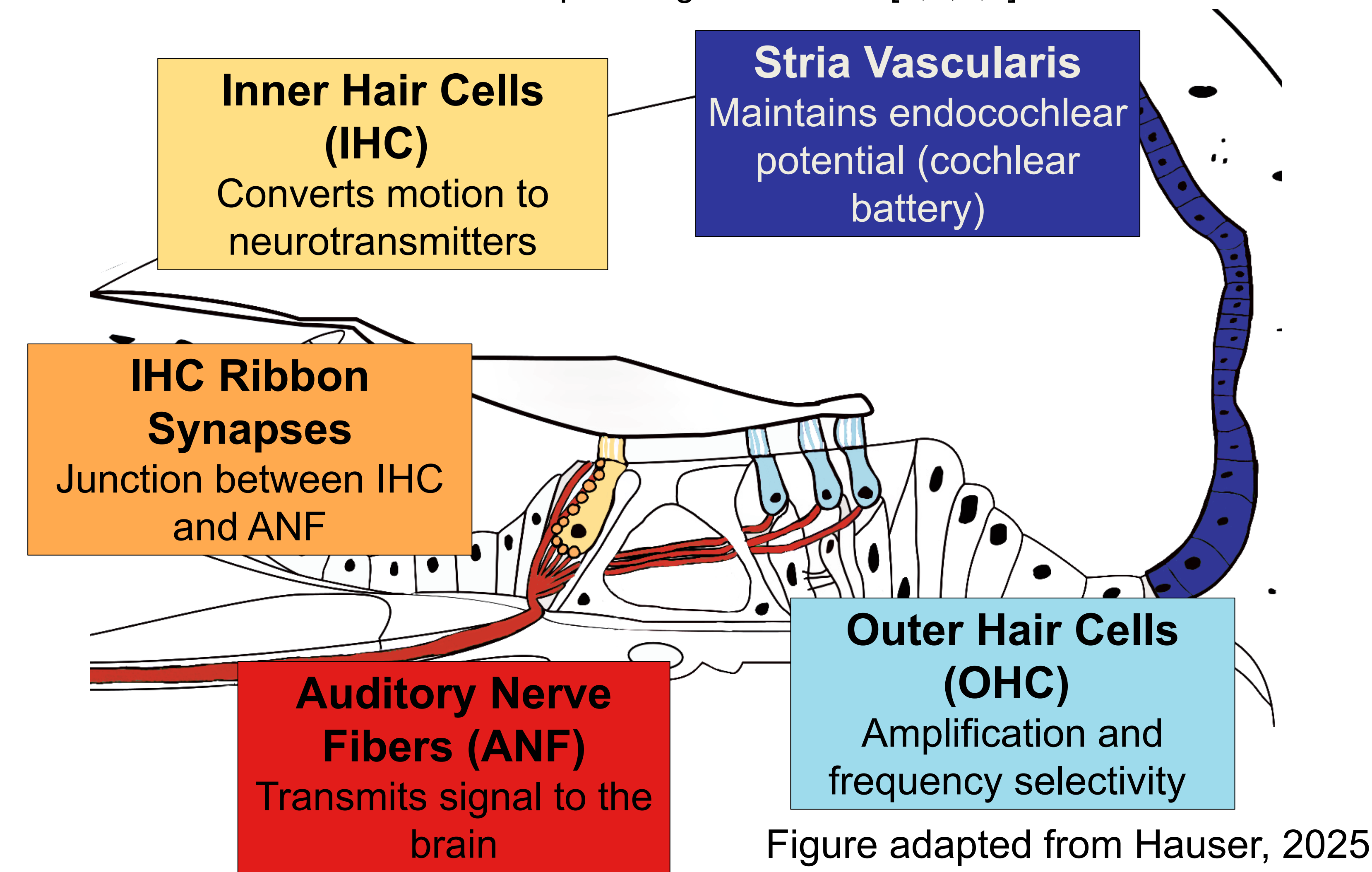# Stratifying Sensorineural Hearing Loss Using Non-invasive Biomarkers: A Replication Study

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## Introduction

- Sensorineural hearing loss (SNHL) is a *complex* disorder, often the result of several etiologies accumulated across the lifespan, resulting in variable treatment outcomes [1,2,3].
- Current audiometric testing cannot distinguish different inner ear pathologies and clinical management focuses on audibility and patient report rather than each patient's cochlear pathophysiology profile.
- Damage of cochlear sensory cells (OHCs and IHCs), afferent synapses, or degeneration of the stria can affect listening outcomes for speech in divergent ways [1,2,4]. For example, metabolic hearing loss and noise-induced hearing loss have been shown to have divergent effects on auditory nerve tuning, including distortion of cochlear tonotopy [5].
- Animal models of SNHL suggest that non-invasive biomarkers may allow for stratification of different cochlear pathologies in SNHL [1,2,3,6].

