# Diminished Whole-brain but Enhanced Peri-sylvian Connectivity in Absolute Pitch Musicians

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## Abstract

■ Several anatomical studies have identified specific anatomical features within the peri-sylvian brain system of absolute pitch (AP) musicians. In this study we used graph theoretical analysis of cortical thickness covariations (as indirect indicator of connectivity) to examine whether AP musicians differ from relative pitch musicians and nonmusicians in small-world network characteristics. We measured "local connectedness" (local clustering = $\gamma$), "global efficiency of information transfer" (path length = $\lambda$), "small-worldness" ($\sigma = \gamma/\lambda$), and "degree" centrality as measures of connectivity. Although all groups demonstrated typical small-world features, AP musicians showed significant small-world alterations. "Degree" as a measure of interconnectedness was globally significantly decreased in AP musicians. These differences let us suggest that AP musicians demonstrate diminished neural integration (less connections) among distant brain regions. In addition, AP musicians demonstrated significantly increased local connectivity in peri-sylvian language areas of which the planum temporale, planum polare, Heschl's gyrus, lateral aspect of the superior temporal gyrus, STS, pars triangularis, and pars opercularis were hub regions. All of these brain areas are known to be involved in higher-order auditory processing, working or semantic memory processes. Taken together, whereas AP musicians demonstrate decreased global interconnectedness, the local connectedness in peri-sylvian brain areas is significantly higher than for relative pitch musicians and nonmusicians. ■

## INTRODUCTION

The advent of neuroimaging has provided unique insight into the brain of musicians, including the findings of a number of specific anatomical features. Most of these features were identified in brain areas involved in the control of psychological functions related to musical skills, which are as follows: sensorimotor cortex (Gaser & Schlaug, 2003a, 2003b), central sulcus in the hand motor area (Bangert & Schlaug, 2006; Amunts et al., 1997), anterior corpus callosum (Schlaug, Jäncke, Huang, Staiger, & Steinmetz, 1995), planum temporale (Keenan, Thangaraj, Halpern, & Schlaug, 2001; Schlaug, Jäncke, Huang, & Steinmetz, 1995), Heschl's gyri (Bermudez, Lerch, Evans, & Zatorre, 2009; Wong et al., 2008; Schneider, Sluming, Roberts, Bleeck, & Rupp, 2005), frontal cortex (Bermudez et al., 2009), and cerebellum (Hutchinson, Lee, Gaab, & Schlaug, 2003). Diffusion tensor imaging (DTI) enables identification of specific features in the fiber tracts of musicians. This innovative technique has been used to show that musicians demonstrate differences in various fiber tracts when compared with nonmusicians (Halwani, Loui, Ruber, & Schlaug, 2011; Loui, Li, Hohmann, & Schlaug, 2011; Imfeld, Oechslin, Meyer, Loenneker, & Jäncke, 2009; Oechslin, Imfeld, Loenneker, Meyer, & Jäncke, 2009; Bengtsson et al., 2005; Schmithorst & Wilke, 2002). These anatomical differences are often interpreted as evidence of training-induced and experience-dependent adaptations because the musicians (especially classical musicians, i.e., the most studied musician group) start to practice early in life and continue to do so throughout their lives (Imfeld et al., 2009; Jäncke, 2009; Bengtsson et al., 2005; Munte, Altenmuller, & Jäncke, 2002; Schlaug, 2001). Although intensive practice of musical instruments is a likely candidate explaining the anatomical differences between musicians and nonmusicians, only longitudinal training studies can definitively demonstrate whether music-related training induces anatomical changes in musicians. First longitudinal studies, however, support the assumption of training-induced anatomical changes in musicians (Hyde et al., 2009).

In this study, we focus on a particular group of musicians, namely, the absolute pitch (AP) musicians, who have received some interest in recent brain imaging studies. These musicians are able to identify tones without relying on an external and internal reference tone. AP is a rare ability for which some authors estimate the occurrence of 1 in 10.000 people (Takeuchi & Hulse, 1993). However, one has to keep in mind that these figures are based on rough estimations. Recent large-scale studies have shown that the incidence of AP ability must be much higher in musicians and is influenced by age of commencement, ethnicity, tonal language background, and anatomical prerequisites (Deutsch, Dooely, Henthorn, & Head, 2009; Deutsch, Henthorn, Marvin, & Xu, 2006; Keenan et al., 2001). It is defined as the ability to either

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identify a pitch class (the chroma) of a tone or produce a specific pitch without use of a reference tone (Levitin & Rogers, 2005; Zatorre, 2003; Takeuchi & Hulse, 1993). The very specific ability of AP may be distinguished from the more common ability of relative pitch (RP), which almost all musicians learn and allows them to identify or produce tone intervals. Although there has been a substantial increase in research on AP musicians over the last 120 years, the psychological, neurophysiological, and neuroanatomical underpinnings of this interesting ability are still far from being entirely understood. Anatomical studies examining the neuroanatomy of AP musicians demonstrated increased left-sided (or decreased right-sided) planum temporale volumes (Luders, Gaser, Jäncke, & Schlaug, 2004; Keenan et al., 2001; Zatorre, Perry, Beckett, Westbury, & Evans, 1998; Schlaug, Jäncke, Huang, & Steinmetz, 1995), altered fiber architecture of the fasciculus arcuatus (Oechslin et al., 2009), and hyperconnectivity in bilateral superior temporal lobe structures (Loui et al., 2011) and the corticospinal tract (Imfeld et al., 2009). Together with several functional brain imaging studies (Oechslin, Meyer, & Jäncke, 2010; Ohnishi et al., 2001), these studies support the notion that the peri-sylvian language-related system is differently organized in AP musicians.

All of the preceding anatomical studies have mainly reported focal anatomical differences. But the human brain is now increasingly conceived of as a highly interconnected network (Bullmore & Sporns, 2009; Herculano-Houzel, 2009; Watts & Strogatz, 1998). It is argued in this context that particular psychological functions are controlled by spatially distributed networks (Langer et al., 2011) rather than by focal brain areas. This specifically pertains to AP in view of the evidence that several brain regions and psychological processes are involved in controlling the AP ability. These processes concern especially those of working memory that are controlled by frontal and parietal areas, which, in turn, are thought to be involved in generating AP (Schulze, Mueller, & Koelsch, 2011; Schulze, Zysset, Mueller, Friederici, & Koelsch, 2011; Schulze, Gaab, & Schlaug, 2009; Zatorre et al., 1998; Hantz, Kreilick, Marvin, & Chapman, 1997; Crummer, Walton, Wayman, Hantz, & Frisina, 1994; Klein, Coles, & Donchin, 1984). If this is indeed the case, then the brain of AP musicians should make efficient use of networks located in temporal, frontal, and parietal brain areas. In other words, the AP brain should be differently interconnected than the brain of RP musicians and nonmusicians.

Recent studies have shown that the functional and anatomical connections of the brain network are organized in a highly efficient small-world manner (Bullmore & Sporns, 2009; Stam & Reijneveld, 2007; Sporns & Kötter, 2004; Sporns, Tononi, & Edelman, 2000). A small-world organization of the brain network implies a high level of local neighborhood clustering (indexed by the clustering coefficient and by the so-called gamma measure) combined with global efficiency of information transfer (indexed by the path length and the lambda measure). Thus, small-world networks explain how the brain minimizes wiring costs while simultaneously maximizing the efficiency of information propagation (Bullmore & Sporns, 2009).

