

# Emotion regulation by cognitive reappraisal – The role of frontal theta oscillations

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## ABSTRACT

The regulation of emotion by cognitive reappraisal has attracted a lot of attention over the last decade. Studies using functional magnetic resonance imaging (fMRI) revealed a wide-spread network of multiple prefrontal and sub-cortical brain regions involved in the successful decrease of negative emotions. However, less is known about the temporal dynamics and the physiological mechanisms underlying these regulation processes. Synchronization of neural oscillations in specific frequency bands plays a key-role in the long-range interaction of different brain regions and oscillatory coupling in the theta frequency range was recently identified to play an important role in the interaction of prefrontal structures, the amygdala and the hippocampus in animal models. Accordingly, we investigated the role of prefrontal theta oscillations during the cognitive reappraisal of aversive pictures in humans. We hypothesized an increase in frontal theta oscillations during emotion regulation and a relationship between frontal theta power and the subjective success of emotion regulation. EEG from 30 healthy participants was recorded while they were asked to passively watch or reappraise the content of pictures with negative content. As expected, we found a significant increase in frequencies around 4 Hz at electrode Fz during the regulation condition 'decrease' compared to the 'maintain' condition ( $p = .006$ ) as well as for the regulation condition 'increase' compared to the 'maintain' condition ( $p = .017$ ). Additionally, the strength of theta power was positively correlated with the regulation success as reported by the participants ( $r = 0.463, p < .05$ ). The estimation of possible generators of the theta oscillations was done using standardized low resolution electromagnetic tomography (sLORETA). Results suggested the left middle/inferior frontal gyrus as a possible generator. The results of the present study are in line with previous findings of fMRI studies suggesting the same regions as part of the regulation network and provide a first direct link between the imaging based knowledge of emotion regulation and a possible physiological mechanism.

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## Introduction

Emotion regulation is a major topic in affective neuroscience as it plays an important role in both the pathogenesis and the treatment of several psychiatric disorders such as borderline personality disorder (BPD), depression or anxiety disorders. Consequently, it has been addressed in a number of recent psychophysiological and neuroimaging studies (Hajcak et al., 2010; Moser et al., 2010; Ochsner et al., 2004; Paret et al., 2011; Wager et al., 2008).

Multiple studies using functional magnetic resonance imaging (fMRI) identified the structural and functional neuroanatomy of emotion regulation. Two systems have been implicated in the processing of emotion and emotion regulation. The ventral emotion system is

involved in emotion detection and includes the amygdaloid complex, the insula and the anterior cingulate cortex (ACC). The dorsal emotion system is involved in emotion regulation and includes the dorso-lateral prefrontal cortex (dlPFC), the ventrolateral prefrontal cortex (vlPFC) and the orbitofrontal cortex (OFC). These structures form a highly interacting functional network that modulates responses to emotional stimuli (Eippert et al., 2007; Goldin et al., 2009; Ochsner and Gross, 2005; Ochsner et al., 2004; Schulze et al., 2011).

Cognitive reappraisal is a strategy used to change the emotional impact of a situation or event by reinterpreting its meaning. Particularly, cognitive reappraisal strategies applied to aversive stimuli have been investigated (Banks et al., 2007; Kanske et al., 2011; Ochsner et al., 2004; Schulze et al., 2011). For example, subjects were asked to reinterpret the context of a scene in a way that it was less negative to them. This approach resulted in the identification of brain areas involved in emotion regulation with high spatial resolution and revealed the prominent role of amygdala–PFC interaction in emotion regulation. Consistently, fMRI studies reported a negative correlation between the amygdala and prefrontal structures and

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demonstrated an inhibitory influence of the PFC on the amygdala and insula during cognitive reappraisal tasks (Delgado et al., 2008; Hariri et al., 2003; Wager et al., 2008).

While fMRI is a perfect tool for describing brain regions involved in emotion regulation, such as the PFC and the amygdala, with high spatial resolution, it offers no direct measurement of neural activity and accordingly the underlying neurophysiological mechanisms involved in the connectivity between brain regions can't be directly addressed. Recently, basic research in animals provided some first hints regarding key mechanisms in the oscillatory coupling of the PFC and the amygdala. Functional brain networks are comprised of neuronal ensembles coupled through synchronization of brain electroencephalographic rhythms in certain frequencies. An investigation of oscillations in fear conditioning and fear extinction processes in mice, revealed increased oscillations in the theta frequency range (4–8 Hz) of the EEG in the medial prefrontal cortex, the amygdala and the hippocampus (Lesting et al., 2011). Moreover, oscillatory coupling between these regions was demonstrated. These results suggest that theta oscillations might play an important role in the connectivity between PFC and amygdala in a fear context. Of particular interest, a causal relationship by means of theta oscillations between PFC and amygdala was shown in a 5-HTT deficient mouse model, examining influences of social experiences and genetic factors on fear extinction (Narayanan et al., 2011). Even theta mediated interaction was shown in a fear conditioning/extinction context these findings indicate that theta oscillations might be one physiological mechanism that mediates the influence of the prefrontal cortex on the amygdala.

While invasive electrophysiological investigations are usually not possible in humans, scalp EEG can be used to investigate neural oscillations generated in cortical brain structures. Most of the previous EEG studies investigating emotion induction or regulation have focused on event-related potentials (Foti and Hajcak, 2008; Hajcak and Sander, 2006; Hajcak et al., 2010; Moser et al., 2006, 2009, 2010; Thiruchselvam et al., 2011). In addition, the investigation of oscillations is of much interest today since it was hypothesized that highly synchronized discharges of neurons in distinct regions are one key mechanism on how neuronal assemblies interact (Engel et al., 2001; Singer, 1999). The synchronization of oscillations has therefore been used to identify networks of interacting brain regions (Başar et al., 2001; Hipp et al., 2011; Liebe et al., 2012; Mulert et al., 2011).

There are various studies pointing out the importance of low frequency oscillations in the delta, theta and alpha bands in the context of emotion regulation and the processing of negative pictures. For example one study (Aftanas et al., 2001) reported differences between positive and negative affective valence of pictures in the theta-band. Additionally, a number of publications with focus on low frequency oscillation patterns in response to facial expressions exist (Balconi and Lucchiari, 2006; Knyazev et al., 2008a). Balconi and Lucchiari (2006) found that the delta and theta bands are sensitive to emotional faces, while other bands are modulated by all types of facial expressions. Knyazev et al. (2008a) used a face evaluation task in order to investigate anxiety and oscillatory responses and found that explicit anxiety is associated with reduced theta band synchronization. They also found higher alpha band de-synchronization in subjects with high anxiety compared to subjects with low anxiety. In a recent emotion regulation study decreased alpha activity was observed over the left hemisphere during cognitive reappraisal compared to passive picture watching which was suggested by the authors to reflect increased PFC activity (Parvaz et al., 2012).

Beside studies in the context of emotion regulation and emotion processing theta oscillations in humans have been demonstrated to be involved in various perceptual (Salisbury and Taylor, 2012) and cognitive tasks (Michels et al., 2010; Raghavachari et al., 2006; Sammer et al., 2007; Schack et al., 2005). For example, several EEG studies generated evidence for an association between theta and

memory processes (Klimesch et al., 2004; Raghavachari et al., 2006; Schack et al., 2005). In addition, it has been shown that several brain regions are able to generate oscillations in the theta range. Along with possible generators of frontal theta oscillations in lateral prefrontal areas during cognitive tasks (Anderson et al., 2010) the medial PFC/ACC has also been suggested as generator of theta oscillations. This was shown by studies using the standardized low resolution brain electromagnetic tomography algorithm (sLORETA) (Pascual-Marqui, 2002, 2007; Pascual-Marqui et al., 1994) approach (Mulert et al., 2007a,b; Pizzagalli et al., 2002) and combined EEG/PET (Pizzagalli et al., 2003). Mulert et al. (2007a,b) and Pizzagalli et al. (2011, 2003) investigated patients with depression and found altered theta-oscillation in the rostral ACC, a structure associated with emotion processing (Bush et al., 2000). While prefrontal structures and the ACC can be detected with EEG, this is not the case for subcortical structures as the amygdala. Accordingly, an observation of the interaction between cortical and sub-cortical structures like the amygdala is impossible using EEG data recorded at the scalp. However, since successful emotion regulation using cognitive reappraisal is typically linked with a modulation of amygdala activity self-reported affect ratings could be used as a surrogate marker for amygdala activation.

In this study we used a set of aversive pictures to induce negative emotions in healthy subjects. Subjects were asked to decrease, increase or maintain the induced emotion. Based on previous findings in animals, we expected an increase in theta oscillations during the 'decrease' condition compared to the 'maintain' condition. We performed frequency specific source localization using sLORETA in order to reveal the brain regions generating theta oscillations during the reappraisal condition. We hypothesized that emotion regulation is related to an increase of theta oscillations in frontal electrodes, that individual regulation success is linked to the strength of theta oscillations and that source localization of theta oscillations during emotion regulation would suggest generators in the prefrontal cortex.

