of a cytosolic protein 60 kD in size over a distance of 150 to 200 μm will be about 3 to 5 min. Simple diffusional signaling between the synapse and cell body could thus account for the delay in the potentiation observed in the present study. Active retrograde transport is known to take place at a rate of about 30 to 180 μm/min [R. D. Allen, J. Metuzals, I. Tasaki, S. T. Brady, S. P. Gilbert, *Science* **218**, 1127 (1985)], which would allow more rapid signaling than diffusion.

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In Vivo Evidence of Structural Brain Asymmetry in Musicians

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Certain human talents, such as musical ability, have been associated with left-right differences in brain structure and function. In vivo magnetic resonance morphometry of the brain in musicians was used to measure the anatomical asymmetry of the planum temporale, a brain area containing auditory association cortex and previously shown to be a marker of structural and functional asymmetry. Musicians with perfect pitch revealed stronger leftward planum temporale asymmetry than nonmusicians or musicians without perfect pitch. The results indicate that outstanding musical ability is associated with increased leftward asymmetry of cortex subserving music-related functions.

A number of studies have demonstrated that the left hemisphere of the brain is dominant in the production and comprehension of language in the vast majority of persons (*1*). Similar attempts to localize musical functions have yielded conflicting data, mainly because studies of amusia—that is, impairment of musical skills as a result of cerebral lesions—have failed to reveal structural-functional maps similar to those of language organization (*2*). This situation has now changed with the introduction of positron emission tomography (PET) to measure regional cerebral blood flow and metabolism during the processing of verbal and nonverbal stimuli. Whereas left hemispheric activation sites are seen during phonological, lexical, or semantic language task performance (*3*), right hemispheric preponderances are found for melodic and pitch perception, at least in musically naïve subjects (*4*). However, processing strategies may differ among individuals depending on prior musical experience (or giftedness), as suggested by PET experiments (*5*) and by behavioral (*6*) and neurophysiological (*7*) studies.

These proposed functional differences have only been related to anecdotal postmortem descriptions of gross anatomical differences in the brains of eminent musicians compared to nonmusicians as well as pronounced interhemispheric asymmetry mainly of temporal lobe structures (*8*). In an unselected postmortem sample that established an anatomical marker for cerebral asymmetry, the size of a well-defined portion of the posterior superior temporal gyrus, termed the planum temporale (PT), was larger on the left side in the majority of brains (*9*). Asymmetry of the PT has been increasingly accepted as a substrate of left hemisphere dominance for language-related auditory processing because (i) asymmetry of the PT first appears in higher primates, suggesting a relation with the evolution of language (*10*); (ii) the left PT coincides with the center of Wernicke's speech area as identified by lesion studies (*11*); (iii) macroscopic asymmetry of the PT correlates with cytoarchitectonic asymmetry of association cortices thought to play a role in higher order auditory processing (*12*); and (iv) asymmetry of the PT is correlated with handedness, with left-handers being anatomically more symmetrical (*13*).

Rightward deviation from the usual pattern of cerebral asymmetry may be associated with increased giftedness for talents for which the right hemisphere is assumed to be important (*14*). This proposed relation has been partially substantiated by connections between nonrighthandedness, atypical visuospatial lateralization, spatial giftedness, and musical talent (*15*). We have used high-resolution in vivo magnetic resonance morphometry of the PT as an index of laterality in 30 healthy, right-handed professional musicians and compared the results with those from nonmusicians matched for age, sex, and handedness (*16–18*).

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Table 1. Means (±SD) for age, degree of anatomical planum temporale asymmetry (δPT), and size of left and right PT determined with in vivo magnetic resonance morphometry in healthy, right-handed musicians and nonmusicians.

Subjects	Age	δPT†	PT size (mm^2)	
			Left	Right
Musicians (*n* = 30)	26 (4)	−0.36 (0.25)*	1063 (189)	750 (187)
Perfect pitch (*n* = 11)	27 (5)	−0.57 (0.21)**	1097 (202)	611 (105)
No perfect pitch (*n* = 19)	26 (4)	−0.23 (0.17)	1043 (183)	830 (178)
Nonmusicians (*n* = 30)	26 (3)	−0.23 (0.24)	896 (236)	736 (263)

†Negative values indicate leftward asymmetry of the PT (*16*). *P = 0.028 compared to nonmusicians. **P < 0.001 compared to musicians without perfect pitch (*21*).

