# White matter matters: aging of the arcuate fasciculus and middle longitudinal fasciculus

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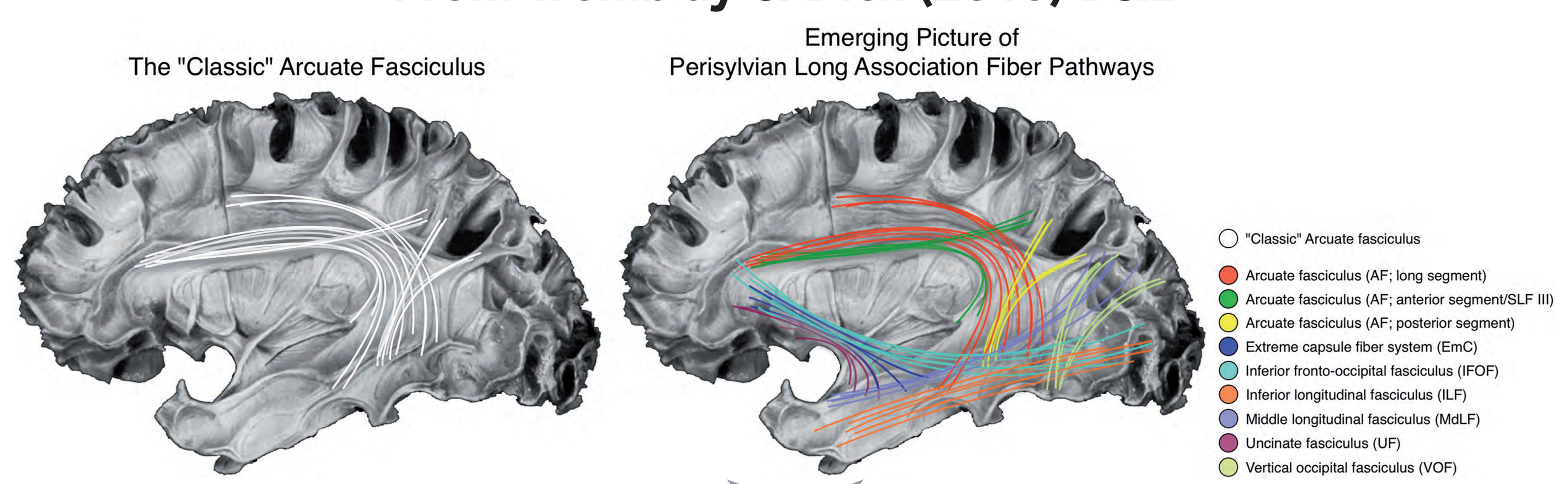
## Introduction

One of the most frequent complaints of elderly adults is a difficulty in perceiving speech in the presence of noise. Traditionally this deficit was ascribed to presbycusis, the biological ageing of the peripheral hearing system [1, 2] . Yet, deficits in elderly speech perception are present even in the absence of hearing deficits. This suggests that factors in addition to the decreasing sensitivity of the peripheral auditory system are contributing to the speech in noise difficulties such as a central processing deficit related to brain aging. Such deficits could originate from white matter (WM) aging, which is known to affect cognition. Here we used High Angular Resolution Diffusion Images (HARDI) with advanced tractography methods to investigate two WM tracts that are thought to be involved in speech and language functions: (1) the Arcuate Fasciculus (AF), with its three components (anterior, posterior and direct)[3], and (2) the Middle Longitudinal Fasciculus (MdLF), with its two components, one connecting the temporal pole (TP) to the inferior parietal lobule (IPL) and one connecting TP to the superior parietal lobule (SPL) [4]. **Figure 1** shows a representation of these tracts.

