Enhanced Cortical Connectivity in Absolute Pitch Musicians: A Model for Local Hyperconnectivity

Psyche Loui[1], Hui C. Charles Li[1], Anja Hohmann[1,2], and Gottfried Schlaug[1]

Abstract

■ Connectivity in the human brain has received increased scientific interest in recent years. Although connection disorders can affect perception, production, learning, and memory, few studies have associated brain connectivity with graded variations in human behavior, especially among normal individuals. One group of normal individuals who possess unique characteristics in both behavior and brain structure is absolute pitch (AP) musicians, who can name the appropriate pitch class of any given tone without a reference. Using diffusion tensor imaging and tractography, we observed hyperconnectivity in bilateral superior temporal lobe structures linked to AP possession. Furthermore, volume of tracts connecting left superior temporal gyrus to left middle temporal gyrus predicted AP performance. These findings extend previous reports of exaggerated temporal lobe asymmetry, may explain the higher incidence of AP in developmental disorders, and may provide a model for understanding the heightened connectivity that is thought to underlie savant skills and cases of exceptional creativity. ■

INTRODUCTION

Since the 19th century with Wernicke's (1874) seminal postulate on neural disconnection, connectivity in the human brain has been a matter of increasing scientific interest (Catani & Mesulam, 2008b; Geschwind, 1965). Over a century of neuroimaging and neuropsychological research has reliably demonstrated that structural and functional connectivity that is altered by acquired lesions or developmental and/or psychiatric disorders can disrupt the normal processes of perception, language, learning, memory, and social functioning, as shown from aphasia, autism, and schizophrenia (Whitfield-Gabrieli et al., 2009; Catani & Mesulam, 2008a; Coben & Myers, 2008; Geschwind, Quadfasel, & Segarra, 1968; Meyer, 1905). Although hypoconnectivity (a loss of connections) generally leads to an inability to perform various perceptual, cognitive, and motor tasks, hyperconnectivity has been less explored but has recently been associated with above-normal perceptual abilities such as synesthesia (Hänggi, Beeli, Oechslin, & Jäncke, 2008; Rouw & Scholte, 2007; Ramachandran et al., 2004; Ramachandran & Hubbard, 2001) and savant skills in autism (Wallace, Happe, & Giedd, 2009). Despite various theoretical accounts for behavioral data suggesting that hyperconnectivity might lead to superior performance in perceptual and cognitive tasks, few studies have established direct associations between the degree of neural connectivity and the graded variations in behavior, especially among normal healthy individuals. Here we use a combination of diffusion tensor imaging and established perceptual testing to demonstrate that hyperconnectivity exists and reflects perceptual categorization ability among possessors of absolute pitch (AP), suggesting that AP may be a new model to investigate issues pertaining to neural connectivity.

AP is the ability to name the pitch class of any given tone without a reference (Miyazaki, 1988). This ability is thought to be rare and is often regarded as a "musical gift" partly because of its possession by historical musical talents such as Mozart (Ward, 1999). Because of its links to both genetic and environmental factors, it has been proposed that studies of AP may offer a model for understanding the influence of genes and development on neural and cognitive function (Zatorre, 2003; Gregersen, Kowalsky, Kohn, & Marvin, 2001). Furthermore, AP has been linked to developmental disorders: Elevated incidences of AP have been documented among populations with autistic spectrum disorders (Brenton, Devries, Barton, Minnich, & Sokol, 2008; Heaton, Davis, & Happe, 2008), Williams syndrome (Levitin, 2005), and synesthesia (Hänggi et al., 2008; Beeli, Esslen, & Jäncke, 2005). These links could suggest that AP may share a common anatomical substrate as the disorders mentioned above. One common thread of these disorders with reports of elevated incidence of AP is that they are also associated with abnormal white matter connectivity within local regions of sensory-processing areas (Lee et al., 2007; Marenco et al., 2007; Rouw & Scholte, 2007). A similar regional hyperconnectivity has not been described in normal healthy individuals with AP, but if it were present, it could suggest that AP is a new model

---

[1]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, [2]Charité-University Medicine Berlin, Germany

to explore the etiology, development, and broader neuroscience implications of hyperconnectivity.

Although AP appears initially to be a binary trait, analyses of behavioral performance on AP suggest that the trait exists along a continuum (Bermudez & Zatorre, 2009b). Some individuals, termed AP1 possessors (Baharloo, Johnston, Service, Gitschier, & Freimer, 1998), are able to label any presented pitch regardless of timbre and spectral region; on the other hand, other individuals (e.g., AP2, AP3, and AP4) perform at a lower, albeit significantly above-chance level in pure-tone tests that give no timbre cues (Baharloo et al., 1998); however, their performance improves for tones with instrumental timbres and for particular tones on each instrument, such as white keys on the piano (Miyazaki, 1988, 1990). In addition, AP appears to predominate for pitch chroma rather than pitch height, as AP possessors are known to make octave judgment errors, misattributing tones to a different register despite accurate performance in pitch class identification (Miyazaki, 1989).

Genetic versus environmental contributions to AP possession is a controversial topic that has received much attention in the literature. AP exhibits a unique and nonuniform distribution among different populations. Musical training may be a prerequisite for AP, with early onset musical training being especially important (Baharloo, Service, Risch, Gitschier, & Freimer, 2000; Gregersen, Kowalsky, Kohn, & Marvin, 1999), although some studies have suggested that AP might be prevalent in the general population if assessment tests did not depend on note naming and therefore on musical training (Ross, Olson, & Gore, 2003a). One case in which onset age of musical training seems to have less influence is in blind musicians, who have an elevated incidence of AP even despite late onset of musical training (Hamilton, Pascual-Leone, & Schlaug, 2004). Furthermore, people of East Asian descent are disproportionally likely to possess AP (Schellenberg & Trehub, 2008; Deutsch, Henthorn, Marvin, & Xu, 2006; Deutsch, Henthorn, & Dolson, 2004; Gregersen et al., 1999). These population differences have been attributed to genetic contributions (Athos et al., 2007; Gregersen et al., 1999; Baharloo et al., 1998), exposure to tone language (Deutsch et al., 2004, 2006), and type of musical training (Gregersen et al., 2001). Some have suggested that AP results from inherited traits (Profita & Bidder, 1988), as supported by the observations of familial aggregation of AP even after controlling for early musical training (Deutsch et al., 2006; Baharloo et al., 2000; Gregersen, 1998) as well as recent evidence for genome-wide linkage on chromosome 8 among AP families (Theusch, Basu, & Gitschier, 2009).

There is also abundant evidence that AP is a result of learning and/or experience during a sensitive period of development. The incidence of AP declines with the increase in age of commencement of musical training: Late-starting musicians are less likely to possess AP (Deutsch et al., 2006; Gregersen et al., 2001). In addition, speakers of tonal languages have much higher incidence of AP after controlling for other possible contributors such as duration or intensity of musical training (Deutsch et al., 2006; Levitin & Rogers, 2005). Furthermore, the incidence of AP is positively correlated with tone language fluency (Deutsch, Dooley, Henthorn, & Head, 2009), suggesting that exposure to and experience with pitched information, possibly within a sensitive period of development, may affect the maturation or pruning of brain networks that give rise to the ability to categorize pitch into pitch chroma classes.