Using graph theoretical analysis, we examined whether AP musicians differ from RP musicians and nonmusicians in terms of their small-world network characteristics. Our network analysis is based on region-wise cortical thickness covariations, for which there is strong evidence that this measure is a valid, albeit an indirect, indicator of structural connectivity (Bernhardt, Chen, He, Evans, & Bernasconi, 2011; Lerch et al., 2006; Mechelli, Friston, Frackowiak, & Price, 2005). Most of the anatomical studies comparing AP musicians with RP musicians have reported anatomical differences in peri-sylvian language-related brain areas (see above for references). Thus, we hypothesized that AP musicians should demonstrate a specific and different small-world organization in this region. In this study, we focused on one particular small-world parameter representing the local connectedness of particular brain areas. This measure is referred to as degree or degree centrality and is the sum of weights incident upon a node (i.e., the sum of weights of the edges that a node has). According to the findings of Loui et al. (2011), who demonstrated hyperconnectivity mainly in the temporal lobe in AP musicians on the basis of DTI data, we hypothesized that AP musicians should demonstrate a stronger connectedness in terms of higher degree measures especially in peri-sylvian brain areas and especially in brain areas involved in auditory analyses.

## METHODS

### Subjects

Thirteen AP musicians (seven women, mean age = 24.8 years, *SD* = 3.1 years), 16 RP musicians (10 women, mean age = 25.4 years, *SD* = 3.2 years), and 12 nonmusicians (five women, mean age = 28.1 years, *SD* = 4.9 years) comparable with respect to age, gender, and handedness participated in the study. Given that most of the participants in all three groups had an academic background, their years of education were closely matched. All participants were consistently right-handed according to the procedure proposed by Annett (1970), had no history of neurological, neuropsychological, or psychiatric disease, and reported no use of drugs or medication. All participants were native German or Swiss German-speaking white adults, except two musicians who were Asians, one in the AP and one in the RP group. The local ethics committee of the Canton of Zurich approved the study, and written informed consent was obtained from all participants.

### Musical Instruments and AP Test

The musicians played a variety of instruments including the violin, piano, trombone, transverse flute, and viola.

The evaluation of the AP ability is reported in more detail elsewhere (Oechslin et al., 2009) but is also described here for completeness. We evaluated AP among professional musicians (AP and RP) with an in-house designed AP test. Participants heard 108 pure sine wave tones, presented in pseudorandomized order, which ranged from A3 (tuning: A4 = 440 Hz) to A5, while each tone was presented nine times (three times in each octave). The accuracy was evaluated by counting correct answers—the semitone errors were taken as incorrect to increase the discriminatory power by means of AP. We did not count octave errors because it is even difficult for AP musicians to identify the correct octaves. Each tone of the AP test had a duration of 1 sec; the ISI of 4 sec was filled with brown noise (the spectral density of this noise is inversely proportional to $f^2$, meaning it has more energy at lower frequency; f is the frequency). Subjects had to write down the tonal label immediately after they heard the accordant tone (i.e., while hearing the 4-sec brown noise; Oechslin et al., 2009).

### MRI Data Acquisition

MRI scans were acquired on a 3.0-T GE Signa Excite whole-body scanner (GE Medical Systems, Milwaukee, WI) equipped with a transmit–receive body coil and a commercial eight-element sensitivity encoding (SENSE) head coil array. A volumetric 3-D T1-weighted fast spoiled gradient-echo scan was obtained with a measured spatial resolution of 0.94 × 0.94 × 1.00 mm (matrix = 256 × 256 pixels, 172 slices). Further imaging parameters were as follows: field of view = 240 × 240 mm, echo time = 2.1 msec, repetition time = 9.2 msec, inversion time = 500 msec, flip angle $\alpha = 20°$. Total acquisition time was about 6 min and 20 sec.

### Surface-based Morphometry

Cortical surface reconstruction was performed with the FreeSurfer image analysis suite (version 4.5.0), which is documented and freely available for download on-line (surfer.nmr.mgh.harvard.edu/). The technical details of these procedures were described in prior publications (Fischl, Salat, et al., 2004; Fischl, van der Kouwe, et al., 2004; Fischl et al., 2002; Fischl, Liu, & Dale, 2001; Fischl & Dale, 2000; Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999). Briefly, the 3-D structural T1-weighted MRI scan was used to construct models of each participant's cortical surface to measure cortical thickness. This is a fully automated procedure involving segmentation of the cortical white matter (Dale et al., 1999), tessellation of the gray–white matter junction, inflation of the folded surface tessellation patterns (Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, et al., 1999), and automatic correction of topological defects in the resulting manifold (Fischl et al., 2001). This surface was then used as the starting point for a deformable surface algorithm designed to find the gray/white and pial (gray matter/cerebrospinal fluid) surfaces with submillimeter precision (Fischl & Dale, 2000). The procedures for measuring cortical thickness have been validated against histological analysis (Rosas et al., 2002) and manual measurements (Salat et al., 2004; Kuperberg et al., 2003). This method uses both intensity and continuity information from the surfaces in the deformation procedure to interpolate surface locations for regions in which the MRI image is ambiguous (Fischl & Dale, 2000). For each participant, cortical thickness of the cortical ribbon was computed on a uniform grid (comprised by vertices) with 1-mm spacing across both cortical hemispheres, with the thickness being defined by the shortest distance between the gray/white and pial surfaces; measures were mapped to the inflated surface of each participant's brain reconstruction, allowing visualization of data across the entire cortical surface (i.e., gyri and sulci) without the data being obscured by cortical folding. In addition, the cerebral cortex was parcellated into units based on gyral and sulcal structure (Destrieux, Fischl, Dale, & Halgren, 2010; Desikan et al., 2006; Fischl, Salat, et al., 2004; Fischl, van der Kouwe, et al., 2004), and cortical thickness within each parcellation was computed.

### Graph Theoretical Network Analysis

#### *Network (Graph) Construction*

One of FreeSurfer's implemented parcellation schemes (aparc.a2009s) was used to compute mean cortical thickness in 148 anatomical structures across both cortical hemispheres (Figure 1). These parcellations were used to construct the association (connectivity) matrix ($A_{ij}$) based on the cortical thickness correlation matrix ($C_{ij}$) between all pairs of parcellations, resulting in a 148 × 148 association matrix (network) for the AP musicians, one for the RP musicians and one for the nonmusicians (Figure 2).

#### *Threshold Selection*

Network graphs were represented by weighted matrices ($A_{ij}$, one matrix for each correlation threshold $r$) with $N$ nodes and $K_r$ edges, where nodes represent cortical regions and edges represent the weighted connections between these cortical regions. There is currently no definitive and generally accepted strategy for applying a particular threshold (Bullmore & Sporns, 2009). Each connectivity matrix was therefore thresholded repeatedly over a wide range of correlation thresholds in increments of $r = .025$ from $r = .15$ to $r = .525$, resulting in 16 networks with different connection densities per group (He, Chen, & Evans, 2007; Watts & Strogatz, 1998).

