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Decrease in Early Right Alpha Band Phase Synchronization and Late Gamma Band Oscillations in Processing Syntax in Music

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Abstract: The present study investigated the neural correlates associated with the processing of musicsyntactical irregularities as compared with regular syntactic structures in music. Previous studies reported an early (~200 ms) right anterior negative component (ERAN) by traditional event-related-potential analysis during music-syntactical irregularities, yet little is known about the underlying oscillatory and synchronization properties of brain responses which are supposed to play a crucial role in general cognition including music perception. First we showed that the ERAN was primarily represented by low frequency (<8 Hz) brain oscillations. Further, we found that music-syntactical irregularities as compared with music-syntactical regularities, were associated with (i) an early decrease in the alpha band (9–10 Hz) phase synchronization between right fronto-central and left temporal brain regions, and (ii) a late (~500 ms) decrease in gamma band (38–50 Hz) oscillations over fronto-central brain regions. These results indicated a weaker degree of long-range integration when the musical expectancy is violated. In summary, our results reveal neural mechanisms of music-syntactic processing that operate at different levels of cortical integration, ranging from early decrease in long-range alpha phase synchronization to late local gamma oscillations. *Hum Brain Mapp 00:000–000, 2008.* **02008 Wiley-Liss, Inc.**

Key words: music; syntax; oscillations; synchronization; phase; EEG; network

INTRODUCTION

Contract grant sponsor: Ministerio de Educación y Cultura, Spain; Contract grant number: AP2002-0421; Contract grant sponsor: Ministerio de Ciencia y Tecnología, Spain; Contract grant number: FIS2005-01729; Contract grant sponsor: JST. Shimojo ERATO project. *Correspondence to: Joydeep Bhattacharya, Department of Psy-

chology, Goldsmiths College, University of London, New Cross SE14 6NW, London, UK. E-mail: pss01jb@gold.ac.uk Music processing is a complex set of perceptive and cognitive operations, which in turn are temporally integrated and linked to previous experiences recruiting extensive memory systems by which emotions emerge. Consequently, the investigation of the neurocognition of music has been increasingly important for the understanding of human cognition and its underlying brain mechanisms [Koelsch and Siebel, 2005]. The present study focused on the syntactic processing in music perception. Music involves perceptually discrete elements (e.g. tones, intervals, and chords) organized into sequences which are

Received for publication 25 July 2007; Revised 31 January 2008; Accepted 12 March 2008

DOI: 10.1002/hbm.20584

Published online in Wiley InterScience (www.interscience.wiley. com).

115 hierarchically structured according to syntactic regularities 116 [Patel, 2003; Tillmann et al., 2000]. In the context of majorminor tonal music, regularities consist of the arrangement 118 of chord functions within harmonic progressions 119 [Krumhansl and Toiviainen, 2001; Schönberg, 1969]. The computation of structural relations between these elements, for instance between a chord function and a pre-122 ceding harmonic context, is part of the analysis of musical structure. The integration of both regular and irregular events into a larger meaningful musical context is required 125 for the emergence of meaning based on the processing of musical structure [Krumhansl, 1997; Meyer, 1956].

127 A multitude of studies have focused on syntax violations in language domain [Eckstein and Friederici, 2006; 129 Friederici et al., 1996; Friederici, 2001, 2002; Gunter et al., 130 1999; Hahne and Friederici, 1999; Palolahti et al., 2005], 131 reporting a robust event-related-potential (ERP) component, the early (100-350 ms) left anterior negativity 133 (ELAN), which is taken to reflect initial syntactic structure 134 building. These studies have shown that the neural genera-135 tors of the ELAN lie in the left inferior frontal cortex (infe-136 rior BA 44), an area which is also involved in the process-137 ing of syntactic information in music [Maess et al., 2001]. 138 A study of speech perception reported an early negativity, 139 which was elicited bilaterally in response to combined pro-140 sodic-syntactic violations. This result indicated that addi-141 tional right hemispheric resources were recruited for the initial structure building processes [Eckstein and Friederici, 143 2006]. On the other hand, syntax violations in mathemati-144 cal expressions (e.g. equations) were recently investigated 145 in an ERP paradigm [Martin-Loeches et al., 2006], which 146 reported parieto-occipital negativities instead of frontal 147 negativities, leading to a conclusion of less overlap 148 between the syntactic processing of language and mathe-149 matics than previously thought [Dehaene and Cohen, 150 1995].

Most of the electrophysiological studies on musical syn-152 tax also adopted the classical ERP paradigm [Koelsch et al., 2000; Koelsch et al., 2002a,b; Patel et al., 1998]. Using chord sequences with final chords that were either har-155 monic syntactically regular or irregular, it has been shown 156 that music-syntactical violations elicit an early right ante-157 rior negative (ERAN) component; this component is maximal at 200 ms after the onset of irregular chords and is 159 strongest over right frontal electrode regions [Koelsch et al., 2000; Koelsch et al., 2002b]. The ERAN can be elicited in absence of directed attention [Koelsch et al., 2002a], in both musicians and nonmusicians [Koelsch et al., 2000; Loui et al., 2005], indicating an inherent human ability to acquire knowledge about musical syntax through everyday listening experiences [Tillmann et al., 2000]. Using magnetoencephalogram, it was found that the 166 mERAN (magnetic-ERAN) was generated predominantly in the inferior fronto-lateral cortex [Maess et al., 2001]. 169 However, using fMRI, it was found that posterior temporal regions (Heschl's gyrus, superior temporal sulcus, planum temporale), in addition to the frontal areas, were also activated during music-syntactic processing [Koelsch et al., 172 2002c].

Although these studies offer invaluable information 174 about the neural correlates of music-syntactic irregularities, they suffer from two primary limitations. First, EEG studies relied heavily on the averaging techniques which do not adequately represent aspects of brain activity that we expect to be relevant for music cognition, such as the information about the underlying oscillatory dynamics. This 180 dynamics is increasingly believed to provide insights into 181 neuronal substrates of perceptual and cognitive processes 182 [Basar et al., 2001; Kahana, 2006; Rizzuto et al., 2003; 183 Singer, 1999; Tallon-Baudry and Bertrand, 1999; Ward, 2003]. Second, fMRI studies suggest that irregularities in 185 musical syntax are processed by multiple brain areas, yet 186 it is not clear whether these regions operate in isolation or 187 interact with each other. This latter information is supposed to be crucial since there is extensive evidence that 189 any cognitive task demands not only simultaneous co-acti-190 vation of various brain regions but also functional interaction between these regions [Bressler and Kelso, 2001; Bressler, 1995; Brovelli et al., 2004; Engel and Singer, 2001; Engel et al., 2001; Friston, 2001]. This dynamical interaction is considered to be best characterized by transient phase relationships between the oscillatory activities of underlying neuronal populations, termed as phase synchronization, at the frequency of interest [Lachaux et al., 1999; Tass 198 et al., 1998; Varela et al., 2001].

Therefore, in this study we aimed to address these limi-200tations by investigating the oscillation and synchronization201content of the electrical brain responses recorded from202human subjects during listening to chord sequences end-203ing in regular or irregular chords.204

MATERIALS AND METHODS

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Stimuli

The stimuli of our experiment consisted of two chord 210 sequences, both with five chords and a pause (half-note). Chord sequences were composed according to the classical 212 rules of harmony (voice leading was performed in a coun- 213 terpoint-like fashion, without parallel fifths or octaves). The presentation time for each of the first four chords was 215 600 ms, and for the final chord was 1200 ms. The first four 216 chords were identical for both types of sequences: tonic, 217 subdominant, supertonic, dominant. The final of the fifth 218 chords was either a tonic (regular) or a supertonic (irregular) chord. In major-minor tonal music, one particular example of a music-syntactic regularity is the end of a harmonic progression, which is usually characterized by a dominant-tonic progression. Thus, the final supertonic 223 chord in our experiment represents a music-structural irregularity. Note that, psychoacoustically, supertonics do not represent physical oddballs, at least not with respect to pitch commonality or roughness. Moreover, the pitches of the supertonics correlated higher with the pitches in the 228

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Figure 1.

