Gamma oscillations are involved in the sensorimotor transformation of pain

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Keywords: Gamma oscillations, pain, motor response, EEG
ABSTRACT

Pain signals threat and initiates motor responses to avoid harm. The transformation of pain into a motor response is thus an essential part of pain. Here, we investigated the neural mechanisms subserving the sensorimotor transformation of pain at the cortical level by using electroencephalography (EEG). In a simple reaction time experiment, brief painful stimuli were delivered to the left hand of healthy human subjects who responded with button presses of the right hand. The results show that the simple reaction time task was associated with neuronal responses at delta/theta, alpha/beta and gamma frequencies. The analysis of the relationship between neuronal activity and response speed revealed that gamma oscillations which were temporally coupled to the painful stimuli – but not temporally coupled to the motor response – predicted reaction times. Lateralization of gamma oscillations indicates that they originate from motor areas rather than from sensory areas. We conclude that gamma oscillations are involved in the sensorimotor transformation of pain whose efficiency they reflect. We hypothesize that the relationship between stimulus-locked gamma oscillations and reaction times reflects a direct thalamo-motor route of nociceptive information that is central to the biological function of pain.
INTRODUCTION

The physical integrity of the individual critically depends on the perception of pain. Central to the biological function of pain is the initiation of motor responses. Such motor responses include immediate withdrawal responses as well as more complex behavioral changes. Whereas withdrawal responses mostly result from spinal reflexes (Sandrini et al. 2005; Skljarevski and Ramadan 2002) more complex motor responses (Fields 2006; Melzack and Casey 1968) which include movements of other body parts or even the entire body require participation of the cerebral cortex. The neural mechanisms which underlie the initiation of such complex motor responses at the cortical level are largely unknown yet.

In the brain, the perception of pain is subserved by an extended network of brain areas (Apkarian et al. 2005; Tracey and Mantyh 2007). Neurophysiological studies disclosed that painful stimuli yield different neuronal responses within this network. Numerous investigations characterized pain-evoked potentials at frequencies below 10 Hz (Garcia-Larrea et al. 2003; Lorenz and Garcia-Larrea 2003). Other studies recorded pain-related suppressions of neuronal oscillations at alpha and beta (8-30 Hz) frequencies (Mouraux et al. 2003; Ploner et al. 2006a). In addition, recent studies revealed pain-induced oscillations at higher gamma (30-100 Hz) frequencies (Gross et al. 2007; Hauck et al. 2007; Schulz et al. 2011). However, how these neuronal responses relate to the behavioral outcome of the pain experience, i.e. a motor response is not yet known.

Here, we investigated the neural processes subserving the sensorimotor transformation of pain at the cortical level by using electroencephalography (EEG). We applied time-frequency analyses to single trial EEG responses during a reaction time task which served as a simple model of a motor response to pain which requires participation of the cerebral cortex. A linear mixed model (LMM) was used to relate neuronal activity to the efficiency of the sensorimotor transformation process, i.e. the speed of the motor response. As neuronal gamma oscillations have been related to the perception of pain (Gross et al. 2007; Hauck et al. 2007; Schulz et al. 2011) as well as to the initiation and execution of movements (Ball et al. 2008; Crone et al. 1998; Darvas et al. 2010; Donner et al. 2009; Miller et al. 2010;
we particularly focused on the functional significance of gamma oscillations for motor responses to pain.
MATERIALS AND METHODS

Subjects. Twenty healthy human subjects participated in the study. Three subjects were excluded from the analysis due to poor data quality and/or prolonged reaction times. The analysis, thus, included 17 subjects (7 male, 10 female, 22 – 33 years) with at least 40 (out of 120) artifact-free trials. Informed consent was given by all subjects. The study was approved by the local ethics committee and conducted in conformity with the declaration of Helsinki.

Paradigm. In a simple reaction time experiment, 120 moderately painful cutaneous laser stimuli were delivered to the dorsum of the left hand. Subjects were instructed to react as fast as possible to the stimuli by pressing a button with the index finger of the right hand. Interstimulus interval was randomly varied between 8 and 12 seconds (Fig. 1). Subjects were exposed to white noise through headphones to cancel out any noise of the laser device.

