Brain wave synchronization and entrainment to periodic acoustic stimuli

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Abstract

As known, different brainwave frequencies show synchronies related to different perceptual, motor or cognitive states. Brainwaves have also been shown to synchronize with external stimuli with repetition rates of ca. 10–40 Hz. However, not much is known about responses to periodic auditory stimuli with periodicities found in human rhythmic behavior (i.e. 0.5–5 Hz). In an EEG study we compared responses to periodic stimulations (drum sounds and clicks with repetition rates of 1–8 Hz), silence, and random noise. Here we report inter-trial coherence measures taken at the Cz-electrode that show a significant increase in brainwave synchronization following periodic stimulation. Specifically, we found (1) a tonic synchronization response in the delta range with a maximum response at 2 Hz, (2) a phasic response covering the theta range, and (3) an augmented phase synchronization throughout the beta/gamma range (13–44 Hz) produced through increased activity in the lower gamma range and modulated by the stimulus periodicity. Periodic auditory stimulation produces a mixture of evoked and induced, rate-specific and rate-independent increases in stimulus related brainwave synchronization that are likely to affect various cognitive functions. The synchronization responses in the delta range may form part of the neurophysiological processes underlying time coupling between rhythmic sensory input and motor output; the tonic 2 Hz maximum corresponds to the optimal tempo identified in listening, tapping synchronization, and event-interval discrimination experiments. In addition, synchronization effects in the beta and gamma range may contribute to the reported influences of rhythmic entrainment on cognitive functions involved in learning and memory tasks.
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Keywords: Synchronization; Entrainment; Brainwaves; Auditory stimuli

Synchronization of oscillatory activities in distributed neural assemblies is a well-studied mechanism in the working of the brain. It can be understood as a reflection of the cooperative activity of neurons within distributed assemblies [10]. It entails the ideas that certain types of neural assemblies are characterized by synchronous activity of their constituent neurons, and that different EEG frequency components reveal synchronies related to different perceptual, motor or cognitive states [2,9,11,21]. Early in the history of human brain physiology it was demonstrated that brain activities could also synchronize to external stimuli [1,25]. Research using auditory stimuli has focused primarily on 'steady-state auditory evoked potentials' [8,9,16], working with stimulus repetition rates in the gamma range from 30 to 50 Hz. An area nearly absent from previous research is the synchronization of brainwaves to auditory stimuli with repetition rates below 10 Hz. This is somewhat surprising in view of a century of research on rhythmic sensorimotor synchronization [20,19],

and the overwhelming evidence for an optimal repetition rate in human repetitive perceptuo-motor behavior of 0.5 and 4 Hz (e.g. preferred tempo in listening to and in making of music, accuracy in detecting deviant event intervals, tapping synchronization, etc.) [6,24]. Recently, entrainment models of rhythmic motor behavior [12,13] have stimulated studies examining intrinsic rhythmicity and frequency coupling in neural systems as well as clinically applied synchronization research [23,22]. Despite the considerable number of studies, however, neurophysiological processes that underlie time coupling between rhythmic sensory input and motor output are still not well understood. The present study explores one aspect of this coupling by investigating whether brainwave oscillations synchronize to rhythmic auditory stimuli with stimulation rates of 1–8 Hz, a range most relevant to human repetitive sensorimotor behavior.

There has been only one previous study reporting a driving response of the EEG amplitude to acoustic stimuli with repetition rates from 3 to 8 Hz [15]. The study used direct, non-averaged EEG measurements, and it is unclear whether the identified responses were neurogenic in origin. Unfortunately, that study has never been replicated independently, probably

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due to the fact that the experimental procedure applied does not easily lead to consistent analysis of the EEG amplitude periodicities: various studies have shown that auditory event related potentials attenuate with stimulus repetition and that degree of attenuation is affected by stimulation rate [14,17,7]. This reduced amplitude, together with the large variability of responses to repeated stimuli [3] causes considerable complications for standard ERP analysis in this experimental paradigm (continuous stimulation). We therefore decided to approach the question of EEG synchronization to periodic auditory stimulation by focusing on the analysis of stimulus related phase coherence.