The link between pitch categorization ability and early exposure implicates an exposure-dependent brain morphology that may be in place for AP possessors that may not be present in the rest of the population. In AP individuals, brain areas used to categorize pitches may be differently connected to auditory areas responsible for pitch perception; specifically, AP individuals may possess more direct (or more extensively developed) connections between perception and categorization areas than the normal population. Although evidence for drug-induced shifting of tuned periodicity detectors had been interpreted as a subcortical (e.g., inferior colliculus) contribution to pitch class mapping (Braun & Chaloupka, 2005), structural and functional neuroimaging studies have implicated a network of cortical areas that are uniquely structured and recruited among AP musicians (Bermudez & Zatorre, 2009a; Oechslin, Meyer, & Jancke, 2009; Schulze, Gaab, & Schlaug, 2009; Wilson, Lusher, Wan, Dudgeon, & Reutens, 2008; Luders, Gaser, Jancke, & Schlaug, 2004; Keenan, Thangaraj, Halpern, & Schlaug, 2001; Ohnishi et al., 2001; Zatorre, Perry, Beckett, Westbury, & Evans, 1998; Schlaug, Jancke, Huang, & Steinmetz, 1995). The planum temporale (PT), as a gross-anatomical marker of auditory association surface area, is more leftwardly asymmetric in AP musicians compared with non-AP controls (Luders et al., 2004; Schlaug et al., 1995). Using gray matter volume of the PT as a metric, Zatorre et al. (1998) found a larger left posterior superior temporal region in AP subjects compared with normal subjects unselected for musical skill, with no differences between the groups on the right side. Furthermore, the left PT volume was associated with lower error scores on the pitch-naming task. This absolute size of the left PT or the leftward PT asymmetry may be the basis for a functional hemispheric dominance in auditory processing, where the left hemisphere is biased toward the processing of pitched information. Functional studies have identified differences in cortical networks recruited by AP and non-AP musicians during pitch processing and categorizing. In this context, it is of interest that there is also a higher than expected incidence of AP among congenitally and early blind musicians compared with sighted musicians (Hamilton et al., 2004). Compared with sighted musicians with AP, blind AP musicians used more parietal and visual association areas during pitch and musical experiments (Gaab, Schulze, Ozdemir, & Schlaug, 2006; Ross, Olson, & Gore, 2003b); this might suggest an increased functional and possibly even a structural hyperconnectivity between early auditory and visual association regions among blind individuals that emerges as a function

of neuroplastic changes. Positron emission tomography conducted during the perception of tones and tone pairs (intervals) (Zatorre et al., 1998) showed that the dorsolateral pFC was more active in AP than non-AP subjects during the perception of pitch, whereas the right inferior frontal cortex was more active in non-AP than in AP subjects during the modal (major vs. minor) assignment of two-tone intervals, suggesting that AP and non-AP individuals recruit different working-memory networks to process pitch information. In electrophysiological studies, AP individuals' processing of pitches results in reduced or absent P300 components compared with non-AP controls (Crummer, Walton, Wayman, Hantz, & Frisina, 1994; Wayman, Frisina, Walton, Hantz, & Crummer, 1992; Klein, Coles, & Donchin, 1984), indexing a smaller working-memory load resulting from AP. However, an enhanced N1 component was shown (Wu, Kirk, Hamm, & Lim, 2008) in an ERP study comparing AP and non-AP musicians during pitch labeling, suggesting a stronger perceptual coding but reduced working-memory dependence among AP musicians. Source localization on ERP differences between AP and non-AP possessors revealed enhanced activity in bilateral STG and MTG, especially in the left hemisphere (Hirata, Kuriki, & Pantev, 1999). A positron emission tomography study investigating AP processing also showed left STG activity during pitch labeling (Wilson et al., 2008), converging with the increased leftward PT asymmetry in AP musicians (Schlaug et al., 1995). Furthermore, a recent fMRI study showed that even when given the same pitch memory task, AP musicians recruited elevated STS activity, whereas non-AP musicians had more activity in the right superior parietal lobule (Schulze et al., 2009). The fact that AP musicians recruited the STS, a region with a known role in sound categorization (Hickok & Poeppel, 2007; Möttönen et al., 2006), suggests that categorization of pitch information early in the auditory encoding phase dominates the neural process that AP musicians employ to perform pitch memory tasks. These findings from cognitive neuroscience studies demonstrate more efficient and effortless access to pitch classes among AP possessors. Although findings focus mainly on the left hemisphere, some also report bilateral increases in processing efficiency, albeit with a greater leftward preponderance among AP musicians.

Taken together, these structural and functional studies make the case for efficient and well-connected auditory perception and association cortices being closely connected with each other among AP possessors, especially in superior temporal regions including STG and MTG. These two regions have a unique pattern of connectivity, as identified in a recent DTI study which investigated connections from STG and MTG to the frontal lobe (inferior frontal gyrus [IFG]) via the arcuate fasciculus (superior longitudinal fasciculus III) (Loui, Alsop, & Schlaug, 2009). The arcuate fasciculus was found to be diminished among individuals with musical disorders, with additional behavioral correlations shown (1) between STG–IFG connections and perceptual behavior and (2) between MTG–IFG connections and

production–perception mismatch. Additional connections between STG and MTG, if identified and linked to musical behavior, would represent the completion of a three-node network between STG, MTG, and IFG, classical areas important to language that also subserve music and auditory perception/categorization behavior more generally. As AP is generally conceptualized as an overabundance of musical ability, we might expect that this enhancement in performance could reflect enhanced connectivity (hyperconnectivity) in the brain, in contrast to the hypoconnectivity among musically disordered individuals. In this context, it is important to note the higher incidences of AP in developmental disorders such as autistic spectrum disorders, Williams syndrome, and synesthesia, which have been linked to local hyperconnectivity. Thus, the link between AP and other heritable and/or neurodevelopmental conditions suggest that local hyperconnectivity may characterize AP in the same way as in other conditions and that AP may offer a new model to explore the etiology, development, and broader neuroscience implications of hyperconnectivity. Using diffusion tensor imaging combined with behavioral testing, we tested the hypothesis that AP possessors may have increased white matter connectivity within their auditory perception and association cortices. Furthermore, we related measures of DTI connectivity to behavioral performance in AP tasks.

METHODS

Subjects

Twelve AP musicians and 12 non-AP musician controls participated in the study. All participants were professional or amateur musicians recruited from musical organizations in the Greater Boston area and were paid for their participation. The two groups were matched for gender, age, handedness (as assessed using the Edinburgh Handedness Inventory; Oldfield, 1971), ethnicity, IQ, age of onset of musical training, and years of musical training. All subjects gave written informed consent, and the study was approved by the institutional review board of Beth Israel Deaconess Medical Center.

Procedure

Behavioral Screening

Before testing, we administered a questionnaire to understand participants' language and musical background: Participants indicated their first language and any other languages they spoke, the musical instrument(s) they played, and their duration and age of onset of musical training. To ensure that the two groups were similar in IQ, subjects also completed verbal and abstract measures on the Shipley–Hartford Retreat Test (Shipley, 1940), which has been shown to be a predictor of IQ (Paulson & Lin, 1970). Table 1 summarizes the demographic information, musical training information,

Table 1. Demographic Information and Pitch-labeling Test Performance of AP and Control Groups

Group	AP Mean (Range)	Control Mean (Range)
No. subjects	12	12
Gender		
Male	8	8
Female	4	4
Age	25 (19–30)	26 (15–34)
Ethnicity		
Asian	5	5
Caucasian	6	6
Other	1	1
Native languages		
Tone languages (Mandarin, Cantonese, Taiwanese)	5	5
Nontone languages (English, French, Spanish, German)	7	7
Handedness		
Right-handed	11	11
Left-handed	1	1
Years of musical training	16 (10–23)	16 (6–24)
Age of onset of musical training	5.2 (3–12)	6.1 (3–10)
Musical instrument(s)[a]		
Strings	8	5
Keyboards	5	8
Winds	2	2
Voice	2	1
Scaled IQ	119 (110–125)	117 (109–125)
AP test performance	97% (92–100)	41% (19–77)

[a]Some subjects report more than one.