Stimulation. Painful stimuli were applied by using cutaneous laser stimulation which activates selectively nociceptive Aδ and C afferents (Plaghki and Mouraux 2003). The laser device was a Tm:YAG laser (Starmedtec GmbH, Starnberg, Germany) with a wavelength of 1960 nm, a pulse duration of 1 ms and a spot diameter of 5 mm. Stimulus intensity was individually adjusted to elicit moderately painful pinprick-like sensation with a rating of 5 on a numerical rating scale ranging from 0 (no pain) to 10 (maximum tolerable pain). Adjustment resulted in a mean stimulus intensity of 500 mJ (range, 400 - 670 mJ). Stimulation site was slightly changed after each stimulus.

Recordings. EEG data were recorded using an electrode cap (EASYCAP, Herrsching, Germany). The electrode montage included 64 electrodes consisting of all 10-20 system electrodes and the additional electrodes Fpz, FCz, CPz, POz, Oz, Iz, AF3/4, F5/6, FC1/2/3/4/5/6, FT7/8/9/10, C1/2/5/6, CP1/2/3/4/5, TP7/8/9/10, P5/6, PO1/2/9/10, plus two electrodes below the outer canthus of each eye. The EEG was referenced to the FCz
electrode, grounded at AFz, sampled at 1 kHz (0.1 µV resolution) and highpass-filtered at 0.5 Hz. The impedance was kept below 20 kΩ.

**Analysis.** Reaction times to painful laser stimuli were calculated as latency between stimulus application and button press. Reaction times longer than 600 ms were discarded in order to focus the analysis on first pain-related responses. EEG data were preprocessed in BrainVision Analyzer 2.0 software (Brain Products, Munich, Germany). The processing steps include downsampling to 512 Hz, high-pass filtering of 0.5 Hz, removal of artifacts from non-cortical sources such as horizontal and vertical eye movements as well as neck muscle activity using ICA (Independent Component Analysis), and data transformation to the average reference. Trials with artifacts exceeding ±100 µV in any channel were automatically rejected. The remaining trials (93 ± 22) were aligned with respect to application of painful stimuli (-1100 ms - 2500 ms) and with respect to button presses (-2100 ms - 1500 ms) and exported to Matlab (The Mathworks, Natick, USA).

Time-frequency analyses were performed in Matlab using custom programming on the basis of standard mathematical and signal analysis functions. To compute time-frequency representations (TFR) we applied a single trial Hamming tapered, moving window short time Fast Fourier Transformation. The window had a length of 100 data points, was padded with zeros up to 512 data points and was shifted for 1 data point. Hence, the displayed frequency resolution was 1 Hz and the displayed temporal resolution was 1/512 sec.

We first determined changes in neuronal activity related to the reaction time task. To determine temporal coupling of neuronal activity to painful stimuli and motor responses, respectively, we analyzed the trials twice; once stimulus-locked (i.e. with respect to painful stimuli) and once response-locked (i.e. with respect to button presses). On a single trial basis, TFRs were computed and transformed into percent signal change with respect to the single trial baseline from -1000 ms to 0 ms before stimulus application. Hence, the same baseline has been applied to both types of alignment. TFRs were visually inspected for artifacts. For each subject and electrode, individual mean TFRs were calculated by
averaging the baseline corrected single trial TFRs across trials. In addition, for each electrode, group mean TFRs were calculated by averaging the individual TFRs across subjects. Statistical significance of changes of neuronal activity was assessed by calculating paired t-tests between poststimulus activity at each data point of the TFRs and the mean activity of the prestimulus baseline period (-1000 to 0 ms) for each electrode without any signal change transformation or baseline correction. To control for type I error, False Discovery Rate (FDR) as correction across time (0 - 1000 ms for stimulus aligned trials, -500 - 500 ms for button press aligned trials), frequency (0 – 100 Hz) and electrodes (65) was performed. Based on the distribution of observed p-values, the FDR correction controls the expected proportion of false positives among supra-threshold values (Benjamini and Hochberg 1995).

To further characterize the sensorimotor transformation process, functional microstates as periods of stable topography of neuronal activity were determined (Lehmann et al. 2009; Pascual-Marqui et al. 1995). A k-means clustering algorithm with 5000 repetitions using Cartool software (http://brainmapping.unige.ch/Cartool.htm; (Brunet et al. 2011) was used. Microstate analyses were performed for the grand average across all trials and subjects. Microstate analysis was applied to the time course of gamma (70 – 90 Hz) and delta/theta (3 – 8 Hz) activity as activity only at these frequencies occur during the sensorimotor transformation process and relate to its efficiency, i.e. the speed of reaction times (see below). Microstate analysis was performed for trials aligned with respect to painful stimuli (0 – 1000 ms) and with respect to button presses (-500 – 500ms). The postprocessing included a sequentializing of similar but temporarily distinct microstates, a cluster threshold of at least 30 time frames (59 ms), as well as a merging of clusters that were highly correlated (92%). To correct for multiple comparisons we used the same threshold as defined by the FDR correction across time, frequency and electrodes. Microstates were considered as significant if more than 5 electrodes exceeded the threshold.

