

Supplemental Methods and Results

Psychological Assessment

The VLMT was extended by instructing participants to remember the items in the correct order if possible, and additionally analyzing scores for absolute (counting correct responses up to the first error) and relative (counting all responses where a correct sequence of minimum two items was reported) temporal order memory. Performance in the VLMT was analyzed by calculating the t-scores for the memory components “Learning”, “Consolidation” and “Recognition”, as well as the temporal order scores separately in the pre and post session. Separate mixed-design Analyses of Variance (ANOVAs) were used to analyze training-related differences in the VLMT t-scores and temporal order scores with the between-subject factors training condition (auditory, tactile, control) and group (congenitally blind, sighted) and the within-subject factor session (pre, post). For the VLMT t-scores the additional factor memory component (Learning, Consolidation, Recognition) and for the VLMT temporal order scores the additional factor type (absolute, relative) were added. Bonferroni correction was used to control for multiple comparisons.

ANOVAs performed on the VLMT t-scores were used to test differences between the blind and sighted participants in verbal working memory and verbal temporal order working memory. The analysis showed a main effect of memory component, with higher t-scores for Learning and Recognition compared to Consolidation across groups, training conditions and sessions ($F(2,92) = 6.62, p < .0100, \eta^2_p = .13$). There was an interaction between the factors memory component and the group ($F(2,92) = 3.36, p < .0500, \eta^2_p = .07$), whereas blind participants showed higher values for the memory components Learning and Recognition, but not for the component Consolidation compared to the sighted. However, post hoc tests did not show significant differences between blind and sighted participants for any memory component (Bonferroni corrected $\alpha = .0167$; Learning, $p = .0993$; Consolidation; $p = .9739$; Recognition, $p = .2170$). The ANOVA performed on the VLMT temporal order scores showed a main effect of type ($F(1,47) = 196.5, p < .0010, \eta^2_p = .81$), with overall higher relative compared to absolute temporal order scores across groups, sessions and training conditions. Importantly, the blind participants showed overall higher temporal order scores compared to the sighted (main effect group: $F(1,47) = 5.40, p < .0500, \eta^2_p = .10$).

In a working memory strategy questionnaire, participants indicated whether they used any of the following strategies: verbal memorization (verbal), internal rehearsal (rehearsal), internal sequencing (sequencing), story telling, visual imaging, spatial imaging, episodic memorizing, or/and whether they performed the task intuitively, or whether they had no strategy. Differences in the reported working memory strategies (verbal, rehearsal, sequencing, story telling, visual imaging, spatial imaging, episodic memorizing, intuitive, no strategy) between groups (sighted versus congenitally blind participants) and the different training conditions (auditory, tactile, control) were tested using Fisher’s exact tests (2-tailed).

Congenitally blind and sighted participants showed no differences in working memory strategies (strategy x group interaction: verbal: $p = .2075$; rehearsal: $p = .2399$; sequencing: $p = .4736$; story: $p = .0847$; visual: $p = .3797$; spatial: $p = .8094$; episodic: $p = .2028$; intuitive: $p = .1584$;

no: $p = .1451$). However, overall participants in the different training conditions differed in whether they used verbal working memory strategies (verbal strategy x training: $F(2) = 6.39$, $p < .0500$; descriptively more participants chose this strategy in the auditory and tactile training condition); and differed in whether they responded intuitively (intuitive strategy x training; $F(2) = 6.41$, $p < .0500$; descriptively participants in the tactile training condition used this strategy the least). There were no further differences in strategy usage between participants of the different training conditions (strategy x training condition interaction: rehearsal; $p = .0554$; sequencing: $p = .3629$; story: $p = .7641$; visual: $p = .2920$; spatial: $p = .3200$; episodic: $p = .3475$; no: $p = .0510$).

Pre-Training Baseline Differences between Blind and Sighted

The same analysis procedure as applied to the 2-back pre-training data contrasted with the RS data was applied to the pre-training connectivity and power data recorded during the RS to access baseline differences in power and connectivity between blind and sighted participants.

Differences in baseline (pre-training resting state) connectivity and power between the blind and sighted were present in the beta-band. The blind participants showed reduced beta-band connectivity compared to the sighted between the occipito-temporal ROI and parts of the visual cortex (Fig. S2 B; $Q = 0.2$; FDR corrected $\alpha = .0091$; p -values $< .0091$). There were no differences at any other ROI or frequency band ($Q = 0.2$; beta-band at all ROIs FDR corrected $\alpha = .0001$, at frontal, parietal, insula, temporal ROIs p -values $\geq .0065$, $\geq .0004$, $\geq .0003$, $\geq .0001$; theta-band at all ROIs FDR corrected $\alpha = .0001$, at frontal, parietal, insula, temporal, occipito-temporal ROIs p -values $\geq .0008$, $\geq .0067$, $\geq .0013$, $\geq .0008$, $\geq .0001$; gamma-band band at all ROIs FDR corrected $\alpha = .0001$, at frontal, parietal, insula, temporal, occipito-temporal ROIs p -values $\geq .0332$, $\geq .4921$, $\geq .0209$, $\geq .2168$, $\geq .4324$). Furthermore, the congenitally blind showed reduced beta-band power, mainly in parts of the visual cortex (Fig. S2 C; FDR corrected $\alpha = .0163$; p -values $< .0163$). There were no power effects in any other frequency band ($Q = 0.2$; at the theta- and gamma-band FDR corrected $\alpha = .0001$; theta-band: p -values $\geq .0046$; beta-band: p -values $\geq .0003$). The findings suggest reduced local connectivity and activity in the visual cortex of congenitally blind individuals, and are consistent with a previous study (Hawellek et al. 2013).