### Figure 1. Fiber pathways for language. From Tremblay & Dick (2016) B&L



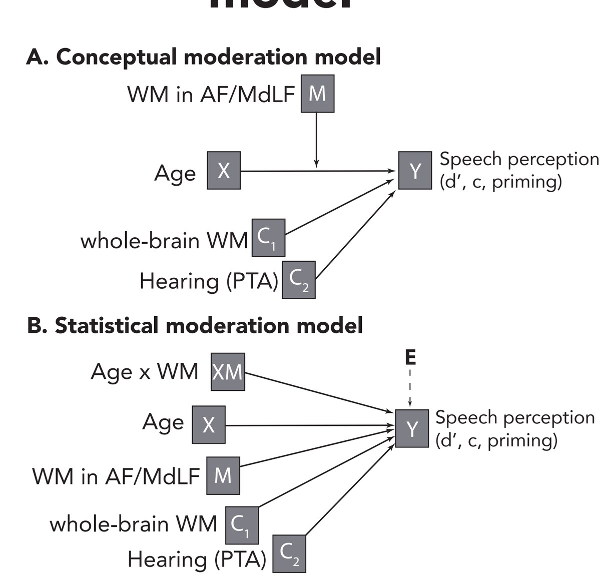

## Methods

- 14 young (mean = 30 ± 10.49 y; 19-46 y) and 15 older (mean 71 ± 5.85 y; 65-84 y) cognitively healthy adults were recruited. Cognitive evaluation (MOCA) and hearing evaluation (pure tone audiometry, speech reception thresholds and distortion products) were conducted.
- **Task**: auditory syllable discrimination task (same/different judgment) at three levels of intelligibility (low, mid, high) with two types of syllable pairs (fricatives [e.g. /fe vs se/] and stops [e.g. /ge vs pe/]). 50% of the experimental pairs were identical.
- **Image acquisition:** Philips 3.0 Tesla Achieva TX, a MPRAGE (1 mm3) and a HARDI sequence were acquired (TR = 8.5 ms; TE = 76.7 ms; b=1500 s/m2, 60 directions, 128 volumes, no gap, 1.8 mm).
- **Image processing** was completed using Freesurfer and FSL. Tractography analyses were conducted with DIPY [13, 14]. DTI and Fiber Orientation Distribution (FOD) metrics (**Table 1**) were computed.
- **Statistical analyses.** A series of ANCOVAs was conducted to examine the effect of age on AF and MdLF. Moderation analyses were conducted to determine whether age related changes in speech perception are moderated by WM. The moderation model is presented in **Figure 2**. The dependent variables (DV) were sensitivity (d'), criterion (C) and a measure of priming (facilitation) computed using reaction times (RT) (RTdiffrent - RT same). All DV were computed from the low intelligibility condition (-5 dB SNR).

### Table 1. Diffusion metrics

| List of diffusion metrics used in the study | | |
|---|---|---|
| Family of metrics | Metrics | Description |
| DTI | Fractional Anisotropy (FA) | FA represents the degree of diffusion within a voxel, with higher values indicating greater directional diffusion (values range between 0 for isotropic diffusion and 1 for anisotropic diffusion). |
| | Axial Diffusivity (AD) | AD represents diffusion in the direction along the length of the tensor and is believed to indicate changes in axonal integrity (higher values suggest greater integrity). |
| | Radial Diffusivity (RD) | RD represents the average of the secondary and tertiary perpendicular eigenvalues. Lower values indicate lower diffusion perpendicular to the primary axis of the axon, which may suggest increased myelination. |
| | Mean Diffusivity (MD) | MD corresponds to the average of the three eigenvalues of the diffusion tensor. A higher value of MD may represent demyelination. |
| FOD | Apparent Fibre Density (AFD) | AFD represents the fraction of space occupied by a fiber bundle. It is robust to crossing and kissing fibers. A decrease in AFD could represent a decrease of white matter integrity. |
| | Number of Fiber Orientations (NuFO) | Number of Fiber Orientations within each voxel. Indicator of white matter complexity. |

### Figure 2. Moderation model




## Results

**WM aging. (A) AF.** As shown in **Figure 3A**, all AF segments were tracked in most participants. In 2 participants, we did not find the direct segment. A mixed 3 x 2 x 2 ANCOVA was conducted with Segment (Direct, Anterior, Posterior) and Hemisphere (Left, Right) as within-subjects factors, Group (Younger, Older) as the between-subjects factor, and whole-brain metric values as covariates. The results are reported in **Table 2A**. There were age differences in each segment (FA, MD, and AFD) with few hemispheric differences. The Posterior segment showed evidence of additional decline in three metrics (RD, AD, Nufo).

