Probing Some Links Among Aging, Vestibular Function, and Balance

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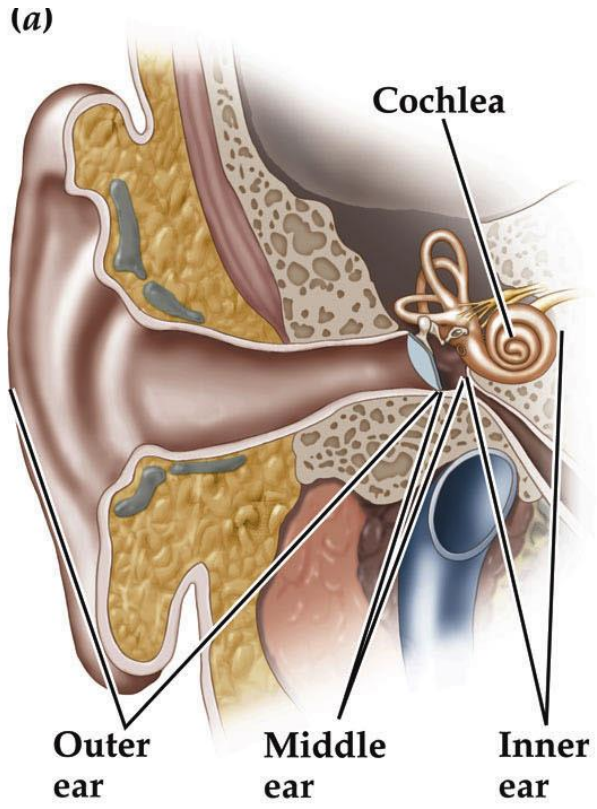
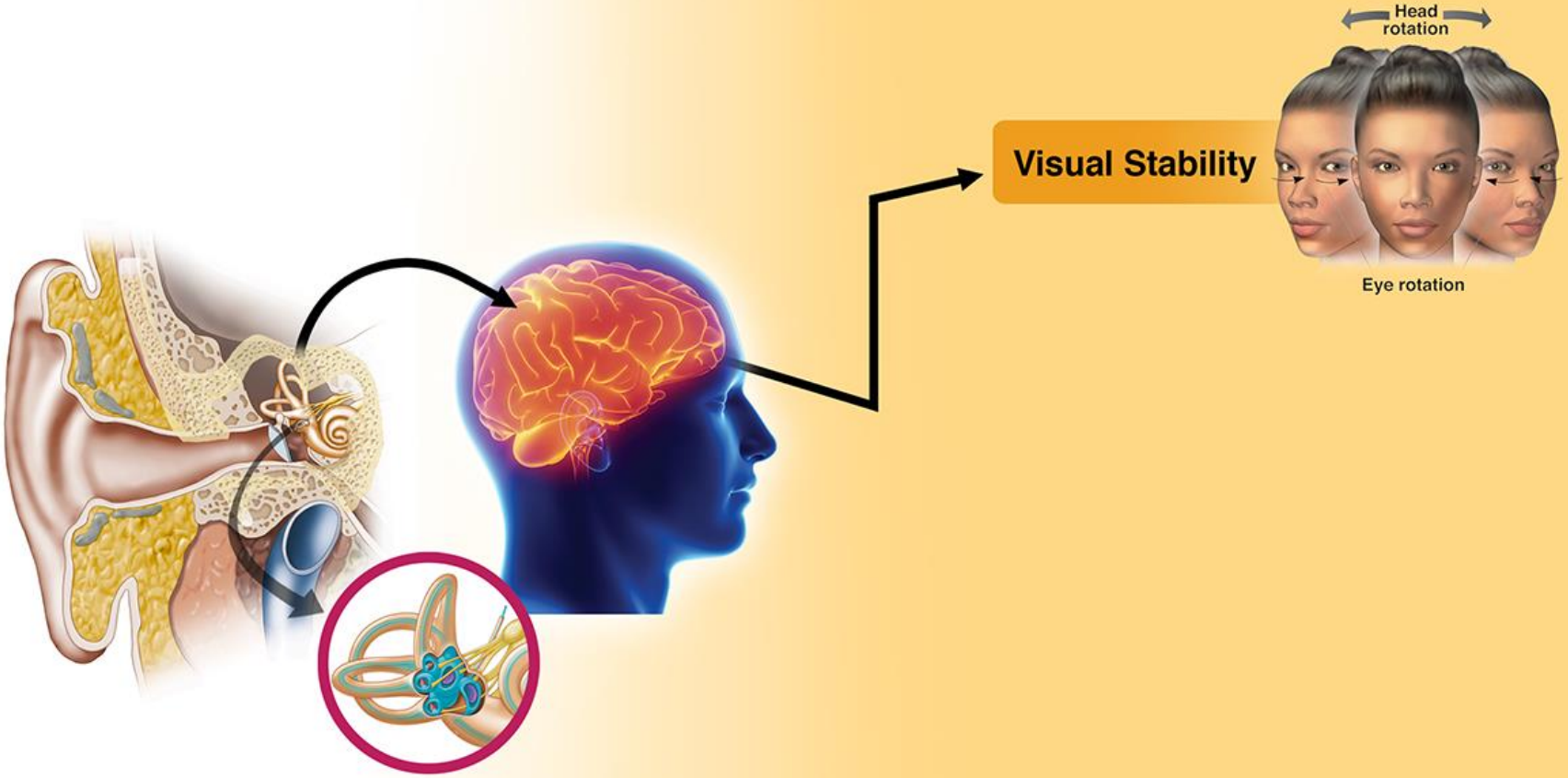
Our vestibular periphery senses rotation, translation, and tilt



SENSATION & PERCEPTION 3e, Figure 12.6

The Vestibular System in Action



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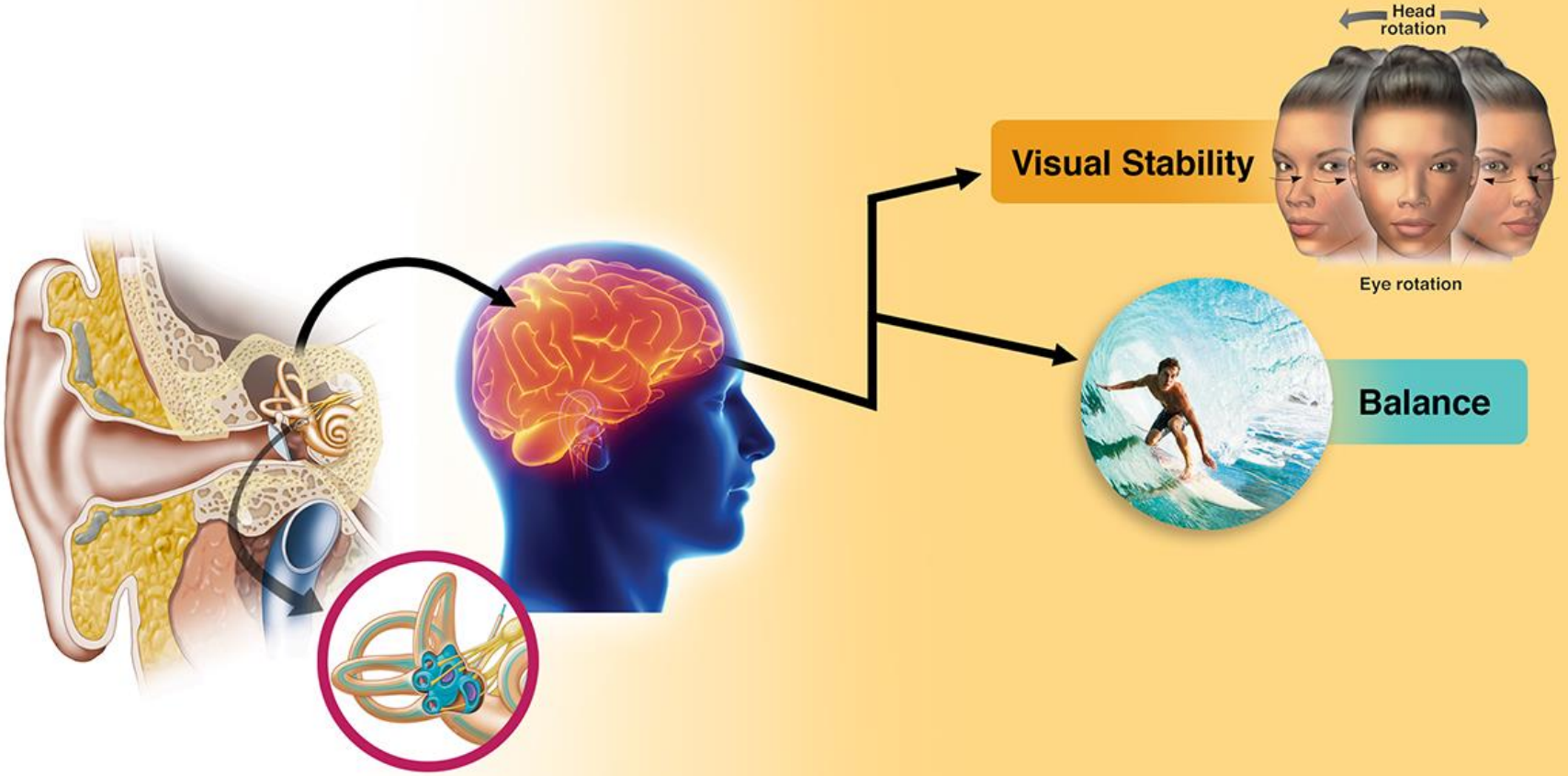

