Vandy Journal Club

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NHANES

- The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States.
- The survey is unique in that it combines interviews and physical examinations.
- NHANES is a program in the National Center for Health Statistics (NCHS).

NHANES

- The survey became a continuous program in 1999.
- There are components on a variety of health and nutrition measurements to meet emerging needs as they are identified.
- The survey examines approximately 5,000 persons each year. These persons are located in counties across the country.

NHANES

- The sample for the survey is selected to represent the U.S. population of all ages.
- The NHANES program samples persons 60 and older, African Americans, and Hispanics.

NHANES

- Health interviews are conducted in respondents’ homes.
- Health measurements are performed in specially-designed and equipped mobile centers, which travel to locations throughout the country.

NHANES

- The study team consists of a
  - physician
  - medical and health technicians
  - dietary and health interviewers.
- Many of the study staff are bilingual (English/ Spanish).

Articles to be Discussed

- Agrawal et al., (2013). Head Impulse Test Abnormalities and Influence on Gait Speed and Falls in Older Individuals. *Otology & Neurotology*, *34*, 1729-1735.
- Agrawal et al., (2010). Diabetes, Vestibular Dysfunction, and Falls: Analyses From the National Health and Nutrition Examination Survey. *Otology & Neurotology*, *31*(9), 1445-1450.

Articles to be discussed (con't)

- Semenov YR, Bigelow RT, Xue Q-L, du Lac S, Agrawal Y. Association between vestibular and cognitive function in U.S. Adults: Data from the National Health and Nutrition Examination Survey. 2015. *J Gerontolog A Biol Sci Med Sci,* 1-8.

Otology & Neurotology
34:1729–1735 © 2013, Otology & Neurotology, Inc.

Head Impulse Test Abnormalities and Influence on Gait Speed and Falls in Older Individuals

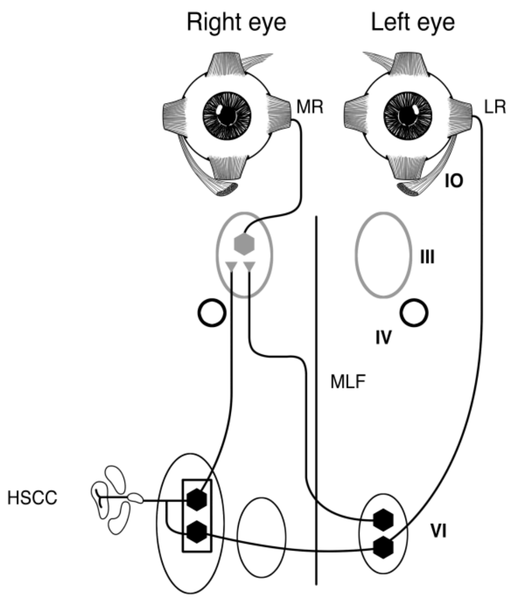
Yuri Agrawal, Marcela Davalos-Bichara, Maria Geraldine Zuniga, and John P. Carey

Department of Otolaryngology–Head and Neck Surgery, The Johns Hopkins University School of Medicine, Baltimore, Maryland, U.S.A.

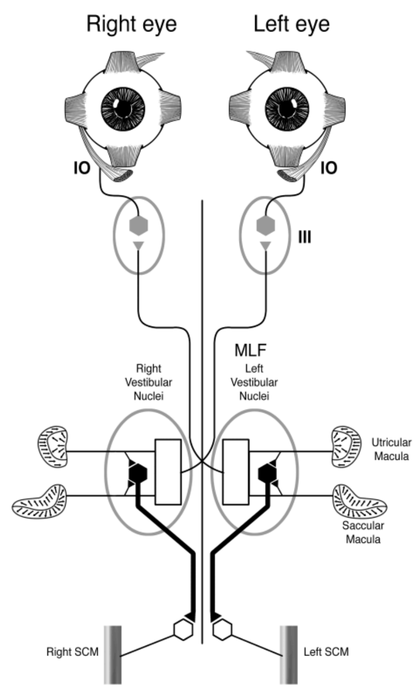
Objectives

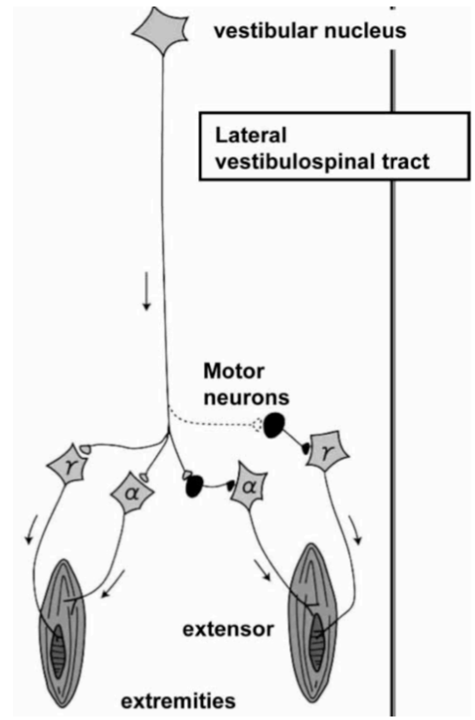
- To assess the prevalence of vestibular dysfunction in older adults using the head impulse test (HIT)
- To assess the independent influence of HIT abnormalities on gait speed and fall risk in older individuals.