## Methods

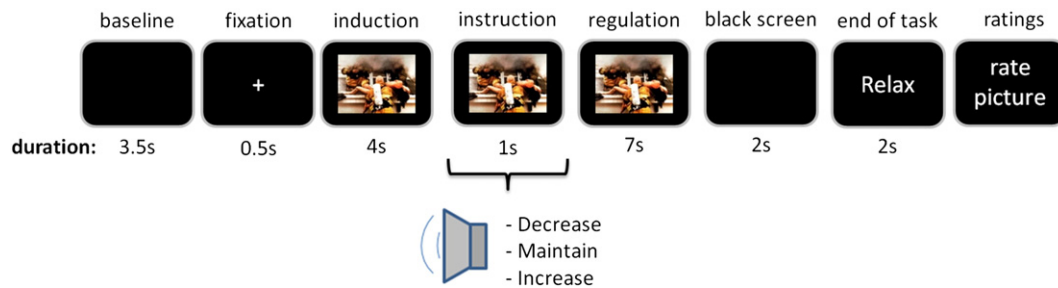
This study was approved by the Ethical Committee of Hamburg. All procedures were explained to each participant and declarations of consent were always signed before the experiment began. Participants were paid €25 for their participation.

### Analytic strategy

In order to test our hypothesis of increased theta oscillations we recorded EEG data of 30 healthy subjects while they performed an emotion regulation task. At first we identified the frequency range and the scalp topography that are predominately modulated by the regulation task. In a second step we compared the theta activity at the found position for three conditions and tested for possible relationships to the behavioral data. Furthermore, we analyzed the strength of theta oscillations at different phases within one condition. Finally, we used the frequency band reflecting task modulated activity and applied a source estimation analyses to reveal possible generators.

### Participants

A total of 30 participants (15 male; mean (M) age of 24.9 years; standard deviation (SD) 3.81 years) completed the study. All participants declared to be free of psychiatric and neurological disorders and not to have a history of drug abuse by a standardized questionnaire used by our laboratory. Participants also declared that they had no first-degree relatives with psychiatric disorders. Finally, participants had no prior exposure to the stimuli.



**Fig. 1.** Schematic diagram showing the design of a trial. Four seconds after the onset of a picture an instruction was given via headphones. Subjects were asked to follow the instruction until the word “relax” occurred on the screen.

## Stimuli

Ninety negative and 30 neutral pictures were taken from the International Affective Picture System<sup>2</sup> (IAPS; Lang et al., 2008). The negative pictures were divided into two sets each containing 45 negative pictures (assessment 1: valence  $M = 1.91$ ,  $SD = 0.30$ ; arousal  $M = 6.10$ ,  $SD = 0.41$ ; assessment 2: valence  $M = 1.90$ ,  $SD = 0.28$ ; arousal  $M = 6.37$ ,  $SD = 0.64$ ). Both sets also included 15 neutral pictures (assessment 1: valence  $M = 5.31$ ,  $SD = 0.66$ ; arousal  $M = 3.27$ ,  $SD = 0.91$ ; assessment 2: valence  $M = 5.06$ ,  $SD = 0.38$ ; arousal  $M = 2.85$ ,  $SD = 0.48$ ). The sets were matched without repetition of pictures. The negative pictures showed scenes such as car accidents or mutilations, while the neutral pictures showed people in everyday life situations with unthreatening objects or people. Additionally, a set of three negative and two neutral pictures was created for the practice block.

## Procedure

Each subject participated in one experimental session. The session consisted of a description of the experiment, the preparation for the EEG measurement and a detailed instruction regarding the use of cognitive reappraisal strategies, including several examples. Before the start of the experiment a resting state EEG (5 min) was acquired and inspected for abnormalities by a physician experienced in the evaluation of clinical EEG (G.L.). In this study's sample no subject had to be excluded for abnormalities in the EEG. Every experimental session consisted of one practice run of five pictures to familiarize the subjects with the protocol and the handling of the equipment and to permit them to practice the regulation strategy in the experimental setup. The practice block was followed by two experimental blocks, which included picture sets of 60 trials each. The pause between the blocks was approximately 3 min. The recording of the entire experiment took about 50 min.

The instruction for the reappraisal given to the subject was based on the instructions described by other groups in previous studies (Jackson et al., 2000; Ochsner et al., 2002, 2004; Wager et al., 2008). In case of a ‘decrease’ task, participants were asked to generate a less negative interpretation of the scene shown by the picture. This could be done in multiple ways. For example by imaging that the shown scene is not real and the people are actors or by focusing on a positive aspect of the picture like the presence of the ambulance

in a car accident scene. Furthermore, participants were instructed to remain within the context of the given scene and not to replace or change their emotion by thinking of a situation which is not related to that scene. This was done to achieve that participants regulate their emotion in accordance with the tested framework. In case of an ‘increase’ trial participants were asked to focus on negative aspects of the picture or to imagine, that the shown person is a friend or family member of them. During the ‘maintain’ condition participants were told to attentively watch the picture and experience the feeling naturally without trying to change the emotional state induced by the picture or to mentally digress. After the instruction participants had the possibility to practice the reappraisal strategy in a training session of five pictures. Afterwards, participants were asked, if they were able to regulate their emotion using cognitive reappraisal.

The structure of a trial is illustrated in Fig. 1. Every trial started with a fixation cross after 3.5 s of black screen. The fixation cross was presented in order to minimize eye-movements, focusing their gaze at the center of the screen for picture onset. The pictures were presented for 12 s. Four seconds post picture onset, a digitized human voice gave a one-word instruction (“verringern” (engl. decrease), “steigern” (engl. increase), “fortfahren” (engl. maintain)). For negative pictures subjects were asked to decrease, increase, or maintain their actual emotional response. When a neutral picture was presented subjects were always asked to maintain their emotional response. This was done to avoid ambiguous instructions to a non-existing emotional response and has been done by other groups before (Jackson et al., 2000).

To regulate their emotions, participants were instructed to decrease, increase or maintain the intensity of their negative affect by using the previously explained and trained strategy of cognitive reappraisal.

Participants were told to continue the given task until the word “relax” occurred on the screen. This happened two seconds after the offset of the picture. After every trial subjects had to evaluate the image they had just viewed. First, participants were asked to rate their first impression of the picture. Second, participants were asked to rate their feeling after cognitive reappraisal of the picture. Both ratings were given by the subject right after every trial. The rating procedure started 4 s after picture offset (see Fig. 1) with the rating of the first impression. Directly after participants gave their first rating the menu for the second rating appeared on the screen. A Likert scale from zero to five was used and subjects were instructed to rate neutral pictures with zero and to use the numbers from one to five to describe the intensity of the aversion, where one equals low aversion and five equals high aversion. For orientation purposes, subjects were told that the first picture of the first set was a three on the scale. This was done to guarantee, that no one rated the first picture too high or low, to avoid rating ceiling and floor effects.

All subjects were instructed not to look away from the monitor during the entire EEG-experiment. Additionally, subjects were asked to try not to move or strain their muscles in order to minimize artifacts during the recording.

<sup>2</sup> The unpleasant IAPS pictures were 2095, 2205, 2352.2, 2375.1, 2703, 2811, 3000, 3001, 3005.1, 3015, 3016, 3017, 3030, 3053, 3059, 3060, 3062, 3063, 3064, 3068, 3069, 3071, 3080, 3100, 3101, 3102, 3103, 3110, 3120, 3130, 3131, 3140, 3150, 3168, 3170, 3180, 3191, 3195, 3220, 3225, 3230, 3261, 3266, 3301, 3350, 3400, 3500, 3530, 6021, 6022, 6212, 6350, 6360, 6415, 6520, 6540, 6560, 6563, 6570, 9040, 9075, 9140, 9163, 9183, 9185, 9187, 9220, 9252, 9253, 9254, 9322, 9325, 9326, 9332, 9405, 9410, 9412, 9413, 9414, 9421, 9433, 9560, 9570, 9571, 9635.1, 9800, 9810, 9910, 9921, and 9940 and the neutral IAPS pictures were 2190, 2191, 2302, 2383, 2384, 2393, 2512, 2570, 2580, 2702, 2745.1, 2840, 5471, 5635, 5720, 5731, 5875, 7025, 7036, 7041, 7060, 7110, 7150, 7161, 7175, 7235, 7490, 7705, 7950, and 8312.

