# Supplementary Methods and Figures for: Subcortical, modality-specific pathways contribute to multisensory processing in humans

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# Supplementary Methods and Information

*Post-hoc control analyses and results.* To strengthen our claim that connectivity within the putatively auditory system determines multisensory processing ability (see Results), we ran a number of post-hoc control analyses. First, to determine the specificity of our findings, we ran a control analysis in which the parietal operculum (S2) served as the seed for probabilistic tractography. This region neighbors A1 and was defined at the group level using the Harvard-Oxford structural probability atlas (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases). Specifically, a mask was created in MNI space based on the isolated probability map of parietal operculum cortex. This mask was then registered non-linearly to subject-native DTI space. By raising the probability threshold of the mask, voxels below the cut-off are set to zero. We used this to titrate the probability threshold for each subject, such that the seed-size equaled 50 voxels, similar to the size of the A1 and V4 seeds. We then conducted probabilistic tractography for each subject using the thus obtained S2 mask as the seed. Next, we correlated multisensory processing ability with tract strength seeded from S2 across subjects using Spearman's rank correlation coefficient and a similar thresholding procedure as described in the main text for A1 and V4. As expected, this analysis did not reveal a significant correlation between tract strength to S2 and multisensory processing ability near the MGN or the cochlear nucleus (see Results in the main text), highlighting the specificity of our findings and supporting the idea that anatomical connections within the *auditory* system contribute to multisensory processing ability.

As a second control analysis, we localized MGN based on our functional localizer fMRI data to determine more precisely the location of the voxels showing a correlation between A1-seeded tract strength and multisensory processing ability relative to MGN (see

Results). As we could not reliably identify MGN at the individual subject level based on our anatomical scans or individual functional localizer fMRI results, we isolated MGN at the group level in MNI space by conducting a group-level t-test on the unsmoothed, non-linearly normalized individual localizer activation maps. The unsmoothed data were used because no sound-related activity was observed in MGN at the group level after smoothing of the individual localizer data using a Gaussian kernel with a FWHM of 5 mm, conceivably due to spatial smearing-related attenuation of meaningful activation in this small structure below the significance threshold. Results are shown in Fig. 3B (main text) and described in more detail the main Results section.

Third, to confirm that our principal tractography results are not driven by variability in individual differences in local DTI metrics, we correlated our behavioral measure with mean diffusivity (MD) and fractional anisotropy (FA) averaged over the voxels that showed a significant correlation between tract strength and multisensory processing ability (see Table 1 of main text) (c.f. Cohen, 2011b). As expected, no significant correlations were found (Fig. S1). Given that FA and MD reflect local tissue properties that are unrelated to connectivity estimates with the seed region, these results highlight the specificity of the findings to tract strength (see Fig. 3).

Fourth, in order to exclude the possibility that individual differences in brain shape affected our correlations between tract strength and behavior, we performed a voxel based morphometry (VBM) analysis (c.f. Cohen, 2011b, de Wit *et al.*, 2012). Specifically, we estimated gray matter density based on skull-stripped T1 anatomical images normalized to MNI space, for the voxels that showed a significant correlation between multisensory processing ability and tract strength seeded from left A1 (see Table 1 of main text). Gray matter density was subsequently correlated with multisensory processing ability. As expected, the resulting correlation was non-significant (Fig. S2, right panel), indicating that our principal tractography results are not driven by variability in gray matter density.

Fifth, because cerebral volume can also affect estimates of tract strength (number of paths crossing a voxel, see Methods of main text), we estimated cerebral volume based on skull-stripped T1 anatomical images, and included it as a covariate in partial correlation analyses for the voxels in which tract strength correlated significantly with multisensory processing ability (see Table 1 of main text). As expected the pattern of results was highly similar to our original analysis (Fig. S3B), indicating that individual differences in cerebral volume did not significantly contribute to our results.

Sixth, to rule out participant age as a possible confound in our analyses, we correlated individual participant age with the following measures: 1) Mean tract strength in the voxels that showed a significant correlation with behavior (See Table 1 in main text) seeded from left A1; 2) Our behavioral measure; 3) peak A1 activity; 4) peak V4 activity. We did not find any significant effects (Figure S4), indicating that age was not a confounding variable in our analyses. Additionally, we ran partial correlations with age included as a covariate for the voxels that showed a significant correlation between fiber strength seeded from left A1 and left V4, and multisensory processing ability. As expected, the pattern of results was highly similar to our original analysis (Fig. S3A), excluding age as a possible confound.