Vestibular Reflexes



Canal Ocular Reflex



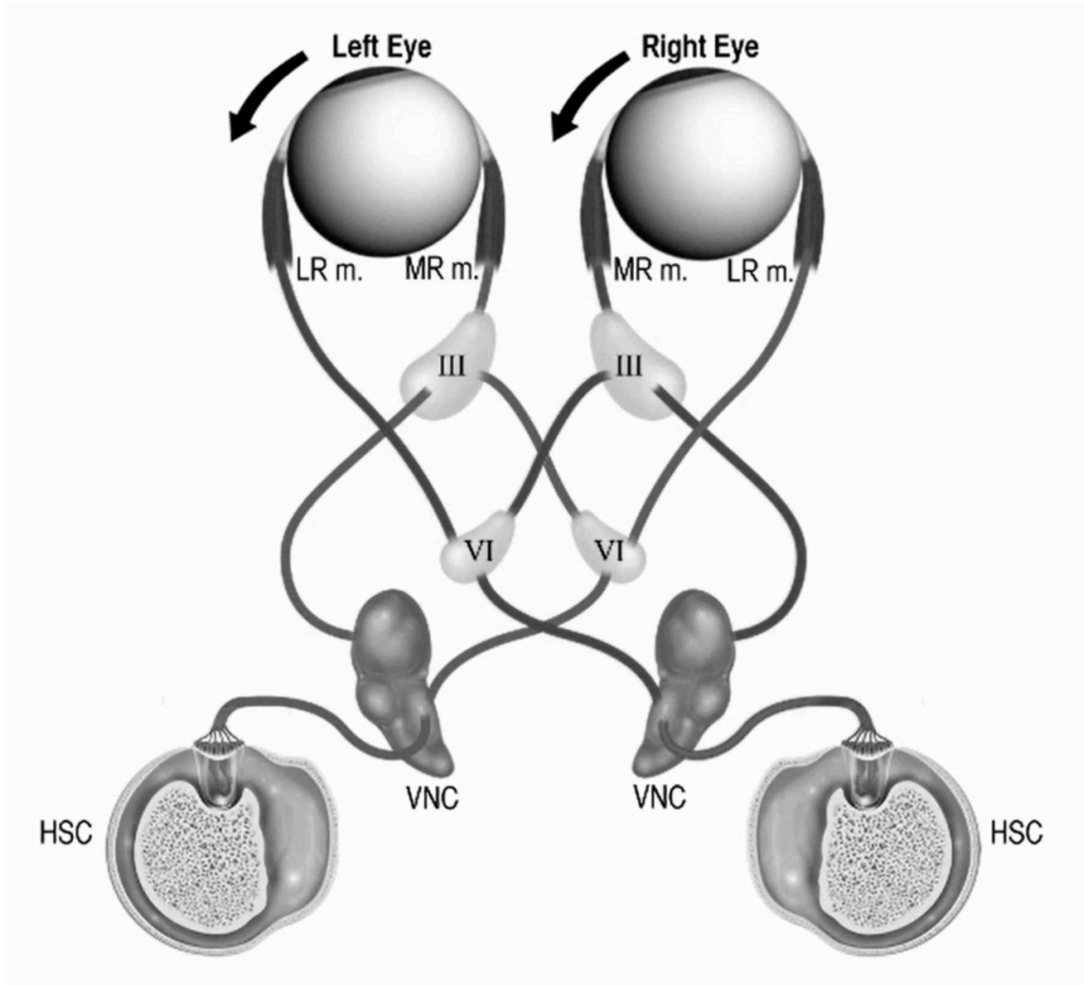


Otolith Ocular Reflex

Otolith Collic Refex

Vestibulo-spinal Reflex

Canal-Ocular Reflex



Head Impulse Test

- Normal Result
  - A translation toward patient's to either side should invoke a corresponding compensatory eye movement.

Head Impulse Test

- Abnormal Result
  - Damage to the left peripheral vestibular system will result in a catch-up saccade movement to the right on left head turn.

Left side impaired

Methods

- Study Design: Cross-sectional study.
- Setting: Tertiary care academic medical center.
- Patients: Fifty community-dwelling individuals age 70 and older.

Exclusion Criteria

- Individuals were excluded if they could not participate in study procedures because of blindness, poor neck range of motion or cervical spine instability (for head impulse testing), or inability to walk unassisted (for gait testing).
- Subjects were also excluded if they had a history of diabetes mellitus.
- History of vestibular disease.