Finally, we aimed to determine neuronal activity which predicts the efficiency of the sensorimotor transformation process, i.e. the speed of the behavioral response. We therefore
analyzed the relationship between neuronal activity and reaction times on a single trial basis. To assess intraindividual (conditional) dependence of reaction times on neuronal activity we applied linear mixed models (LMM) to the single trial time-frequency transformed EEG data. The LMM parameters were estimated by solving the Henderson's mixed model equations (Searle et al. 1992). LMM were estimated for each data point of the baseline corrected single trial TFRs (1744 time frames x 100 frequency steps for each of the 65 electrodes). This analysis yields TFRs containing t-values which do not show neuronal activity but the relationship between neuronal activity and response speed as a function of time and frequency. Before estimating the LMM, the reaction times were multiplied by -1 to ensure that positive t-values indicate that faster reaction times are associated with greater amplitudes. We estimated LMM for stimulus-locked and response-locked neuronal activity, respectively. This analysis shows how neuronal activity which is temporally coupled to the stimulus and the motor response, respectively, predicts the speed of the motor response. To control for type I error, FDR correction across time, frequency and electrodes was performed as done for the signal change TFRs (Benjamini and Hochberg 1995). Again, a microstate analysis was performed for the resulting time course of t-values for gamma and delta/theta responses (see above).
RESULTS

Subjects reported moderately painful pinprick-like sensations to individually adapted laser stimuli. Reaction time to painful laser stimuli was $417 \pm 53$ ms (mean $\pm$ SD).

Neuronal activity during the reaction time task. We first determined changes in neuronal activity related to the reaction time task. Stimulus-locked time-frequency representations (TFRs) were calculated for each trial and electrode. These TFRs show neuronal activity as a function of time and frequency and include phase-locked as well as non-phase-locked neuronal activity. The group mean stimulus-locked TFR at exemplary electrode FCz (Fig. 2A) shows that painful stimuli and subsequent button presses yielded four different neuronal responses at latencies between 150 and 2000 ms after stimulus application. First, we found a strong increase of neuronal activity below 10 Hz (55 % max. signal change, $t_{\text{max}} = 5.8$) with a maximum at latencies between 150 and 400 ms corresponding to pain-evoked (Garcia-Larrea et al. 2003; Lorenz and Garcia-Larrea 2003) and movement-related (Colebatch 2007; Tamas and Shibasaki 1985) potentials. Second, we observed an increase of neuronal activity (19 % max. signal change; $t_{\text{max}} = 5.1$) in the gamma frequency band between 70 and 90 Hz at latencies between 150 and 400 ms confirming recent descriptions of pain- and motor-induced gamma oscillations (e.g. Ball et al. 2008; Gross et al. 2007). Third, we identified a pain-related decrease in neuronal activity (-11 % max. signal change; $t_{\text{min}} = -6.1$, all $p < 0.05$, FDR corrected) around 20 Hz between 200 and 600 ms after stimulus application (Mouraux et al. 2003; Ploner et al. 2006a) as well as, fourth, a beta activity rebound starting after behavioral responses at about 800 ms. Comparison of stimulus-locked and response-locked TFRs (Fig. 2A and 2B, respectively) showed qualitatively similar patterns of neuronal activity indicating that all neuronal responses were temporally coupled to the stimuli as well as to motor responses.

We next assessed the dynamics of neuronal activity by defining functional microstates as periods of stable topography representing functionally distinct states of neuronal processing (Lehmann et al. 2009; Pascual-Marqui et al. 1995). For stimulus-locked activity, the k-means
clustering analysis revealed 2 significant microstates of delta/theta and gamma activity, respectively, before and during the button press. Initially, the topographies of gamma and delta/theta activity showed a right-sided lateralization of power (Fig. 2A, right panel), suggesting - due to the lateralization contralateral to the stimulus - sensory processing. Subsequently, we observed a left-sided lateralization of delta/theta and gamma power (Fig. 2A, right panel) suggesting – due to the lateralization contralateral to the motor response - motor processing. Again, the microstate analysis for the response-locked neuronal activity showed a qualitatively similar pattern (Fig. 2B, right panel).