IQ test results, and AP test performance for each group. The AP test is described below.

AP Testing

AP was confirmed using an established listening test (Keenan et al., 2001; Zatorre & Beckett, 1989; Ward & Burns, 1982) in which subjects had to identify 52 sine wave tones. Each trial contained one computer-generated sine wave tone (500-msec duration with a 50-msec rise and decay time) with a fundamental frequency that was tuned to a pitch in the equal-tempered Western scale ranging from 370 Hz (F#3) to 739.97 Hz (F#4). Participants' task was to label each pitch by writing down the letter name (including any accidentals) on an answer sheet upon hearing each tone. The intertone time interval was 2 sec.

Image Acquisition

High-resolution anatomical and diffusion-weighted images were acquired in a 3-T General Electric scanner. Anatomical images were obtained using a strongly T1-weighted, three-dimensional, magnetization-prepared, rapid-acquisition, gradient-echo (MPRAGE) volume acquisition with a voxel resolution of 0.93 × 0.93 × 1.5 mm. Diffusion-weighted images were obtained with a single-shot, spin-echo, EPI sequence (echo time = 86.9 msec, repetition time = 10000 msec, field of view = 240 mm, matrix size = 128 × 128 voxels, slice thickness = 5.0 mm, no skip, NEX = 1, axial acquisition). Twenty-five noncollinear directions with a b value of 1000 sec/mm^2 and one direction with a b-value of 0 sec/mm^2 were acquired. Fractional anisotropy (FA) values, a measure of the degree of directional preference of water diffusion (Basser, 1995), were calculated within each brain voxel. This diffusion sequence lasted under 7 min and had been shown to be sufficient in detecting between-group differences in tracts terminating in the superior and middle temporal gyri (Loui & Schlaug, 2009).

Data Analysis

Behavioral Data

Participants' responses were scored in two ways. First, responses were scored as correct if they fell within one semitone of the actual pitch. For example, if the actual pitch was B, acceptable responses included A#/B-flat, B, and C. Thus, chance level of correct performance was 3/11 = 27%.

In a secondary analysis, full credit was given for correctly identifying the tone, and half credit was assigned if the participant's response was one semitone away from the actual pitch.

For both types of analyses, subjects received no credit if the responses were two semitones or more away from the actual pitch.

Diffusion Imaging Data

Tractography was applied to the DTI data to reconstruct white matter tracts by successively following the path of preferred direction of water diffusion when FA is higher than a selected threshold (Basser, Pajevic, Pierpaoli, Duda, & Aldroubi, 2000). Using MedINRIA software version 1.7 (Fillard, Toussaint, & Pennec, 2006), diffusion tensors were calculated from all voxels within the brain, and fiber tracts were calculated by connecting adjacent voxels with similar principal eigenvectors, using a threshold FA value of 0.2 and

a smoothness factor (a parameter ranging from 0 to 1 corresponding to the straightness of each fiber; Weinstein, Kindlmann, & Lundberg, 1999) of 0.2 for continuous fiber reconstruction. Only fibers with lengths of >10 mm were included. These parameters had been used in previous studies with similar ROIs (Loui et al., 2009) and are similar to those used by others who applied a fiber assignment by continuous tracking algorithm (Schaechter, Perdue, & Wang, 2008; Weinstein et al., 1999).

To constrain fiber tracts and to determine regional FA values, ROIs were drawn bilaterally on each brain in white matter immediately underlying the posterior superior temporal gyrus (pSTG) and posterior middle temporal gyrus (pMTG). ROIs were hand drawn on a single sagittal slice of the FA map of each hemisphere of each subject where the pSTG and the pMTG were most clearly distinguishable. ROI volumes and locations were defined according to published DTI atlas segmentations (temporal superior posterior and temporal middle posterior regions; Lawes et al., 2008) and were identifiable in each hemisphere of each individual's brain on the sagittal FA-weighted image. ROIs were drawn by one coder and were verified by a second coder, both of whom were blind to the subjects' identity and group assignment. Mean ROI volumes were 250 mm^3 (SD = 85 mm^3) for pSTG and 285 mm^3 (SD = 93 mm^3) for pMTG. Volumes and slice coordinates of each of the four ROIs between APs and non-AP subjects did not differ: all $t(22) < 2$, all $p > .1$. Intercoder reliability (r^2) of volumes and locations of identified tracts was 98% and 89%, respectively (see Figure 1 for location and size of the ROIs). This eliminates the possibility that any between-group differences observed might be an artifact of differences in ROI location or volume.

To test the hypothesis that these differences might result from larger tract volume or connectivity in the whole brain and/or in regions not specific to auditory perception and categorization areas in the temporal lobe, we also traced the corticospinal tracts, motor-related bundles of white matter unrelated to pitch categorization ability, and tested for differences between AP and non-AP groups

in these tracts. Pyramidal tracts were identified in each hemisphere of each brain using ROIs drawn over a single axial slice in the precentral gyrus, posterior limb of the internal capsule, and basis pontis, with methods described in Figure 1 in Lindenberg et al. (2010). Average ROI volume was 2200 mm^3 (SD = 950 mm^3) in the precentral gyrus, 1186 mm^3 (SD = 543 mm^3) in the internal capsule, and 1288 mm^3 (SD = 608 mm^3) in the pons. Left and right hemispheres did not differ in volume or in location (all p's > .1). Left and right pyramidal tracts were identified and compared between AP and non-AP groups.

Mean FA value was calculated for each ROI of each subject by averaging the mean FA in all voxels. After applying tractography, the identified fiber bundles were compared for tract volume, fiber count, and averaged tract FA values. Tract volume, fiber count, tract FA values, and ROI volume and FA values were exported into Excel and SPSS for further analyses.

RESULTS

Behavioral Data

We obtained behavioral and diffusion imaging results from 12 self-reported AP-possessors and 12 controls matched in age, gender, ethnicity, first language, and number of years and onset age of musical training. In a behavioral test of pitch categorization, the AP group outperformed normal controls robustly: All self-identified AP possessors performed significantly above chance, with a mean performance of 97% (range = 92–100%). Non-AP musician control subjects, on the other hand, did not perform significantly above chance (mean = 36%, range = 19–77%). This highly significant difference between scores, $t(22) = 5.8, p < .001$, confirms that individuals in the AP group were superior at pitch categorization.

