

Adults and children processing music: An fMRI study

Stefan Koelsch,^{a,b,*} Thomas Fritz,^b Katrin Schulze,^b David Alsop,^a and Gottfried Schlaug^{a,*}

^aMusic and Neuroimaging Laboratory, Department of Neurology, Beth Israel Deaconess, Medical Center and Harvard Medical School, Boston, MA 02215, USA

^bMax Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany

Received 8 July 2004; revised 25 October 2004; accepted 6 December 2004
Available online 2 March 2005

The present study investigates the functional neuroanatomy of music perception with functional magnetic resonance imaging (fMRI). Three different subject groups were investigated to examine developmental aspects and effects of musical training: 10-year-old children with varying degrees of musical training, adults without formal musical training (nonmusicians), and adult musicians. Subjects made judgments on sequences that ended on chords that were music-syntactically either regular or irregular. In adults, irregular chords activated the inferior frontal gyrus, orbital frontolateral cortex, the anterior insula, ventrolateral premotor cortex, anterior and posterior areas of the superior temporal gyrus, the superior temporal sulcus, and the supramarginal gyrus. These structures presumably form different networks mediating cognitive aspects of music processing (such as processing of musical syntax and musical meaning, as well as auditory working memory), and possibly emotional aspects of music processing. In the right hemisphere, the activation pattern of children was similar to that of adults. In the left hemisphere, adults showed larger activations than children in prefrontal areas, in the supramarginal gyrus, and in temporal areas. In both adults and children, musical training was correlated with stronger activations in the frontal operculum and the anterior portion of the superior temporal gyrus.

© 2005 Elsevier Inc. All rights reserved.

Keywords: Auditory processing; Music; fMRI; Children; Musical expertise; Functional plasticity; BA 6; BA 21; BA 22; BA 37; BA 44; BA 45; BA 47

Introduction

Music is one of the oldest and most basic sociocognitive domains of the human species. It is assumed that human musical abilities played a key phylogenetical role for the evolution of language, and that music making behavior covered important

evolutionary functions such as communication, group coordination and social cohesion (Zatorre and Peretz, 2001). Likewise, it is assumed that, ontogenetically, infants' first steps into language are based on prosodic information, and that musical communication in early childhood (such as maternal music) plays a major role for emotional, cognitive, and social development of children (Trehub, 2003). However, despite the biological relevance of music, only a relatively small number of studies has so far investigated the neural basis of music processing in adults, and there is only one published study that investigated music processing in children using functional brain imaging (Overy et al., 2004, for a study investigating music perception in children with EEG see Koelsch et al., 2003). Thus, only little is known about the cerebral correlates of music processing in children, and so far, no direct comparison of such correlates between children and adults is available.

The present study aimed at further investigating the functional neuroanatomy of music perception in children and adults with functional magnetic resonance imaging (fMRI). Three different experimental groups (each group consisted of ten subjects) were investigated to examine developmental aspects and functional plasticity of music processing: (a) 10-year-old children with varying degrees of musical training, (b) adults without formal musical training (nonmusicians), and (c) adult musicians.

We investigated music processing with a chord sequence paradigm that was similar to paradigms employed in some previous experiments using electroencephalography (EEG) and magnetoencephalography (MEG; for an overview, see Koelsch and Friederici, 2003, see also below). In major–minor tonal music, chord functions are arranged within chord sequences according to regularities. These regularities build a musical structure and have been considered to represent part of a musical syntax (Koelsch and Friederici, 2003; Sloboda, 1985; Tillmann et al., 2000). The dominant-tonic progression (i.e., the progression of chords built on the fifth and on the first scale tone) at the end of a chord sequence is a prominent marker for the end of a harmonic sequence and has been considered as a basic syntactic structure of major–minor tonal music (Riemann, 1877/1971). Each sequence used in the present study consisted of five chords. The first four chords were arranged according to the classical rules of harmony and established a musical context toward the end of the sequence (Fig. 1A). The

* Corresponding authors. Stefan Koelsch is to be contacted at Max Planck Institute for Human Cognitive and Brain Sciences, Stephanstrasse 1a, Leipzig D-04103, Germany. Fax: +49 341 9940113.

E-mail addresses: mail@stefan-koelsch.de, koelsch@cbs.mpg.de (S. Koelsch), gschlaug@bidmc.harvard.edu (G. Schlaug).

Available online on ScienceDirect (www.sciencedirect.com).

fourth chord of all sequences was a dominant seventh chord, which induced a strong expectancy for a tonic chord at the fifth position of a sequence (Bharucha and Stoeckig, 1986; Bigand et al., 1999; Krumhansl and Kessler, 1982). Seventy percent of the chord sequences fulfilled this expectancy and ended on a dominant-tonic progression. That is, they ended with the harmonic structure that appropriately marked the end of the harmonic progression after the presentation of the dominant seventh chord. In contrast, 30% of the sequences ended on a deceptive cadence, in which the dominant was not succeeded by a regular tonic, but by an irregular subdominant variation (a so-called Neapolitan sixth chord, see Methods; deceptive cadences and Neapolitan sixth chords are prominent stylistic elements of major–minor tonal music). Thus, the latter sequence type violated the expectancy of a regular musical structure.

Based on previous studies using similar chord sequence paradigms (Koelsch et al., 2002a; Maess et al., 2001; Tillmann et al., 2003), we expected that the musical irregularities would activate inferior frontolateral cortex, supratemporal cortex (both anterior and posterior STG), as well as the superior temporal sulcus (STS); activations were expected to be present in both hemispheres, with right-hemispheric weighting. In a previous study investigating music processing in children using EEG (Koelsch et al., 2003), children showed similar electrophysiological correlates of music processing as adults. Thus, we expected that similar anatomical structures would be activated in children compared to adults. With respect to effects of musical expertise on music processing in adults, a previous EEG study indicated that musicians react more sensitively to music-syntactic irregularities than nonmusicians (Koelsch et al., 2002b, in this study, irregular chords elicited a larger early right anterior negativity in musicians). Because previous studies suggest that neural correlates of music-syntactic processing are at least partly localized in the inferior frontolateral cortex (inferior pars opercularis, Maess et al., 2001) and in the anterior portion of the STG (Koelsch and Friederici, 2003), we expected differences in activation in these regions between musicians and nonmusicians.