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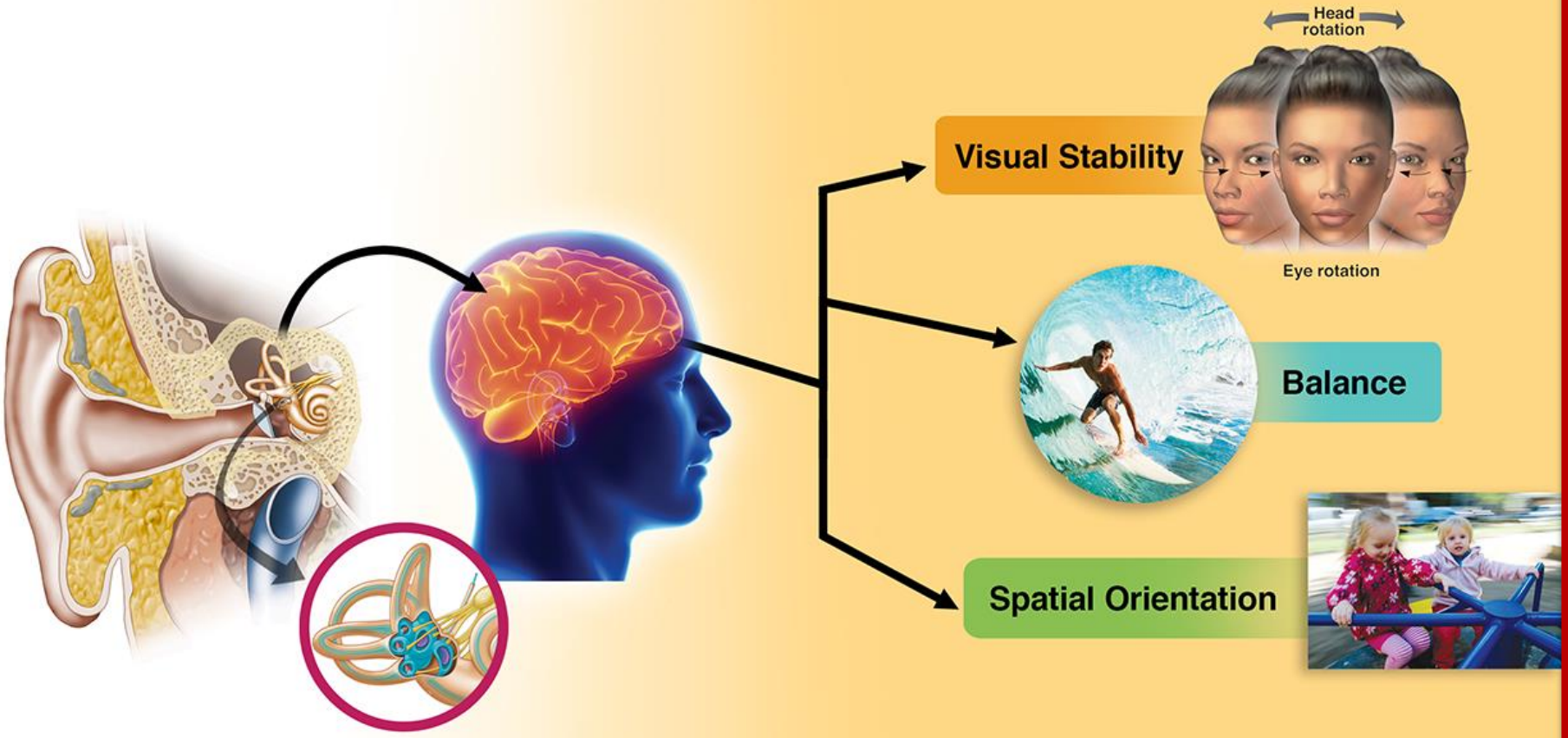

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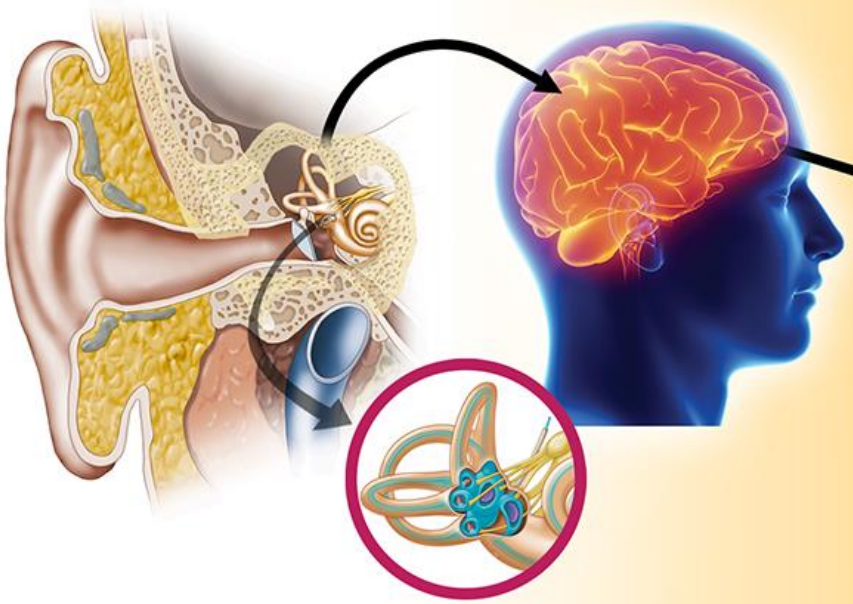
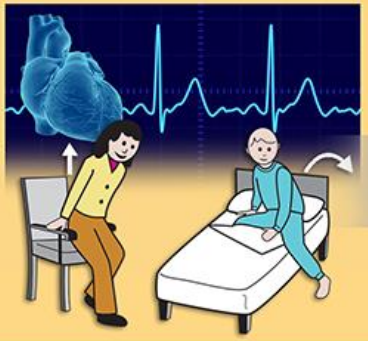