ROI Statistics

ROIs were drawn bilaterally on the pSTG and the pMTG of each individual brain. Volumes and locations of ROIs

Figure 1. An example of left-hemisphere ROIs drawn over T1-weighted images that were spatially coregistered with FA and diffusion tensor images to identify tracts between pSTG and pMTG. (A) pSTG. (B) pMTG.
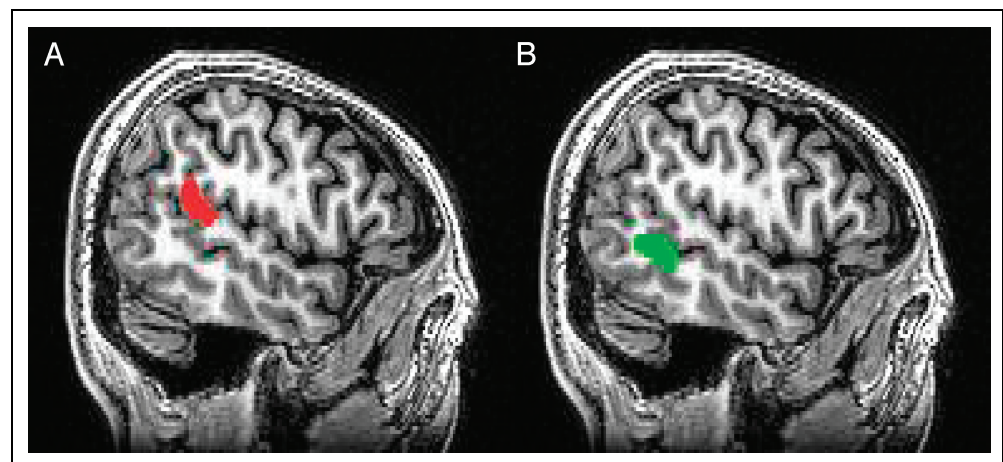
were similar between regions and between groups (see Methods). A two-way ANOVA with factors of group (AP vs. non-AP) and ROI (left pSTG, left pMTG, right pSTG, right pMTG) was performed on the dependent variable of FA, a value between 0 and 1 representing the degree of constrained diffusion in each voxel of the diffusion image. This confirmed a significant difference in FA between AP and non-AP groups, $F(1, 88) = 4.0, p < .05$, with the AP group showing higher FA values overall ($M = 0.28$, var $= 0.002$) than the non-AP group ($M = 0.26$, var $= 0.002$). A significant overall effect of regional FA value was also observed, $F(1, 88) = 5.7, p = .001$, with highest FA in the right pMTG ($M = 0.30$, var $= 0.002$), followed by the right pSTG ($M = 0.29$, var $= 0.001$) and then the left pMTG ($M = 0.25$, var $= 0.002$) and the left pSTG ($M = 0.25$, var $= 0.002$). Individual t test contrasts did not reveal significant between-group differences in FA values of specific regions, nor was a significant interaction observed between group and ROI, $F(1, 88) = 0.34, p = .80$, suggesting that all ROIs contributed small effects equally to the observed elevation in preferential diffusivity in white matter of the AP group over the non-AP controls. ROI volumes did not differ between AP and non-AP groups by region, hemisphere, or group (all p's $> .1$), eliminating the possibility of tract volume or regional FA value differences resulting from confounds in ROI volume.

Tract Statistics

Tracts connecting pSTG to ipsilateral pMTG were identified in both hemispheres of all subjects. Volume and fiber number of these tracts were significantly higher in the AP group. A two-way ANOVA on the dependent variable of tract volume (in mm^3), with the factors of group (AP vs. non-AP) and hemisphere (left vs. right), showed a highly significant effect of group, $F(1, 44) = 16.6, p < .001$, confirming that tract volumes connecting STG to MTG were larger among AP possessors compared with non-AP possessors. Independent samples t tests on left and right tract volumes comparing APs and non-APs confirmed that differences were robust on both hemispheres: left hemisphere, $t(22) = 3.8, p = .001$; right hemisphere, $t(22) = 2.3, p = .03$. Total tract volume (left plus right) was significantly larger in AP than non-APs, $t(22) = 3.9, p < .001$. No significant between-group differences were observed in tract FA values. Total number of fibers was also significantly higher in APs, $t(22) = 2.4, p < .05$, with individual t tests confirming larger fiber numbers for APs in the left hemisphere, $t(22) = 2.4, p < .05$, but not in the right hemisphere, $t(22) = 1.0, ns$. Figure 2 illustrates the differences in tract volume between APs and non-APs.

Having observed these AP-related group differences in STG–MTG connectivity in performance-matched groups, one question that arises is whether individuals who possess predictors of AP that were controlled for in our sample, such as early onset musical training and exposure to tone language, may also have the AP-like tract morphology. To
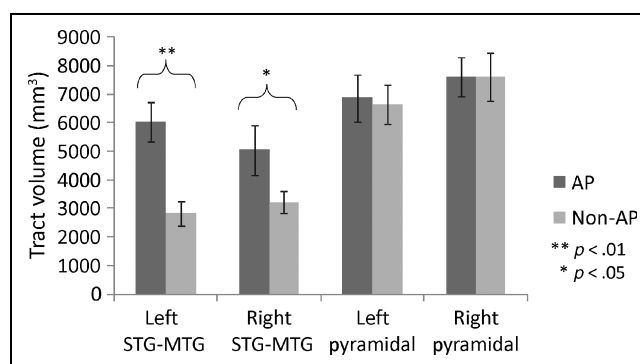

Figure 2. Main comparisons in tract volume. Bars represent means; error bars represent standard error.

compare tract volumes between early and late onset musicians, a median split was done on all subjects (collapsed across AP abilities) by age of onset of musical training. A comparison between tract volume of early and late onset groups revealed that the left tract volume was significantly larger in early onset musicians than late-onset musicians, $F(1, 22) = 5.23; p = .03$, whereas the same trend was not observed for the right tract, $F(1, 22) = 0.44, p = .52$. No significant difference was observed in a comparison of tract volume between tone-language speakers and nontone language speakers or between Asian and non-Asian subjects.

Testing for Between-group Differences in Nonauditory Tracts

Although AP-related differences in tract volume were observed in connections between superior and middle temporal gyri in the temporal lobe, it was unclear whether these differences might result from larger tract volume or connectivity differences in the whole brain and/or in regions not specific to auditory perception and categorization areas in the temporal lobe. If AP possessors also show hyperconnectivity in tracts thought to be unrelated to auditory processing, such as the corticospinal tracts, then we could infer that hyperconnectivity was not specific to regions responsible for pitch perception and categorization ability. A two-way ANOVA was conducted on the dependent variable of tract volume in the left and right corticospinal tracts, with factors of group (AP vs. non-AP) and hemisphere (left vs. right). Results showed no main effect of group, $F(1, 44) = 0.02, p = .87$, no main effect of hemisphere, $F(1, 44) = 1.24, p = .27$, and no interaction between group and hemisphere, $F(1, 44) = 0.02, p = .88$. Corticospinal tracts were not significantly different between AP and non-AP groups, suggesting that differences in tract volume in superior temporal regions were not due to hemispheric differences within the whole brain or overall differences in long-range connectivity. Heightened connectivity among AP musicians appears to affect local structures specific to the temporal lobe.
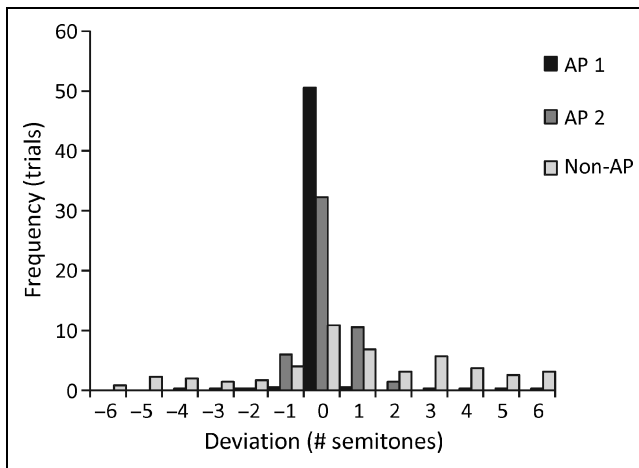
Figure 3. Results from pitch-labeling task averaged within AP1, AP2, and control groups, plotted as distributions over number of semitone deviations from target pitches.