### EEG recording

Recordings took place in a sound-attenuated and electrically shielded room. Subjects were seated in a slightly reclined chair in front of a 19" computer monitor and asked to keep their eyes open. The distance between the eyes of the subject and monitor was approximately 1 m. The EEG was recorded using 32 active electrodes (ActiCaps, Brain Products, Munich, Germany). Electrodes were positioned according to the international 10/20 system with FCz as the reference electrode. Data were collected at a rate of 1000 samples per second. The impedances were always kept below 5 k $\Omega$ . The EEG recording was acquired using the Brain Vision Recorder software Version 1.10 (Brain Products, Munich, Germany).

### EEG pre-processing

Data analysis was done using the Brain Vision Analyzer software Version 2.0 (Brain Products, Munich, Germany). Data were band-pass filtered (0.1–45 Hz) and down-sampled to 250 Hz. Next, all sets were corrected for eye-blink artifacts by applying an ICA. Afterwards the data were re-referenced to the common average and FCz was recovered as a regular channel.

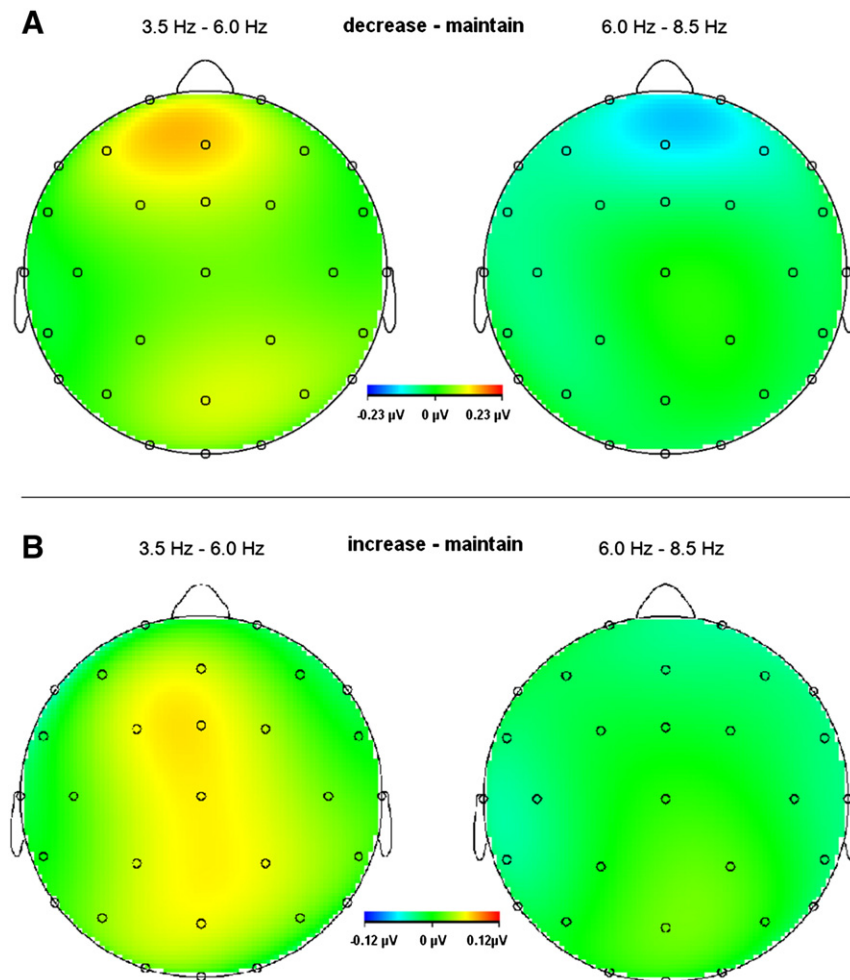
Epochs of 16 s including the baseline, induction, instruction and regulation period were created for each of the conditions (decrease, increase, maintain, neutral). Upon a visual inspection trials that continued to contain residuals artifacts were removed from further analyses.

### Voltage maps

Since low theta oscillations around 4 Hz were shown to be most relevant for the interaction between PFC and the amygdala in mice (Lesting et al., 2011) we calculated separated voltage distribution maps for low (3.5–6 Hz) and high theta (6–8.5 Hz) for the 'increase', 'decrease' and 'maintain' conditions. In order to avoid overlapping event-related brain potentials caused by instructions with the regulation outcome, maps were calculated taking into account the entire regulation interval starting after the 1 s instruction period. Similar definitions of low and high theta were used in previous studies (Fellinger et al., 2011; Salisbury and Taylor, 2012) in humans. Fellinger and colleagues defined theta as ranging from 3.58 to 5.52 Hz and Salisbury and Taylor investigated (low-) theta from 3 to 5 Hz. The differences between the 'increase' and 'maintain' as well as between the 'decrease' and 'maintain' conditions are displayed in Fig. 2.

### FFT-analysis

For each trial, the 4000 ms (= 1000 data points) interval before the picture onset was used for baseline correction in the time domain and has been applied to the entire epoch. Every trial was subdivided into sub-segments of 2 s each. This resulted in 2 segments during baseline and induction and 3 segments during regulation. A Fast Fourier Transformation (FFT) with 1 Hz resolution and periodic 'hanning' window was calculated for every segment. An average was calculated for every subject and for every condition. The mean theta-power from



**Fig. 2.** Topography of the contrasts decrease–maintain (A) and increase–maintain (B) for the 7 s regulation phase for frequencies from 3.5 to 6.0 Hz and for 6.0 to 8.5 Hz.



electrode Fz for the frequency band ranging from 3 to 8 Hz was extracted in steps of 1 Hz and imported to SPSS for the complete regulation interval (7 s) as well as for the three sub-segments. For the correlation with the behavioral data the mean activity of the baseline intervals (mean of both 2 s segments) was subtracted frequency wise from the corresponding activity of the complete regulation interval during the regulation in order to take into account slow baseline drifts or vigilance effects.

### Wavelet analysis

A continuous wavelet transformation using a complex morlet wavelet was calculated for the frequencies from 3 to 8 Hz for every segment. Complex morlet wavelets have frequently been used for time–frequency analysis by our (Leicht et al., 2010, 2011) and other laboratories (Digiacoio et al., 2008; Herrmann et al., 1999; Knyazev et al., 2008b). The activity during the 4 s baseline has frequency-wise been subtracted from the trial. The results of the wavelet transformation were averaged within a subject and grand averages containing all 30 subjects were calculated for every condition. This procedure resulted in time–frequency analyses reflecting the induced part of the brain response (Chen et al., 2012; Tallon-Baudry et al., 1998). Analogous, to the FFT-analyses, the theta activities were exported to SPSS.

### Source localization (sLORETA)

The standardized low resolution electromagnetic tomography algorithm (sLORETA) is an improvement of the widely used LORETA algorithm (Pascual-Marqui et al., 1994). sLORETA has frequently been used to estimate possible generators of neuronal oscillations (Meltzer et al., 2009) or evoked potentials (Mobascher et al., 2009) and the results have been validated using combined EEG–fMRI (Mulert et al., 2004) and EEG–PET data (Pizzagalli et al., 2003). In sLORETA localization inference is based on images of standardized current density. This standardization improves the accuracy of sLORETA compared to LORETA (Pascual-Marqui, 2002) and calculates the smoothest possible solution to the observed scalp distribution. Therefore sLORETA as implemented in the freely available LORETA-KEY software (<http://www.uzh.ch/keyinst/loreta.htm>) has been used here to find possible generators of oscillations ranging from 4 to 5 Hz. This frequency range was selected on the results of the wavelet analysis, since it reflects the main effect. Sources were estimated using an inverse transformation based on the location of the electrodes for both, the ‘decrease’ and the ‘maintain’ conditions and a voxel-by-voxel contrast (decrease-maintain) has been calculated to reveal the sources which might be linked to the decrease of aversive pictures.

### Behavioral data

As described above, subjects rated every picture twice, reflecting their emotional response before and after regulation instructions. To create a measure of regulation success, we subtracted the rating after performing the task from the initial rating for each picture. Negative picture trials with positive difference rating values, therefore, showed successful reappraisal. The average reappraisal for every subject was calculated and exported to SPSS. Due to reported problems with the rating scale one subject has been excluded from the analysis.