Methods

- Interventions:
  - HIT (abnormal HIT defined as right or left HIT abnormality)
  - visual acuity
  - monofilament testing
  - grip strength.
- Main Outcome Measures:
  - Gait speed on a 4-meter walk
  - Case history

Results

- The participants' mean age was 77 years (range, 70-95 yr); 52% were female subjects.
- An abnormal HIT (50% abnormal) was significantly associated with;
  - 0.23 m/s reduction in gait speed
  - 0.44 more falls in the last 1 year
  - 5-fold increase in the odds of falling in the last 5 years

Results

TABLE 3. *Multiple logistic regression analyses of gait speed and fall risk in study population*

	Gait speed[g]		1-year fall history[h]		5-year fall history[i]	
Risk factor	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Horizontal HIT[a]	**5.04 (1.21–21.0)**	**0.026**	3.56 (0.86–14.7)	0.079	**5.17 (1.25–21.4)**	**0.024**
Age[b]	0.88 (0.77–1.01)	0.074	0.92 (0.81–1.05)	0.205	1.00 (0.89–1.14)	0.962
Sex[c]	0.89 (0.11–6.68)	0.909	2.23 (0.27–18.3)	0.453	1.67 (0.24–11.5)	0.601
Somatosensory function[d]	0.51 (0.22–1.17)	0.113	0.98 (0.44–2.18)	0.951	0.96 (0.46–2.01)	0.916
Visual acuity[e]	**1.88 (1.06–3.32)**	**0.031**	**2.02 (1.14–3.60)**	**0.016**	0.88 (0.55–1.41)	0.607
Grip strength[f]	0.94 (0.85–1.04)	0.204	0.97 (0.88–1.08)	0.605	1.02 (0.93–1.12)	0.663

Conclusions

- Approximately half of the community-dwelling older individuals in our study had evidence of vestibular dysfunction
- Vestibular dysfunction was significantly associated with gait speed and fall risk in adjusted analyses.

Conclusions

- Approximately half of the subjects in the cohort showed evidence of vestibular impairment!
- Screening for vestibular impairment using the simple HIT and directing targeted vestibular therapy may be important to reduce gait impairment and fall risk in older individuals.

Questions

Review article: Agrawal, Y., Carey, J. P., Della Santina, C. C., Schubert, M. C., & Minor, L. B. (2010). Diabetes, Vestibular Dysfunction, and Falls: Analyses From the National Health and Nutrition Examination Survey. *Otology & Neurotology*, *31*(9), 1445-1450.

Diabetes Mellitus

- Diabetes affects 380 million people world wide and 29 million people in the United States.
- Definition: Diabetes mellitus is a chronic disease where cells do not generate insulin or they resist against insulin, and as a result there are high levels of glucose in the blood.

Mayo Clinic, 2014

Diabetes Mellitus

- After a person eats, insulin moves glucose into the bloodstream. Glucose is then used as fuel for the body.
- People develop diabetes when they have high blood sugar, because their body does not move the glucose into the muscle, fat, and liver cells.

Mayo Clinic, 2014

Background

- The risk of falling is increased in patients with diabetes
  - Peripheral neuropathy and retinopathy are associated complications and are risk factors for falls
  - Patients with diabetes are 70% more likely to have vestibular impairments (Agrawal, 2009)

Background

- Possible causes of impairment on the vestibular system from diabetes mellitus
  - Histopathologic analyses: Previous studies support pathologic changes from diabetic microangiopathy in rat vestibular end organs as well as Type 1 hair cell degeneration (Smith, 1995)
  - Other animal studies have indicated pathologic myelin-sheath thinning around vestibular nerves in those with diabetes mellitus (Myers, 1998)

Background

- Diabetes mellitus and vestibular dysfunction
  - Electronystagmographic testing revealed evidence of abnormal vestibular dysfunction in several small samples of patients with Type 1 diabetes (Rigon, 2007)
  - One study found a significant difference in the time constant of the vestibulo-ocular reflex on rotary chair testing in those with diabetes mellitus (Nicholson, 2002)

Objective

- Study the effect of diabetes mellitus on the vestibular system
- Assess whether vestibular impairments have an independent effect on fall risk with those that have diabetes

Methods

- Balance questionnaire with the primary focus on history of falls
- Balance testing involved a modified Romberg Test
  - Participants were assessed unassisted in 4 test conditions (designed to specifically test the sensory components of the balance system)

