REVIEW

Time–Frequency Analysis of Event-Related Potentials: A Brief Tutorial

Christoph S. Herrmann · Stefan Rach · Johannes Vosskuhl · Daniel Strüber

Abstract Event-related potentials (ERPs) reflect cognitive processes and are usually analyzed in the so-called time domain. Additional information on cognitive functions can be assessed when analyzing ERPs in the frequency domain and treating them as event-related oscillations (EROs). This procedure results in frequency spectra but lacks information about the temporal dynamics of EROs. Here, we describe a method—called time–frequency analysis—that allows analyzing both the frequency of an ERO and its evolution over time. In a brief tutorial, the reader will learn how to use wavelet analysis in order to compute time–frequency transforms of ERP data. Basic steps as well as potential artifacts are described. Rather than in terms of formulas, descriptions are in textual form (written text) with numerous figures illustrating the topics. Recommendations on how to present frequency and time–frequency data in journal articles are provided. Finally, we briefly review studies that have applied time–frequency analysis to mismatch negativity paradigms. The deviant stimulus of such a paradigm evokes an ERO in the theta frequency band that is stronger than for the standard stimulus. Conversely, the standard stimulus evokes a stronger gamma-band response than does the deviant. This is interpreted in the context of the so-called match-and-utilization model.

Introduction

Event-related potentials (ERPs) represent the standard technique in cognitive neuroscience to assess the temporal-spatial dynamics of cognitive processes (Handy 2004; Luck 2005). They are computed by averaging the electroencephalogram (EEG) across a number of experimental trials. An ERP consists of a series of positive and negative deflections. These deflections are called components if they respond to experimental manipulations of sensory or cognitive processes. They are named according to their polarity and latency, for example the P300 refers to a positive component that peaks around 300 ms after stimulus onset.

Ongoing (*spontaneous*) brain activity is typically described in the frequency or spectral domain, since it reflects a mixture of oscillations. Interestingly, also *event-related* brain responses to sensory and cognitive events can be described as event-related oscillations (EROs) in the spectral or time–frequency domain (Başar et al. 2001). Every ERP component can be viewed as an ERO of a specific frequency or a superposition of multiple EROs with different frequencies. A P100 typically peaks at 100 ms and has a temporal width of around 50 ms. If this ERP component is viewed as one half cycle of an oscillation, the 50 ms corresponds to an oscillation with a period of 100 ms (i.e. 10 Hz) which corresponds to the alpha band (8–12 Hz). Later components of longer duration like the P300 are reflected in the slower delta (0–4 Hz)

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and theta (4–8 Hz) frequency range (Başar-Eroglu et al. 1992). Thus, it is the superposition of the EROs in all frequency bands that constitute the morphology and amplitude of the ERP (Karakaş et al. 2000).

It has been shown that spontaneous oscillations before stimulus onset influence the post-stimulus ERP in amplitude and latency. Intriguingly, spontaneous alpha activity modulates ERP components that are reflected in the alpha range such as the auditory N1 (Rahn and Başar 1993; Haig and Gordon 1998; Barry et al. 2004) and the visual P1 (Fellinger et al. 2011), whereas spontaneous theta activity rather modulates later ERP components that are reflected in the theta range (Başar et al. 1998). If alpha modulation resulted in enhanced N1 amplitudes, this in turn led to faster reaction times (Haig and Gordon 1998). The findings about the close relation of brain oscillations and ERP components have been taken as evidence for the notion that ERP components are more appropriately considered to be a superposition of oscillatory brain responses. An extreme version of this view is that an ERP is purely generated by the resetting of the phase of spontaneous oscillations (Makeig et al. 2002; Klimesch et al. 2007). The phase of a spontaneous oscillation usually increases continuously from zero to 2π, jumps back to zero and so forth. Certain events have been shown to influence the phase of oscillations. In case of a phase reset, the phase is reset to the same phase value for every event, such as the onset of a sensory stimulus. Phase-reset as a mechanism for ERP generation, however, is a matter of debate (Mäkinen et al. 2005; Mazaheri and Jensen 2006; Risner et al. 2009)—a critical review is given by Sauseng et al. (2007). Most probably, the ERP is a combination of two mechanisms referred to as *additive power* and *phase resetting* (Min et al. 2007; Mishra et al. 2012). Regardless of whether ERPs are generated by a phase reset of spontaneous oscillations or not, there are good reasons to perform frequency or time–frequency analysis of brain responses in order to assess EROs.

Assessment of Induced Brain Oscillations

As will be shown in more detail below, oscillatory brain responses can either be phase-locked to stimulus onset or can vary in phase with respect to stimulus onset. In the former case, oscillations would show up in the ERP and are considered to be *stimulus-evoked* oscillations. In the latter case, oscillations would nearly cancel out in the averaged ERP and are considered to be *stimulus-induced* oscillations (Herrmann et al. 2004b). Although this distinction has mainly been used in the context of oscillatory alpha (Klimesch et al. 1998; Busch and Herrmann 2003; Herrmann et al. 2004b) and gamma responses (Tallon-Baudry et al. 1998; Gruber et al. 2008), it is also valid for oscillations in other frequency bands such as the theta band.

For example, Klimesch et al. (2000) were able to show that induced theta oscillations are enhanced for remembered as compared to forgotten items in a memory paradigm. Furthermore, Bastiaansen et al. (2002) have demonstrated that stimuli that disappear from the screen and have to be remembered, result in stronger modulation of induced theta responses than stimuli which were presented continuously but did not have to be remembered. In addition, Guderian and Düzel (2005) were able to demonstrate that induced theta oscillations are stronger for recollection than for recognition in a memory paradigm. A comprehensive review on theta oscillations in memory paradigms is given by Bastiaansen and Hagoort (2003).

### Predicting Human Behavior with Brain Oscillations

A further advantage of analyzing brain oscillations lies in their predictive value for subsequent behavior even before stimulus onset. For example, it has been demonstrated that the amplitude of pre-stimulus EEG alpha oscillations predicts whether or not subjects are able to detect near-threshold visual stimuli (Ergenoglu et al. 2004; Hanslmayr et al. 2007). In addition, discriminability of above-threshold stimuli was shown to depend upon pre-stimulus alpha power (Van Dijk et al. 2008). More recently, Busch et al. (2009) showed that also the phase of pre-stimulus alpha oscillations is predictive for subsequent visual perceptual performance. Not only alpha but also other oscillations such as for example in the delta range (0–4 Hz) have been demonstrated to predict subsequent behavior (Stefanics et al. 2010).