Visual Stability

Balance

Spatial Orientation



Autonomic

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Sensing gravity is among the most fundamental activities for our brain

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Overview of today's "main event"

- Talk focuses on three recently published papers from my lab that focus on balance and the exquisite sensitivity of gravity perception
  - "Vestibular Perceptual Thresholds Increase above the Age of 40", Frontiers in Neurology, (2016)
  - "Multivariate Analyses of Balance Test Performance, Vestibular Thresholds and Age", Frontiers in Neurology, (2017)
  - "Vestibular roll tilt thresholds partially mediate age-related effects on balance", Progress in Brain Reports, (2019)

frontiers in Neurology

ORIGINAL RESEARCH
published: 03 October 2016
doi: 10.3389/fneur.2016.00162

Check for updates

Vestibular Perceptual Thresholds Increase above the Age of 40

*María Carolina Bermúdez Rey[1,2], Torin K. Clark[1,2,3], Wei Wang[1,4], Tania Leeder[2], Yong Bian[1,2] and Daniel M. Merfeld[1,2]**

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Three Primary Goals for this Study

- Determine if males and female show differences in their vestibular thresholds
- Determine how self-motion perception thresholds vary with age
- Determine if vestibular thresholds correlate with balance performance **in healthy asymptomatic "normals"**

Vestibular **Dysfunction** Previously Shown to Impact Balance (4 of 100's of examples)

- Nashner, Black, and Wall (1982) showed that patients with well-defined clinical disorders were unable to suppress the influence of visual and kinesthetic signals
- Horak, Nashner, Diener (1990) compared the responses of normals and severe bilateral vestibular loss patients to elucidate the functional role played by vestibular function
- Peterka (2002). Tested normals and patients and modeled vestibular contributions.
- Stapley, Ting, Kuifo, Evaraert, Macpherson (2006) showed the instability that resulted in cats following bilateral vestibular ablation

“Big Picture” Methodological Goals

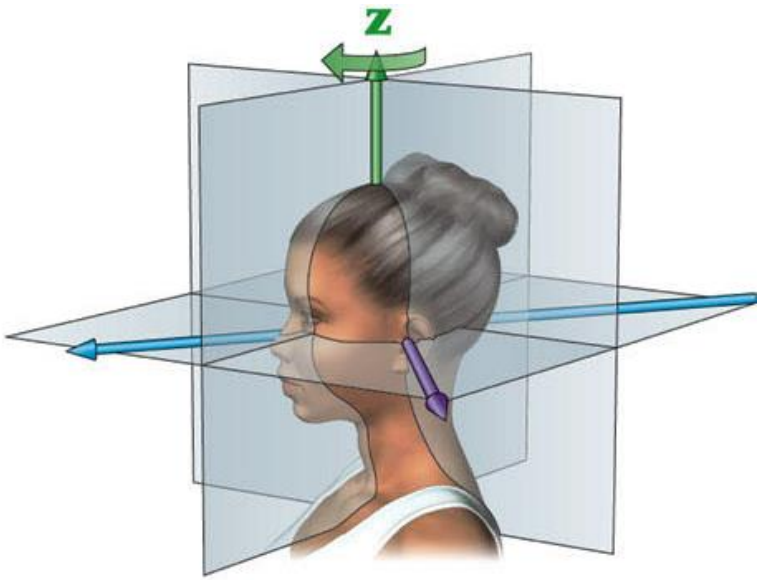
- Quantify balance using a simple standard variant of the Romberg test with foam
- Quantify vestibular function by measuring self-motion (“vestibular”) thresholds for 5 different motions

Threshold Methods

- Use Moog 6DOF motion platform to provide motion
- Direction recognition task

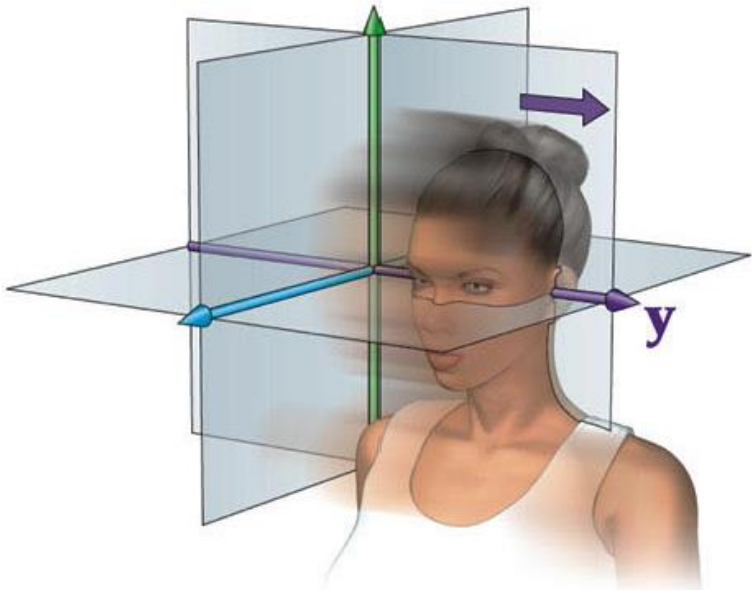
Threshold Motions

- Yaw (“Horizontal Canals”)



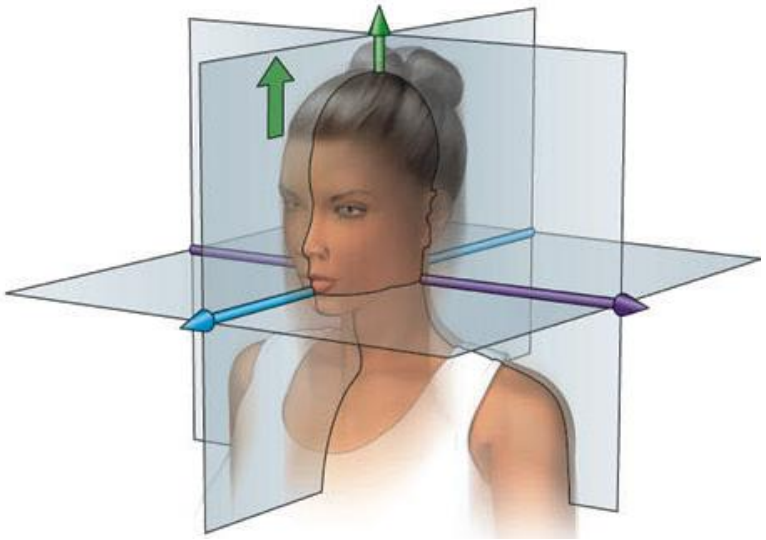
Threshold Motions

- Yaw, Y-translation (“Utricle”)



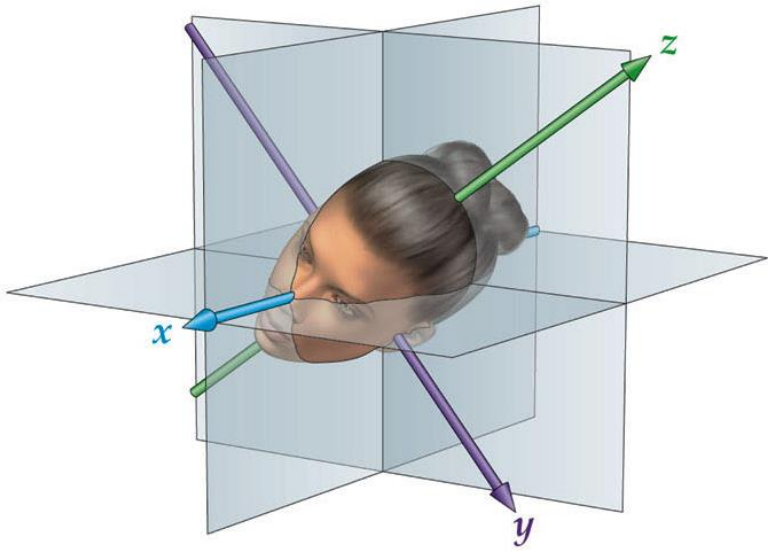
Threshold Motions

- Yaw, Y-translation, Z-translation (“Saccule”)