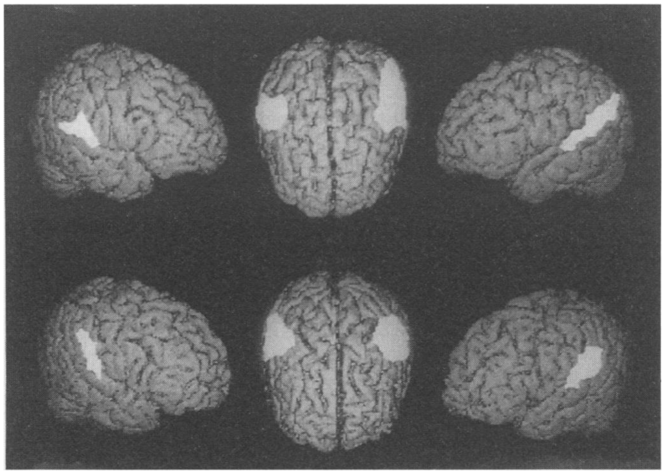

Fig. 1. Brain surface projections of the right and left planum temporale (PT) in a musician with perfect pitch (upper) and a nonmusician (lower). (Left) Views from the right; (middle) views from above with the left brain hemispheres to the reader's right; (right) views from the left. The images were reconstructed from stacks of 128 contiguous sagittal magnetic resonance image slices where the PT had been highlighted on each slice. The δPT values are −0.77 for the musician and −0.39 for the nonmusician (*16*).

We found that the PT was more lateralized to the left in musicians ($P = 0.028$). Possession of perfect pitch explained most of the variation in the degree of PT asymmetry among musicians ($P < 0.001$) (*19–21*). Musicians with perfect pitch showed stronger leftward PT asymmetry compared to other musicians, whereas musicians without perfect pitch did not differ from controls (Table 1 and Fig. 1).

Our finding of increased leftward PT asymmetry among musicians should be seen in the following context. First, PET has demonstrated that the posterior superior temporal region, including the PT, is involved in music perception (*5*). Second, in one postmortem myeloarchitectonic study of a musician with melody deafness after circumscribed brain injury, the lesion was centered on the left PT, sparing the primary auditory and inferior parietal cortex (*22*). Third, gross left-right asymmetry of the PT, as measured in our study, reflects cytoarchitectonic asymmetries of auditory association areas located on the PT (*12*). Thus, our morphometric findings in musicians may suggest that the functional capacity of cortex shown to subserve musical functions increases with leftward structural asymmetry of this neural system. This result lends anatomical support to behavioral and electrophysiological evidence of a difference in lateralization of musical processing between musicians and nonmusicians, with more left-lateralized representation in musicians (*6, 7*). Our data concur with the general concept that, because of time constraints of interhemispheric transfer, efficiency of neuronal assemblies is expected to increase with the number of elements clustered in one hemisphere (*23*). In fact, this principle may be the essence of hemispheric specialization (*23*).

Our study does not reveal the mechanism creating structural asymmetry. Leftward PT asymmetry usually appears in the human fetus between the 29th and 31st gestational week (*24*), so that prenatal factors are likely to play a role. Nevertheless, considering that the maturation of fiber tracts and intracortical neuropil, two presumed determinants of gyral shape (*25*), are still progressing by the age of seven (*26*), it remains uncertain whether gross anatomy may also be susceptible to some postnatal plastic change, such as in response to specific stimulation (*20*). Our study demonstrates that individual variability in cognitive performance can covary with features of external brain morphology.

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17. The professional musicians were recruited through announcements in three well-known music schools in Germany, as well as through personal contacts. All were classical musicians who had either finished their education or were receiving formal training at a music school. No amateur musicians were included. All string players ($n = 14$) were keyboard players as well but had a preference for string instruments; the others were keyboard players ($n = 16$). The age-, sex-, and handedness-matched nonmusicians were recruited through announcements in the local medical school. Most of them were medical students or young faculty members in university hospitals. None of them had ever played a musical instrument or received formal musical training. All subjects gave informed consent.
18. Handedness was assessed with the 12-item questionnaire of M. Annett [*Br. J. Psychol.* **61**, 303 (1970)]. Consistent right-handedness was defined as performance of all 12 tasks with the right hand, with up to two "either" preferences being acceptable. Three male musicians and three male nonmusicians were nonconsistent righthanders; all other subjects were consistent righthanders. Also, non-

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musicians and musicians did not differ in body length ($P > 0.05$).
19. No formal test for perfect pitch was applied. Subjects were asked if they would be able to sing any tone without a reference tone and if they could name any tone that was given to them without a reference tone. In those musicians who described themselves as having perfect pitch (n = 11), this information was confirmed by review of their music school examination records for pitch discrimination task performance.
20. In distinguishing between musicians with or without perfect pitch, we were guided by a study of D. Sergeant [*J. Res. Mus. Educ.* **17**, 135 (1969)] investigating the possession of perfect pitch in a large sample of professional musicians. In this study almost all musicians who began training before the age of seven had perfect pitch, but almost none of those beginning after the age of 11. Similar results were also found by others suggesting that early exposure and disposition may underly this ability [A. Bachem, *J. Acoust. Soc. Am.* **27**, 751 (1955); C. L. Krumhansl, *Annu. Rev. Psychol.* **42**, 277 (1991); M. Klein, M. G. H. Coles, E. Donchin, *Science* **223**, 1306 (1984)].
21. For statistical analysis, δPT values (*16*) were subjected to a one-way analysis of variance (ANOVA) with three levels (musicians with or without perfect pitch, and controls). In this ANOVA two planned orthogonal (linear) contrasts were computed, comparing musicians versus controls and musicians with perfect pitch versus musicians without [R. E. Kirk, *Experimental Design: Procedures for the Behavioral Sciences* (Wadsworth, Belmont, CA, 1968), pp. 69–98]. The results were as follows: orthogonal contrast for musicians versus controls: [$F(1,57) = 5.12$, $P = 0.028$]; orthogonal contrast for musicians with perfect pitch versus musicians without: [$F(1,57) = 16.18$, $P < 0.001$]. Prior to the ANOVA, a Bartlett-Box-test for homogeneity of variances of δPT had revealed no deviation from the homogeneity assumption {[$F(2,4840) = 1.25$, $P = 0.32$]}.
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TECHNICAL COMMENTS