Power Differences at the ROIs

In order to retrieve time frequency maps of the source power at each ROI (Fig. S4 A, B), cross-spectra were computed over the delay (-1 to -0.2 s pre-stimulus) and the encoding time window (0 to 0.7 s post-stimulus) and not averaged across segments. Note, that here we display the encoding time window to provide insights into the auditory stimulus processing. All analysis however focuses on the delay window, as the encoding window is superimposed by the participant's responses. Source power was computed separately for each time point. The source power contrast between pre and post session was averaged across all voxels of each ROI separately. For a detailed description see *Materials and Methods* section. For statistical analyses source power was averaged across the time points of the delay window.

Mixed-design ANOVAs with the between-subject factors group (blind, sighted), training conditions (auditory, control) and the within-subject factors ROIs (frontal, parietal, insula,

temporal, occipito-temporal), and frequency-bands (theta-, beta-, gamma-band) were performed to test whether training-related changes in power at the ROIs differed between the sighted and blind group.

There was a significant main effect of group ($F(1,32) = 5.33$, $p < .0500$, $\eta^2_p = .14$), whereas sighted participants compared to the blind showed an overall higher power increase across sessions. Power changes varied across frequency-bands (main effect frequency-band: $F(2,64) = 5.5$, $p < .0500$, $\eta^2_p = .15$). Power overall increased significantly stronger in the theta-band compared to the gamma-band, where it decreased from the pre- to the post-training session. Increases in the beta-band did not significantly differ from the other frequency bands (post hoc paired-sample t-tests, Bonferroni corrected $\alpha = .0167$; theta- vs. gamma-band: $p = .0128$; beta- vs. gamma-band, $p = .0176$; theta- vs. beta-band: $p = .1587$). There were no significant interactions.

Correlation between the Speech Acoustics and the Neuronal Signal

An additional analysis was performed to test whether the recruitment of the visual cortex in congenitally blind individuals during the auditory working memory delay period results from the fact that the visual cortex is processing some aspects of the speech signal. In sighted participants, slow neuronal activity (theta-band) in the auditory cortex has been shown to correlate with the speech envelope during speech comprehension (e.g. Luo and Poeppel 2007; Peelle et al. 2012). Such *speech-tracking* might occur in the absence of a speech stimulus during internal rehearsal-like processing such as mental imagery (Tian and Poeppel 2012).

The envelope of the speech waveform (length: 0.45 s) and the neural signal (delay and encoding window: -1 to 0.7 s) at the temporal ROI and the occipito-temporal ROI were band-pass filtered using a 2nd order Butterworth filter, either in the theta-band (2.5-5 Hz) or in the beta-band (17.5-22.5 Hz) (Fig. S 6). Therefore, first, the envelope of the speech waveform was calculated as the absolute of the Hilbert transform of the signal separately for each of the 10 speakers. The envelope was down sampled (500 Hz) and band-pass filtered. The filtered envelopes were averaged across speakers. In a first step, the neural signal was projected to source space based on the individual Nx3 spatial filter for three orthogonal dipole orientations, and in a second step the dipole orientation was chosen as the one which maximizes the power for each voxel for the specific frequency band (for details of the spatial filter: *Materials and Methods* section). Then, the neural signal was filtered and averaged across all voxels of each ROI (temporal, occipito-temporal). Iterative (time shift: 0.01 s) Spearman's rank-correlations between the filtered speech signal and the filtered neuronal signal were performed across trials separately for each ROI, each frequency band, the pre and post session, the auditory training and control condition and the congenitally blind and sighted.

As expected from previous literature (Luo and Poeppel 2007; Peelle et al. 2012), during the encoding period (0-0.7 s post-stimulus) significant correlations were observed (p-values $< .0500$; r-values between -0.57 and 0.65) between neural activity in the theta-band at the temporal ROI and the speech acoustics in both the congenitally blind and sighted, for pre and post sessions and all training conditions. Although, there were a few data points in the theta-band at the occipito-temporal ROI in both groups with p-values $< .0500$, the r-values were very small (between -0.2 and 0.18), and should be interpreted cautiously. In the delay window we found no significant correlations at any ROI or frequency band. These findings do not provide any evidence that the

recruitment of visual cortex in the congenitally blind was related to the auditory processing of the speech signal.

Supplemental References

Hawellek DJ, Schepers IM, Roeder B, Engel AK, Siegel M, Hipp JF. 2013. Altered Intrinsic Neuronal Interactions in the Visual Cortex of the Blind. *J Neurosci.* 33:17072–17080.

Luo H, Poeppel D. 2007. Phase patterns of neuronal responses reliably discriminate speech in human auditory cortex. *Neuron.* 54:1001–1010.

Peelle JE, Gross J, Davis MH. 2012. Phase-locked responses to speech in human auditory cortex are enhanced during comprehension. *Cereb Cortex.* in press.

Tian X, Poeppel D. 2012. Mental imagery of speech: linking motor and perceptual systems through internal simulation and estimation. *Front Hum Neurosci.* 6:314.