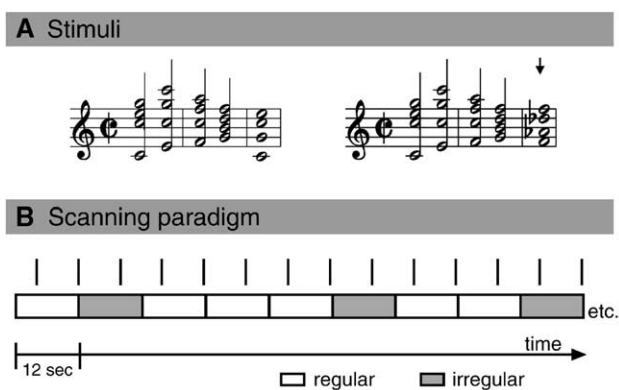


Fig. 1. (A) Examples of stimuli: chord sequence ending on a regular tonic chord (left), and on an irregular Neapolitan sixth chord (right, the Neapolitan chord is indicated by the arrow). In the experiment, 72 different chord sequences were presented in all 12 major keys. (B) Experimental design: the rectangles indicate mini-blocks, each comprising three chord sequences (resulting in a duration of 12 s per mini-block). White rectangles indicate mini-blocks with sequences ending on (regular) tonic chords, grey rectangles indicate mini-blocks with sequences ending on (irregular) Neapolitan chords. Vertical lines indicate scans (TR: 6 s, clustered volume acquisition).

In contrast to a previous fMRI study with a similar experimental design (Koelsch et al., 2002a), the present study has the advantage that (1) fMRI scanning covered the whole brain, (2) less frequent acquisitions were used (so that the musical stimulus was mostly presented during the silence period between two scans), (3) both adults and children were measured, (4) subjects with and without formal musical training were measured, and (5) Neapolitan chords were used as music-structural irregularities, enabling us to relate the present study to previous studies that employed a very similar musical stimulus using EEG (Koelsch et al., 2000, 2001, 2002b,c, 2003) and MEG (Maess et al., 2001).

Methods

Subjects

Three groups of subjects were investigated. Each group consisted of 10 participants (5 males and 5 females): (a) nonmusicians (age range 20–36 years, mean 25.6 years), none of them had any formal musical training (except normal school education), and none of them played a musical instrument; (b) musicians (age range 21–34 years, mean 26.8 years), who had learned an instrument for 4–18 years (mean: 9.4 years); (c) children (age range 9.5–10.9 years, mean 10.2 years). Three children did not play any musical instrument, four children had played an instrument for less than 1 year, and three children had played an instrument for more than 1 year (2, 4, and 8 years). Children were categorized into three groups (children with no, medium, and extensive musical training) to conduct a regression analysis between the activation pattern and musical training. All subjects were right-handed and reported to have normal hearing.

Stimuli

Stimuli were 72 chord sequences, each consisting of five chords (see Fig. 1A for two examples). The first chord was always the tonic of the following sequence. Chords at the second position were tonic, mediant, or subdominant. Chords at the third position were subdominant, dominant, or dominant six–four chords. Chords at the fourth position were dominant seventh chords. The chord at the fifth position was either a tonic (regular) or a Neapolitan chord (irregular, a Neapolitan is a minor subdominant with a diminished sixth instead of a fifth). Classically, Neapolitan chords are sixth chords, but for a proper comparison between Neapolitans and tonics, both tonic and Neapolitan chords were presented equiprobably in root position and as sixth chords. Chord sequences were presented with different melodic outlines (e.g., starting with the third, the fifth, or the octave in the top voice). Presentation time of chords 1–4 was 666.7 ms, chord 5 had a duration of 1333.2 ms, resulting in a total duration of 4000 ms per sequence. All chords had the same decay of loudness, sequences were played in direct succession, creating the sensation of a musical piece (there was no silence period between chords or chord sequences, sound examples can be downloaded from www.stefan-koelsch.de/fMRI_AdultsAndKids). Chords were presented under computerized control via MIDI on a synthesizer (ROLAND JV 1010; Roland Corporation, Hamamatsu, Japan) with a piano timbre (General MIDI #1). The musical stimulus was played with approximately 75 dB SPL using an MRI compatible headphone with piezo-electric transmission.

Procedure

Each subject performed two directly succeeding runs. For each run, 32 mini-blocks were constructed, each mini-block consisted of three sequences, resulting in a total number of 96 sequences per run (each mini-block had a duration of 12 s). There were two types of mini-blocks: (a) mini-blocks consisting of sequences ending on regular (tonic) chords, and (b) mini-blocks in which sequences ended on irregular (Neapolitan) chords (see Fig. 1B for illustration of the experimental setup). 22 mini-blocks of type a and 10 mini-blocks of type b were presented in each run (that is, in each run 66 sequences ended on a tonic, and 30 sequences on a Neapolitan chord, resulting in a probability for Neapolitans of about 30%). Both types of mini-blocks were randomly intermixed in a way that 1–3 mini-blocks of type a were presented before the presentation of a mini-block of type b (Fig. 1B). In each mini-block with Neapolitans, the tonal key was shifted one semitone upwards with the onset of the second sequence (corresponding to the tonal key of a Neapolitan). For example, in a mini-block with Neapolitans that started in C major, the second sequence, as well as the following sequences, was presented in C# major (because a Neapolitan chord sounds in C major like a C# major chord, the second sequence thus continued in the key of the Neapolitan of the first sequence). This key shift was used to prevent the musical stimulus from becoming monotonous. No key shift occurred in type b sequences. That is, type a sequences differed from type b sequences in three respects: (1) they contained Neapolitan chords, (2) they contained a change of key, and (3) they were less frequent. Note that points 1 and 2 represent music-syntactic irregularities. With respect to point 3, EEG studies indicate that an increase of the probability of irregular chords from 25% to 50% percent mainly results in a decrease of effect size (while effect patterns essentially remain the same). Because of the short duration of the experimental session (required for the children), we opted for a probability of 30%.

Subjects were asked to press a button on the last chord of each sequence: one button for the regular sequence ending (tonic chord) using the index finger, and another button for the irregular ending (Neapolitan chord) using the middle finger of the same hand. Before the functional MR experiment, samples of the two sequence types were presented to the participants until they were able to differentiate between regular and irregular sequence endings.

Data acquisition and analysis

Functional magnetic resonance imaging (fMRI) was performed on a GE 3-T whole-body MR scanner. To minimize interferences with the MR scanner noise as well as auditory masking effects, fMRI data were acquired with an effective repetition time (TR) of 6 s using a clustered volume acquisition lasting 1.75 s (i.e., 1.75 s scanner noise were followed by 4.25 s silence). Two scans were acquired during the presentation of a mini-block (Fig. 1B). In each of the two runs, a total of 74 scans were acquired (44 during the presentation of the 22 mini-blocks ending on tonic chords and 20 during the 10 mini-blocks with Neapolitans). Additionally, 6 scans were acquired during silence at the beginning of a run, and 4 scans were acquired during silence at the end of a run. Initiation of the first set of 24 slices was synchronized with stimulus presentation. A high resolution T1 weighted scan (1 × 1 × 1.5 mm voxel size) was acquired for each subject for anatomical co-registration prior to the functional imaging experiment. fMRI data were analyzed using the SPM99 software package (Institute of Neurology,

London, UK). After realignment, co-registration, normalization, and smoothing (8 mm FWHM), condition, and subject effects were estimated using a general linear model. The effects of global differences in scan intensity were removed by scaling each scan in proportion to its global intensity. Data were convolved with the hemodynamic response function (hrf), low frequency drifts were removed using a temporal high-pass filter with a cut-off of 108 s (as suggested by the SPM algorithm). In addition, a low-pass filter (hrf) was applied. For both adult and children data, a block design analysis was used (fixed effects) to contrast the experimental condition irregular (Neapolitan chord at the end of the chord sequence) with the control condition regular (tonic chord at the end of the chord sequence).

