

## ABSTRACT

**Introduction:** Meniere's disease (MD) is largely diagnosed with clinical criteria supported by audiometry. Recently, vestibular evoked myogenic potential (VEMP) testing has emerged as a diagnostic tool despite variability in the assessment and application of frequency tuning criteria. This study aims to analyze the diagnostic value of the 1000/500 Hz amplitude ratio (AR) of ocular VEMP (oVEMP) and cervical VEMP (cVEMP) in patients with MD and non-MD vestibulopathy.

**Setting:** A retrospective review of patients with vestibular testing from 2020 to 2022 at a tertiary care center. Patients were grouped by MD or non-MD vestibulopathy. A subset analysis was performed on MD with vestibular migraine (VM). The primary outcome was the 1000/500 Hz AR. A positive ratio cutoff was >0.94 for cVEMP, >0.92 for oVEMP, and absent response was designated a value of 1. Value designations were determined from preexisting literature. Descriptive statistics, univariate and regression analyses were performed.

**Results:** Review yielded 93 ears in 91 patients (Mean Age 47.9, range 18-77), with 41 MD and 50 non-MD patients. Differences in age, gender, and ethnicity were not significant ( $p = 0.81$ ,  $p = 0.53$ ,  $p = 0.45$ , respectively). There was no significant difference in the 1000/500 Hz AR between MD and non-MD ( $p = 0.91$ ), nor in subset analyses of MD cohort disease activity ( $p = 0.28$ ), stage ( $p = 0.18$ ), or concomitant VM ( $p = 1.00$ ). Increasing age correlated with decreasing 500 Hz values in the MD ( $p = 0.005$ ) and non-MD cohort ( $p = 0.002$ ). Increasing age correlated with decreasing 1000 Hz values only in MD ( $p = 0.039$ ). Age corrected linear regression showed no significant association between VEMP amplitudes and MD diagnosis. ROC curve analysis demonstrated cVEMP and oVEMP to be poor predictors of MD diagnosis (AUCs of 0.47 and 0.46 respectively). Ideal cutoff for cVEMP was determined to be 0.45 (sensitivity 90.7%, specificity 16.0%), and ideal cutoff for oVEMP was 1.78 (sensitivity 7.0%, specificity 98%).

**Conclusion:** The 1000/500 Hz AR, or the "VEMP tuning," may not distinguish MD from non-MD vestibulopathy. To our knowledge, this is the largest study to date on the diagnostic utility of VEMP to distinguish MD from non-MD vestibulopathy, including those with VM, superior semicircular canal dehiscence, benign paroxysmal positional vertigo, labyrinthitis, and uncompensated vestibulopathy of unknown etiology.

## INTRODUCTION

MD is largely diagnosed with clinical criteria supported by audiometry, but it remains a tricky diagnosis with inconsistent and sometimes conflicting findings<sup>1-6</sup>

oVEMP measures utricular and superior vestibular nerve function while cVEMP measures saccular and inferior vestibular nerve function<sup>7-8</sup>

VEMP response at 500 Hz yields the largest response amplitude in young normal adults; **it has been suggested that 1,000 Hz becomes the dominant stimulating frequency in MD**, hence making the 1,000/500 Hz AR a promising diagnostic metric

Preliminary studies have demonstrated the ability of multi-frequency VEMPs to accurately detect MD compared to healthy controls,<sup>13,14</sup> however the ability to differentiate between MD, vestibular migraine, vestibular neuritis, and benign paroxysmal positional vertigo based on VEMPs alone remains unclear<sup>15-17</sup>

**Thus, the objective of this study was to analyze the diagnostic value of the 1000/500 Hz AR of oVEMP and cVEMP in patients with MD versus non-MD vestibulopathy**

## METHODS

• **Retrospective chart review** approved by the Mount Sinai IRB

• **Setting/Population:** Patients with vestibular symptoms evaluated with multi-frequency VEMP (MF-VEMP) testing at a tertiary care center from 2020 to 2022. Patients were grouped as MD (probable or definite MD) versus non-MD (vestibular migraine, superior semicircular canal dehiscence, benign paroxysmal positional vertigo, labyrinthitis, and uncompensated vestibulopathy of unknown etiology)

• **Primary outcome:** 1000/500Hz amplitude ratio (AR)