Single-Trial Analysis

A fundamental goal in psychophysiology is to link human behavior to electrophysiology on a trial-by-trial basis. This has been difficult to achieve due to the low signal-to-noise ratio (SNR) of ERPs. An ERP amplitude (i.e. the signal) is in the range of a few microvolts (μV), whereas the amplitude of the spontaneous EEG (i.e. mainly the alpha rhythm which is considered 'noise' in this respect) is on the order of a few tens of μV, resulting in an SNR of −20 decibels (dB). However, some researchers have succeeded in identifying at least ERPs with high voltage, such as the P300, in single-trial data (Wetter et al. 2004; Jongsma et al. 2006). Especially, the so-called ERPIMAGE that plots single ERP trials in color and sorts them according to behavioral measures such as reaction time has proven useful in this respect (Jung et al. 2001).

Analyzing single-trials within a narrow frequency band bears the advantage that the amplitude of the 'noise' is considerably reduced. Both, other frequencies that are not of interest and technical noise have a spectral density that

Fig. 1 Principle of frequency and time–frequency analysis. **a** 10 s of posterior EEG from a wake human subject with eyes closed, depicting strong alpha activity. **b** A spectrum shows that the alpha rhythm has a frequency of 10 Hz. **c** The time–frequency plot displays the temporal dynamics of the alpha rhythm, revealing the waxing and waning over time. Note, that the 10 Hz peak in the spectrum (**b**) represents the average of the 10 Hz activity over the time interval of 10 s whereas the time–frequency plot (**c**) reveals maxima and minima during the time course
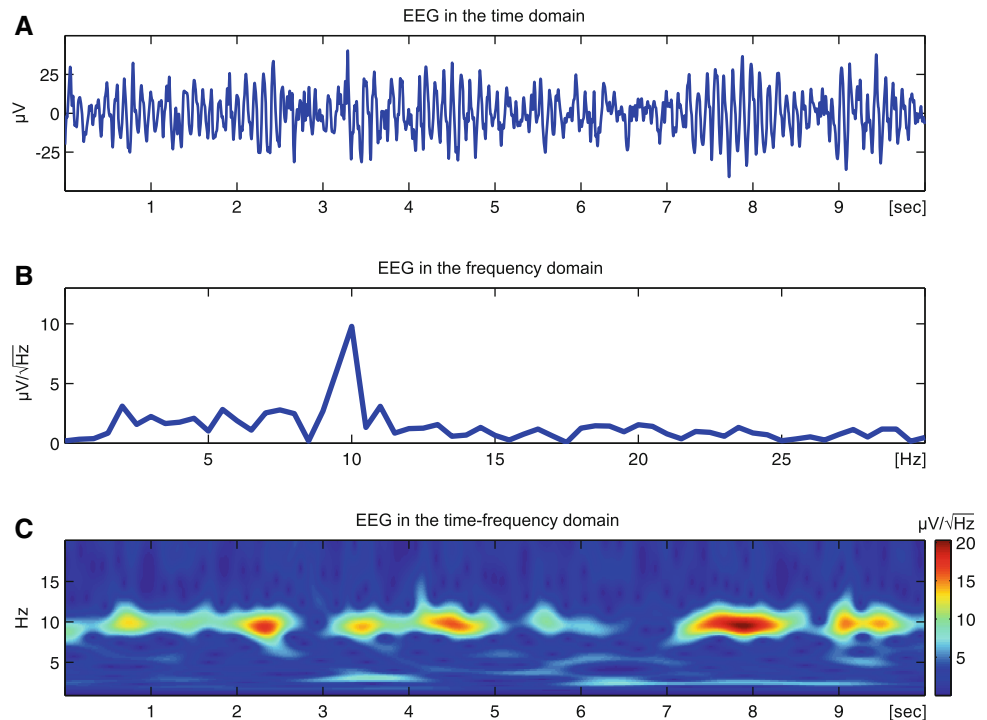
is specified per Hertz (Hz). Thus, wider bands yield increased levels of noise.[1] Therefore, analyzing single-trial data in narrow frequency bands becomes feasible (Schürmann et al. 1995) and has revealed interesting results about cognitive processes (Debener et al. 2005) including auditory mismatch detection (Atienza et al. 2005; Bishop and Hardiman 2010). For the purpose of single-trial classification, time–frequency analysis is often combined with independent component analysis (ICA) such that every ICA component has a time–frequency representation and topography (De Vos et al. 2012).

In the following, we will at first describe how to perform time–frequency analyses of event-related EEG data in form of a brief tutorial. Then, since this article is part of a special issue on MMN, we review studies that have applied time–frequency analysis to MMN paradigms.

Tutorial

Time Domain, Frequency Domain, and Time–Frequency Domain

Figure 1a depicts 10 s of ongoing EEG at a posterior electrode in the so-called time domain. The EEG is

dominated by the alpha activity which typically oscillates in the range of 8–12 Hz. Its amplitude varies over time which can easily be observed in the time domain. The exact frequency of the alpha rhythm, however, cannot be extracted at first glance from this graph. This is easier in the frequency domain or spectral domain (cf. Fig. 1b). A frequency transform converts the EEG signal into a spectrum. Typically, a fast Fourier transform (FFT) is used for this purpose. The resulting spectrum displays which frequencies are contained in the EEG.

The temporal dynamics of the frequency components, however, cannot be accessed. The so-called time–frequency domain combines the best of both worlds and shows the amplitude and frequency of brain oscillations including their variation over time (cf. Fig 1c). Here, the color indicates the amplitude of a brain oscillation, as illustrated in Fig. 1c for the alpha rhythm, depicting its amplitude variation with a maximum around 8 s as well as a relatively stable frequency around 10–11 Hz.