**Inner Hair Cells (IHC)** Converts motion to neurotransmitters

**Stria Vascularis** Maintains endocochlear potential (cochlear battery)

**IHC Ribbon Synapses** Junction between IHC and ANF

**Auditory Nerve Fibers (ANF)** Transmits signal to the brain

**Outer Hair Cells (OHC)** Amplification and frequency selectivity

Figure adapted from Hauser, 2025

**Can the addition of non-invasive biomarkers to clinical factors improve predictions of speech-in-noise scores?**

## Methods

**Participants:**
- 34 adults aged 18+ (23 female)
- Normal hearing group: no conductive components and clinically normal audiometric thresholds through 8kHz (N=13)
- Hearing loss group: Symmetric sensorineural hearing loss with no threshold exceeding 70 dB HL up to 8 kHz (N=21)
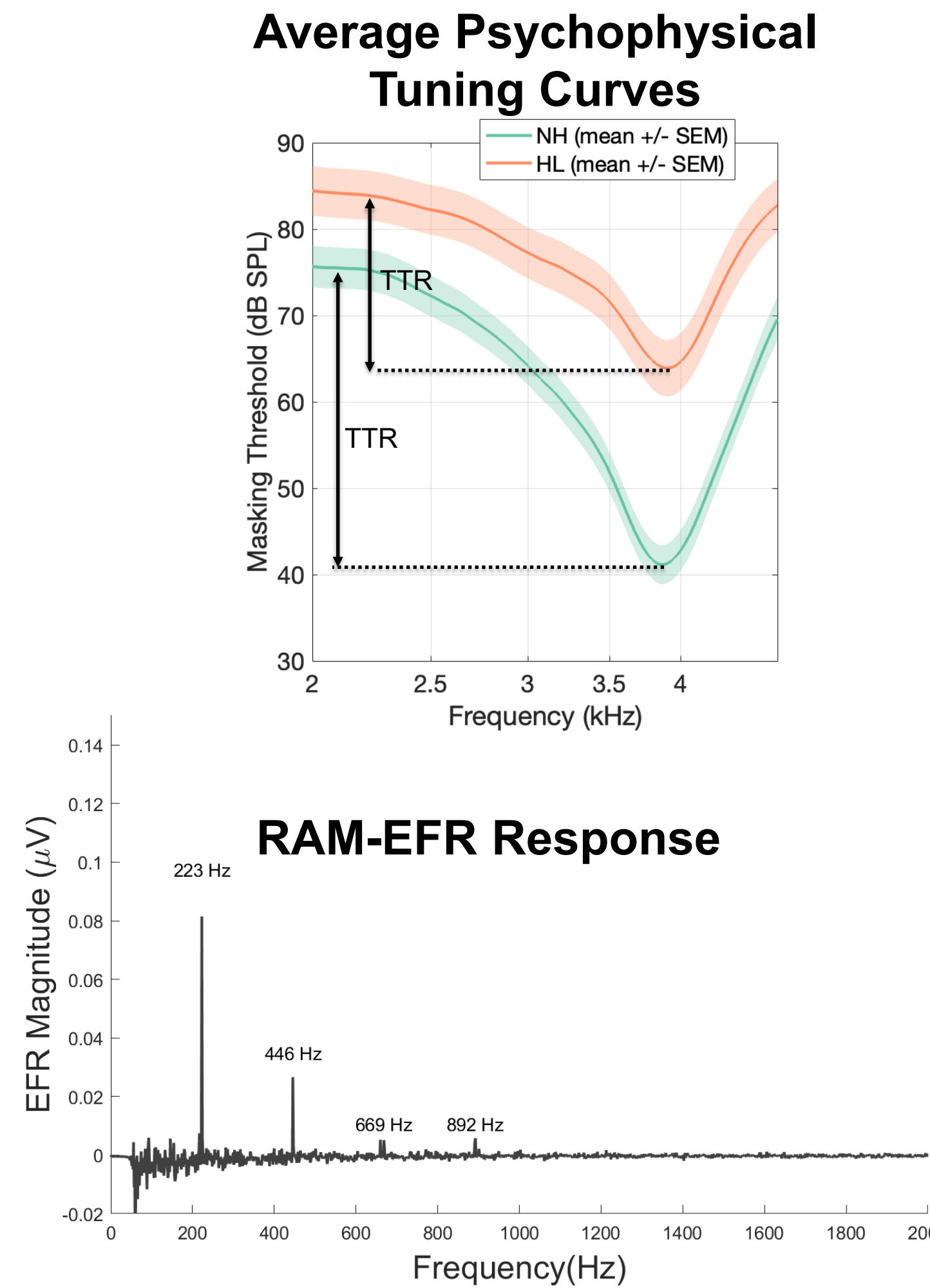
**Clinic-style Measurements:**
- Conventional pure tone air and bone audiometry
  - AC: 250-16000 Hz
  - BC: 500, 1000, 2000, and 4000Hz
- Basic demographic information (e.g., age, noise exposure history)

**Non-Invasive Biomarkers:**
- Psychophysical Tuning Curve (PTC) centered at 4000 Hz [6,7]
- Rectangular Amplitude Modulated Envelope Following Response (RAM EFR), 223 Hz modulation of 4000 Hz tone [8,9]

**Speech Measurement:**
- Modified Rhyme Test (MRT) with linear amplification for participants with hearing loss [10]
- Lapse rate was calculated as the error rate at the highest tested SNR and provides a metric for attention during the task [11]