• **Variables:**

- Demographics: age, gender, race/ethnicity, insurance, and comorbidities
- Audiometric: Pure tone average (PTA)
- Vestibular: diagnosis, 1000Hz and 500Hz amplitudes on MF-VEMP

• **Statistical Analysis:** Univariate and Bivariate analyses, Linear Regression, Receiver-operating Curves (ROC)

## RESULTS

- 93 ears in 91 patients met inclusion criteria. 40 were men, 51 were women
- The mean age of our cohort was 47.9 years, with 41 in the MD cohort, and 50 in the non-MD vestibulopathy cohort
- **The distribution between cohorts was balanced, with no significant differences by demographics (Table 1, right)**

• **There was no significant difference in the number of positive or negative MF-VEMP tests between the MD and non-MD, nor in subset analyses of MD cohort disease activity, stage by PTA, or the presence of concomitant vestibular migraine (Table 2, below)**

	MD	Non-MD	<i>p</i>		
<b>Positive MF-VEMP</b>	35	42	0.91		
<b>Negative MF-VEMP</b>	6	8			
Disease Activity					
	Active MD	Inactive MD	<i>p</i>		
<b>Positive MF-VEMP</b>	16	8	0.28		
<b>Negative MF-VEMP</b>	5	0			
Disease Stage					
	Stage 1	Stage 2	Stage 3	Stage 4	<i>p</i>
<b>Positive MF-VEMP</b>	9	6	11	2	0.18
<b>Negative MF-VEMP</b>	4	1	0	1	
Concomitant VM					
	MD Only	MD with VM	<i>p</i>		
<b>Positive MF-VEMP</b>	30	5	1.0		
<b>Negative MF-VEMP</b>	6	0			

Table 2: Contingency tables for positive/negative MF-VEMP testing and vestibular diagnosis, MD disease activity, MD disease stage, and concomitant VM

- For cVEMP: we performed linear regression to assess the impact of age on ARs and found that increasing age correlated with decreasing 500Hz and 1000 Hz amplitudes in MD, and only with decreasing 500Hz response in the non-md group
  - *We selected cVEMP for further analysis, as saccular hydrops has been shown to be more pronounced in MD<sup>12</sup>*

• **There was no significant association on multivariate linear regression correcting for age (Figure 1, below)**

