

Clinical characterisation of auditory and vestibular function in autosomal recessive type IX collagen-related Stickler syndrome (COL9A1, COL9A2 and COL9A3)

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Introduction

Autosomal recessive type IX collagen-related Stickler syndrome (COL9A1, COL9A2 and COL9A3) is a **rare inherited connective tissue disorder associated with sensorineural hearing loss** (Boothe *et al.*, 2020 and Acke *et al.*, 2022). However, vestibular and middle ear function have not previously been systematically characterised in this subtype.

Objectives

This study aimed to clinically evaluate **auditory, middle ear and peripheral vestibular function** in individuals with genetically confirmed COL9-related Stickler syndrome

Methods

DESIGN: A cross sectional population-based study

SAMPLE: Given the rarity of autosomal recessive type IX collagen-related Stickler syndrome, all known eligible UK cases were invited to participate. 8 subjects (three adults and five children) with a genetically confirmed (Genomics England PanelApp, 2026) pathogenic variant in COL9A1, COL9A2 or COL9A3 (limited to approximately 20 nationwide) were recruited from the NHS England Stickler Syndrome Highly Specialised Service (HSS).

PROCEDURE: The auditory function was studied using pure-tone audiometry (PTA) and tympanometry; Peripheral vestibular function was assessed using video head impulse test (vHIT) as a measure of the vestibulo-ocular-reflex (using ICS impulse goggles and OTOsuite Vestibular software, v.5). A questionnaire: the dizziness handicap inventory (DHI) was used to assess the self-perceived effect of dizziness.

Results

AUDIOMETRY: Hearing loss was identified in **7 out of 8 participants**, predominantly presenting as **bilateral, sloping, mild-to-moderate sensorineural hearing loss** [Figure 1 and 2]

TYMPANOMETRY: Middle ear function was within **normal limits in 11 of 16 ears**. [Figure 3]

VESTIBULAR:

- Peripheral vestibular function assessed using the video head impulse test (vHIT) demonstrated **no evidence of semicircular canal dysfunction**. [Figure 4]
- Self-perceived dizziness, measured using the Dizziness Handicap Inventory (DHI), was **absent in 6 out of 8 participants**. The **mean total DHI score was 5.71 +/- 9.62** (well below the mild handicap threshold of 16). Only 1 adult participant scooped in the mild handicap range (DHI=26), likely attributed to the concurrent visual/mucoskeletal issues.

Conclusions

Vestibular dysfunction and middle ear abnormalities do not appear to be consistent features of autosomal recessive type IX collagen-related Stickler syndrome. The predominant audiometric finding of mild-to-moderate sloping sensorineural hearing loss is consistent with previous reports. As the first study to systematically assess vestibular, middle ear and self-reported balance function in this subtype, these findings provide important clinical insight into the auditory and vestibular phenotype of type IX collagen-related Stickler syndrome.

References

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- Genomics England PanelApp. Stickler syndrome panel (R45), version 4.0: NHS Genomic Medicine Service PanelApp, Genomics England; 2026 [Available from: <https://nhsgms-panelapp.genomicsengland.co.uk/panels/3/v4.0>].