**(B) MdLF.** As shown in **Figure 3B**, all components of the MdLF were found in all participants. A mixed 2 x 2 x 2 ANCOVA was performed with Segment (IPL, SPL) and Hemisphere (Left, Right) as within-subjects factors, Group (Younger, Older) as the between-subjects factor, and whole-brain metric values as covariates. The results are reported in **Table 2B**. There were age differences in both segments (FA, MD, and Nufo) with few hemispheric differences. The IPL was more strongly affected by aging than the SPL, across multiple metrics (FA, AD, Nufo, AFD).

### Table 2. Results of the ANCOVA analyses*

| Tract | Metrics | Group | Segment | Hemisphere | Group * Segment | Group * Hemisphere | Group * Segment * Hemisphere | Segment * Hemisphere |
|---|---|---|---|---|---|---|---|---|
| A. AF | FA | 0.036 (0.171) | 0.026 (0.141) | 0.323 (0.041) | 0.072 (0.104) | 0.331 (0.039) | 0.521 (0.027) | 0.386 (0.039) |
| | RD | 0.653 (0.008) | 0.013 (0.154) | 0.344 (0.034) | 0.034 (0.122) | 0.436 (0.023) | 0.978 (0.001) | 0.260 (0.051) |
| | MD | 0.023 (0.182) | 0.008 (0.171) | 0.148 (0.079) | 0.375 (0.037) | 0.660 (0.008) | 0.377 (0.037) | 0.510 (0.020) |
| | AD | 0.570 (0.015) | 0.010 (0.190) | 0.342 (0.041) | 0.012 (0.182) | 0.228 (0.050) | 0.023 (0.158) | 0.081 (0.108) |
| | NuFO | 0.219 (0.065) | 0.085 (0.102) | 0.058 (0.148) | 0.002 (0.245) | 0.140 (0.092) | 0.264 (0.056) | 0.194 (0.069) |
| | AFD Max | 0.600 (0.017) | 0.289 (0.070) | 0.941 (≥ 0.001) | 0.062 (0.151) | 0.190 (0.099) | 0.904 (0.006) | 0.816 (0.012) |
| | AFD Sum | 0.006 (0.293) | 0.067 (0.115) | 0.032 (0.193) | 0.007 (0.203) | 0.880 (0.001) | 0.454 (0.035) | 0.584 (0.024) |
| | Afd Total | 0.078 (0.141) | 0.762 (0.013) | 0.099 (0.124) | 0.170 (0.081) | 0.738 (0.005) | 0.872 (0.007) | 0.788 (0.011) |
| B. MdLF | FA | 0.008 (0.241) ↓ | 0.009 (0.233) ↓ IPL | 0.460 (0.021) | 0.015 (.208) ↓ IPL | 0.850 (0.001) | 0.628 (.009) | 0.620 (0.010) |
| | RD | 0.580 (0.012) | 0.082 (0.112) | 0.157 (0.076) | 0.829 (0.002) | 0.528 (0.016) | 0.135 (0.084) | 0.091 (0.106) |
| | MD | 0.035 (0.166) ↑ | 0.333 (0.037) | 0.010 (0.238) ↑ R | 0.008 (0.248) ↑ SPL | 0.508 (0.018) | 0.054 (0.141) | 0.440 (0.024) |
| | AD | 0.111 (0.116) | 0.058 (0.160) | 0.453 (0.027) | 0.002 (0.362) ↓ IPL | 0.947 (≥ 0.001) | 0.233 (0.067) | 0.039 (0.187) ↑ SPL/R |
| | NuFO | 0.042 (0.168) ↓ | 0.746 (0.005) | 0.259 (0.055) | 0.007 (0.279) ↑ IPL | 0.900 (0.001) | 0.300 (0.047) | 0.713 (0.006) |
| | AFD Max | 0.802 (0.003) | 0.499 (0.019) | 0.782 (0.003) | 0.014 (0.226) ↑ IPL ↓ IPL | 0.476 (0.021) | 0.978 (≥ 0.001) | 0.650 (0.009) |
| | AFD Sum | 0.563 (0.015) | 0.462 (0.025) | 0.650 (0.010) | 0.019 (0.226) ↑ IPL ↓ IPL | 0.429 (0.029) | 0.914 (0.001) | 0.506 (0.020) |
| | AFD Total | 0.165 (0.090) | 0.420 (0.031) | 0.175 (0.086) | 0.087 (0.133) | 0.393 (0.035) | 0.694 (0.008) | 0.279 (0.056) |