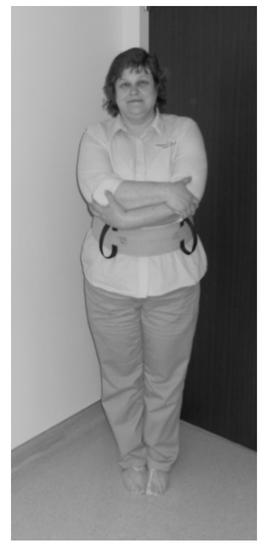
Balance Tests

- **Romberg Test of Standing Balance on Firm and Compliant Surfaces**
  - **Condition 1:** Stand eyes open on firm surface
    - Roughly equivalent to SOT condition 1
  - **Condition 2:** Stand eyes closed on firm surface
    - Eliminates vision, proprioception is available
    - Roughly equivalent to SOT condition 2
  - **Condition 3:** Stand eyes open on a compliant surface (6 inch thick foam square)
    - Distorts proprioceptive sense
    - Roughly equivalent to SOT condition 4
  - **Condition 4: Stand eyes closed on a compliant surface (6 inch thick foam square)**
    - **Eliminates vision and distorts proprioceptive sense**
    - **Roughly equivalent to SOT condition 5**

“Balance Testing”

“Romberg Test of Standing Balance on Firm and Compliant Support Surfaces”

- **Condition 1:** Firm surface, feet together, eyes open
- **Condition 2**: Firm surface, feet together, eyes closed (eliminates visual input)



C1

C2

"Balance Testing"

"Romberg Test of Standing Balance on Firm and Compliant Support Surfaces"

- **Condition 3:** Compliant surface, feet together, eyes open (obscures proprioceptive input)

- **Condition 4:** Compliant surface, feet together, eyes closed (obscures visual and proprioceptive inputs)

C3

C4

Methods

- **Only subjects who passed conditions 1-3 were included in the study**
- The authors contended:
  - **"…condition 4 in this study, assesses** a patient's ability to maintain balance when **vestibular** information is the only reliable sensory input (i.e. in the absence of parallel visual and proprioceptive cues)."

Methods

- **What is a "pass?"**
  - **Ability to stand stable for**
    - **15 seconds for conditions 1 and 2 and**
    - **30 seconds for conditions 3 and 4**

Methods

- **What is a "fail?"**
  - **open eyes,**
  - **moving arms or feet to achieve stability,**
  - **beginning to fall requiring intervention by operator**
- A fail…
  - resulted in repeat if desired.
  - A (second) fail ended the test

Methods

- Examinations for peripheral neuropathy were completed in participants aged 40 years and older
- Participants were in a supine position and a standard monofilament was used to apply pressure to the bottom of the feet (3 sites)
    1) plantar-first metatarsal head
    2) Plantar-fifth metatarsal head
    3) Plantar-hallux
- 1 to 3 insensate areas was considered as mild neuropathy
- 4 to 6 insensate areas was considered as severe neuropathy

Methods

- Visual examinations were performed to measure visual acuity and used as a proxy for retinopathy in this study
- Nidek Auto Refractor Model ARK -760 was used to assess visual acuity
  - 20/20 was considered to have no visual acuity impairment
  - 20/20 to 20/40 was considered to be a mild visual acuity impairment
  - Worse than 20/40 was considered to be a severe visual acuity impairment

Results

- From the total sample of US adults aged 40 years and older, 17% (n=1,136) had diabetes mellitus
  - Prevalence of vestibular dysfunction among individuals with diabetes mellitus was 54%
  - 22% of participants with diabetes had a 6 to 10 year duration of disease
  - 38% had a greater than 10 year duration of disease

Results

- Hemoglobin A1c levels were 7.0% and greater in 41% of individuals with diabetes mellitus
- The prevalence of mild and severe peripheral neuropathy among patients with diabetes were 19% and 7.1%
- Prevalence of mild and severe retinopathy in patients with diabetes were 54% and 22%
- The prevalence of falls in individuals with diabetes mellitus was 12%

Results

TABLE 1. *Prevalence (95% CI) of vestibular dysfunction, measures of diabetes severity, diabetes-related complications, and falls in US adults aged 40 years and older with diabetes mellitus (n = 1,136), NHANES 2001–2004*[a]

Characteristics	Prevalence, % (95% CI)
Vestibular dysfunction[b]	
No	46 (42–51)
Yes	54 (49–58)
Duration of diabetes exposure (yr)[c]	
0–5	40 (36–44)
6–10	22 (19–24)
>10	38 (34–43)
Hemoglobin A_{1c} (%)[d]	
<7.0	59 (54–63)
≥7.0	41 (37–46)
Peripheral neuropathy[e]	
None	74 (70–78)
Mild (1–3 insensate sites)	19 (15–23)
Severe (4–6 insensate sites)	7.1 (5.1–9.2)
Retinopathy[f]	
None	24 (20–28)
Mild (20/40 and better)	54 (51–58)
Severe (worse than 20/40)	22 (19–25)
History of falls[g]	
No	88 (85–91)
Yes	12 (8.6–15)

CI indicates confidence interval.
[a]n = 1,136, sample weights applied.
[b]Participants had objective evidence of vestibular dysfunction based on Romberg testing; 86 participants had missing data.
[c]A total of 166 participants had missing data.
[d]A total of 120 participants had missing data.
[e]A total of 263 participants had missing data.
[f]A total of 197 participants had missing data.
[g]Participants reported falling in the past 12 months; 10 participants had missing data.