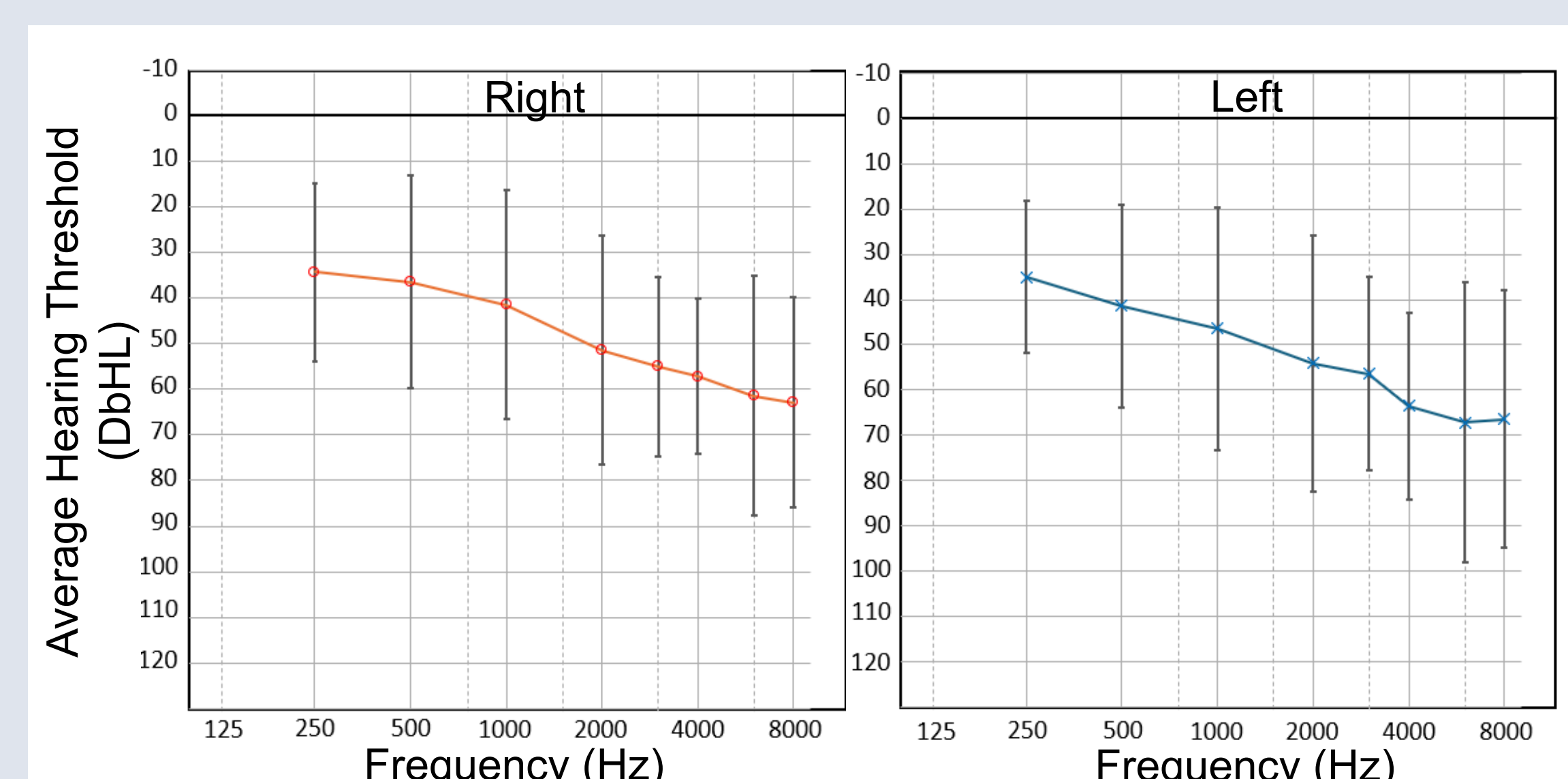


Figure 1: The mean average of PTA air-conduction thresholds of participants measured at; 250-8000 Hz (+/- SD).