Supplemental Figures and Tables

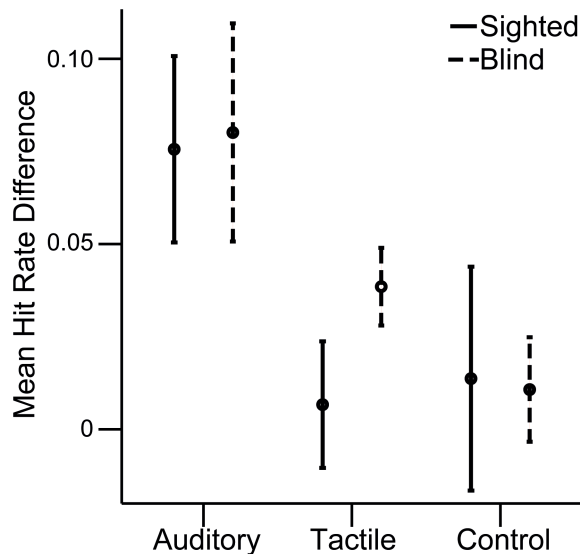


Figure S 1 Working Memory Training with Voices Increased Performance The post-minus-pre-training session differences in hit rate are displayed separately for the congenitally blind and sighted participants and the training conditions (auditory: working memory training with voices; tactile: working memory training with tactile motion stimuli; control: training-control condition). The only significant increase in hit rates was observed for participants with working memory training with voices (auditory) in both congenitally blind and sighted participants.

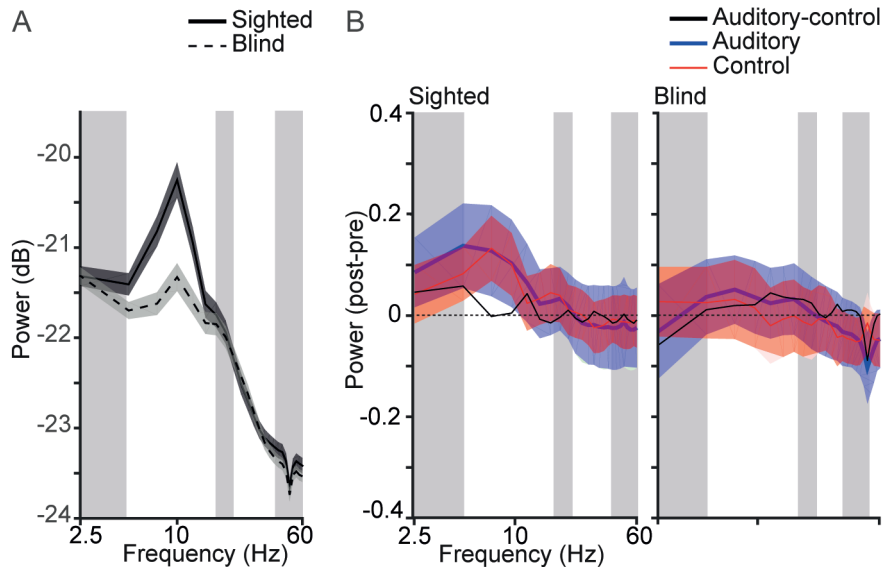


Figure S 2 Power Spectrum (A) The mean overall power spectrum (SE, shaded area) is displayed in dB separately for the sighted (black line) and the congenitally blind (black dashed line) participants. Power values were averaged across all voxels, across pre- and post-training 2-back sessions and across participants of all training conditions. Overall, the congenitally blind show reduced alpha-band power compared to the sighted. (B) The mean power spectrum (SE, shaded area) across sessions (contrast post/pre session) is displayed separately for the sighted (left) and congenitally blind (right) and for the auditory working memory training (Auditory), the training-control condition (control) and the difference

between the auditory training and training-control conditions (Auditory-control). Power values were averaged across all voxels separately for each participant. Alpha-band power was similar across training conditions, suggesting that the difference in alpha-band power between sighted and congenitally blind was not related to the working memory training. In (A) and (B) the gray transparent boxes indicate the frequency bands used for the analysis: theta (2.5-5 Hz), beta (17.5-22.5 Hz) and gamma (40-60 Hz). The x-axis is logarithmically scaled.