ERP Versus ERO

Like spontaneous EEG, event-related changes in the EEG can either be analyzed in the time, frequency, or time–frequency domain (cf. Fig. 2). In the beginning of ERP research, it was most common to display ERPs in the time domain (Walter et al. 1964; Sutton et al. 1965), as depicted in Fig. 2a. Making use of the Fourier Transform allowed to perform spectral analysis of ERPs, transforming the signal into the frequency domain (Dietsch 1932). The spectrum of

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[1] Imagine that an EEG amplifier records technical noise with a spectral density of 0.01 μV/Hz. Then the noise in a frequency band that is 1 Hz wide would be 0.01 μV while it would be 0.1 μV in a band that is 10 Hz wide.
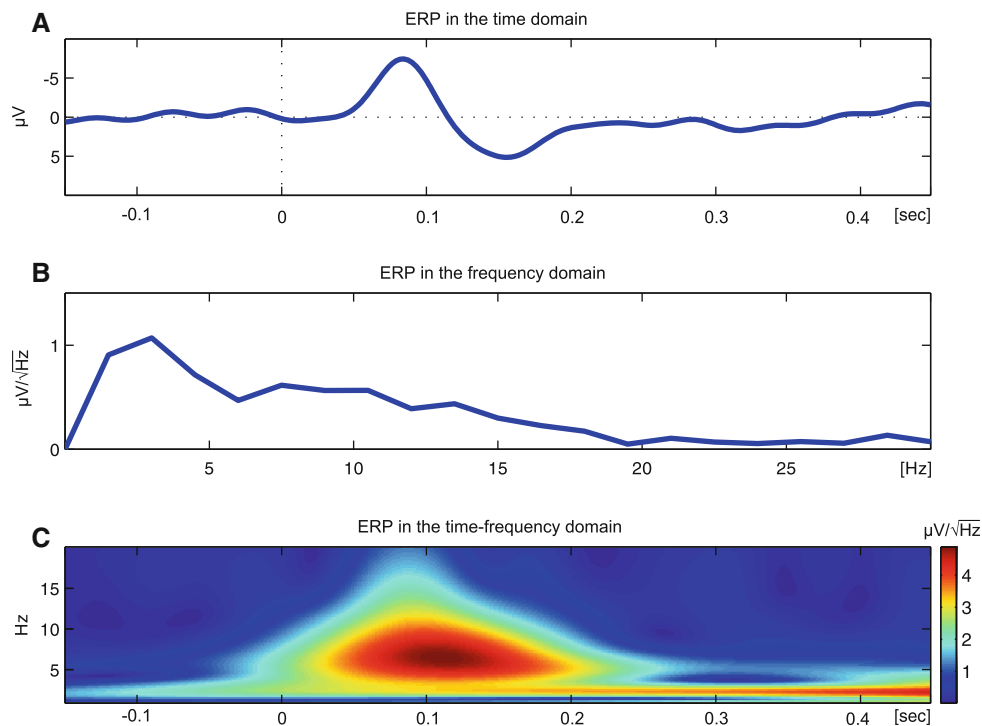
Fig. 2 An ERP in different domains. **a** ERP in response to a deviant stimulus from a MMN paradigm (Schadow et al. 2009) plotted in the time domain. The *dotted line* at 0 s on the time axis indicates stimulus onset. **b** The same ERP represented in the frequency domain (i.e. the spectrum of the ERP). A peak occurs around 2–3 Hz. **c** The same ERP in the time–frequency domain. Here, two spectral components (2–3 and 6 Hz) and their evolution over time are clearly visible, whereas in the spectrum only one peak can be discerned. One frequency component at 6 Hz peaks at 0.1 s after stimulus onset and another at 2–3 Hz around 0.4 s. Interestingly, the 2–3 Hz component is also visible in the frequency domain while the 6 Hz component is not. This is due to the fact that the spectrum was computed for one second and the 6 Hz component appears only for a fraction of that second whereas the 2–3 Hz component has a longer duration

the ERP in Fig. 2a is shown in Fig. 2b. However, spectra do not provide information on how frequency components evolve over time and some frequency components cannot be observed in the spectrum, because they are only of short duration in relation to the total duration of the frequency transform (often one second). Early approaches that tried to visualize temporal dynamics of frequency components plotted multiple EEG spectra in succession—a method that was referred to as 'compressed spectral array' (Bricolo et al. 1978).

Current time–frequency analyses typically use so-called *wavelet transforms* to reveal the temporal evolution of spectral components (Bartnik et al. 1992). In principle, time–frequency analyses can also be computed by using short-term FFTs or multiple band-pass filters combined with a Hilbert Transform, but wavelet transform have become more popular. A recent tutorial review of the similarities and differences of the most-frequently used time–frequency techniques is given by Wacker and Witte (2013). The result of a wavelet transform of the ERP in Fig. 2a is displayed in Fig. 2c, revealing two distinct frequency components and their temporal evolution. Every single line of a time–frequency plot is the result of a separate wavelet transform. This means that the ERP is convolved with a wavelet of one center frequency with a limited bandwidth around this frequency. For the next line, the ERP is convolved with a wavelet of another frequency and so forth.

Time Versus Frequency Resolution

Figure 3 illustrates why a wavelet can be optimized for either high time or frequency resolution but not both with the same quality. A wavelet is computed by multiplying a Gaussian with a complex-valued oscillation. Depending on the Gaussian that is used, the wavelet has a different time and frequency resolution. The top row of Fig. 3 depicts two exemplary Gaussians with different standard deviations. The second row illustrates the real part of a complex-valued oscillation at 20 Hz. In the third row, the real and imaginary parts of the resulting complex-valued wavelet are shown.[2]