### Statistical analysis

All statistical analyses were performed using the SPSS-software package (16.0). Comparisons between the ‘decrease’, ‘increase’ and ‘maintain’ conditions were done using two-tailed t-tests. At first we

calculated t-tests for contrasts ‘decrease’ vs. ‘maintain’, ‘increase’ vs. ‘maintain’ and ‘decrease’ vs. ‘increase’ based on the entire regulation period (1–7 s) for the mean 4 Hz activity. Afterwards, we divided the regulation interval of each condition into three sub time windows (1–3 s, 3–5 s, 5–7 s) and calculated t-tests for contrasts ‘decrease’ vs. ‘maintain’ and ‘increase’ vs. ‘maintain’ for those time-frames. The subdivision into 2 s intervals was done to be able to observe a possible temporal dynamic also in the FFT data. The tests were done for both the FFT segments and the wavelets. Additionally, we calculated further contrasts for the mean 4 Hz activity only based on the FFT data. An ANOVA and post-hoc t-tests were calculated to compare the theta activity of the different parts (baseline, induction, decrease/increase/maintain) within the ‘decrease’ and ‘increase’ trials. Post-hoc t-tests were calculated comparing the ‘decrease’ period vs. the 4 s baseline, the ‘decrease’ period vs. the 4 s ‘induction’ period and the ‘induction’ period vs. the ‘baseline’. For analyzing the behavioral data, ANOVAs were calculated comparing the first ratings of the ‘decrease’, ‘increase’ and ‘maintain’ conditions and the second ratings of the ‘decrease’, ‘increase’ and ‘maintain’ conditions. In order to compare the contrast ‘decrease’ vs. ‘increase’ regarding the second rating a two-tailed t-test was done. The correlation between the FFTs/wavelets and the regulation success was based on the theta activity of the entire 7 s regulation period and calculated using the Spearman correlation coefficient.

## Results

### Behavioral results

The average rating for the first impression of the pictures did not significantly differ between the conditions ‘decrease’ ( $M = 2.71$ ;  $SD = 0.64$ ), ‘increase’ ( $M = 2.98$ ;  $SD = 0.64$ ) and ‘maintain’ ( $M = 2.56$ ;  $SD = 0.65$ ). The ratings of the neutral pictures ( $M = 0.17$ ;  $SD = 0.17$ ) were lower compared to the emotional pictures in the ‘decrease’ ( $t = 59.32$ ;  $p < .001$ ), ‘maintain’ ( $t = 54.55$ ;  $p < .001$ ) and ‘increase’ ( $t = 67.34$ ;  $p < .001$ ) conditions. The second rating indicating the regulation performance was reduced for the ‘decrease’ ( $M = 1.91$ ;  $SD = 0.69$ ) and increased for the ‘increase’ ( $M = 3.76$ ;  $SD = 0.49$ ) conditions compared to the ‘maintain’ ( $M = 2.64$ ;  $SD = 0.70$ ) condition. Both differences were statistically significant ( $p < .001$ ).

### Voltage maps

Visual inspection of voltage maps displaying the differences between the ‘decrease’ and ‘maintain’ conditions as well as the ‘increase’ and ‘maintain’ conditions showed an increase in low theta-power (3–5 Hz; see Fig. 2) with a maximum over electrode Fz. Based on this voltage distribution, the further analyses were performed for electrode Fz and focused on low theta.

### FFT analysis (decrease–maintain)

Statistically contrasting the condition ‘decrease’ vs. ‘maintain’ gave a significant increase of  $0.43 \mu V$  ( $p = .006$ ) in 4 Hz theta activity at electrode Fz. This increase was observed for the entire regulation period (1–7 s). A more detailed analysis using intervals of two seconds, revealed some variability in this effect over time. The 4 Hz theta activity was increased by  $0.53 \mu V$  ( $p = .028$ ) in the interval from 3 to 5 s after the instruction. In the other two time windows of the ‘decrease’ condition only a modestly higher activity that did not reach statistical significance  $0.37 \mu V$  ( $p = .090$ ; 1–3 s) and  $0.35 \mu V$  ( $p = .225$ ; 5–7 s) could be observed.

### FFT analysis (increase–maintain)

The comparison of theta activity at Fz between the ‘increase’ and the ‘maintain’ conditions (1–7 s) showed significantly stronger theta oscillations of 0.37  $\mu\text{V}$  ( $p = .017$ ) during the ‘increase’ condition. The analyses of the subtime windows showed a modestly higher but not significant increase for the early windows by 0.06  $\mu\text{V}$  (1–3 s;  $p = .819$ ) and the late windows by 0.41  $\mu\text{V}$  (5–7 s;  $p = .108$ ). However, during the time interval from 3 to 5 s the theta activity was increased by 0.51  $\mu\text{V}$  ( $p = .014$ ).

### FFT analysis (decrease–increase)

The comparison of theta activity at Fz between the ‘decrease’ and the ‘increase’ conditions did not reach a significant level for the entire regulation period ( $p = .649$ ). Also the analyses of the subtime windows did not reveal any significant differences.

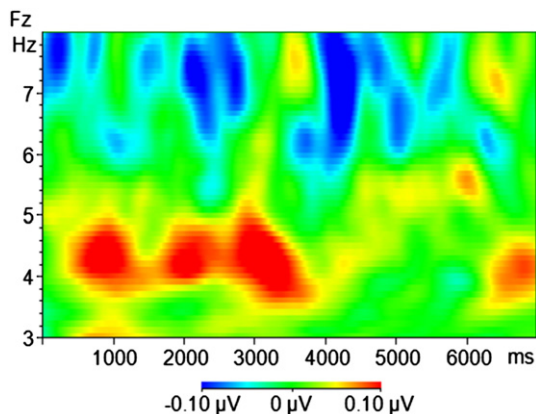
### FFT analysis (within conditions)

The ANOVA comparing the 4 Hz activity within the different periods of the ‘decrease’ trials revealed a significant difference ( $F = 7.76$ ;  $p < .001$ ) at electrode Fz. The post-hoc t-tests, comparing the regulation period to the baseline period (4 s before picture onset) showed a significant increase of 1.86  $\mu\text{V}$  ( $p < .001$ ). Also the 4 Hz theta at electrode Fz was increased during the ‘decrease’ period compared to the induction period 0.69  $\mu\text{V}$  ( $p < .001$ ). Additionally, we observed more theta activity in the induction phase compared to the baseline 1.16  $\mu\text{V}$  ( $p < .001$ ). The ANOVA comparing the 4 Hz activity within the different periods of the ‘increase’ trials did not reach a significant level ( $p = .85$ ) and therefore post-hoc t-test was not calculated.

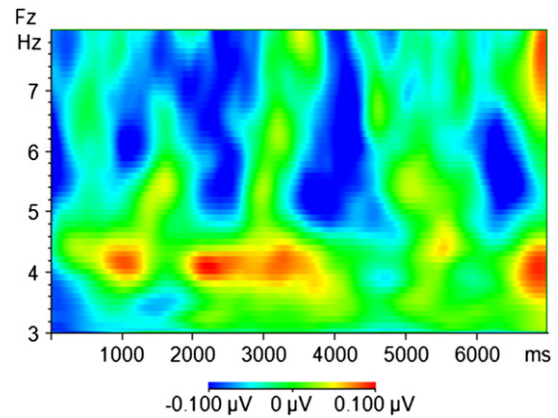
### Wavelet analysis

As expected, the analysis of the regulation interval using wavelets revealed similar results as the FFT analysis. The theta power was significantly increased comparing the ‘decrease’ and the ‘maintain’ conditions (see Fig. 3) for the time window from 1 to 3 s ( $p = .011$ ) and the time window from 3 to 5 s ( $p = .007$ ) but not for the window from 5 to 7 s ( $p = .940$ ). The theta power in the entire 7 s regulation interval was also significantly increased ( $p = .018$ ).

The comparison of the 4 Hz activity at electrode Fz between the ‘increase’ and ‘maintain’ conditions as calculated by the wavelet transformation revealed the following results (see Fig. 4). No significant difference was observed for the 1–3 s ( $p = .372$ ) and the 5–7 s



**Fig. 3.** Time–frequency analyses of the contrast decrease–maintain. There is a significant increase in the range from 4 to 5 Hz. The time–frequency representation starts with the regulation interval (time = 0 ms) and ends with the offset of the picture (time = 7000 ms).



**Fig. 4.** Time–frequency analyses of the contrast increase–maintain. There is a significant increase around 4 Hz.

( $p = .748$ ) intervals while there was a significant increase in the 3–5 s ( $p < .002$ ) interval. The 7 s regulation interval did not reach a significant level ( $p = .090$ ).

### Theta and behavior

There was a significant relationship between regulation success of the ‘decrease’ condition, as measured by the ratings, and 4 Hz theta activity, as calculated by the FFTs, during the entire regulation interval ( $r = 0.463$ ,  $p < .05$ ; see Fig. 5). The correlation between regulation success in the ‘decrease’ condition and 4 Hz activity, as calculated by the wavelet transformation was also significant ( $r = 0.37$ ,  $p < .05$ ). However a relationship between theta activity during the increase condition and the ratings given by the participants was not observed.