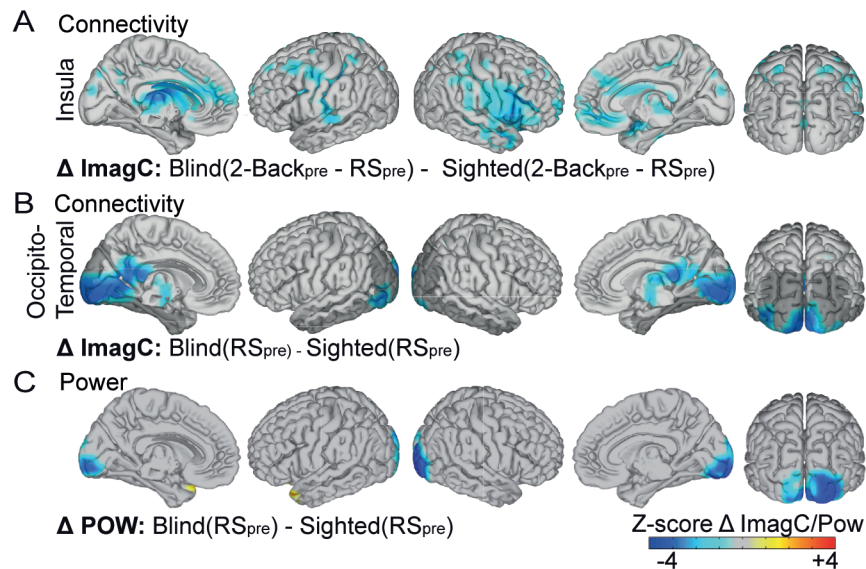
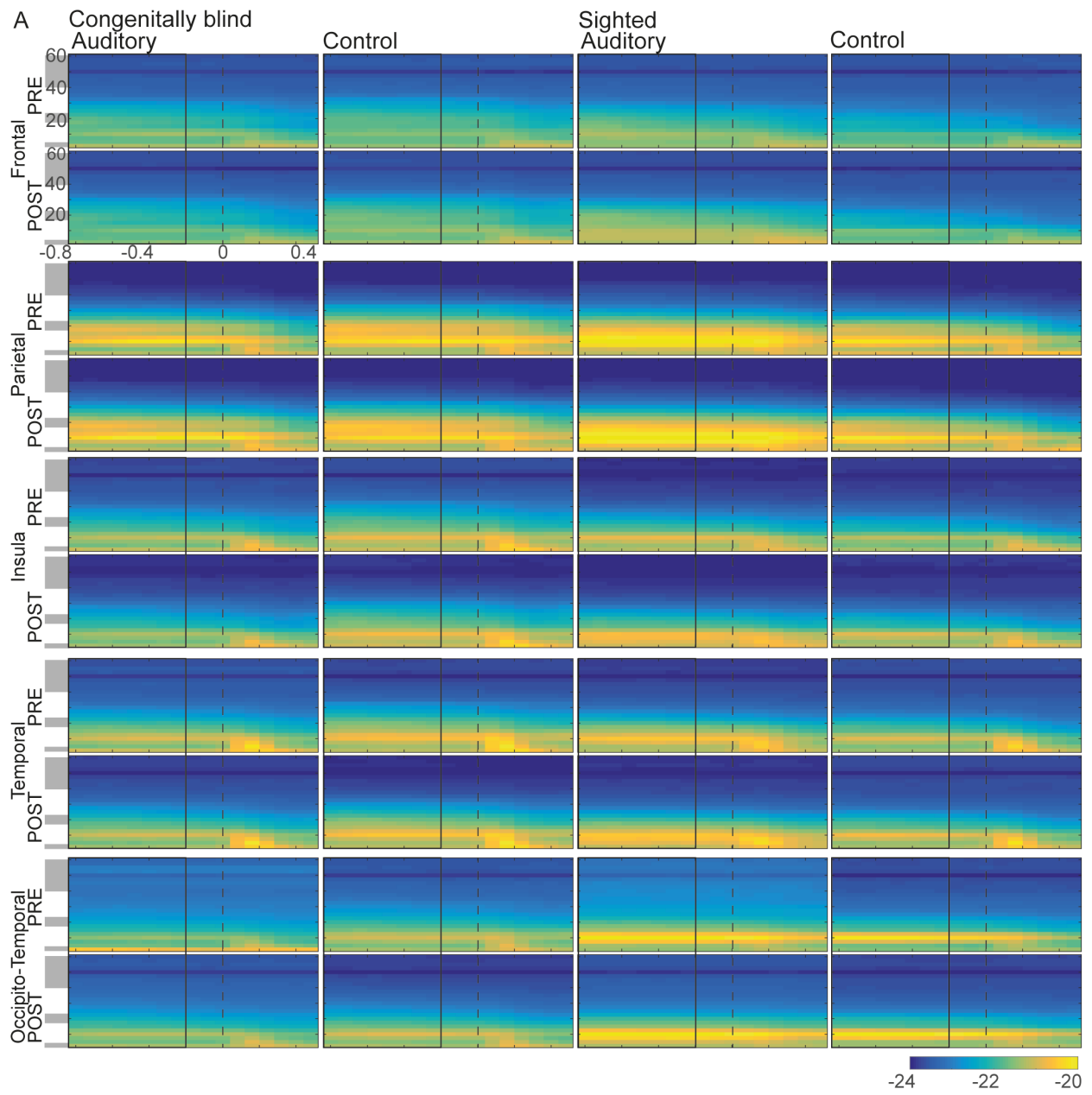


Figure S 3 Pre-Training Differences Between Congenitally Blind and Sighted (A) Congenitally blind participants compared to the sighted showed reduced (auditory 2-back task, contrasted to the resting state data) connectivity in the theta-band between the insula ROI (displayed in dark transparent gray) and the voxels displayed in color. Smaller connectivity values in the blind compared to the sighted participants are displayed in blue. (B) The baseline (pre-training resting state) connectivity in the beta-band between the occipito-temporal ROI and the voxels displayed in color was reduced in congenitally blind participants compared to sighted participants. (C) The baseline (pre-training resting state) power in the beta-band was reduced in congenitally blind participants compared to sighted participants in visual brain areas. In (A-C) connectivity/power differences are displayed as z-scores (differences/contrasts divided by the SD of the permutations).