To test for hemispheric differences in the group of adults, the original functional images were again pre-processed, normalizing the images onto a symmetrical T1 template. This symmetrical template was generated in a first step by calculating a flipped version of the SPM T1 template, and in a second step by creating a mean image of the original and the flipped template. After smoothing, two sets of functional images were created, one that was flipped and one that was unflipped, resulting in two sets of functional images. Then, contrast images were calculated (irregular vs. regular) for each subject using the flipped and unflipped images. These individual contrast images were used within a second level analysis for a paired *t* test to evaluate differences between the flipped and the unflipped functional images. A mask image was generated, which took only positive voxels of the contrast Neapolitan > tonic chords of the main analysis into account. By applying this mask to the results of the second-level asymmetry analysis we were able to investigate hemispheric differences of activations in this condition.

To investigate effects of musical expertise on the activation pattern in adults, a fixed effects analysis was conducted. The contrast musicians (unexpected > expected) > nonmusicians (unexpected > expected) was masked exclusively with the contrast nonmusicians (expected > unexpected) in order to evaluate which brain areas were more strongly activated in musicians compared to nonmusicians for the contrast unexpected > expected. The analogous analysis for the contrast nonmusicians (unexpected > expected) > musicians (unexpected > expected) did not reveal any significant effects.

Results

Behaviorally, adult nonmusicians had 97.8% correct responses, adult musicians 98.9%, and children 96.9%. Differences between groups were not significant. The behavioral data indicate that all subject groups could easily differentiate regular and irregular sequence endings.

Adults

Fig. 2A shows the activations elicited in adults by music-syntactically irregular (Neapolitan) chords contrasted to regular (tonic) chords (Neapolitan > tonic chords, see also Table 1). In both hemispheres, irregular chords activated inferior frontolateral cortex (IFLC, Brodmann areas [BA] 44, 45, extending anteriorly into BA 46), the inferior ventrolateral premotor cortex (vlPMC, BA 6), the orbital frontolateral cortex (OFLC, BA 47), the anterior insula, the anterior portion of the superior temporal gyrus, the posterior half of

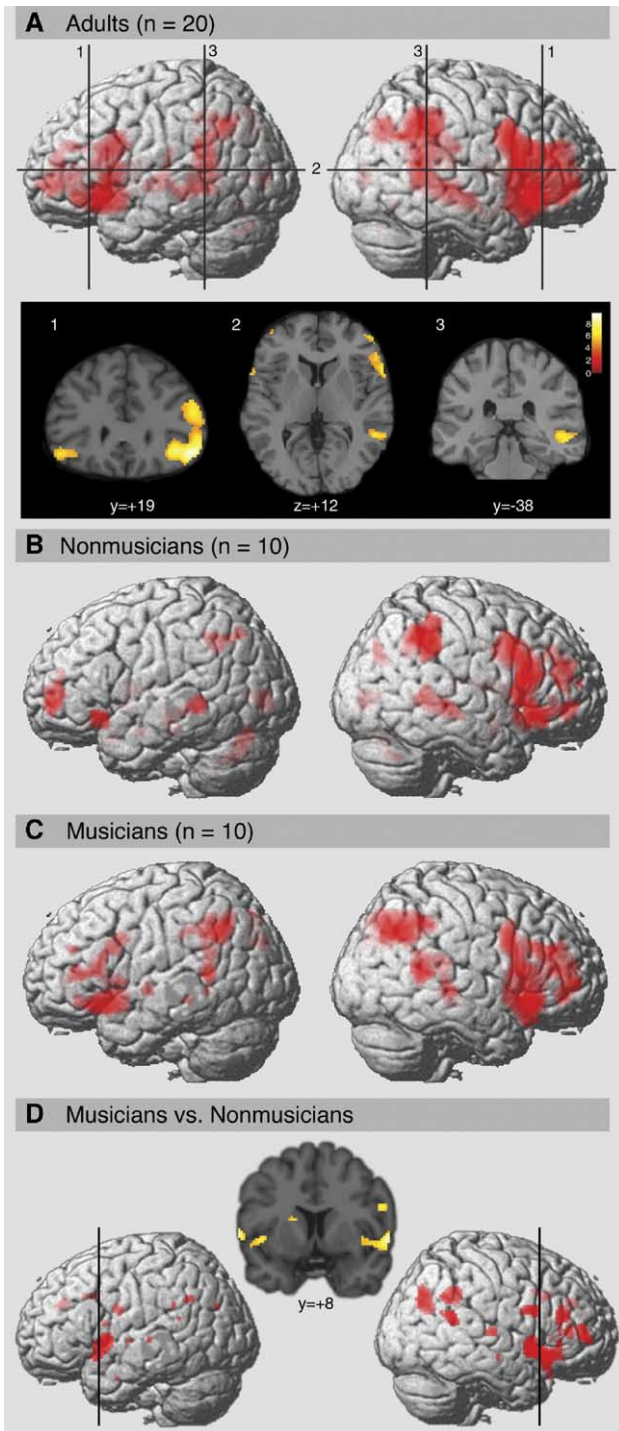


Fig. 2. Adults. Activations of Neapolitans contrasted to tonic chords (Neapolitan > tonic chords, FDR-corrected, thresholded at $P = 0.05$, voxel extent: 10), for all adults ($n = 20$; upper panel of A), and separately for nonmusicians ($n = 10$; B), as well as musicians ($n = 10$; C). The lower panel of A shows activations of Neapolitans contrasted to tonic chords, depicted on slices of an individual brain (y - and z -coordinates correspond to standard stereotaxic space; Talairach and Tournoux, 1988, FEW-correction, thresholded at $P = 0.05$, voxel extent: 10). (D) Effects of musical training (uncorrected SPMs, thresholded at $P = 0.005$), group comparison of adults (10 musicians > 10 nonmusicians) for the contrast Neapolitan > tonic chords, rendered onto an individual brain (left and right). The coronal slice (middle) shows the group differences in the frontal operculum and the right anterior STG.

the superior temporal sulcus (STS, BA 22), the posterior portion of the middle and the superior temporal gyrus (BA 21/37, BA 22p), and the supramarginal gyrus (SMG). Fronto-opercular (BA 44, BA 45) as well as posterior temporal activations (STS/MTG, and STG/BA 22p) were slightly lateralized to the right ($P < 0.001$, uncorrected; for details of the second-level analysis see Methods). Activations of the OFLC and the anterior insula were bilateral (see also left image of lower panel of Fig. 2A). No significant activations of the primary auditory cortex were observed (see also middle image of lower panel of Fig. 2A).