Threshold Motions

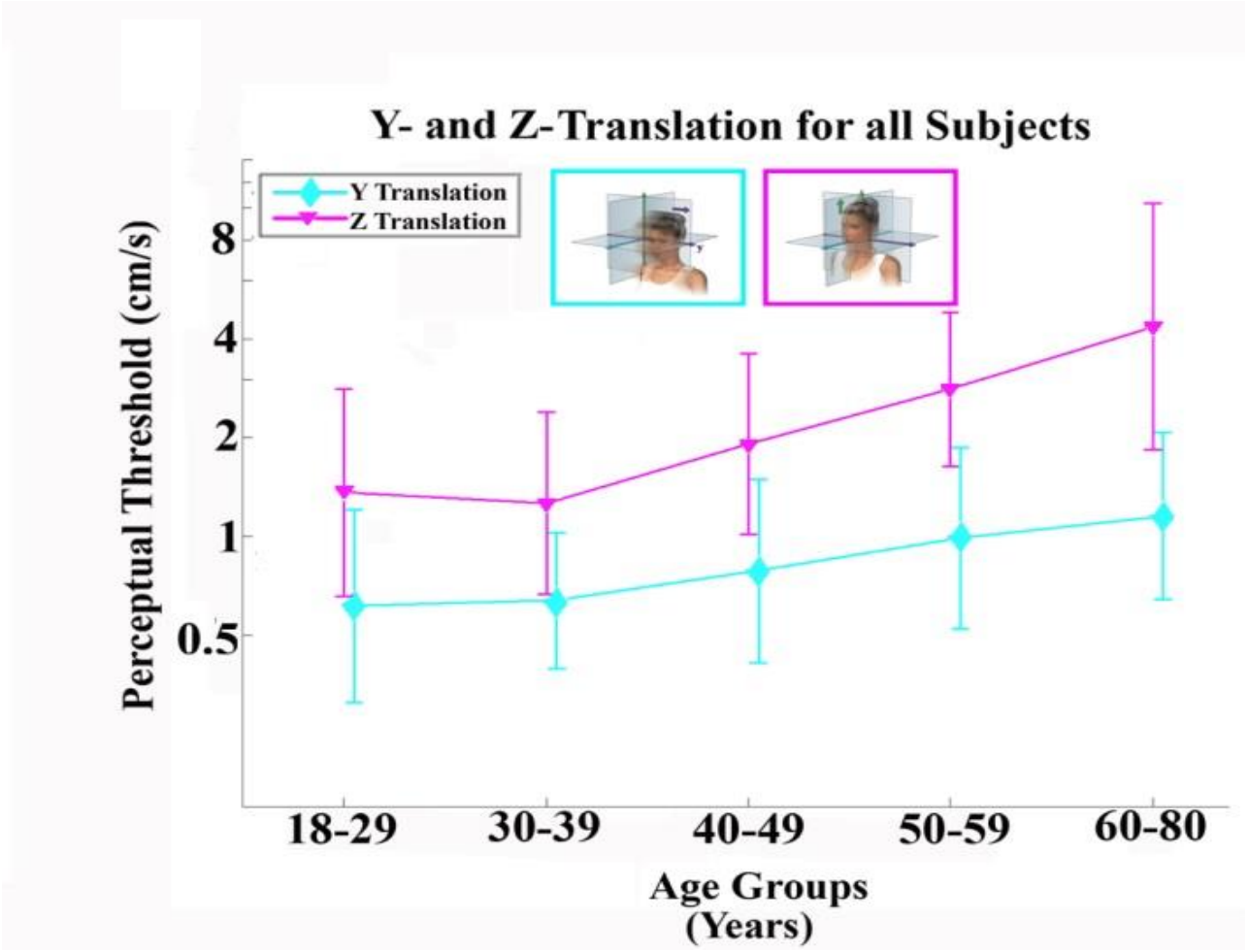
- Yaw, Y-translation, Z-translation, Roll tilt



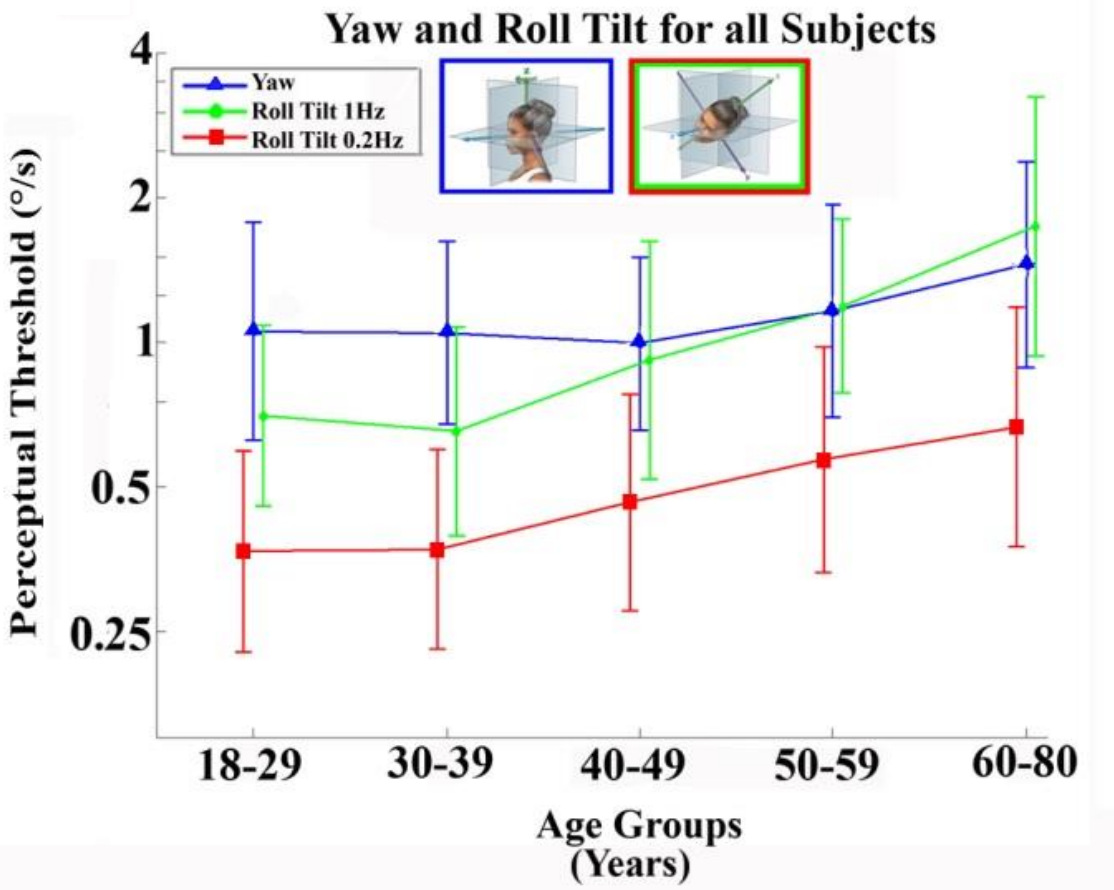
Threshold Methods (Bermúdez Rey et al.)