**Relationship between neuronal activity and reaction times.** To determine neuronal activity which predicts the efficiency of the sensorimotor transformation process we related amplitudes of neuronal activity to reaction times on a single trial basis. We specifically applied linear mixed models (LMM) to the single trial time-frequency transformed EEG data. This analysis yields TFRs which do not show neuronal activity but the relationship between neuronal activity and reaction times as a function of time and frequency. First, we analyzed neuronal activity aligned with respect to stimulus application. Figure 3A shows that amplitudes of delta/theta ($t_{\text{max}} = 5.9$) and gamma ($t_{\text{max}} = 6.9$, all $p < 0.05$, FDR corrected) activity were related to reaction times. The positive t-values indicate that higher amplitudes of neuronal activity were associated with shorter reaction times (see Methods). In addition, beta activity was also related to reaction times but occurred after the button presses and can therefore not be related to the sensorimotor transformation. Thus, delta/theta and gamma responses which were temporally coupled to the stimulus predicted the efficiency of the sensorimotor transformation process. Notably, topographies reveal that gamma activity predicting reaction times was lateralized to the left hemisphere which suggests involvement in motor rather than in sensory processes. Second, we analyzed neuronal activity aligned with respect to button presses (Fig. 3B). We found that only delta/theta ($t_{\text{max}} = 7.8$, $p < 0.05$, FDR corrected) but not gamma activity predicted reaction times. Thus, stimulus-locked
gamma oscillations which most probably originate from motor areas but not response-locked

gamma oscillations predicted reaction times.
DISCUSSION

Here, we investigated the cortical mechanisms subserving the sensorimotor transformation of pain. To this end, healthy human subjects performed a simple reaction time task as an elementary model of the cortical transformation of pain into a motor response. Our results show that speeded motor responses to painful stimuli are associated with neuronal activity at delta/theta, alpha/beta and gamma frequencies. Neuronal activity at all frequencies was temporally coupled to the painful stimuli as well as to the motor responses. Analysis of the relationship between neuronal activity and reaction times revealed that activity at delta/theta and gamma frequencies predicted response speed, i.e. the efficiency of the sensorimotor transformation process. Intriguingly, gamma oscillations which were temporally coupled to the painful stimulus but - according to the topography - most probably originate from motor areas predicted reaction times. Gamma oscillations are, thus, involved in the sensorimotor transformation of pain whose efficiency they reflect.

Neuronal activity at delta/theta frequencies and its functional significance. The simple reaction time task was associated with neuronal activity at delta/theta frequencies. Delta/theta activity is likely to include evoked responses to painful stimuli (Garcia-Larrea et al. 2003; Lorenz and Garcia-Larrea 2003) as well as movement-related potentials (Colebatch 2007; Tamas and Shibasaki 1985). Early activity at delta/theta frequencies was strongest at vertex electrodes which is compatible with stimulus-related (Garcia-Larrea et al. 2003; Lorenz and Garcia-Larrea 2003) as well as movement preparation-related (Colebatch 2007; Tamas and Shibasaki 1985) activity. Later activity around the button press shows a left lateralized topography, indicating that this activity represents motor-related activity (Caldara et al. 2004; Kirsch et al. 2010). The analysis of the relationship between delta/theta activity and reaction times reveals that the amplitude of delta/theta activity was significantly related to reaction times. However, neither the topography nor the temporal coupling of the LMM analysis to the stimulus and the motor responses provides clear evidence whether sensory- and/or motor-related activity predicts the efficiency of the sensorimotor transformation.
Furthermore, to the very best of our knowledge, no previous study has as yet related single trial amplitudes of evoked responses to reaction times. Nevertheless, as the subjective intensity (Schulz et al. 2011) and the saliency (Iannetti et al. 2008) of physically identical stimuli can vary the relationship between delta/theta activity and reaction times could well reflect spontaneous variations in the perceived intensity and/or saliency of painful stimuli.