**Average Psychophysical Tuning Curves**

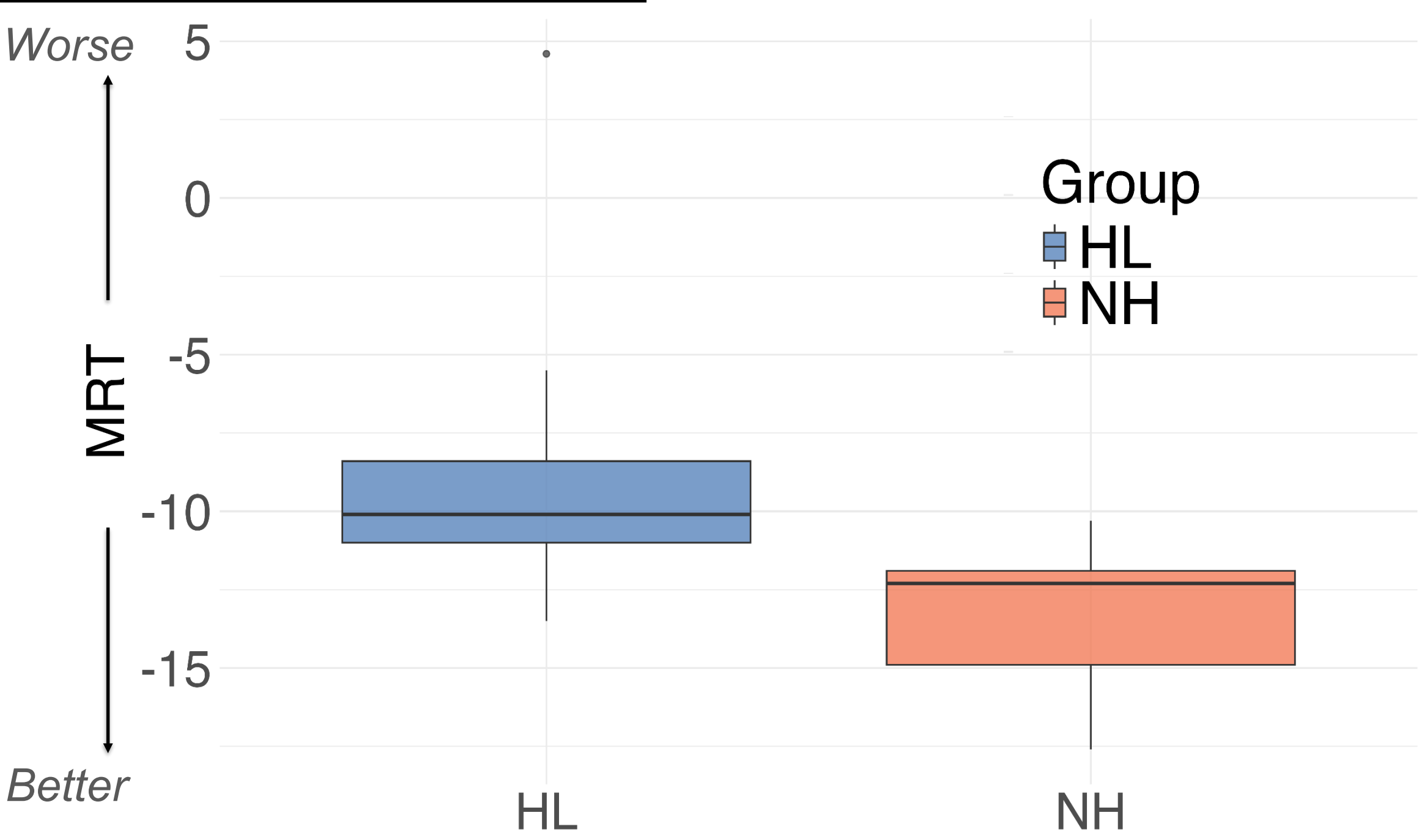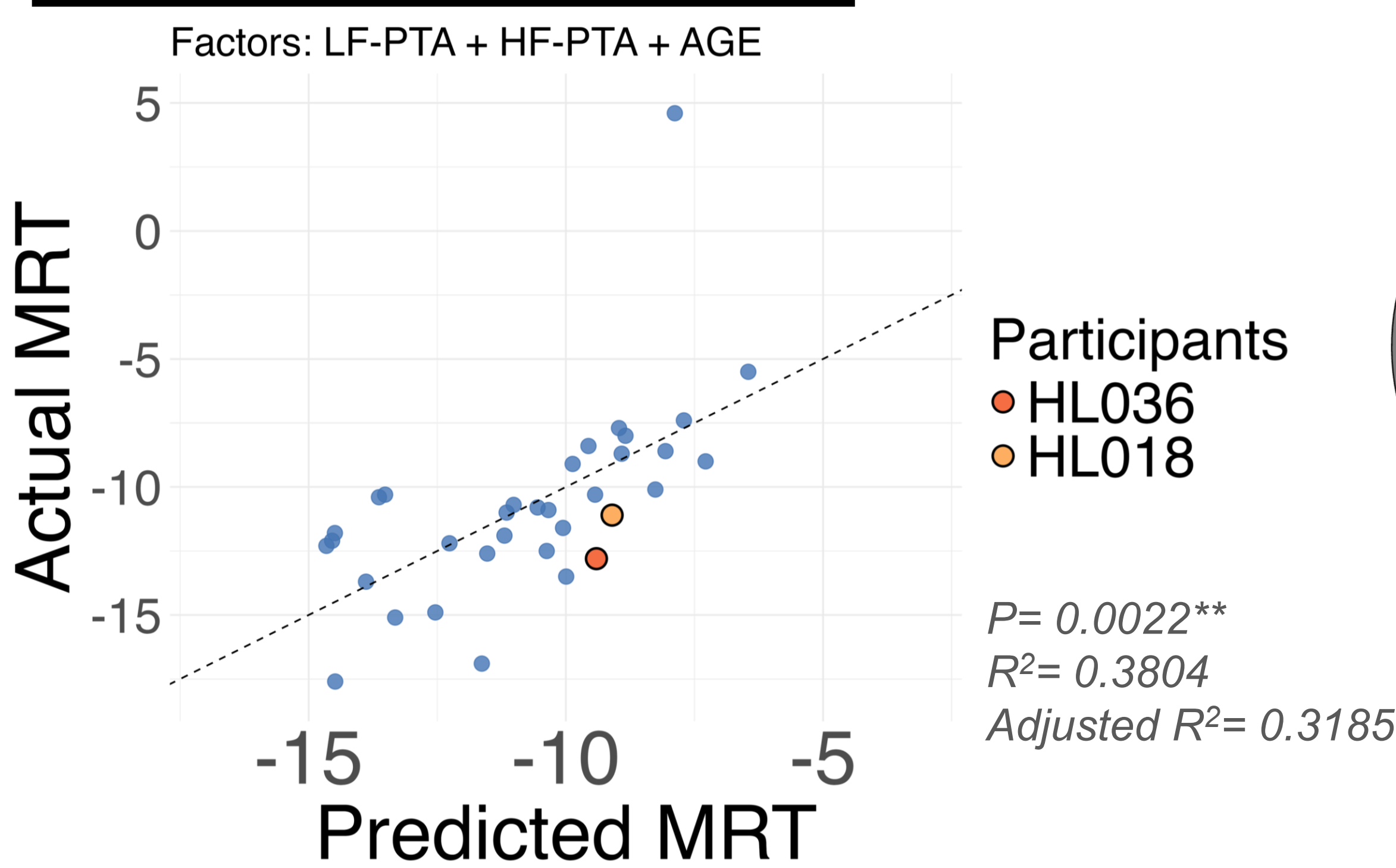**RAM-EFR Response**

