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Introduction

Background

- Headache has been known comorbidity of many Méniere's attacks ever since Prosper Ménière proposed his namesake disease in 19th century
- Current estimates of migraine prevalence in Méniere's disease is reported around 50%-c.f. 12% prevalence in the general population
- Despite this well-known comorbidity, systemic characterization of migraine effects on clinical presentation of MD is lacking

Objectives

- Herein we undertook comparison of Méniere's Disease (MD) and Migrainous Méniere's Disease (MMD) patients to characterize migraine effects on three specific clinical features of MD:
 - 1) Duration of definite vertigo attacks
 - 2) Saccular function as assessed by cVEMP amplitude
 - 3) Cochleosaccular endolymphatic hydrops severity as assessed by grading 4-hr delayed 3D-FLAIR MR imaging

Methodology

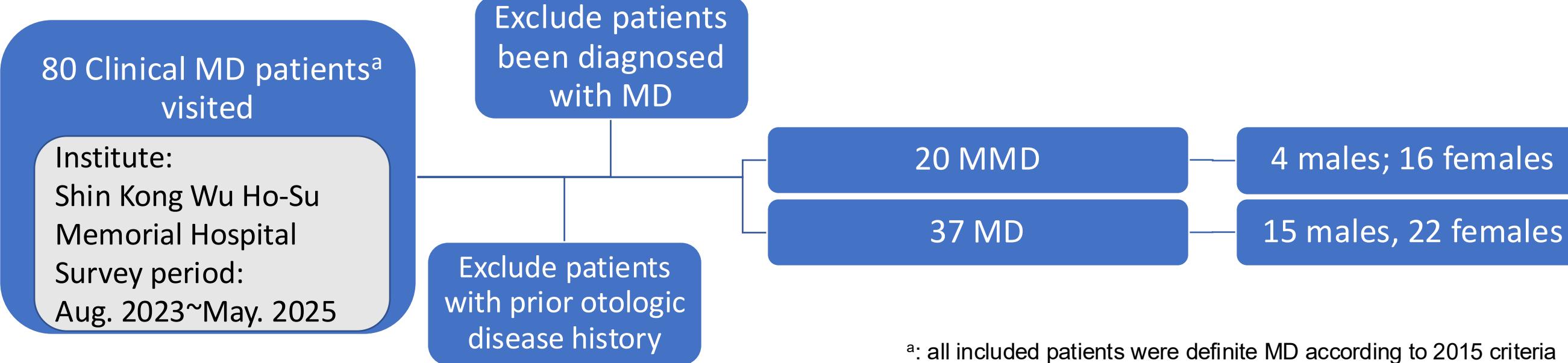


Figure 1 Flow chart of patient selection

Patient Selection

- Prospective consecutive MD and MMD patients in a tertiary care hospital "dizzy clinic" setting. The details are as shown in the flow chart (Figure 1)

Diagnosis Criteria

- Definite MD was diagnosed according to 2015 international consensus diagnostic criteria and was limited to newly diagnosed patients with no prior otologic history or treatment
- Migraine headache was diagnosed according to the ICHD-3 criteria
- MMD indicates patients having migraine headache temporally (before, during, or after) associated with Méniere attacks

Méniere Attack Duration

- Duration of Méniere attacks were classified as <1 hour (mild), 1-6 hours (moderate), and ≥6 hours (severe)

Saccular Function Assessment

- All MD and MMD participants and an age-matched control group were included for the cVEMP comparisons

- 500Hz tonebursts at 95dB intensity acoustic stimuli and standard cervical VEMP electrode montage were used. Response amplitude was recorded for each affected ear of MD and MMD participants and for both ears of each normal control participant.

