

Enhanced anterior-temporal processing for complex tones in musicians

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Abstract

Objective: To examine how auditory brain responses change with increased spectral complexity of sounds in musicians and non-musicians.

Methods: Event-related potentials (ERPs) and fields (ERFs) to binaural piano tones were measured in musicians and non-musicians. The stimuli were C4 piano tones and a pure sine tone of the C4 fundamental frequency (f_0). The first piano tone contained f_0 and the first eight harmonics, the second piano tone consisted of f_0 and the first two harmonics and the third piano tone consisted of f_0 .

Results: Subtraction of ERPs of the piano tone with only the fundamental from ERPs of the harmonically rich piano tones yielded positive difference waves peaking at 130 ms (DP130) and 300 ms (DP300). The DP130 was larger in musicians than non-musicians and both waves were maximally recorded over the right anterior scalp. ERP source analysis indicated anterior temporal sources with greater strength in the right hemisphere for both waves. Arbitrarily using these anterior sources to analyze the MEG signals showed a DP130m in musicians but not in non-musicians.

Conclusions: Auditory responses in the anterior temporal cortex to complex musical tones are larger in musicians than non-musicians.

Significance: Neural networks in the anterior temporal cortex are activated during the processing of complex sounds. Their greater activation in musicians may index either underlying cortical differences related to musical aptitude or cortical modification by acoustical training.

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1. Introduction

How we perceive a musical sound is determined by its pitch and timbre. The pitch is determined mainly by the fundamental frequency of the sound and timbre by its temporal pattern and frequency spectrum. Several studies have revealed a right hemisphere advantage for processing musical cues (Samson and Zatorre, 1988, 1994; Zatorre and Samson, 1991; Brancucci and San Martini, 1999; Tervani-

emi et al., 2000; Samson et al., 2002; Warrier and Zatorre, 2004), although others have shown equal hemispheric contributions (Menon et al., 2002) or task-specific hemispheric specialization (Platel et al., 1997) – with left hemisphere advantage for pitch, rhythm and familiarity tasks, and right hemisphere advantage for timbre tasks. Lesion studies (Robin et al., 1990) and functional neuroimaging studies (Zatorre and Belin, 2001; Schönwiesner et al., 2005) have shown that temporal variations of sounds are mainly processed in the left hemisphere and spectral variations in the right hemisphere.

Subjects with extensive musical training respond differently to musical sounds than subjects with no musical background (Pantev et al., 1998; Shahin et al., 2003; Kuriki

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et al., 2006). Electromagnetic studies, using event-related potentials (ERPs) and fields (ERFs), have reported enhanced cortical representations in musicians compared to non-musicians for musical tones with increased amplitude of the middle latency (15–30 ms) responses (Schneider et al., 2002), the N1m at 100 ms (Pantev et al., 1998) and the P2(m) at 185 ms (Shahin et al., 2003, 2005; Kuriki et al., 2006). Increased responses in musicians might be attributed to enhanced grey matter in the auditory region of musicians (Schlaug et al., 1995; Schneider et al., 2002). This may occur as an inherited characteristic associated with a natural aptitude for music, or to synaptic modifications in the brains of musicians owing to the musicians' acoustical training history, or to both factors. The N1m and P2 have been shown to augment after a period of frequency discrimination training (N1m: Menning et al., 2000; P2: Bosnyak et al., 2004). The N1m and P2 have also been reported to reflect changes in the spectral characteristics of sounds. The N1m is affected by the bandwidth of pure tones (Seither-Preisler et al., 2003) and the P2(m) by the number of higher harmonics contained in piano tones (Shahin et al., 2005). These effects may reflect neural networks underlying auditory perception in musicians which are tuned to process the spectral characteristics of complex sounds.

ERPs and ERFs are usually generated by multiple overlapping sources and decomposing these sources is a complex task. Changes in the N1(m) and P2(m) wave, for example, may have obscured other, smaller, music-related responses. In such cases, source analysis (SA: Scherg, 1990) and current source density (CSD: Perrin et al., 1987) are useful because they can dissociate scalp distributions into components that reflect underlying independent processes. However, the accuracy of both these methods is limited by the proximity and similarity of the underlying sources. For example, two sources that are close in location and similar in orientation will be difficult to distinguish by either method. To simplify SA or CSD, responses recorded under different conditions can be subtracted from each other to give the electromagnetic activity related to whatever is different between the conditions. This subtraction method has been used extensively in ERPs to measure the Mismatch Negativity (MMN) (Näätänen et al., 1978; Brattico et al., 2002), the Negative difference wave (Nd) related to attention (Hillyard and Hansen, 1986) and the Object-Related Negativity (ORN) (Alain et al., 2001).

In the present study, we applied the subtraction method to data from Shahin et al. (2005). Shahin et al. (2005) contrasted ERPs/ERFs for piano tones matched in pitch (C4, $f_0 = 262$) and temporal envelope, but varied in the number of higher harmonics. The objective of the Shahin et al. (2005) study was to measure the effect of increased spectral content of tones on the N1(m) and P2(m). They showed that the P2(m) but not the N1(m) increased in amplitude with increased spectral complexity. Here, we subtracted ERPs of the tone containing only the fundamental from ERPs of the spectrally rich piano tones in order to isolate

activities related to processing the added spectral content. A related analysis was done on ERFs using the source space method. We hypothesized that the extra harmonics in piano tones should affect the response in the auditory areas of the temporal lobe, particularly in the right hemisphere, and that this effect would likely be larger in musicians than in non-musicians.

2. Methods

2.1. Participants

Eight musicians (age 28 ± 8 years; four females) and eight non-musician subjects (age 29 ± 4 years; one female) participated in the study. Musicians were recruited by posters placed in the Faculty of Music at the University of Toronto. All subjects were right-handed. All musicians played the piano, with six musicians identifying the piano as their principal instrument and the other two identifying either the flute or percussion. The musicians practiced their principal instrument an average of 9 ± 5 h a week. The mean age of beginning of musical training was 7 ± 3 years old (mean years of practice 15 ± 7 years). Non-musician subjects had never played a musical instrument and had no formal musical training. Normal auditory thresholds (less than 20 dB HL) for both ears were confirmed for each subject for frequencies between 250 and 8000 Hz. Subjects gave written informed consent prior to the experimental session in accordance with the guidelines of the Research Ethics Committee of Baycrest.