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[2] A so-called complex number (z) consists of a real part (a) and an imaginary part (b) such that $z = a + bi$ where i is the imaginary number that results from taking the square root of -1.
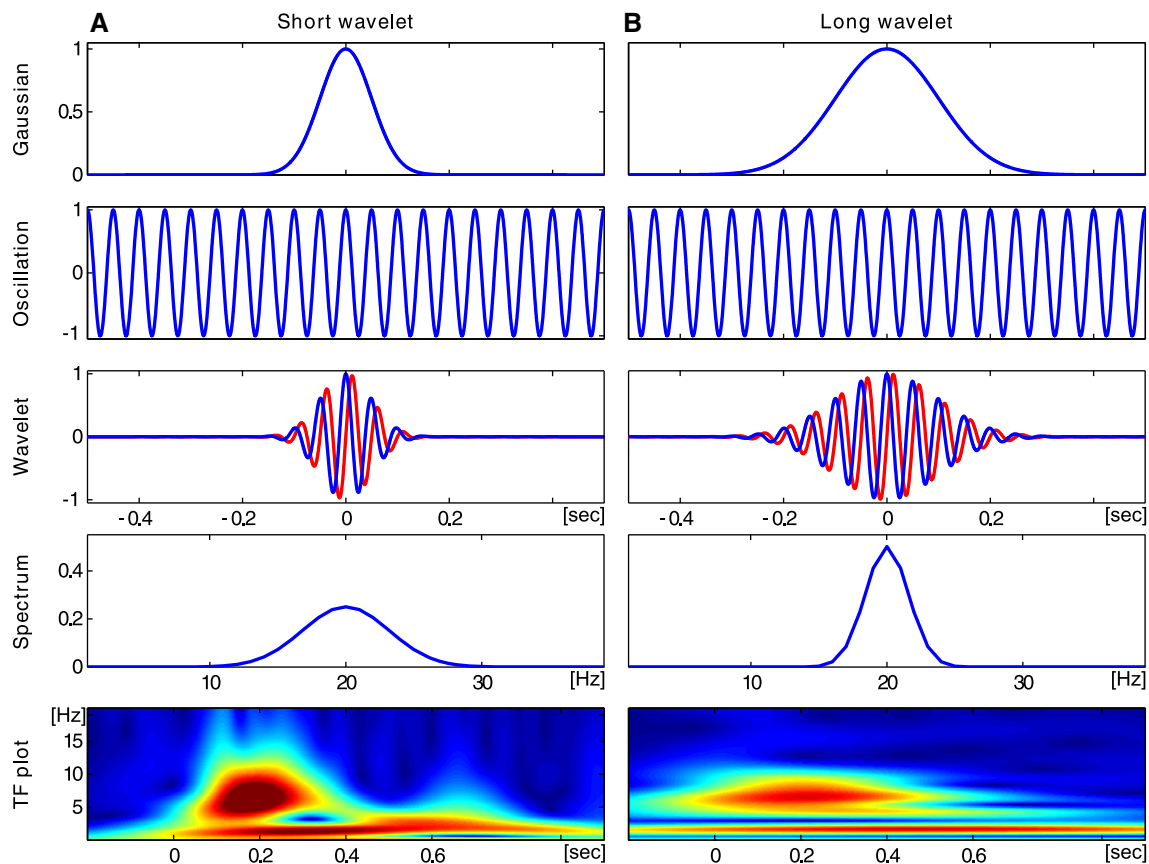
Fig. 3 Time and frequency resolution of a wavelet transform. **a** Multiplying a Gaussian with short standard deviation in the time domain (*top row*) with a complex-valued oscillation (*second row*, only real part shown) results in a wavelet (*third row*, real part: red; imaginary part: blue). The spectrum of this wavelet is shown in the fourth row. Convolving the ERP from Fig. 2 with this wavelet yields the time–frequency plot (*bottom row*). The short wavelet has a high time resolution but low frequency resolution, resulting in an overlap of two responses above and below 5 Hz. **b** Using a Gaussian with a longer duration (*top row*) results in a wavelet with more cycles (*third row*), a narrower spectrum (*fourth row*), and, thereby, a better frequency resolution. Here, the two responses are clearly separated (*bottom row*)

The time resolution of the wavelets is determined by the standard deviation in time. Therefore, a brief wavelet with few cycles (Fig. 3a, third row) has a better time resolution than a wider wavelet with more cycles (Fig. 3b, third row). The frequency resolution of wavelets is inversely related to their time resolution. This can be determined by computing a spectrum of these wavelets and is shown in the fourth row of Fig. 3. The short wavelet (Fig. 3a) will pick up oscillations in the range of approx. 5–35 Hz, whereas the longer wavelet of Fig. 3b has a better frequency resolution and will pick up oscillations in a more restricted range of approx. 15–25 Hz.

The bottom row of Fig. 3 shows two time–frequency (TF) plots of the ERP of Fig. 2 computed for wavelets with short (Fig. 3a) and long (Fig. 3b) durations. Both TF plots show two distinct oscillatory responses at 2 and 6 Hz. The short wavelet with the low frequency resolution results in an overlap of the two responses. The longer wavelet with the higher frequency resolution results in a better separation of the two responses. However, here the duration of the responses is smeared out due to the low time resolution.

Evoked Versus Induced Oscillations

Sensory stimulation elicits two types of EROs—called evoked and induced (cf. Fig. 4a). If multiple trials are averaged to compute an ERP, the peaks and troughs of this type of EROs occur always at the same latency and are strongly phase-locked to stimulus onset and, therefore, add up in the ERP. These oscillations are considered *evoked* EROs. The second type of EROs varies in phase from trial to trial. Therefore, multiple trials can exhibit peaks and troughs at the same latency (i.e. peaks in some trials and troughs in other trials). If a number of troughs coincides temporally with a similar number of peaks—as may be expected if amplitudes were distributed randomly—they would nearly cancel out in the averaged ERP. These responses are considered *induced* EROs. Note, that the jitter in phase but not in latency is responsible for the cancellation of the oscillations as explained in more detail in Herrmann et al. (2005).