AP Category Differentiation

On the basis of subjects' behavioral performance on the pitch-labeling task, we found that AP subjects fell into two categories: more accurate possessors (which we label here as AP1) and less accurate but highly above-chance possessors (labeled here as AP2). Category assignment was based on the criterion of 97% performance on the pitch-labeling task. This cutoff resulted in a median split between AP subjects, with six subjects falling into the AP1 category (mean performance = 99.7%) and six in the AP2 category (mean performance = 94.6%). Furthermore, if half credit were given (instead of full credit) for semitone errors, the AP2 group's performance suffered (mean performance = 77.7%, range = 71–93%), whereas AP1 performance remained largely unchanged (mean performance = 98.4%, range = 95.2–100%), indicating that AP2 possessors were more likely to make semitone errors. Figure 3 shows the performance of AP1, AP2, and non-AP groups as a histogram of number of semitone deviations from the correct pitch. The difference in spread among the three distributions, especially between AP1 and AP2 subcategories, provides

support for a performance-based distinction between sub-categories of AP possession.

We examined the relationship between tract volume and the degree of AP possession. A comparison of the morphology of pSTG-to-pMTG tracts among AP1, AP2, and non-AP possessors would reveal the degree to which AP category was reflected by tract volume. To characterize this relationship between tract volume and pitch-labeling ability, AP possession was coded for each individual subject as one of three categories: 1 = AP1, 2 = AP2, and 3 = non-AP. A comparison of tract volume revealed visible differences between AP1, AP2, and non-AP brains, as shown in Figure 4.

Confirming the observed differentiation between categories of AP possession, we observed a highly significant difference in left tract volume, $F(2, 21) = 10.2, p < .001$, surviving Bonferroni correction for multiple comparisons, in a post hoc ANOVA with the three-level factor of AP category. The same relationship was not significant for right tract volume, $F(2, 21) = 2.1, p = .14$ (Figure 5). A partial correlation between variables of AP category and left tract volume was significant even after partialling out the effects of age of onset and tone language ($r = -.67, p = .001$). This dissociation between AP category and hemispheric tract volume provides further support for the dependence of pitch-labeling abilities on the leftward asymmetry of temporal lobe connectivity.

AP as a Continuous Variable

The assignment of AP subjects into AP1 and AP2 represents one of many possible ways to categorize the degree of AP possession based on a subject's performance. As a last follow-up behavioral analysis to capture the possibility of a continuous rather than categorical degree of AP possession, we computed the average absolute deviation (in semitones) for each subject on the pitch categorization task (Bermudez & Zatorre, 2009b). Subjects' response in each trial of the behavioral task was calculated as a number of semitone deviations against the target response (0 is correct, 1 represents one semitone deviation from target,
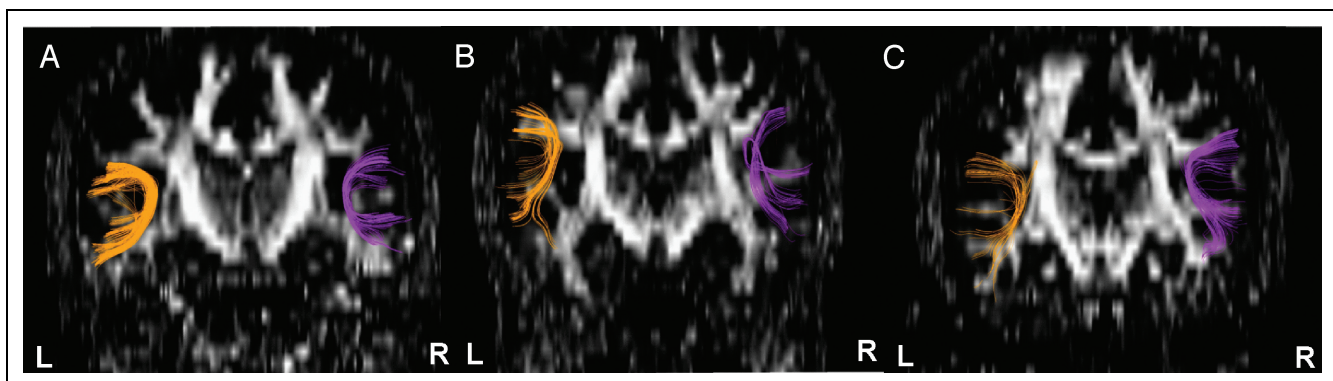

Figure 4. Tractography overlaid on FA images of representative AP1, AP2, and non-AP individuals. Orange = tracts connecting left pSTG and left pMTG. Purple = tracts connecting right pSTG and right pMTG. (A) AP1 possessor; (B) AP2 possessor; (C) non-AP control.
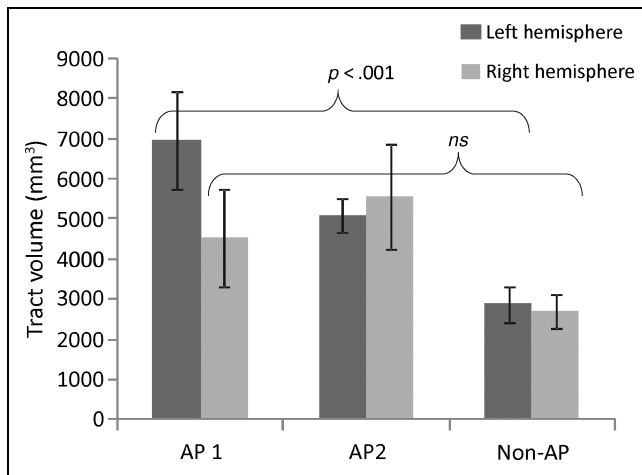
Figure 5. Average left and right tract volumes in AP1, AP2, and non-AP subjects.

etc.), and mean performance for all trials was calculated for each subject. The resulting distribution of absolute deviation (in semitones) was a nonnormal distribution clustered around 0–1 semitones (AP1 subjects in this sample). To correlate the DTI measure of tract volume with this measure of AP ability, a nonparametric correlation (Spearman rank-order correlation) between absolute deviation and pSTG-to-pMTG tract volume revealed a significant negative correlation in the left tract ($r_s = -.52$, $p = .01$) and no correlation in the right tract ($r_s = -.14$, $p = .53$). This confirms that the left pSTG–pMTG tract volume is a neural correlate of AP ability: Individuals who possess more accurate AP also possess larger connections in the left superior temporal lobe.

DISCUSSION

Results showed that people with AP possess higher white matter connectivity in temporal lobe regions responsible for the perception and association of pitch. These hyperconnected regions include the posterior superior and middle temporal gyri in both left and right hemispheres. AP possessors had significantly higher tract volume than non-AP individuals; these differences were especially robust in the left hemisphere as shown by significant correlations between left tract volume and both continuous and categorical behavioral performance on an AP task. The number of identified fibers was also higher in the left hemisphere among AP than non-AP individuals, suggesting that the hyperconnectivity may reflect a larger-than-normal number of fibers in the AP brain.

As the current samples are well matched for IQ, native language, ethnicity, and onset and duration of musical training, results observed are not due to ethnicity or IQ differences nor are they attributable to overall musical training or to tonal language exposure. Median-split analyses suggest that tone language and Asian ethnicity did not contribute significantly to the AP tract morphology, but age of onset of musical training did result in larger left tract volume. However, the AP effects observed in this study cannot be explained by early musical training alone, as confirmed by partial correlation results and the matching of training-onset between AP and non-AP groups.