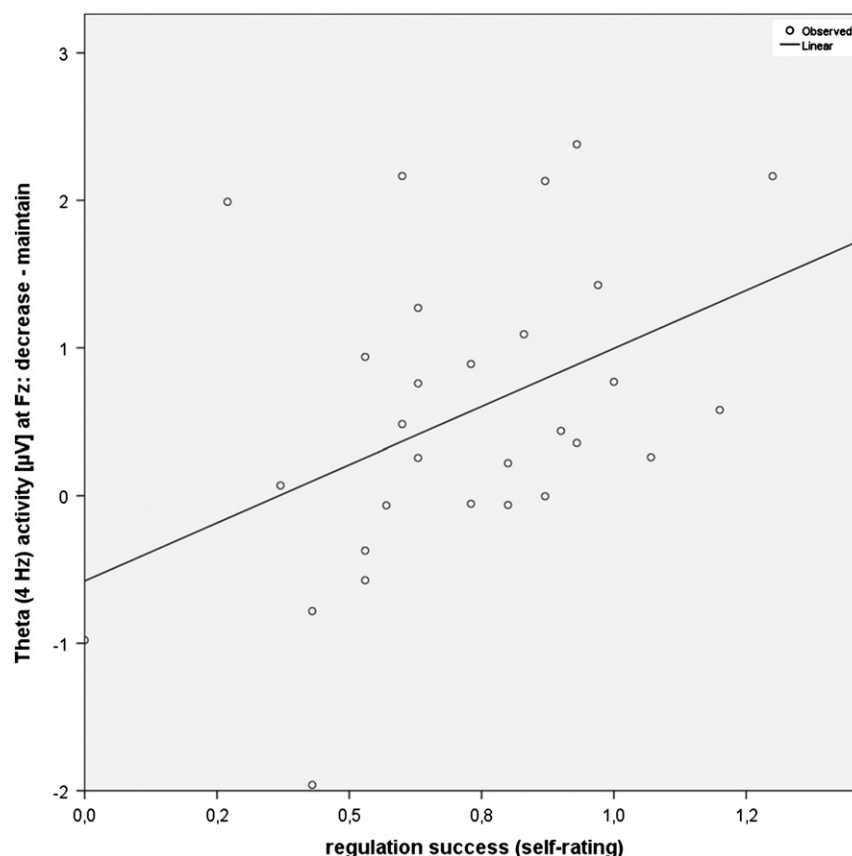
### Source estimation

The localization of the theta oscillations in the ‘decrease’ time window resulted in significant ( $p < .05$ ;  $t = 3.37$ ) activations in the left middle/inferior frontal gyrus (Brodmann area 9) at Talairach coordinates (Tal:  $-54$ ;  $11$ ;  $32$ ). At a trend level ( $p < .1$ ) we additionally found increased activity of the medial frontal gyrus ( $t = 2.54$ ; Brodmann area 32; Tal:  $-15$ ;  $30$ ;  $26$ ) during the reappraisal condition. The results of source localization are demonstrated in Fig. 6.

### Discussion

In accordance with our hypothesis we found that cognitive reappraisal of aversive pictures is correlated with an increase in theta oscillations at prefrontal brain regions. This finding was observed in both, the ‘increase’ and the ‘decrease’ conditions. Furthermore, it was shown that increased theta activity was positively correlated with the success of participants to decrease their emotional response. Moreover, source localization suggested possible generators of the theta oscillations in the left middle/inferior frontal gyrus, which is in accordance with findings of recent fMRI studies (Schulze et al., 2011; Winecoff et al., 2011).

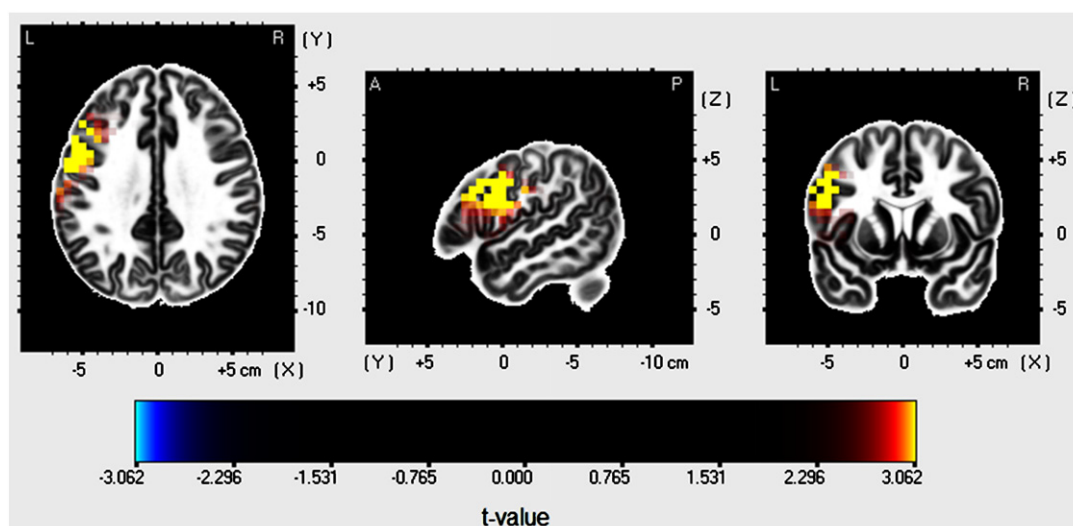
Emotion regulation by cognitive reappraisal involves the interaction between regions in the prefrontal cortex and other structures like the amygdala or insula. Theta oscillations are known to be involved in the interaction between cell assemblies located at different brain regions. Such long range connectivity by means of theta oscillations has for example been observed between frontal and parietal regions in humans performing finger tapping combined with varying tasks (Sauseng et al., 2007). Furthermore, animal research



**Fig. 5.** Correlation between self-reported emotion regulation success and the difference of theta activity at electrode Fz between the decrease and the maintain conditions.

suggested a potential role of theta oscillations as a potential key mechanism in the coupling between the prefrontal cortex and the amygdala (Lesting et al., 2011; Narayanan et al., 2011). Nevertheless, emotion regulation is a complex process including various cognitive processes, such as emotion processing, attention to emotion or memory, which all might be related to an increase of frontal theta oscillations. Accordingly, our finding of increased frontal theta oscillations during cognitive reappraisal could be related to processes that are not directly involved in PFC–amygdala coupling. However, our result of a correlation between the strength of theta oscillations and the individual success in the ‘decrease’ condition

could be interpreted as hint for PFC–amygdala interaction since successful emotion regulation has been shown to be related to a decrease in amygdala activity (Lee et al., 2012; Wager et al., 2008; Winecoff et al., 2011). Though, theta oscillations are also discussed as a mechanism of interaction between cortical and sub-cortical brain structures in the context of memory processes (Fujisawa and Buzsáki, 2011; Klimesch et al., 1996, 2000; Sederberg et al., 2003). Klimesch et al. (1996) demonstrated significantly higher theta power during the encoding of successfully remembered words and discussed their finding in the context of hippocampo–cortical feedback loops. In a later work Klimesch and colleagues linked theta



**Fig. 6.** sLORETA estimation for the contrast decrease vs. maintain for frequencies from 4 to 5 Hz. Only significant voxels ( $p < .05$ ; two-tailed) are displayed.

oscillations to a memory-related increase in the P300 amplitude. The work by Klimesch is in line with intracranial recordings by Sederberg et al. (2003). They also demonstrated an increase in theta activity during the encoding of successfully recalled words in the right temporal and frontal cortex.

The voltage distribution of theta oscillations with a maximum over frontal, central electrodes is a common finding for theta oscillations in cognitive processing and has been observed in a variety of tasks such as working memory, calculation and even musical imagining (Sasaki et al., 1996). It is also known that theta activity plays an important role in emotion processing (Aftanas et al., 2001) as well as in disorders associated to pathological emotional perception like depression (Mulert et al., 2007b; Pizzagalli et al., 2003). In our data we found low theta oscillations to be increased comparing the 'increase' and 'maintain' as well as the 'decrease' and 'maintain' conditions. In both cases the increase was most pronounced around electrode Fz. This might lead to the conclusion that in both tasks overlapping brain networks are involved. Such a network overlap is a robust finding in fMRI research on emotion regulation. Using a similar experiment than we did, Schulze et al. (2011) found along other regions in particular the inferior frontal gyrus to be involved in both an 'increase' and 'decrease' conditions. Similar results were reported by Ochsner et al. (2004). They found comparable activation patterns in the left lateral prefrontal cortex in the 'decrease' and 'increase' conditions. However, both studies did also report differences in the networks. Since we did not observe any differences between the theta activity in the 'decrease' and 'increase' conditions it is likely, that the main source generating those oscillations is a structure that is active during both conditions. This is supported by the investigation of the temporal dynamics of the theta oscillations. In both, the 'decrease' as well as the 'increase' conditions, the increase of theta oscillation was most pronounced 3 to 5 s after the instruction and less pronounced at other times.