When looking at the data of nonmusicians and musicians separately (Figs. 2B and C), musicians showed slightly stronger activations in the frontal cortex (especially in the left hemisphere), in the anterior portion of the STG, in the SMG, and in posterior temporal areas. When data of musicians and nonmusicians were directly compared (contrast: Neapolitan > tonic chords for musicians > nonmusicians), FDR-corrected SPMs (thresholded at $P < 0.05$) did not reveal significant differences between the two groups, probably due to the relatively low number of subjects. However, as noted in the Introduction, the early right anterior negativity (ERAN) has been shown to be larger in (adult) musicians than nonmusicians, and the ERAN has been suggested with MEG and EEG to be generated in the IFLC (pars opercularis, BA 44), and in the anterior portion of the STG. Thus, possible activation differences between groups in these structures were tested directly (i.e., guided by our hypotheses) using uncorrected SPMs (thresholded at $P = 0.005$). This test indicated that activations of irregular chords were stronger in musicians than in nonmusicians in both left and right IFLC (pars opercularis), and in the anterior portion of the right STG (Fig. 2D, see Methods for details about the group statistics).

Children

In the right hemisphere, the activation pattern of children was very similar to that of adults (Fig. 3A, and Table 1), except that no

Table 1

Local maxima of activations elicited by music-syntactically irregular (Neapolitan) chords contrasted to regular (tonic) chords (Neapolitan > tonic chords), separately for adults and children

Anatomical location	Adults	Children		
<i>Left hemisphere</i>				
BA 44	-55, 10, 7	6.06		
BA 45	-46, 24, 10	2.84		
BA 47	-41, 16, -6	8.29	-43, 19, -6	4.27
BA 6	-50, 1, 23	5.98		
STS	-52, -34, 2	4.64		
STG/BA 22p	-59, -49, 15	6.33		
<i>Right hemisphere</i>				
BA 44	52, 9, 11	8.44	53, 10, 10	4.72
BA 45	44, 29, 12	7.31	52, 18, 7	5.56
BA 47	47, 19, -6	9.67	44, 19, -6	6.14
BA 6	43, -1, 28	8.24	44, 1, 30	3.40
STS	50, -32, 2	6.26	46, -30, -1	4.47
STG/BA 22p	57, -49, 13	6.62	50, -42, 13	3.89
SMG	57, -49, 13	8.09		

Coordinates refer to standard stereotaxic space (Talairach and Tournoux, 1988), z values (bold) are FDR-corrected (thresholded at $P < 0.05$, voxel extent: 10). Note that 10 children and 20 adults were measured, leading to a stronger statistical power for the data of adults.

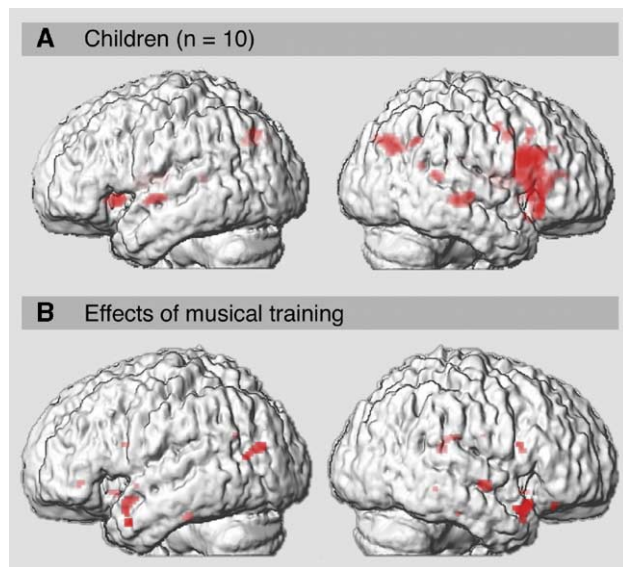


Fig. 3. Children. (A) Activations of Neapolitans contrasted to tonic chords, rendered on the average brain of children (Neapolitan > tonic chords, FDR-corrected, thresholded at $P = 0.05$, voxel extent: 10). (B) Regression analysis, activations of Neapolitans (Neapolitan > tonic chords) \times degree of musical training (see Methods), rendered onto the average brain of children (uncorrected SPMs, thresholded at $P = 0.005$).

SMG activation was observed. In the left hemisphere, only the OFLC and the anterior portion of the STG were significantly activated in children.

To investigate effects of musical training in children, possible activations in the IFLC and the anterior STG were tested directly (as in adults) using uncorrected SPMs thresholded at $P = 0.005$ (regression analysis, activations of [Neapolitans > tonic chords] \times degree of musical training; see Methods). Similar to adults, musical training appeared to be correlated with increased activation in the right IFLC and the anterior portion of the right STG (Fig. 3B).

Discussion

In all three groups (nonmusicians, musicians, and children), unexpected chords (contrasted to expected chords) elicited activations of IFLC, vIPMC, anterior and posterior temporal lobe structures, OFLC, and anterior insula. Activations of each of these structures were observed in both hemispheres, although activations of IFLC, vIPMC, and temporal lobe structures had a right-hemispheric weighting.

IFLC (BA 44) and vIPMC

Activations of these regions have been reported in some previous functional imaging studies on auditory processing using musical stimuli (e.g., Janata et al., 2002a,b; Koelsch et al., 2002a; Maess et al., 2001; Parsons, 2001; Platel et al., 1997, 2003; Tillmann et al., 2003), linguistic stimuli (for a review, see Friederici, 2002), auditory oddball paradigms (Doeller et al., 2003; Opitz et al., 2002), pitch discrimination tasks (Gaab et al., 2003; Gandour et al., 2000; Griffith, 2001, 2003; Zatorre et al., 1992, 1994), and serial prediction tasks

(e.g., Schubotz and von Cramon, 2002). On a more abstract level, IFLC (BA 44) and the vIPMC may be regarded to be involved in the analysis, recognition, and prediction of sequential auditory information (Conway and Christiansen, 2001; Huettel et al., 2002; Schubotz and von Cramon, 2002): Fronto-opercular cortex, along with vIPMC, recognizes structural properties (rather than simple acoustic properties) of complex auditory sequences, and these areas are involved in a fast short-term prediction of upcoming events. Violations of predictions activate these areas compared to events that do not violate the prediction.