Examples of musical stimuli. Top row: chord sequences (in **D**major), ending either on a tonic chord (regular, **A**), or on a supertonic (irregular, **B**). (**C**) In the experiment, sequences from all twelve major keys were presented in pseudo-ran-

preceding harmonic context than those of the tonic chords (calculated according to the echoic memory based model [Martens et al., 2005]; see also Koelsch et al. [2007] for detailed correlations of local context (pitch image of the current chord) with global context (echoic memory representation as established by previously heard chords).

We presented 1,350 sequences, half of them ending on a tonic, and the other half ending on a supertonic (see Fig. 1). That is, each sequence type (A/B) was assigned equal probability. Both sequences were presented in each of the twelve major keys and randomly in a tonal key different from the key of the preceding sequence (see Fig. 1C). Additionally, they were randomly intermixed. All chords had the same decay of loudness and were played with a piano-sound (General Midi sound No. 2) under computer-ized control on a synthesizer (ROLAND JV 8010; Roland Corporation, Hamamatsu, Japan). See Koelsch and Jentschke, [2007] for more details.

Another 120 chord sequences (half of them ending on a tonic, and half of them ending on a supertonic) were played with an instrumental timbre other than piano (e.g., trumpet, organ, and violin). Participants were informed a priori about these chords played by a deviant instrument and their task was to detect them, but these deviant chords were not analyzed. This task was used to focus the participants on the timbre, in order to avoid directed attention to the musical syntax. Participants were not informed of the occurrence of music-syntactic irregularities.

Participants

Twenty right-handed participants (11 females, age range 20–30 years, mean 24.5 years) participated in this study.

dom order. Each sequence was presented in a tonal key that differed from the key of the preceding sequence; regular and irregular sequence endings occurred equiprobably (P = 0.5).

309 Eleven of them were nonmusicians, who had never attended a music lesson, and 9 of them were amateur musicians, who had learned to play an instrument or sung in a choir for 2-10 years (average of 5.4 years). All participants reported normal hearing. The experimental session was of ~ 2 h length. During the session the participants were watching a silent movie with subtitles and performing the timbre change detection task at the same time. The inclusion of a subtitled movie served two purposes: (i) it made the daunting task of listening for 120 min to detect the deviant stimuli feasible, and (ii) it reduced the amount of directed attention to the music syntactically regular or irregular chords, thereby reducing the effect of attentional modulation of the brain responses associated with processing the syntax in music.

EEG Recording and Pre-Processing

Multivariate EEG signals were recorded from 40 electrodes placed over the scalp according to the extended 10–20 329 system referenced to the left mastoid. Additionally, electrooculogram was recorded to monitor blinks and eye movements. We used the EEGLAB Matlab Toolbox [Delorme and Makeig, 2004] for visualization and filtering purposes. 333 After rejecting segments of data with artefacts like blinks, eye movements and muscle artefacts as determined by visual inspection, we applied a high-pass filter at 0.5 Hz to remove linear trends and a notch filter at 50 Hz (49– 51 Hz) to eliminate power-line noise. The filtering option in EEGLAB used the MatLab routine filter (zero-phase forward and reverse digital filtering). The sampling rate was 250 Hz. The data epochs representing single experimental trials time locked to the onset of the last chord were

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extracted from -500 ms to 1,000 ms, resulting in approximately n = 600 epochs per condition and participant.

Data Analysis

We performed the following three types of analysis: (i) standard averaging technique to analyze ERP components, wavelet based time-frequency representations (TFR) to analyze (ii) the spectral power of the oscillatory contents and (iii) the spatiotemporal dynamics of the phase synchronization. This last analysis was done by means of bivariate synchronization and synchronization cluster analysis (SCA).

Neural phase synchrony refers to the phenomenon in which neurons coding for a common representation synchronize their oscillatory firing activity within a restricted frequency band [Trujillo et al., 2005; Varela et al., 2001]. The analysis of the spectral power of the oscillatory activity focuses on the local synchrony of neuronal populations (synchrony *within* neighboring cortical areas), whereas the phase synchronization analysis refers to the phase coupling *between* neuronal assemblies, which lie either within the same hemisphere or at different hemispheres. This large-scale integration is believed to be required for the manifestation of a complete cognitive structure [Varela et al., 2001]. Thus, the two approaches provide complementary information about the underlying neuronal processing [Le Van Quyen and Bragin, 2007].

Time-frequency analysis

We studied the oscillatory brain responses by means of wavelet based TFR analysis [Tallon-Baudry et al., 1997]. We chose a complex Morlet wavelet with a Gaussian shape both in time and in frequency [Mallat, 1999]:

$$\psi(t) = \sqrt[4]{\frac{2}{\pi}} \exp(-t^2) \exp(i\eta t). \tag{1}$$

The convolution of translated (t') and rescaled (s) versions of this wavelet with a signal x(t) gives the wavelet transform for each scale and time instant,

$$W_x(t',s) = \left\langle x \middle| \psi_{t',s} \right\rangle = \int_{-\infty}^{\infty} x(t) \psi_{t',s}^*(t) \ dt, \tag{2}$$

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$$\psi_{t',s}(t) = \frac{1}{\sqrt{s}} \psi\left(\frac{t-t'}{s}\right). \tag{3}$$

In the time domain, the wavelet spreads around t = t' with a standard deviation $\sigma_t = s/2$, and in the frequency domain its centre frequency is $f = \eta/2\pi s$ with a standard deviation $\sigma_f = 1/2\pi s$ [Allefeld, 2004]. The value η defines the constant relation between the centre frequency and the bandwidth $\eta = f/\sigma_f$, and therefore is characteristic of the

wavelet family in use; y determines the temporal resolu- 400 tion ($\sigma_t = \eta/4\pi f$) and frequency-resolution ($\sigma_f = f/\eta$) 401 which is always within the limit imposed by the uncer-402 tainty principle $\sigma_f \sigma_t = 1/4\pi$ [Mallat, 1999]. For the analysis 403 of the fast cognitive processes, the temporal-resolution is 404critical to detect possible functional states occurring close 405 in time [Schack et al., 1999; Trujillo et al., 2005]. We chose 406 $\eta = 7$ ($\eta > 5$ is needed for the convergence of the convolu- 407 tion integral in numerical calculations [Grossman et al., 408 1989]), which provides a good compromise between high 409 frequency resolution at low frequencies and high time re- 410 solution at high frequencies (for example, $\sigma_t = 55$ ms and 411 σ_{f} = 1.4 Hz at 10 Hz; σ_{t} = 11 ms and σ_{f} = 7 Hz at 412 50 Hz). The frequency domain was sampled from 2 to 413 60 Hz with a 1 Hz interval between frequencies. 414

To study changes in the spectral content of the oscillatory 415 activity, we used the wavelet energy, which was computed 416 as the squared norm of the complex wavelet transform: 417

$$E_x(t,f) = \left| W_x\left(t,\frac{\eta}{2\pi f}\right) \right|^2 \tag{41}$$

We distinguished between two types of oscillatory brain 422 423 responses: (i) evoked response or response phased-locked to the stimulus onset, and (ii) induced response or response not 424 phased-locked to the stimulus onset [Galambos, 1992]. The 425 former response was estimated by applying the wavelet 426 transform to the averaged ERP profile, thus keeping the 427 phase-locked information across epochs. The joint response 428 (evoked + induced) was obtained by applying wavelet 429 transform of each trial followed by averaging. Thus, the 430 induced activity was computed by subtracting the evoked 431 response from the joint response. Although this technique 432 is valid to distinguish evoked from induced responses, in 433 the case of extensive latence variability in the onset of the 434 ERP, the phase-locked activity could be underestimated. A 435 more detailed study of the evoked and induced responses 436 in our paradigm should take that into account. 437

For both types of responses, the mean TFR energy 438 $\mu_{\text{base}}(f)$ of the pre-stimulus period (between -300 and 439 -100 ms) was subtracted. The wavelet energy was further 440 normalized by the standard deviation $\sigma_{\text{base}}(f)$ of the baseline period as follows: 442

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$$E_{\text{norm}}(t,f) = \frac{E_x(t,f) - \mu_{\text{base}}(f)}{\sigma_{\text{base}}(f)} \tag{5} \quad \begin{array}{c} 44\\ 44 \end{array}$$

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Our investigation of the TFR energy emphasized high 447 frequency oscillations (>30 Hz) due to the relevance of the 448 fast gamma oscillations for both the binding of temporal 449 (and spatial) information necessary to build a coherent 450 perception [Tallon-Baudry et al., 1997] and the integration 451 of bottom-up and top-down processes [Engel and Singer, 452 2001; Herrmann et al., 2004a; Pulvermuller et al., 1997; 453 Varela et al., 2001].