*The numbers in the table represent p values and effect sizes (in parentheses) for each of the effect and interactions. Dark green indicates a significant p value while light green indicates a near significant effect.

**Speech perception. (A) AF.** Moderation analyses revealed complex patterns of effects, which are reported in **Table 3A**. Overall, decline in the discrimination of stop consonants was more strongly related to WM decline than the discrimination of fricative consonants representing ~70% of all moderations. Decline in all segments moderated the effect of age on speech perception, with the Direct segment accounting for 50% of the moderations. Moderations were found mostly on FOD metrics (56%). An example of a moderation is shown in **Figure 4A** for the Anterior segment. For younger adults, more fibres in the Anterior segment is associated with facilitation while for the older adults, this relationship is absent.

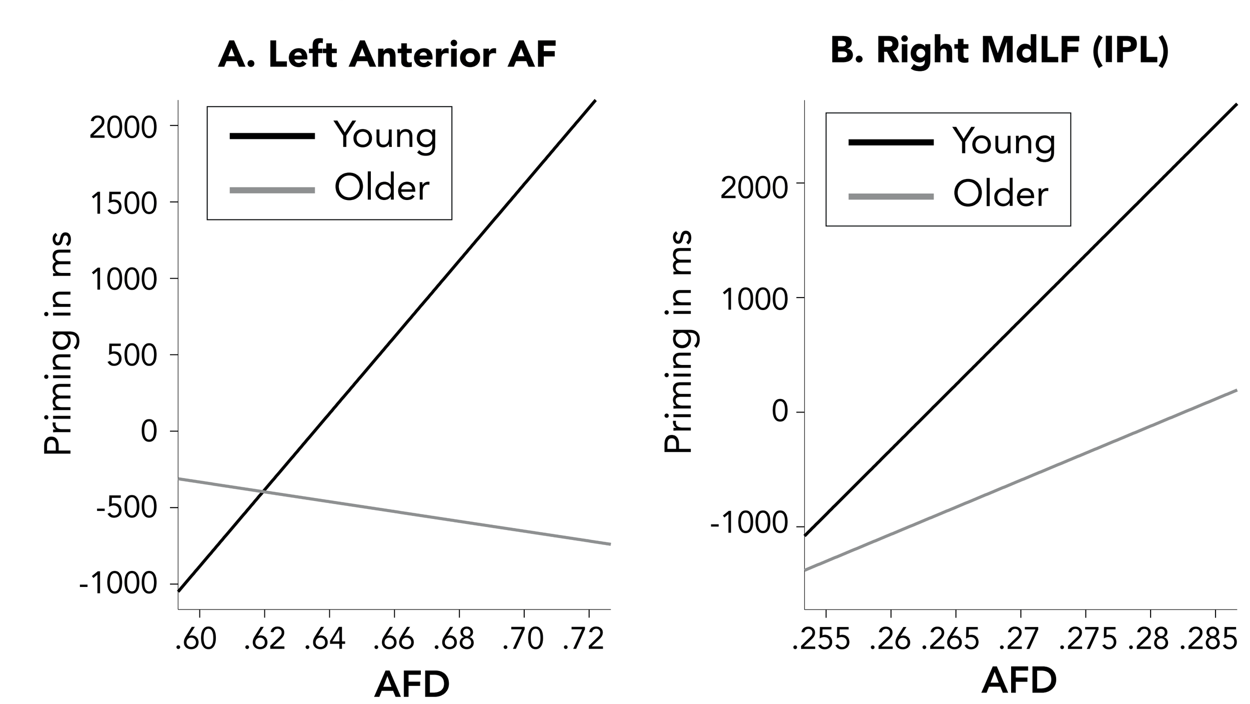
**(B) MdLF.** Moderation results for the MdLF are reported in **Table 3B**. Overall, decline in the discrimination of stop consonants was more strongly related to WM decline compared to fricative consonants representing 73% of all moderations. Decline in both segments moderated the effect of age on speech perception, with the SPL accounting for 60% of the moderations. Moderation effects were found mainly on FOD metrics (80%). An example of a moderation is shown in **Figure 4B** for the IPL. For younger adults, more fibres in the IPL is associated with facilitation while for the older adults, this relationship is reduced.