2.2. Stimuli

The stimuli were four tones 500 ms in duration: (1) a C4 piano tone (Fundamental $f_0 = 262$ Hz) containing the fundamental and eight harmonics (called “piano”); (2) a tone matched in the temporal envelope to the piano tone containing the C4 fundamental and the first two harmonics (called “piano2”); (3) a tone matched in envelope to the piano tone containing only the C4 fundamental (called “piano0”); and (4) a pure tone with only the C4 fundamental (called “pure”). The piano stimuli were prepared by applying a Fourier transform to a natural piano sound and then a bandpass filter (Hanning window) was applied in the Fourier domain that kept f_0 for piano0, f_0 , f_1 and f_2 for piano2 and f_0 and f_1 – f_8 for piano. Time series were constructed by inverse Fourier transform. Fig. 1 shows the waveforms and spectra for all tones.

2.3. Procedure

ERPs and ERFs were recorded simultaneously using a CTF EEG amplifier (VSM MedTech, British Columbia, Canada; 32 Ag/AgCl electrodes placed in an Easy Cap, 10-20 system) and a 151-channel whole head MEG system (VSM MedTech, British Columbia, Canada), respectively. The channel configuration for EEG was as follows: Frontal

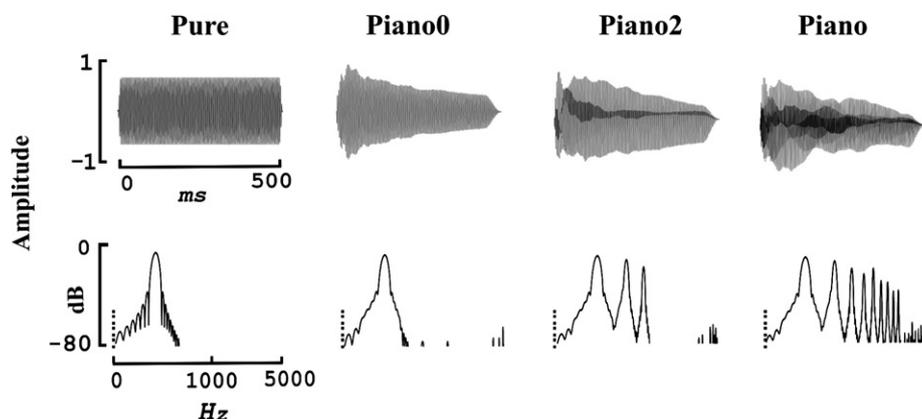


Fig. 1. Time domain (top) and spectra (bottom) for the C4 stimuli. From left to right: pure tone with the C4 fundamental, piano0 tone with piano temporal envelope and the C4 fundamental, piano2 tone with piano temporal envelope and the C4 fundamental and the first two harmonics, piano tone with piano temporal envelope and the C4 fundamental and the first eight harmonics. Dashed lines indicate the zero frequency.

F3, F4, F7, F8, Fz, FPz; Fronto-central FC1, FC2, FC5, FC6; Central C3, C4; Parieto-central CP1, CP2, CP5, CP6; Parietal P3, P4, P7, P8, Pz; Parieto-occipital POz; Occipital O1, O2; Temporal T7, T8; Mastoid channels M1, M2; Posterior channels CB1, CB2 and the Inion channel Iz. The reference electrode was Cz and the ground electrode was placed at the collarbone. Skin impedances were reduced to less than 10 k Ω at all electrode sites. EEG and MEG were low-pass filtered at 100 Hz (0-Hz high pass) and sampled at 312.5 Hz. The experiments were conducted in an acoustically silent and electrically and magnetically shielded room.

Tones were presented binaurally through plastic tubes at 60 dB above thresholds measured individually for each subject, tone and ear prior to the session (60 dB SL). The tubes acted as low-pass filters which attenuated the sounds for frequencies greater than 2200 Hz (-3 dB cut off frequency 2500 Hz; slope -40 dB/octave). Subjects watched a silent movie during the session. Eight blocks each containing 60 stimuli of the same type of tone were arranged and presented in the following order for all subjects: blocks 1 and 8 were designated for pure tone; blocks 2 and 7 were designated for piano2 tone; blocks 3 and 6 were designated for piano tone; blocks 4 and 5 were designated for piano0 tone. The interstimulus interval between tone presentations varied from 3 to 4 s offset to onset.

Continuous EEG/MEG files for each subject were loaded into BESA 2000 (MEGIS Software, Gräfelfing, Germany), digitally filtered between 0.1 and 20 Hz (zero phase shift), and divided into epochs of 600 ms duration including a 100-ms pre-stimulus interval. Trials containing shifts in any channel greater than ± 200 μ V in EEG were rejected and the same exact trials were rejected in MEG. EOG signals were monitored in the frontal EEG leads. Accepted trials (mean 86%, range 75–98%) were re-referenced to an average reference (of all channels) offline. Finally, the trials were baselined to the pre-stimulus interval (-100 to 0 ms) and averaged according to stimulus type (pure, piano0, piano2, and piano) and block (each tone type contained two blocks).

2.3.1. ERP channel analysis

The two averages (two blocks) for each tone type were collapsed into one average. Average ERPs for piano0 were then subtracted from ERPs for piano2 (piano2 – piano0) and piano (piano – piano0) tones for each subject. Average ERPs for pure tones were also subtracted from ERPs of piano0 tones. Fig. 2 shows the subtraction of group average waveforms of piano0 from piano and piano2 {mean(piano + piano2)}. This resulted in an average difference waveform that exhibited three distinct peaks (most clearly identified in the musicians group): a peak around 130 ms (DP130), a peak around 180 ms (referred to, herein, as P2 because it reflects the same process as the unsubtracted P2), and a peak around 300 ms (DP300) – DP for Difference Positivity. The difference waveforms were then interpolated onto a 47-channel montage depicting the current source density (CSD) scalp distribution. The CSD montage contained the original electrodes (except for CB1 and CB2) and additional multiple inter-electrode locations: Frontal AF1, AF2, AF5, AF6, AF9, AF10, FP1, FP2; Fronto-temporal FT9, FT10; Parieto-occipital PO1, PO2, PO5, PO6, PO9, PO10; and the Nasion channel Nz. CSD (Perrin et al., 1987), also called Scalp Surface Laplacian, is calculated by taking the second spatial derivative of the voltage data. This transformation of the voltage scalp distributions into scalp maps depicting the local radial current density is useful because it increases the spatial resolution of the measured scalp potentials by eliminating common activities between neighboring electrodes due to tangential current flow (mainly in the scalp). Because the current flow through the skull is primarily radial, CSDs give a good approximation of the actual voltage at the level of the cortex (Nunez, 1990). To apply the Surface Laplacian operator to the scalp potentials, spherical spline interpolations (Perrin et al., 1989) of the recorded scalp potentials are first carried out. Spherical spline maps interpolate the recorded scalp potentials at the individual sites so that they sum to zero over the whole head, including the part not covered by electrodes. Doing so allows interpolation for the area covered by the electrodes as well as