The behavioral paradigm we used for assessing AP relies on participants' knowledge of pitch classes and their ability to label pitches. The fact that our non-AP control sample is recruited specifically to match our AP group for age of onset and number of years of musical training ensures that both AP and non-AP groups are equally familiar with the set of note names based on training. Thus, the behavioral paradigm adopted here is robust to potential differences in performance that may result from lack of knowledge. Our behavioral testing allowed us to separate AP possessors into AP1 and AP2 groups and also in more fine-grained detail by calculating the mean absolute deviation from target response in semitones for each subject to obtain a continuum of AP ability. It remains to be seen whether the phenotype of AP is categorical or continuous, but our results suggest that both views have merit. Another issue that remains to be determined is whether the degree of AP possession might differ between other covariates such as tone language exposure, Asian ethnicity, or age of onset of musical training in larger sample populations.

Although increased tract volume was observed in the initial AP-versus-non-AP comparison in both hemispheres, only the left pSTG–pMTG connection reflected the behaviorally defined degree of AP possession, as indicated by a significantly positive correlation between left pSTG–pMTG tract volume and absolute semitone deviation on the behavioral task, suggesting that local hyperconnectivity in the left hemisphere was responsible for the absolute categorization of pitch. Although right hemisphere tracts were also significantly larger in AP than non-AP subjects, this difference did not covary with the degree of AP possession. The finding that hyperconnectivity between left pSTG and pMTG is predictive of the behaviorally defined degree of pitch categorization ability is consistent with recent fMRI results indicating more STS activity among AP musicians (Schulze et al., 2009) in providing support for the left STS as a center for automatic and effortless categorization, possibly as a way station along the STG-to-MTG pathway that sends information from a fine-grained, controlled perceptual representation to an unconscious and automatic category-based representation. Because the present diffusion tractography methods rely on the use of seed regions of white matter, we could not include the STS (which has little white matter) among our ROIs. Nevertheless, more efficient connectivity in the STG-to-MTG pathway among AP possessors may explain extended functional activation in the STS that lies along the course of that pathway. Because the AP-related tract volume differences are observed between pSTG and pMTG but not in the control corticospinal tracts, the present results suggest that AP differences may be unique to the temporal lobe. However, as we

have only investigated a small fraction of all possible tracts in the human brain, it is possible that other tracts that are yet to be traced within the present sample may play a role in AP possession as well. Thus, although the current results are suggestive of local hyperconnectivity, future research is needed to define the specificity and focality of this hyperconnectivity in the AP brain.

Although FA and tract volume as identified by tractography methods provide useful measures that are correlated with cortical connectivity, it is important to note that increases in FA and tract volume might result from a combination of factors including increased intra-axonal viscosity, increased myelination, decreased crossing fibers, and increased straightness within fibers. Although each one of these factors or combination thereof could all contribute to structural differences, using the current diffusion imaging and analysis methods, we cannot readily distinguish which one or which combination of factors is the most important one. Nonetheless, the present results indicate significant differences between AP musicians and matched controls, providing evidence for increased connectivity between pSTG and pMTG that is uniquely linked to AP possession.

Another outstanding issue concerns the distinction between AP proper and heightened tonal memory and its relationship to AP2 according to our present criterion. It may be possible that AP2 individuals in our sample converge or partly overlap with the population of individuals with heightened tonal memory (Ross, Gore, & Marks, 2005), which results in superior and facilitated performance when given a test of pitch-labeling characteristic of AP. The fact that these individuals made more semitone errors than AP1 individuals in a test using pure tones suggests that their encoding of pitch may be dependent upon instrumental timbre and/or may be more dependent on training. In that regard, analyses of errors made in the AP behavioral test are relevant here; for instance, one AP2 subject, whose main instrument is piano, labeled all tones as white keys (without accidentals), reflecting a preference for pitch classes that are more readily accessible in his primary instrument. Such effects of learning converge with previous reports (Miyazaki, 1988) but are not observed in our AP1 group. These differences between AP1 and AP2 groups demonstrate dependence on instrumental training primarily among AP2 possessors, as was previously shown (Baharloo et al., 1998); however, in the present testing procedures, we rely on tests that use pure tones to avoid biasing our results in favor of participants who have training in the instrument chosen as the testing timbre. For instance, by using pure tones, we eliminate the possible advantage that piano players might have toward tests that use piano tones.

The observed distinction between AP and control groups cannot be explained by training duration or onset because the two groups in our sample were matched for both age of onset and duration of musical training. However, early musical training does result in a larger left tract volume, as revealed by a median-split analysis. The enlarged left tract in early onset musicians is similar to AP1 individuals and may reflect a sensitive period of developmental neuroplasticity during which musical training may stimulate the maturation of superior temporal regions that may subserve AP ability in some (but not all) individuals. As previous reports have noted that the incidence of AP depends on early musical training (Zatorre, 2003; Gregersen et al., 2001), differences in early exposure due to musical training may have contributed to more extensive white matter development in the AP group. However, the fact that the tract differences are still significantly correlated with degree of AP possession after partialling out the age of onset of musical training suggests that the AP morphology can exist over and above early musical training.

Results suggest that a combination of predispositions and environmental factors lead to the development of superb pitch categorization ability: Local hyperconnectivity in both temporal lobes may be one of the prerequisites for the neural structure necessary for AP, whereas exposure (due to early onset musical training) may influence and shape the hyperconnectivity in the left more than in the right hemisphere. Thus, our results appear to support the hypothesis that early musical training is "necessary but not sufficient" for developing AP. Although a brain that is predisposed with local hyperconnectivity, such as that observed within both temporal regions as in our sample, may have the ability to develop above-normal categorization skills, early exposure may lead to stronger left-lateralized neural connectivity necessary for the exceptional AP1 possessor's ability to categorize sounds. Early exposure to pitched information may have elicited rapid development of connections between auditory perception and association cortices. Alternately, early exposure could have triggered a reduction in pruning processes in the leftward auditory cortices, resulting in leftward hemispheric asymmetry characteristic of AP1 possessors.

Cases of hyperconnectivity have also been observed in other conditions such as autism (Herbert et al., 2002), color grapheme synesthesia (Hänggi et al., 2008; Rouw & Scholte, 2007; Ramachandran & Hubbard, 2001), and documented cases of exceptional heightened creativity (Carson, Peterson, & Higgins, 2003). Interestingly, these conditions also share an increased incidence of AP. Furthermore, hyperconnectivity in the temporal lobe has been observed in a musician with interval-taste and tone-color synesthesia (Hänggi et al., 2008). Although these two lines of evidence do not offer a causal conclusion to the possible connection between AP and autism or between AP and general developmental disorders that are characterized by local hyperconnectivity, results are suggestive that the compulsion to categorize, subserved by increased local connectivity in temporal regions, is a common feature among AP, synesthesia, and autism (Lee et al., 2007; Rouw & Scholte, 2007; Ramachandran et al., 2004; Ramachandran & Hubbard, 2001). The link between AP and other unusual conditions, such as savant skills and cases of exceptional creativity, remains to be explored.

The current study shows that the rare ability to categorize and to associate labels to pitch is subserved by heightened connectivity in white matter between auditory perception and association cortices. Such a pitch categorization process is instinctive, fast, and effortless, especially among AP1 possessors, and can be independent of IQ, ethnic background, and experience with tonal languages. This enhanced cortical connectivity among AP possessors is predominant in bilateral superior temporal regions and furthermore reflects the degree of AP ability in the left hemisphere, in regions thought to be responsible for the categorization of speech sounds (Hickok & Poeppel, 2007). This leftward preponderance in hyperconnectivity converges with previous reports of leftward asymmetry in AP musicians (Schlaug et al., 1995) and suggests that asymmetry in brain development may be an interaction of genetic factors and early experience-dependent cortical plasticity or pruning processes affecting temporal lobe structures during brain development.