Finally, because gender can affect brain-based measures (Tomasi *et al.*, 2008), and our sample consisted largely of females, we reran the correlation analysis as described in the main text for the clusters of voxels that exhibited a correlation between tract strength and multisensory processing ability (see Table 1 in the main text) but now excluding the three male subjects. This did not change the pattern of results (i.e., all correlations listed in Table 1 of the main text, and shown in Fig 3 of the main text remained significant).

# Supplementary Figures

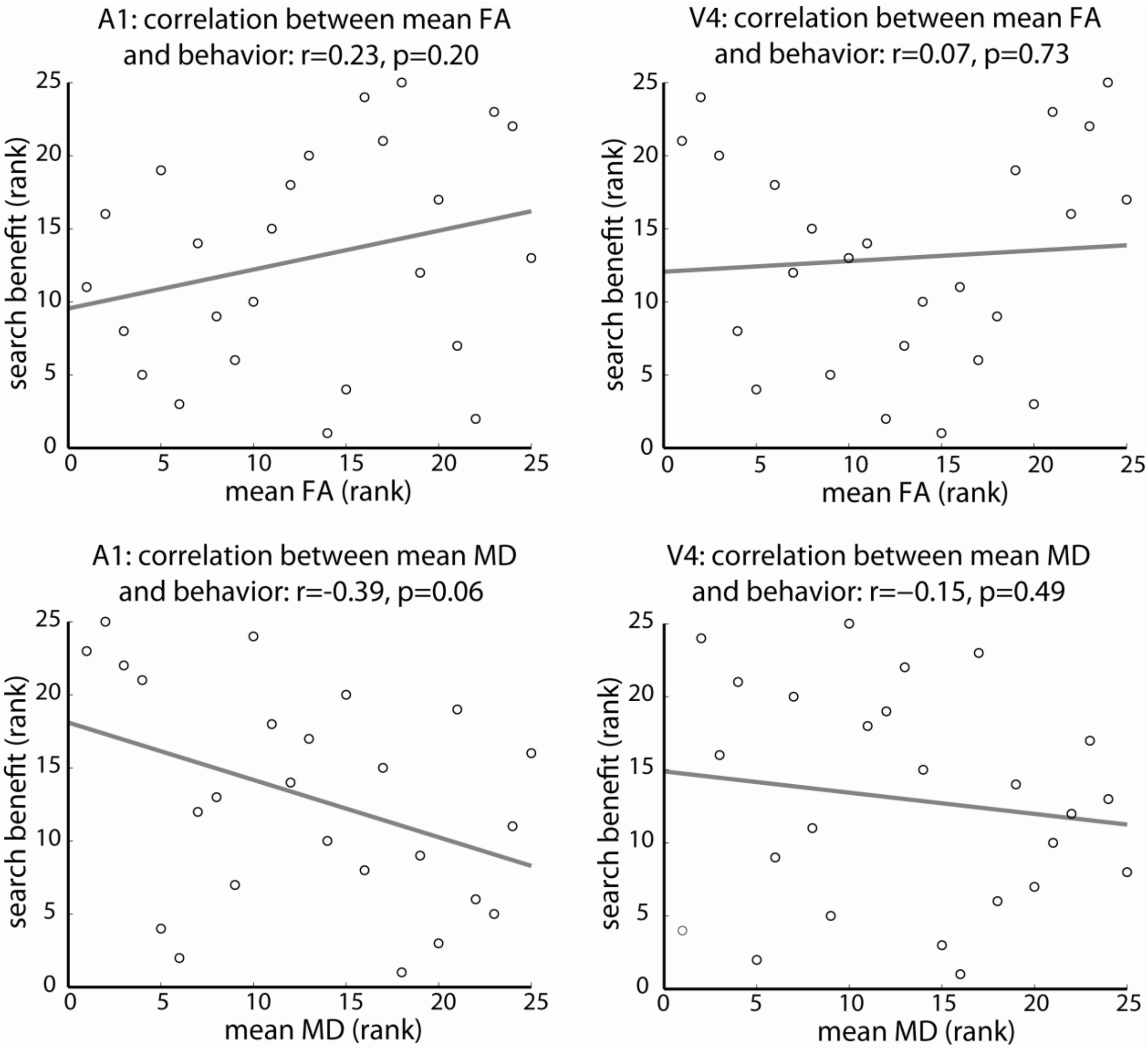


Figure S1. Results from control analyses examining the relationship between local tissue properties - the diffusion metrics fractional anisotropy (FA) and mean diffusivity (MD) - and our behavioral measure. Multi-sensory processing ability did not correlate significantly with FA or MD, averaged over voxels in which tract strength significantly predicted multisensory processing ability (see Table 