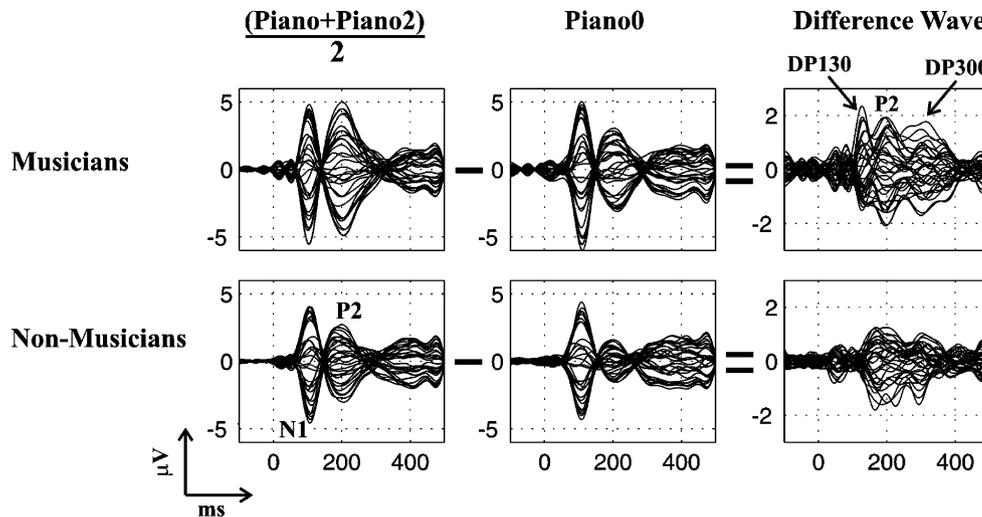


Fig. 2. Overlay of ERP traces of all channels of the group average waveforms for musicians and non-musicians collapsed over the two waveforms of the piano and piano2 tones (left) and only piano0 tone (middle) and their difference waveform (right). The two difference grand mean waveforms were merged because their effects did not differ statistically. The positive peaks DP130 (130 ms), DP300 (300 ms) are identified in the musician group difference waveform. Also, the N1 and P2 are identified in the mean (piano + piano2) tone for non-musicians. The size of the ERP difference wave is doubled compared to the original waveforms.

extrapolation to the part of the sphere not covered by electrodes.

Original potential and CSD difference waveforms were exported to Matlab for peak analysis. Peak latencies for the DP130 and DP300 were determined from the difference group average waveforms (Potential and CSD), and based on these latencies, peak amplitudes were determined for each subject and tone difference (piano – piano0 and piano2 – piano0). We used group average latencies to obtain amplitude values for individuals because prior inspection of the waveforms indicated that many of the non-musicians, waveforms did not show a clear peak between 100 and 150 ms (DP130). Group average difference waveforms for musicians had positive DP130 and DP300 peaks, maximally exhibited at FPz, occurring at 126 ms for the DP130 and 308 ms for the DP300. Group average waveforms for the controls did not show a positive peak in the period between 100 and 150 ms (DP130) so the latency of 126 ms was assigned arbitrarily to their DP130. The DP300 of the control group average waveforms had a latency of 305 ms. Based on the above latency values (126 ms for the DP130 and 305 ms for the DP300) an automated Matlab routine obtained the corresponding peak values for the DP130 and DP300 for each subject and tone difference waveform for channels F7, FPz, F8 of the Potential data and FP1, FPz, FP2 of the CSD data. There were no clear peaks for the piano0 – pure difference waveforms so no further analysis was carried out for these waveforms. The FP1 and FP2 channels in CSD analysis were substituted for the F7 and F8 channels because the original potential maps configuration did not have the FP1 and FP2 channels and we felt it would be wise to look at these frontal locations because they showed larger CSD magnitudes for the DP130 and DP300 than the more lateral F7 and F8 channels.

2.3.2. ERP source analysis

A source model for the DP130 and DP300 components was constructed using the group average ERPs of the two difference waveforms (piano – piano0 and piano2 – piano0) of the musicians' and non-musicians' data. The source analysis procedure used a Single Equivalent Dipole (SED) method (Scherg, 1990). SED is a theoretical current dipole placed inside the brain which produces theoretical potentials at the surface of the head (Forward Solution). The default four-shell ellipsoidal head model of BESA was used for the forward solution. The modeling procedure iteratively manipulates the location and orientation of SED(s) to achieve a model that best fits the actual measured scalp potentials (Inverse Solution). The final result is an estimate of the location, orientation and current strength of each postulated generator. Here, source fitting followed a procedure where the largest peak was fitted first and then fitting of peaks in the residuals followed, with sources constrained to localize within the brain boundaries. One dilemma in source analysis is that closely situated generators, especially ones similar in orientation, are difficult to separate in the time domain. A model of one source for such generators will show overlap of several activities, but can still be informative, as will be demonstrated below for the DP130 and DP300.

Fig. 3 (left panel) shows the average of the two difference waveforms (top left) for the musicians' data and the residual waveforms after each fitting procedure. The locations and orientations of the P2 and DP130 components in the musicians group are shown on the right. First, to account for the P2 wave of the musicians group, two symmetrically constrained sources were fitted for the P2 using a window of ± 10 ms around its peak (peak at 192 ms). The two sources were localized medially in the temporal gyrus (Fig. 3 right panel; grey dipoles). When projected onto