Acknowledgments

REFERENCES

Athos, E. A., Levinson, B., Kistler, A., Zemansky, J., Bostrom, A., Freimer, N., et al. (2007). Dichotomy and perceptual distortions in absolute pitch ability. *Proceedings of the National Academy of Sciences, U.S.A., 104,* 14795–14800.

Baharloo, S., Johnston, P. A., Service, S. K., Gitschier, J., & Freimer, N. B. (1998). Absolute pitch: An approach for identification of genetic and nongenetic components. *American Journal of Human Genetics, 62,* 224–231.

Baharloo, S., Service, S. K., Risch, N., Gitschier, J., & Freimer, N. B. (2000). Familial aggregation of absolute pitch. *American Journal of Human Genetics, 67,* 755–758.

Basser, P. J. (1995). Inferring microstructural features and the physiological state of tissues from diffusion-weighted images. *NMR in Biomedicine, 8,* 333–344.

Basser, P. J., Pajevic, S., Pierpaoli, C., Duda, J., & Aldroubi, A. (2000). In vivo fiber tractography using DT-MRI data. *Magnetic Resonance in Medicine, 44,* 625–632.

Beeli, G., Esslen, M., & Jäncke, L. (2005). Synaesthesia: When coloured sounds taste sweet. *Nature, 434,* 38–38.

Bermudez, P., & Zatorre, R. (2009a). The absolute pitch mind continues to reveal itself. *Journal of Biology, 8,* 75.

Bermudez, P., & Zatorre, R. J. (2009b). A distribution of absolute pitch ability as revealed by computerized testing. *Music Perception, 27,* 89–101.

Braun, M., & Chaloupka, V. (2005). Carbamazepine induced pitch shift and octave space representation. *Hearing Research, 210,* 85–92.

Brenton, J. N., Devries, S. P., Barton, C., Minnich, H., & Sokol, D. K. (2008). Absolute pitch in a four-year-old boy with autism. *Pediatric Neurology, 39,* 137–138.

Carson, S. H., Peterson, J. B., & Higgins, D. M. (2003). Decreased latent inhibition is associated with increased creative achievement in high-functioning individuals. *Journal of Personality and Social Psychology, 85,* 499–506.

Catani, M., & Mesulam, M. (2008a). The arcuate fasciculus and the disconnection theme in language and aphasia: History and current state. *Cortex, 44,* 953–961.

Catani, M., & Mesulam, M. (2008b). What is a disconnection syndrome? *Cortex, 44,* 911–913.

Coben, R., & Myers, T. E. (2008). Connectivity theory of autism: Use of connectivity measures in assessing and treating autistic disorders. *Journal of Neurotherapy, 12,* 161–179.

Crummer, G. C., Walton, J. P., Wayman, J. W., Hantz, E. C., & Frisina, R. D. (1994). Neural processing of musical timbre by musicians, nonmusicians, and musicians possessing absolute pitch. *Journal of the Acoustical Society of America, 95,* 2720–2727.

Deutsch, D., Dooley, K., Henthorn, T., & Head, B. (2009). Absolute pitch among students in an American music conservatory: Association with tone language fluency. *Journal of the Acoustical Society of America, 125,* 2398–2403.

Deutsch, D., Henthorn, T., & Dolson, M. (2004). Absolute pitch, speech, and tone language: Some experiments and a proposed framework. *Music Perception, 21,* 339–356.

Deutsch, D., Henthorn, T., Marvin, E. W., & Xu, H. (2006). Absolute pitch among American and Chinese conservatory students: Prevalence differences, and evidence for a speech-related critical period. *Journal of the Acoustical Society of America, 119,* 719–722.

Fillard, P., Toussaint, N., & Pennec, X. (2006). *MedINRIA: DT-MRI processing and visualization software.* Paper presented at the Similar Tensor Workshop.

Gaab, N., Schulze, K., Ozdemir, E., & Schlaug, G. (2006). Neural correlates of absolute pitch differ between blind and sighted musicians. *NeuroReport, 17,* 1853–1857.

Geschwind, N. (1965). Disconnexion syndromes in animals and man: I. *Brain, 88,* 237–294.

Geschwind, N., Quadfasel, F. A., & Segarra, J. (1968). Isolation of the speech area. *Neuropsychologia, 6,* 327–340.

Gregersen, P. K. (1998). Instant recognition: The genetics of pitch perception. *American Journal of Human Genetics, 62,* 221–223.

Gregersen, P. K., Kowalsky, E., Kohn, N., & Marvin, E. W. (1999). Absolute pitch: Prevalence, ethnic variation, and estimation of the genetic component. *American Journal of Human Genetics, 65,* 911–913.

Gregersen, P. K., Kowalsky, E., Kohn, N., & Marvin, E. W. (2001). Early childhood music education and predisposition to absolute pitch: Teasing apart genes and environment. *American Journal of Medical Genetics, 98,* 280–282.

Hamilton, R. H., Pascual-Leone, A., & Schlaug, G. (2004). Absolute pitch in blind musicians. *NeuroReport, 15,* 803–806.

Hänggi, J., Beeli, G., Oechslin, M. S., & Jäncke, L. (2008). The multiple synaesthete E.S.—Neuroanatomical basis of interval-taste and tone-colour synaesthesia. *Neuroimage, 43,* 192–203.

Heaton, P., Davis, R. E., & Happe, F. G. (2008). Research note: Exceptional absolute pitch perception for spoken words in an able adult with autism. *Neuropsychologia, 46,* 2095–2098.

Herbert, M. R., Harris, G. J., Adrien, K. T., Ziegler, D. A., Makris, N., Kennedy, D. N., et al. (2002). Abnormal asymmetry in language association cortex in autism. *Annals of Neurology, 52,* 588–596.

Hickok, G., & Poeppel, D. (2007). The cortical organization of speech processing. *Nature Reviews Neuroscience, 8,* 393–402.

Hirata, Y., Kuriki, S., & Pantev, C. (1999). Musicians with absolute pitch show distinct neural activities in the auditory cortex. *NeuroReport, 10,* 999–1002.

Keenan, J. P., Thangaraj, V., Halpern, A. R., & Schlaug, G. (2001). Absolute pitch and planum temporale. *Neuroimage, 14,* 1402–1408.

Klein, M., Coles, M. G., & Donchin, E. (1984). People with absolute pitch process tones without producing a P300. *Science, 223,* 1306–1309.

Lawes, I. N. C., Barrick, T. R., Murugam, V., Spierings, N., Evans, D. R., Song, M., et al. (2008). Atlas-based segmentation of white matter tracts of the human brain using diffusion tensor tractography and comparison with classical dissection. *Neuroimage, 39,* 62–79.

Lee, J. E., Bigler, E. D., Alexander, A. L., Lazar, M., DuBray, M. B., Chung, M. K., et al. (2007). Diffusion tensor imaging of white matter in the superior temporal gyrus and temporal stem in autism. *Neuroscience Letters, 424,* 127–132.

Levitin, D. J. (2005). Musical behavior in a neurogenetic developmental disorder: Evidence from Williams syndrome. *Annals of the New York Academy of Sciences, 1060,* 325–334.

Levitin, D. J., & Rogers, S. E. (2005). Absolute pitch: Perception, coding, and controversies. *Trends in Cognitive Sciences, 9,* 26–33.

Lindenberg, R., Renga, V., Zhu, L. L., Betzler, F., Alsop, D., & Schlaug, G. (2010). Structural integrity of corticospinal motor fibers predicts motor impairment in chronic stroke. *Neurology, 74,* 280–287.