**Sensory- and motor-related gamma oscillations.** In line with previous investigations (Gross et al. 2007; Hauck et al. 2007; Schulz et al. 2011; Tiemann et al. 2010) we observed gamma oscillations which were lateralized to the right hemisphere, i.e. contralateral to the painful stimulus. The lateralization strongly suggests that these gamma oscillations are related to sensory processes. In addition, we also observed later left-lateralized gamma oscillations. Lateralization of oscillations to the hemisphere contralateral to the button press indicates that these oscillations are related to motor rather than to sensory processes. The lateralised topography of gamma responses is in line with recent findings of pain-related (Schulz et al. 2011) and motor-related (Ball et al. 2008) gamma activity and argues against the possibility that the responses are due to muscle activity or miniature saccades which exhibit a spatially different distribution with maxima at peripheral (Goncharova et al. 2003) and parietooccipital (Yuval-Greenberg et al. 2008) electrodes, respectively. The result is also in agreement with previous studies showing that gamma oscillations may occur slightly before (Crone et al. 1998; Donner et al. 2009; Miller et al. 2010) but also during (Cheyne et al. 2008; Huo et al. 2010) motor execution. Consequently, motor-related gamma oscillations have been related to the initiation and execution of movements. The present results provide further evidence for an involvement of gamma oscillations in both processes. First, we observed that gamma oscillations which were temporally coupled to the stimulus predicted the speed of the motor response. The coexistence of temporal coupling to the stimulus and functional coupling to the motor response i.e. a significant correlation between neuronal activity and response speed, indicates that these oscillations are involved in the sensorimotor transformation process whose efficiency they reflect. Second, we observed that gamma
oscillations which were temporally coupled to the motor response did not relate to reaction
times. Temporal coupling without functional coupling is likely to indicate that these gamma
oscillations are uniformly related to the execution rather than to the initiation of motor
responses. We thus hypothesize that different aspects of gamma oscillations relate to the
initiation and execution of motor responses, respectively.

Functional significance of pain-related gamma oscillations. Pain can be conceptualized
as a motivational state which drives the individual into complex and variable patterns of
behavioral responses ranging from spinally mediated withdrawal reflexes (Sandrini et al.
2005; Skljarevski and Ramadan 2002) to complex motor responses at the cortical level
(Fields 2006; Melzack and Casey 1968). Here, we used a simple reaction time paradigm as
a most simple model of the sensorimotor transformation of pain at the cortical level. Our
results show that gamma oscillations are significantly related to the efficiency of the
sensorimotor transformation of pain. Our findings complement previous studies in monkeys
(Womelsdorf et al. 2006) and humans (Bauer et al. 2009; Gonzalez Andino et al. 2005;
Hoogenboom et al. 2010; Koch et al. 2009; Schoffelen et al. 2005) which related gamma
oscillations to the speed of behavioral responses. Those studies provided converging
evidence that gamma oscillations in sensory (Bauer et al. 2009; Hoogenboom et al. 2010;
Koch et al. 2009; Womelsdorf et al. 2006) as well as in motor areas (Gonzalez Andino et al.
2005; Schoffelen et al. 2005) determine reaction times. This was taken as evidence for a role
of gamma oscillations as a neuronal communication which controls information flow across
the brain (Fries 2009; Wang 2011). Our observations would be well compatible with this
hypothesis by showing that gamma oscillations relate to the efficiency of the sensorimotor
transformation of pain that critically depends on information flow across the brain.

Alternatively, but not mutually exclusively, our observations could also indicate a cortically
mediated release of spinal inhibition (Duque et al. 2010) induced by the application of painful
stimuli. Moreover, the present data do not provide evidence on the causal relationship
between gamma oscillations and reaction times. Fluctuations of gamma oscillations and
reaction times might eventually reflect fluctuations of vigilance and/or peripheral nociceptive input.

Notably, gamma oscillations which predicted the efficiency of the sensorimotor transformation process were observed in the left hemisphere, i.e. contralateral to the button press. Thus, these oscillations are most likely related to motor rather than to sensory processes. The occurrence of motor-related gamma oscillations which were, however, temporally coupled to the stimulus in predicting reaction times could indicate that pain-related information is not only conveyed via sensory areas to the motor cortex but is also directly routed from the thalamus via the cingulate cortex to the motor system as shown in anatomical studies (Craig 2008; Dum et al. 2009) and suggested by a recent functional imaging study (Liang et al. 2012). Our results would thus be compatible with the recent suggestion that the anterior midcingulate cortex integrates information about negative affect including pain to initiate adaptive motor responses (Shackman et al. 2011). The direct thalamo-motor route of nociceptive information could well reflect the particular biological relevance of complex but coordinated motor responses to pain and complements other evidence for a parallel organization of pain pathways in the human brain (Frot et al. 2008; Ploner et al. 2006b; Ploner et al. 1999).