Since it has been shown that induced oscillations reflect important information about cognitive processes, methods
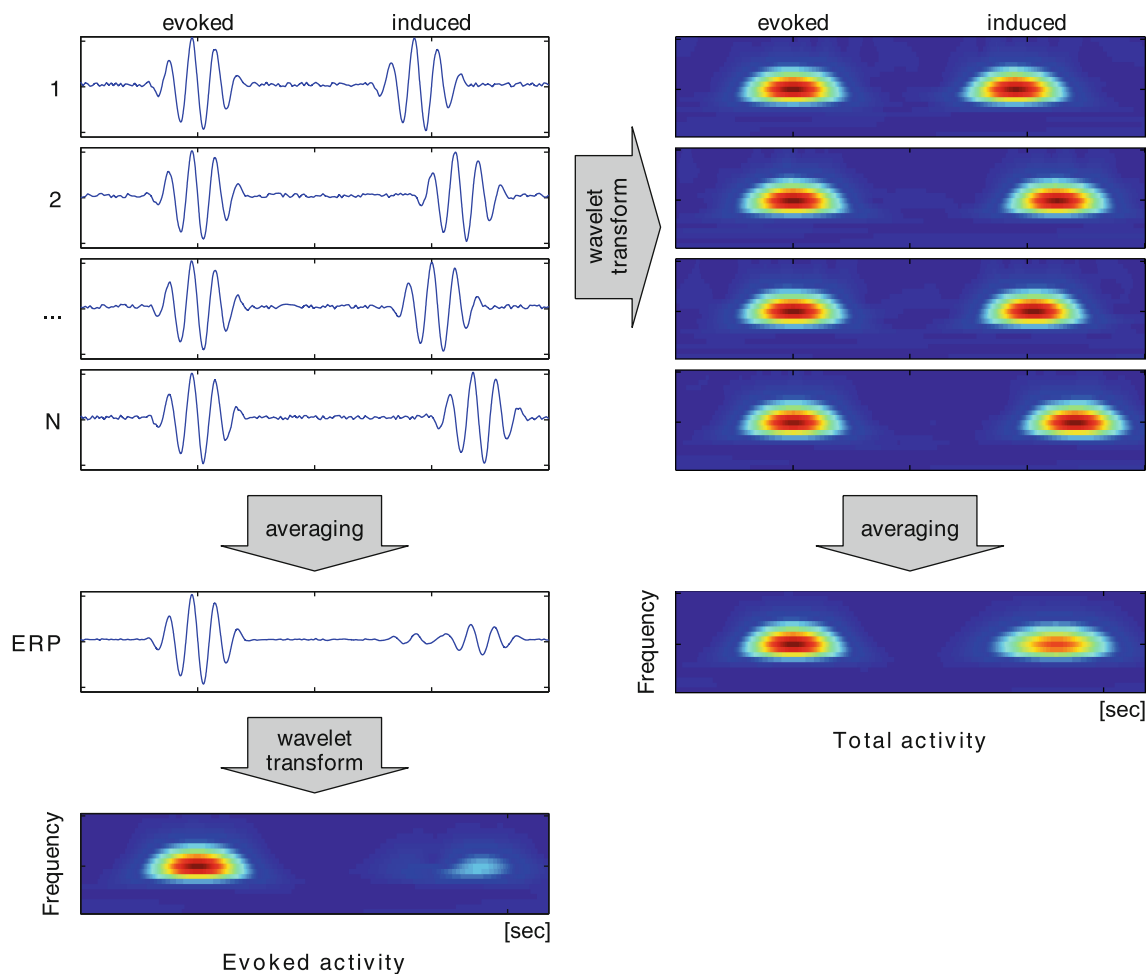
Fig. 4 Evoked and induced EROs. *Left panel* In order to compute evoked EROs, it is sufficient to average across all single trials (1···N) and compute a wavelet transform of the averaged ERP. *Right panel* In order to analyze also induced EROs, each single trial has to be subjected to a WT and absolute values have to be computed in order to prevent cancellation by negative values. Then, WTs are averaged yielding the total oscillatory brain response which comprises evoked and induced EROs. Those responses that appear only in the total but not in the evoked time–frequency plot are considered induced EROs. Adapted from Herrmann et al. (2004a)

such as time–frequency analysis have been developed to analyze them on a single-trial basis. If each single trial of an EEG experiment is at first subjected to a wavelet transform and absolute values are then computed, this results in only positive values which cannot cancel out. The resulting average contains both, evoked and induced EROs, and is therefore referred to as *total activity* (cf. Fig. 4) or *event-related spectral perturbation* (ERSP). The computed absolute values of the complex numbers that result from the wavelet transform represent the magnitude or amplitude of the oscillations.

Phase-Locking

Evoked and induced EROs mainly differ in their degree of phase-locking to stimulus onset which can be assessed in terms of a parameter that is referred to as *phase-locking factor* (PLF) or *inter-trial phase coherence* (ITC). If the phase of an oscillation at a given latency after stimulus onset were completely random across trials, the PLF would be zero. If, however, the phases were identical in all trials, the PLF/ITC would be one. The method is described schematically in Fig. 5. The PLF/ITC can be computed for every point in time and every frequency of a time–frequency analysis resulting in a time–frequency plot of PLF.[3]

Scaling Issues

The amplitude or power of a time–frequency representation can be scaled in different ways. A straight-forward method would be an absolute scale (i.e. amplitude in μV or power in

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[3] The phase-locking factor can also be used to estimate the coherence between two electrodes that is believed to represent whether two brain regions are functionally coupled (i.e. work together). For the sake of brevity, we do not want to go into the details of coherence measures at this point. Good reviews on this topic can be found elsewhere (Varela et al. 2001; Siegel et al. 2012).
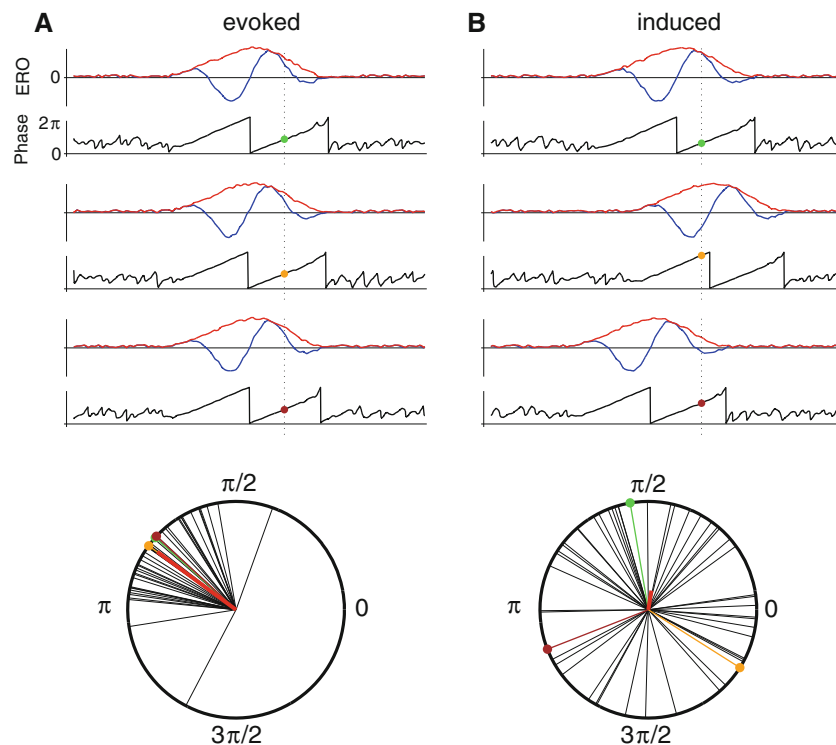
Fig. 5 Phase-locking. **a** Three consecutive trials of evoked EROs with their real part (*blue*), amplitude (*red*), and phase (*black*). If the amplitude is near zero, the phase cannot be reliably estimated. If the amplitude is significantly different from zero, the phase of the oscillations continuously increases from zero to 2π, jumps back to zero and so forth. If the phase is extracted at a given point in time (*dotted black line*), the resulting phase values can be mapped onto the unit circle (*bottom*) represented as three colored dots for the three trials. If all trials of an experiment are mapped onto the unit circle (*black* vectors), the average of all vectors can be computed (*thick red line*). The length of this vector represents the PLF or ITC. **b** In case of induced EROs, the variability of phase across trials is larger, resulting in a wider distribution of the black vectors on the unit circle. Correspondingly, the average vector is shorter and the degree of phase-locking is lower