This kind of thresholding resulted in different number of edges between the networks of the groups because of differences in their interregional cortical thickness correlations (see Figure 2). Thus, between-group differences in network

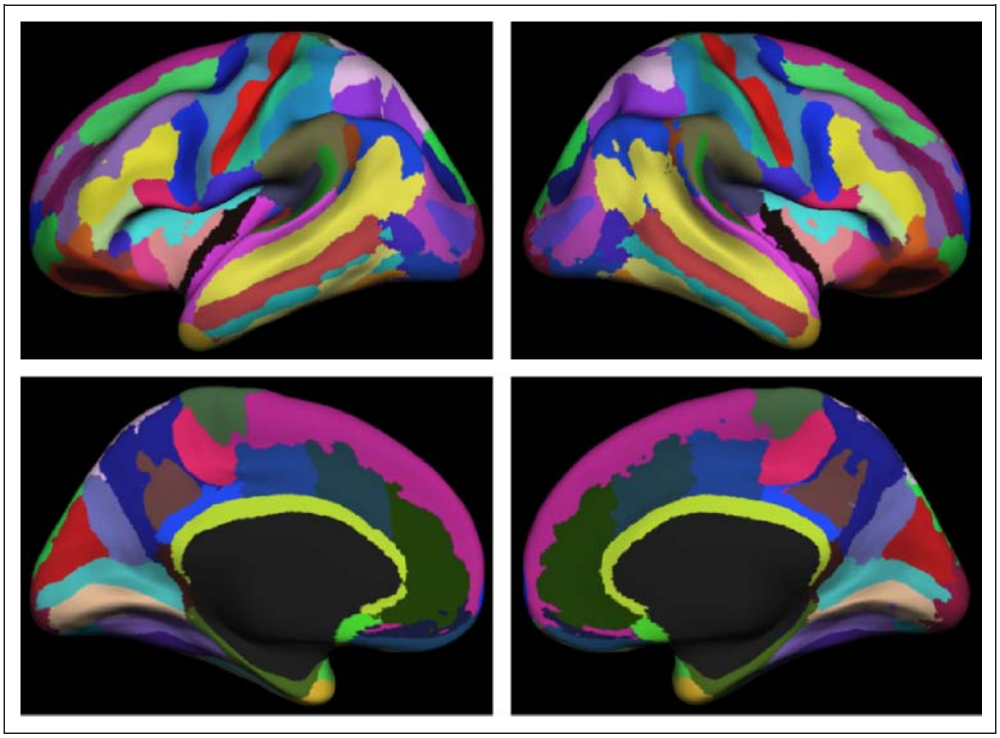

**Figure 1.** Parcellation scheme: Shown are the mean parcellation schemes of the left (lateral view, top left; medial view, bottom left) and right hemispheres (lateral view, top right; medial view, bottom right) used to define the 148 network nodes. Note that the brain models are inflated to have also a look at sulcal cortical regions.



characteristics might also reflect changes in wiring costs and not only alterations in the topological organization of the network (Achard & Bullmore, 2007; Stam & Reijneveld, 2007). In general, networks constructed under the sparsity condition, that is, with fixed percent of edges, are not state of the art in graph theoretical data modeling. Therefore, we did not force our networks to have equal connection densities. However, in a network study that investigated structural brain networks in grapheme–color synesthesia, we found similar results independent of whether absolute or relative correlation thresholds (sparsity) were used (Hänggi, Wotruba, & Jäncke, 2011).

### *Small-world Analysis*

The network analysis software tnet (running in R; www.r-project.org/) was used to analyze the networks (Opsahl, Agneessens, & John, 2010; Opsahl, 2009; Opsahl & Panzarasa, 2009; Opsahl, Colizza, Panzarasa, & Ramasco, 2008). tnet allows analyzing weighted networks (opsahl.co.uk/tnet/). The networks were analyzed according to the theory of small-world networks as introduced by Watts and Strogatz (Bullmore & Sporns, 2009; Watts & Strogatz, 1998). To make our network parameters comparable with those parameters obtained in similar studies that used cortical thickness correlations, we followed their procedures as closely as possible (Bernhardt et al., 2011; Hänggi et al., 2011; Gong et al., 2009; He, Chen, Gong, & Evans, 2009; He, Chen, & Evans, 2008). Small-world indices were derived from the comparison of the real network with 100 random network realizations comprising the same number of nodes, edges, mean degree, and degree distribution. The procedure for constructing the random networks is described in more detail elsewhere (Opsahl et al., 2008).

On the basis of these structural brain networks, key characteristics that describe the overall architecture of a network were computed, including the clustering coefficient $C_r$ and the characteristic path length $L_r$ (Watts & Strogatz, 1998; Figure 3). In binary networks, the $C_r$ is the ratio between the number of connections between the direct neighbors of a node and the total number of possible connections between these neighbors and provides information about the level of local connectedness within a network. The characteristic $L_r$ of a binary network gives the average number of connections that have to be crossed to travel from each node to every other node in the network and provides information about the level of global communication efficiency of a network (van den Heuvel, Stam, Kahn, & Hulshoff Pol, 2009). The definitions of $C_r$ and $L_r$ in weighted networks, as implemented in tnet (opsahl.co.uk/tnet/), are based on the sum of the weights, and these formulas are reported elsewhere (Opsahl et al., 2008, 2010; Opsahl & Panzarasa, 2009; Panzarasa, Opsahl, & Carley, 2009).

Networks with small-world organization have a $C_r$ that is higher than the $C_r$ of a comparable random organized network ($C_r$ random), although still having a short characteristic $L_r$ similar in length to that of an equivalent random network ($L_r$ random). Formally, small-world networks show a ratio $\gamma_r$ defined as $C_r$ real/$C_r$ random of >1 and a ratio $\lambda_r$ defined as $L_r$ real/$L_r$ random of ≈1

(Humphries & Gurney, 2008; Humphries, Gurney, & Prescott, 2006; Sporns & Zwi, 2004; Watts & Strogatz, 1998). A high $\gamma_r$ reflects a high level of local neighborhood clustering within a network, and a short normalized travel distance $\lambda_r$ expresses a high level of global communication efficiency within a network (Bullmore & Sporns, 2009; Sporns & Zwi, 2004; Watts & Strogatz, 1998).

### *Nodal Centrality Analysis*

Hub regions were evaluated by weighted degree centrality measures that were originally proposed for binary networks by Freeman (Freeman, 1978). Degree in weighted networks is taken as the sum of weights and labeled node strength (Barrat, Barthelemy, Pastor-Satorras, & Vespignani, 2004; Newman, 2004). The formula of this measure for weighted networks is described in more detail elsewhere (Opsahl et al., 2008, 2010; Opsahl, 2009; Panzarasa et al., 2009). Centrality of a node expresses its structural or functional importance. Highly central nodes may serve as way stations for network traffic (betweenness centrality) or as centers for information integration (degree centrality). Degree centrality is the sum of weights incident upon a node (i.e., the sum of weights of the edges that a node has). Degree is often interpreted in terms of the capability of a node to catch whatever is flowing through the network. We used Pajek software (vlado.fmf.uni-lj.si/pub/networks/pajek/) to visualize weighted, averaged (across all networks) degree centrality scores of the nodes in the networks of the three groups under investigation.