Discussion

- Findings suggest that diabetes mellitus increases the risk of vestibular dysfunction (condition four of Romberg)
  - It was observed that those with diabetes mellitus and vestibular dysfunction had a significantly longer duration of the disease and/or a higher serum hemoglobin A1c level
  - There was a higher prevalence of vestibular dysfunction among participants with diabetes that also had other complications indicative of long-standing and more severe disease (neuropathy and retinopathy)

Discussion

- In the comparison among the different complications, (i.e. peripheral neuropathy, retinopathy, and vestibular dysfunction) vestibular dysfunction had the most effect on the association between diabetes and falls risk
- These findings suggest that vestibular dysfunction may represent a newly recognized diabetes-related complication

Discussion

- As diabetes progresses or hemoglobin A1c levels are increased, the person is at greater risk for vestibular impairments and other complications (i.e. neuropathy and retinopathy)
- Diabetes management is important to help control for additional complications
- Strategies to reduce fall risk in this population is crucial
- Further research is needed to characterize the relationship between diabetes mellitus and vestibular impairments

Review article: Semenov YR, Bigelow RT, Xue Q-L, du Lac S, Agrawal Y. Association between vestibular and cognitive function in U.S. Adults: Data from the National Health and Nutrition Examination Survey. 2015. *J Gerontolog A Biol Sci Med Sci,* 1-8.

Background

- **Age results in a reduction in the function of the peripheral and central vestibular system, and balance system, and this contributes to falls**
- **Recent information** (early 2000's [see references]) suggests that the **vestibular system contributes to:**
  - **memory,**
  - **attention and,**
  - **executive functions (e.g. working memory, reasoning, problem-solving etc.)**

Background

- **Behavior of animals and humans after bilateral vestibular deafferentation,** suggests that **vestibular system provides information about spatial orientation (i.e. spatial memory and spatial navigation)**
  - **Clinicians have noted the connection between bilateral vestibular impairment and**
    - **memory loss**
    - **"foggy-headed" sensation**

Definition: Visuo-spatial Memory

- **Visuo-spatial memory: the part of memory responsible for recording information about one's environment and its spatial orientation.**
  - a person's **spatial memory is required in order to navigate around a familiar city,**
    - just as a **rat's spatial memory is needed to learn the location of food at the end of a maze.**

Background: Visuo-spatial Ability

- **Deteriorates with age**
  - **Older individuals have greater difficulty than younger subjects navigating in real world** and virtual environments
  - Make more **errors in returning to their starting places (car in a parking lot?)**
  - **Have greater difficulty remembering the locations of previous targets**
    - ***"How difficult is it to find your shopping cart at Costco once you leave it?"***
    - ***"How difficult is it to find your car after you park it at a big shopping mall?"***

Background: Visuo-spatial Ability

- **Unknown whether age-related vestibular loss plays a role in the impairment of spatial cognitive function in older adults**

Background: NHANES

- From 1999-2002 NHANES evaluated the relationship between "balance function" and "cognitive function" in this data set

NHANES

- **1999 – 2000, 2001 – 2002 NHANES**
- **Conducted "balance testing" 40 years of age and older (Romberg Test of Standing Balance on Firm and Compliant Surfaces)**
- **Conducted "cognitive tests" for persons 60+ years of age**
  - Excluded from cognitive testing if: unable to complete the testing without help from a "proxy respondent."
- **Subject filters reduced the balance test to N = 3270**
- **Subject filters reduced the cognitive test to N = 1,303.**

“Balance Testing”

Romberg Test of Standing Balance on Firm and Compliant Support Surfaces

- **“categorized subjects *as having vestibular dysfunction* if they did not pass test Condition 4.”**

Cognitive Testing

- **Digital Symbol Substitution (DSS)** subtest of the Wechsler Adult Intelligence Scale, 3rd edition **(WAIS III)**
  - **Subject was given a "key" that paired symbols with numbers.**
  - **Then they were given a series of numbers**
  - **Subjects had to draw in 120 seconds as many of the symbols associated with the numbers as possible**
  - **Maximum score = 133**
  - **DSS believed to assess: psychomotor speed, attention, <u>visuospatial skills</u>, associative learning and memory**

Digital Symbol Substitution Test

1	2	3	4	5
␣	]	ꝏ	^	≃

Key

5	4	4	3	4	2	2	2	5	5	5	3	1	5	5
1	1	2	1	5	4	4	4	2	1	3	5	5	1	5
4	3	1	3	1	3	4	3	1	3	2	5	4	3	4

Results (Highlights)

- **Mean total score on DSS was 45.5 pts**
  - **range 0-100 pts**
- **"Vestibular dysfunction"(Romberg test) occurred in 58% of the study population**
- **"Vestibular dysfunction" was associated with:**
  - **a mean reduction in the DSS score of 3.4 points** (95% confidence interval = -5.2 points and -1.6 points, p = .001)
    - **<u>equivalent to a loss of 5 years of age in cognitive function</u>**
- **Vestibular dysfunction explained 8.8% of the association between age and DSS score**