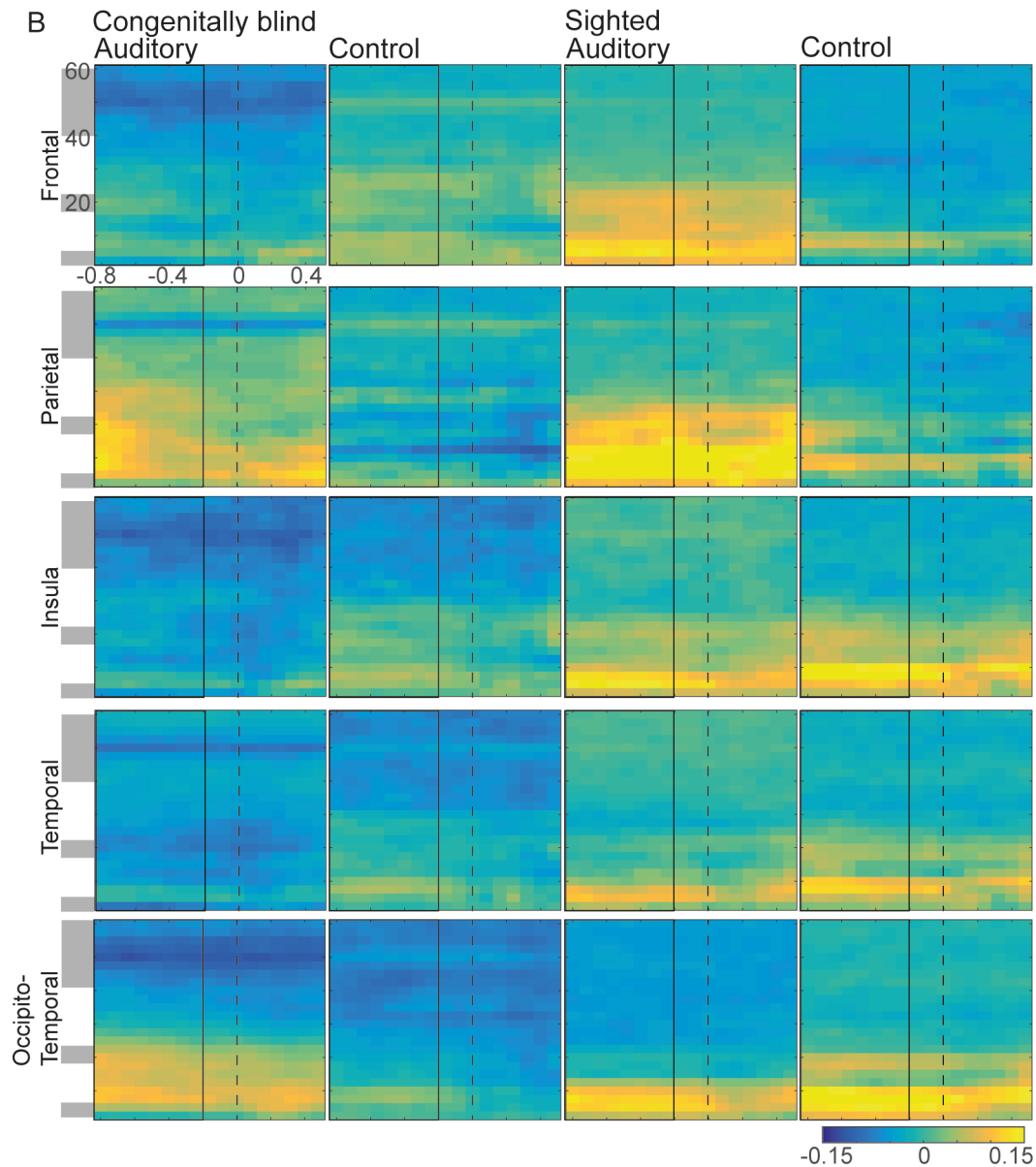