### *Statistical Analysis*

For the statistical comparisons of age, intracranial volume, global cortical white matter volume, cortical thickness, cortical volume, and cortical surface area, we used ANOVA models. The variable sex was compared using a $\chi^2$ test. Age of musical training onset, total amount of musical training, and performance in the AP test were compared between AP and RP musicians using independent samples $t$ tests. The network parameters connection density, clustering coefficient, path length, gamma, lambda, and sigma were compared between groups across the different thresholds using the nonparametric Mann–Whitney U test. These statistical tests are interpreted with caution because the measures are intercorrelated. The best

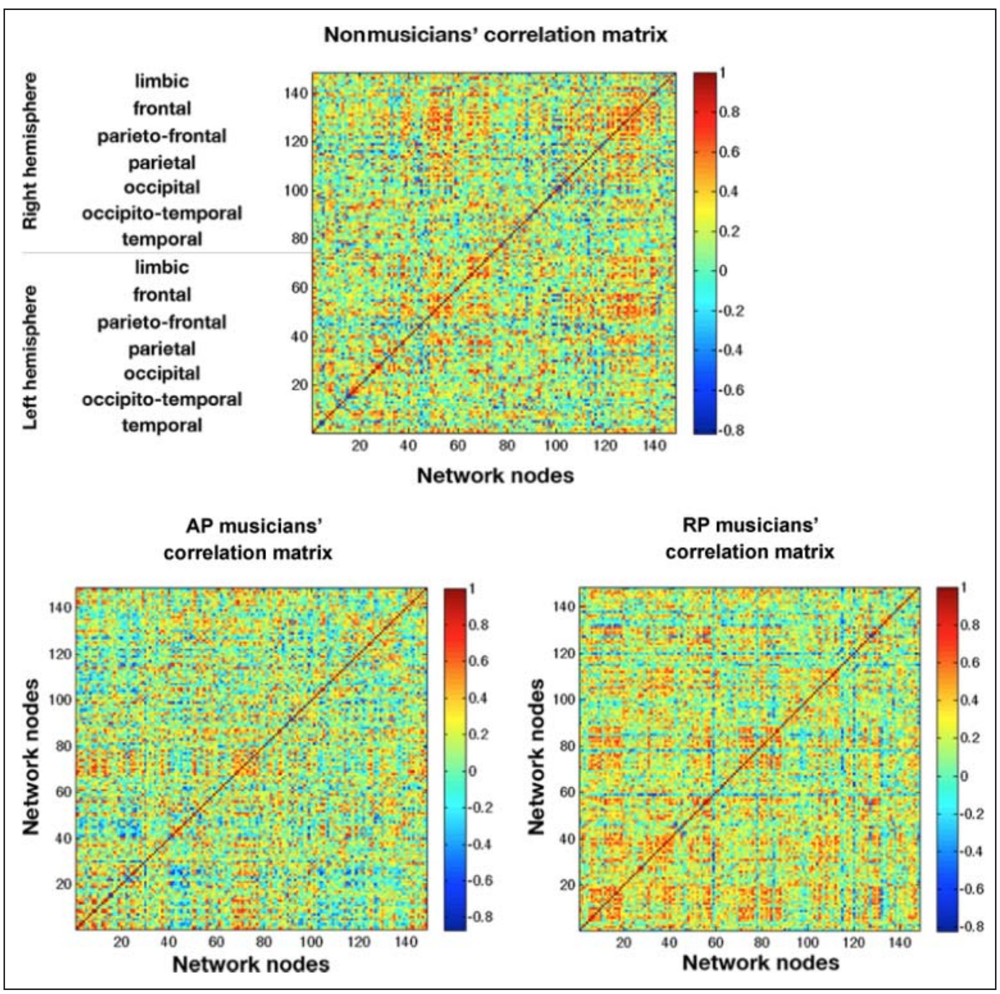


**Figure 2.** Shown are the connectivity matrices (region-wise cortical thickness correlations) of the nonmusicians, RP musicians, and AP musicians, representing the undirected weighted edges of the group-specific networks.

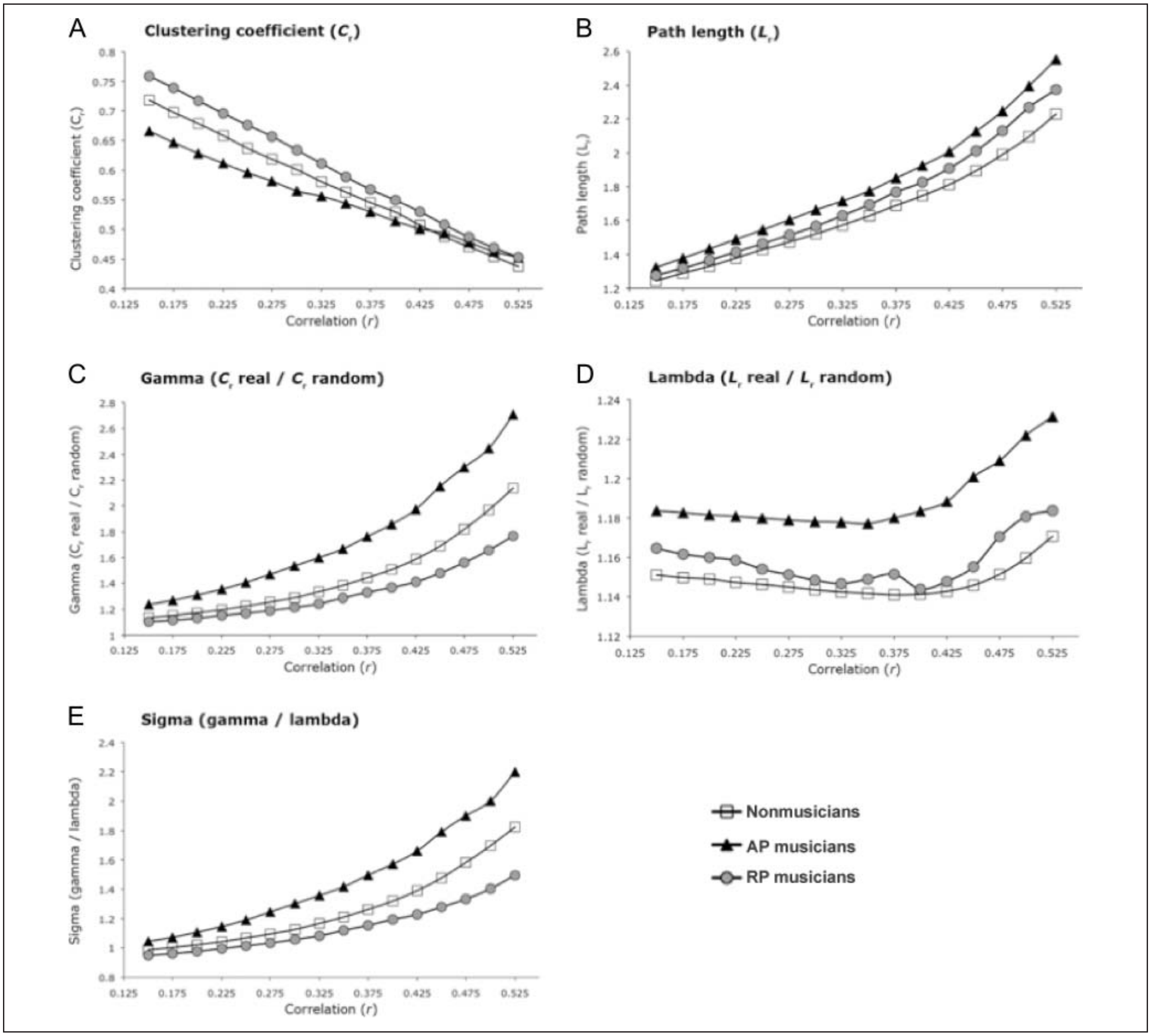


**Figure 3.** Small-world network indices. Whole cortical small-world network indices are shown for the AP musicians' network (black triangles), RP musicians' network (gray circles), and nonmusicians' network (white squares). (A) Mean weighted clustering coefficients ($C_r$). (B) Mean weighted path lengths ($L_r$). (C) Weighted clustering coefficient parameters $\gamma_r$ defined as $C_r$ real/$C_r$ random. (D) Weighted path length parameters $\lambda_r$ defined as $L_r$ real/$L_r$ random. (E) Small-world index $\sigma_r$ defined as $\gamma_r/\lambda_r$. The $x$ axis represents the particular correlation coefficient at which the association matrix was thresholded.