A *post-hoc* analysis of the TFR energy in the delta and 455 theta band was performed due to the fact that the domi-456

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nant frequencies of the EEG signal which contributed to the generation of the ERAN component were below 8 Hz.
Here the non-normalized form of the wavelet energy Eq. (4) was used to compare explicitly energy for each condition the poststimulus with the prestimulus TFR, because of the possible influence of the prestimulus brain state on the event-related brain responses [Doppelmayr et al., 1998].

Phase synchrony analysis

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The wavelet transform Eq. (2) can be expressed explicitly in terms of frequency and time by using the relationship between the scale $s = \eta/2\pi f$ and the frequency f, and from this complex-valued signal the corresponding frequency-specific instantaneous phase can be calculated as follows:

$$\phi(t,f) = \arg W_x\left(t,\frac{\eta}{2\pi f}\right). \tag{6}$$

For each trial we computed the complex phases $\phi_{ik}(t_i f)$ of the channel *i* at an epoch *k* and used them for the subsequent synchronization analysis. It has been widely reported in the literature [Hurtado et al., 2004; Lachaux et al., 1999; Pereda et al., 2005; Rodriguez et al., 1999; Tass et al., 1998] that the assessment of phase synchronization between neurophysiological signals is better understood in a statistical sense. One of the approaches taking this into account is use of the concept of directional statistics [Mardia, 1972] in bivariate phase synchronization.

The strength of the phase synchronization between two electrodes i and j, at time t and with centre frequency f, is:

$$\overline{R}_{ij} = \left| \frac{1}{n} \sum_{k=1}^{n} \exp(i(\phi_{jk} - \phi_{ik})) \right|,\tag{7}$$

where n is the number of epochs. This index is nearly 0 when there is no phase relationship between the considered electrode pair across the epochs, and approaches 1 for strong phase synchronization. In the context of directional statistics, this reflects whether the distribution of the relative phase between two electrodes is spread or concentrated on the unit circle, respectively.

In the case of large number of recording electrodes a measure of global synchronization strength can be computed, from the pair-wise synchronization matrix, \overline{R}_{ij} , for each time point *t* and centre frequency *f*:

$$\overline{R} = \frac{2}{N(N-1)} \sum_{i,j>i} \overline{R}_{ij}.$$
(8)

But this measure conceals the spatial distribution of the synchronization, an issue of fundamental importance in cognitive neuroimaging where one has to look for possible short- or long-range phase synchronization between different cortical areas. Recently a new method was proposed that can provide information about both the global synchronization strength and the topographical details of the synchronization in event-related brain-responses: the SCA 515 [Allefeld and Kurths, 2004], which has been applied to visual attention and language processing experiments 517 [Allefeld, 2004; Allefeld et al., 2005]. 518

The underlying idea is to model the array of electrodes 519 as individual oscillators that take part in different strength 520 c_i in a single synchronized cluster *C*. This individual cluster characterizes, in each epoch *k*, the dynamics of the 522 array as a whole through the cluster phase Φ_k , which is 523 the result of a circular weighted mean of the oscillator 524 phases, 525

$$\Phi_k = \arg \sum_j c_j \exp(i\phi_{jk}), \tag{9} 527$$

where the participation indices c_i are calculated as a (monotonously increasing) function $f(\overline{R}_{iC})$ of the phase locking between each individual oscillator and the cluster,

$$\overline{R}_{iC} = \left| \frac{1}{n} \sum_{k} \exp(i(\phi_{ik} - \Phi_k)) \right|, \qquad (10)$$

The basic premises that are relevant to this approach are that the dynamics of the phase differences can be decoupled by introducing a mean field, i.e. that the assumption of a single synchronized cluster holds, and that its stochastic part is independent for each of them. 541 Taking this into account, the population values ρ_{ij} of the empirical estimate of bivariate synchronization \overline{R}_{ij} can be 543 factorized as ρ_{iC} ρ_{jC} and a self-consistent solution of this 545 set of equations can be found. The SCA algorithm pro-546 vides a maximum likelihood estimation of the ρ_{iC} , repre-547 senting the phase synchronization index between the oscillator *i* and the cluster, \overline{R}_{iC} .

By computing the index \overline{R}_{iC} , we could detect subpopulations of electrodes that adjust differently to the global 550 rhythm and obtain a topographical picture of the synchronization and its temporal dynamics. As a measure of the global synchronization strength we used the cluster mean, 553

$$\overline{R}_C = \frac{1}{N} \sum_i \overline{R}_{iC}.$$
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It is important to mention that the SCA assumes phase differences distributed around zero, whereas the bivariate 559 synchronization analysis can detect a more general case of 560 phase differences bounded by a constant value different 561 from zero. Consequently, the index \overline{R}_{iC} would not detect a 562 delay in the phase synchronization between electrodes and 563 cluster. However, a combined use of the SCA and the 564 bivariate synchronization analysis could clarify this issue. 565 If both approaches deliver converging results, we could 566 assume that the distribution of phase differences is around 567 zero, but if the data of the bivariate synchronization analysis shows different results, they could be due to a constant 569 (non-zero) phase different between electrodes.

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ID: 40410 Date: 9/4/08

With the SCA we explored low (< 15 Hz) and high (15– 50 Hz) frequency bands, but the SCA delivered weak effects in the beta (15–30 Hz) and gamma (30–50 Hz) bands which, consequently, were left out from this study.

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In a number of studies synchronization in EEG signals has been investigated using classical magnitude-squared coherence function [Schack et al., 1999; Srinivasan et al., 1998; von Stein and Sarnthein, 2000; von Stein et al., 2000], which is equivalent to a correlation coefficient in the frequency domain, as a linear measure of bivariate synchronization. Magnitude-squared-coherence mixes both phase and amplitude correlation [Womelsdorf et al., 2007], and there exists no clear-cut way to extract the phase synchronization information from the coherence function [Lachaux et al., 1999]. Further, Tass et al. [1998] pointed out that synchronization of two oscillators is not equivalent to the linear correlation of two signals that is measured by coherence. For instance, if the oscillators are chaotic and their amplitudes are varying without any temporal correlation yet their phases are coupled, coherence would be very low and it would not be possible to detect synchronization of their phases. Since phase synchronization requires an adjustment of phases but not of amplitudes, it is a more general approach to address the study of synchronization between EEG signals.