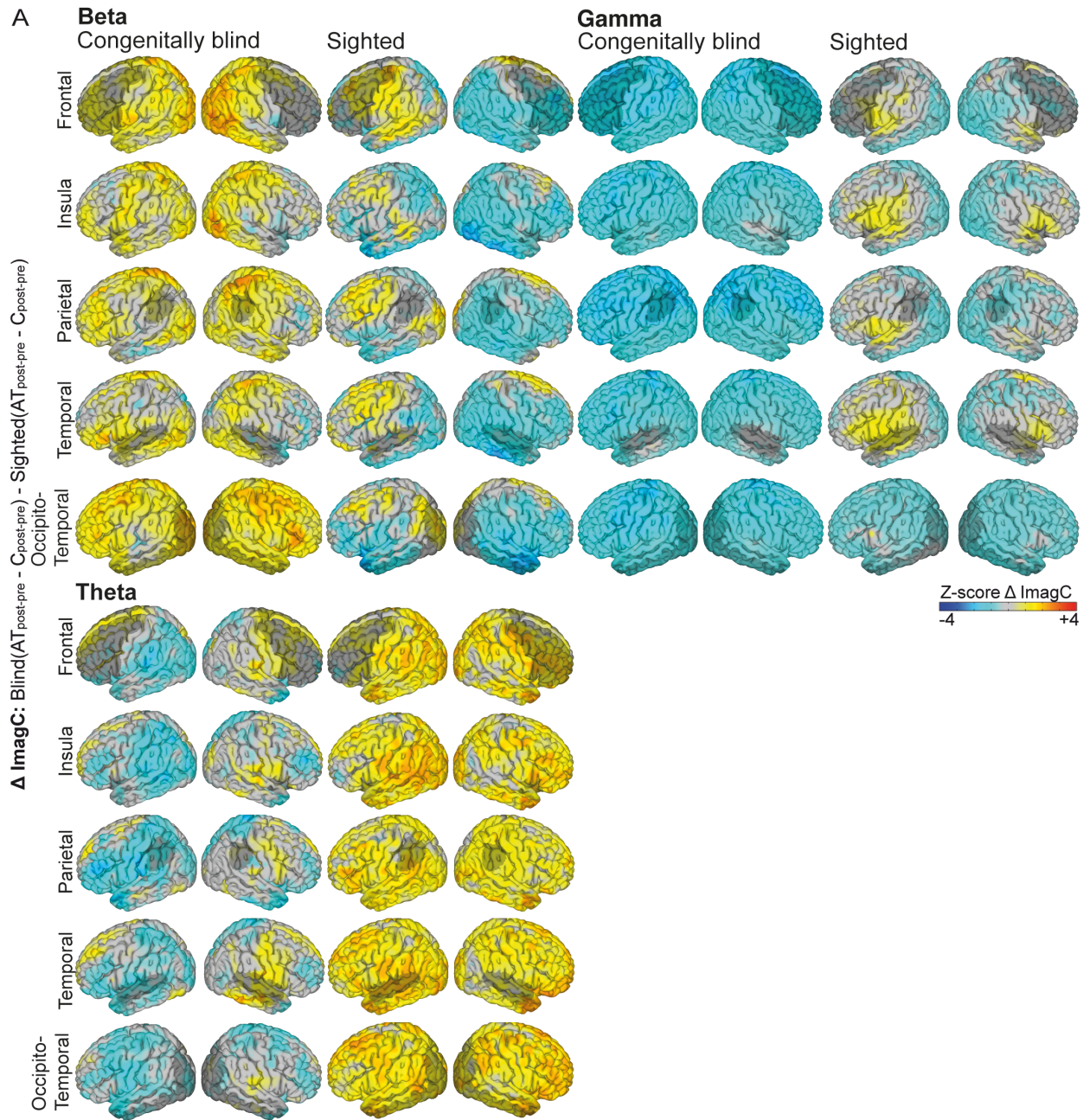