- Yaw Rotation, Y-translation, Z-translation, Roll tilt
  - 1 s (1 Hz) motion for all four directions
  - Roll tilt also tested with 5 s duration (0.2 Hz)
- 105 healthy subjects with no vestibular symptoms
  - 54 Female, 51 Male
  - Age range: 18 to 80

Translation thresholds increase above age 40



Rotation/Tilt thresholds increase above age 40



Threshold Summary

- These increases are both significant and substantial
- As a percentage of the baseline, the average threshold increased:
  - 83% of baseline for 1Hz *z*-translation over 10 years
  - 56% of baseline for 1Hz roll tilt over 10 years
  - 46% of baseline for 1Hz *y*-translation over 10 years
  - 32% of baseline for 0.2Hz roll tilt over 10 years
  - 15% of baseline for 1Hz yaw rotation over 10 years

Balance Methods (Bermúdez Rey et al.)

- 99 of the 105 “threshold” subjects also participated in a Romberg foam balance test
- Same test as that used for previous National Health and Nutrition Examination Survey (NHANES)
  - Four conditions

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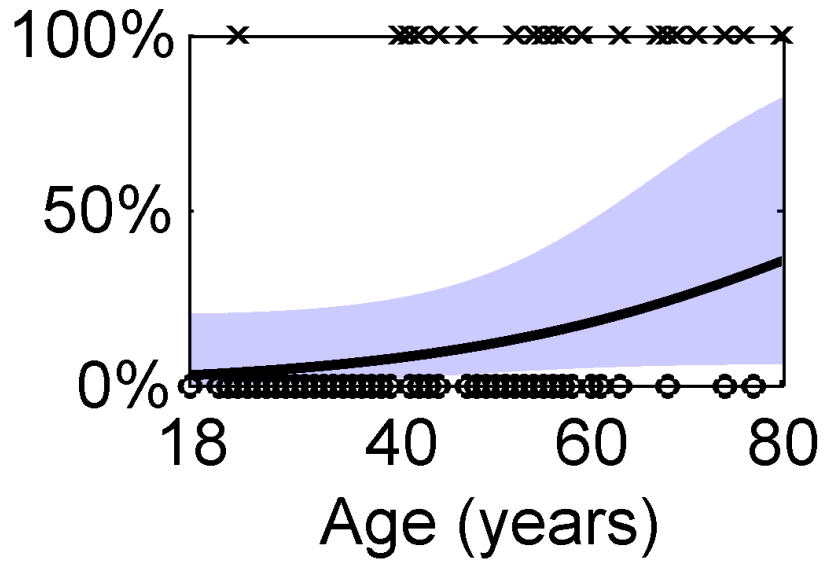
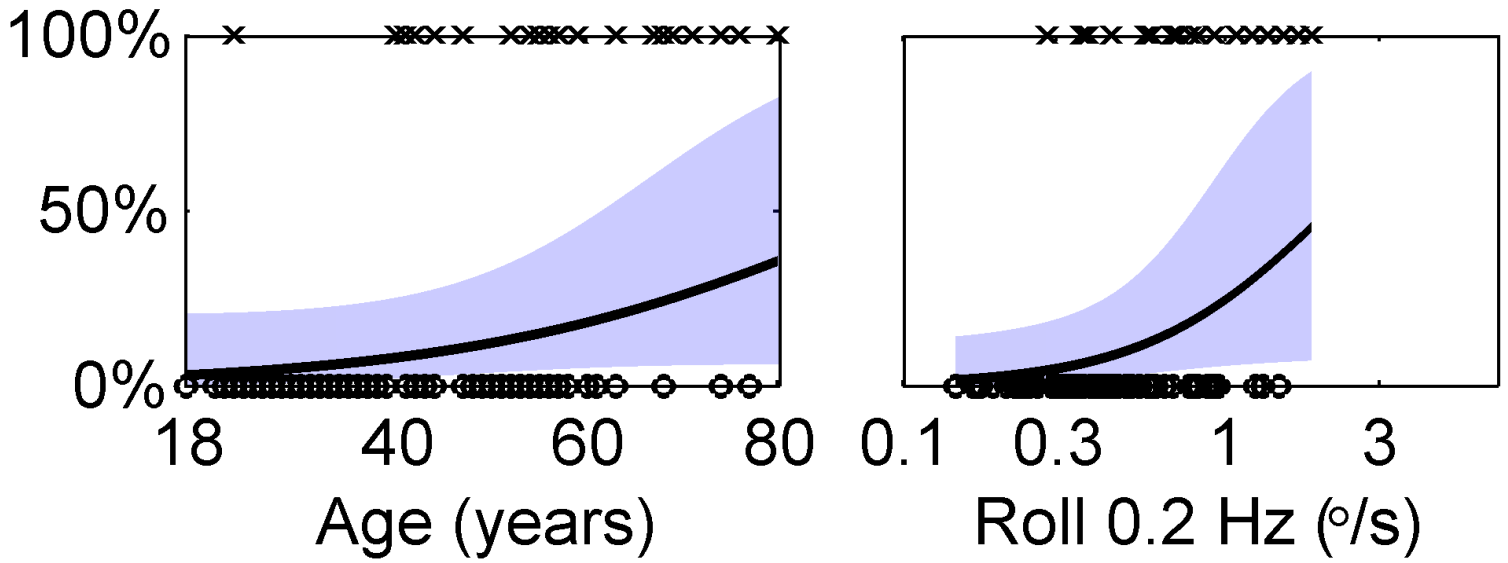
Balance findings

- 99 of 99 subjects completed the first 3 conditions (C1, C2, and C3) of the Romberg foam balance test
- 20 of 99 subjects failed to complete the 4th condition (C4) – the so-called “vestibular” condition

Balance Test Failure Rate Increased with Age



Balance Test Failure Rate Increased with Roll Tilt Thresholds



Provocation/Speculation

- According to US CDC, over 25,000 Americans die each year as a direct result of an unintentional fall
- Roughly another 80,000 Americans die each year within a year of a fall-related hip fracture
- Recent national survey data suggest that risk of falling is about 6 times higher for those who fail the ”vestibular component” of the Romberg balance test on foam (Agrawal et al, 2011)
- Combining these various facts with a few calculations suggests that deaths in US due to vestibular dysfunction likely falls between 50,000 Americans (10th leading cause of death) and 150,000 Americans (3rd leading cause of death) each year

Summary of Primary Novel Findings (Bermúdez Rey et al)

- Data showed that vestibular thresholds, including roll tilt thresholds, broadly increased with age above the age of 40
- Even after taking age into account via a mixed-model, higher roll tilt thresholds at 0.2Hz were highly correlated with balance test failures ($p=0.003$)
- We found these findings compelling, especially given the rudimentary nature of our balance assay, so we immediately began a re-analysis

frontiers in Neurology

ORIGINAL RESEARCH
published: 08 November 2017
doi: 10.3389/fneur.2017.00578

Check for updates

Multivariate Analyses of Balance Test Performance, Vestibular Thresholds, and Age