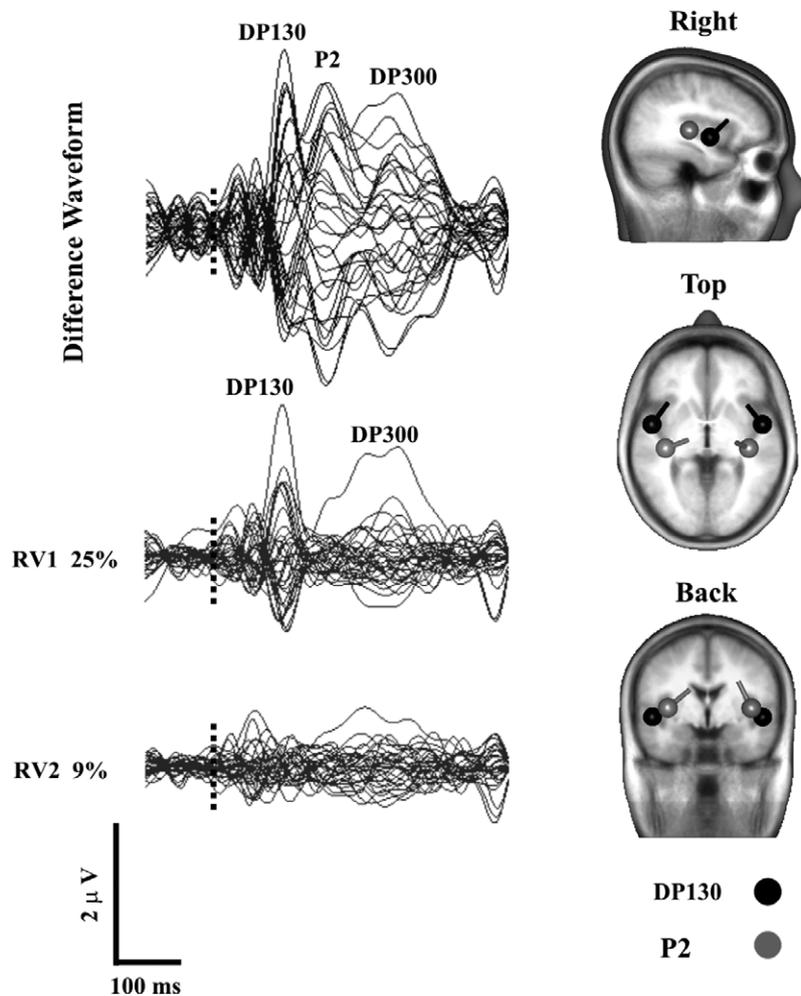


Fig. 3. (Left) Average of the (piano – piano0 + piano2 – piano0) difference waveforms, followed by the residual variance (RV) waveforms after each fitting procedure for the musicians group. (Right) Locations and orientations of the P2 (grey) and DP130 (black) sources superimposed on the average MRI brain of BESA 2000 shown for right (sagittal), top (axial) and back (coronal) views.

the average MRI brain of BESA the dipoles had Talairach coordinates – right source – of x (Medial Lateral) = 37, y (Anterior Posterior) = –23, z (Inferior Superior) = 5.3 (Brodmann 13, 22, and 41; in the medial transverse temporal gyrus), consistent with activities originating close to the core region of the auditory cortex. The sources were oriented upward and medially. This resulted in residual waveforms (Fig. 3, RV1 = 25%) which still contained the DP130 and DP300. Second, two symmetrically constrained sources were fitted to the DP130 component using a window of ± 10 ms around its peak. The two sources localized anterior and lateral to the P2 in the temporal lobes (Fig. 3; black dipoles; Talairach coordinates – right source – $x = 49$, $y = -2$, $z = -2$; Focus point: superior temporal gyrus). The DP130 source waveforms also contained much of the DP300 wave, which indicated that the DP130 and DP300 are generated in close proximity and orientation. The combination of the P2 and DP130 sources explained over 90% of the variance (RV2) for the entire waveforms in the musicians' data. To assess the closeness of the DP130 and DP300 sources, we separately modeled the

non-musicians' data in the same way we modeled the musicians' data. Two symmetrically constrained sources were fitted to the P2 component, which localized to the same locations of the musicians' P2 (above). Because there was no DP130 in the control group, we fitted the DP300 with two symmetrically constrained sources which localized (Talairach coordinates – right source – $x = 40.1$, $y = -8.5$, $z = -9.1$) close to the DP130 sources seen in the musicians' data and hence explain the difficulties of modeling the DP130 and DP300 by separate sources in the musicians group. Finally, to compare the temporal dynamics of the anterior temporal cortex activities in both groups, the musicians' source solution for the DP130 was applied as a spatial filter onto the non-musicians' data.

2.3.3. ERF source analysis

Since we were not able to subtract MEG signals due to changes in head position between blocks, the source analysis was done on individual blocks. The source model for MEG was constructed by fitting the N1m first using two SEDs, constrained to be symmetrical, on each individual,

tone type and block. The N1m had a mean source location Talairach coordinates collapsing over the 16 subjects and tone types of $x = 47$, $y = -17$, $z = 6.5$, consistent with sources originating in the supratemporal plane. An MEG source model was then constructed that consisted of two symmetrical sources for the N1m with the above group mean coordinates and two symmetrical sources for the DP130 with the coordinates obtained from the ERP source model. The N1m sources were tangential and oriented toward the mid-frontal region. The DP130 sources had the same orientation as the DP130 sources of the ERPs minus the radial tilt. The MEG model was then applied back as a spatial filter onto each subject, tone type and block data to obtain the corresponding waveforms. The waveforms for the two blocks for each tone type were collapsed into one average. The DP130 source waveforms were then extracted and the waveforms for the piano0 were subtracted from the source waveforms of piano2 and piano. The musicians' mean difference source waveforms exhibited a peak at 126 ms (DP130) but no clear peak at 300 ms (DP300). A Matlab routine obtained the corresponding peak values for individual subjects at 126 ms for the DP130 and 305 ms for the DP300 (assigned arbitrarily according to the ERP DP300).

2.3.4. Statistical analysis

DP130 and DP300 amplitudes – Potential, CSD and source waveforms – were evaluated separately by repeated measures analyses of variance (ANOVAs) using the General Linear Model module of Statistica Version 6.0 (Statsoft Inc, Tulsa, OK, USA). In ERPs, peaks of the DP130 and DP300 were first evaluated separately at the midline frontal channel FPz, using the variables group (musician vs. control) and tone difference (piano2 – piano0 vs. piano – piano0). Then peaks were evaluated at the bilateral channels (F7/F8 in Potential analysis and FP1/FP2 in CSD analysis) including group, hemisphere (left and right) and tone difference as variables. In ERFs, peaks of the DP130 and DP300 in the source waveforms were evaluated with group, hemisphere (left and right) and tone difference as variables. Post hoc comparisons were made with the least significant difference (Fisher LSD) test. All tests were two-tailed ($\alpha = 0.05$) and corrected for sphericity violations (Greenhouse–Geisser) where appropriate.