As noted in the Introduction, the first four chords of the sequences established, from a music-theoretical view, a musical structure whose most regular ending is the tonic. The presentation of a Neapolitan instead of a tonic at the fifth position of the chord sequences thus violates music-syntactic regularities. Previous studies have shown that listeners familiar with the regularities of major–minor tonal music (whether or not they received formal musical training) build up expectancies, or predictions, for music-syntactically regular chord functions during the perception of harmonic sequences (Bharucha and Krumhansl, 1983; Koelsch et al., 2000; Krumhansl and Kessler, 1982). Thus, it seems likely that violations of musical syntax (that are perceived as expectancy violations) activated BA 44 and vIPMC in the present study. Note that, corroboratingly, an electrophysiological correlate of music-syntactic processing, the early right anterior negativity (ERAN, Koelsch et al., 2000), has been localized with MEG in BA 44 (Maess et al., 2001), and with EEG in BA 44 and the anterior portion of the STG (Koelsch and Friederici, 2003). Moreover, syntactic processing of language has also been shown to activate IFLC (particularly inferior BA 44, often along with the anterior STG; Friederici, 2002; Kaan and Swaab, 2002), although usually with a different hemispheric weighting (i.e., usually with left hemispheric dominance).

Taken together, it thus appears that the recognition of musical syntax, and the detection of a music-syntactic irregularity (the irregularity also representing a violation of a serial prediction) involves a network comprising the pars opercularis in the IFLC (possibly along with the anterior STG) and the vIPMC. Note that it has been suggested that there might be an immediate link between the prediction of upcoming events and a representation of corresponding motor schemas in the lateral PMC to enable an immediate mapping of perception onto action, in the present study premotor programs for articulation, or “vocal plans” (Schubotz and von Cramon, 2002, see also Rizzolatti et al. (1996)). Such a mapping is needed, e.g., when singing along in a group, and such a mapping is presumably also involved in the learning and understanding of musical syntax.

The extent of activation of IFLC and vIPMC was larger in the present study compared to some previous studies (e.g., Schubotz and von Cramon, 2002; Opitz et al., 2002), presumably due to the high complexity of the musical sequences used in the present study (the arrangement of sequences was based on complex regularities of major–minor tonal music).

Other areas of the frontal lobe have been implicated in the tracking of tonal keys (Janata et al., 2002a): Tonality-tracking areas had been located in the rostromedial PFC (that is, more medially, and more anteriorly than the IFLC). Such rostromedial prefrontal regions were not activated in the present study, possibly because no tonality tracking was required by the subjects.

Posterior temporal activations (STS, MTG, and STG)

The areas comprising the posterior MTG (BA 21/37) and STG (BA 22p) have been reported to be involved in the processing of lexical-semantic aspects, i.e., meaning, of language (Baumgaertner et al., 2002; Démonet et al., 1992; Friederici, 2002; Friederici et al., 2000; Halgren et al., 2002; Helenius et al., 1998; Kuperberg et al., 2000; Ni et al., 2000; Price et al., 1997). Although there is still no clear consensus of how musical semantics might be defined, a recent EEG study indicates involvement of BA 21/37 in the semantic processing of words when a word is semantically unrelated to musical information (Koelsch et al., 2004). Music-psychologically, the interplay of formal structures in creating patterns of tension and resolution (e.g., the presentation of a Neapolitan instead of a tonic) has been regarded as an important aspect of musical meaning (Meyer, 1956, see also Krumhansl (1997)). Note (a) that Neapolitan chords belonged, within the contextual (and hence meaningful) harmonic environment, to a different semantic category compared to the tonic chords, and (b) that Neapolitan has a musical meaning which is utilized by composers as a means of expression. It is thus possible that the irregular chords activated cortical structures that are involved in the processing of meaning information (with right-hemispheric weighting, in contrast to studies using linguistic stimuli). A similar activation (comprising BA 21/37 and BA 22p) was observed in a study from Satoh et al. (2001). In that study, a condition in which subjects listened more globally to musical pieces under the instruction to detect minor chords was compared with a condition in which subjects performed a selective attention task on the same musical stimulus (subjects were asked to follow the alto-voice of the music). It is possible that the activation of the mentioned areas was a result of the semantic processing of the music during a more global listening to the musical pieces.

The regions along the banks of the STS have been suggested to be involved in pre-lexical processing (Mummery et al., 1999) and in the perception of acoustic-phonological features of speech (Binder et al., 1994; Pöppel, 1996). It is possible that, analogously, these regions have been activated during the acoustic analysis of the interval structure of the Neapolitan chords; this issue remains to be specified.

BA 45 and supramarginal gyrus (SMG)

Because of the involvement of BA 45 and SMG, it appears that the processing of the irregular chord functions also activated working memory functions (enabling to relate the irregular chord functions to the subsequent musical context). BA 45 and regions within the inferior frontal sulcus (IFS) have been implicated in working memory for both musical (pitch) and linguistic information (Friederici, 2002; Janata et al., 2002b; Zatorre et al., 1994). Likewise, the SMG has been shown to be involved in short-term memory processes for musical (pitch) information (Celsis et al., 1999; Gaab et al., 2003; Janata et al., 2002b), as well as in short-term auditory-verbal memory processes and phonological store (Caplan et al., 1995; Clarke et al., 2000; Paulesu et al., 1993; Salmon et al., 1996; Vallar et al., 1997).

Orbital frontolateral cortex

The OFLC has been implicated in the evaluation of the emotional significance of a sensory stimulus (Mega et al., 1997).

The Neapolitan chords sound odd to listeners familiar with major-minor tonal regularities and violate the sensory expectancies of listeners (Koelsch et al., 2000). The violation of musical expectancies has been regarded as an important aspect of generating emotions when listening to music (Krumhansl, 1997; Meyer, 1956). Moreover, the perception of irregular chord functions has been shown to lead to an increase of perceived tension (Bigand et al., 1996), and the perception of tension has been linked to emotional experience during music listening (Krumhansl, 1997). The assumption that unexpected chords may generate emotional responses is supported by a recent study in which Neapolitan chords occurring in Bach-chorales led to changes in electrodermal activity (Steinbeis et al., submitted for publication). With this respect, it is possible that the activation of OFLC reflects emotional processes during the perception of the Neapolitan chords. It is likely that the activation of OFLC is related to the activation of the anterior insula (the insula is involved in the organization of reactions of the autonomous nervous system when stimuli with emotional valence are processed; Augustine, 1996). Note that activations of OFLC and anterior insula (which appear to reflect rather emotive aspects of music processing) were not lateralized in contrast to fronto-opercular and posterior temporal activations (which appear to reflect rather cognitive aspects of music processing, see also below; for another music study reporting activation of OFLC, see Levitin and Menon, 2003).