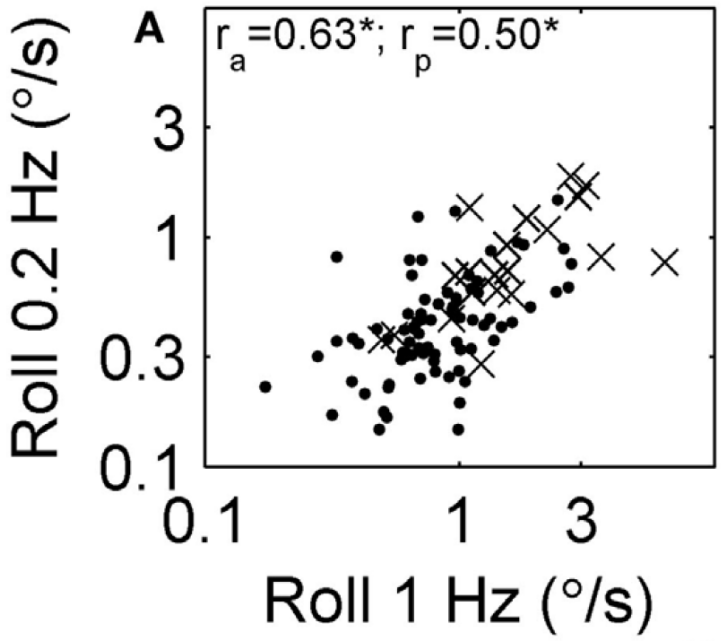
Faisal Karmali[1,2], María Carolina Bermúdez Rey[1,2], Torin K. Clark[1,2,3], Wei Wang[2,4] and Daniel M. Merfeld[1,2]*

[1] Jenks Vestibular Physiology Laboratory, Mass Eye and Ear Infirmary, Boston, MA, United States, [2] Otolaryngology, Harvard Medical School, Harvard University, Boston, MA, United States, [3] Smead Aerospace Engineering Sciences, University of Colorado, Boulder, CO, United States, [4] Division of Sleep Medicine, Brigham and Women's Hospital, Boston, MA, United States

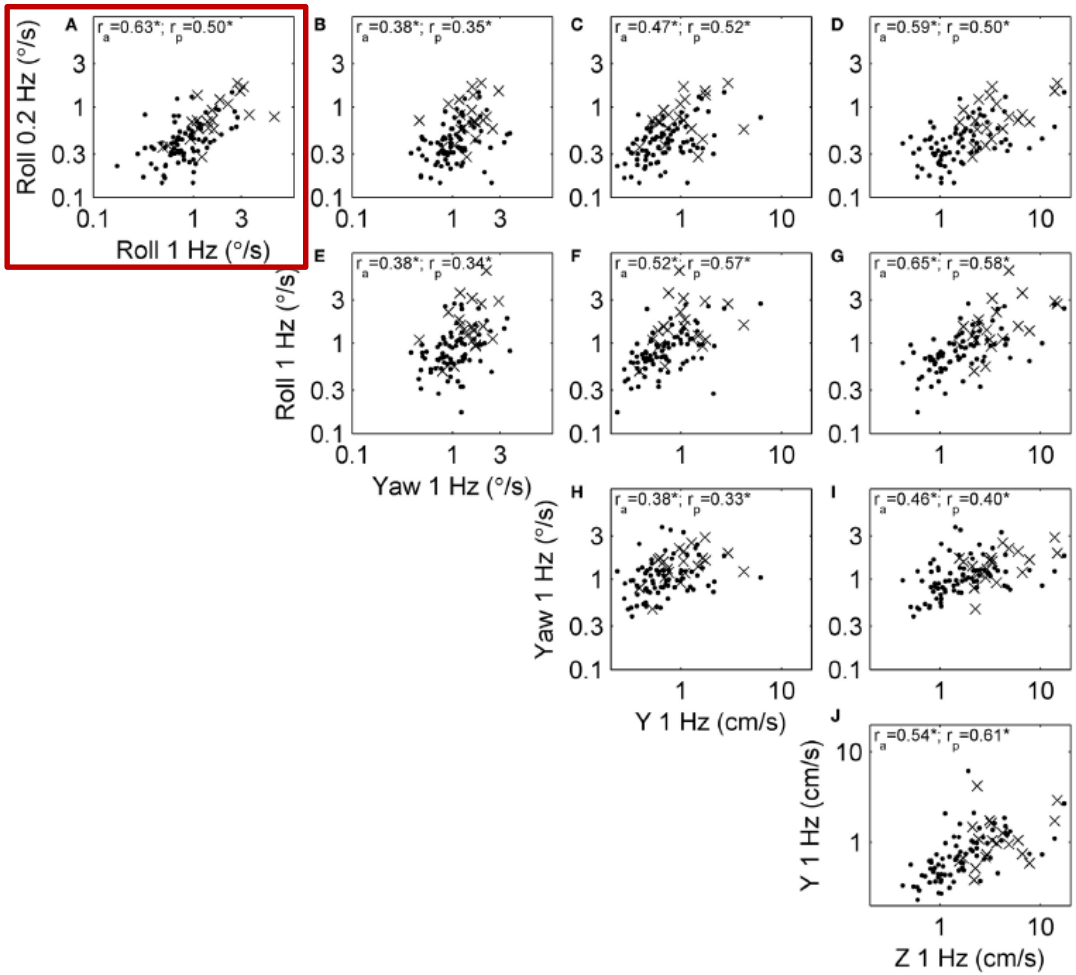
Goals for this Multi-variate Re-analysis

- Focus on correlations
  - Correlations in the various multiple threshold measures themselves
  - Multi-variate correlations between thresholds, age, and balance

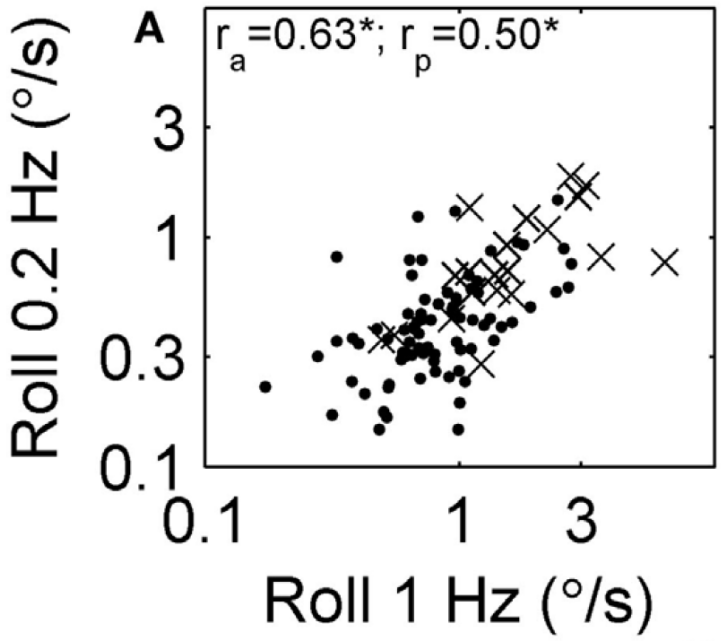
0.2Hz and 1Hz Roll Tilt Thresholds Are Correlated



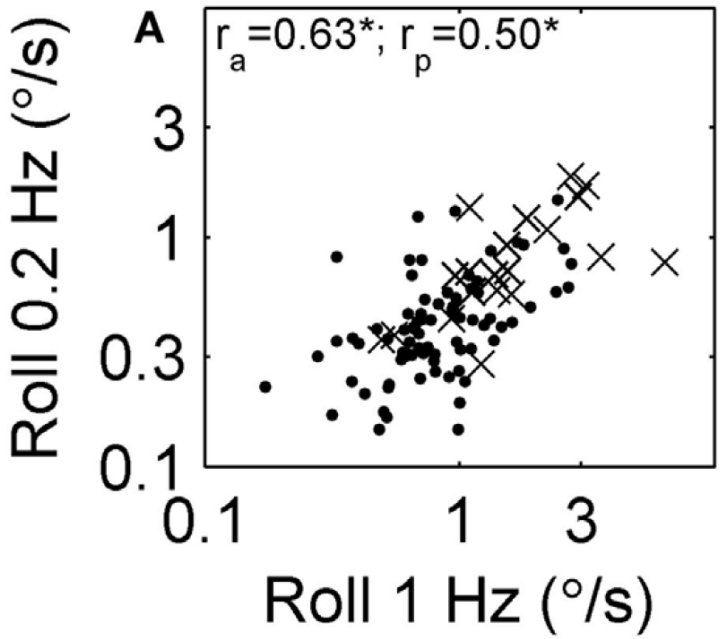
All 10 Threshold Pair Correlations are Significant