### Table 3. Moderation results*

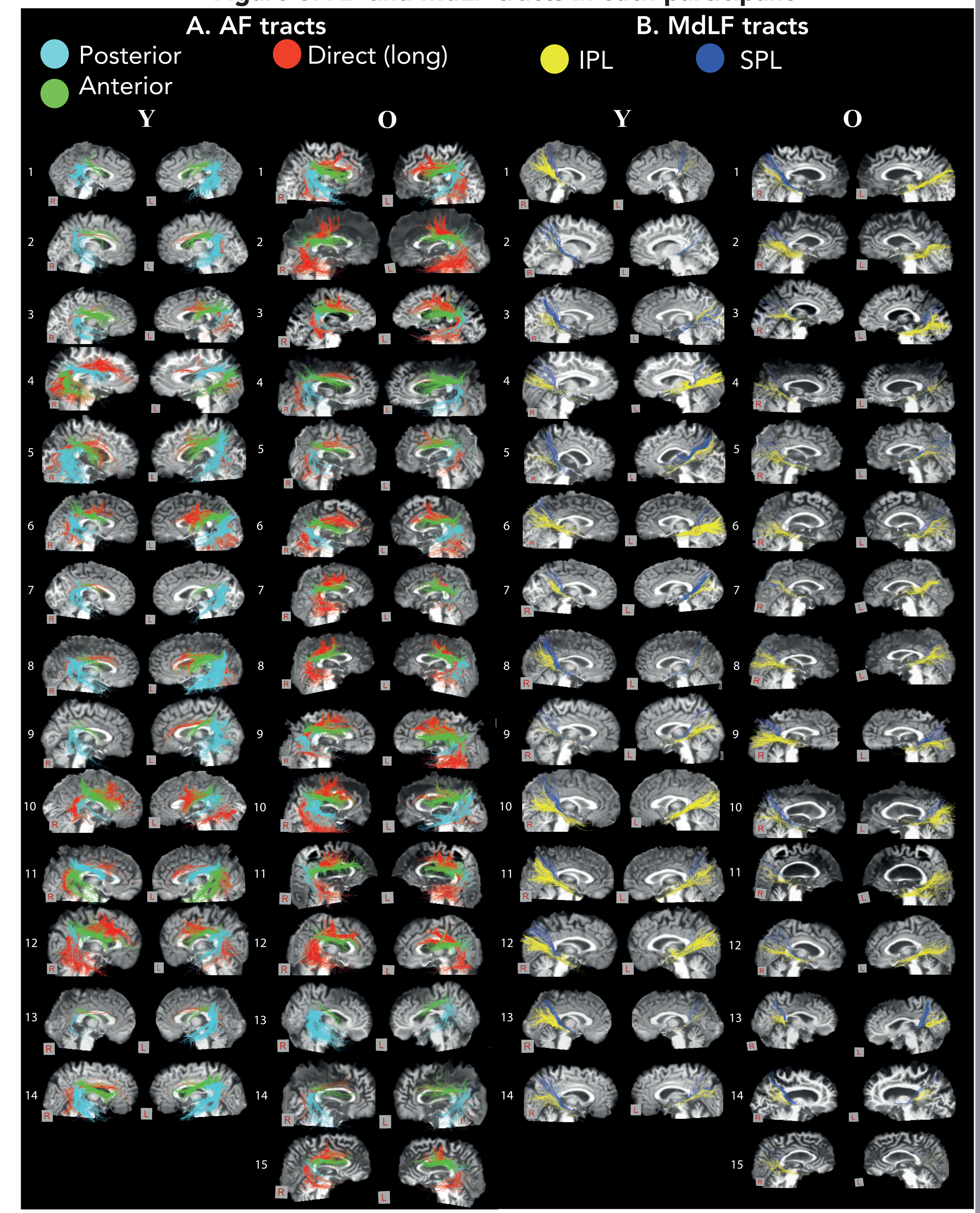
| Tract | Segments | Metrics | Priming F | Priming S | | Sensitivity (d') F | Sensitivity (d') S | | Criterion (c) F | | Criterion (c) S |
|---|---|---|---|---|---|---|---|---|---|---|---|
| A. AF | Direct | FA | | | | | | | | | |
| | | RD | | XM | | | | | | | X, XM |
| | | MD | | XM | | | | | | | X, XM |
| | | AD | | | | | | | | | X, XM |
| | | NuFO | | | | | | | | | |
| | | AFD max | | X, XM | | | | | XM | | |
| | | AFD sum | | | | | | | | | |
| | | AFD Total | | | | X, XM | | | | | |
| | Anterior | FA | | | | X, XM | | | | | |
| | | RD | | | | X, XM, M | | | | | |
| | | MD | | | | | | | | | |
| | | AD | | | | | | | M | | |
| | | NuFO | | M | | | | | | | |
| | | AFD max | M | X, XM, M | | | | | | | |
| | | AFD sum | | | | | X, XM | X, XM | X, XM, M | | |
| | | AFD Total | X | | | | | | | | |
| | Posterior | FA | | | | | | | | | |
| | | RD | | | | | | | | | |
| | | MD | | | | | | | | | |
| | | AD | | | | | | | | | |
| | | NuFO | | | | | | | | | |
| | | AFD max | | | | | | | | | |
| | | AFD sum | | | | | X, XM | X, XM | | | |
| | | AFD Total | | | | | | | | | |
| B. MdLF | IPL | FA | XM | X, XM, M | | | | | | | |
| | | RD | | | | | | | | | |
| | | MD | | | | | | | | | |
| | | AD | | | | | | | | | |
| | | NuFO | | X,XM | | | | | | | |
| | | AFD max | | X, XM, M | | | X, XM, M | | | | |
| | | AFD sum | | X | | | X, XM, M | | | | |
| | | AFD Total | M | M | | | | | M | | |
| | SPL | FA | | | | | | | X, XM, M | | |
| | | RD | | | | | | | | | |
| | | MD | | | | | | | | | |
| | | AD | | | | | | | M | | |
| | | NuFO | | X, XM | X, XM, M | | | | X, XM | X, XM | |
| | | AFD max | | X | | | X, XM | X, XM, M | | | |
| | | AFD sum | | | | | X, XM | X, XM | | | |
| | | AFD Total | | | | | | | | | |

*Green indicates a moderating effect of WM in the right hemisphere while blue indicates a moderating effect of WM in the left hemisphere.

### Figure 4. Exemples of moderations




### Figure 3. AF and MdLF tracts in each participant




## Conclusions

- The finding that a decline in the integrity of AF -which forms the bulk of the dorsal speech stream connecting auditory to premotor areas, which are believed to contain speech sound representations – moderates speech perception decline suggest a role for phonological processing in the aetiology of speech perception decline.The role of the MdLF, in contrast, is more elusive. Its connectivity suggests that is could be involved in connecting primary to non-primary auditory areas within the temporal lobe as well as connecting these regions to the parietal lobe, which is known to be involved in working memory. Other possible functions include attention and audiovisual integration. Our results suggest a role for this tract in speech perception in adulthood, possibly suggesting that a decline in cognitive functions such as working memory and attention may play a part in decline in speech perception with age. The finding of age independent effects of MdLF decline (also AF) on speech perception suggests that this tract plays a general role in speech perception. In sum, our results suggest a multifactorial etiology for age-related speech perception decline that goes beyond peripheral decline to include brain connectivity within multiple pathways.

## References

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