Effects of musical training

When tested directly, both left and right IFLC (pars opercularis), and the anterior portion of the right STG, were activated more strongly in musicians than in nonmusicians, in both adults and children. The greater activation of these areas in musicians appears to reflect a stronger involvement of neural resources engaged in music-syntactic processing: Previous studies indicate (a) that neurophysiological correlates of music-syntactic processing are localized in these areas (Koelsch and Friederici, 2003; Maess et al., 2001, see also above), and (b) that music-syntactic irregularities activate these neurophysiological correlates more strongly in musicians than in nonmusicians (Koelsch et al., 2002b). This difference in activation between musicians and nonmusicians reflects that musicians have a more specific representation of musical regularities and thus presumably react more sensitively to the violation of these regularities. The data of children suggest that this difference between musicians and nonmusicians can be observed already at the age of 10 years (probably even earlier).

fMRI data of children

In the right hemisphere, the activation pattern of children was very similar compared to the pattern of adults, except that no activation of the SMG (and probably less activation of BA 45/46) was found in children. In contrast to adult musicians, no left hemisphere activations were observed in BA 44, BA 45/46, vIPMC, and the SMG. In contrast to adult nonmusicians, less activations of prefrontal areas (BA 45/46) and SMG were found in the left hemisphere.

That is, activations of SMG and BA 45 were strongest in adult musicians and weakest in children (especially in the left hemisphere). Because working memory-related activations of the SMG have recently been shown to correlate with performance competence in a pitch discrimination task (Gaab et al., 2003), the present

data suggest that the musical experience of subjects led to a stronger engagement of working memory-based pitch processing while performing the task (despite the similar behavioral performance; Gaab et al., 2003). That is, it appears that adult musicians relied most, and children least, on working memory-based pitch processing while differentiating regular and irregular chords.

Neapolitan chords and primary auditory analysis

No significant activations of primary or peri-primary auditory areas (BA 41, roughly corresponding to Heschl's gyrus, and BA 42) have been observed in response to the Neapolitans, neither in adults, nor in children, reflecting that the psychoacoustical difference between tonic and Neapolitan chords was minor and did, thus, not play a major role for processes of primary auditory analysis. That is, the present results render it unlikely that a possible processing of the "sensory dissonance" of Neapolitans (electrically presumably reflected in the N1; Näätänen, 1992), or auditory sensory memory operations activated by the out-of-key notes of the Neapolitans (electrically reflected in the mismatch negativity, MMN, e.g., Näätänen, 1992) were considerably involved in the processing of Neapolitans. Instead, results reveal that the pattern activated by the Neapolitan chords considerably differs from the activation pattern of the (physical) MMN: physical irregularity detection mainly activates primary (and adjacent) auditory cortex, with additional (but smaller) contributions from frontal cortical areas (Alho et al., 1996; Giard et al., 1990; Opitz et al., 2002). These differences between the activation patterns indicate that the experimental stimuli used in the present study activated music-specific processing rather than only processes of primary auditory analysis. With this respect, the present results also corroborate the assumption that the early electrical effect elicited by Neapolitan chords (the ERAN) reflects processing of musical structure, rather than auditory sensory memory operations, or other basic processes of auditory analysis such as the processing of sensory dissonance. Future studies could further clarify the role of the frontal cortex in processing music-syntactic irregularities on the one hand, and sensory oddballs on the other, by directly comparing activations elicited by both deviance types.

In contrast to the present study, primary (and adjacent) auditory cortices were activated in our previous study using a similar chord sequence paradigm (Koelsch et al., 2002a), even in a condition in which unexpected deviant chords did not represent a physical deviance (tonal modulations). We assume that this difference between studies is due to the use of less frequent acquisitions in the present study (that allowed to present the musical stimulus mainly during silence): because of the continuous scanning in the previous study (which made the acoustic analysis of the stimuli more difficult), subjects had to focus their attention strongly to the stimulus when unexpected events occurred (to press the correct button). This strong focussing on the stimulus in the previous study presumably led to a strong activation of the auditory cortices following the presentation of deviant events (Jäncke et al., 1999).

Conclusions

In summary, irregular chord functions activated cerebral structures with patterns that were similar for adult nonmusicians and 10-year-olds. We suggest that the activated structures can be assigned to four different cortical networks: (a) a network compris-

ing IFLC (along with the anterior STG) and vIPMC involved in the processing of musical structure, (b) a network comprising posterior temporal areas (BA 21, BA 22p, and BA 37) involved in the processing of musical meaning, (c) a network comprising SMG and pre-frontal cortex (BA 45) related to working memory, and (d) a network comprising OFLC (BA 47), and anterior insula, possibly involved in emotional aspects of music processing. Future experiments could be directed at dissociations between these different networks, and at further clarifying the functional significance of the mentioned structures for the processing of auditory information.

Differences between participants with and without musical training in the IFLC and the anterior STG presumably reflect competence differences in music-syntactic processing. Moreover, differences between groups in the SMG and BA 45 suggest that musicians relied most, and children least, on working memory-based pitch processing.

The activation pattern elicited by the music-syntactically irregular chords clearly differs from the activation pattern elicited by acoustic events that physically deviate from standard events in an auditory oddball paradigm: physically deviant events are detected mainly based on operations of the auditory sensory memory (Näätänen, 1992; Schröger, 1998) and activate auditory areas to a greater extent than fronto-opercular areas (Alho et al., 1996; Opitz et al., 2002; see also Tervaniemi et al., 2000). This suggests that music-syntactic irregularity detection relies on different cognitive modules (located in at least partly different cerebral structures) than those underlying physical irregularity detection. Instead, the activation pattern observed in the present study is rather reminiscent to activations observed in language experiments, particularly those investigating syntax processing (Friederici, 2002), suggesting that the processing of musical and linguistic information relies on strongly overlapping neural resources (see also Patel, 2003).

Notably, activations were observed in both adults and children with no formal musical training, in line with findings indicating that humans have a general ability to effortlessly acquire complex musical knowledge, and to process musical information fast and accurately according to this knowledge (the implicit knowledge about musical regularities is presumably acquired during listening experiences in everyday life; Tillmann et al., 2000). This ability underlines the inherent interest of the human brain in music and thus stresses the biological relevance of music.

Acknowledgments

This study was supported by a grant from the International Foundation for Music Research (IFMR) and in part by grants from the National Science Foundation (BCS-0132508), the German Academic Exchange Service (DAAD), the Dana Foundation, and the Doris Duke Charitable Foundation Clinical Scientist Development Award.

References

- Alho, K., Tervaniemi, M., Huotilainen, M., Lavikainen, J., Tiitinen, H., et al., 1996. Processing of complex sounds in the human auditory cortex as revealed by magnetic brain responses. *Psychophysiology* 33, 369–375.
- Augustine, J.R., 1996. Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res. Rev.* 22, 229–244.