3. Results

Fig. 4A shows the Potential waveforms for the average of the two difference waveforms (piano-piano0 and piano2-piano0) at frontal (F7, FPz, and F8) and vertex sites (C3, Cz, and C4) for musicians and non-musicians with the DP130 and DP300 identified at FPz and the P2 at Cz. Fig. 4B shows the peak values and the 95% confidence intervals for DP130 and DP300 in musicians and non-musicians at F7, FPz, and F8 in the Potential analysis and at FP1, FPz, and FP2 in the CSD analysis. Fig. 4C shows the CSD maps for the DP130, P2 and DP300 for musicians

and non-musicians. The P2 was more posterior in its scalp distribution (amplitude maximum at Cz) than the other two peaks in the difference waveform. P2 was larger at Cz in musicians than non-musicians ($p = 0.021$) but was not analyzed further since it had been found in the previous report of Shahin et al. (2005) to be enhanced by the presence of upper harmonics preferentially in musicians compared to non-musicians. From the waveforms and CSD topographies of Fig. 4, it is evident that the DP130 is present in musicians but not in non-musicians, while the P2 and DP300 appear in both groups especially in musicians. Both the DP130 and DP300 waves were larger over the right hemisphere (comparing F7 and F8 channels).

Separate ANOVAs for the DP130 and DP300 at FPz revealed only a group main effect for the DP130 component (Potential: $F_{(1,14)} = 23.1$, $p = 0.0003$; CSD: $F_{(1,14)} = 13.96$, $p = 0.0022$) and no interaction. An ANOVA of the DP130 at F7 and F8 for the Potential analysis or at FP1 and FP2 for the CSD analysis revealed a group main effect (Potential: $F_{(1,14)} = 5.2$, $p = 0.039$; CSD: $F_{(1,14)} = 25.2$, $p = 0.0002$), an interaction, significant for the CSD analysis and approaching significance for the Potential analysis, between group and hemisphere (Potential: $F_{(1,14)} = 3.34$, $p = 0.089$; CSD: $F_{(1,14)} = 7.5$, $p = 0.016$) and no interaction between group and tone difference. The group main effect indicated a larger DP130 for musicians and the interaction between group and hemisphere indicated a greater right-sided asymmetry in musicians. Similar ANOVAs of the DP300 at F7 and F8 for the Potential analysis and at FP1 and FP2 for the CSD analysis suggested only a main effect of hemisphere approaching or at significance (Potential: $F_{(1,14)} = 3.96$, $p = 0.066$; CSD: $F_{(1,14)} = 4.53$, $p = 0.05$) and no interaction of group with hemisphere or tone difference. The main effect of hemisphere was attributed larger DP300s over the right hemisphere for both groups and tone differences.

Fig. 5A shows the source waveforms for the DP130 in musicians and non-musicians (EEG top, MEG bottom) collapsed over the two tone differences. Fig. 5B shows the grand mean root mean square group average for the piano and piano2 original (unsubtracted) waveforms in musicians and non-musicians for the purpose of comparing the N1 and P2 latencies to the DP130 and DP300. In EEG, the DP130 was absent in the source waveform of non-musicians and was right lateralized in musicians. The DP300 exhibited right dominance for both groups. In MEG the DP130 appeared in the source waveform of the musicians group only. It was not as right lateralized as in the EEG source waveforms. Instead of the DP130, the non-musicians exhibited an earlier negative peak around 100 ms. No DP300 was evident in the MEG source waveforms of Fig. 5A.

For the MEG waveforms obtained from ERF source data an ANOVA of the DP130 revealed only a group main effect ($F_{(1,14)} = 8.7$, $p = 0.01$) and no interaction with hemisphere. The group main effect indicated a larger DP130m for musicians compared to non-musicians.