## Results

### MRT Score by Group

Figure 1: Participants with hearing loss have a poorer signal to noise (SNR) threshold on average compared to subjects with normal hearing sensitivity; however, there is overlap between the distributions.

Group: HL, NH

### Model 1: Clinical Factors

Factors: LF-PTA + HF-PTA + AGE

Participants: HL036, HL018

$P = 0.0022$**
$R^2 = 0.3804$
Adjusted $R^2 = 0.3185$

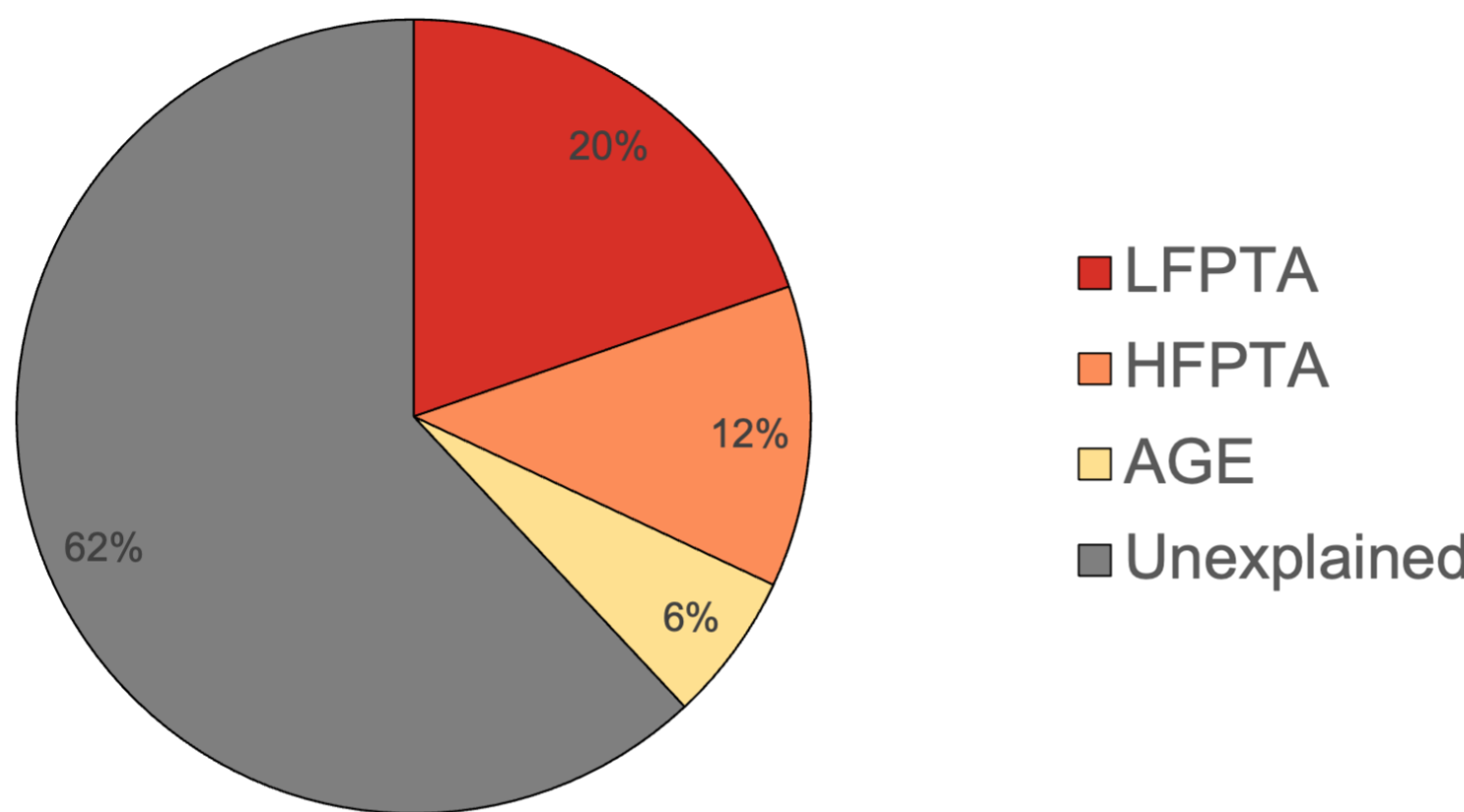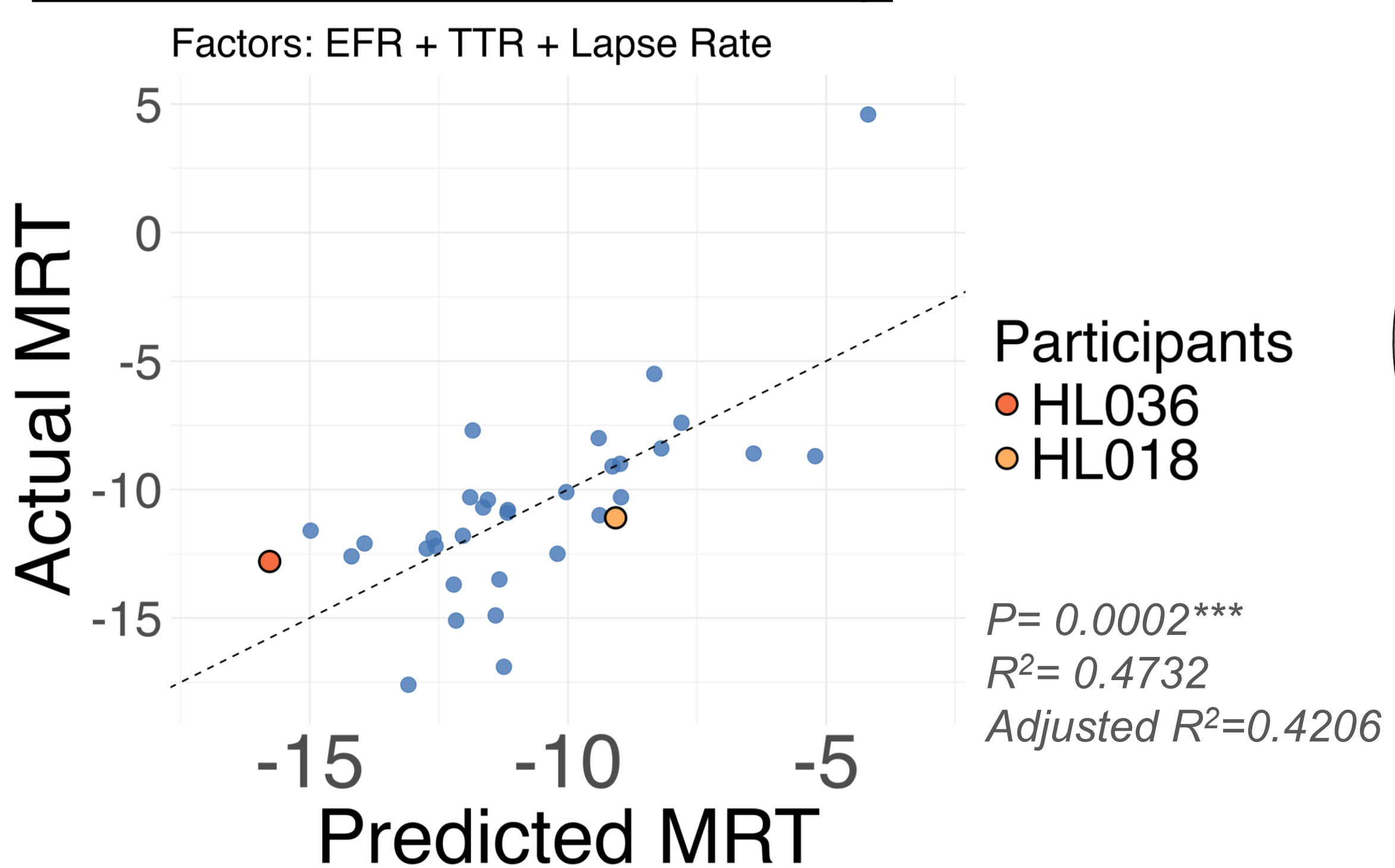Variance Explained: LFPTA 20%, HFPTA 12%, AGE 6%, Unexplained 62%