In the present study we recorded EEGs from 10 subjects (5 females; mean age 26) who had been asked to listen to sound stimuli passively. Periodic acoustic stimuli consisted of clicks (0.005 s rectangular pulses) and drum sounds, each presented with repetition rates of 1–6, and 8 sounds/s (Hz); recordings with silence (no acoustic stimulation) and continuous pink noise (noise with an energy distribution matching human auditory frequency sensitivity) served as controls and reference measures. Subjects were seated in an upright chair, wearing an EEG cap and listening to the stimuli via headphones with eyes closed. The peak SPL for the click and drum sounds at headphones was adjusted to 79 dB. Continuous EEG recordings were made while subjects listened to 120-s periods of randomly selected periodic stimuli, silence, or pink noise. The presentation sequence of repetition rates and control trials was counterbalanced across subjects. EEGs were recorded from 19 non-polarizable Ag/AgCl electrodes (impedance < 5 kΩ) according to the international 10–20 system, referenced against common linked earlobes. Sampling rate was 256 Hz with a time constant of 0.3 s (upper frequency limit = 70 Hz). Data segments containing eye movements or voltage fluctuations > 250 μV were excluded from further data processing. The analyses reported here were performed on recordings from the vertex electrode (Cz) yielding largest responses.

Synchronization between periodic auditory stimuli and EEG responses was analyzed with the stimulus-locked inter-trial coherence (ITC) applied to 3-s epochs of the EEG recordings, with each epoch-start aligned with a stimulus onset. ITC, also referred to as "phase-locking factor"(Tallon-Baudry [21]), is a measure of consistency across epochs (or trials) of the EEG spectral phase at each frequency and latency window. Calculations for the spectral estimate of the normalized power spectrum were run on 3-s epochs using a three-cycle Hanning-windowed sinusoidal wavelet. ITC values were calculated for 21 EEG frequency bands (ten 1-Hz bands from 1 to 10 Hz, five 2-Hz bands from 12 to 20 Hz and six 4-Hz bands from 22 to 44 Hz). Because of the window effects only ITC values from the middle 1-s epoch were considered in the following. For each stimulus condition and frequency band we obtained epoch-length × sample-rate = 256 ITC values. ITC calculations were done with our own MATLAB-script using the 'phasecoher' function from EEGLAB [5].

As the experimental paradigm does not allow for determination of a significance level for the ITC through comparison with a 'pre-stimulus' baseline we tested the significance in an analysis of variance of ITC values for the three experimental conditions (no stimulation, noise, and periodic stimulation). For this analysis ITC values were averaged over the 1-s epochs to obtain mean ITCs for each frequency band, stimulus condition, and subject.

Analysis of variance (ANOVA) of the mean ITC showed a significant effect for stimulus condition (periodic stimuli, noise, and silence), but not for EEG frequency bands (condition: $F(2, 9) = 79.06$, $p < 0.001$; frequency band: $F(20, 9) = 0.39$, $p = 0.9618$). The main effect for condition was due to increased phase coherence under periodic stimulation (Fig. 1a), whereas pink noise slightly reduced phase coherence in comparison
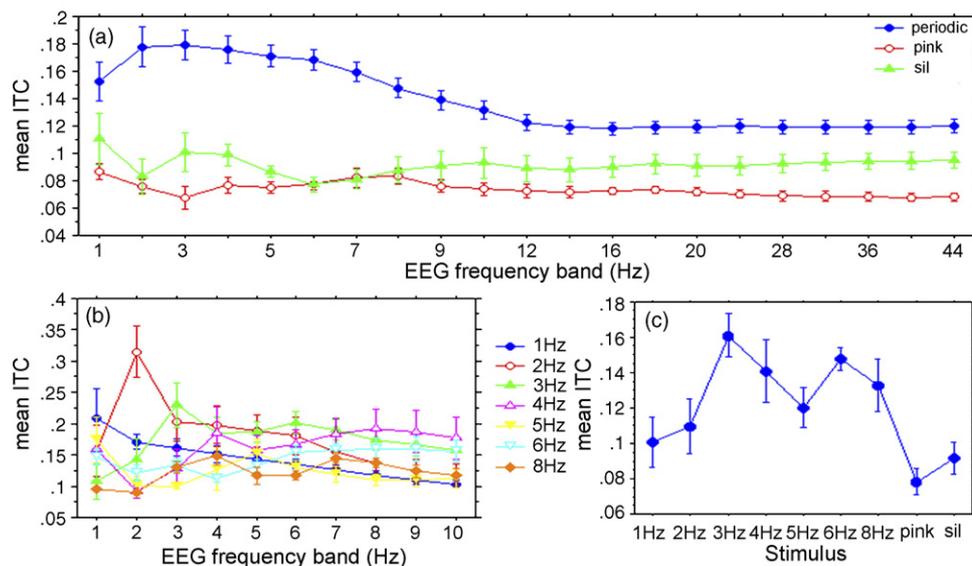
Fig. 1. Grand average (*n* = 10) of mean ITC. (a) Mean ITC for silent condition (sil), continuous pink noise stimulation (pink) and the mean for periodic stimulations (periodic) for all analyzed EEG frequency bands. (b) Mean ITC responses for 1–8 Hz repetition rates in the delta, theta, and alpha range. (c) Mean ITC in the lower gamma range (20 Hz). Error bars = ±1S.E.

