Session Title: More common than you think: Vestibulo-ocular and vestibulospinal dysfunction in aging and neurodegenerative disease

Presenters: LE Dibble, PT, PhD; CD Hall, PT, PhD; MC Schubert, PT, PhD

Learning Objectives:
- Describe/discuss the evidence for vestibular damage with aging and two model neurodegenerative diseases (Diabetes, MS)
- Identify crucial examination tools to measure gaze and postural stability in patients with advancing age or diabetes and MS.
- Understand the relationship between alterations in gaze stability and postural stability.
- Describe/discuss the evidence for motor learning within the vestibulo-ocular and vestibulo-spinal pathways in the context of aging and neuro-degeneration.

I) VOR/VSR declines in aging and neurodegenerative disease
   a) Vestibular Anatomy Review
   b) Age related anatomic and physiologic decline
      i) Sensors
      ii) Ganglia / Peripheral nerve
      iii) Vestibular nuclei
      iv) Tests for documentation of VOR / VSR deficits

   c) Evidence of VOR/VSR deficits in aging, Diabetes, and MS
      i) In fallers with these conditions, abnormal vestibular findings are common.
      ii) Clinical tests (ie head thrust) may not reveal deficits present on vHIT

   \[\text{Horizontal canal: Yaw Plane HIT}\]
   \[\text{Anterior canal: Pitch Down HIT}\]
   \[\text{Utricular macula: Ocular VEMP}\]
   \[\text{Posterior canal: Pitch Up HIT}\]
   \[\text{Saccular macula: Cervical VEMP}\]

From Curthoys et al, 2013
II) Examination and differential diagnosis of vestibulo-ocular reflex (VOR) and vestibulospinal reflex (VSR)
   a) Clinical / Instrumented tests of body structure and function

Table 1. Vestibular function test findings in the context of aging and neurodegenerative diseases

<table>
<thead>
<tr>
<th>Measure</th>
<th>Vestibular Dysfunction</th>
<th>Older Adults</th>
<th>MS</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head Impulse Test</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Horizontal and Anterior Canal &lt;~0.8&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Yaw &gt;~0.8&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Horizontal canal: greater aVOR variability, CS /HR, and CS latency than controls&lt;sup&gt;50&lt;/sup&gt;</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>Posterior Canal &lt;~0.55&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Unknown for vertical canals</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Caloric</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>&gt;25% unilateral asymmetry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dynamic Visual Acuity</strong></td>
<td>&lt; 0.118 ± 0.184 across ages 3-85 years&lt;sup&gt;6&lt;/sup&gt; (active)</td>
<td>&lt; 0.207 ± 0.216 ages &gt; 50 years&lt;sup&gt;6&lt;/sup&gt; (active)</td>
<td>Reduced canal plane DVA&lt;sup&gt;14&lt;/sup&gt;</td>
<td>Abnormal passive canal plane DVA horizontal and anterior SCC&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Rotary Chair</strong></td>
<td>Abnormal high velocity step and high frequency (sinusoid) gains</td>
<td>Reduced VOR gain at all HZ &gt;50years&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Unknown</td>
<td>No difference in active or passive head rotation VOR gain (&gt; 0.9, ~ 100d/s)</td>
</tr>
<tr>
<td></td>
<td>Recovers at low velocity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Ocular VEMP</strong></td>
<td>Lengthened N1 or P1 latency (delayed)</td>
<td>Delayed N10 latency with 0.12ms/decade progression (n=257)&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Delayed or absent&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Reduced amplitude&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Reduced threshold</td>
<td>Amplitude decreased by 2.9µV/decade. (n=257)&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Less commonly have reduced magnitude&lt;sup&gt;7,8&lt;/sup&gt;</td>
<td>Delayed N1/ P1 latencies&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Reduced or magnified amplitude</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asymmetry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cervical VEMP</strong></td>
<td>Lengthened N1 or P1 latency (delayed)</td>
<td>Amplitude decreased by 0.14µV/decade</td>
<td>May be less commonly affected compared to oVEMP&lt;sup&gt;7,8&lt;/sup&gt;</td>
<td>Reduced N1 amplitude&lt;sup&gt;3&lt;/sup&gt;, Delayed N1/ P1 latency&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Reduced threshold</td>
<td>P13 latency was 0.38ms longer in males (n=257)&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Delayed in absent&lt;sup&gt;7,8&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Reduced or magnified amplitude</td>
<td>Reduced amplitude&lt;sup&gt;13&lt;/sup&gt;</td>
<td>Less commonly have reduced magnitude to oVEMP&lt;sup&gt;7,8&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Asymmetry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SVV</strong></td>
<td>&gt;2deg&lt;sup&gt;17-18&lt;/sup&gt;</td>
<td>&gt; 3 deg in 5/51 individuals aged 70–95 years&lt;sup&gt;19&lt;/sup&gt;</td>
<td>48% patients had mean 0.82° ± 2.32 Healthy (0.22°±1)&lt;sup&gt;15&lt;/sup&gt;</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td>&gt;3deg bucket test&lt;sup&gt;19, 20&lt;/sup&gt;</td>
<td></td>
<td>&gt;7deg&lt;sup&gt;16&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>
b) Critical examination tools to measure activity limitations and participation restrictions of VSR

- Systems model of postural control involves biomechanical system, limits of stability, anticipatory postural adjustments, automatic postural responses, sensory integration, and dynamic balance during gait.  