Reference Analysis

The use of a common reference for coherence and phase synchronization analysis has been criticized in recent years based on the argument that the common reference introduces spurious correlations uniformly distributed over the scalp [Fein et al., 1988; Guevara et al., 2005; Nunez et al., 1997; Schiff, 2005]. Instead, the use of surface Laplacians has been encouraged because they are essentially reference-free and additionally reduce the volume conduction effect [Nunez, 1995; Pernier et al., 1988; Perrin et al., 1987, 1989; Schiff, 2005]. Nevertheless, Nunez et al. [1997, 1999] demonstrated that although surface Laplacian methods remove most of the distortions caused by the common reference electrode and volume conduction, common reference methods, like average reference and digitally linked mastoids, produce reasonably reliable results for longrange coherence. Moreover, the surface Laplacian acts as a spatial band-pass filter of scalp potential, thus emphasizing the locally synchronized sources and deemphasizing the long-range synchronized sources. Further, it is less accurate near the edges of the electrode array due to a lack of neighboring electrodes [Nunez et al., 1997; Srinivasan et al., 1998]. However, it provides a more precise representation of the underlying source synchronization, as it is a rather good estimate of the local dura potential. Therefore, this reference scheme is preferred when studying the topography of the synchronization. In any study of (phase) synchronization, all of these issues should be taken into consideration in order to avoid the systematic rejection of any particular scheme of reference: both common reference

and surface Laplacian supply useful information, but that 628 has to be interpreted within the limitations of each 629 approach. An interesting new approach to the problem of 630 volume conduction and active reference is the use of the 631 phase lag index, a novel measure of phase synchronization, which has been recently shown to be less affected by 633 the influences of common sources and active reference 634 electrodes [Stam et al., 2007]. 635

In this study, we used both average reference (as common reference) and Laplacian methods. Both recommend 637 high density EEG (\geq 48 electrodes) to perform optimally. 638 We had 40 EEG electrodes, montage which is not ideal but 639 still useful. We chose the spherical spline Laplacian [Perrin 640 et al., 1989], assigning idealized positions on the unit 641 sphere to the electrodes. We selected spline of order m = 4 642 after Perrin et al. [1989]. 643

Statistics

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Statistical analysis for the ERP components and the TFR based oscillation and phase synchronization indices was performed with the use of a non-parametric pair-wise per-649 mutation test [Good, 1994]. It was necessary to use a nonparametric test because the distributions cannot be 651 assumed to be Gaussian. Also, the permutation test pro-652 vides exact significance levels even for small sample sizes 653 and small differences between conditions. For all indices, with the exception of the theta and delta band TFR energy for each condition separately, the test statistic was the difference between the two sample means: irregular (super-657 tonic) chords minus regular (tonic) chords. In the case of 658 the delta and theta spectral power, the maximum peak of 659 the non-normalized TFR energy Eq. (4) within a time win- 660 dow from 0 to 300 ms poststimulus was compared statisti- 661 cally with the mean value of the TFR energy averaged 662 between 300 and 100 ms prior to the stimulus onset. When 663 comparing the difference between conditions, also in this 664 case test statistic was the difference between the two sam- 665 ple means (normalized expression, Eq. (5)).

Additionally, we tested whether the induced gamma 667 spectral power for each separated condition was significantly different of the pre-stimulus levels. In this case, the 669 test statistic was the difference between the sample mean 670 after stimulation and the mean pre-stimulus value. 671

In all cases, the permutation tests were computed by taking the first and second half of 5,000 random permutations of the joint sample and calculating replications of the 674 test statistics. The *p*-values were then obtained as the frequencies that the replications had larger absolute values than the experimental difference. When multiple permutation tests are performed, the Bonferroni correction of the *p*-678 values gives usually exceedingly conservative results when 679 applied to EEG signals, due to the violation of the assump- 680 tion of independent tests. Consequently, we complemented 681 the permutation test with a step-down approach [Good, 682 2005; Troendle, 1995]. This step-down method explicitly takes into account the correlations between the tests and, 684

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as a consequence, the final *p*-values do not need to be extra corrected. Therefore, when several tests were computed via this stepwise algorithm the threshold values used were the standard 0.05 and 0.01 significance levels.

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To study the spatiotemporal progression of ERP components, electrodes were grouped into six regions of interest (ROIs): LA (left anterior: FP1, F9, AF7, F7, F3), LC (left central: FT7, FC3, T7, C3, TP7, CP5, CP3), LP (Left posterior: P7, P3, P9, P07, O1), RA (right anterior: FP2, AF8, F10, F4, F8), RC (right central: FC4, FT8, C4, T8, CP4, CP6, TP8), RP (right posterior: P4, P8, PO8, P10, O2). These same six ROIs were used in the analysis of the spectral power distributions of evoked and total theta oscillatory activities.

To search for significant differences between conditions, and between each condition separately and the pre-stimulus level, in terms of the gamma band spectral power, we evaluated a permutation test for each of the 20 frequencies in the range of 30-50 Hz. To study the topographical differences in the phase synchronization indices obtained after computing the surface Laplacian, electrodes were grouped into eight ROIs. Some of the groups of electrodes were the same as those used in the ERP analysis (LA, LP, RA, RP), but the electrodes of central regions were separated into central ROIs and temporal ROIs: RC (Right central: FC4, C4, CP4, CP6), RT (Right temporal: FT8, T8, TP8), LC (left central: FC3, C3, CP5, CP3) and LT (Left temporal: FT7, T7, TP7).

RESULTS

ERP Analysis

ERPs were derived by averaging the raw trials for each subject and condition after re-referencing to the mean potential of the mastoids and performing a baseline correction between 500 and 0 ms prior to the onset of the final chord. The grand-averaged ERP waveforms for the regular tonic and irregular supertonic chords show that the irregular chords elicited a clear ERAN compared with the regular chords (see Fig. 2). The ERAN component peaked F2 around 200 ms and was widely distributed over the scalp with slightly higher amplitudes at right anterior electrodes than at their left counterparts. Figure 3A depicts the 6 F3 ROIs, whereas in Figure 3B the significant (P < 0.01) statistical differences between the two chord types for the 6 ROIs are plotted. This representation offers a picture of the spatiotemporal progression of the ERAN, indicating clusters of scalp areas showing significant differences in the waveforms. The earliest effect was found at right anterior electrode regions, mainly at the right fronto-central region with a temporal spread of 160-220 ms. This effect then manifested in central and posterior electrode regions bilaterally.

Since the ERAN component almost disappeared when the ERPs were recomputed after filtering the raw signal with 8 Hz low-pass (figure not shown), we concluded that



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Figure 2.

ERP analysis. Grand average of the ERPs obtained for the following: processing of regular chords (represented by black lines), processing of irregular chords (blue), and the difference profiles (blue-black, red). The response to the irregular chords is less positive than the response to the regular chords, leading to a negative component known as the ERAN.

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this component was mainly constituted of brain oscillations with frequencies lower than 8 Hz.

Spectral Power Analysis

Theta band responses

Since the ERAN disappeared with 8 Hz low-pass filtering, we further tested whether this ERP component was manifested as a decrease in the evoked or total (evoked + induced) slow oscillations. Around the latency of the 779 ERAN, we investigated whether the changes in the evoked 780 and total spectral power distributions relative to prestimulus levels were more specifically localized in the delta (< 4 Hz) or in the theta (4-7 Hz) frequency bands. For this purpose we used the average reference scheme. The time 785 courses of the total and evoked TFR energy for the delta and theta bands are presented in Figure 4 at the right elec-764 trodes F4 and FT8, within the average reference scheme. A poststimulus increase in these measurements can be observed for both regular and irregular chords (Fig. 4A-789 H), with higher increases for the regular condition. 790

Curves in Figure 4A-H exhibit local maxima in the spec-791 792 tral power relative to baseline levels in all cases consid-793 ered, with more dramatic changes in the regular condition. These results indicate that the processing of regular chords 794 795 elicits increases in phase-locked but also non-phase locked 796 oscillatory activity in delta and theta frequency bands, increases which are weaker when processing irregular 798 chords.

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Figure 3.

(A) Head positions of the electrodes and 6 ROI used for the ERP and spectral power analysis. (B) Latency periods of statistically significant (P < 0.01) differences between the grand averages of the ERPs of the irregular and the regular conditions, calculated with respect to a pair-wise non-parametric permutation test (over

The difference (irregular minus regular) curves confirm the lower spectral power for irregular chords relative to regular chords, difference which is more pronounced in the total spectral power (Fig. 4I–L, dotted curves).

For statistical analyses, total and evoked theta and delta activities, for each condition separately, were first averaged across the electrodes of the 6 ROIs (see Statistics in Materials & Methods). Next, the maximum values between 100 and 300 ms poststimulus of the indices were compared for each condition separately (via permutation test) with the mean baseline level between 300 and 100 ms prior to the stimulus onset at each ROI (Fig. A–H). Finally, we tested for differences between conditions for the evoked and total theta and delta activities at each ROI, by comparing in the time window 100–300 ms the normalized spectral power Eq. (5) of irregular and regular chords.