The left middle/inferior frontal gyrus as estimated by the sLORETA analysis, is a very consistent finding in fMRI based emotion regulation research (Johnstone et al., 2007; Ochsner et al., 2002; Schulze et al., 2011; Winecoff et al., 2011). The Euclidean distance between the voxel with the strongest activity in this study (Tal: −54; 11; 32) and the strongest activation in BA9 as reported by Ochsner et al. (2004): (MNI: −56; 8; 40 ~ Tal: −53; 2; 40) is 12 mm and the distance to coordinates observed by Schulze et al. (2011): (MNI: −52; 20; 26 ~ Tal: −49; 15; 28) is less than 8 mm. Despite the relatively poor spatial resolution of EEG source estimations our results almost perfectly map onto these fMRI findings. Such a good estimation is in line with previous source localization studies that compared EEG source localization to results obtained using PET (Oakes et al., 2004; Pizzagalli et al., 2003), showing great overlap between the PET data and the source estimated of the EEG calculated by sLORETA. In both studies only 28 electrodes were used. Unlike various fMRI studies we did not find a significant activation in mid-line structures but there was a statistical trend in Brodmann area 32. This is relevant since recently published neuroimaging studies indicated that the amygdaloid complex, the insula, the anterior cingulate cortex (ACC), the ventrolateral PFC, the dlPFC and the mPFC constitute a functional brain network involved in emotion detection/experience and emotion regulation processes (Ochsner et al., 2004, 2009; Schulze et al., 2011; Wager et al., 2008). While the mPFC seems to be involved in outcome based forms of fear regulation, for example after extinction of conditioned and instructed fear, the dlPFC appears to be more important for regulatory processes such as cognitive reappraisal and monitoring of behavior. Based on this observation the hypothesis that the mPFC/ACC only passes information judged as relevant to higher dlPFC regions for deeper analyses was established (Mechias et al., 2010). Consequently, the dlPFC seems to be one of the key players in the network for conscious reappraisal of stimuli. In fact there is evidence that the PFC exerts inhibition on

the amygdala during cognitive reappraisal (Urry et al., 2006; Wager et al., 2008; Winecoff et al., 2011) and that the decrease of amygdala activity was positively associated with reported regulation success. Given the findings of our study, of a plausible theta generator in the PFC and a correlation between the theta activity and self-ratings, the assumption of theta mediated interactions in the emotion regulation network could be drawn. However, the exact function of theta oscillations has to be addressed in future work.

In this study we investigated theta oscillations around 4 Hz at electrode Fz. Interestingly, oscillations of higher frequencies ( $f > 5$  Hz) were not modulated by the emotion regulation task (Figs. 2–4). However, theta sub-bands, in particular low theta oscillations around 4 Hz have been described in various tasks before. Fellingner and colleagues (Fellinger et al., 2011) reported theta effects in an auditory selective attention paradigm for frequencies between 3.58 and 5.52 Hz. An increase of theta power (4–5 Hz) in the left hemisphere along with an increased inter trial phase synchrony during semantic priming has also been observed (Salisbury and Taylor, 2012). This raises the question if specific, distinct theta sub-bands exist.

## Limitations

Here, EEG was recorded with 32 electrode channels. The quality of the source localization could be probably improved using a higher number of electrodes. Nevertheless, the results of source estimation are well in line with recent fMRI findings. Moreover, since the amygdala is a sub-cortical structure, a possible contribution to the electrical potentials observed at the scalp, if any, is very small and therefore EEG-based source localization of amygdala activity cannot be performed. Accordingly, with the present study, amygdala activity was not directly assessed and only indirect clues about PFC–amygdala interaction were possible based on the assessment of subjective success of emotion regulation which is known to be related to amygdala activity (Wager et al., 2008). Finally, the fact that in this study both ratings were given after the entire block might have biased the rating of the first impression. However, this design offered the chance to investigate the induction and regulation without any interruptions which also might influence the emotional state induced by the pictures.

In further studies, the hypothesis that the interaction between prefrontal structures such as the dlPFC or the vlPFC with limbic structures like the amygdala or the insula is mediated by the synchronization of theta frequencies could be tested using the approach of simultaneous EEG–fMRI (Jaspers-Fayer et al., 2012; Mulert et al., 2008, 2010). Indeed, EEG informed fMRI has already successfully been used to couple theta information with the BOLD signal during a working memory task (Michels et al., 2010) and in a mental arithmetic task (Sammer et al., 2007). Sammer and colleagues created a regressor based on the single-trial theta activity on the scalp and found significant activity in the hippocampal regions, the cingulate and the frontal superior regions. This demonstrates that EEG–fMRI can be used to characterize a network coupled by theta oscillations including both cortical and subcortical structures.

In this paper we presented first data suggesting the relevance of oscillations around 4 Hz in emotion regulation processes. Disturbed emotion regulation plays a major role in several psychiatric disorders such as borderline personality disorder (Schulze et al., 2011), depression (Joormann and Gotlib, 2009) or anxiety disorders (Kim et al., 2011). Therefore, cognitive reappraisal is used with cognitive behavioral therapy during the treatment of these conditions (Smits et al., 2012). In fact, disturbed connectivity between PFC and amygdala has been suggested to play a major role in the pathophysiology of borderline personality disorder and accordingly it would be very interesting to investigate the role of theta oscillations in these conditions. A deeper understanding of the mechanism of PFC–amygdala



interaction in humans might be the basis for new therapeutic options. Additional insights into regulation mechanisms as well as therapeutic approaches might be offered by techniques such as neurofeedback or transcranial electric stimulation. Both of these approaches have successfully been used to influence specific oscillation patterns in defined brain regions (Marshall et al., 2006; Salari et al., 2012).

In summary, we found an increase in theta oscillations around 4 Hz at electrode Fz while subjects tried to decrease or increase emotions induced by negative pictures. A positive correlation between EEG oscillations in the theta range and successful usage of cognitive reappraisal in order to decrease negative emotions was observed. The possible generator of the theta oscillations as estimated by sLORETA was identified in the left prefrontal cortex, a brain region previously associated with cognitive reappraisal in fMRI studies.