Figure 2: Traditional clinical factors significantly predict 38% of the variance in participants' MRT threshold.

### Model 2: Biomarkers Only

Factors: EFR + TTR + Lapse Rate

Participants: HL036, HL018

$P = 0.0002$***
$R^2 = 0.4732$
Adjusted $R^2 = 0.4206$

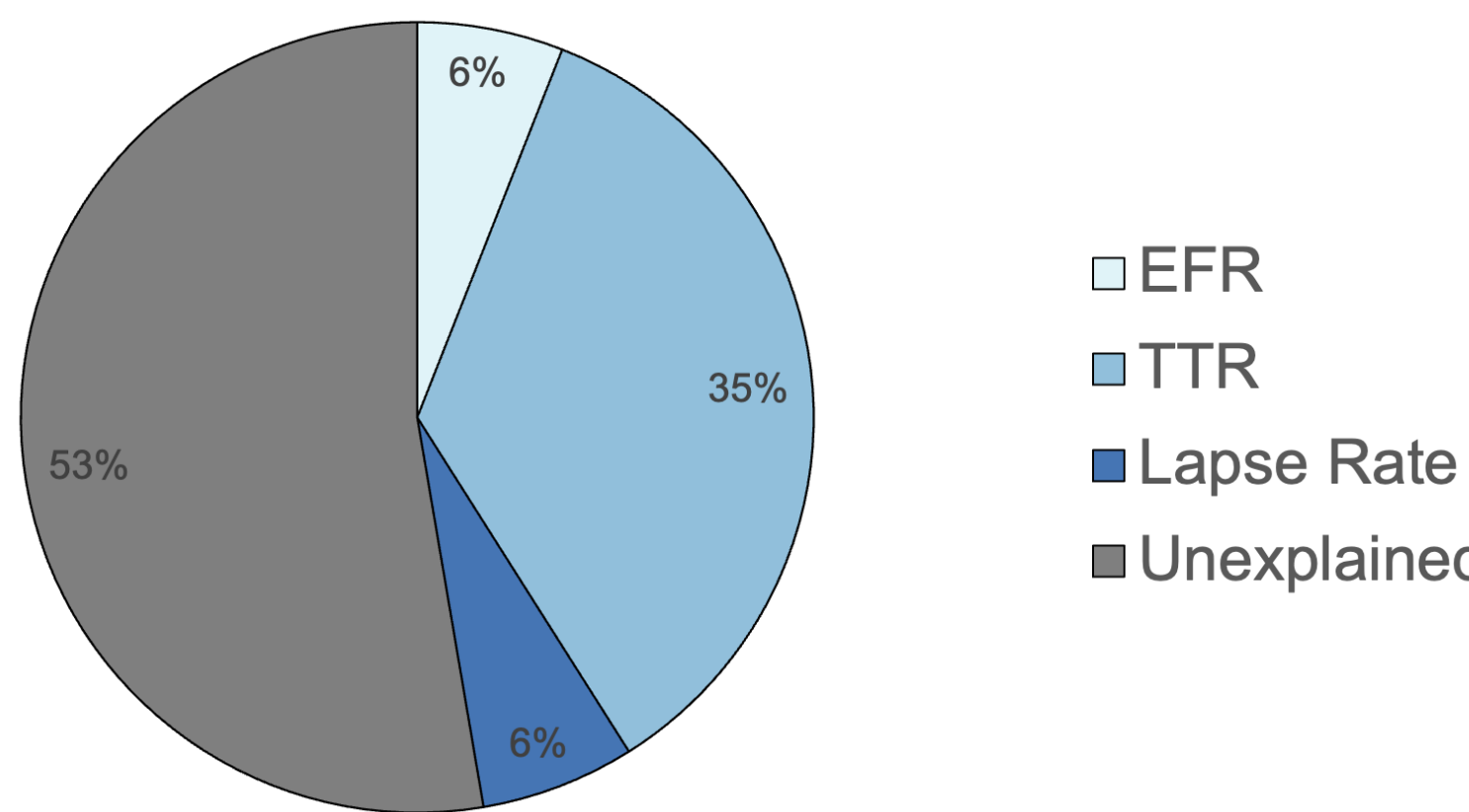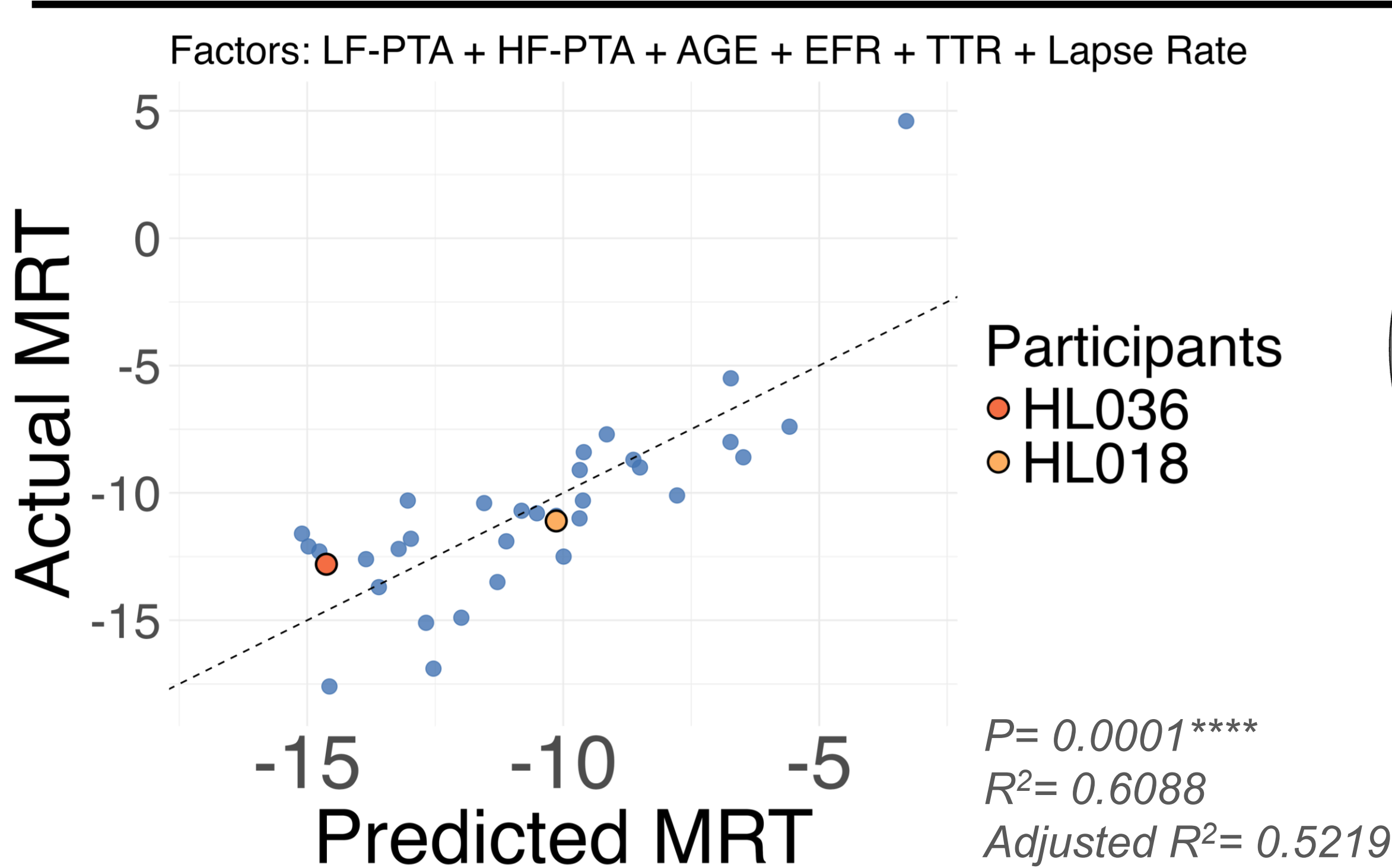Variance Explained: EFR 6%, TTR 35%, Lapse Rate 6%, Unexplained 53%