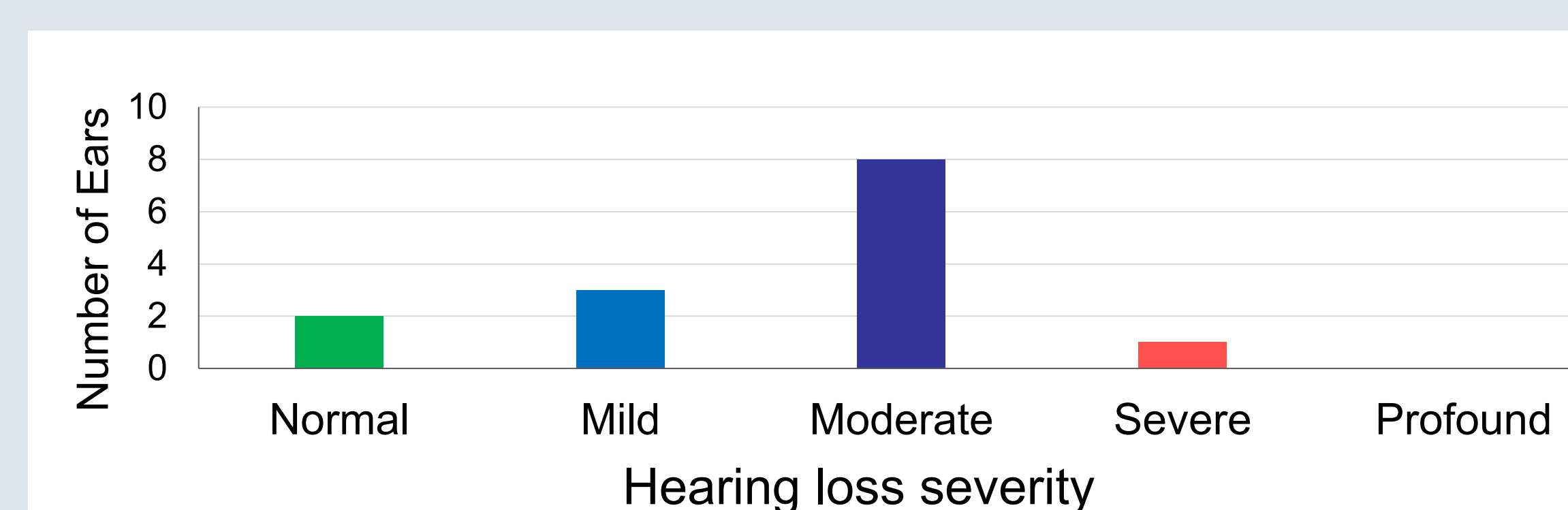


Figure 2: **Frequency distribution of hearing loss severity;** 5-frequency pure tone mean average a-c hearing thresholds for each ear, for all participants (excl. participant 6^a) as per the BSA guidelines for hearing loss severity reporting (BSA, 2018).

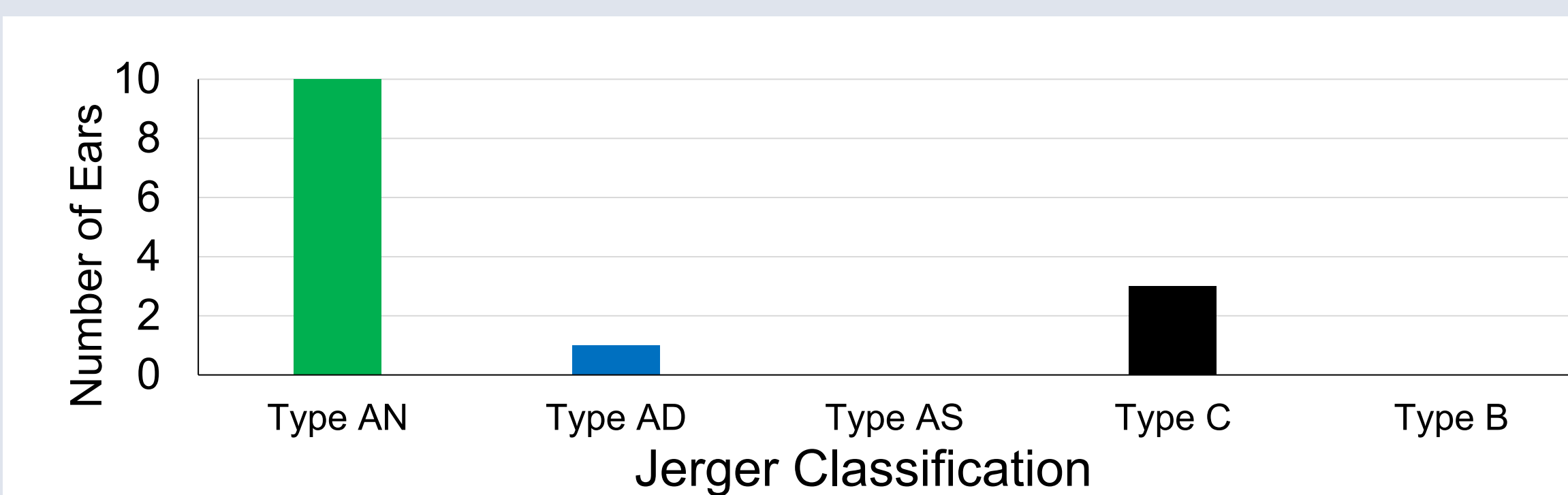


Figure 3: Frequency distribution of tympanometry by Jerger classification; Participant (excluding participant 6) tympanic membrane compliance (ml), peak pressure (mm ug) and ear canal volume (ECV) measured through 226 Hz tympanometry.

