeuro 5:1–13.

Iemi L, Chaumon M, Crouzet SM, Busch NA (2017) Spontaneous Neural Oscillations Bias Perception by Modulating Baseline Excitability. J Neurosci 37:807–819.

JASP Team (2018) JASP (Version 0.9)[Computer Software].

Kastner-Dorn AK, Andreatta M, Pauli P, Wieser MJ (2018) Hypervigilance during anxiety and

selective attention during fear: Using steady-state visual evoked potentials (ssVEPs) to disentangle attention mechanisms during predictable and unpredictable threat. Cortex 106:120–131.

Keil A, Stolarova M, Moratti S, Ray WJ (2007) Adaptation in human visual cortex as a mechanism for rapid discrimination of aversive stimuli. Neuroimage 36:472–479.

Klimesch W (2012) Alpha-band oscillations, attention, and controlled access to stored information. Trends Cogn Sci 16:606–617.

Klimesch W, Fellinger R, Freunberger R (2011) Alpha oscillations and early stages of visual encoding. Front Psychol 2:118.

Klimesch W, Sauseng P, Hanslmayr S (2007) EEG alpha oscillations: The inhibition-timing hypothesis. Brain Res Rev 53:63–88.

Lang PJ, Bradley MM (2010) Emotion and the motivational brain. Biol Psychol 84:437–450.

Lavie N (2005) Distracted and confused?: Selective attention under load. Trends Cogn Sci 9:75–82.

Lebron-Milad K, Abbs B, Milad MR, Linnman C, Rougemount-Bücking A, Zeidan MA, Holt DJ, Goldstein JM (2012) Sex differences in the neurobiology of fear conditioning and extinction: a preliminary fMRI study of shared sex differences with stress-arousal circuitry. Biol Mood Anxiety Disord 2:7.

LeDoux JE (2014) Coming to terms with fear. Proc Natl Acad Sci 111:2871–2878.

Lee TW, Girolami M, Sejnowski TJ (1999) Independent component analysis using an extended infomax algorithm for mixed subgaussian and supergaussian sources. Neural Comput 11:417–441.

Lissek S, Powers AS, McClure EB, Phelps EA, Woldehawariat G, Grillon C, Pine DS (2005) Classical fear conditioning in the anxiety disorders: A meta-analysis. Behav Res Ther 43:1391–1424.

Lonsdorf TB et al. (2017) Don't fear 'fear conditioning': Methodological considerations for the design and analysis of studies on human fear acquisition, extinction, and return of fear. Neurosci Biobehav Rev 77:247–285.

Löw A, Weymar M, Hamm AO (2015) When Threat Is Near, Get Out of Here: Dynamics of Defensive Behavior During Freezing and Active Avoidance. Psychol Sci 26:1706–1716.

Lundqvist D, Flykt A, Öhman A (1998) The Karolinska Directed Emotional Faces - KDEF. CD ROM from the Department of Clinical Neuroscience, Psychology Section, Karolinska Institutet.

MacLeod C, Rutherford E, Campbell L, Ebsworthy G, Holker L (2002) Selective Attention and Emotional Vulnerability: Assessing the Causal Basis of Their Association Through the Experimental Manipulation of Attentional Bias. J Abnorm Psychol 111:107–123.

Merz CJ, Tabbert K, Schweckendiek J, Klucken T, Vaitl D, Stark R, Wolf OT (2012) Neuronal correlates of extinction learning are modulated by sex hormones. Soc Cogn Affect Neurosci 7:819–830.

Michalowski JM, Pané-Farré CA, Löw A, Hamm AO (2015) Brain dynamics of visual attention during anticipation and encoding of threat- and safe-cues in spider-phobic individuals. 10:1177–1186.

Milad MR, Quirk GJ (2012) Fear Extinction as a Model for Translational Neuroscience: Ten Years of Progress. Annu Rev Psychol 63:129–151.

Miskovic V, Keil A (2012) Acquired fears reflected in cortical sensory processing: A review of electrophysiological studies of human classical conditioning. Psychophysiology 49:1230–1241.

Mogg K, Bradley BP (2018) Anxiety and Threat-Related Attention: Cognitive-Motivational Framework and Treatment. Trends Cogn Sci 22:225–240.

Morey RD, Rouder JN (2018) BayesFactor: Computation of Bayes Factors for Common Designs.

Mueller EM, Panitz C, Hermann C, Pizzagalli DA (2014) Prefrontal Oscillations during Recall of Conditioned and Extinguished Fear in Humans. J Neurosci 34:7059–7066.

Mueller EM, Pizzagalli DA (2016) One-year-old fear memories rapidly activate human fusiform gyrus. Soc Cogn Affect Neurosci 11:308–316.

Muench HM, Westermann S, Pizzagalli DA, Hofmann SG, Mueller EM (2016) Self-relevant threat contexts enhance early processing of fear-conditioned faces. Biol Psychol 121:194–202.