with silence, the reduction being significant for the 14–44 Hz (beta and gamma) EEG bands (post–hoc Bonferroni–Dunn test: $p < 0.0001$). There was no significant interaction between factors condition and frequency band. Also, a post–hoc test did not show any significant differences between the effects of periodic drum and click stimuli ($F(1, 9) = 0.112$, $p > 0.7$).

Further analysis shows that the increase in inter-trial coherence is not just a consequence of the stimulus sequence but generated by specific brain responses to these stimuli:

(1) If the mean ITC is analyzed with respect to stimulation rates (Fig. 1b and c) we find frequency specific maxima that cannot be explained in terms of stimulus characteristics (all periodic stimuli had constant duration and amplitude):

   (a) Responses in the delta and theta range show a marked stimulus rate dependency, with rates from 1 to 5 Hz producing maxima in the respective EEG frequency bands and 2-Hz stimulations generating the largest responses (in the 2 Hz EEG band mean ITC for 2 Hz stimulation rates is about double than that for 1 or 3 Hz; Fig. 1b). This finding is incompatible with the idea that the increased ITC is a mere reflection of stimulus sequence.

   (b) The increased coherence throughout the EEG frequency bands from 13 to 44 Hz also show stimulus rate dependency with an absolute maximum for 3 Hz and a second, smaller maximum for 6 Hz stimulus rates (Fig. 1c). A posthoc analysis for stimulus rate shows that mean ITC for 3 and 6 Hz in the 20 Hz EEG band are not only

significantly different from the silent and pink condition (Bonferroni–Dunn test $p < 0.0001$) but also from the 1 Hz stimulation (Bonferroni–Dunn test $p < 0.0001$), whereas mean ITCs for 1 and 2 Hz stimulation are not different from the control conditions (Bonferroni–Dunn test $p > 0.2$ for 1 Hz and $p > 0.06$ for 2 Hz).

(2) Fig. 1b also suggests that the responses in the delta and theta range may be composite responses, consisting of frequency-band-specific components centered in the delta range and non-specific components with maxima in the theta band. Responses up to 5 Hz repetition rates each have a maximum in the corresponding frequency bands, with 2 Hz producing considerable larger values than the other rates (for 1–3 Hz the maxima are absolute, for 4 and 5 Hz relative). Stimulation rates of 6 and 8 Hz do not produce response peaks at the corresponding EEG frequency band but show relative maxima at the subharmonics of 3 and 4 Hz, respectively. All stimulation rates produce a second, broader response peak (only a raised level for 2 Hz stimuli) in the theta/alpha range.