approach would be to perform randomization tests with these data. However, complete randomization was considered to be too time- and resource-consuming because that would imply a kind of "double" randomization for the small-world measures lambda and gamma. In a first step, one would have to generate randomized cluster coefficients ($C_r$) and path lengths ($L_r$) for the three groups, whereas in a second step, these randomized measures would have been compared with random distributions of networks. According to our calculations, that would have required several weeks of computation for our workstations and data set. Thus, we avoided this time-consuming approach and concentrated our statistical analysis and interpretation on the degree measure, which does not need a comparison with random networks. Degree is also the most important measure for our article. For degree, we performed between-group randomization tests by calculating different degree values on the basis of 1,000 randomized assignments of the participants to the groups and computed a correlation matrix for each randomization. Error probability was set to $p < .05$ (two-tailed hypothesis testing if not otherwise stated) for a single comparison, and Bonferroni correction was applied in analyses where multiple comparisons occurred.

## RESULTS

### Demographic and Global Brain Measures

Demographic and global brain measures are summarized in Table 1. There were no significant differences between nonmusicians and the two musician groups with respect to age, sex, intracranial volume, left and right total cortical white matter volume, left and right total cortical gray matter volume, left and right total cortical surface area, and left and right mean cortical thickness. No significant differences between AP musicians and RP musicians were found with respect to the total amount of time spent for musical training. However, age of musical training onset was statistically significant different between AP and RP musicians, with AP musicians having started earlier with musical training than RP musicians (AP musicians: mean = 6.1 years, $SD$ = 1.9 years; RP musicians: mean = 8.5 years, $SD$ = 3.4 years; $p$ = .027).

### Small-world Analysis

The densest whole cortical 148-node network of the AP musicians is composed of 10,528 edges (connection density = 0.484) and the sparsest network of 2,176 edges (density = 0.100). In RP musicians, the densest whole cortical network contained 12,906 edges (density = 0.593) and the sparsest network of 2,578 edges (density = 0.118). In nonmusicians, the densest whole cortical network is composed of 12,474 edges (density = 0.573) and the sparsest network of 2,810 edges (density = 0.129). These networks correspond to absolute correlation thresholds between $r$ = .15 to $r$ = .525, and between-group differences in connection density were statistically not significant (all $p$s > .21). Across the whole range of correlation thresholds, mean weighted clustering ($C_r$), and path lengths ($L_r$) were not statistically significantly different between groups (all $p$ values > .13; Figure 3A and B). In all three groups (AP, RP, and NMus), we observed a small-world index σ greater than 1 over the entire range of density thresholds. This was reflected in $\gamma = C_r/C_r$ random > 1 and $\lambda = L_r/L_r$ random ≈ 1, indicating a small-world organization in all groups (Figure 3C–E).

### Degree Centrality Analysis

Hub regions were evaluated by weighted degree centrality scores. Across all nodes and differently thresholded networks, AP musicians showed lowest absolute degree centrality (mean = 19.1, $SD$ = 8.0), whereas degree centrality scores of the RP musicians and nonmusicians were similar (mean = 23.4, $SD$ = 24.1 and mean = 11.9, $SD$ = 9.9, respectively; Figure 4). AP musicians showed a trend toward significantly reduced degree centrality scores compared with RP musicians ($p$ = .083; $p$ < .05, after 1,000 permutations), degree was significantly lower in AP musicians compared with nonmusicians ($p$ = .046; $p$ < .05, after 1,000 permutations), and RP musicians and nonmusicians did not differ in degree ($p$ = .82; $p$ > .05, after 1,000 permutations).

However, when focussing on the 20 most highly connected nodes (20 of 148 nodes is about 13.5%, and these nodes are denoted as hubs), it is quite impressive that there is only one peri-sylvian structure among the 20 hubs in nonmusicians (hypergeometric probability, $p$ = .12), that is, the right pars triangularis, whereas in AP and RP musicians, there are 11 and 5 peri-sylvian regions among their 20 hubs, respectively (Table 2). The hypergeometric probability for RP musicians to demonstrate five peri-sylvian hubs in the group of the 20 largest hubs is $p$ = .099 and thus fails to be statistically significant, although there is trend for slightly more peri-sylvian hubs in this group. However, the hypergeometric probability for AP musicians to demonstrate 11 peri-sylvian hubs in the group of the 20 largest hubs is $p = 4.26\text{E}^{-06}$ and is thus highly significant. The distribution of the degree centrality scores across the whole network is visualized for each group separately in Figure 5.

## DISCUSSION

We performed graph theoretical network analysis on MRI-based region-wise cortical thickness correlations and compared the small-world features of the structural networks between AP musicians, RP musicians, and nonmusicians. In examining differences in anatomical features between these groups, the present approach addressed the whole-brain network organization rather than that of the more classical "univariate" approach with its focus on particular brain regions. Our study is based on the analysis of important small-world parameters that express the characteristics of the whole-brain network. Here, we focus on four measures: "local connectedness" (local clustering = γ), "global efficiency of information transfer" (path length = λ), "small-worldness" (σ = γ/λ), and "degree." "Degree" is particularly important because it is considered to be the most fundamental network measure, is associated with other network measures, and is taken as a measure of connectivity (Bullmore & Sporns, 2009). The higher the "degree" measure, the stronger the interconnectivity of the network. Our network analysis revealed a typical small-world organization of the region-wise cortical thickness correlations for all groups, thus, again, supporting the idea that the human brain is organized anatomically according to the small-world principle. All three groups revealed relatively short "path lengths" (λ ≈ 1) and demonstrated strong "local clustering" (γ > 1), resulting in a typical small-world measure (σ > 1) regularly found for healthy brains. Thus, our data are in line with those of previous graph theoretical analyses of structural networks that were derived from DTI tractography and cortical thickness correlations. Those analyses suggested a small-world-like organization of brain networks in healthy participants (Hänggi et al., 2011; Guye, Bettus, Bartolomei, & Cozzone,