The permutation test did not reveal significant (P >0.05) changes at any of the ROIs in response to stimulation in the total spectral power elicited by the regular or irregular chords. However, significant (P < 0.01) increases in the delta and theta evoked spectral power were found. More specifically, the theta evoked spectral power differed from baseline levels in all 6 ROIs for processing both regular and irregular chords. The mean latency across ROIs of this effect was 203 ms, for the regular chords, and 189 ms, for the irregular chords. Similar increases relative to baseline levels in the delta evoked spectral power were found to be significant (P < 0.01) at anterior and central electrode regions, bilaterally, with a mean latency across ROIs of 237 ms for music-syntactically regular chords and 260 ms for music-syntactically irregular chords. Interestingly, the peaks in the delta evoked spectral power were delayed relative to the peaks in the theta evoked spectral power.

subjects). The p values are presented for different areas of electrodes: LA (left anterior), LC (left central), LP (left posterior), RA (right anterior), RC (right central) and RP (right posterior). The most pronounced significance values were obtained in RA and RC electrodes, followed by the RP electrodes.

The difference (supertonic minus tonic) total spectral 879 power was not significant (P > 0.05) in the theta frequency 880 range, but in the delta band (P < 0.01) at RA and RC electrode regions with a latency period of 100–150 ms. Significant differences in the spectral power of phase-locked 883 theta activity were obtained between 100 ms and 160 ms at left- and right-anterior (P < 0.05) brain areas. 885

As indicated in this section, the poststimulus changes 886 were due to a smaller spectral power for irregular relative 887 to regular chords. 888

Gamma band responses

The TFR analysis was extended to investigate the spec-892 tral power distribution of evoked and induced oscillatory 893 activities in the high frequency range (30–50 Hz). The early 894 processing of irregular and regular chords elicited similar 895 bursts of gamma oscillations (50-100 ms, 30-37 Hz, figure 896 not shown) but no statistically significant differences 897 between the two conditions were found. The difference 898 TFR, irregular-regular, is plotted in Figure 5 for both com-893 mon reference (A) and Laplacian algorithm (B). Only one significant zone of reduced spectral power was found, 901 which was similar for both reference schemes: a decrease 902 between 40 and 50 Hz in the time span of 510-560 ms for 903 the common reference, and a broader decrease between 38 904 and 50 Hz and with a latent period of 500-550 ms for the 905 Laplacian scheme. This decrease was due to both an 906 increase (from the baseline) in the induced gamma spectral 907 power during regular chord processing and a decrease 908 (from the corresponding baseline) in the induced gamma 909 spectral power during irregular chord processing (see Fig. 910 6). Only the increase relative to pre-stimulus levels in the 9F6 regular condition was significant (P < 0.01), indicating that 912

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ID: 40410 Date: 9/4/08 Time: 18:40 Path: J:/Production/HBM#/Vol00000/080051/3B2/C2HBM#080051



Time course of the spectral power distribution of total and evoked delta and theta oscillatory activity (non-normalized expression, Eq. (4) at the right-hemisphere electrodes F4 and FT8 with average reference scheme. (A–D) Total oscillatory activity in the delta band (A,B) and theta band (C,D) for the irregular (dashed lines) and regular (solid lines) conditions showing clear larger values for the regular condition. (E–H) Same for the evoked oscillatory activity. Significant differences (P < 0.01) between the maximum poststimulus peak and mean baseline level are indicated at

irregular chords (vertical dashed lines). (I–L) Difference (irregular minus regular) total (dotted lines) and evoked (solid lines) oscillatory activity indicated in standard deviations from the 100–300 prestimulus baseline Eq. (5). Irregular chords exhibit less spectral power as compared with regular chords, both in the phase-locked and in the total oscillations. The vertical lines represent regions of significance (P < 0.05) for the comparison conditions in the delta band phase-locked and total spectral power.

for the processing of irregular chords late changes in induced oscillatory activity were absent.

The topography of the decrease in the spectral power of the induced oscillatory activity averaged over the frequency range 38–50 Hz and the time window 500–550 ms is illustrated in Figure 5C. In this plot the TFR energy obtained after applying the surface Laplacian was aver-
aged across trials for the irregular versus the regular1021
1022chord. Peaks of reduced spectral power emerged at the
frontal electrodes FZ, AF8, F8, and F9 as well as at the cen-
tro-parietal CPz, temporo-parietal electrode TP8 and parie-
tal electrodes P8 and P9.1021
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ID: 40410 Date: 9/4/08 Time: 18:40 Path: J:/Production/HBM#/Vol00000/080051/3B2/C2HBM#080051

for each frequency $<\!15$ Hz and time instant, the cluster mean was computed as an index of spatial global synchronization strength as indicated by the SCA approach (see Materials and Methods for details). The difference values

Synchronization cluster analysis

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Materials and Methods for details). The difference values are shown in Figure 7A. The main effect is that irregular chords, as compared with regular chords, were associated with a robust decrease in the degree of global phase synchrony in the lower alpha band with the frequency span of 8–10 Hz and the time span of 175–250 ms. The analyses were repeated after Laplacian, and the result was very similar to that based on common reference (see Fig. 7B).

Phase Synchrony Analysis

After re-referencing the data using a common reference,

To obtain the topography of this decrease in phase synchronization effect, we averaged the 8–9 Hz index \overline{R}_{iC} of 1044 the electrode i over the time window 175–250 ms for each condition separately and analyzed the difference (irregular 1046 minus regular chords, Fig. 7C). For both conditions separately, the main synchronized structure was localized 1048 mainly at the left temporal region but also at the electrode FC4 (not shown). It is important to note that the synchron-1050 ized cluster denotes which electrodes are more dynamically coupled between them in a time-frequency window, information which is not necessarily related to the local spectral power at the electrodes. The R_{iC} measure in each separate condition ranged from 0.2, for EEG channels weakly synchronized to the cluster, to 0.8 for the electro-1056 des FT7, T7 and TP7.

The between-conditions difference in the phase synchronization topography showed a strong localization of the decrease in synchronization at fronto-central right electrodes (F4, FC4, C4) with a maximal decrease at the FC4 electrode (Fig. 7C). According to the permutation test across participants computed at the 8 ROIs (see Materials & Methods), significant differences (P < 0.01) were predominantly found at right central electrodes (see marked white ellipse in Fig. 7C).

Next we studied the temporal dynamics of the strength of alpha band phase synchronization both when comparing the two conditions (Fig. 8A) and for each condition separately (Fig. 8B–D). For the electrode FC4, the irregular chord exhibited a steep decrease in phase synchronization relative to the regular chord. This effect began almost immediately after stimulus presentation, reaching a maximum between 175 and 210 ms (Fig. 8B). Differences between two conditions were also evident for electrodes C4 and F4 (Fig. 8C,D), but the earlier sharp decrease was not found.