Discussion

- **Significant association between "vestibular function" (i.e. balance function) and cognitive function**
  - **"…vestibular loss associated with aging may contribute to the far more common cognitive deficits observed in older adults.** ***Indeed, it has been hypothesized that vestibular loss contributes to the onset to Alzheimer's disease."*** [italics ours] Semenov et al. 2015

Discussion

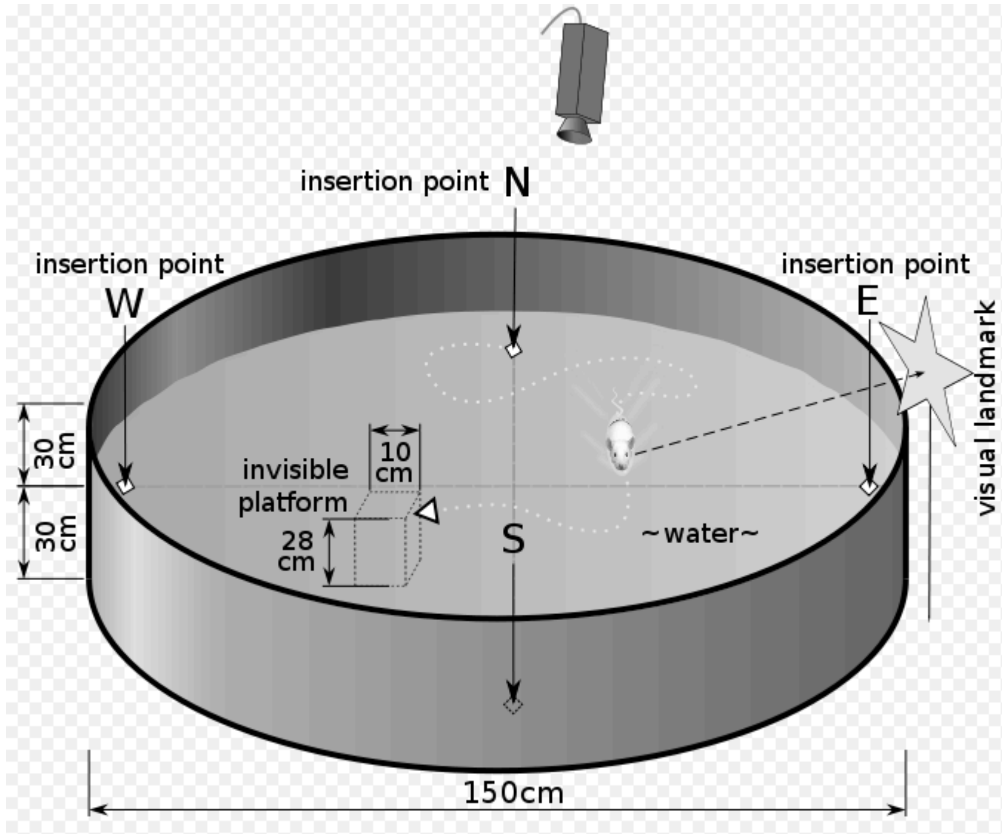
- "…**lower cognitive performance related to vestibular loss was associated with …**
  - **a 2.6 fold increase in the odds of falling** (95% confidence interval = 1.2 and 5.5, p = .017
  - Individuals with vestibular loss have been shown to have **impairments in the ability to generate internal representations of their external world.**
    - "…**difficulty remembering the locations of previously seen targets, and navigating towards these targets or back to their starting locations."** Semenov et al. 2015

Discussion

Brandt et al. 2005

- **Human studies have focused on patients with bilateral vestibular loss (e.g. post-surgery for NF 2) compared to age and sex-matched controls**
- **Test: Human adaptation** of the **Morris Water Test** (MWT = test of spatial navigation)
  - **Patients showed impaired performance when required to retrace their path to a hidden target (i.e. a platform)**
  - <u>Other memory functions were normal</u>

Morris Water Test



The rat is inserted at the points indicated. At first the platform is raised and visible. However, after the rats identify correctly the location of the platform the platform is submerged a bit. Then the rat must use the location of the "visual landmark" to guide it to the partially submerged platform. Rats with bilateral loss of vestibular function have difficulty navigating to the partially submerged platform.

There are three tactics for the rats to escape the maze: a praxic strategy (remembering the movements needed to get to the platform), a taxic strategy (the rat uses visual cues to reach their destinations), or spatial strategy (using distal cues as points of reference to locate themselves) https://en.wikipedia.org/wiki/Morris_water_navigation_task

Discussion

- The inability to generate mental maps of the environment may make it difficult for patients with vestibular loss to:
  - navigate around obstacles in their way (e.g. obstacles in the hallway that we keep tripping over in the dark), leading to falls and fall-related hip and wrist fractures
  - Re-locate targets in the environment (e.g. car in parking lot, shopping cart in big lot store)

Discussion

- Also, may result in a **“Reduction in the ability to spatially interact with ones environment** may have implications for instrumental activities of daily living (ADLs) including **shopping and traveling in the community.”**

Discussion

What are explanations for the association between vestibular impairment and cognitive dysfunction?