Mammalian Vestibular Hair Cell Regeneration

Birds and mammals are born with a full complement of inner ear hair cells, which were thought to be irreversibly lost when damaged (*1*). It is now well known that birds have the capacity to regenerate hair cells in their auditory and vestibular organs after damage by acoustic trauma or ototoxic drugs (*2*) and that these new cells can mediate functional recovery (*3*). Recent studies by A. Forge *et al.* (*4*) and by M. E. Warchol *et al.* (*5*) suggest that the vestibular epithelium of the mature mammalian inner ear may also have the ability to produce new hair cells by renewed mitotic activity in response to aminoglycoside injury in vivo (*4*) and in vitro (*5*). However, these reports do not provide convincing evidence that the DNA labeling, seen at a low frequency in vitro, is the source of the apparent recovery of hair cell apical surfaces observed in vivo.

Our study was undertaken to determine if cell division can be shown to give rise to new hair cells in normal mature mammalian vestibular epithelium or during the first 6 weeks after aminoglycoside ototoxicity. Three groups of young mature albino Hartley guinea pigs were used. The experimental animals in each group were treated with a single transtympanic injection of the ototoxic aminoglycoside, gentamicin, in the left ear (*6*). Animals in each control group were given an identical volume of 0.9% saline. The first group of animals was killed after 1 to 16 weeks and used for light microscopic evaluation of damage produced in the sensory epithelium of the utricle (*7*). The second group, killed after 1 to 16 weeks, was used for scanning electron microscopy (SEM) (*8*) in order to compare our results with those of Forge *et al.* (*4*). In animals of the third group, an osmotic pump filled with [^{3}H]thymidine was implanted under the skin of the back with its output leading to a cannula inserted into the perilymphatic space before treatment with aminoglycoside (*9*). These animals were killed after 1 to 16 weeks (*10*).

Hair cell damage and loss was evident in the light microscopic sections and SEM analyses of tissue from gentamicin-treated animals (Fig. 1). Experimental animals had fewer hair cells than controls, particularly in the striolar region. Other signs or damage observed by light microscopy of SEM included nuclear pyknosis, nuclear swelling, vaccuolization, cytoplasmic extrusion, and stereocilia fusion. The extent of damage was variable at all survival times. At 1 or 2 weeks after gentamicin treatment, hair cell injury was limited primarily to the striolar region in 10 of 16 animals examined by SEM. In three of the animals damage was observed over a larger area, extending from the striola toward the periphery of the organ. Complete destruction of the sensory hair cells was observed in the remaining three animals. Four weeks after gentamicin administration, one animal displayed hair cell damage extending out from the striolar region; in the other animal blebbing and fusion of stereocilia were seen over the entire surface of the sensory epithelium. In the animal killed 4 months after gentamicin, the surface of the utricle continued to show damaged stereocilia bundles throughout the entire sensory epithelium. The average length of the sensory epithelium and the linear support cell density remained constant between the control and experimental animals (Table 1) (*11*). However, the linear hair cell density was 51 to 85% lower in experimental animals than controls ($P < 0.001$).

Table 1. Results of treatment with gentamicin on guinea pig utricle: Length of sensory epithelium, hair cell density, and support cell density. Measurements are averages (± standard deviation).

Animal number	Treatment (weeks)	Sensory epithelium length (× 0.1 mm)	Hair cell density (per 0.1 mm)	Support cell density (per 0.1 mm)
94-01	1	7.2 (±2.0)	1.6 (±0.7)	11.6 (±4.6)
94-13	1	9.3 (±2.1)	3.4 (±0.8)	9.9 (±3.1)
93-42	1	7.2 (±1.6)	2.6 (±1.4)	10.4 (±1.5)
94-06	4	7.4 (±1.5)	1.3 (±1.5)	8.4 (±1.5)
94-05	6	8.7 (±2.0)	1.6 (±0.6)	7.1 (±1.6)
93-55	6	7.2 (±1.9)	4.3 (±0.8)	10.7 (±2.8)
93-57	0*	7.4 (±1.6)	8.7 (±1.7)	12.6 (±3.3)
93-38	6*	8.9 (±2.1)	6.6 (±1.9)	10.2 (±1.2)

*Control group received no gentamicin.

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