Bivariate synchronization analysis

1080To study changes in the functional connectivity pattern1081during the processing of music-syntactical irregularities,1082we used the pair-wise synchronization index \overline{R}_{ij} Eq. (6).1083Following the robust decrease in alpha band phase syn-

chronization at right fronto-central regions (as found by 1084 the SCA method), we investigated whether this effect was due to a decrease in either short-range synchronization between adjacent electrodes or a long-range synchronization between the right fronto-central electrodes and other distant electrodes. Consequently, for the same time and 1089 frequency windows, where the reported reduction of phase synchronization was maximal, we computed the mean pair-wise synchronization index between the electrode FC4 and each of the other EEG channels. Similarly, the phase synchrony indices between electrode C4 and each of the other EEG channels were calculated. FC4 and C4 were selected because the difference (ST minus T) 1096 index R_{iC} was maximal at these 2 electrodes (see Fig. 8). 1097 Additionally, we investigated the index \overline{R}_{ij} for the pairs 1098 FC4-F4, C4-F4 and FC4-C4. Thus, we could test whether 1099 these EEG channels constitute a cluster themselves. Significant outcomes of the permutation tests for the differences 1101 in the pair-wise synchronization index between conditions 1102 in this time-frequency range are depicted in Figure 9, and 1F93 show a reduction of long-range interaction between electrode FC4 and each of the left temporo-parietal electrodes T7, TP7, P7. Similar tests on time ranges earlier than 1106 175 ms or later then 300 ms produced no statistically sig-1107 nificant differences between the two conditions. 1108

We did not find a significant difference between conditions for the short-range phase coupling of the pairs FC4-F4, C4-F4 or FC4-C4. However, interestingly, the index \overline{R}_{ij} 1110 for these pairs did show maximum values for each of the conditions separately (Fig. 10A,B), indicating that the three electrodes constituted a synchronized cluster for processing both the supertonic and tonic chords. 1109

Additionally, Figure 10 depicts for each condition the phase coupling for channels TP7 and P7, separately, with the rest of the electrodes. We can observe the higher values at electrode numbers No. 22 (TP7) and No. 30 (P7), which indicates a stronger phase synchronization between these electrodes for processing both harmonical regularities and irregularities. The aforementioned difference between conditions for the bivariate index of the EEG channel FC4 is illustrated in Figure 10E.

DISCUSSION

Neapolitan vs. Supertonic Chords

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Most of the earlier studies using similar chord sequence 1130 paradigms presented Neapolitan chords as music-structural irregularities [Koelsch et al., 2000; Koelsch et al., 1132 2002a,b; Maess et al., 2001]. Though this choice elicited 1133 very large ERAN amplitudes, the following two problems 1134 arise: (a) The Neapolitan chords have fewer pitches in common with the directly preceding chords than the other regular or tonic chords have, thus creating a larger degree 1137 of 'sensory dissonance'. Therefore, it is difficult to dissociate the processing of sensory dissonance from the processing of musical syntax. (b) Neapolitan chords also constitute 1140

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Figure 5.

Late gamma activity. Difference between conditions of the global spectral power averaged across trials in the band 30-50 Hz for common reference (**A**) and spline Laplacian (**B**). The white contours denote regions where the difference between the two conditions is significant at 0.01 and 0.05 levels according to the permutation test over subjects. (**C**) Topographical map of the 38-50 Hz spectral power averaged in the time window 500-550 ms for spline Laplacian. The decrease in induced gamma activity is maximal at frontal electrodes (FZ, AF8, F8, and F9) and at parietal electrodes (CPZ, TP8, P8, and P9).

an audible frequency deviation because the previous chords are presented in the same tonal key whereas the Neapolitan chords introduce pitches which are less frequent than the pitches of the regular tonic chords. Thus, the processing of frequency deviance (neurally represented 1198 by a frequency MMN component) and the processing of 1199 musical syntax could be overlapped. For this reason, it is 1200 crucially important to minimize the acoustic differences 1201 between music-syntactically irregular and regular chords 1202 by taking into account various acoustical features. Consequently, we used supertonics as our choice of irregular 1204 chords, which are in-key chord functions, and have even higher pitch correlations with the preceding harmonic context than those of the regular/tonic chords. So, in short, 1207 the reported findings indicate the component of the brain responses which is specifically associated with processing syntax in music since the other components due to acoustical differences were minimized. 1210

ERP Analysis: Anterior Frontal Negativity

We reconfirmed the result of previous studies [Koelsch et al., 2000; Koelsch et al., 2002a,c], that processing of music-syntactically irregular chords relative to regular chords elicited an early right anterior negativity (ERAN).



Figure 6.

Late gamma activity. Induced spectral power in the 30–50 Hz 1249 band for spline Laplacian computed for the music-syntactically 1250 regular (**A**) and irregular (**B**) chords. The increase relative to 1251 pre-stimulus levels in the time window between -100 ms and 1252 -300 ms was significant (P < 0.01) only in the regular condition. 1254

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ID: 40410 Date: 9/4/08 Time: 18:40 Path: J:/Production/HBM#/Vol00000/080051/3B2/C2HBM#080051



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Figure 7.

SCA. Time-frequency plot of the difference between supertonic condition and regular condition for the cluster strength, in the frequency range <15 Hz, (A) using the mean of the mastoids behind the ears as reference and (B) after spherical spline Laplacian. (C) Topographical distribution of the difference between conditions of the synchronization strength between each electrode and cluster, obtained for 8 ROIs by averaging the 8-9 Hz index between 185 and 210 ms. A ROI-wise paired permutation test over subjects in each ROI was computed to detect the statistical differences between supertonic and tonic condition. The permutation test yielded significant differences (P < 0.01) at right central electrodes, the ROI which is indicated by the white ellipse.

This negativity was statistically significant in the time win- 1312 dow from 160 to 220 ms and represented predominantly 1313 by frequencies below 8 Hz. The ERAN was more significant when the difference mean amplitude values were averaged over the ROIs at right fronto-central regions, but also clearly present in the left hemisphere. The ERAN component was assumed to reflect neural activity related to the processing of a harmonic expectancy violation [Koelsch et al., 2002a, 2005a; Tillmann et al., 2006]. Like earlier studies, the present data showed that the ERAN can be elicited under task-irrelevant conditions and also in nonmusicians, supporting the notion that listeners familiar with Western tonal music normally possess an implicit 1324 knowledge of music-syntactic regularities, even when not 1325 formally trained.

Spectral Power Analysis: Low Frequency Response

We investigated whether this ERAN component was mainly generated by a decrease in the spectral content of slow (<8 Hz) evoked oscillations, total power, or both. Evoked oscillations have a fixed phase latency across trials relative to the stimulus onset, whereas total oscillatory activity refers to oscillations both phase-locked and nonphase-locked to the stimulus onset. Our results demonstrated that the delta and theta total spectral power increases were concurrent with a phase-alignment in the

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Figure 8.

Temporal profiles of cluster synchronization. (A) Temporal evolution of the difference between the indices of the synchroniza-1361 tion strength between cluster and oscillator, R_{iC} , for both conditions (supertonic vs. tonic), computed for all electrodes. Additionally, the temporal profile of \overline{R}_{iC} for the supertonic (dotted) and tonic condition (line) is depicted for electrodes FC4 (B), C4 (C) and F4 (D). Contrary to the channels C4 and F4, the electrode FC4 elicits a steep decrease in the synchronization index 1367 for the irregular final chord. 1368

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Time 185–250 ms •FP1 •FP2 •AF7 •AF8 •AFZ •F9 •F10 •F7 •F8 •F3 •FZ •F4 •FT8 ₩FC4 6.7 •C4 •T8 •CPZ ·CP4CP6TP8 •PZ •P4 •P8 •P10 •POZ PO8 O2 •01

Figure 9.

Bivariate synchronization analysis. Differences between conditions of the pair-wise synchronization index in the frequency band 8–9 Hz and time window 185–250 ms. Differences between electrode FC4 and the rest of electrodes significant at the level P < 0.01, according to a permutation test over subjects, are plotted by a dashed line. The test yielded three significant effects, namely a decrease in synchronization between channel FC4 and each of the left temporo-parietal electrodes T7, TP7 and P7.

1402 delta and theta band, respectively, after the final chord 1403 onset, and these effects were weaker in irregular than in 1404 regular chords. However, only the changes in the evoked 1405 spectral power were significant. Fronto-central regions 1406 bilaterally were involved in significant poststimulus 1407 changes in delta frequency phase-locked oscillations, while 1408 all scalp areas selected exhibited poststimulus changes in 1409 the spectral power of theta band evoked oscillations. These 1410 findings support the arguments against a strict lateraliza-1411 tion of music processing to the right hemisphere [Koelsch 1412 et al., 2002], and rather show that neural resources for syn-1413 tactic processes are shared between two hemispheres, in 1414 which inferior frontal regions play a major role [Tillmann 1415 et al., 2006]. The poststimulus increases in the theta phase-1416 locked oscillations had a latency similar to that of the ERAN component (~190 to 200 ms), whereas the effect in 1417 1418 the delta band was delayed, indicating that the different 1419 poststimulus bursts of oscillations could be complementary 1420 but not identical. When studying differences between con-1421 ditions, the delta band revealed an effect for both phase-1422 locked and total spectral power at fronto-central regions 1423 bilaterally.