Figure S 4 Time-frequency maps of the power changes at each ROI (A) The logarithmized power is displayed separately for each ROI (rows), the pre and post sessions (labeled on the left), the training conditions (columns) and the congenitally blind (left) and sighted (right) participants for the delay and encoding window. A black box indicates the delay window (-0.8 to -0.2 s pre-stimulus) and a black dashed line the stimulus onset (encoding window: 0 to 0.5 s). Gray bars on the left indicate the analyzed frequency bands (theta, beta, gamma). In the delay window, continuous power in a narrow beta- and theta-band is visible at some ROIs (e.g., theta-band: frontal, insula, temporal and occipito-temporal; beta-band: insula, temporal and occipito-temporal). Continuous, broadband gamma-band activity is visible at all ROIs. Auditory stimulus processing can be seen in the low-frequency bands in the encoding window. (B) The power contrast across pre-post sessions is displayed separately for the congenitally blind and sighted, each training condition and each ROI. In the delay window, power changes across session were continuous. Although, power changes were overall larger in the sighted compared to the blind and in lower frequency bands compared to higher bands, the training conditions did not affect power significantly differently in the congenitally blind and sighted (supplemental methods).



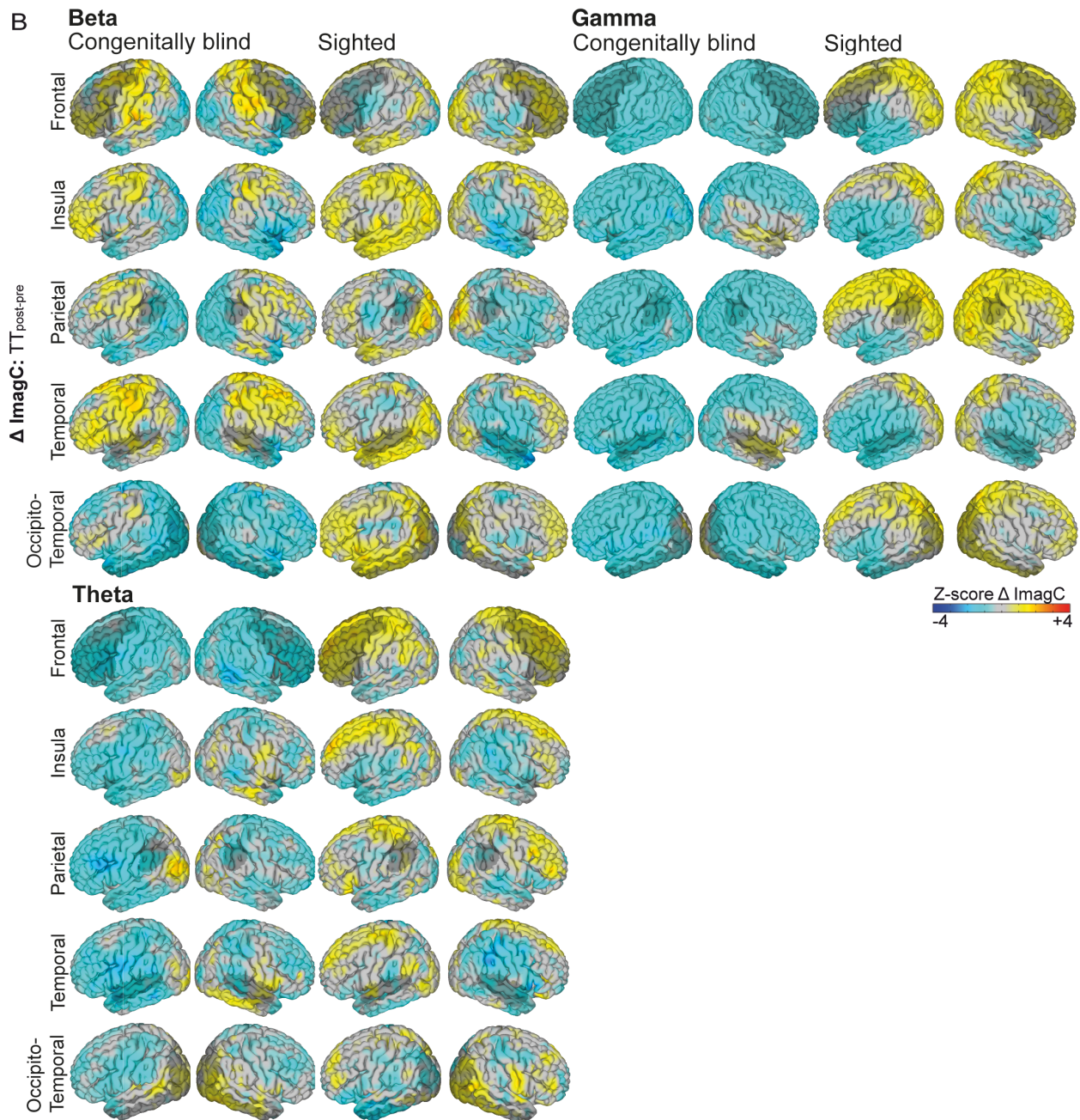


Figure S 5 Unthresholded theta-, beta- and gamma-band connectivity (A) The post-minus-pre connectivity between training conditions (auditory-minus-control; AT, auditory training; C, control condition) is displayed at all ROIs and frequency bands, separately for the congenitally blind and sighted participants. The connectivity differences are displayed as z-scores (connectivity differences divided by the SD of the permutations). Congenitally blind participants showed training-related increases in connectivity in the beta-band compared to the sighted between the frontal, insula, temporal and occipito-temporal regions of interest (ROIs; displayed in dark transparent gray) and the voxels displayed in red. Sighted participants showed increased training-related connectivity in the theta-band compared to the congenitally blind between the frontal, parietal, insula, and temporal ROIs (displayed in dark transparent gray) and the voxels displayed in red. There were no significant group and training condition differences in the gamma-band. Each row shows connectivity for the ROI labeled on the left. (B) The post-minus-pre connectivity in the tactile training (TT) condition is displayed at all ROIs and frequency bands, separately

for the congenitally blind and sighted participants. Note that neuronal data of this training condition were not analyzed.