μV^2). However, amplitudes of low-frequency oscillations are significantly higher than those of high-frequency oscillations due to the 1/f-characteristics of EEG data. Thus, if the color scale were chosen to resolve high-frequency responses, the color scale would be saturated for low-frequency responses. If, on the other hand, the color scale were adapted to low-frequency amplitudes, high-frequency responses would no longer be visible in the plot.

A logarithmic scale has been used to solve this problem. For this purpose, all post-stimulus values are represented with respect to a defined pre-stimulus baseline in the time–frequency domain[4] and are scaled in decibel (dB). The decibel is a logarithmic unit that represents the ratio of two signals. If amplitudes are considered, 6 dB roughly represent a two-fold increase of signal amplitude with respect to baseline. If the

signal were 10 μV and the baseline were 5 μV, the signal to baseline ratio (S/B) would be computed as follows: S/B [dB] = $20 \log_{10}$ (S/B) = $20 \log_{10}$ (10 μV/5 μV) = 6.02. Note, that for power values 3 dB roughly represent a two-fold increase, since then the S/B ratio is computed as follows: S/B [dB] = $10 \log_{10}$ (S/B). Instead of dB, the values could also be presented in percent of the baseline values. Both scales, however, apply a baseline division which assumes a gain model for ERP generation that is multiplicative in nature. Alternatively, baseline values can also be subtracted from post-stimulus values if assuming an additive model of ERP generation. Post-stimulus values can then be represented in μV. Refer to Grandchamp and Delorme (2011) for a discussion on this topic and advanced methods of normalization for single-trial EEG analyses. Care must be taken when choosing the time interval for the baseline. As is the case with ERP components when filtering ERPs, frequency components are smeared out in time by time–frequency analysis. Therefore, frequency components that occur early after stimulus onset can be smeared into the pre-stimulus time interval. Baselines should then be chosen to cover an earlier time interval before the

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[4] Note, that typically two baseline corrections are carried out during a time–frequency analysis. First, a baseline subtraction in the time domain removes direct current (DC) components of the signal (i.e. constant offsets from zero). Subsequently, the time–frequency plot can either be represented as absolute values or with respect to a baseline in the time–frequency domain.
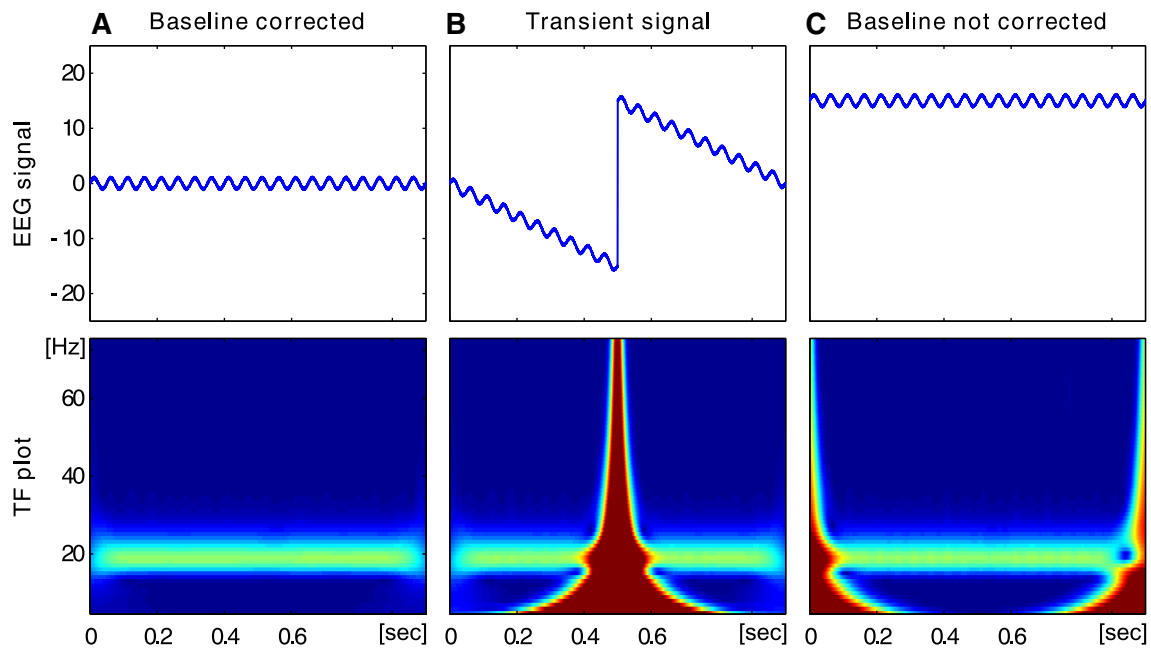
Fig. 6 Possible artifacts. **a** Simulated EEG signal after applying a baseline correction in the time domain (*top*) and the corresponding TF plot (*bottom*) showing a straight line at 20 Hz. **b** If a sharp transient occurs in the middle of the EEG, this results in an artifact that spans a wide range of frequencies. Since low-frequency wavelets are longer in time than high-frequency wavelets, the shape of the artifact represents an arrow-head. **c** If the EEG signal contains a DC shift that has not been removed via a baseline correction, two artifacts appear at the borders of the graph—each representing one half of the arrow-head

onset of the smeared frequency component—depending on the actual smearing of components.