## Conflict of interest

The authors declare no conflict of interest

## References

- Aftanas, L.I., Varlamov, A.A., Pavlov, S.V., Makhnev, V.P., Reva, N.V., 2001. Affective picture processing: event-related synchronization within individually defined human theta band is modulated by valence dimension. *Neurosci. Lett.* 303, 115–118.
- Anderson, K.L., Rajagovindan, R., Ghacibeh, G.A., Meador, K.J., Ding, M., 2010. Theta oscillations mediate interaction between prefrontal cortex and medial temporal lobe in human memory. *Cereb. Cortex* 20, 1604–1612.
- Balconi, M., Lucchiarini, C., 2006. EEG correlates (event-related desynchronization) of emotional face elaboration: a temporal analysis. *Neurosci. Lett.* 392, 118–123.
- Banks, S.J., Eddy, K.T., Angstadt, M., Nathan, P.J., Phan, K.L., 2007. Amygdala–frontal connectivity during emotion regulation. *Soc. Cogn. Affect. Neurosci.* 2, 303–312.
- Başar, E., Başar-Eroglu, C., Karakaş, S., Schürmann, M., 2001. Gamma, alpha, delta, and theta oscillations govern cognitive processes. *Int. J. Psychophysiol.* 39, 241–248.
- Bush, G., Luu, P., Posner, M.I., 2000. Cognitive and emotional influences in anterior cingulate cortex. *Trends Cogn. Sci.* 4, 215–222.
- Chen, C.-C., Kiebel, S.J., Kilner, J.M., Ward, N.S., Stephan, K.E., Wang, W.-J., Friston, K.J., 2012. A dynamic causal model for evoked and induced responses. *Neuroimage* 59, 340–348.
- Delgado, M.R., Nearing, K.I., LeDoux, J.E., Phelps, E.A., 2008. Neural circuitry underlying the regulation of conditioned fear and its relation to extinction. *Neuron* 59, 829–838.
- Digiacomo, M.R., Marco-Pallarés, J., Flores, A.B., Gómez, C.M., 2008. Wavelet analysis of the EEG during the neurocognitive evaluation of invalidly cued targets. *Brain Res.* 1234, 94–103.
- Eippert, F., Veit, R., Weiskopf, N., Erb, M., Birbaumer, N., Anders, S., 2007. Regulation of emotional responses elicited by threat-related stimuli. *Hum. Brain Mapp.* 28, 409–423.
- Engel, A., Fries, P., Singer, W., 2001. Dynamic predictions: oscillations and synchrony in top-down processing. *Nat. Rev. Neurosci.* 2, 704–716.
- Fellinger, R., Klimesch, W., Schnakers, C., Perrin, F., Freunberger, R., Gruber, W., Laureys, S., Schabus, M., 2011. Cognitive processes in disorders of consciousness as revealed by EEG time–frequency analyses. *Clin. Neurophysiol.* 122, 2177–2184.
- Foti, D., Hajcak, G., 2008. Deconstructing reappraisal: descriptions preceding arousing pictures modulate the subsequent neural response. *J. Cogn. Neurosci.* 20, 977–988.
- Fujisawa, S., Buzsáki, G., 2011. A 4 Hz oscillation adaptively synchronizes prefrontal, VTA, and hippocampal activities. *Neuron* 72, 153–165.
- Goldin, P.R., Manber, T., Hakimi, S., Canli, T., Gross, J.J., 2009. Neural bases of social anxiety disorder: emotional reactivity and cognitive regulation during social and physical threat. *Arch. Gen. Psychiatry* 66, 170–180.
- Hajcak, G., Nieuwenhuis, S., 2006. Reappraisal modulates the electrocortical response to unpleasant pictures. *Cogn. Affect. Behav. Neurosci.* 6 (4), 291–297.
- Hajcak, G., MacNamara, A., Olvet, D.M., 2010. Event-related potentials, emotion, and emotion regulation: an integrative review. *Dev. Neuropsychol.* 35, 129–155.
- Hariri, A.R., Mattay, V.S., Tessitore, A., Fera, F., Weinberger, D.R., 2003. Neocortical modulation of the amygdala response to fearful stimuli. *Biol. Psychiatry* 53, 494–501.
- Herrmann, C.S., Mecklinger, A., Pfeifer, E., 1999. Gamma responses and ERPs in a visual classification task. *Clin. Neurophysiol.* 110, 636–642.
- Hipp, J.F., Engel, A.K., Siegel, M., 2011. Oscillatory synchronization in large-scale cortical networks predicts perception. *Neuron* 69, 387–396.
- Jackson, D.C., Malmstadt, J.R., Larson, C.L., Davidson, R.J., 2000. Suppression and enhancement of emotional responses to unpleasant pictures. *Psychophysiology* 37, 515–522.
- Jaspers-Fayer, F., Ertl, M., Leicht, G., Leupelt, A., Mulert, C., 2012. Single-trial EEG–fMRI coupling of the emotional auditory early posterior negativity. *Neuroimage* 62 (3), 1807–1814. <http://dx.doi.org/10.1016/j.neuroimage.2012.05.018>.
- Johnstone, T., van Reekum, C.M., Urry, H.L., Kalin, N.H., Davidson, R.J., 2007. Failure to regulate: counterproductive recruitment of top-down prefrontal–subcortical circuitry in major depression. *J. Neurosci.* 27, 8877–8884.
- Joormann, J., Gotlib, I.H., 2009. Emotion regulation in depression: relation to cognitive inhibition. *Cogn. Emot.* 24, 281–298.
- Kanske, P., Heissler, J., Schönfelder, S., Bongers, A., Wessa, M., 2011. How to regulate emotion? Neural networks for reappraisal and distraction. *Cereb. Cortex* 21, 1379–1388.
- Kim, M.J., Loucks, R.A., Palmer, A.L., Brown, A.C., Solomon, K.M., Marchante, A.N., Whalen, P.J., 2011. The structural and functional connectivity of the amygdala: from normal emotion to pathological anxiety. *Behav. Brain Res.* 223, 403–410.
- Klimesch, W., Doppelmayr, M., Russegger, H., Pachinger, T., 1996. Theta band power in the human scalp EEG and the encoding of new information. *Neuroreport* 7, 1235–1240.
- Klimesch, W., Doppelmayr, M., Schwaiger, J., Winkler, T., Gruber, W., 2000. Theta oscillations and the ERP old/new effect: independent phenomena? *Clin. Neurophysiol.* 111, 781–793.
- Klimesch, W., Schack, B., Schabus, M., Doppelmayr, M., Gruber, W., Sauseng, P., 2004. Phase-locked alpha and theta oscillations generate the P1–N1 complex and are related to memory performance. *Cogn. Brain Res.* 19, 302–316.
- Knyazev, G.G., Bocharov, A.V., Levin, E.A., Savostyanov, A.N., Slobodskoj-Plusnin, J.Y., 2008. Anxiety and oscillatory responses to emotional facial expressions. *Brain Res.* 1227, 174–188.
- Knyazev, G.G., Levin, E.A., Savostyanov, A.N., 2008. Impulsivity, anxiety, and individual differences in evoked and induced brain oscillations. *Int. J. Psychophysiol.* 68, 242–254.
- Lang, P.J., Bradley, M.M., Cuthbert, B.N., 2008. International affective picture system (IAPS): affective ratings of pictures and instruction manual. Technical Report A-8. University of Florida, Gainesville, FL.
- Lee, H., Heller, A.S., van Reekum, C.M., Nelson, B., Davidson, R.J., 2012. Amygdala–prefrontal coupling underlies individual differences in emotion regulation. *Neuroimage* 62, 1575–1581.
- Leicht, G., Kirsch, V., Giegling, I., Karch, S., Hantschk, I., Möller, H.-J., Pogarell, O., Hegerl, U., Rujescu, D., Mulert, C., 2010. Reduced early auditory evoked gamma-band response in patients with schizophrenia. *Biol. Psychiatry* 67, 224–231.
- Leicht, G., Karch, S., Karamatskos, E., Giegling, I., Möller, H.-J., Hegerl, U., Pogarell, O., Rujescu, D., Mulert, C., 2011. Alterations of the early auditory evoked gamma-band response in first-degree relatives of patients with schizophrenia: hints to a new intermediate phenotype. *J. Psychiatr. Res.* 45 (5), 699–705. <http://dx.doi.org/10.1016/j.jpsychires.2010.10.002>.
- Lesting, J., Narayanan, R.T., Kluge, C., Sangha, S., Seidenbecher, T., Pape, H.-C., 2011. Patterns of coupled theta activity in amygdala–hippocampal–prefrontal cortical circuits during fear extinction. *PLoS One* 6, e21714.
- Liebe, S., Hoerzer, G.M., Logothetis, N.K., Rainer, G., 2012. Theta coupling between V4 and prefrontal cortex predicts visual short-term memory performance. *Nat. Neurosci.* 15, 456–462.
- Marshall, L., Helgadottir, H., Molle, M., Born, J., 2006. Boosting slow oscillations during sleep potentiates memory. *Nature* 444, 610–613.
- Mechias, M.-L., Etkin, A., Kalisch, R., 2010. A meta-analysis of instructed fear studies: implications for conscious appraisal of threat. *Neuroimage* 49, 1760–1768.
- Meltzer, J.A., Fonzo, G.A., Constable, R.T., 2009. Transverse patterning dissociates human EEG theta power and hippocampal BOLD activation. *Psychophysiology* 46, 153–162.
- Michels, L., Bucher, K., Luchinger, R., Klaver, P., Martin, E., Jeanmonod, D., Brandeis, D., 2010. Simultaneous EEG–fMRI during a working memory task: modulations in low and high frequency bands. *PLoS One* 5, e10298.
- Mobascher, A., Brinkmeyer, J., Warbrick, T., Musso, F., Wittsack, H.J., Stoermer, R., Saleh, A., Schnitzler, A., Winterer, G., 2009. Fluctuations in electrodermal activity reveal variations in single trial brain responses to painful laser stimuli – a fMRI/EEG study. *Neuroimage* 44, 1081–1092.
- Moser, J.S., Hajcak, G., Bukay, E., Simons, R.F., 2006. Intentional modulation of emotional responding to unpleasant pictures: an ERP study. *Psychophysiology* 43, 292–296.
- Moser, J.S., Krompinger, J.W., Dietz, J., Simons, R.F., 2009. Electrophysiological correlates of decreasing and increasing emotional responses to unpleasant pictures. *Psychophysiology* 46, 17–27.
- Moser, J.S., Most, S.B., Simons, R.F., 2010. Increasing negative emotions by reappraisal enhances subsequent cognitive control: a combined behavioral and electrophysiological study. *Cogn. Affect. Behav. Neurosci.* 10, 195–207.
- Mulert, C., Jäger, L., Schmitt, R., Bussfeld, P., Pogarell, O., Möller, H.-J., Juckel, G., Hegerl, U., 2004. Integration of fMRI and simultaneous EEG: towards a comprehensive understanding of localization and time-course of brain activity in target detection. *Neuroimage* 22, 83–94.
- Mulert, C., Juckel, G., Brunnenmeier, M., Karch, S., Leicht, G., Mergl, R., Möller, H.-J., Hegerl, U., Pogarell, O., 2007a. Prediction of treatment response in major depression: integration of concepts. *J. Affect. Disord.* 98, 215–225.
- Mulert, C., Juckel, G., Brunnenmeier, M., Karch, S., Leicht, G., Mergl, R., Möller, H.-J., Hegerl, U., Pogarell, O., 2007b. Rostral anterior cingulate cortex activity in the theta band predicts response to antidepressive medication. *Clin. EEG Neurosci.* 38, 78–81.
- Mulert, C., Seifert, C., Leicht, G., Kirsch, V., Ertl, M., Karch, S., Moosmann, M., Lutz, J., Möller, H.-J., Hegerl, U., Pogarell, O., Jäger, L., 2008. Single-trial coupling of EEG and fMRI reveals the involvement of early anterior cingulate cortex activation in effortful decision making. *Neuroimage* 42, 158–168.
- Mulert, C., Leicht, G., Hepp, P., Kirsch, V., Karch, S., Pogarell, O., Reiser, M., Hegerl, U., Jäger, L., Möller, H.J., McCauley, R.W., 2010. Single-trial coupling of the gamma-band response and the corresponding BOLD signal. *Neuroimage* 49, 2238–2247.
- Mulert, C., Kirsch, V., Pascual-Marqui, R., McCauley, R.W., Spencer, K.M., 2011. Long-range synchrony of gamma oscillations and auditory hallucination symptoms in schizophrenia. *Int. J. Psychophysiol.* 79, 55–63.