- Baumgaertner, A., Weiller, C., Büchel, C., 2002. Even-related fMRI reveals cortical sites involved in contextual sentence integration. *NeuroImage* 16, 736–745.
- Bharucha, J., Krumhansl, C., 1983. The representation of harmonic structure in music: hierarchies of stability as a function of context. *Cognition* 13, 63–102.
- Bharucha, J., Stoeckig, K., 1986. Reaction time and musical expectancy: priming of chords. *J. Exp. Psychol.: Hum. Percept. Perform.* 12, 403–410.
- Bigand, E., Parncutt, R., Lerdahl, J., 1996. Perception of musical tension in short chord sequences: the influence of harmonic function, sensory dissonance, horizontal motion, and musical training. *Percept. Psychophys.* 58, 125–141.
- Bigand, E., Madurell, F., Tillmann, B., Pineau, M., 1999. Effect of global structure and temporal organization on chord processing. *J. Exp. Psychol.: Hum. Percept. Perform.* 25, 184–197.
- Binder, J., Rao, S., Hammeke, T., Yetkin, F., Jesmanowicz, A., et al., 1994. Functional magnetic-resonance-imaging of human auditory-cortex. *Ann. Neurol.* 35, 662–672.
- Caplan, D., Gow, D., Makris, N., 1995. Analysis of lesions by MRI in stroke patients with acoustic-phonetic processing deficits. *Neurology* 45, 293–298.
- Celsis, P., Boulanouar, K., Doyon, B., Ranjeva, J., Berry, I., et al., 1999. Differential fMRI responses in the left posterior superior temporal gyrus and left supramarginal gyrus to habituation and change detection in syllables and tones. *NeuroImage* 9, 135–144.
- Clarke, S., Bellmann, A., Meuli, R., Assal, G., Steck, A., 2000. Auditory agnosia and auditory spatial deficits following left hemispheric lesions: evidence for distinct processing pathways. *Neuropsychologie* 38, 797–807.
- Conway, C., Christiansen, M., 2001. Sequential learning in non-human primates. *Trends Cogn. Sci.* 5, 539–546.
- Démonet, J., Chollet, F., Råmsay, S., Cardebat, D., Nespoulous, J., et al., 1992. The anatomy of phonological and semantic processing in normal subjects. *Brain* 115, 1753–1768.
- Doeller, C.F., Opitz, B., Mecklinger, A., Krick, C., Reith, W., Schröger, E., 2003. Prefrontal cortex involvement in preattentive auditory deviance detection: neuroimaging and electrophysiological evidence. *NeuroImage* 20 (2), 1270–1282.
- Friederici, A.D., 2002. Towards a neural basis of auditory sentence processing. *Trends Cogn. Sci.* 6, 78–84.
- Friederici, A.D., Opitz, B., von Cramon, D.Y., 2000. Segregating semantic and syntactic aspects of processing in the human brain: an fMRI investigation of different word types. *Cereb. Cortex* 10, 698–705.
- Gaab, N., Gaser, C., Zaehle, T., Jancke, L., Schlaug, G., 2003. Functional anatomy of pitch memory—an fMRI study with sparse temporal sampling. *NeuroImage* 19, 1417–1426.
- Gandour, J., Wong, D., Hsieh, L., Weinzapfel, B., Van Lancker, D., et al., 2000. A crosslinguistic PET study of tone perception. *J. Cogn. Neurosci.* 12, 207–222.
- Giard, M., Perrin, F., Pernier, J., 1990. Brain generators implicated in processing of auditory stimulus deviance. A topographic ERP study. *Psychophysiology* 27, 627–640.
- Griffith, T., 2001. The neural processing of complex sounds. *Ann. N. Y. Acad. Sci.* 930, 211–231.
- Griffith, T., 2003. Functional imaging of pitch analysis. *Ann. N. Y. Acad. Sci.* 999, 40–49.
- Halgren, E., Dhond, R.P., Christensen, N., Van Petten, C., Marinkovic, K., et al., 2002. N400-like magnetoencephalography responses modulated by semantic context, word frequency, and lexical class in sentences. *NeuroImage* 17, 1101–1116.
- Helenius, P., Salmelin, R., Service, E., Connolly, J.F., 1998. Distinct time courses of word and context comprehension in the left temporal cortex. *Brain* 121, 1133–1142.
- Huetzel, S., Mack, P., McCarthy, G., 2002. Perceiving patterns in random series: dynamic processing of sequence in prefrontal cortex. *Nat. Neurosci.* 5, 485–490.
- Janata, P., Birk, J., Van Horn, D., Leman, M., Tillmann, B., et al., 2002a. The cortical topography of tonal structures underlying Western music. *Science* 298, 2167–2170.
- Janata, P., Tillmann, B., Bharucha, J., 2002b. Listening to polyphonic music recruits domain-general attention and working memory circuits. *Cognitive Affect. Behav. Neurosci.* 2, 121–140.
- Jäncke, L., Mirzazade, S., Shah, N., 1999. Attention modulates activity in the primary and the secondary auditory cortex: a functional magnetic resonance imaging study in human subjects. *Neurosci. Lett.* 266, 125–128.
- Kaan, E., Swaab, T., 2002. The brain circuitry of syntactic comprehension. *Trends Cogn. Sci.* 6, 350–356.
- Koelsch, S., Friederici, A.D., 2003. Towards the neural basis of processing structure in music: comparative results of different neurophysiological investigation methods (EEG, MEG, fMRI). *Ann. N. Y. Acad. Sci.* 999, 15–27.
- Koelsch, S., Gunter, T.C., Friederici, A.D., Schröger, E., 2000. Brain indices of music processing: ‘non-musicians’ are musical. *J. Cogn. Neurosci.* 12, 520–541.
- Koelsch, S., Gunter, T.C., Schröger, E., Tervaniemi, M., Sammler, D., et al., 2001. Differentiating ERAN and MMN: an ERP-study. *NeuroReport* 12, 1385–1389.
- Koelsch, S., Gunter, T.C., von Cramon, D.Y., Zysset, S., Lohmann, G., et al., 2002a. Bach speaks: a cortical ‘language-network’ serves the processing of music. *NeuroImage* 17, 956–966.
- Koelsch, S., Schmidt, B.H., Kansok, J., 2002b. Influences of musical expertise on the ERAN: an ERP-study. *Psychophysiology* 39, 657–663.
- Koelsch, S., Schröger, E., Gunter, T.C., 2002c. Music matters: preattentive musicality of the human brain. *Psychophysiology* 39, 1–11.
- Koelsch, S., Grossmann, T., Gunter, T.C., Hahne, A., Friederici, A.D., 2003. Children processing music: electric brain responses reveal musical competence and gender differences. *J. Cogn. Neurosci.* 15, 683–693.
- Koelsch, S., Kasper, E., Sammler, D., Schulze, K., Gunter, T.C., et al., 2004. Music, language, and meaning: brain signatures of semantic processing. *Nat. Neurosci.* 7, 302–307.
- Krumhansl, C.L., 1997. An exploratory study of musical emotions and psychophysiology. *Can. J. Exp. Psychol.* 51, 336–352.
- Krumhansl, C.L., Kessler, E., 1982. Tracing the dynamic changes in perceived tonal organization in a spatial representation of musical keys. *Psychol. Rev.* 89, 334–368.
- Kuperberg, G., McGuire, P., Bullmore, E., Brammer, M., Rabe-Hesketh, S., et al., 2000. Common and distinct neural substrates for pragmatic, semantic and syntactic processing of spoken sentences: an fMRI study. *J. Cogn. Neurosci.* 12, 321–341.
- Levitin, D., Menon, V., 2003. Musical structure is processed in “language” areas of the brain: a possible role for Brodmann area 47 in temporal coherence. *NeuroImage* 20, 2142–2152.
- Maess, B., Koelsch, S., Gunter, T.C., Friederici, A.D., 2001. ‘Musical Syntax’ is processed in the area of Broca: an MEG-study. *Nat. Neurosci.* 4, 540–545.
- Mega, M., Cummings, J., Salloway, S., Malloy, P., 1997. The limbic system: an anatomic, phylogenetic, and clinical perspective. In: Salloway, S., Malloy, P., Cummings, J. (Eds.), *The Neuropsychiatry of Limbic and Subcortical Disorders*. American Psychiatric Press, Washington, DC, pp. 3–18.
- Meyer, L.B., 1956. *Emotion and Meaning in Music*. University of Chicago Press, Chicago.
- Mummery, C., Ashburner, J., Scott, S., Wise, R.J., 1999. Functional neuroimaging of speech perception in six normal and two aphasic subjects. *J. Acoust. Soc. Am.* 106, 449–457.
- Näätänen, R., 1992. *Attention and Brain Function*. Erlbaum, Hillsdale, NJ.
- Ni, W., Constable, R., Mencl, W., Pugh, K., Fulbright, R., et al., 2000. An even-related neuroimaging study distinguishing form and content in sentence processing. *J. Cogn. Neurosci.* 12, 120–133.
- Opitz, B., Rinne, T., Mecklinger, A., von Cramon, D.Y., Schröger, E., 2002. Differential contribution of frontal and temporal cortices to