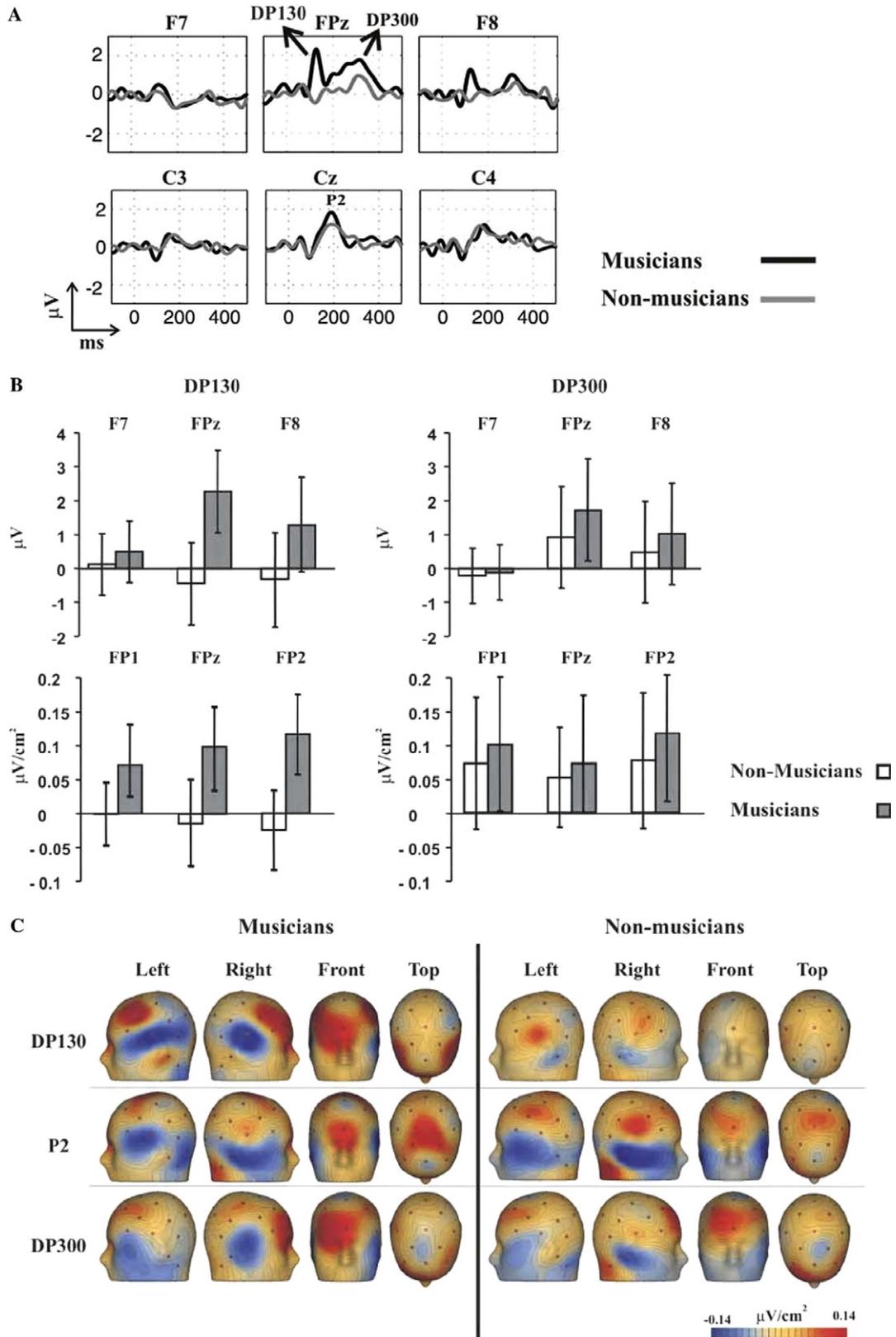


Fig. 4. (A) Potential waveforms at frontal (F7, FPz, and F8) and vertex (C3, Cz, and C4) sites for musicians and non-musicians with the DP130 and DP300 identified at FPz and the P2 at Cz. (B) Peak amplitudes of the DP130 (left) and DP300 (right) for musicians and non-musicians at F7, FPz and F8 sites for Potential analysis and at FP1, FPz and FP2 sites for CSD analysis. Vertical bars denote 0.95 confidence intervals. (C) CSD maps for the DP130, P2 and DP300 for musicians and non-musicians.

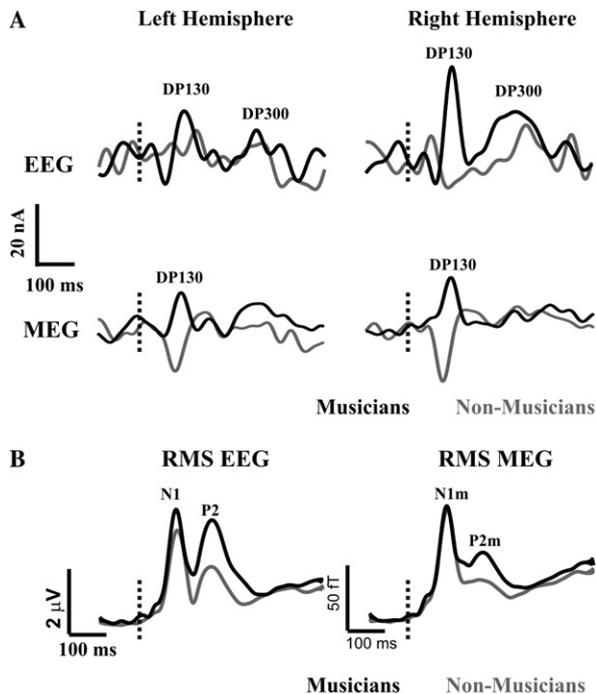


Fig. 5. (A) Grand average source waveforms, based on data from all channels, of the left and right DP130 for musicians and non-musicians in EEG (top) and MEG (bottom). (B) The grand root mean square (RMS) of musicians and non-musicians of the unsubtracted waveforms collapsing over piano and piano2 waveforms. The RMS waveforms indicate the timing of the N1(m) and P2(m) responses.

Similar ANOVAs of the DP300 revealed no main effects or interactions between variables ($F = 2.4$ or smaller).

4. Discussion

Our study revealed anterior temporal cortex activities – the DP130 and DP300 – that are evoked during processing of piano tones in musicians and non-musicians. DP130 and DP300 appeared when subtracting piano tones containing only the fundamental from piano tones with more complex spectra. Because the piano tones differed in their spectral bandwidths but shared the same temporal envelope and pitch, we suggest that the DP130 and DP300 are associated with the processing of the spectral characteristics of the tones. DP130 was mainly present in the musicians group (EEG and MEG) suggesting its enhancement by musical training or by musical aptitude, while DP300 was common to both groups (EEG data). Both components were largest over the right hemisphere which may be specialized for processing of spectral information. Our results do not rule out a contribution of other sound manipulations to DP130 and DP300 such as temporal variations. Griffiths et al. (1998) reported that increased regularity in the temporal structures of sounds while holding the spectral structure constant increased activities in the auditory cortex. Nevertheless, temporal variation did not appear to contribute to the results presented here. Subtraction of pure and piano0 tones which had similar spectral content but different temporal envelopes did not reveal a DP130 or DP300.

Difference waveforms allow us to directly compare activities between conditions rather than to a baseline – as in unsubtracted waveforms – and can show small components of the ERP/ERF that are not easily visible in unsubtracted waveforms. They are particularly effective when the component occurs between large peaks in the waveform – as is the case for the DP130 which occurs between N1(m) and P2(m). This approach assumes that the ERPs/ERFs are the same in the two conditions other than for the addition of the difference waveform in one condition. One has to be careful that there is not just a shift in latency of some parts of the ERPs. In the present case, we feel that the DP130 cannot be explained by an earlier P2 evoked by the spectrally rich stimuli because the scalp topography of the DP130 is clearly different from that of the P2.

Right dominance of the DP130 and DP300 as seen in ERPs is consistent with previous studies assessing musical specialization of the hemispheres. Examining patients with unilateral (right or left) temporal lobe excisions for various musical tasks, revealed a right hemisphere advantage for pitch (Zatorre and Samson, 1991; Warrier and Zatorre, 2004), and timbre processing (Samson and Zatorre, 1988; Samson et al., 2002) and during melodic discrimination (Samson and Zatorre, 1994). Moreover, Zatorre and Belin (2001) have shown that spectral variation of tones modulates the anterior superior temporal gyrus (STG) bilaterally with the right predominating, while temporal variation mainly activates the core regions of the auditory cortex, with the left predominating. Zatorre and Belin (2001) posited that because right hemisphere neurons when compared with the left hemisphere neurons are characterized by higher synaptic density and reduced myelination, they may be more specific to processing spectral than temporal information. The spectral characteristics (e.g., harmonics) of a sound are part of its timbre. Platel et al. (1997) revealed that right hemisphere advantage is specific to the timbre of musical notes as opposed to pitch, rhythm and familiarity, which weighted toward the left. A right hemisphere advantage was also revealed in musicians, specifically in musicians who are inclined to process sounds based on the spectral content rather than the pitch of sounds (Schneider et al., 2005). Schneider et al. (2005) contrasted hemispheric specialization based on the pitch or the spectral bandwidth of tones. They classified a group of musicians into f_0 and f_{sp} listeners, where f_0 and f_{sp} musicians inherently judged the direction of pitch shift between pairs of complex tones according to the tones fundamental frequency (f_0) or to the spectral envelope frequency ($f_{sp} = n \times f_0$; where n is the number of harmonics present in the tones), respectively. They showed that f_{sp} listeners, when compared to f_0 listeners, showed markedly rightward asymmetry of grey matter in the lateral Heschl's gyrus. Accordingly, right hemisphere advantage for the piano tone containing the more complex spectra (DP130 and DP300), especially in musicians trained on the piano (DP130), is consistent with the right hemisphere dominance for spectral or timbre processing.