Beware of Artifacts

Steep transients in the time domain result in artifactual oscillatory responses spanning a wide range of frequencies because wavelets of all frequencies will pick up this transient signal. A true wavelet transform uses multiple wavelets with a fixed number of cycles across frequencies. The different wavelets span different time ranges for different frequencies, for example a 10 Hz wavelet with 6 cycles has a duration of 600 ms, whereas 6 cycles of 50 Hz correspond to 150 ms. Therefore, these artifacts have the typical shape of an arrow-head, since slow-frequency wavelets will result in temporally broad responses and high-frequency wavelets in temporally narrow responses. The resulting arrow-head can easily be identified (see Fig. 6b). Such sharp transients can result from electrode artifacts or saccadic eye movements. Refer to Yuval-Greenberg et al. (2008) for a detailed discussion of how micro-saccades can lead to artifactually induced gamma-band responses that can be projected to occipital electrodes if a nose reference is used. Recently, advanced methods have been developed in order to subtract the artifactual responses (Hassler et al. 2011).

Furthermore, it is important to conduct a baseline correction before computing a wavelet transform (cf. Fig. 6a). If an ERP is subjected to a wavelet transform without at first subtracting the baseline of the ERP in the time domain, two artifacts at the beginning and the end of the ERP result (see Fig. 6c).

How to Present Data in a Publication

If the results of an ERP study are to be published in a journal article, a number of criteria have to be fulfilled in order to meet the guidelines for physiology journals (Picton et al. 2000). No such guidelines have been developed thus far for frequency or time–frequency analysis of EEG data. Here, we would like to give a few recommendations on how to present data properly.

In principle, almost all of the criteria of ERP analysis also apply to spectral and time–frequency analysis, for example it is important to specify hypotheses, behavioral results should be reported if assessed, and the experimental setup needs to be described in sufficient detail. Other parameters, however, are especially crucial for frequency analysis including the EEG amplifier that was used and its settings (i.e. sampling rate of the analog–digital converter, amplitude resolution, and filter parameters). The method used for analysis must be described in sufficient detail (i.e.

number of data points for computation of frequency spectrum, number of wavelet cycles, baseline correction, etc.).

Among other criteria, ERP articles should not only report amplitudes or latencies of ERP components (e.g. in tables or bar plots), but should also display complete ERPs (Picton et al. 2000). This helps to identify the morphology of the ERP and, thereby, allows to evaluate possible contamination of the baseline, linear drifts, and so on. The same holds for frequency and time–frequency analysis. Articles should always display frequency spectra or time–frequency plots. If differences between conditions are reported, spectra or time–frequency plots should also be shown for each condition separately. This allows to assess whether there was an oscillatory brain response at the time/frequency of reported differences between conditions. For the interpretation, it is crucial whether two significant oscillatory responses are different in intensity or whether two conditions differ without significant oscillatory responses in either condition.

Whenever many data points are analyzed, a statistical problem arises due to multiple comparisons. This has been an issue for data from functional magnetic resonance imaging where more than 100,000 voxels are analyzed statistically (Bennett et al. 2009). It has been shown that the problem of multiple comparisons also occurs for EEG and MEG data (Vecchiato et al. 2010), especially when computing frequency responses for many electrodes. If one second of ERP data that was recorded at a sampling rate of 1,000 Hz is analyzed in a time–frequency plot with 100 frequencies, this results in 100,000 data points per electrode. Different correction methods have been suggested to cope with this problem and are implemented in some of the available software packages (Kilner et al. 2005).

Software Packages and Further Literature

Many commercial software packages offer wavelet analysis for the computation of time–frequency analysis—among others, asa (ANT Neuro HQ, Enschede, The Netherlands), BESA (BESA GmbH, Gräfeling, Germany), Brain Vision Analyzer (Brain Products, Munich, Germany), and CURRY Neuroimaging Suite (Neuroscan, Compumedics, Charlotte, NC, USA).

In addition, many freely available packages are available that run under MATLAB (The MathWorks, Natick, MA, USA). Among others, EEGLAB offers many additional routines for organizing EEG data as well as a variety of signal analysis tools. Further packages that build up on MATLAB are SPM8 (Functional Imaging Laboratory, London, UK) and FieldTrip (Donders Center for Cognitive Neuroimaging, Nijmegen, The Netherlands).

A comprehensive tutorial on the application of wavelet analysis to EEG is given by Samar et al. (1999). Many

details on phase-locking, time and frequency resolution as well as other parameters can be found in Herrmann et al. (2005). A very instructive tutorial on the software package EEGLAB is available from Delorme and Makeig (2004).

Review on Studies Using Time–Frequency Analysis for MMN Paradigms

In cognitive neuroscience, different experimental paradigms are used in order to investigate specific cognitive functions. For example, in the auditory target-oddball paradigm, frequent and infrequent sounds are presented with the instruction to respond to the infrequent sound, which then elicits a strong P300 indexing the allocation of attention towards this sound (Polich and Kok 1995).

If subjects are not required to respond to the stimuli and attention is drawn away from auditory stimulation by watching a video, the same oddball paradigm can be employed to investigate automatic auditory change detection (Duncan et al. 2009). If the ERP in response to the standard stimulus is subtracted from the ERP in response to the deviant stimulus, a negativity is visible that starts roughly 100 ms after stimulus onset and extends to 250 ms—it is referred to as the mismatch negativity or MMN (Näätänen et al. 2007).

Theta Oscillations and Mismatch Negativity

Applying time–frequency analysis to ERP data obtained in a mismatch negativity paradigm revealed that both the standard and the deviant stimulus elicit a theta response—albeit stronger in response to the deviant (Fuentemilla et al. 2008). Especially the theta phase-locking (as reflected by ITC) was responsible for this difference but not power (as reflected in the ERSP). The notion that the processing of deviant stimuli is associated with theta oscillations was further substantiated by studies using magnetoencephalography (MEG) recordings (Lin et al. 2007; Hsiao et al. 2009). Also the finding that the differences in theta oscillations in response to standard and deviant tones are reflected in the phase-locking received further support by a replication study (Ko et al. 2012).

Interestingly, Bishop and Hardiman (2010) were able to demonstrate that investigating theta oscillations can be advantageous over analyzing the MMN in the time domain. These authors addressed the question why some individuals have the ability to identify auditory deviants but show no MMN in their ERPs. When analyzing theta-band ITC in single trials, they were able to identify a mismatch-related enhancement in 82 % of their subjects but only in 70 % if the MMN was analyzed in the time domain. The importance of analyzing theta-band oscillations when looking for

MMNs is further supported by a study investigating how newborn infants react in response to auditory deviants (Isler et al. 2012). Taken together, these findings suggest that analyzing theta oscillations can be very fruitful when studying auditory deviant detection.