The present findings complement and extend previous studies in which pain-induced gamma oscillations have been related to the subjective experience of pain (Gross et al. 2007) and its involuntary attentional effects (Tiemann et al. 2010). These observations can be well reconciled with the recent hypothesis (Donner and Siegel, 2011) that neuronal gamma oscillations are related to the local representation of sensory and motor variables which determine further neuronal processing at the network level.

Limitations. We used a simple reaction time task as a model of a motor response to pain which requires participation of the cerebral cortex. However, button presses do certainly not represent behaviorally appropriate motor responses to painful events. Nevertheless, the
reaction time task can well serve as a most simple model of complex motor responses to pain – as a first approach to the understudied field of the association between pain and motor behavior. Moreover, the spatial dissociation between stimulus and motor response to opposite limbs facilitates disentangling stimulus- and response-related neuronal responses. However, considering the close proximity of sensory and motor areas in post- and precentral cortex, an unequivocal assignment of neural activity to sensory and motor areas is beyond the spatial resolution of EEG.

**Conclusions.** In a simple reaction time task to painful stimuli, we investigated the role of neuronal gamma oscillations for the sensorimotor transformation of pain. We found that gamma oscillations are involved in both the initiation and execution of motor responses. Our finding that stimulus-locked gamma oscillations which are suggested to originate from motor regions predict the speed of behavioral responses may complement other evidence for a direct thalamo-motor route of nociceptive information. This finding extends evidence for a parallel organization of pain processing pathways in the human brain that are central to the biological function of pain.

**ACKNOWLEDGMENTS**

The study was supported by the Deutsche Forschungsgemeinschaft (PL 321/6-1, Research Training Group 1373) and the Studienstiftung des deutschen Volkes. We thank Mark Mühlau for fruitful discussions of the study.
REFERENCES


FIGURE LEGENDS

Figure 1. Paradigm. 120 painful laser stimuli were applied to the left hand with an interstimulus interval of 8 – 12 s. Subjects were instructed to react as fast as possible to the stimuli by pressing a button with the right hand.

Figure 2. Neuronal activity during the simple reaction time task. A, Left, Stimulus-locked time-frequency representation (TFR) of neuronal activity at electrode FCz coded as percent signal change with respect to a prestimulus baseline. The dashed line indicates the mean latency of the button press. Neuronal activity which is significantly different from baseline activity (see Methods) is accentuated by a black line. Right, Topographies of significant gamma (70 – 90 Hz) and delta/theta (3 – 8 Hz) microstates. The location of the electrode shown in the TFR is marked by a black dot. B, Response-locked TFR of neuronal activity at electrode FCz coded as percent signal change with respect to a prestimulus baseline. The dashed line indicates the mean latency of stimulus application. Right, Topographies of significant gamma and delta/theta microstates. The location of the electrode shown in the TFR is marked by a black dot. The color bar refers to both TFRs as well as to the topographical maps.

Figure 3. Relationship between neuronal activity and reaction times. A, Left, Stimulus-locked relationship between neuronal activity and reaction times as time time-frequency representation (TFR) at electrode CP1 based on Linear mixed models (LMM, t-values). The dashed line indicates the mean latency of the button press. Significant t-values are accentuated by a black line. Right, Topographies of significant LMM gamma and delta/theta microstates. The location of the electrode shown in the TFR is marked by a black dot. Bottom, Time course (LMM, t-maps) of the relationship between stimulus-locked gamma oscillations during the significant microstate (142 – 408 ms) in 25 ms steps. B, Left, Response-locked relationship between neuronal activity and reaction times as time time-frequency TFR at electrode Cz based on LMM (t-values). The dashed line indicates the
mean latency of stimulus application. Right, Topography of the significant LMM delta/theta microstate. The location of the electrode shown in the TFR is marked by a black dot. The color bar refers to both TFRs as well as to the topographical maps.
A. Relationship between stimulus-locked neuronal activity and reaction time

- Significant gamma microstate (142 - 408 ms)
- Significant theta microstate (99 - 238 ms)

*Time course of the relationship between stimulus-locked gamma activity and reaction time during the significant microstate

B. Relationship between response-locked neuronal activity and reaction time

- No significant gamma microstate
- Significant theta microstate (-192 - 121 ms)