Shahin et al. (2003) reported a component (N1c) that is similar in its characteristics to the DP130 reported here. The N1c of Shahin et al. (2003) and the DP130 are similar in their latencies (DP130: 130 ms; N1c: 138 ms) and positions in the lateral belt of the auditory cortex. Also, both are augmented in musicians and exhibit right-sided asymmetry. As such one might consider that both of these components reflect similar perceptual processes. However, the DP130 and N1c appear to differ in their source locations. The DP130 source was anterior compared to P2 in the present results, whereas in the study of Shahin et al. (2003) P2 and N1c sources overlapped in the anterior posterior coordinate. Our judgment is that these two activities do not reflect the same perceptual/cognitive process, although they are both components in the auditory processing stream.

The MEG analysis also demonstrated differences related to spectral processing, but the results were not exactly the same as the EEG analysis. The DP130 was clearly present in MEG but did not show hemispheric dominance as in the EEG. Also, the DP300 was not present in the MEG recordings. Some of these differences may have been caused by our use of source locations based on the EEG analysis to model the magnetic equivalent of the DP130. At the present state of MEG technology we cannot subtract the recorded waveforms in the same way as we can in EEG because the position of MEG sensors with respect to the brain shifts with head movements (EEG electrodes stay fixed). EEG/MEG differences are also probably related to the fact that MEG is relatively blind to activities that are radially oriented. The DP130 and DP300 were lateral in their locations and could represent activities in the gyri where a portion of the sources orient radially to the scalp and go undetected by MEG. The similar lateral and radial EEG N1c component (Shahin et al., 2003) has also not been reported in MEG studies. These factors may explain the absence of the DP300 in MEG and the smaller amplitude of the DP130 seen in MEG than EEG (Fig. 5A). The MEG source waveforms of the non-musicians showed a negative peak around 100 ms which may be a residual of the N1m surviving our subtraction technique. Working with the present data set, Shahin et al. (2005) observed that the N1(m) was slightly larger for the spectrally rich piano tone compared to the other tones. Although the effect was not significant, the results accord with those of Lütkenhöner et al. (2006) who found larger N1m for piano tones compared to pure tones. Also, the N1(m) was slightly, but not significantly, larger in the musicians group than controls as evidenced by Fig. 5B of the grand mean group root mean square average for the piano and piano2 original (unsubtracted) waveforms. In musicians, commencement of the DP130 wave at frontal sites (~30 ms following the N1m) may have overlapped and diminished the N1m frontally in this group.

The DP300 was very anterior in its scalp topography. This, possibly, may have represented some residual artifact from blinks or ocular movements that were not removed by

our artifact rejection procedure. However, the asymmetry of the fields is not characteristic for blinks and it is difficult to imagine lateral eye movements related to spectral processing. We therefore conclude that this represents brain activity. Although the CSD showed distinct topographies for the DP130 and the DP300, the two activities were not separable in source analyses of the musicians' data. However, the absence of the DP130 in the non-musicians' data provided us with an opportunity to fit the DP300 component alone, uncontaminated by the DP130 activities. This analysis ultimately confirmed that both activities were generated in nearby regions of the anterior temporal lobe with greater activity in the right hemisphere than in the left hemisphere. We also considered the possibility that the inferior frontal lobes might have been involved in stimulus processing and in the generation of the DP130 and DP300 ERP waveforms. Left middle-frontal activities have been reported during passive musical perception tasks (Ohnishi et al., 2001). However, activities in various frontal regions (anterior cingulate, inferior, superior and middle frontal gyri) have mainly been associated with music processing when tasks required attention (Platel et al., 1997) or when they involved processing auditory imagery where perceptual information is accessed from memory (Zatorre and Halpern, 1993; Zatorre et al., 1996; Halpern and Zatorre, 1999). In the study of Ohnishi et al. (2001) subjects were presented with a musical piece (Bach) that may have commanded some attention. Platel et al. (1997) reported that when attended to, rhythm, pitch, timbre, and familiarity modulate different regions of the cortex. In our study the subjects were instructed to ignore repetitive sounds differing in spectral content and to concentrate on a silent movie (dual task control). The asymmetry we observed was opposite that reported by Ohnishi et al. (2001), and because our subjects watched a silent movie, we feel frontal activities time locked to our auditory stimuli were unlikely in our experiment. We acknowledge, however, generators in frontal regions can be difficult to distinguish from those in the anterior temporal lobe when the signal to noise ratio of the recording is not high.

Our source analysis indicated that the DP130 was right sided and localized anterior and lateral to the auditory P2 generators, hence pointing to sources originating in the anterior belt region (Rauschecker and Tian, 2000) of the superior temporal gyrus (STG). Animal studies (Rauschecker et al., 1995; Rauschecker and Tian, 2000; Tian et al., 2001) have shown that the lateral belt responds preferentially to complex sounds compared to pure tones which are mainly processed in the core regions of the auditory cortex. The same animal studies have also shown that there exists a hierarchical organization for the lateral belt of the STG – anterolateral (AL), middle lateral (ML) and caudolateral (CL) – where AL is sensitive to sounds of spectrally broad bandwidths (“What”) and CL is associated with determining the location of sounds (“Where”). The anterolateral location for the DP130 and DP300 is therefore consistent with the above animal studies where the piano

tones with the more complex spectra exhibited these activities as compared to the piano tone with only the fundamental, suggesting involvement of the anterior “what” stream (Rauschecker and Tian, 2000).