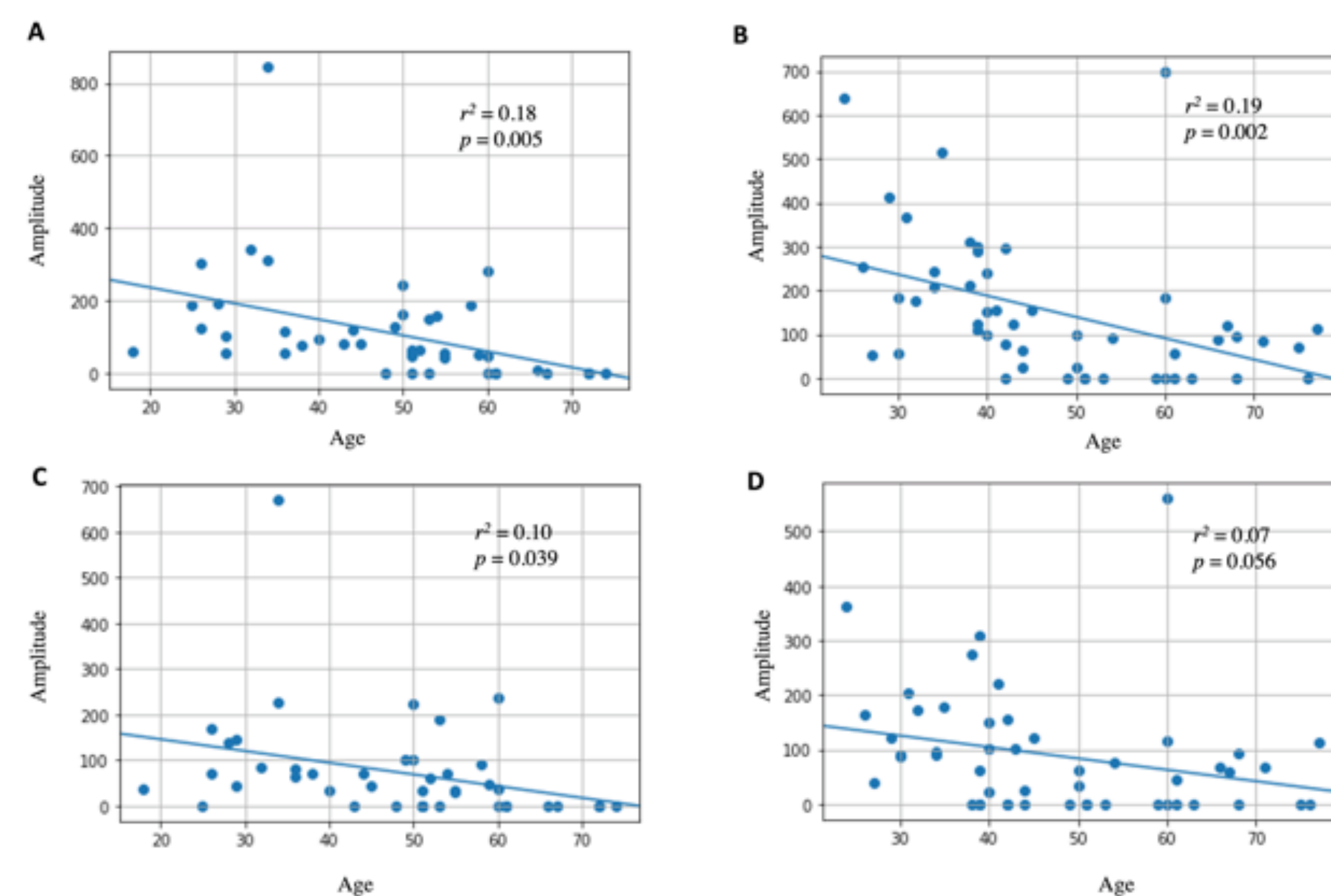


Figure 1: Linear regression of (A) cVEMP 500 Hz amplitude and age in definite/probable MD, (B) cVEMP 500 Hz amplitude and age in those with non-MD, (C) cVEMP 1000Hz amplitude and age in those with definite/probable MD, (D) cVEMP 1000Hz and age for those with non-MD

	Definite/Probable MD (n = 41)	Non-MD (n = 50)	P-value
<b>Sex</b>			
Male	20 (48.8%)	20 (40.0%)	0.53
Female	21 (51.2%)	30 (60.0%)	
<b>Age</b>			
mean (SD)	48.3 (14.4)	47.5 (14.4)	0.81
<b>Ethnicity</b>			
White	18	23	0.45
African-American	0	2	
Asian	5	3	
Other/Unknown	18	22	
<b>Comorbidities</b>			
Diabetes Mellitus	1	3	0.47
Hypertension	2	6	0.16
Hyperlipidemia	4	8	0.19
Depression	3	6	0.70
Cancer	2	2	0.76
Coronary Artery Disease	0	2	0.39
Thyroid disease	2	4	0.50
Asthma	2	6	0.16
Anemia	0	2	0.39
ADHD	3	0	0.31
Anxiety	6	3	0.70

Table 1: Differences in Demographics between those with MD and those with non-MD

- We calculated the Area under the curve (AUC) for the ROC curve of ARs = 0.47 for cVEMP and 0.46 for oVEMP
  - *The AUC is an effective way to summarize the overall diagnostic accuracy of a test. It takes values from 0 to 1, where a value of 0 indicates a perfectly inaccurate test, and a value of 1 reflects a perfectly accurate test. Generally an AUC of .5 suggests no discrimination (which is the ability to diagnose patients with and without the disease or condition based on the test)*

- Ideal cutoff for cVEMP was determined to be 0.45 (sensitivity 90.7%, specificity 16.0%, PPV 0.48)
- Ideal cutoff for oVEMP was 1.78 (sensitivity 7.0%, specificity 98%, PPV 0.75)

• **Here our results suggest that the 1000/500Hz AR may not be a reliable diagnostic marker (Figure 2, below)**