Figure 3: Biomarkers alone significantly predict 47% of the variance in participants' MRT threshold

### Model 3: Clinical and Biomarkers Combined

Factors: LF-PTA + HF-PTA + AGE + EFR + TTR + Lapse Rate

Participants: HL036, HL018

$P = 0.0001$****
$R^2 = 0.6088$
Adjusted $R^2 = 0.5219$

Variance Explained: LFPTA 16%, HFPTA 9%, AGE 7%, EFR 4%, TTR 16%, Lapse Rate 9%, Unexplained 39%
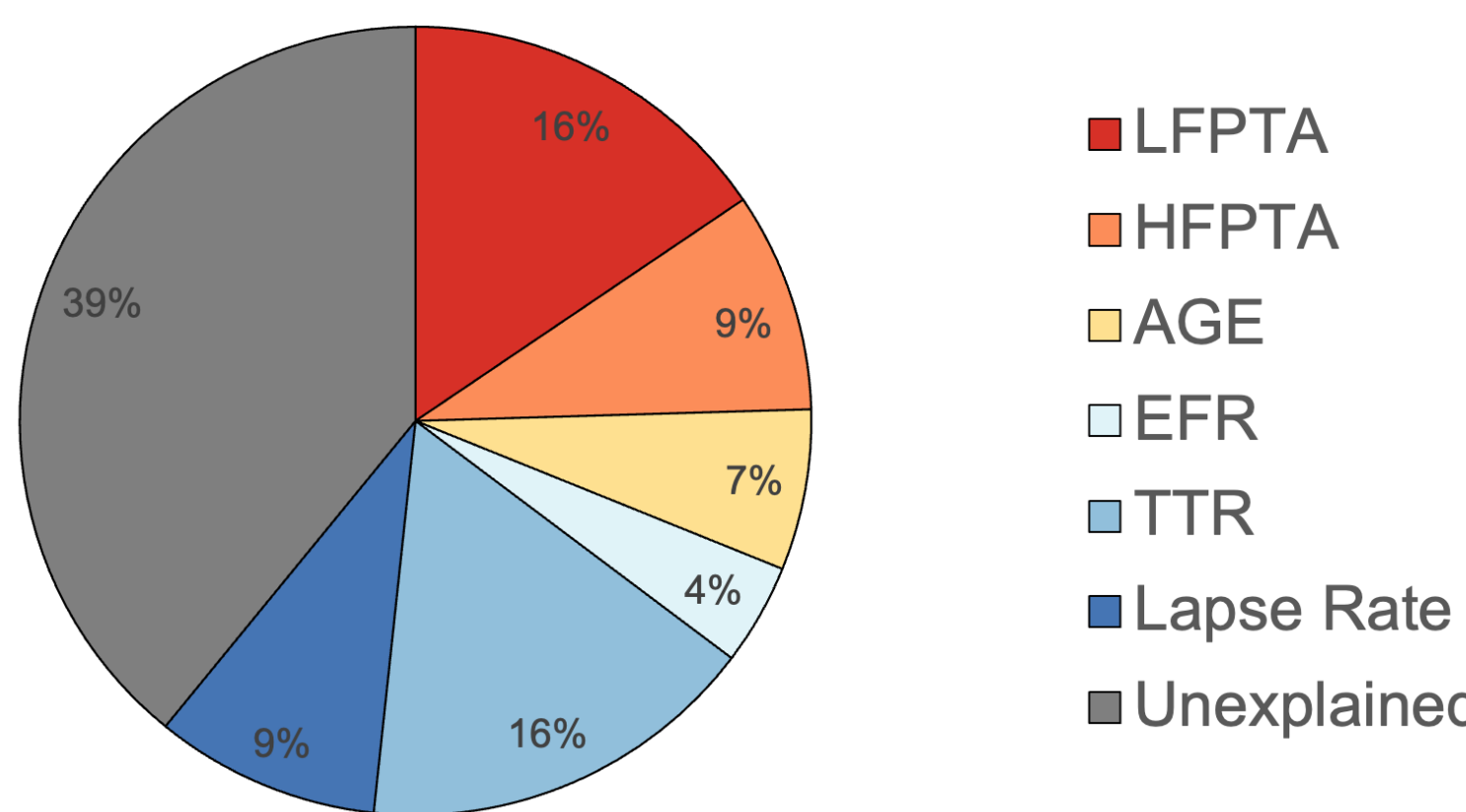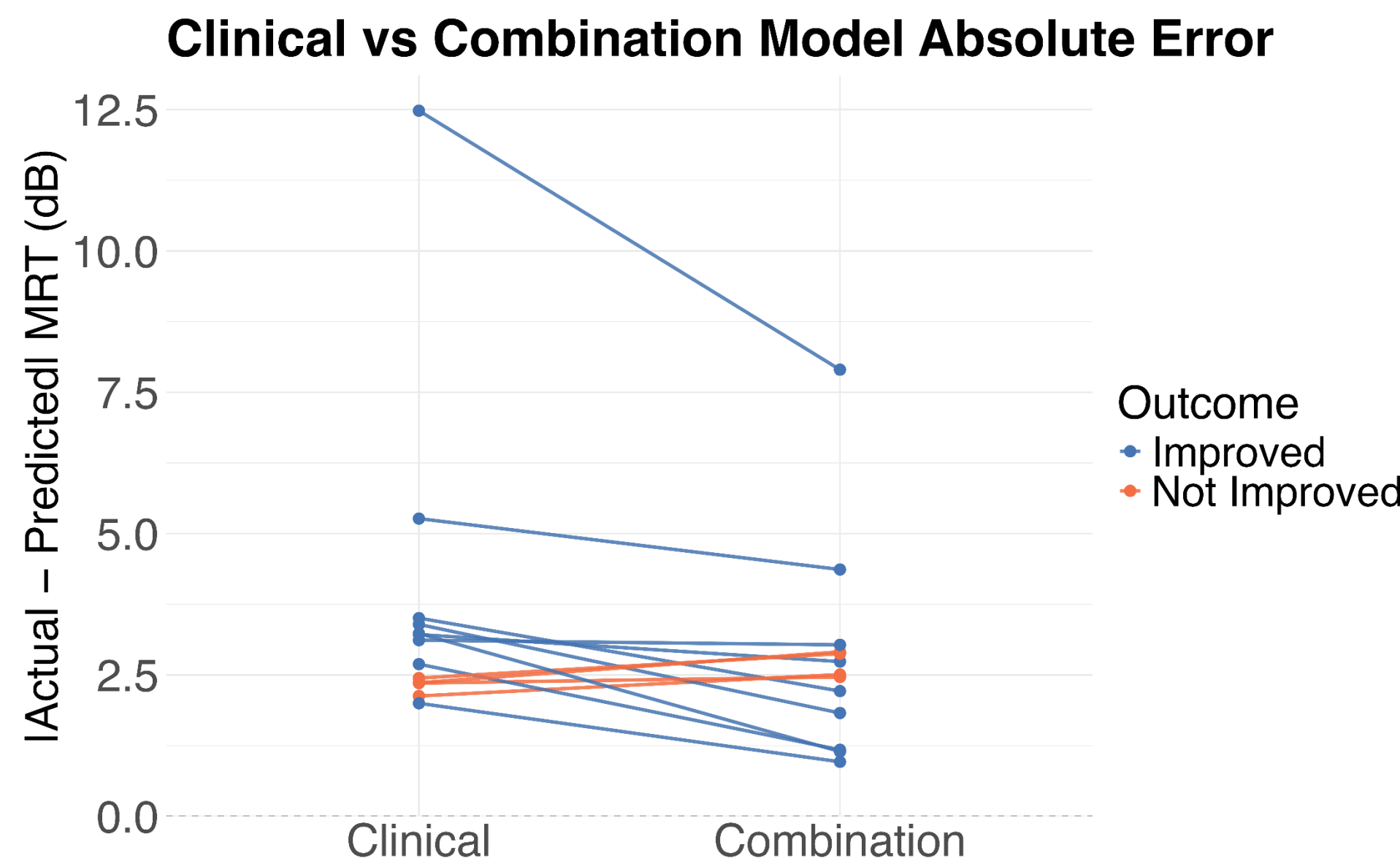
Figure 4: With the combination model, an additional 22% of the variance is explained by adding the biomarkers to the clinical factors