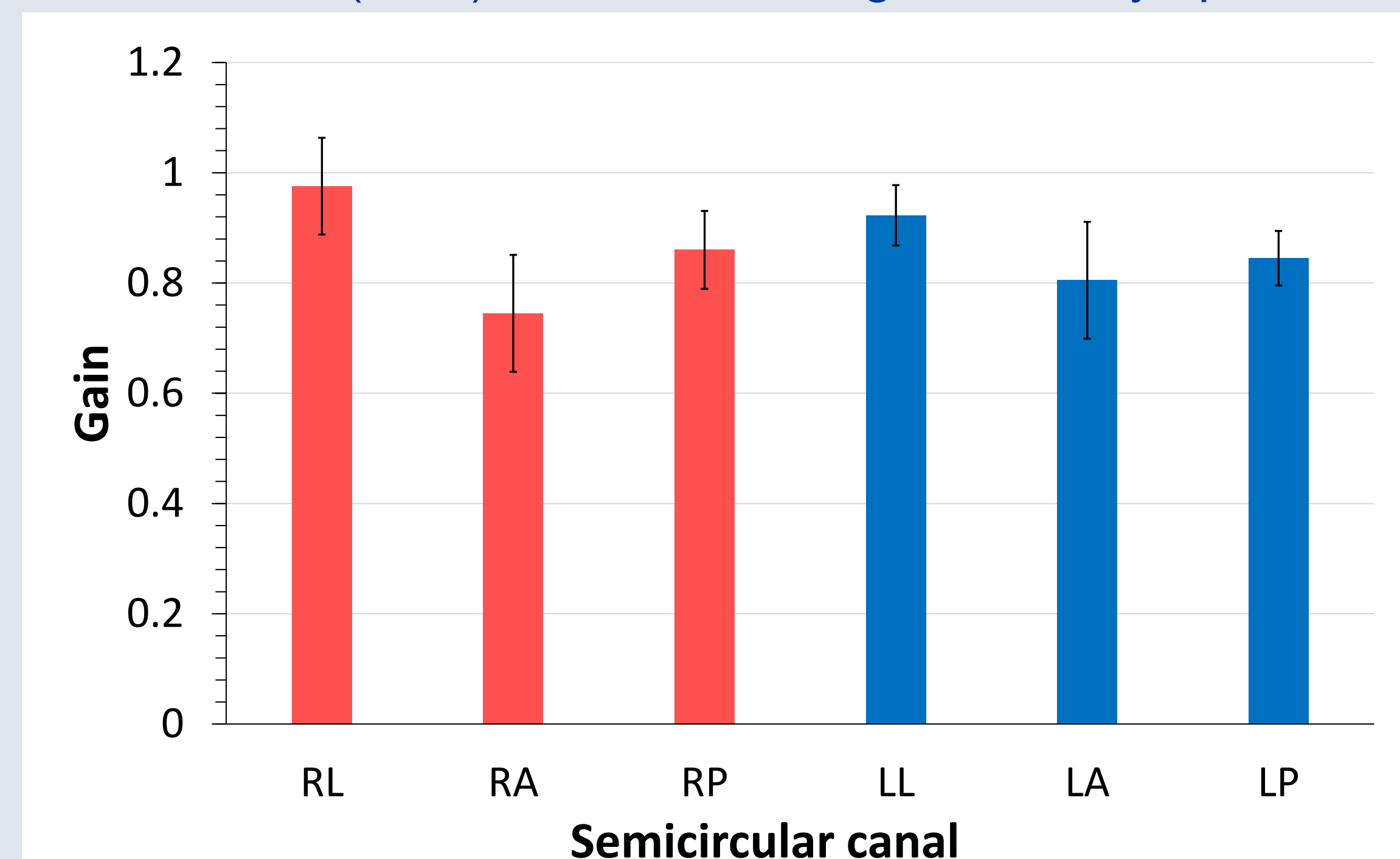


Figure 4. Average VOR gain. The mean gain (+/- SD) of vHIT assessed lateral VOR gain of 7 participants^a and vertical canals of 2 participants^b (participant 4 and 8). right lateral (RL), right anterior (RA), right posterior (RP), left lateral (LL), left anterior (LA) and left posterior (LP). The right and left lateral canals (RL and LL). ^aparticipant 6 was excluded from all vHIT testing due to non-compliance and participant 7 vertical canal data was excluded due to technical (pupil tracking) issue.

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