**Table 1.** Demographic and Global Brain Characteristics

| | *AP Musicians (n = 13)* | | | | *RP Musicians (n = 16)* | | | | *Nonmusicians (n = 12)* | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Measures* | *Mean* | *SD* | *Min.* | *Max.* | *Mean* | *SD* | *Min.* | *Max.* | *Mean* | *SD* | *Min.* | *Max.* | *ANOVA (p)* | *AP–RP (p)* |
| Age (years) | 24.8 | 3.1 | 19.0 | 31.0 | 25.4 | 3.24 | 20.0 | 32.0 | 28.1 | 4.93 | 19.0 | 34.0 | .078 | |
| Age of musical training onset (years) | 6.1 | 1.9 | 3.0 | 10.0 | 8.5 | 3.4 | 4.0 | 15.0 | | | | | | .027 |
| Total amount of musical training (years) | 18.5 | 2.5 | 14.0 | 22.0 | 16.6 | 3.93 | 8.0 | 24.0 | | | | | | .16 |
| Correct answers, AP test (%) | 85.0 | 13.8 | 54.6 | 100.0 | 7.5 | 4.53 | 0.0 | 18.5 | | | | | | $1.4E^{-11}$ |
| Sex (female/male) | 7/6 | | | | 10/6 | | | | 5/7 | | | | .55 | |
| ICV ($cm^3$) | 1452.2 | 223.3 | 1013.0 | 1781.9 | 1520.4 | 116.6 | 1307.9 | 1726.6 | 1574.0 | 174.5 | 1291.4 | 1906.0 | .22 | |
| Total left cortical white matter ($cm^3$) | 230.9 | 23.9 | 207.7 | 272.5 | 213.0 | 26.6 | 172.6 | 265.9 | 240.1 | 37.6 | 181.7 | 298.6 | .056 | |
| Total right cortical white matter ($cm^3$) | 241.6 | 25.4 | 209.8 | 282.2 | 222.1 | 29.3 | 176.7 | 271.7 | 244.3 | 39.0 | 177.1 | 299.1 | .13 | |
| Total left cortical volume ($cm^3$) | 252.0 | 26.2 | 220.3 | 304.7 | 241.2 | 25.7 | 192.9 | 284.1 | 260.2 | 21.2 | 236.3 | 292.3 | .14 | |
| Total right cortical volume ($cm^3$) | 253.7 | 24.7 | 220.8 | 309.1 | 243.6 | 25.3 | 192.6 | 285.9 | 260.8 | 23.0 | 237.1 | 295.7 | .19 | |
| Total left cortical surface area ($cm^2$) | 816.3 | 75.3 | 734.9 | 983.2 | 786.8 | 62.8 | 642.9 | 928.9 | 836.6 | 80.6 | 715.0 | 987.2 | .20 | |
| Total right cortical surface area ($cm^2$) | 823.8 | 72.7 | 745.1 | 986.4 | 786.7 | 68.6 | 644.2 | 925.8 | 838.3 | 89.3 | 705.0 | 1004.5 | .19 | |
| Mean left cortical thickness (mm) | 2.756 | 0.099 | 2.583 | 2.925 | 2.714 | 0.118 | 2.475 | 2.932 | 2.749 | 0.104 | 2.567 | 2.899 | .54 | |
| Mean right cortical thickness (mm) | 2.756 | 0.093 | 2.581 | 2.888 | 2.745 | 0.091 | 2.588 | 2.940 | 2.766 | 0.096 | 2.594 | 2.903 | .85 | |

For the evaluation of the gender frequency, a $\chi^2$ test was applied. The comparisons between AP musicians and RP musicians with respect to the musical variables were done with independent samples *t* tests. All other variables were assessed with ANOVA models. Max. = maximum; Min. = minimum.

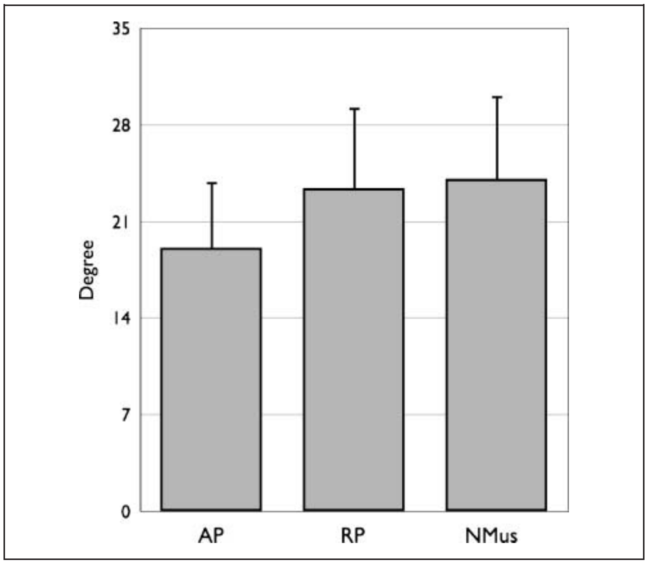


**Figure 4.** Mean degree (and standard deviations) broken down for the three groups. NMus = nonmusicians.

2010; Bullmore & Sporns, 2009; Gong et al., 2009; He et al., 2009).

One of our main goals was to analyze between-group differences with respect to the local specialization or local clustering in peri-sylvian language areas. For this, we used the "degree" measure and found that, among the 20 largest hubs, defined as the nodes with the 20 highest degree measures, peri-sylvian hubs are overproportionally represented in AP musicians. Within these 20 hubs, there were 11 hubs located within the peri-sylvian language areas (five in the left and six in the right hemisphere) in AP musicians. Eight of them are located in the temporal lobe, including the planum temporale, planum polare, Heschl's gyrus, and the lateral aspect of the superior temporal gyrus. On the left hemisphere, the STS also forms a hub with a relatively strong degree. Three additional hubs are located in the inferior frontal gyrus, specifically in the left and right pars triangularis and the left pars opercularis. These brain areas are all known to be involved in higher-order auditory processing, working memory, language and semantic memory processes, and auditory–motor mapping as well as in feedforward and feedback control of vocal production. The planum temporale is conceptualized as a "computational" hub for the processing of complex auditory stimuli (Griffiths & Warren, 2002) and responds differently in AP musicians in the context of auditory information processing (Elmer, Meyer, & Jäncke, 2012; Ohnishi et al., 2001). The planum polare is involved in controlling prosodic and attention-related auditory processes (Jäncke, Buchanan, Lutz, & Shah, 2001; Meyer, Friederici, & von Cramon, 2000), and the STS is a brain area known to integrate information from different modalities (Oechslin et al., 2010; Hugdahl, Løberg, & Nygård, 2009; Schulze et al., 2009; Hein & Knight, 2008). Interestingly, the left-sided STS region, where we identified a strong hub in AP musicians, is strongly involved in phonetic, linguistic, and prosodic processing especially in AP (Oechslin et al., 2010) and RP musicians (Elmer et al., 2012). Finally, the inferior frontal gyrus is involved in higher-order phonological processing, analysis of semantic information, auditory–motor mapping, and feedforward and feedback control of vocal production (Tourville, Reilly, & Guenther, 2008; Lahav, Saltzman, & Schlaug, 2007; Noesselt, Shah, & Jäncke, 2003). Taken together, most of the strongest hubs in AP musicians are clustered adjacently in peri-sylvian brain areas known to be involved in processing auditory, auditory–visual, speech, and semantic information. This unusual clustering of peri-sylvian language areas with relative high "degree" measures might suggest that AP musicians are specifically reliant on the use of these hubs for pitch analysis.

Interestingly, the absolute degree size of the hubs, even of those located in peri-sylvian brain areas, is much smaller in AP musicians compared with RP musicians and nonmusicians, thus meaning that these hubs are less strongly interconnected in AP musicians than in the other participant groups. In other words, there is a general hypoconnectivity in the entire brain of AP musicians combined with a relative hyperconnectivity in peri-sylvian language areas.