1424 Several EEG studies have reported two mechanisms that 1425 contribute to the generation of ERPs: a *phase-resetting* of the ongoing oscillatory activity and a neuronal response 1426 added to the ongoing oscillations [Basar, 1980; Brandt et al., 1427 1991; Lopes da Silva, 1999; Makeig et al., 2002]. We consider that each model separately can only account for 1429 ERPs occurring in simple paradigms, involving basic sensory stimulus configurations, whereas for complex paradigms, such as in music processing, a contribution of both additive power and phase-resetting of oscillations is to be expected [Mazaheri and Jensen, 2006; Min et al., 2007]. 1434 Thus, our results can be interpreted within the framework 1435 of the current debate as an indication that both amplitude and phase-locking vary in response to stimulation [Herrmann et al., 2004b]. 1438

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A previous study using oscillatory analysis in language 1439 comprehension paradigms has reported that grammatical 1440 violations lead to a higher degree of stimulus-evoked ac- 1441 tivity in the lower theta band than the grammatical condi- 1442 tions [Roehm et al., 2003]. This study claimed that an irresolvable conflict in language processing produces a reor- 144 ganization in the sense of phase resetting. Rather, our 1445 results would indicate that it is the regular in-key chord, which may reorganize more coherently the spontaneous 1447 distribution of phase in the EEG and simultaneously elicit 1448 higher increases in the amplitude of the oscillations. Fur-1449 ther investigations comparing specifically syntax process-1450 ing in music and language should address this issue. 1451

Spectral Power Analysis: High Frequency Gamma Response

Early evoked gamma activity did not differ between the 1456 conditions, yet significant differences were found in the 1457 induced gamma oscillations at a later stage of processing 1458 (around 500-550 ms). The lack of significant differences in 1459 the initial processing stage was possibly due to the fact 1460 that both regular (tonic) and irregular (supertonic) chords 1461 were correct musical objects themselves that would pro- 1462 vide a similar outcome after the initial acoustical feature 1463 extraction and binding processes. In major keys, the super- 1464 tonic is the in-key chord built on the second scale tone, 1465 which implies that this chord function cannot be detected 1466 as irregular by the occurrence of out-of-key tones. Only af- 1467 ter the integration of the initial processes of feature extrac- 1468 tion with the working memory representing the previous 1469 musical context, the differences between the final chords 1470 would be apparent and the subsequent stage of harmonic 1471 integration would differ. This is nicely reflected by the dif- 1472 ferences in the induced gamma activity appearing at a 1473 later stage of processing, due to a significant increase in 1474 the gamma spectral power during regular chord process- 1475 ing and the absence of a similar increase in the gamma 1476 spectral power during irregular chord processing. There- 1477 fore, our results suggest that induced gamma responses 1478 reflect the integration of bottom-up and top-down proc- 1479 esses, within the framework of the match-and-utilization 1480 model (MUM) of Herrmann et al. [2004a]. According to 1481 the MUM, the comparison of stimulus related information 1482

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ID: 40410 Date: 9/4/08 Time: 18:41 Path: J

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Figure 10.

Bivariate synchronization analysis. (**A**,**B**) Pair-wise synchronization index versus channel number (1–40) for electrodes F4 (No. 10), FC4 (No. 15) and C4 (No. 20) averaged in the frequency band 8–9 Hz and time window 185–250 ms, presented during processing regular (A) and irregular (B) chords. Note that the index R_{ii} (phase coupling of en electrode with itself) is always I. (**C**,**D**) Same but for electrodes TP7 (No. 22) and P7 (No. 30). Maximum values appear at these same channels, No. 22 and No. 30. (**E**) Difference (supertonic minus tonic) of the bivariate synchronization index for electrode FC4 (No. 15), showing decreases in the phase synchronization with electrode positions T7, TP7, and P7 (No. 17, 22, 30).

1531 with the memory contents produces a "match" or "mismatch" output, reflected in the early gamma band 1533 responses. This output can then be used for coordinating 1534 behavioral performance, for redirecting attention or for 1535 storage in memory. This "utilization" processes modulate 1536 the late gamma response. Similarly, in our context, after 1537 the processing of stimulus-related information and build-1538 ing up of a musical context, the comparison of these proc-1539 esses with long-term memory contents (such as abstract

representations of music-syntactic regularities, possibly 1540 implemented at the right inferior frontal cortex) would 1541 lead to the different induced gamma activity. Conse- 1542 quently, these data also suggest that the harmonic integra- 1543 tion requires the consolidation of bottom-up and top-down 1544 processes. We propose that the successful consolidation of these processes was manifested in the increase of induced gamma oscillations for the processing of regular chords. 1547 The irregular supertonic chords did not match so well 1548 with the harmonic long-term memory and, consequently, 1549 the gamma spectral power decreased. Our interpretation is further supported by Lentz et al. [2007], who recently demonstrated that matches of auditory patterns which are 1552 stored as representations in long-term memory are 1553 reflected in increased induced γ -band oscillations.

It is noteworthy to mention that the latency of this 1555 gamma effect (500–550 ms) is strongly reminiscent of the 1556 latency of the N5, which is an ERP component followed 1557 by ERAN in very similar paradigms [Koelsch et al., 2000, 1558 2002a; Koelsch, 2005]. The N5 has been taken to reflect 1559 processes of harmonic integration: the final irregular 1560 chords are more difficult to integrate into the preceding 1561 harmonical context [Koelsch et al., 2000], and as a consequence they elicit a reduction of the amplitude of the late ERP waveforms, leading to the negative ERP component. 1564 This observation is coherent with the decrease of γ -band activity for the irregular chords relative to the regular 1560 chords in our study.

The spline Laplacian localized the induced gamma activ-1568 ity at the frontal (Fz, AF8, F8, and F9) and parietal (CPZ, 1569 TP8, P7, and P9) brain regions. This demonstrated the pre- 1570 dominance of the prefrontal cortex in processing of musi- 1571 cal syntax including the integration of final chord with the 1572 preceding harmonic context. The present data also showed 1573 an important role of temporo-parietal regions, which is 1574 consistent with previous data of activations in the supra- 1575 temporal cortex (anterior and superior STG) reported in 1576 both fMRI and EEG studies [Koelsch and Friederici, 2003; 1577 Koelsch et al., 2002c, 2003, 2005b]. Previous studies impli- 1578 cated the parietal lobe in harmonic processing [Beisteiner 1579 et al., 1999] and in auditory working memory [Platel et al., 1997]. Here, we propose that the gamma oscillations that 1581 mediate the integration of top-down and bottom-up processes at later stages are elicited in regions responsible for 1583 auditory working memory and long-term memory processing. This proposal is also consistent with previous reports of activations in response to music-syntactic irregularities in both inferior parietal regions and regions along the inferior frontal sulcus, both of which are known to play a role in auditory working memory [Janata et al., 2002; Koelsch et al., 2005b]. Notwithstanding, fMRI activations and changes in y-band activity do not always correlate positively, because an *increase* in regional cerebral blood flow detected by fMRI could concur with a *decrease* in the γ band activity. The former would be linked to an increased 1594 neural activity, but the latter would indicate that the local 1595 neural population is less synchronized. 1596