Endolymphatic Hydrops Imaging

- All MD and MMD participants underwent 4-hr delayed 3D-FLAIR MR scanning on a 3T scanner (Ingenia 3.0T, Philips, Best, Netherland) according to the protocol of Naganawa S and Nakashima T [2014]
- Hydrops grading was according to Bernaert's 4-stage grading system [2019] and the evaluations were done by an experienced neuroradiologist blinded to clinical case details

Results

Demographics of Pathological and Control Groups

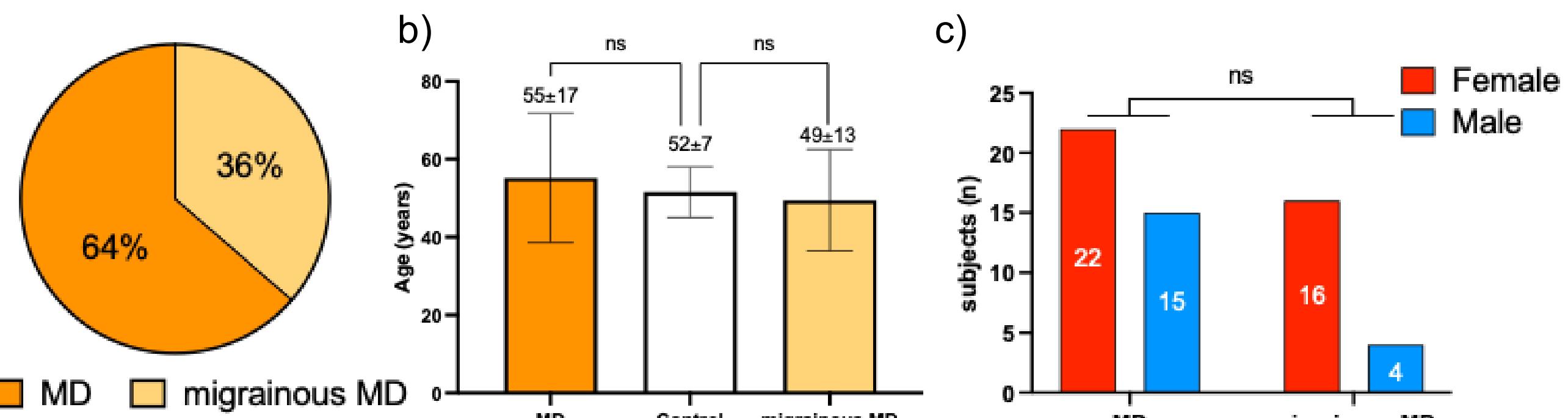


Figure 2 Demographics of MD, MMD, and healthy control cohorts

- The MMD cohort accounted for 36% of the entire study population, consistent with previous reports of MMD prevalence (Figure 2a)
- Age at disease onset in the MD cohort was 55±16 (mean±SD) years, slightly older than 49±13 years of the MMD cohort (Figure 2b). There were no age difference between control and pathological groups.
- Female-to-male ratio in the MMD cohort was 4:1, substantially greater than the 1.5:1 ratio in the MD cohort, but not statistically significant for this sample size (Figure 2c)