- auditory change detection: fMRI and ERP results. *NeuroImage* 15, 167–174.
- Overy, K., Norton, A., Cronin, K., Gaab, N., Alsop, D., Schlaug, G., 2004. Imaging melody and rhythm processing in young children. *NeuroReport* 15, 1723–1726.
- Parsons, L., 2001. Exploring the functional neuroanatomy of music performance, perception, and comprehension. *Ann. N. Y. Acad. Sci.* 930, 211–231.
- Patel, A.D., 2003. Language, music, syntax and the brain. *Nat. Neurosci.* 6, 674–681.
- Paulesu, F., Frith, C., Frackowiak, R., 1993. The neural correlates of verbal component of working memory. *Nature* 362, 342–345.
- Platel, H., Price, C., Baron, J., Wise, R., Lambert, J., et al., 1997. The structural components of music perception. A functional anatomical study. *Brain* 120, 229–243.
- Platel, H., Baron, J., Desgranges, B., Bernard, F., Eustache, F., 2003. Semantic and episodic memory of music are subserved by distinct neural networks. *NeuroImage* 20, 244–256.
- Pöppel, D., 1996. A critical review of PET studies of phonological processing. *Brain Lang.* 55, 317–351.
- Price, C., Moore, C., Humphreys, G., Wise, R.J., 1997. Segregating semantic from phonological processes during reading. *J. Cogn. Neurosci.* 9, 727–733.
- Riemann, H., 1877/1971. *Musikalische Syntaxis: Grundriss einer harmonischen Satzbildungslehre*. Sändig, Niederwalluf.
- Rizzolatti, G., Fadiga, L., Gallese, V., Fogassi, L., 1996. Premotor cortex and the recognition of motor actions. *Cogn. Brain Res.* 3, 131–141.
- Salmon, E., Van der Linden, M., Colette, F., Delfiore, G., Maquet, P., et al., 1996. Regional brain activity during working memory tasks. *Brain* 119, 1617–1625.
- Satoh, M., Takeda, K., Nagata, K., Hatazawa, J., Kuzuhara, S., 2001. Activated brain regions in musicians during an ensemble: a PET study. *Cogn. Brain Res.* 12, 101–108.
- Schröger, E., 1998. Measurement and interpretation of the mismatch negativity (MMN). *Behav. Res. Meth. Instrum. Comput.* 30, 131–145.
- Schubotz, R.I., von Cramon, D.Y., 2002. Predicting perceptual events activates corresponding motor schemes in lateral premotor cortex: an fMRI study. *NeuroImage* 15, 787–796.
- Sloboda, J., 1985. *The musical mind: the Cognitive Psychology of Music*. Oxford Univ. Press, New York.
- Steinbeis, N., Koelsch, S., Sloboda, J., submitted for publication. The role of musical structure in emotion: investigating neural, physiological, and subjective emotional responses to harmonic expectancy violations.
- Talairach, J., Tournoux, P., 1988. *Co-planar Stereotaxic Atlas of the Human Brain. 3-Dimensional Proportional System: An Approach to Cerebral Imaging*. Thieme, Stuttgart.
- Tervaniemi, M., Medvedev, S., Alho, K., Pakhomov, S., Roudas, M., et al., 2000. Lateralized automatic auditory processing of phonetic versus musical information: a PET study. *Hum. Brain Mapp.* 10, 74–79.
- Tillmann, B., Bharucha, J., Bigand, E., 2000. Implicit learning of tonality: a self-organized approach. *Psychol. Rev.* 107, 885–913.
- Tillmann, B., Janata, P., Bharucha, J.J., 2003. Activation of the inferior frontal cortex in musical priming. *Cogn. Brain Res.* 16, 145–161.
- Trehub, S., 2003. The developmental origins of musicality. *Nat. Neurosci.* 6, 669–673.
- Vallar, G., DiBetta, A., Silveri, M., 1997. The phonological short-term store-rehearsal system: patterns of impairment and neural correlates. *Neuropsychologia* 35, 795–812.
- Zatorre, R., Peretz, I. (Eds.), 2001. *The Biological Foundations of Music*, *Annals of the New York Academy Sciences*, vol. 930.
- Zatorre, R.J., Evans, A., Meyer, E., Gjedde, A., 1992. Lateralization of phonetic and pitch discrimination in speech processing. *Science* 256, 846–849.
- Zatorre, R.J., Evans, A., Meyer, E., 1994. Neural mechanisms underlying melodic perception and memory for pitch. *J. Neurosci.* 14, 1908–1919.