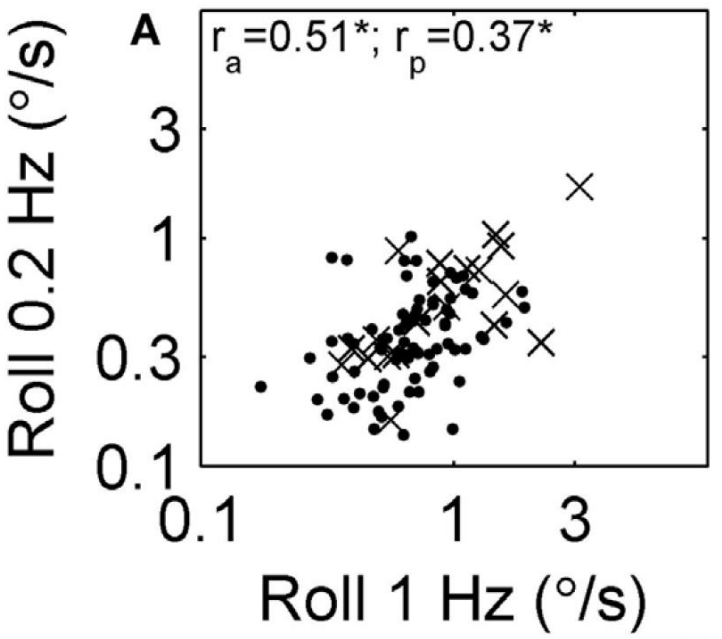


But what about age?

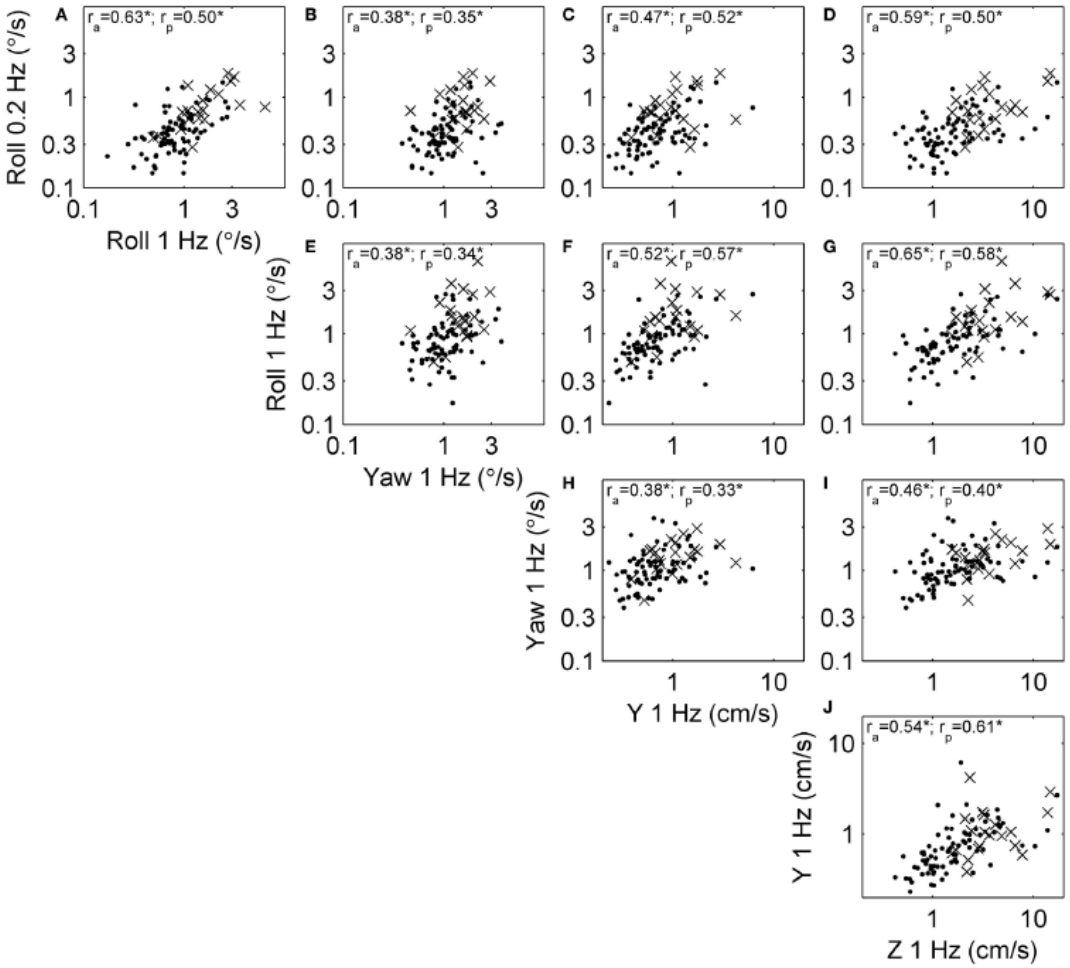


But what about age?
0.2Hz and 1Hz roll tilt thresholds are still correlated





All 10 Age-Corrected Threshold Pair Correlations are Significant



Principal Component Analysis (PCA) of the 5 standardized thresholds after removing age-effect

TABLE 4 | Principal component analysis of age-adjusted, log-transformed thresholds for all subjects.

	First	Second	Third	Fourth	Fifth
Contribution (%)	**52**	15	13	10	10
Yaw	**0.38**	0.84	−0.29	−0.22	0.15
Y	**0.43**	0.03	0.85	−0.28	−0.07
Z	**0.48**	0.05	0.00	0.82	−0.30
Roll tilt 1 Hz	**0.47**	−0.40	−0.15	0.03	0.77
Roll tilt 0.2 Hz	**0.46**	−0.38	−0.41	−0.45	−0.53

The component with the largest contribution is shown in bold.

Summary (Karmali et al) **for thresholds**

- Thresholds (Yaw Rotation, Y- & Z-Translation, Roll Tilt) are all moderately correlated with one another even after accounting for age-effects
- PCA shows that a single principal component (PC) explains about half of the variance found in the threshold data
- This principal component weighs the 5 thresholds more-or-less evenly, suggesting that high (or low) thresholds are an individual characteristic

Goals for this Multi-Variate Re-Analysis

- Focus on correlations among the various measures
  - Correlations between the threshold measures
  - Correlations among thresholds, age, and balance

Of 7 Independent Variables, only 0.2Hz Roll Thresholds Correlate with Balance

TABLE 6 | Results of a multiple logistic regression to predict the chance of failing condition 4 of the balance test based on age and log-transformed vestibular thresholds.