Although the DP300 appeared larger in musicians than non-musicians, this difference in enhancement did not reach significance. Given that the DP130 and DP300 reflect mechanisms associated with spectral processing, we would expect both components to be enhanced in musicians owing to either their musical aptitude or training histories. Alternatively, these two processes may represent earlier (DP130) and later (DP300) activities in the sound processing stream, with the earlier component responsible for discriminating specific frequency variations and the later component associated with processing spectra of broad bandwidths in general. Our musicians were trained on the piano and hence they may have developed a mechanism (DP130) that enabled them to make fine spectral discriminations, inherent to the harmonic structure present in the spectrum of piano tones. This may render neurons underlying such a mechanism more selective to their inputs. Rauschecker and Tian (2000) showed that anterolateral neurons in the Rhesus monkey, although broadly tuned, were highly selective to monkey calls, which suggests their selectivity to learned spectral bandwidths. This suggests that the enhancement of the anterolateral DP130 seen in our pianists may be specific to the timbre of training and not necessarily to all bandwidths. Timbre specificity in violinists and trumpeters has been reported by Pantev et al. (2001), but was not shown when comparing violinists and pianists (Shahin et al., 2003).

The DP130 followed the middle latency (ML: N19–P30–P50) and N1(m) responses and preceded the P2(m). These components have been shown to localize to primary core and non-primary belt/parabelt auditory cortices (sometimes, for simplicity, referred to as A1 and A2, respectively) with the ML responses localizing to A1 (Yvert et al., 2001; Schneider et al., 2002, 2005) and the N1(m) to non-primary auditory cortex (Scherg et al., 1989; Picton et al., 1999; Engelien et al., 2000), while localization to the border of A1 or to non-primary auditory regions has been reported for the P2(m) (A1: Lütkenhöner and Steinstrater, 1998; non-primary auditory cortex: Pantev et al., 1996; Hari et al., 1987; Bosnyak et al., 2004). N1m and P2 have been shown to augment after training at frequency discrimination tasks (N1m: Menning et al., 2000; P2: Tremblay et al., 2001; Atienza et al., 2002; Reinke et al., 2003; Bosnyak et al., 2004). Also, all of the above mentioned components (ML, N1m, P2(m)) have been reported to be larger in musicians (ML and P50: Schneider et al., 2002, 2005; Shahin et al., 2004; N1m: Pantev et al., 1998; Kuriki et al., 2006; P2(m): Shahin et al., 2003, 2005; P2m: Kuriki et al., 2006). However, enhancement of the N1(m) in musicians compared to non-musicians has not been revealed in other studies (Shahin et al., 2003; Lütkenhöner et al., 2006) including the N1(m) of the current data set reported in Shahin et al. (2005). Therefore, the DP130 likely reflects

a different processor (anterior temporal) than the N1(m), which represent activities closer to or originating from the core region of the auditory cortex and may be more related to indexing non-specific sound characteristics (Seither-Preisler et al., 2003; Shahin et al., 2003; Lütkenhöner et al., 2006).

The parallel enhancement in musicians of the right-lateralized anterior DP130 and other AEPs and AEFs (ML and P2) localizing to distributed regions of the auditory cortex, and of P2 and a right-sided N1c by behavioral training in non-musicians (Bosnyak et al., 2004), suggests that there exists an experience-directed neural mechanism which drives this enhancement in accordance with Hebbian mechanisms. Modification of components that occur early in the temporal stream of information processing, such as ML responses localizing to A1 and N1(m) reflecting current sinks in non-primary auditory cortex, appear to require experience with musical sounds during brain development (N1m: Pantev et al., 1998; P1/N1/P2: Shahin et al., 2004) and correlate with anatomical changes (Schneider et al., 2002) whereas DP130/N1c/P2/DP300 which occur at longer latencies and are modified by training in adults appear to reflect greater flexibility in the learning system. Activity in the learning system may be modulated by cholinergic pathways that signal behavioral relevance (Buonomano and Merzenich, 1998; Kilgard and Merzenich, 1998; Weinberger, 2004) and enable long range and local interactions to sculpt cortical changes in a laminar-specific fashion via Hebbian mechanisms (Diamond et al., 1994; Finnerty et al., 1999). The long latency brain events DP130 and DP300 localizing to anterior structures may relate cortical modifications to context and memory while retaining their sensitivity to spectral content more than the N1(m) which occurs earlier in the stream of information processing and was less affected by acoustical training or musical aptitude (Bosnyak et al., 2004; Lütkenhöner et al., 2006) and with spectral manipulations as reported in the present study.

The enhanced processing (DP130) in musicians may partly be related to attentional factors. Although our subjects were instructed to ignore the stimuli and concentrate on the silent movie, the familiarity and saliency of the musical cues, especially the more complex piano tones, may still have captured the attention of musicians to a greater degree than in non-musicians owing to the musicians' acoustical learning history. In ERPs, selective attention can be evidenced by early anterior negativities (Hillyard and Hansen, 1986; Woldorff and Hillyard, 1991) which may indicate an early mechanism for gating the perceptual analysis (Woldorff and Hillyard, 1991). The anterior negativities are most visible when subtracting ERPs for unattended from attended stimuli with sources likely generating in the inferior frontal and superior temporal gyri (Jemel et al., 2003). Sieroka et al. (2003) showed that selective auditory attention can also induce a negative sustained potential anteriorly, with sources likely generating in the precuneus or posterior cingulate gyrus. There was no evidence for such negative components in the

current work – the salient harmonic-rich piano tones were more positive than the simple tones. Moreover, the anterior negativities have been shown to sum with and enhance the auditory N1 (Hillyard, 1981), which again was unaffected by the bandwidth complexity of the tones in our study. These observations do not favor attributing the enhanced DP130 to attention exclusive of other factors. However, mechanisms for attention and plasticity appear to interact. When stimuli are attended to, the brain response to those stimuli can become larger beyond the specific period of attention by means of plastic changes in the cortex. Expansion of cortical representations by training history appears to be gated by cholinergic mechanisms in the basal forebrain that make cortical neurons more sensitive to their afferent inputs (Metherlate and Weinberger, 1990; Buonomano and Merzenich, 1998; Weinberger, 2004). It is possible that enhanced cortical representations reflected in the DP130 may themselves come to command attention in the experienced subject by means of feedback to subcortical nuclei (Sarter et al., 2005) that appear able to modulate cortical activity in an area-specific fashion (Jiménez-Capdeville et al., 1997).

Physiological and anatomical differences between the brains of musicians and non-musicians might relate as much to inherited predispositions as to acquired expertise (Schneider et al., 2002, 2005). Subjects who develop larger and more responsive areas of auditory cortex as a consequence of intrinsic factors may have an aptitude for music since they are naturally better able to discriminate and remember musical sounds. This aptitude may lead to their entering musical training, because music is something that they can readily succeed in. The training itself may then affect the anatomy and physiology of the brain. Disentangling the interactions between aptitude and training are difficult in the adult brain, but perhaps may be possible in developmental studies.

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