1597 Finally, there has been some debate on the possible relationship between the ERAN and the mismatch negativity 1599 (MMN). The MMN is a negative ERP component, which is 1600 elicited by deviant auditory stimuli in an otherwise repetitive auditory environment [Naatanen, 1992]. Both MMN and ERAN can be elicited in the absence of attention 1603 [Koelsch et al., 2001], while their amplitudes can be influ-1604 enced by attentional demands [Loui et al., 2005; Woldorff et al., 1998]. These findings were based on traditional ERP 1606 averaging techniques which ignore the oscillatory content 1607 of the underlying neural response. Several studies have 1608 shown early oscillatory components of the MMN in the 1609 gamma band, particularly a decrease of stimulus-locked or evoked gamma activity onset [Fell et al., 1997], and a transient decrease in the induced gamma response [Bertrand 1612 et al., 1998]. In contrast to the MMN, no oscillatory components in the gamma band were found for the ERAN. The 1614gamma band effect occurring at later processing stages (around 500-550 ms), presumably reflects primarily har-1616 monic integration (i.e., top-down, rather than bottom-up 1617 processing). Thus, our data also reflect that the processing 1618 of irregular chord functions involves implicit knowledge 1619 about the complex regularities of major-minor tonal music [Koelsch et al., 2001], whereas MMN mainly involves processing related to sensory aspects of acoustic information (different assumptions apply for abstract-feature MMNs [Paavilainen et al., 2001]). 1624

Decrease in Long-Range Alpha Band Phase Synchronization

1628 The global decrease in phase synchronization in the 1629 lower alpha band (8-10 Hz) evoked by the syntactically 1630 irregular chords (relative to the regular chords) 185-250 ms was primarily represented by the neural sources in right fronto-central and frontal electrode regions (FC4, C4 and F4). This decrease appeared to be due to a reduction of the phase coupling between these electrodes and other 1634 scalp regions. Using a bivariate synchronization index, we 1636 found that the phase locking between electrode FC4 and left temporo-parietal regions was significantly reduced during the similar time-frequency window. This character-1638 1639 ized the decrease in the alpha band synchronization as a 1640 spatial long-range effect. Interestingly, the right fronto-central electrodes, where the reduction of phase synchroniza-1641 1642 tion was maximal, also elicited the strongest significant 1643 decrease in the spectral power of local theta oscillations 1644 and the larger amplitude of the ERAN. In a related study on musical expectancy [Janata and Petsche, 1993], EEG pa-1645 1646 rameters, such as amplitude and magnitude-squared-co-1647 herence in various frequency bands, change over right frontal regions for varying degrees of violations of musical 1648 1649 expectancy.

1650 The relevance of long-range alpha synchronization in 1651 paradigms of complex multiple integration has been 1652 recently reported [von Stein and Sarnthein, 2000; von Stein 1653 et al., 2000] based on the functional measure of coherence or synchrony. More specifically, in the first of the men- 1654 tioned studies, perception of stimuli with varying behavioral significance was shown not to be only driven by "bottom-up" processes but also to be modified by internal constraints such as expectancy or behavioral aim. The neu-1658 ral correlates of the internal constraints were interaeral 1659 synchronization in the alpha (and theta) band. The hypothesized role of the alpha band in providing top-1661 down control was explained as follows: alpha activity is 1662 present in the "idling" brain states (such as the activity in the visual cortex while closing the eyes). These brain states may thus reflect states without bottom-up input, and as 1665 such, the alpha rhythm may be an extreme case of top- 1666 down processing, which is modulated by purely internal 1667 mental activity (e.g. imaginary, thinking or planning) or by 1668 the degree of expectancy [Chatila et al., 1992]. The authors 1669 showed that top-down alpha and theta band cortical inter- 1670 actions are integrated with bottom-up γ band activity dur- 1671 ing the successful processing of stimuli that are associated 1672 with behavioral relevance. This view of the alpha band is 1673 compatible with our results, showing that after the initial 1674 processing of the musical stimuli, the violation of the harmonic expectations was reflected in the top-down mechanism. Notice that the role of interaeral phase coupling in the alpha band does not require lack of bottom-up proc-1678 esses, rather it may be just a second stage of processing, 1679 once the bottom-up interactions have taken place and the internal constraints dominate the modulation of the brain responses.

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Further increases in between-regions coherences in the 1683 alpha band have been found in studies on mental imagery 1684 and mental performance of music [Petsche et al., 1997] and 1685 have also been claimed to be critically important for maintaining spontaneous functioning of the healthy brain [Bhattacharya, 2001]. These findings support the role of the 1688 alpha band in providing top-down control, by mediating the integration from multiple cortical areas which are activated during the task. 1691

Our results indicate that the violation of musical expectancy was reflected in the electrical brain responses as a decrease in long-range alpha phase coupling due to topdown processing. The integration of the multiple cortical areas responsible for the early processing stages (such as the left temporo-parietal brain regions) with higher areas (mainly the inferior frontal gyrus), where the abstract rules of harmonic regularities are implemented, was weaker for the supertonic chord relative to the regular chord because it deviates from the stored harmonic expectations. Thus, a decrease in the alpha oscillations that possibly mediate this top-down processing was manifested.

Similar evidence for the interplay between right auditory 1704 and prefrontal cortex has been described for an MMN paradigm [Doeller et al., 2003]. Several studies support that 1706 many aspects of melodic processing rely on both superior 1707 temporal and frontal cortices. More specifically, functional 1708 imaging studies indicate that areas of the auditory cortex 1709 within the right superior temporal gyrus are involved in 1710

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1711 the processing of pitch and timbre [Zatorre, 1988; Zatorre 1712 and Samson, 1991], and that working memory for pitch 1713 entails interaction between temporal and frontal cortices 1714 [Zatorre et al., 1994]. Hyde et al. [2006] found, in a music (with tone deafness) brains, white matter changes in the right IFG area (BA 47) as correlates of a musical pitch processing, which was interpreted as an anomalous connectivity 1718 between frontal and auditory cortical areas. A PET study 1719 [Blood et al., 1999] reported positive correlations of activity in orbitofrontal and bilateral frontopolar cortex with increasing dissonance, and the predominance of inferior frontal areas has been further demonstrated in an fMRI study investigating musical syntax processing where activation of 1724 this region increased for strong musical expectancy violations [Tillmann et al., 2003], but also for more subtle harmonic irregularities [Tillmann et al., 2006]. A recent extensive review of musical disorders provides further evidence 1728 for the interaction of frontal and temporal brain regions [Stewart et al., 2006]. More specifically, the left posterior 1730 planum temporale has been reported to be involved in the 1731 processing and primary storage of various complex sound 1732 patterns [Griffiths and Warren, 2002] and to play a role in 1733 bridging the external auditory information with further 1734 judgment [Saito et al., 2006].

Overall the phase synchronization analysis provided the 1736 first evidence for a role of the integration between the right inferior frontal cortex and left temporo-parietal regions in processing structural relations in music. Considering that 1739 the early stages of extraction of acoustic features and audi-1740 tory sensory memory are already completed at this time, 1741 this information together with the auditory Gestalts and 1742 analysis of intervals would have to be implemented in the 1743 working memory. Here, we suggest that the decoupling 1744between left temporo-parietal and right anterior regions for 1745 the harmonically incorrect chords reflected the mismatch 1746 between the working memory contents, which could lie in 1747 the left temporo-parietal regions, and the long-term memory 1748 contents (abstract model of harmonic regularities), stored in 1749 the prefrontal cortex. Nevertheless, future experiments should further elucidate the generality of this mechanism in syntactic processing of music.

> In sum, the interesting outcome of our study was that different neural processes, which were distributed across the brain, complemented each other in order to perceive the harmonic structure of music. Different scales of cortical integration, ranging from local delta, theta and gamma oscillations, to long-range alpha phase synchronization, were here demonstrated to mediate the processing of syntax in music and, as a result of their interplay, to contribute to the emergence of a "unified cognitive moment" [Varela et al., 2001].

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ACKNOWLEDGMENTS

The authors were thankful to Carsten Allefeld for providing the source code of SCA and for useful discussions and valuable comments.

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◆ Ruiz et al. ◆

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AQ1: Kindly check whether the short title is OK as given.

AQ2: Please note that the year in reference Roehm et al., 2004 has been changed to 2003 in accordance with 2226 that given in the reference list. OK?

AQ3: Allefeld et al., (In press); Bialonski and Lehnertz, 2007 are not cited anywhere in the text. Kindly insert 22 its citation at an appropriate place or delete it from the reference list.]

AQ4: "Please check and confirm that the spelling of names, ordering of first and surnames (First MI Last), des ignations and spelling of affiliations are correct for all authors."