Analysis of the actual time course of the ITC supports the idea of a composite response in the delta and theta range (Fig. 2): the frequency-specific peaks in the mean ITC responses are produced by a 'tonic' ITC component in the frequency band corresponding to the stimulation rate (marked by arrows in Fig. 2). This component has a pronounced maximum at around 2-Hz stimulation rate, falling off sharply at lower and higher rates. Such a response is obviously not a reflection of stimulus features: as a tonic
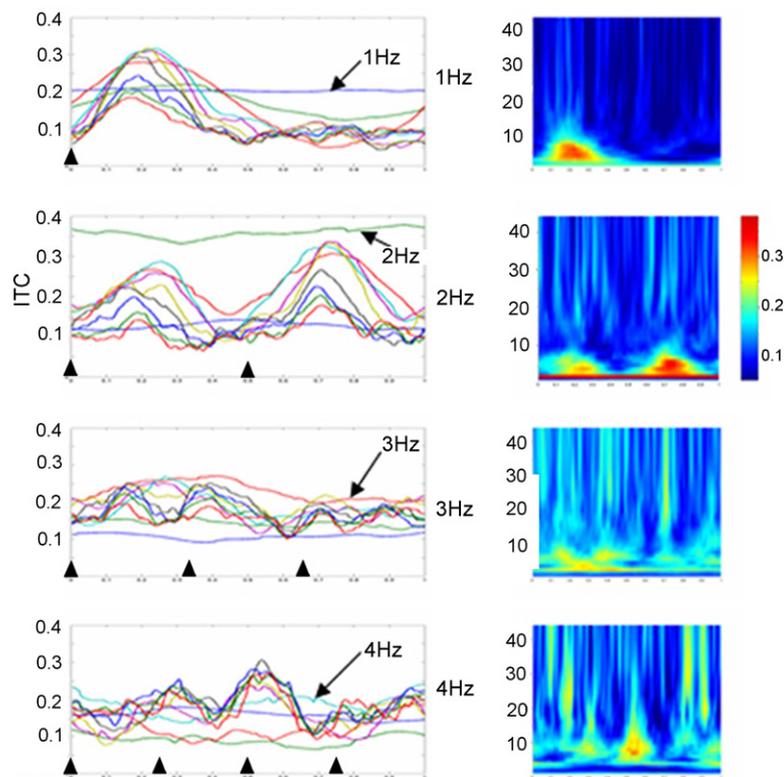
Fig. 2. Grand average ($n = 10$) of ITCs during 1 s EEG epochs for stimulus rates from 1 to 4 Hz Left column: time/ITC plots for EEG frequency bands 1–10 Hz. Arrows point to the tonic component of the ITC response. Right column: time/EEG frequency bands (1–44 Hz) with ITC colour-coded. Triangles mark onsets of periodic stimuli.

response it shows no periodicities corresponding to the stimulus events and seems to be an induced response that, because of its frequency specificity, can be described as delta wave entrainment to the periodicity of the external acoustic stimuli. The second component is a phasic ITC response in all frequency bands above the band corresponding to the stimulation rate. The fact that its peak amplitude decreases with repetition rate might suggest that this component mainly reflects the coherence of stimulus-evoked activity as described in previous studies [14,17]. However, as it has been demonstrated that stimuli in a sequence – except for the first one – do not lead to stimulus related increase in spectral power [7], it is possible that the phasic response reflects a stimulus-induced activity. This stimulus-induced phase synchronization, however, instantly dissipates and does not lead to entrainment. The loss of stimulus evoked periodicity in the grand mean of this phasic response at rates higher than 2 Hz (see Fig. 2) seems to be due to several factors: higher stimulus rates reduce the amplitude of the evoked activity [14], and repeated stimulation leads to increased response variability [3]. As demonstrated in Fig. 3, this means that responses are not sharply time locked, and that there is subject specific variability in latency and amplitude of this response.

(3) ITC time plots for the 14–44 Hz EEG bands (Fig. 4a) suggest that synchronization response in this range is different from those in the lower frequency ranges. Increased ITC in this range is marked by a strong 20–26 Hz modulation

(Fig. 4b), an activity that is also present in the absence of auditory stimulation (Fig. 4b). The modulation frequency appears to be independent of the stimulus repetition rate, but the degree of modulation is strongest for 3 Hz stimulation rates. The mean power spectral density of the 22–25 Hz modulation was found to be 12.5 dB higher (for the subject displayed in Fig. 4; mean = 7.2 dB for all 10 subjects) than in the silent condition. Additionally there is also a pronounced modulation by the periodic stimuli (Fig. 4a). For 3 Hz repetition rates the power spectral density of the 3 Hz modulation was found to be 19.3 dB higher (for the subject displayed in Fig. 4; mean = 12.7 dB for all 10 subjects) than in the silent condition. In contrast, non-periodic (noise) stimulation decreases the ongoing 'background' synchronization, as indicated by the above ANOVA (see Fig. 1a).