The current findings appear to contradict those of a recently published article in which the authors suggest (absolute) hyperconnectivity in the superior temporal gyrus region on the basis of DTI data (Loui et al., 2011). In our study, the strongest hubs with the highest degree measures in AP musicians were identified in the peri-sylvian language region. Thus, relative to brain areas outside the peri-sylvian language areas, there is indeed some kind of hyperconnectivity in AP musicians, even when we use a different measurement and analysis technique than in the study of Loui et al. However, this study also shows that the absolute amount of interconnectedness (within and outside the peri-sylvian brain area) is much lower in AP musicians and suggests a general hypoconnectivity in the brain of AP musicians. To reconcile our findings with those of Loui et al., one should keep in mind that both studies used different MRI methods to estimate the connectivity pattern. Loui et al.'s study used DTI and tractography, whereas we used cortical thickness measures and applied graph theoretical approaches to estimate small-world parameters. Both methods have their merits, but further research is needed to disentangle the differences and similarities of the measures obtained with both methods. Although there are some differences between these two studies, they do converge in finding the peri-sylvian language area to be differently connected and organized in AP musicians.

This pattern of interconnectedness in AP musicians with an unusually high number of hubs in peri-sylvian areas and many small hubs outside peri-sylvian brain areas might indicate a less efficiently organized global network. It is possible that this network is specialized to process auditory or language information differently or

**Table 2.** Hub Regions Evaluated by Weighted Degree Centrality Scores

| | *AP Musicians* | | *RP Musicians* | | *Nonmusicians* | |
|---|---|---|---|---|---|---|
| *Rank* | *Degree* | *Node* | *Degree* | *Node* | *Degree* | *Node* |
| 1 | 39.8 | Right subcentral gyrus and sulcus | 50.3 | Right supramarginal gyrus | 47.5 | Left posterior dorsal cingulate cortex |
| 2 | 38.0 | **Left pars triangularis** | 48.9 | Left orbital gyrus | 46.0 | Right mid-posterior cingulate cortex |
| 3 | 35.6 | **Right posterior segment of SF** | 48.9 | Left precuneus | 45.4 | Left inferior part of precentral sulcus |
| 4 | 34.5 | **Left pars opercularis** | 47.2 | Right orbital gyrus | 44.4 | Right superior circular insular sulcus |
| 5 | 33.8 | Left superior circular insular sulcus | 45.4 | **Left STS** | 43.1 | Left mid-posterior cingulate cortex |
| 6 | 33.5 | **Left lateral aspect of STG** | 44.9 | Right precuneus | 42.4 | Right subcentral gyrus and sulcus |
| 7 | 32.8 | **Right lateral aspect of STG** | 44.3 | Right middle temporal gyrus | 41.5 | Left parieto-occipital sulcus |
| 8 | 32.4 | **Right anterior vertical segment of SF** | 43.1 | Left supramarginal gyrus | 41.2 | Left superior part of precentral sulcus |
| 9 | 32.4 | Right insular long gyrus and central sulcus | 42.7 | **Right STS** | 40.0 | Right superior frontal sulcus |
| 10 | 32.0 | **Left planum polare** | 41.3 | **Right planum temporale** | 39.8 | **Right pars triangularis** |
| 11 | 32.0 | Left subcentral gyrus and sulcus | 41.2 | Left middle temporal gyrus | 39.8 | Right middle frontal sulcus |
| 12 | 32.0 | Left temporal pole | 41.0 | Left subcentral gyrus and sulcus | 39.6 | Left marginal cingulate sulcus |
| 13 | 30.4 | Right fusiform gyrus | 40.7 | Right parieto-occipital sulcus | 39.0 | Left superior frontal gyrus |
| 14 | 30.4 | **Left STS** | 40.1 | Right parahippocampal gyrus | 38.0 | Right marginal cingulate sulcus |
| 15 | 30.3 | Left subparietal sulcus | 40.1 | Left parahippocampal gyrus | 37.9 | Left precuneus |
| 16 | 30.1 | Right supramarginal gyrus | 38.4 | **Left Heschl's gyrus** | 36.8 | Left subcentral gyrus and sulcus |
| 17 | 30.0 | Left inferior occipital gyrus and sulcus | 38.2 | Left superior frontal gyrus | 36.6 | Right superior part of precentral sulcus |
| 18 | 29.9 | **Right pars triangularis** | 37.6 | Left parieto-occipital sulcus | 36.4 | Right intraparietal sulcus |
| 19 | 29.7 | **Right planum temporale** | 37.5 | Right middle frontal gyrus | 36.0 | Right middle frontal gyrus |
| 20 | 29.6 | **Right Heschl's gyrus** | 37.3 | **Right posterior segment of SF** | 36.0 | Right posterior collateral sulcus |

Shown are the 20 nodes (hubs) with the highest degree centrality scores within each network. Statistical testing revealed that peri-sylvian areas are significantly more often hub regions within the network of AP musicians ($p$ = 4.26E$^{-06}$). In RP musicians, there is a trend for peri-sylvian brain areas being more often hubs ($p$ = .43) and nonmusicians ($p$ = .099). The hubs within the peri-sylvian brain are printed in **bold**. SF = Sylvian fissure; STG = superior temporal gyrus.

preferentially. This fits well with findings from an earlier study of our group showing lower hemodynamic responses in the Heschl's gyrus but stronger hemodynamic responses in the STS when AP musicians are confronted with different variants of auditory language information (Oechslin et al., 2010). The specific architecture of the peri-sylvian language areas could result in "automatic and effortless categorization," as Loui et al. propose. However, the network we have identified could also have several disadvantages. For example, it is conceivable that the integration of auditory information into a broader context is computationally more demanding for AP musicians and that this might thus require more executive control during music and tone processing (without necessarily implying that AP performance is controlled or driven by conscious cognition). This could explain the stronger hemodynamic responses in brain areas known to be involved in working memory processes (Zatorre et al., 1998). This very specific