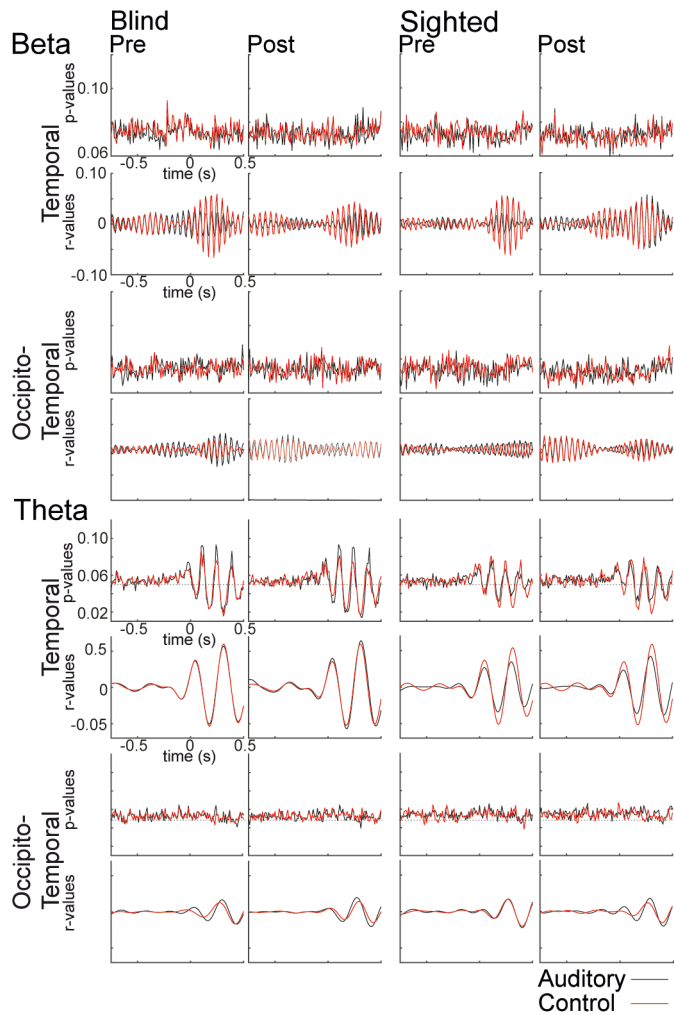


Figure S 6 Correlation between the Speech Acoustics and the Neuronal Signal The iterative Spearman's rank-correlations (r - and p -values) between the speech waveform and the neural signal are displayed across time (window: 0.45 s; shift: 0.01 s; epoch: -1 to 0.7) in the theta- (2-7 Hz) and beta-band (17-24 Hz) at the temporal and the occipito-temporal ROI (labeled on the left) separately for the pre/post session (columns), the training conditions (auditory training condition: red; control condition: black) and the congenitally blind and sighted (columns). A dashed line indicates the significance level ($p = 0.05$). The speech waveform correlated significantly with the neuronal signal in the theta-band at the temporal ROI in all sessions, training conditions and groups. No correlations were observed in the delay window.

Table S1 Experimental Procedure

| <u>Pre MEG/EEG</u> | | Behavioral Training | | <u>Post MEG/EEG</u> | <u>MRI</u> |
|------------------------------|--|--------------------------------|---------------------------------|------------------------------|---------------------------------|
| Session 1-2 | | Session 3-6 | | Session 7-8 | Session 9 |
| All participants (n = 54) | <u>Auditory</u> Training (n = 9) | Tactile Training (n = 9) | Training- Control (n = 9) | All participants (n = 54) | All participants (n = 54) |
| <u>Resting State1</u> | | | | <u>Resting State1</u> | <u>MRI</u> |
| <u>Auditory</u> | Auditory | Tactile | Auditory | <u>Auditory</u> | |
| <u>2-Back Task</u> | n-Back Task | n-Back Task | 1-Back Task | <u>2-Back Task</u> | |
| | | | | n-Back Task | DTI |
| Tactile | | | Tactile | Tactile | |
| 2-Back Task | | | 1-Back Task | 2-Back Task | |
| | | | | n-Back Task | |
| <u>Resting State2</u> | | | | <u>Resting State2</u> | |

^aAbbreviations: MEG, magnetoencephalography; EEG, electroencephalography; MRI, magnetic resonance imaging; Pre, prior to the training; post, after the training; The session were data is reported in the current study are underlined;

S2 Table Regions of Interest Description

| ROI Label | Atlas Labels | Number of Voxels |
|-------------------|---------------------|------------------|
| Frontal | Frontal_Inf_Tri_L/R | 82 LH |
| | Frontal_Mid_L/R | 90 RH |
| | Frontal_Sup_L/R | |
| Parietal | Parietal_Inf_L | 18 LH |
| | | 11 RH |
| Insula | Insula_L/R | 14 LH |
| | | 14 RH |
| Temporal | Temporal_Sup_L/R | 23 LH |
| | Heschl_L/R | 29 RH |
| Occipito-Temporal | Calcarine_L/R | 116 LH |
| | Occipital_Inf_L/R | 119 RH |
| | Occipital_Supl_L/R | |
| | Occipital_Mid_L/R | |
| | Temporal_Inf_L/R | |
| | Fusiform_L/R | |
| V1 | Calcarine_L/R | 20 LH |
| | | 12 RH |
| V2 | Occipital_Inf_L/R | 19 LH |
| | Occipital_Supl_L/R | 15 RH |
| FFA | [-37 -46 -18] LH | 1 LH |
| | [43 -44 -20] RH | 1 RH |
| +hMT/V5 | [-47 -73 -1] LH | 1 LH |
| | [45 -71 -1] RH | 1 RH |

For the regions of interest (ROIs) voxels were selected based on the brain areas defined in the Automated Anatomical Labeling (AAL) atlas. The number of voxels across all AAL areas within a ROI is displayed separately per hemisphere (LH, RH). The Brede Atlas was used to define the center coordinates of the fusiform face area (FFA), and the medial temporal lobe including V5 ROI (+hMT/V5). Coordinates are displayed as MNI coordinates in mm.

S3 Table Working Memory Strategies

| | Verbal* | Rehearsal | Sequencing | Story | Visual | Spatial | Episodic | Intuitive* | No |
|----------------|---------|-----------|------------|-------|--------|---------|----------|------------|----|
| Sighted | | | | | | | | | |
| Auditory | 4 | 1 | 3 | 0 | 3 | 1 | 0 | 3 | 1 |
| Tactile | 5 | 4 | 1 | 1 | 3 | 0 | 2 | 1 | 2 |
| Control | 1 | 1 | 1 | 0 | 0 | 0 | 0 | 5 | 5 |
| Blind | | | | | | | | | |
| Auditory | 5 | 0 | 3 | 0 | 1 | 1 | 0 | 5 | 0 |
| Tactile | 5 | 3 | 4 | 0 | 2 | 0 | 1 | 1 | 3 |
| Control | 2 | 2 | 1 | 2 | 1 | 0 | 2 | 3 | 2 |

*The frequency (number of participants) of usage of the different strategies (columns) in the 2-back task with voices is displayed separately for the sighted and congenitally blind participants in the different training conditions (rows: auditory working memory training; tactile working memory training; training-control condition). *Participants in the different training conditions only differ in their usage of verbal and intuitive memory strategies (using Fishers exact test, 2-tailed; $p < .05$). There were no differences between the sighted and blind in strategy usage.*