- **1) Bilateral vestibular loss may produce atrophy of areas associated with the cortical vestibular network** (dorsal thalamus, temporo-parietal junction, and hippocampus; [**17-18% reduction in mass of the hippocampus**, Brandt, 2005, Schautzer, 2003])
  - **Atrophy could result in impairments in visuospatial memory and perception.** Study of bilateral peripheral loss (N = 10; Brandt et al. 2005) showed patients with hippocampal atrophy showed impairment in the virtual maze
    - **Effects have been reported for patients with <u>unilateral de-afferentation</u>** (Eulenburg et al. 2010)

doi:10.1093/brain/awh617 *Brain* (2005), **128**, 2732–2741

Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans

Thomas Brandt,[1] Franz Schautzer,[2] Derek A. Hamilton,[3] Roland Brüning,[4] Hans J. Markowitsch,[5] Roger Kalla,[1] Cynthia Darlington,[6] Paul Smith[6] and Michael Strupp[1]

Table 1 Mean hippocampal, GM, WM, CSF and whole-brain volume (± SD) measured by MRI volumetry in NF2 patients and controls*

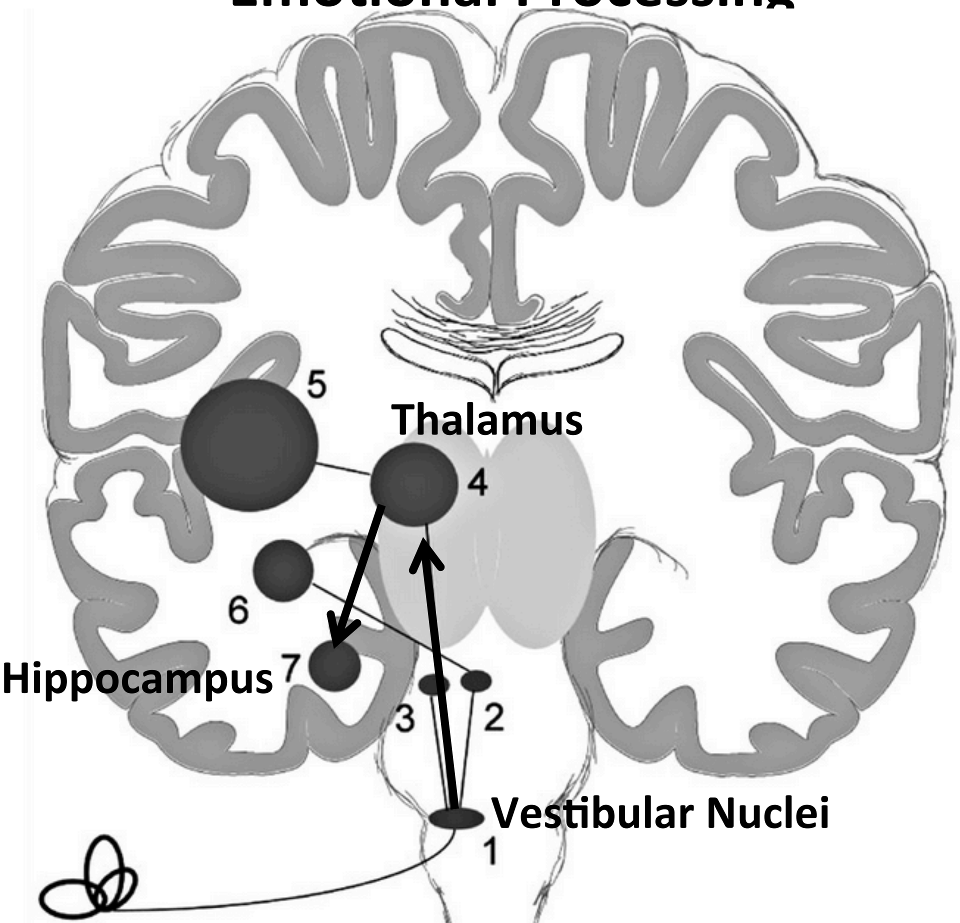
	Control (male)	Control (female)	BVL (male)	BVL (female)
Right HPC (cm^3)	2.67 (0.14)	2.55 (0.23)	2.31 (0.40)	2.02 (0.24)
Left HPC (cm^3)	2.91 (0.26)	2.42 (0.31)	2.33 (0.47)	2.06 (0.15)
Total HPC (cm^3)	5.59 (0.38)	4.98 (0.52)	4.64 (0.83)	4.08 (0.38)
Grey matter (cm^3)	594.32 (27.38)	577.48 (30.94)	648.79 (58.64)	503.64 (60.01)
White matter (cm^3)	687.33 (101.07)	596.53 (40.47)	690.90 (83.22)	532.29 (48.26)
Whole brain (GM + WM, cm^3)	1281.65 (103.1)	1174.01 (65.60)	1339.69 (139.8)	1035.94 (99.94)
CSF (cm^3)	170.16 (27.11)	168.25 (20.20)	240.34 (42.81)	197.65 (30.80)
Right HPC/whole brain	0.209 (0.013)	0.211 (0.021)	0.174 (0.06)	0.195 (0.015)
Left HPC/whole brain	0.228 (0.019)	0.198 (0.020)	0.177 (0.024)	0.199 (0.015)
Total HPC/whole brain	0.437 (0.032)	0.408 (0.036)	0.351 (0.051)	0.394 (0.027)