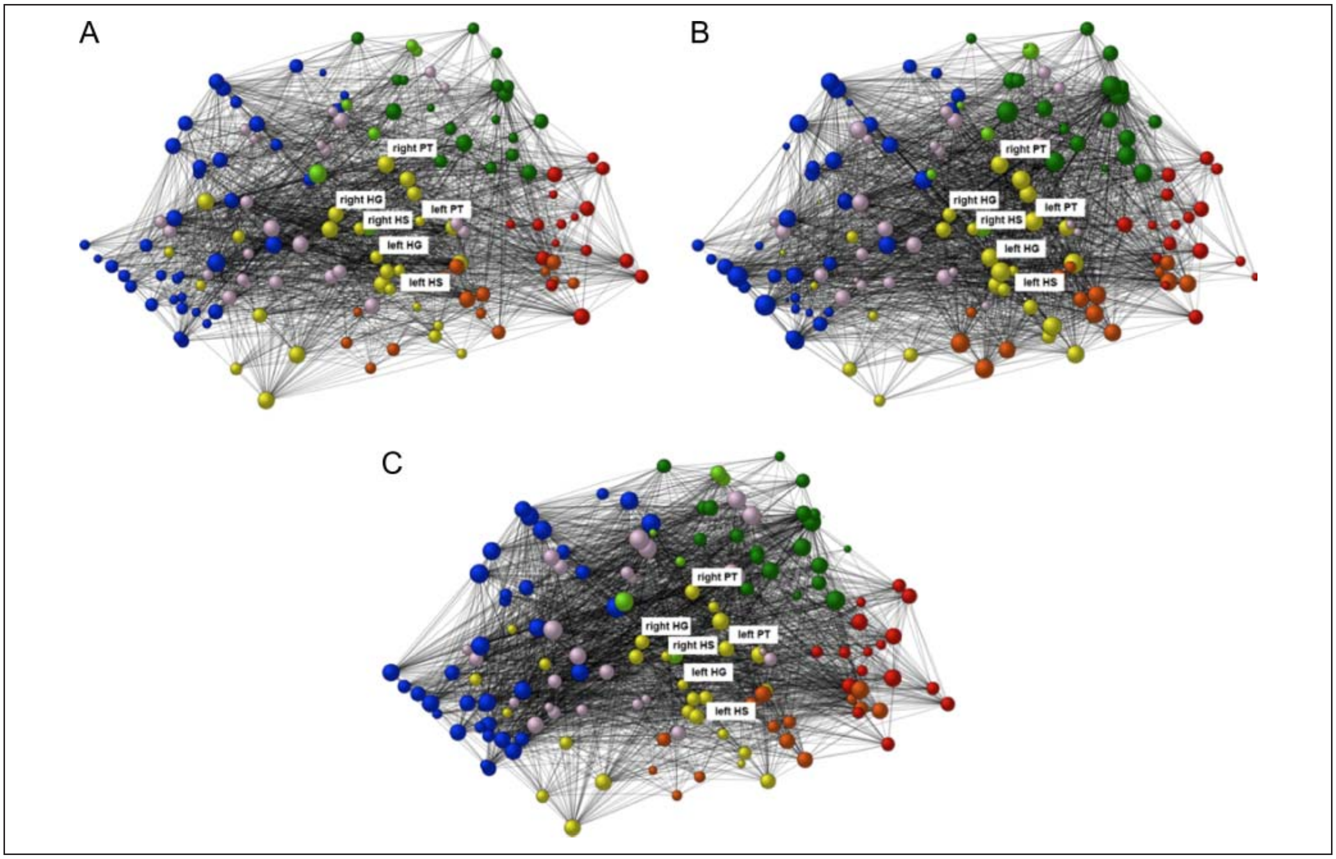


**Figure 5.** Degree centrality distribution of the nodes in the average network of the groups. Note that the size of the spheres represents the weighted degree centrality scores, the black lines represent the edges (connections) between the nodes, and the different colors represent the nodes within the different lobes. The degree centrality distribution in the network of the AP musicians is shown in A, that of the RP musicians is represented in B, and the degree centrality distribution in the network of the nonmusicians is shown in C. Central auditory nodes are indicated. HG = Heschl's gyrus; HS = Heschl's sulcus; PT = planum temporale. Lobar color code: frontal = blue, occipital = red, temporal = yellow, parietal = dark green, limbic = pink, temporo-occipital = orange, parieto-frontal = light green.

local concentration of hubs in peri-sylvian brain areas might be the reason why AP processing occurs at the expense of less efficient processing of other information (e.g., AP musicians are less efficient in transposing of tone intervals; Miyazaki, 1993, 1995, 2004; Miyazaki & Rakowski, 2002).

The decrease in whole-brain connectivity in AP musicians (as indicated by the decreased degree measure in AP musicians) resembles the decrease of connectivity in participants from the autism spectrum disorder (ASD; Barttfeld et al., 2011; Belmonte et al., 2004). This decrease in connectivity in ASD patients is often accompanied by an increase of gray matter density in primary sensory and motor brain areas, suggesting that these areas are preferentially involved in cognitive and perceptual processing (enhanced perceptual functioning model; Hyde, Samson, Evans, & Mottron, 2010; Mottron, Dawson, Soulières, Hubert, & Burack, 2006). Interestingly, there are several reports of superior pitch processing and AP abilities in ASD patients. (Soulieres et al., 2010; Brenton, Devries, Barton, Minnich, & Sokol, 2008; Heaton, Davis, & Happe, 2008; Bonnel et al., 2003; Brown et al., 2003; Heaton, 2003).

A further finding of our study is that the networks of RP musicians and nonmusicians do no substantially differ from each other. Although not statistically significant, it should be pointed out that 5 of the 20 largest hub regions in RP musicians were located in peri-sylvian language areas. In nonmusicians, only one hub was located in peri-sylvian language regions. This indicates, therefore, a tendency at least toward more local clustering in the peri-sylvian brain area in RP musicians and supports the hypothesis that the brain of musicians is partly prepared to process auditory language information differently (see, for further support of this hypothesis, the special issue on the relation between music and language; Ettlinger, Margulis, & Wong, 2011; Giuliano, Pfordresher, Stanley, Narayana, & Wicha, 2011; Ott, Langer, Oechslin, Meyer, & Jäncke, 2011; Patel, 2011; Schon & Francois, 2011).

It is noteworthy that the network pattern identified for AP musicians is entirely different to the one we recently identified for grapheme–color synesthetes (Hänggi et al., 2011). In that study, we identified a reduced global small-world network organization in concert with a strong local hyperconnectivity. This organization was driven by increased clustering, suggesting global hyperconnectivity within the synesthetes' brain. In contrast, the AP musicians in this study demonstrated global hypoconnectivity. AP ability may therefore be understood as relying on an entirely different global network organization than synesthesia. In our opinion, this difference is quite remarkable because two groups (synesthetes and AP musicians) demonstrating enhanced perceptual processing show the different global network characteristics. However, although AP musicians demonstrate global hypoconnectivity, they also demonstrate relative hyperconnectivity in peri-sylvian language areas, although the absolute degree values are still smaller than for the other two groups.

In summary, our study revealed structural alterations in AP musicians in terms of "degree," which is a small-world measure reflecting the interconnectedness of brain areas. These differences were most prominent in peri-sylvian language areas. This leads to the suggestion that the specific AP ability is causally attributable to these specific anatomical alterations. But great caution is due when drawing conclusions on the basis of anatomical differences between experts and nonexperts (Jäncke, 2009) and, therefore, between AP musicians and non-AP musicians. It is possible that the detected anatomical differences are a consequence of and not the primary reason for the life-long experience of AP ability. Several studies have shown that short- and long-term motor and cognitive training is associated with selective and transient neuroanatomical changes in gray and white brain matter in young and older participants (Bezzola, Merillat, Gaser, & Jäncke, 2011; Hyde et al., 2009; Boyke, Driemeyer, Gaser, Buchel, & May, 2008; Driemeyer, Boyke, Gaser, Buchel, & May, 2008; Draganski et al., 2004, 2006). The amount of practice and age of commencement are also known to be important factors in defining the extent of anatomical reorganizations (Imfeld et al., 2009; Aydin et al., 2007; Cannonieri, Bonilha, Fernandes, Cendes, & Li, 2007; Bengtsson et al., 2005; Gaser & Schlaug, 2003b; Amunts et al., 1997). It is possible that the difference between AP and non-AP musicians that we (and others) have identified are simply because of life-long usage of a specific strategy to process auditory information. This strategy might have been implemented into the behavioral hierarchy during childhood and strengthened during explicit and implicit practice ultimately resulting in automatization of AP processing (Meyer et al., 2011).

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