This study demonstrates some hitherto unknown synchronization responses of brainwaves to periodic auditory stimuli. Stimulation with repetition rates of 1–8 Hz leads to increased phase synchronization in all EEG frequency bands and three distinct components can be distinguished. The first is a tonic ITC response (i.e. not reflecting the periodicity of the stimulus sequence) in the delta range and appears to represent an 'entrainment' response: repetition rates between 1 and 5 Hz produce ITC response peaks in the corresponding EEG frequency bands and the response has an absolute maximum at around 2 Hz. This maximum corresponds well with the optimal rate (or tempo) identified in various studies on repetitive human
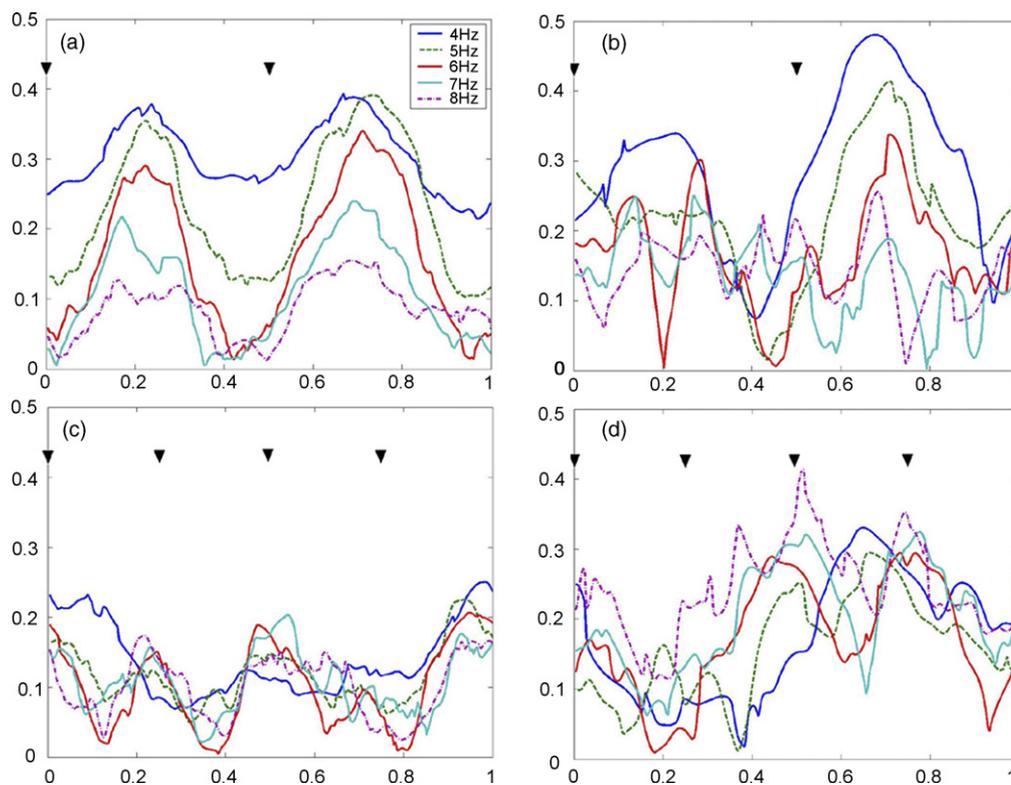
Fig. 3. Inter-subject variability of ITC responses in the theta band (4–8 Hz). Mean ITC responses for 120 1-s epochs from four subjects. (a, b) responses from two subjects for a stimulus rate of 2 Hz. Note the patterned response to the stimulus periods in subject b though all stimuli had constant amplitude. (c, d) responses from two different subjects for a stimulus rate of 4 Hz (the periodicity of the stimulus sequence is largely lost). Triangles mark onsets of periodic stimuli.
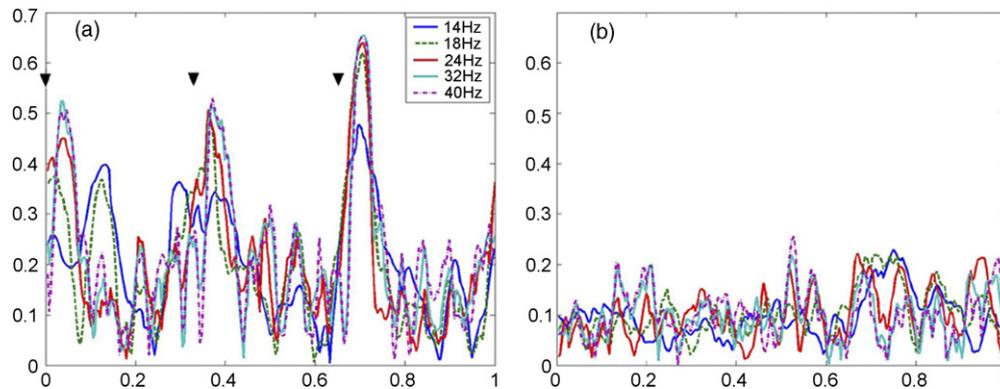
Fig. 4. Pattern of mean ITC responses in the beta and gamma bands for 120 1-s epochs from one subject (only five EEG bands are displayed: 14, 18, 24, 32, 40 Hz). (a) ITC responses for a stimulus rate of 3 Hz. Note increased modulation in low gamma range (ca. 20–26 Hz) that is also present in b, though with smaller amplitude. In addition there is a patterned modulation by the stimuli (3 Hz). (b) Background ITC for the silent condition is still modulated by ongoing activity in the low gamma range, though with considerably reduced amplitude. Triangles in (a) mark onsets of the periodic stimuli.