1 of main text). Thus, multisensory processing ability was selectively predicted by tract strength (Fig. 3 in the main text). Note that the trend in the lower left panel is in the opposite direction as the correlations in Fig. 3 of the main text. A1: voxels that correlated significantly with tract strength seeded from primary auditory cortex. V4: voxels that correlated significantly with tract strength seeded from occipital fusiform cortex area V4.

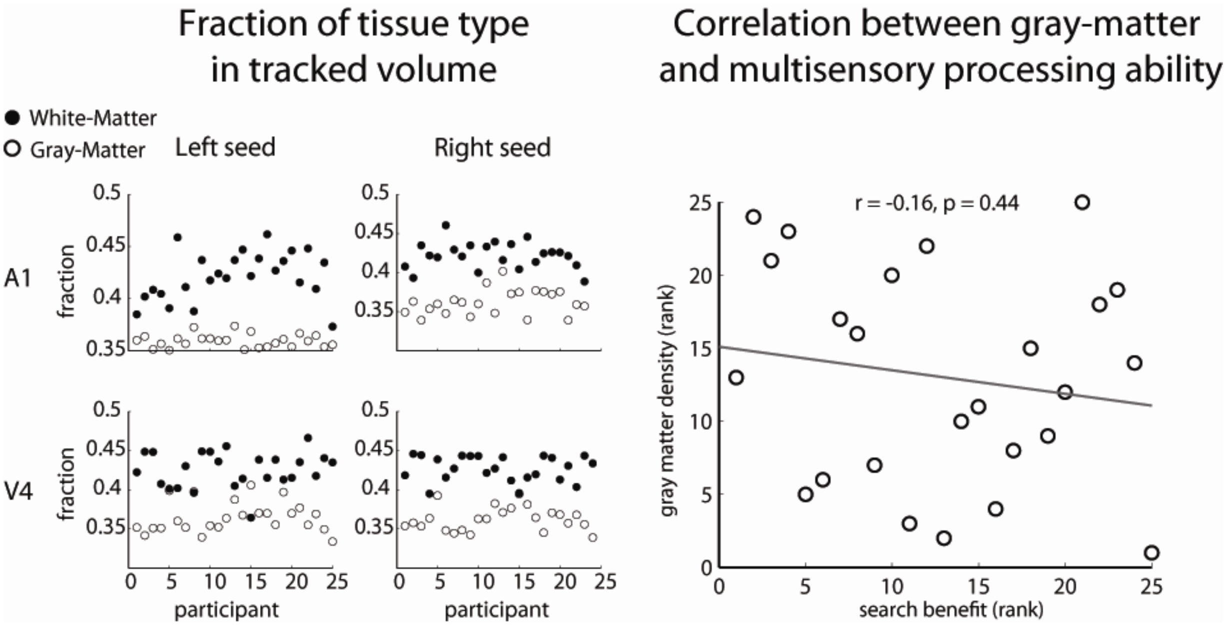


Figure S2. Left panels show the fraction of white and gray matter in the tracked volume per seed and hemisphere. As expected, the largest proportion of tissue was white matter, supporting the idea that our tractography analysis was successful in tracking white-matter pathways. The right panel shows that average gray-matter density in the voxels that showed a significant correlation between multisensory processing ability and tract strength seeded from left primary auditory cortex, does not predict behavior.