Attack Duration in MD vs. MMD

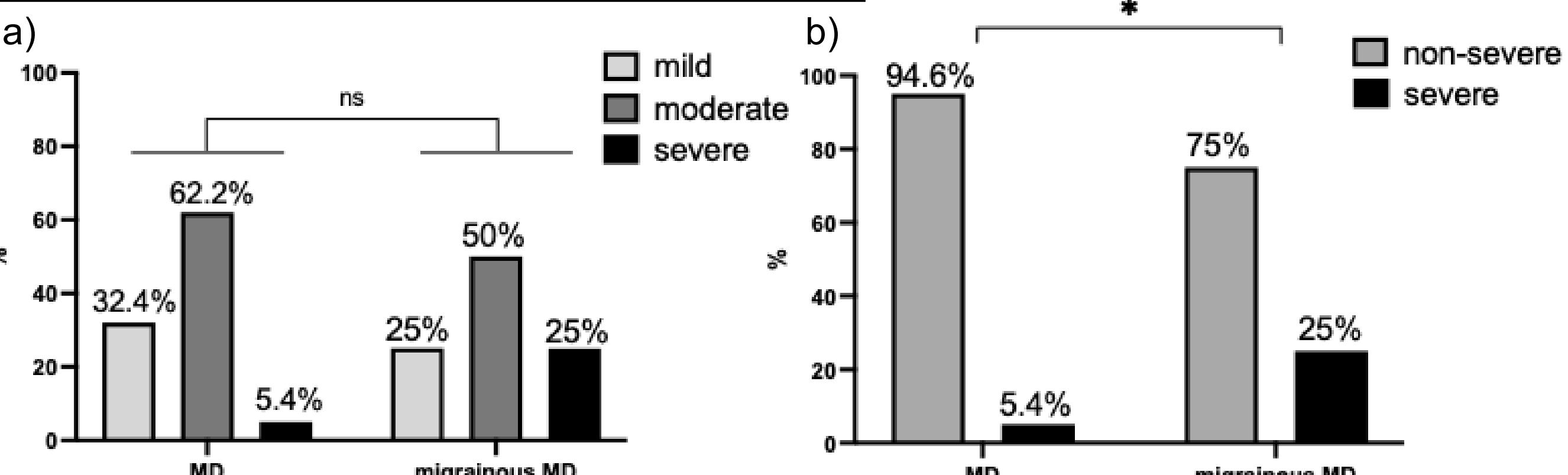


Figure 3 Attack duration across MD and MMD cohorts

- The proportion of mild, moderate, and severe attacks were 32.4%(n=12), 62.2%(n=23), and 5.4%(n=2) in the MD cohort vs. 25%(n=5), 50%(n=10), and 25%(n=5) in the MMD cohort, showing no significant difference (2x3 Chi-square test, Figure 3a)
- When the attack duration data were re-stratified as mild/moderate (<6hr duration) vs. severe (≥6hr duration), severe attacks were significantly more common in the MMD than MD cohort ($p<.05$, Chi-square test, Figure 3b)