## Physiological Biomarkers Improve Predictions of Speech-in-Noise Over Clinical Metrics

### Improving Predictions

13 participants (out of 34 total) had a greater than or equal to 2 dB error with the Clinical Model. The majority of those participants showed a reduction in the error with the Combination Model.

**Clinical vs Combination Model Absolute Error**

Outcome: Improved, Not Improved

### Example Participants

Two examples of listeners with similar clinical metrics, but different speech in noise (SPIN) outcomes. The addition of biomarkers better accounts for these differences compared to the clinical model.

| Subject ID | Age (Y) | LF-PTA (dB HL) | HF-PTA (dB HL) | EFR (dB uV) | Lapse Rate | TTR (dB) | Actual MRT | Clinical Model | Combo Model |
|---|---|---|---|---|---|---|---|---|---|
| HL036 | 71 | 28.75 | 37.5 | 0.95 | 0.19 | 29.2 | -12.8 | -9.4 | -14.63 |
| HL018 | 41 | 26.25 | 46.25 | -0.55 | 0.11 | 12.4 | -11.1 | -9.1 | -10.14 |

## Conclusions

- Using a combination model improves accuracy of the predictive model over clinical metrics alone.
- MRT scores that are poorly predicted by the audiogram can generally be improved by the addition of biomarker factors to the model.
- Incorporation of the biomarkers with the clinical factors (i.e., the combination model) does not disrupt prediction of MRT scores.

## Future Directions

- In future work, we will add wideband middle ear muscle reflex (WB-MEMR) measurements to the models as a biomarker of cochlear synaptopathy and test whether this improves the predictions of speech.
- We will integrate audiological and otologic history of participants into our analyses.
- Ultimately, we hope to relate physiological profiles to estimated cochlear pathology profiles.

**References**: [1] Hauser et al., MoH, 2024. [2] Hauser, 2025. [3] Whitcomb, Clin Transl Gastroenterol, 2019. [4] Bharadwaj et al., Comm Biol, 2022. [5] Henry et al., J Neuroscience, 2019 [6] Parida & Heinz, Hearing Research, 2022. [7] Bharadwaj et al., MoH, 2024. [8] Vasilkov et al., Hearing Research, 2021. [9] Garrett et al., eNeuro, 2025. [10] Stone & Moore, JASA 2014. [11] Brojigin et al., eNeuro, 2022.