Loui, P., Alsop, D., & Schlaug, G. (2009). Tone-deafness: A disconnection syndrome? *Journal of Neuroscience, 29,* 10215–10220.

Loui, P., & Schlaug, G. (2009). Investigating musical disorders with diffusion tensor imaging: A comparison of imaging parameters. *Annals of the New York Academy of Sciences, 1169,* 121–125.

Luders, E., Gaser, C., Jancke, L., & Schlaug, G. (2004). A voxel-based approach to gray matter asymmetries. *Neuroimage, 22,* 656–664.

Marenco, S., Siuta, M. A., Kippenhan, J. S., Grodofsky, S., Chang, W. L., Kohn, P., et al. (2007). Genetic contributions to white matter architecture revealed by diffusion tensor imaging in Williams syndrome. *Proceedings of the National Academy of Sciences, U.S.A., 104,* 15117–15122.

Meyer, A. (1905). Aphasia. *Psychological Bulletin, 2,* 261–277.

Miyazaki, K. (1988). Musical pitch identification by absolute pitch possessors. *Perception & Psychophysics, 44,* 501–512.

Miyazaki, K. I. (1989). Absolute pitch identification: Effects of timbre and pitch region. *Music Perception, 7,* 1.

Miyazaki, K. I. (1990). The speed of musical pitch identification by absolute-pitch possessors. *Music Perception, 8,* 177.

Möttönen, R., Calvert, G. A., Jääskeläinen, I. P., Matthews, P. M., Thesen, T., Tuomainen, J., et al. (2006). Perceiving identical sounds as speech or non-speech modulates activity in the left posterior superior temporal sulcus. *Neuroimage, 30,* 563–569.

Oechslin, M. S., Meyer, M., & Jancke, L. (2009). Absolute pitch—Functional evidence of speech-relevant auditory acuity. *Cerebral Cortex, 20,* 447–455.

Ohnishi, T., Matsuda, H., Asada, T., Aruga, M., Hirakata, M., Nishikawa, M., et al. (2001). Functional anatomy of musical perception in musicians. *Cerebral Cortex, 11,* 754–760.

Oldfield, R. C. (1971). The assessment and analysis of handedness: The Edinburgh Inventory. *Neuropsychologia, 9,* 97–113.

Paulson, M. J., & Lin, T. (1970). Predicting WAIS IQ from Shipley–Hartford scores. *Journal of Clinical Psychology, 26,* 453–461.

Profita, J., & Bidder, T. G. (1988). Perfect pitch. *American Journal of Medical Genetics, 29,* 763–771.

Ramachandran, V. S., & Hubbard, E. M. (2001). Synaesthesia-A window into perception, thought and language. *Journal of Consciousness Studies, 8,* 3–34.

Ramachandran, V. S., Hubbard, E. M., Butcher, P. A., Calvert, G. A., Spence, C., & Stein, B. E. (2004). Synesthesia, cross-activation, and the foundations of neuroepistemology. In *The handbook of multisensory processes* (pp. 867–883). Cambridge, MA: MIT Press.

Ross, D. A., Gore, J. C., & Marks, L. E. (2005). Absolute pitch: Music and beyond. *Epilepsy and Behavior, 7,* 578–601.

Ross, D. A., Olson, I. R., & Gore, J. C. (2003a). Absolute pitch does not depend on early musical training. *Annals of the New York Academy of Sciences, 999,* 522–526.

Ross, D. A., Olson, I. R., & Gore, J. C. (2003b). Cortical plasticity in an early blind musician: An fMRl study. *Magnetic Resonance Imaging, 21,* 821–828.

Rouw, R., & Scholte, H. S. (2007). Increased structural connectivity in grapheme-color synesthesia. *Nature Neuroscience, 10,* 792–797.

Schaechter, J. D., Perdue, K. L., & Wang, R. (2008). Structural damage to the corticospinal tract correlates with bilateral sensorimotor cortex reorganization in stroke patients. *Neuroimage, 39,* 1370–1382.

Schellenberg, E. G., & Trehub, S. E. (2008). Is there an Asian advantage for pitch memory? *Music Perception, 25,* 241–252.

Schlaug, G., Jancke, L., Huang, Y., & Steinmetz, H. (1995). In vivo evidence of structural brain asymmetry in musicians. *Science, 267,* 699–701.

Schulze, K., Gaab, N., & Schlaug, G. (2009). Perceiving pitch absolutely: Comparing absolute and relative pitch possessors in a pitch memory task. *BMC Neuroscience, 10,* 106.

Shipley, W. C. (1940). A self-administering scale for measuring intellectual impairment and deterioration. *Journal of Psychology, 9,* 371–377.

Theusch, E., Basu, A., & Gitschier, J. (2009). Genome-wide study of families with absolute pitch reveals linkage to 8q24.21 and locus heterogeneity. *American Journal of Human Genetics, 85,* 112–119.

Wallace, G. L., Happe, F., & Giedd, J. N. (2009). A case study of a multiply talented savant with an autism spectrum disorder: Neuropsychological functioning and brain morphometry. *Philosophical Transactions of the Royal Society of London, Series B, Biological Sciences, 364,* 1425–1432.

Ward, W. D. (1999). Absolute pitch. In D. Deutsch (Ed.), *The psychology of music* (pp. 265–298). San Diego: Academic Press.

Ward, W. D., & Burns, E. (1982). Absolute pitch. In D. Deutsch (Ed.), *The psychology of music* (pp. 431–451). New York: Academic Press.

Wayman, J. W., Frisina, R. D., Walton, J. P., Hantz, E. C., & Crummer, G. C. (1992). Effects of musical training and absolute pitch ability on event-related activity in response to sine tones. *Journal of the Acoustical Society of America, 91,* 3527–3531.

Weinstein, D. M., Kindlmann, G. L., & Lundberg, E. C. (1999). Tensorlines: Advection-diffusion based propagation through diffusion tensor fields. In *Proceedings of the 10th IEEE Visualization 1999 Conference* (pp. 249–254). Washington, DC: IEEE Computer Society.

Wernicke, C. (1874). *Der aphasische Symptomencomplex.* Breslau: Cohn & Weigert.

Whitfield-Gabrieli, S., Thermenos, H. W., Milanovic, S., Tsuang, M. T., Faraone, S. V., McCarley, R. W., et al. (2009).

Hyperactivity and hyperconnectivity of the default network in schizophrenia and in first-degree relatives of persons with schizophrenia. *Proceedings of the National Academy of Sciences, U.S.A., 106,* 1279–1284.

Wilson, S. J., Lusher, D., Wan, C. Y., Dudgeon, P., & Reutens, D. C. (2008). The neurocognitive components of pitch processing: Insights from absolute pitch. *Cerebral Cortex, 19,* 724–732.

Wu, C., Kirk, I. J., Hamm, J. P., & Lim, V. K. (2008). The neural networks involved in pitch labeling of absolute pitch musicians. *NeuroReport, 19,* 851–854.

Zatorre, R. J. (2003). Absolute pitch: A model for understanding the influence of genes and development on neural and cognitive function. *Nature Neuroscience, 6,* 692–695.

Zatorre, R. J., & Beckett, C. (1989). Multiple coding strategies in the retention of musical tones by possessors of absolute pitch. *Memory & Cognition, 17,* 582–589.

Zatorre, R. J., Perry, D. W., Beckett, C. A., Westbury, C. F., & Evans, A. C. (1998). Functional anatomy of musical processing in listeners with absolute pitch and relative pitch. *Proceedings of the National Academy of Sciences, U.S.A., 95,* 3172–3177.