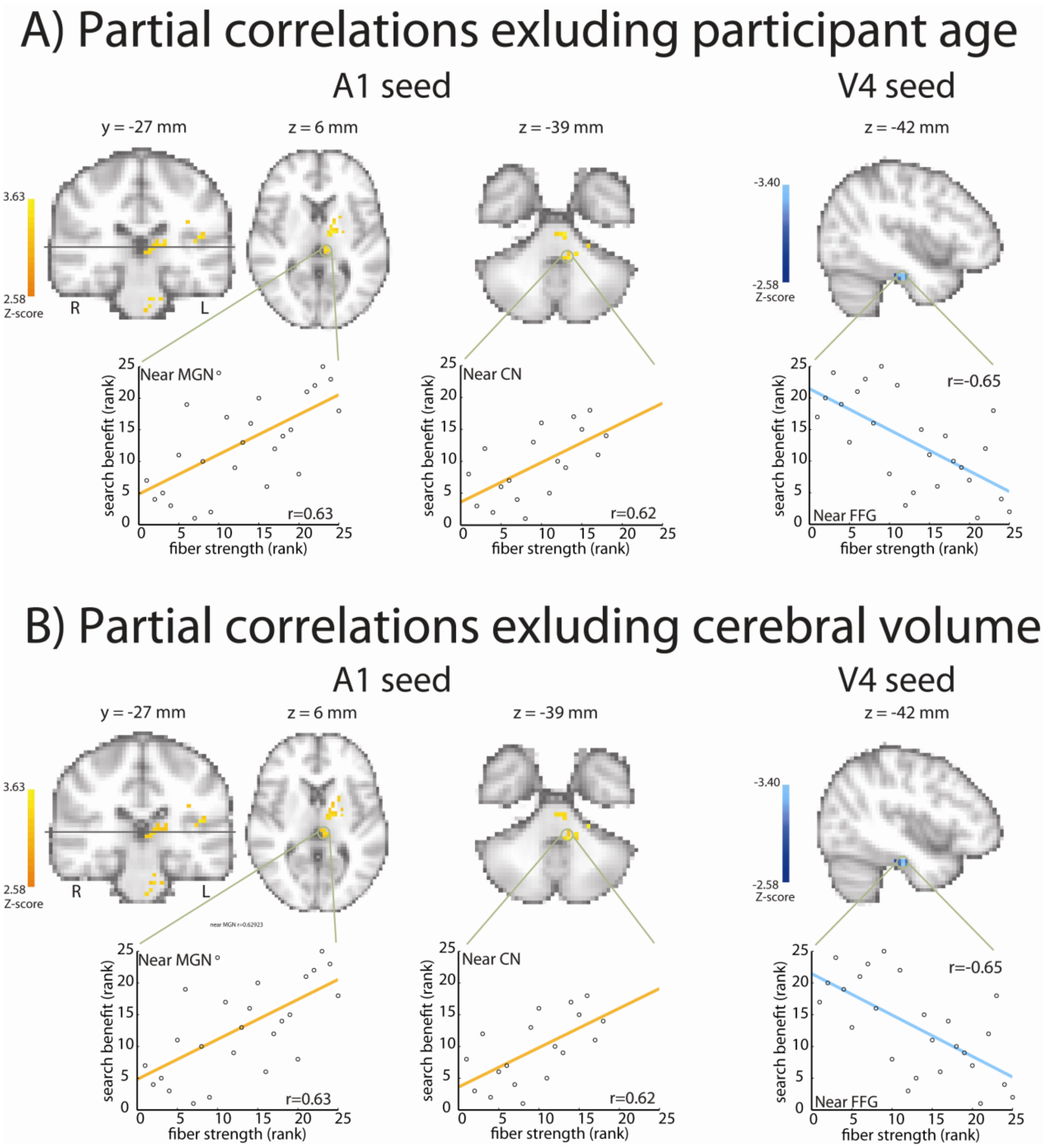


Figure S3. Results of partial correlation analysis examining the relationship between multisensory processing ability and tract strength when excluding the effect of individual participant age (A), and cerebral volume (B). As can be seen, results were highly similar to our original results (see Fig. 3 of main text), suggesting that individual differences in age and cerebral volume contributed minimally, if at all, to our main findings.

