rats without metyrapone treatment. These findings strongly suggest that the metyrapone-induced attenuation of retention impairment is due to inhibition of corticosterone synthesis.

The retention-probe trial findings confirm previous reports that CA3 lesions impair retention of water-maze spatial training (H.-A. Steffenach, E.I. Moser & M.-B. Moser, *Soc. Neurosci. Abstr.* **25**, 649.4, 1999)[5] and elevate plasma corticosterone[2,3]. We found that normalizing corticosterone levels at the time of the probe trial is sufficient to block the retention impairment induced by CA3 damage. These findings strongly suggest that CA3 damage-induced retention deficits of this magnitude are due to influences on memory retrieval mediated by HPA-axis dysregulation. We reported previously that acute exposure to stress of glucocorticoids shortly before retention testing impairs memory retrieval[6,8]. Importantly, the plasma corticosterone elevation obtained with CA3 lesions was highly comparable to levels produced by doses of acutely administered corticosterone that induce memory retrieval impairment in intact rats[6,8]. Furthermore, our finding that the CA3 lesions did not impair acquisition performance is congruent with previous evidence indicating that glucocorticoids do not impair acquisition or immediate recall[6,8]. The effects of hippocampal damage on hypersecretion of glucocorticoids are temporary and dissipate after several weeks (rodents) or months (primates)[9]. It is not yet known whether the cognitive deficits induced by lesioning of the CA3 recover with the same time course. The present findings may have implications for understanding the complex relationship between glucocorticoids, hippocampal integrity and memory function. Prolonged exposure to stress levels of glucocorticoids can induce atrophy of CA3 pyramidal neurons and reduce hippocampal volume, changes associated with cognitive impairments[10–12]. Our findings suggesting that such cognitive impairments result directly from elevated glucocorticoid levels or HPA-axis dysregulation may contribute to the development of new strategies in the treatment of memory disorders following hippocampal damage or sustained hypercortisolemia.

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Visual stimuli activate auditory cortex in the deaf

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Previous brain imaging studies have demonstrated responses to tactile and auditory stimuli in visual cortex of blind subjects, suggesting that removal of one sensory modality leads to neural reorganization of the remaining modalities[1–3]. To investigate whether similar 'cross-modal' plasticity occurs in human auditory cortex, we used functional magnetic resonance imaging (fMRI) to measure visually evoked activity in auditory areas of both early-deafened and hearing individuals. Here we find that deaf subjects exhibit activation in a region of the right auditory cortex, corresponding to Brodmann's areas 42 and 22, as well as in area 41 (primary auditory cortex), demonstrating that early deafness results in the processing of visual stimuli in auditory cortex.