HPC, hippocampus. *Measures were not obtained or could not be computed for four participants (3 BVL patients and 1 control).

Gurvich C. et al. 2013. Vestibular insights into cognition and psychiatry. *Brain Research*, 1537: 244-259

- **Cognitive deficits in spatial memory remain at least 5-10 years post-deafferentation** (Brandt et al. 2005, Schautzer et al, 2003)
  - **Suggests existence of anatomical links between vestibular nuclei and the hippocampus**
- **Role of hippocampus in spatial memory is known**
  - **Vestibular inputs update brain representations of spatial information**
- **However pathway connecting vestibular system to the hippocampus are unclear**
  - **the link may be between the thalamus and the hippocampus**

Known and Hypothesized Connections Between the Central Vestibular System and Centers for Spatial and Emotional Processing



Posterior CNS projections of the vestibular nuclei subserving spatial and emotional processing. 1 = Vestibular nuclei, 2 = locus coeruleus, 3 = parabrachial nucleus, 4 = posterolateral thalamus, 5 = parietoinsular cortex, 6 = amygdala, 7 = hippocampus. From: Franke LM, Walker WC, Cifu D, Ochs AL, Lew HL. Sensorintegrative dysfunction underlying vestibular disorders after traumatic brain injury: A review. J Rehabil Res Dev 49: 985-994.

Discussion

What are (other) possible explanations for the association between vestibular impairment and cognitive dysfunction?

- **2) Postural and gaze instability (from bilateral impairment) requires the brain to allocate more attentional resources for mental tasks for balance and orientation**
  - i.e. **patient has less of a cognitive reserve**
- **3) Cognitive dysfunction may result from anxiety and depression that is common for dizzy patients**

What we know now that we didn't know before

- **Connections exist between the vestibular nuclei and the hippocampus (via the thalamus?)**
- **Patients with impaired balance (not explicitly vestibular impairment) demonstrate evidence of impaired visuospatial memory**
- **(Past research shows) bilateral vestibular deafferentation results in a 17-18% reduction in hippocampal mass and degradation in visuospatial memory**

What we know now that we didn't know before

- Real world consequences of bilateral loss may include a corruption of the visuospatial map that a person has of their environment (location of: stairs, shopping cart, car etc.) and may predispose patients to falls
- Visuo-spatial memory may represent a dimension we need to assess in patients with bilateral vestibular impairments

Other References and Readings

- Bigelow RT, Agrawal Y. 2015. Vestibular involvement in cognition: Visuospatial ability, attention, executive function, and memory. J Vestib Res 25: 73-89.
- Bigelow RT, Semenov MA, Trevino C, Ferrucci L, Resnick SM, Simonsick EM, Xue, Q-L, Agrawal Y. 2015. Association between visuospatial ability and vestibular function in the Baltimore Longitudinal Study of Aging. J Am Geriatr Soc
- Brandt T. 2005. Vesstibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain 128: 2732-2741.
- Brandt T, Schautzer F, Hamilton DA, Bruning R, Markowitsch HJ, Kalla R, Darlingtion C, Smith P, Strupp M. 2005. Vestibular loss causes hippocampal atrophy and impaired spatial memory in humans. Brain 128: 2732-2741.
- Franke LM, Walker WC, Cifu D, Ochs AL, Lew HL. Sensorintegrative dysfunction underlying vestibular disorders after traumatic brain injury: A review. J Rehabil Res Dev 49: 985-994.
- Hanes DA, McCollum G. 2006. Cognitive-vestibular interactions: A review of patient difficulties and possible mechanisms. J Vestib Res 16: 75-91.
- Previc FH, Krueger WW, Ross RA, Roman MA, Siegel G. 2014. The relationship between vestibular function and topographical memory in older adults. Front Int Neuro 46: 1-8.
- Smith PF, Zheng Y, Horii A, Darlington CL. 2005. Does vestibular damage cause cognitive dysfunction in humans? J Vestib Res 15: 1-9.
- Schautzer F. 2003. Chronic bilateral vestibular failure. Ann NY Acad Sci 1004: 316-324.

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