sensorimotor behavior (e.g. experiments on listening, tapping synchronization, and event-interval discrimination experiments) [24,6,12,13]. We suggest that this synchronization component forms an essential part of the neurophysiological processes underlying time coupling between rhythmic sensory input and motor output.

In contrast, the second component, a phasic response centered in the theta range, does not qualify as an entrainment response as all stimulus rates tested influence the ITC over a broad range of EEG frequencies. To a large part this component seems to reflect EEG activity induced by the sequence of stimuli. Loss of the stimulus periodicity in the grand average for stimulation rates larger than 2 Hz appears to be attributable to its reduced amplitude, considerable inter-subject variability, and the fact that it is not strictly time-locked. This variability in phase synchronicity is probably one of the chief reasons why previous analyses of auditory driving by 3–8 Hz stimuli, working with amplitude analysis of ERP, had not been very successful.

The third component, the synchronization responses in the 14–44 Hz EEG bands consist of an evoked (ITC modulation by the stimulus periodicity) and an induced (increased 20–26 Hz ITC modulation) subcomponent that have not been identified in studies using short stimulus sequences. Fuentemilla et al. [7], using three-stimuli trains with ISIs of 584-ms, did not find significant ERSP or ITC responses in the 20–49 Hz frequency range. These different results could be due to the slightly different analytical methods (ITC significance in Ref. [7] is calculated in reference to a 1000 ms pre-stimulus baseline) or, more likely, the different experimental design. As augmented synchronization in the 14–44 Hz EEG bands seems to be mediated by increased activity in the 20–26 Hz range, it seems possible that this is either not present in short stimulus sequences or rises to significance only under prolonged stimulation. This is supported by a recent study that reported gamma band responses to 60-tone acoustic stimulus trains with 390 ms ISIs [18]. The fact that these responses were also observed for omitted stimuli, together with the 'mediated' synchronization reported here, suggest that synchronization responses in the 14–44 Hz range may involve higher level of processing and hence may take part in

the reported influences of rhythmic 'entrainment' on cognitive functions involved in learning and memory tasks [22]. Başar-Eroglu and Başar [4] have shown that in cats visual and auditory stimuli evoke gamma responses in various brain regions. They demonstrated induced, evoked, and emitted gamma responses, the latter being bursts of gamma band oscillations time-locked to a stimulus (in a series of stimuli) that has not been presented. Their results suggest that these gamma activities may also be part of processes involved in anticipation, expectation and attention.

Acknowledgements

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