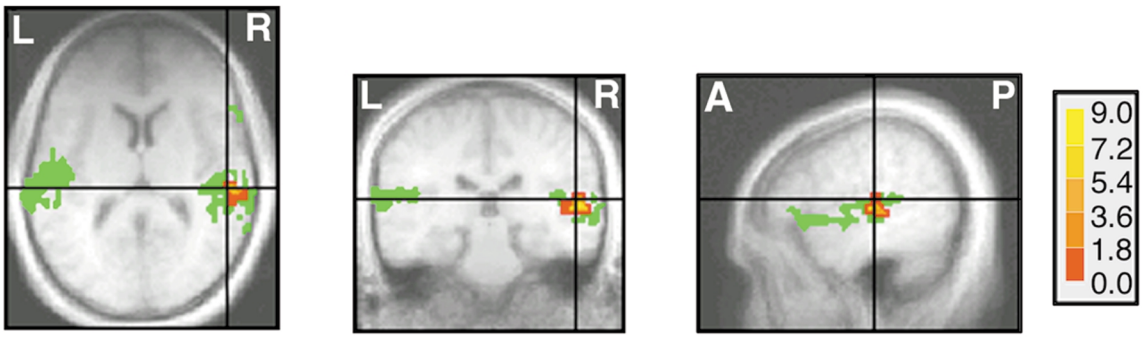

Fig. 1. Visual stimuli activate auditory cortex in the deaf. Shown is an anatomical scan averaged across all deaf and hearing subjects. Auditory regions of interest (ROIs, green regions) and voxels activating differentially in deaf versus hearing subjects in response to the visual motion stimulus (colors defined in scale bar) are shown on axial (left), coronal (middle) and sagittal (right) sections of an averaged anatomical brain, transformed into the standard stereotaxic space of Talairach and Tournoux[5]. The area of visual responsiveness falls within Brodmann's areas 41, 42 and 22 in the right auditory ROI. Crosshairs highlight a voxel within the area of main effect that maps to Brodmann's area 41 (primary auditory cortex). Scale bar indicates the functional intensity (FIT) value, or magnitude of activation. L, left; R, right; A, anterior; P, posterior side of brain.

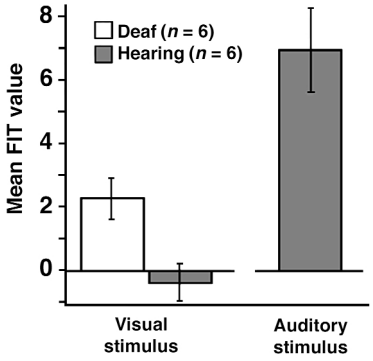

Fig. 2. Mean activation in deaf versus hearing subjects to visual stimuli. Mean functional intensity (FIT) values, corresponding to magnitude of activation, for deaf (white bars) and hearing (gray bars) subjects within the area of main effect shown in Fig. 1. Visual stimuli produced significant activation in deaf but not hearing subjects. For comparison, auditory-evoked activity in this region of hearing subjects is also shown. Error bars denote standard errors of the means.

Six profoundly deaf and six hearing subjects were tested (3 females in each group; deaf, 27.0 ± 5.7 years old; hearing, 26.8 ± 2.6 years old). All subjects were right handed with normal or corrected-to-normal vision. All protocols were conducted in compliance with the University of California at San Diego's Human Subjects Committee Institutional Review Board. Using fMRI (AFNI software[4], 1.5 T BOLD; 28 slices; TR, 4 s; voxel size, $3 \times 3 \times 6$ mm), we defined an auditory region of interest (ROI) by measuring responses elicited by auditory stimuli (music sequences) in our hearing subjects. In Fig. 1, auditory ROIs (green regions) are plotted on an anatomical scan averaged across all deaf and hearing subjects, after transforming individual anatomies into standard Talairach and Tournoux coordinate space[5]. Based on Talairach and Tournoux coordinates, auditory stimuli were found to activate regions in both right and left auditory cortex, including Brodmann's areas 41, 42 and 22, although, consistent with known hemispheric asymmetries for music processing[6], the total volume of the right auditory ROI (26.1 cm^3) was larger than that of the left (14.5 cm^3). Analysis of visually evoked fMRI responses was limited to within these functionally defined auditory ROIs.

Our visual stimulus consisted of a moving dot pattern (size, 10° diameter; speed, 7°/s; dot luminance, 590 candelas/m^2 against a black background; dot size, 0.2°; dot density, 2.7%; percent dots moving coherently, 87%). On alternate runs, the stimulus was presented in either the right or left visual field (15° eccentric to a central fixation spot). The two subject groups performed comparably on a dimming task on the motion stimulus to control for attentional state (deaf, 91.5 ± 12.2% correct; hearing 94.0 ± 2.9%; deaf, 609 ± 107 ms reaction time; hearing, 654 ± 255 ms). Visually evoked activity within the right and left auditory ROIs was computed by correlating fMRI signal amplitude in individual ROI voxels to a reference function corresponding to the time course of the visual stimulus, after first correcting for individual subject movements in six dimensions by realigning images to a single reference image.