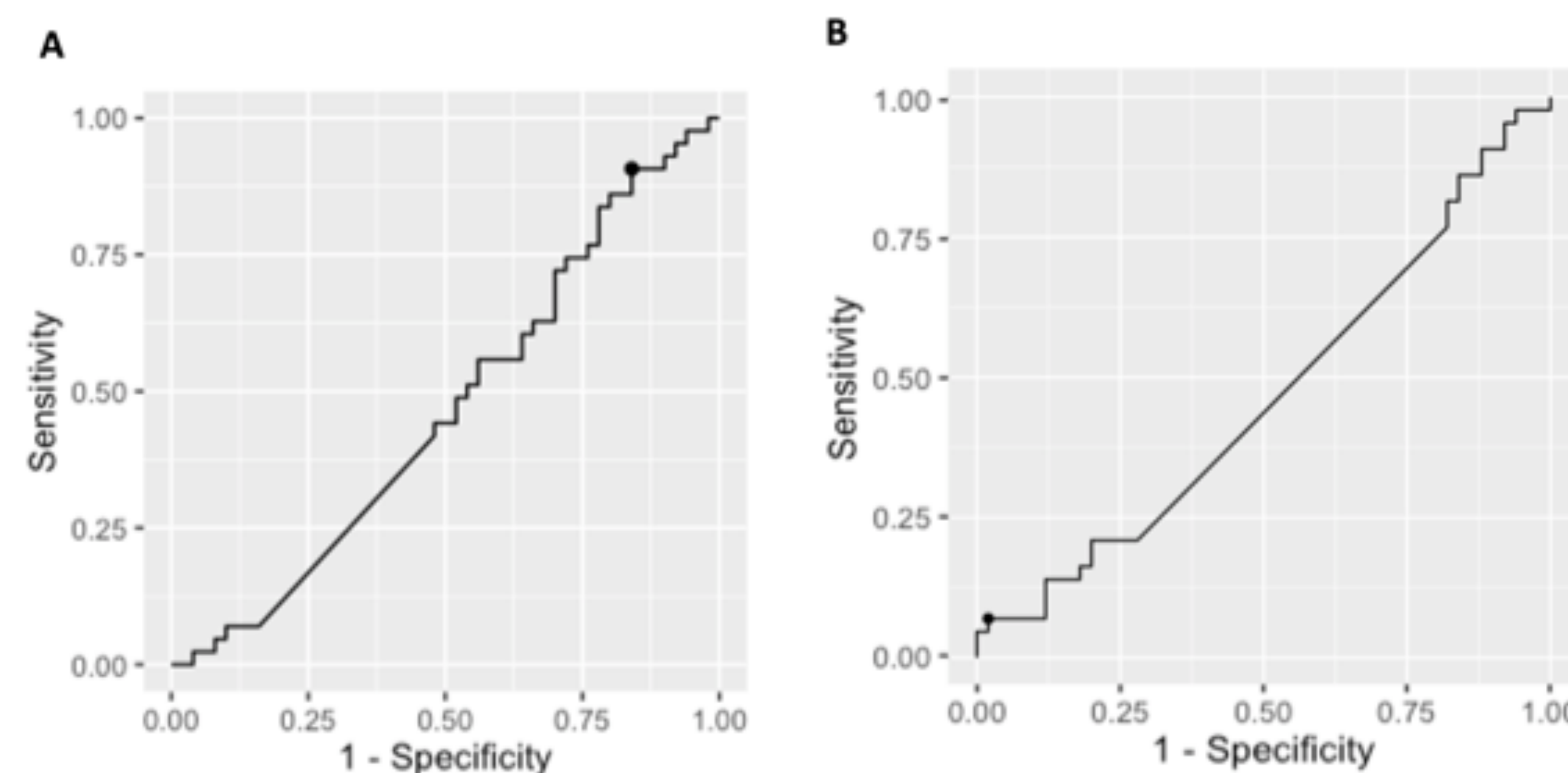


Figure 2: ROC curves for (A) cVEMP 1000/500Hz AR and (B) oVEMP 1000/500 Hz AR. Ideal cutoff (see above) indicated by black circle.

## DISCUSSION/CONCLUSION

- Increased age has been correlated with a shift in frequency tuning of cVEMP and oVEMP to higher frequencies, usually 1000 Hz or beyond
- Prior studies have found that cVEMP 1,000/500 Hz amplitude ratio increases by a decrease of the 500 Hz amplitude with increasing age, and can discern between active and inactive MD activity.
- Our data suggests the 1000/500 Hz AR may not distinguish MD from non-MD vestibulopathy.
- Larger sample sizes with standardized VEMP testing protocols are necessary to definitely make this association.
- This is the largest study to date evaluating the diagnostic utility of the 1000/500 Hz AR comparing MD or non-MD vestibulopathy

## REFERENCES

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