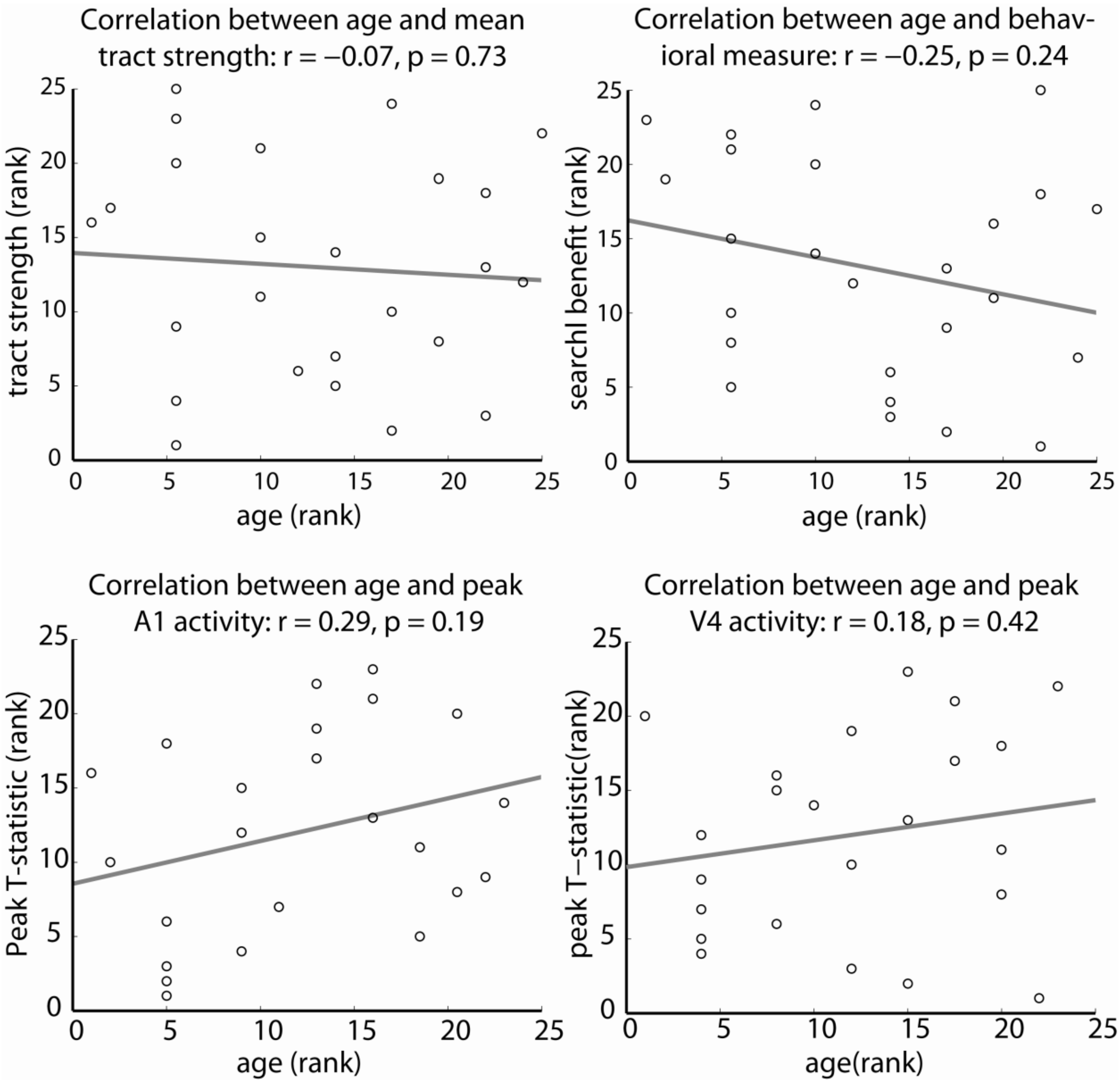


Figure S4. Results from control analyses examining the relationship between age and several brain and behavioral measures. Age did not predict mean tract strength in the voxels that showed a significant correlation between behavior and tract strength seeded from left primary auditory cortex (A1). Age also did not predict multisensory processing ability or peak BOLD activity in A1 or V4.