Gamma Oscillations in Mismatch Paradigms

Evoked gamma-band EROs can reflect two types of processes. On the one hand, they reflect low-level processes of stimulus encoding that depend upon physical stimulus parameters such as intensity in a bottom-up fashion (Schadow et al. 2007). On the other hand, they can also reflect higher-level processes of conscious memory access when subjects actively listened to sounds (Lenz et al. 2007; Lenz et al. 2008). In this context, a model has been proposed for the visual modality—called the match and utilization model or MUM model (Herrmann et al. 2004b). According to the MUM model, stimuli that match with contents of long-term or short-term memory evoke stronger oscillatory brain responses in the gamma frequency band than those that do not match.

Since not only visual, but also auditory stimuli evoke gamma-band EROs and auditory gamma oscillations are thought to reflect memory processes (Kaiser and Lutzenberger 2005), the MUM model might also be valid for the auditory domain. Consistent with this assumption, a study using ringing tones of cell phones showed that evoked gamma-band EROs were stronger for subjects' own ringing tones than for others' (Roye et al. 2010). Given that the MUM model is valid for the auditory domain, one would expect a double dissociation between the electrophysiological process reflecting the match (i.e. early evoked gamma-band EROs) and the mismatch (i.e. theta oscillations at the latency range of the MMN). More specifically, standard stimuli that match the expectation and thus the content of short-term memory should evoke stronger gamma responses, whereas deviant stimuli which do not match this expectation and memory contents should evoke stronger theta responses (Yordanova et al. 2012).

A study comparing a broad-band ERP and an ERP that was band-pass filtered in the gamma-band supported this hypothesis by demonstrating that standard tones that match the auditory expectation evoke stronger gamma responses than deviant sounds (Yabe et al. 2005). Audio-visual experiments further supported this notion in showing that auditory stimuli evoke enhanced gamma-band responses when they match expectations that were built up by visual stimuli (Widmann et al. 2007; Schneider et al. 2008). More recently, Schadow et al. (2009) performed time–frequency analysis to reveal that the auditory gamma-band response that reflects such a match is centered around 40 Hz and stems from auditory cortex.

Even though these studies suggest that the MUM model may be applied to the auditory domain, it is still questionable whether the early gamma-band response also reflects pre-attentive processes. In recent experiments, subjects processed the auditory stimuli attentively. Future studies are needed to resolve the issue whether early gamma-band responses reflect only attentive or also pre-attentive processing of auditory stimuli.

A recent scheme of auditory processing presents the ERP and oscillatory indicators of auditory prediction from multiple latencies and frequency ranges in a common descriptive framework (Bendixen et al. 2012). We hope that this encourages researchers to use the wealth of available time–frequency data to gather information that complements the more traditional ERP-based analyses.

Taken together, EROs of two frequency bands dominate the ERP in response to auditory stimuli in mismatch paradigms—namely the theta and the gamma band. So far, it has been demonstrated that the early gamma-band response reflects a conscious comparison of stimuli with short-term memory, whereas the later theta-band response reflects the MMN. Recently, it has been demonstrated that these two frequency bands closely interact. For example, the phase of theta oscillations modulates the amplitude of gamma oscillations (Canolty et al. 2006; Demiralp et al. 2007). It would be worthwhile to investigate the interaction of theta and gamma oscillations in the context of mismatch paradigms as follows. In MMN paradigms, time–frequency analysis reveals a double dissociation between the processing of matches and mismatches with memory contents if gamma and theta EROs are analyzed, respectively. Since both, standards and deviants, of a mismatch negativity paradigm evoke theta and gamma oscillations—albeit to different degrees—it is conceivable that the two oscillations interact functionally. The following paragraph describes possible interactions of the two frequencies in auditory deviant detection:

The early gamma-band response (peaking around 20–80 ms) reflects whether a stimulus matches with the content of short-term memory (i.e. standard stimuli evoke high gamma amplitudes reflecting a match, whereas deviants evoke low amplitudes reflecting a mismatch). In case of high gamma amplitudes, the subsequent theta response (peaking around 150–200 ms) is suppressed or low in amplitude. In contrast, if gamma amplitudes are low, the theta-band response reflects a detected mismatch as indexed by high theta amplitudes and thus informs the brain about a possibly required action to the deviant stimulus.

This assumption could be tested in future experiments, for example by modulating one of the two oscillations and investigating the influence on the other frequency as well as on detection performance. In principle, three

methods are available that can modulate EEG oscillations non-invasively. (1) EEG oscillations can be modulated by applying repetitive sensory stimulation across a wide range of frequencies resulting in so-called steady-state evoked potentials (Herrmann 2001). (2) EEG neurofeedback has been successfully applied to both the gamma (Keizer et al. 2010) and the theta frequency range (Enriquez-Geppert et al. 2013). (3) Repetitive transcranial magnetic stimulation (rTMS) as well as transcranial alternating current stimulation (tACS) have been demonstrated to enhance EEG oscillations (Thut et al. 2011; Herrmann et al. 2013). If the above assumption holds true, modulating gamma oscillations should in turn influence theta oscillations. If the oscillations are functionally relevant for the cognitive processes, a modulation of them should also result in altered detection rates or reaction times. Future experiments may also shed light on the direction of modulation. Does the gamma response modulate the theta response as suggested by their latencies (gamma peaks earlier than theta)? Or does the slower frequency (theta) modulate the faster frequency (gamma) as has been previously shown?

Conclusion

Time–frequency analysis of spontaneous EEG and ERP data allows to investigate oscillatory brain activity. This offers three advantages over conventional ERP analysis: (1) Induced EROs are not represented in the ERP but carry important information about cognitive processes. They can be assessed with the help of time–frequency analysis. (2) It has been demonstrated that behavioral performance can be predicted from oscillatory brain activity even before stimulus onset. (3) Single-trial analyses have become feasible due to time–frequency analysis—often in combination with ICA—and are of utmost importance for brain computer interfaces (Blankertz et al. 2011).

In mismatch paradigms, the two most prominent brain oscillations occur in the theta and gamma frequency band. Data from other experiments suggest that these two frequency bands are closely linked. MMN paradigms may be ideally suited to further investigate this interaction.

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