	Estimate	SE	*t*-Stat	*p*-Value
(Intercept)	–3.24	1.39	–2.34	0.0193
Age	0.0457	0.0278	1.65	0.100
Sex	0.349	0.639	0.546	0.585
Yaw 1 Hz	0.543	0.763	0.711	0.477
Y 1 Hz	–0.484	0.700	–0.692	0.489
Z 1 Hz	0.173	0.600	0.289	0.773
Roll tilt 1 Hz	0.502	0.751	0.668	0.504
Roll tilt 0.2 Hz	1.51	0.757	2.00	0.0457*

**Signifies statistical significance ($p < 0.05$).*

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**Signifies statistical significance ($p < 0.05$).*

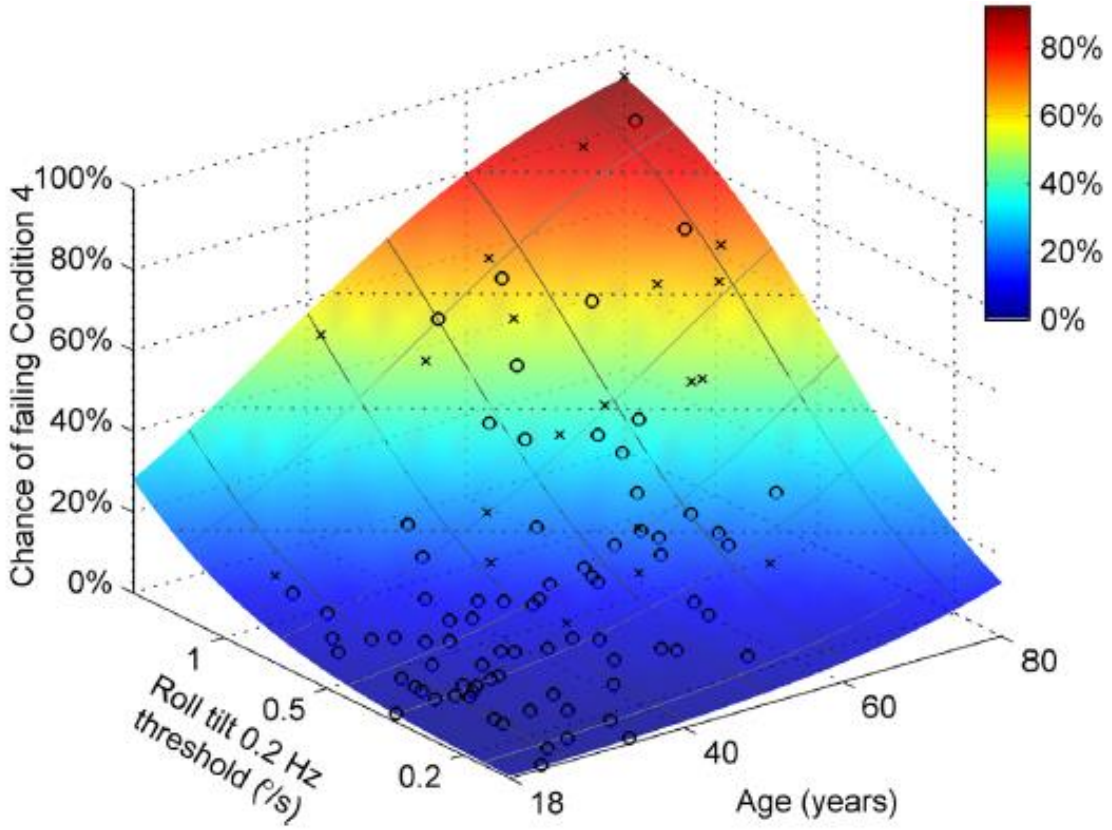
If we remove all independent variables with p-values greater than 0.4, both age and 0.2Hz roll tilt thresholds show statistically significant impacts on C4 failure

TABLE 8 | Results of a multiple logistic regression after application of a stepwise algorithm to provide a simplified model.

	Estimate	SE	*t*-Stat	*p*-Value
(Intercept)	–4.05	1.21	–3.34	0.000834
Age	0.0867	0.0231	3.76	0.000171*
Roll tilt 0.2 Hz	1.75	0.618	2.83	0.004723*

Analyses were done using age-adjusted, log-transformed thresholds.
**Signifies statistical significance ($p < 0.05$).*

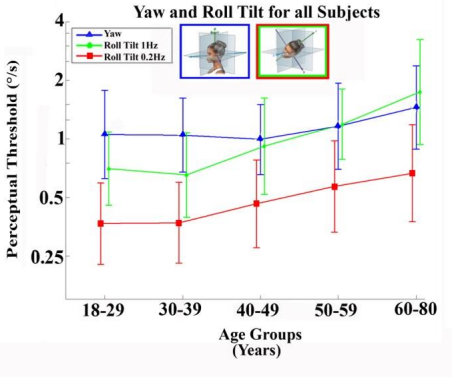
Balance Test Failure Rate Skyrockets for Old Subjects with High Roll Tilt Thresholds

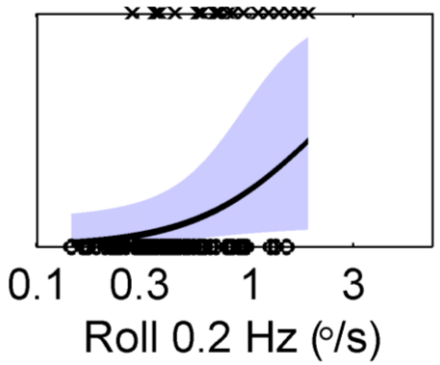


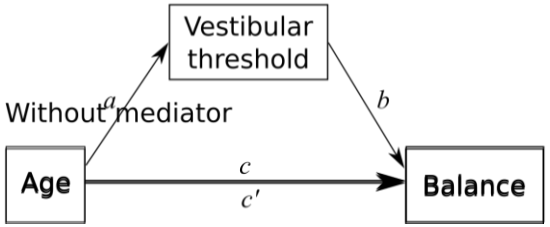
Summary (Karmali et al) re balance

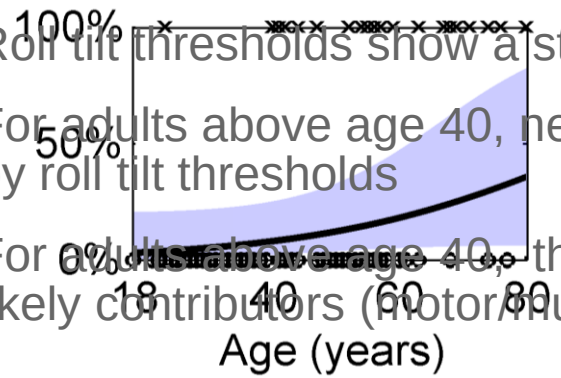
- Roll tilt thresholds showed higher correlation with balance failure on condition 4 than any other measure (even age!)
- Being 60 yo and having roll tilt thresholds that are:
  - Average: Yields a 43% chance of failing Condition 4
  - High: Yields an 80% chance of failing Condition 4
  - Low: Yields a 5% chance of failing Condition 4

Age-Related Mediation Analysis









- Roll tilt thresholds show a statistically significant ($p<0.05$) mediation effect.
- For adults above age 40, nearly half (46.1%) of the age-effect is mediated by roll tilt thresholds
- For adults above age 40, this leaves just half of the age-effect for all other likely contributors (motor/muscle, kinesthesia, neural processing, etc.)

Summary

- We showed:
  - That vestibular function degraded with age above age 40
  - That population variations in vestibular thresholds of healthy asymptomatic humans contribute to balance
  - That vestibular thresholds are moderately correlated and appear to suggest that these thresholds represent an individual characteristic (of unknown origin)
  - That vestibular threshold increases – specifically roll tilt threshold increases - explain nearly half of the impact of age on balance

Thank You!

Questions?

- Support Provided by:
  - NIH/NIDCD R01-DC01458 (PI: Merfeld), including Supplement provided by NIH Women's Health Office
  - NIH/NIDCD R01-DC014924 (PI: Merfeld/Lewis)
  - NIH/NIDCD R03-DC013635 (PI: Karmali)

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  - Co-authors: Torin Clark, Wei Wang, Tania Leeder, Yong Bian
  - Other lab members:, Raquel Galvan-Garza, Wangsong Gong, Bob Grimes, Csilla Haburcakova, Kristen Kirk, Rick Lewis, Koeun Lim, and Yongwoo Yi