Myers KM, Davis M (2007) Mechanisms of fear extinction. Mol Psychiatry 12:120–150.

Panitz C, Hermann C, Mueller EM (2015) Conditioned and extinguished fear modulate functional corticocardiac coupling in humans. Psychophysiology 52:1351–1360.

Panitz C, Keil A, Mueller EM (2019) Extinction-resistant attention to long-term conditioned threat is

indexed by selective visuocortical alpha suppression - Open Data and Materials. Available at: osf.io/bfqjc.

Panitz C, Sperl MFJ, Hennig J, Klucken T, Hermann C, Mueller EM (2018) Fearfulness, neuroticism/anxiety, and COMT Val158Met in long-term fear conditioning and extinction. Neurobiol Learn Mem 155:7–20.

Perrin F, Pernier J, Bertrand O, Echallier JF (1989) Spherical splines for scalp potential and current density mapping. Electroencephalogr Clin Neurophysiol 72:184–187.

Pfurtscheller G (2001) Functional brain imaging based on ERD / ERS. Vision Res 41:1257–1260.

Pintzinger NM, Pfabigan DM, Pfau L, Kryspin-Exner I, Lamm C (2017) Temperament differentially influences early information processing in men and women: Preliminary electrophysiological evidence of attentional biases in healthy individuals. Biol Psychol 122:69–79.

Quirk GJ, Mueller D (2008) Neural mechanisms of extinction learning and retrieval. Neuropsychopharmacology 33:56–72.

R Core Team (2018) R: A Language and Environment for Statistical Computing.

Rescorla RA, Wagner AR (1972) A theory of Pavlovian conditioning: Variations in the effectiveness of reinforcement and nonreinforcement. In: Classical conditioning II: Current research and theory (Black AH, Prokasy WF, eds), pp 64–99. New York: Appleton-Century-Crofts.

Richards HJ, Benson V, Donnelly N, Hadwin JA (2014) Exploring the function of selective attention and hypervigilance for threat in anxiety. Clin Psychol Rev 34:1–13.

Rinck M, Reinecke A, Ellwart T, Heuer K, Becker ES (2005) Speeded Detection and Increased Distraction in Fear of Spiders: Evidence From Eye Movements. J Abnorm Psychol 114:235–248.

Roelofs K (2017) Freeze for action: Neurobiological mechanisms in animal and human freezing. Philos Trans R Soc B 372:20160206.

Rouder JN, Engelhardt CR, McCabe S, Morey RD (2016) Model comparison in ANOVA. Psychon Bull Rev 23:1779–1786.

Sass SM, Heller W, Stewart JL, Levin Silton R, Edgar JC, Fisher JE, Miller GA (2010) Time course of attentional bias in anxiety: Emotion and gender specificity. Psychophysiology 47:247–259.

Scheeringa R, Koopmans PJ, van Mourik T, Jensen O, Norris DG (2016) The relationship between

oscillatory EEG activity and the laminar-specific BOLD signal. Proc Natl Acad Sci 113:6761–6766.

Schupp HT, Flaisch T, Stockburger J, Junghöfer M (2006) Emotion and attention: event-related brain potential studies. Prog Brain Res 156:31–51.

Sperl MF, Panitz C, Hermann C, Mueller EM (2016) A pragmatic comparison of noise burst and electric shock unconditioned stimuli for fear conditioning research with many trials. Psychophysiology 53.

Team Rs (2016) RStudio: Integrated Development Environment for R. Boston, MA: RStudio, Inc. http://www.rstudio.com/.

Thigpen NN, Bartsch F, Keil A (2017) The malleability of emotional perception: Short-term plasticity in retinotropic neurons accompanies the formation of perceptual biases to threat. J Exp Psychol Gen 146:464–471.

Uusberg A, Uibo H, Kreegipuu K, Allik J (2013) EEG alpha and cortical inhibition in affective attention. Int J Psychophysiol 89:26–36.

Vagnoni E, Lourenco SF, Longo MR (2015) Threat modulates neural responses to looming visual stimuli. Eur J Neurosci 42:2190–2202.

Van Bockstaele B, Verschuere B, Tibboel H, Houwer J De, Crombez G, Koster EHW (2014) A Review of Current Evidence for the Causal Impact of Attentional Bias on Fear and Anxiety. Psychol Bull 140:682–721.

Wendt J, Löw A, Weymar M, Lotze M, Hamm AO (2017) Active avoidance and attentive freezing in the face of approaching threat. Neuroimage 158:196–204.

Wieser MJ, Reicherts P, Juravle G, von Leupoldt A (2016) Attention mechanisms during predictable and unpredictable threat — A steady-state visual evoked potential approach. Neuroimage 139:167–175.

Winkler I, Debener S, Muller KR, Tangermann M (2015) On the influence of high-pass filtering on ICA-based artifact reduction in EEG-ERP. Proc Annu Int Conf IEEE Eng Med Biol Soc EMBS 2015–Novem:4101–4105.