Visually evoked activity significantly differed between deaf and hearing subjects in the right auditory ROI (**Fig. 1**, colors defined in scale bar, main effect of subject group, $F_{1,10} = 11.12$, $p = 0.0038$), encompassing a volume of 0.95 cm^3. Although differences were also observed in the left auditory ROI, the region of effect was extremely small (0.054 cm^3) and did not survive stringent statistical standards for safeguarding against false positives. Within the right ROI region of main effect, the visual stimulus caused significant activation in deaf subjects (**Fig. 2**), with a mean functional intensity (FIT, which reflects the magnitude of activation) value of 2.26 ± 1.37 ($p = 0.0049$), whereas no significant activation occurred in hearing subjects (mean FIT, –0.31 ± 1.30, $p = 0.59$). In comparison, the mean FIT value produced by auditory stimuli in these same voxels within hearing subjects was 6.90 ± 2.65 ($p = 0.0069$). Based on Talairach and Tournoux coordinates, this region of visual activation in the deaf corresponds to Brodmann's areas 42 and 22 (secondary and association auditory areas, respectively), which includes part of the planum temporale. In addition, several voxels (0.22 cm^3, ~23% of the total region of effect) fell within area 41 (primary auditory cortex), which encompasses the medial portion of Heschl's gyrus. We also cross-checked these coordinates against probabilistic atlases[7,8] and confirmed that our region of effect included both A1 and the planum temporale. There was no main effect of visual field or interaction between visual field and subject group within this region.

In a second version of these experiments, we collected fMRI responses when subjects were instructed to ignore the motion stimulus and instead perform a dimming task on the fixation spot. Here, deaf and hearing subjects differed significantly ($F_{1,10} = 4.09$, $p = 0.036$) within a region of the right auditory ROI (0.54 cm^3, a subset of the region of difference obtained from the attend condition) that mapped onto area 42. Deaf subjects exhibited significant activity in this region (FIT coefficient, 2.85 ± 2.91, $p = 0.031$) and, as before, hearing subjects did not (FIT coefficient, 0.175 ± 1.43, $p = 0.78$). The smaller region of effect observed under the ignore condition is consistent with the general tendency for sensory cortical areas to activate less strongly to ignored than attended stimuli[9,10]. Nonetheless, the fact that visual activation in auditory cortex was observed in deaf subjects even when the motion stimulus was ignored attests to the robustness of the cross-modal plasticity effect.

Related to the present findings, results from previous fMRI and positron emission tomography studies have suggested that the auditory regions in which we found visual activation in the deaf include areas that may also be involved in visual language processing in both deaf and hearing subjects. Specifically, Brodmann's areas 42 and 22 in deaf subjects are activated to visual images of sign language[11,12], and these same areas are activated in hearing subjects during a silent lip reading task[13] (and during auditory speech tasks[13]). In addition, there has been previous suggestion that these auditory areas may be used for processing purely visual (that is, non-linguistic) stimuli in the deaf. However, these earlier studies used techniques with poor spatial resolution, such as electroencephalography, that could not distinguish whether visual responses in deaf subjects originated from auditory cortex or nearby visual areas[14].

In sum, the results of the present study using fMRI demonstrate the recruitment of auditory cortex in the deaf for the processing of purely visual stimuli. The cross-modal plasticity observed in the present study appeared predominantly in the right auditory cortex. Because our experiment used moving visual stimuli, this hemispheric asymmetry may simply reflect a predisposition for motion processing in the right auditory cortex. This possibility is supported by the finding that in hearing subjects, the right auditory cortex (specifically, the planum temporale) is specialized for processing auditory motion[15]. Thus, right auditory cortex in the deaf, devoid of its normal auditory input,

may come to serve motion processing in the visual modality. Remarkably, the reciprocal result has recently been reported in blind subjects. Here, responses to moving auditory stimuli are observed predominantly in the right visual cortex of the blind[2], again suggesting a predisposition toward motion processing in the right hemisphere. Most importantly, our demonstration of cross-modal plasticity in deaf subjects, in conjunction with that observed in the blind, attests to the robust ability of the human brain to reorganize in response to the removal early in development of input from one sensory modality.

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