cVEMP Amplitude in MD vs. MMD

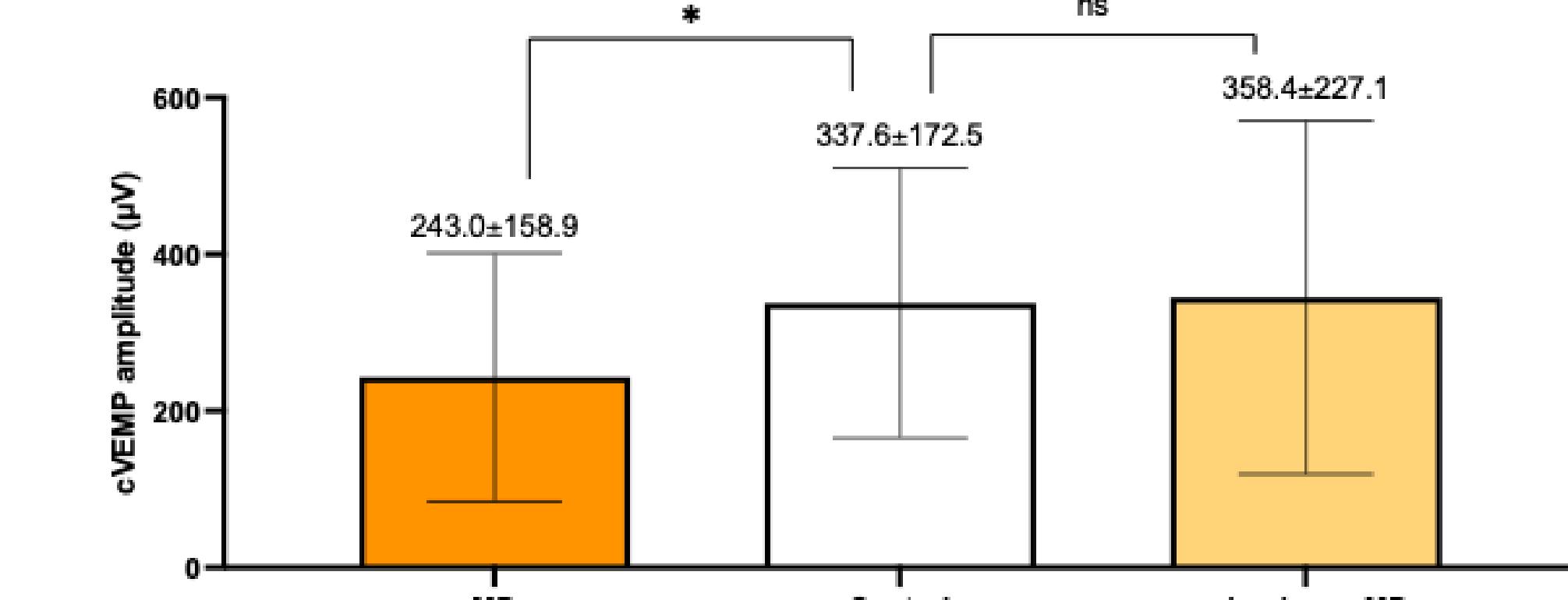


Figure 4 cVEMP amplitude among MD, MMD, and control cohorts

- Mean cVEMP amplitude of ears in the MD cohort was significantly lower than in the healthy control group ($p<.05$, unpaired t test, Figure 4)
- In contrast, mean cVEMP amplitude in the MMD cohort did not differ significantly from the control group (Figure 4)

Hydrops Grading in MD vs. MMD

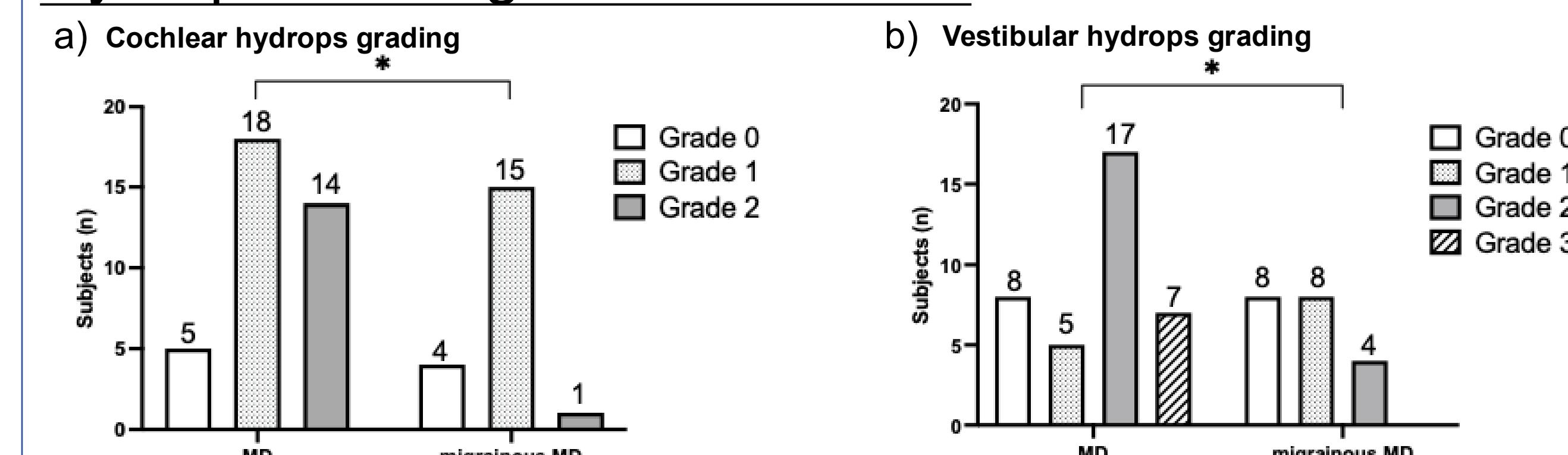


Figure 5 Hydrops grading between MD and MMD cohorts

- 54/57 (95%) of all MD and MMD participants exhibited cochlear and/or saccular endolymphatic hydrops. All 3 off the non-hydropic ears were in MMD subjects.
- In both cochlear and vestibular hydrops grading, MD cohort exhibited significantly different grading distribution than MMD cohort ($p<.05$, 2x3 and 2x4 Chi-square test, Figure 5a and 5b). For both cochlear and vestibular grading, MD ears showed greater severity of hydrops than MMD ears

Conclusion

- MMD showed a greater female preponderance than did MD
- Longer attack duration were significantly more common in the MMD than MD cohort
- The MD cohort exhibited both worse saccular function and greater degree of hydrops than the MMD cohort
- The observed discordance between objective measures of inner ear damages and subjective reports of disease symptoms aligns well with current understanding of migraine as a CNS disorder causing global intensification and/or distortion of sensory signal processing, while "simple" MD is purely an inner ear disorder
- Controlling or mitigating potential migraine contributions to Méniere symptoms should be considered an essential early step in MMD treatment