- Narayanan, V., Heiming, R.S., Jansen, F., Lesting, J., Sachser, N., Pape, H.-C., Seidenbecher, T., 2011. Social defeat: impact on fear extinction and amygdala–prefrontal cortical theta synchrony in 5-HTT deficient mice. *PLoS One* 6, e22600.
- Oakes, T.R., Pizzagalli, D.A., Hendrick, A.M., Horras, K.A., Larson, C.L., Abercrombie, H.C., Schaefer, S.M., Koger, J.V., Davidson, R.J., 2004. Functional coupling of simultaneous electrical and metabolic activity in the human brain. *Hum. Brain Mapp.* 21, 257–270.
- Ochsner, K.N., Gross, J.J., 2005. The cognitive control of emotion. *Trends Cogn. Sci.* 9, 242–249.
- Ochsner, K.N., Bunge, S.A., Gross, J.J., Gabrieli, J.D.E., 2002. Rethinking feelings: an fMRI study of the cognitive regulation of emotion. *J. Cogn. Neurosci.* 14, 1215–1229.
- Ochsner, K.N., Ray, R.D., Cooper, J.C., Robertson, E.R., Chopra, S., Gabrieli, J.D.E., Gross, J.J., 2004. For better or for worse: neural systems supporting the cognitive down- and up-regulation of negative emotion. *Neuroimage* 23 (2), 483–499.
- Ochsner, K.N., Ray, R.R., Hughes, B., McRae, K., Cooper, J.C., Weber, J., Gabrieli, J.D.E., Gross, J.J., 2009. Bottom-up and top-down processes in emotion generation. *Psychol. Sci.* 20, 1322–1331.
- Paret, C., Brennkemeyer, J., Meyer, B., Yuen, K.S., Gartmann, N., Mechias, M.-L., Kalisch, R., 2011. A test for the implementation–maintenance model of reappraisal. *Front. Psychol.* 2.
- Parvaz, M., MacNamara, A., Goldstein, R., Hajcak, G., 2012. Event-related induced frontal alpha as a marker of lateral prefrontal cortex activation during cognitive reappraisal. *Cogn. Affect. Behav. Neurosci.* 1–11.
- Pascual-Marqui, R.D., 2002. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. *Clin. Pharmacol.* 24, 5–12.
- Pascual-Marqui, R.D., 2007. Instantaneous and lagged measurements of linear and nonlinear dependence between groups of multivariate time series: frequency decomposition. eprint arXiv:07111455.
- Pascual-Marqui, R.D., Michel, C.M., Lehmann, D., 1994. Low resolution electromagnetic tomography: a new method for localizing electrical activity in the brain. *Int. J. Psychophysiol.* 18, 49–65.
- Pizzagalli, D., Hendrick, A.M., Horras, K.A., Davidson, R.J., 2002. Anterior cingulate theta activity is associated with degree of treatment response in major depression. *Int. Congr. Ser.* 1232, 711–717.
- Pizzagalli, D.A., Oakes, T.R., Davidson, R.J., 2003. Coupling of theta activity and glucose metabolism in the human rostral anterior cingulate cortex: an EEG/PET study of normal and depressed subjects. *Psychophysiology* 40, 939–949.
- Pizzagalli, D., Pascual-Marqui, R.D., Nitschke, J.B., Oakes, T.R., Larson, C.L., Abercrombie, H.C., Schaefer, S.M., Koger, J.V., Benca, R.M., Davidson, R.J., 2011. Anterior cingulate activity as a predictor of degree of treatment response in major depression: evidence from brain electrical tomography analysis. *Am. J. Psychiatry* 158 (3), 405–415.
- Raghavachari, S., Lisman, J.E., Tully, M., Madsen, J.R., Bromfield, E.B., Kahana, M.J., 2006. Theta oscillations in human cortex during a working-memory task: evidence for local generators. *J. Neurophysiol.* 95, 1630–1638.
- Salari, N., Büchel, C., Rose, M., 2012. Functional dissociation of ongoing oscillatory brain states. *PLoS One* 7, e38090.
- Salisbury, D.F., Taylor, G., 2012. Semantic priming increases left hemisphere theta power and intertrial phase synchrony. *Psychophysiology* 49, 305–311.
- Sammer, G., Blecker, C., Gebhardt, H., Bischoff, M., Stark, R., Morgen, K., Vaitl, D., 2007. Relationship between regional hemodynamic activity and simultaneously recorded EEG-theta associated with mental arithmetic-induced workload. *Hum. Brain Mapp.* 28, 793–803.
- Sasaki, K., Nambu, A., Tsujimoto, T., Matsuzaki, R., Kyuhou, S., Gemba, H., 1996. Studies on integrative functions of the human frontal association cortex with MEG. *Cogn. Brain Res.* 5, 165–174.
- Sauseng, P., Hoppe, J., Klimesch, W., Gerloff, C., Hummel, F.C., 2007. Dissociation of sustained attention from central executive functions: local activity and interregional connectivity in the theta range. *Eur. J. Neurosci.* 25, 587–593.
- Schack, B., Klimesch, W., Sauseng, P., 2005. Phase synchronization between theta and upper alpha oscillations in a working memory task. *Int. J. Psychophysiol.* 57, 105–114.
- Schulze, L., Domes, G., Krüger, A., Berger, C., Fleischer, M., Prehn, K., Schmahl, C., Grossmann, A., Hauenstein, K., Herpertz, S.C., 2011. Neuronal correlates of cognitive reappraisal in borderline patients with affective instability. *Biol. Psychiatry* 69, 564–573.
- Sederberg, P.B., Kahana, M.J., Howard, M.W., Donner, E.J., Madsen, J.R., 2003. Theta and gamma oscillations during encoding predict subsequent recall. *J. Neurosci.* 23, 10809–10814.
- Singer, W., 1999. Neuronal synchrony: a versatile code for the definition of relations? *Neuron* 24, 49–65.
- Smits, J.A.J., Julian, K., Rosenfield, D., Powers, M.B., 2012. Threat reappraisal as a mediator of symptom change in cognitive–behavioral treatment of anxiety disorders: a systematic review. *J. Consult. Clin. Psychol.* 80, 624–635.
- Tallon-Baudry, C., Bertrand, O., Peronnet, F., Pernier, J., 1998. Induced  $\gamma$ -band activity during the delay of a visual short-term memory task in humans. *J. Neurosci.* 18, 4244–4254.
- Thiruchselvam, R., Blechert, J., Sheppes, G., Rydstrom, A., Gross, J.J., 2011. The temporal dynamics of emotion regulation: an EEG study of distraction and reappraisal. *Biol. Psychol.* 87, 84–92.
- Urry, H.L., van Reekum, C.M., Johnstone, T., Kalin, N.H., Thuro, M.E., Schaefer, H.S., Jackson, C.A., Frye, C.J., Greischar, L.L., Alexander, A.L., Davidson, R.J., 2006. Amygdala and ventromedial prefrontal cortex are inversely coupled during regulation of negative affect and predict the diurnal pattern of cortisol secretion among older adults. *J. Neurosci.* 26, 4415–4425.
- Wager, T.D., Davidson, M.L., Hughes, B.L., Lindquist, M.A., Ochsner, K.N., 2008. Prefrontal–subcortical pathways mediating successful emotion regulation. *Neuron* 59, 1037–1050.
- Winecoff, A., LaBar, K.S., Madden, D.J., Cabeza, R., Huettel, S.A., 2011. Cognitive and neural contributors to emotion regulation in aging. *Soc. Cogn. Affect. Neurosci.* 6, 165–176.