(Figure adapted from Horak et al., *PTJ*, 2009)
Table 2. Psychometric properties of commonly used outcome measures for activity and participation limitations

<table>
<thead>
<tr>
<th>Population Measure</th>
<th>Vestibular Dysfunction</th>
<th>Older Adults</th>
<th>MS</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activities-specific Balance Confidence scale</td>
<td>Excellent reliability\cite{22}; &gt;80% high function\cite{25}; Cut-off: &lt; 67% fall risk\cite{26}</td>
<td>Excellent reliability; cut-off: 40 w/ Se: 65%; Sp: 77%\cite{27}</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness Handicap Inventory</td>
<td>Excellent reliability; Mild: 0-30 Moderate: 31-60 Severe: 61-100; MDC: 17, MDIC: 18 points\cite{28}</td>
<td>Excellent reliability; cut-off: total score &lt; 260 sec fall risk w/ 44% Se and 90% Sp\cite{31}</td>
<td>Excellent reliability; cut-off: 59; Se: 50%, Sp: 74%; MDC: 22.5\cite{27}</td>
<td></td>
</tr>
<tr>
<td>Modified Clinical Test of Sensory Interaction on Balance</td>
<td>C1-3: 30s; C4: x=26.6 s; C5: x=13.8 s\cite{30}</td>
<td>Excellent reliability; cut-off: &gt; 13.5 s fall risk\cite{33}</td>
<td>cut-off: 13.6s; Se: 73%, Sp: 54%\cite{34}</td>
<td>Cut-off 10.7 s; Se: 90%, Sp: 89%\cite{35}</td>
</tr>
<tr>
<td>Timed up and go</td>
<td>Cut-off: &gt; 11.1 s fall risk, Se: 80%, Sp: 56%\cite{32} (Whitney)</td>
<td>Excellent reliability; cut-off: &gt; 13.5 s fall risk\cite{33}</td>
<td>cut-off: 13.6s; Se: 73%, Sp: 54%\cite{34}</td>
<td></td>
</tr>
<tr>
<td>Berg Balance scale</td>
<td>Cut-off: 45 impaired balance, 75% sensitivity/specificity\cite{30}</td>
<td>Excellent reliability; Cut-off = &lt;45/56 balance deficits/fall risk (Berg); MDC = 3.3-6.3\cite{37}</td>
<td>Excellent reliability; w/ different cut-offs, Se: 32-94%, Sp: 32-90%\cite{37,34,38}</td>
<td>Cut-off: 52; Se: 90%, Sp: 77%\cite{35}</td>
</tr>
<tr>
<td>Dynamic Gait Index</td>
<td>Excellent reliability; MDC=3.2 points\cite{39}; cut-off: &lt;19/24 fall risk\cite{40}</td>
<td>Excellent reliability; MDC=2.9 points\cite{41}; MDIC=1.9 points; cut-off= &lt;19/24 fall risk Se: 59%, Sp: 64%\cite{42}</td>
<td>Excellent reliability; MDC=4.2-5.5 points; cut-off=12, Se: 45%, Sp: 80%\cite{27}</td>
<td>Cut-off: ≤ 22; Se: 90%, Sp: 85%\cite{35}</td>
</tr>
<tr>
<td>Functional Gait Assessment</td>
<td>Excellent reliability\cite{43}; MCID=8 points\cite{44}</td>
<td>Excellent reliability; cut-off =&lt; 22/30 fall risk w/ 85% sensitivity, 86% specificity\cite{45}</td>
<td>Excellent test-retest reliability (0.98), SEM = 1.0 points, MDD = 2.77 points\cite{51}</td>
<td></td>
</tr>
</tbody>
</table>

MDC: Minimal detectable change; MCID: Minimal clinically important difference; Se: Sensitivity; Sp: Specificity; SEM: Standard Error of the Mean; MDD: Minimal detectable difference
III) Vestibular motor learning and reduction of disability during VOR/VSR Rehabilitation
   a) Improving gaze stability to reduce fall risk
   b) Dosage and error signals necessary for VOR/gaze stability motor learning and retention
   c) Prognosis for recovery / progression of disability

Table 3. Vestibular rehabilitation in non-peripheral vestibular deficits

<table>
<thead>
<tr>
<th>Study</th>
<th>Population</th>
<th>Vestibular function test</th>
<th>Intervention</th>
<th>Dose</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beling, JGPT, 200946</td>
<td>Older adults (x=80 years); n=19</td>
<td>None</td>
<td>Balance rehabilitation; Gaze stability (VORx1 horiz/vert)</td>
<td>3x/wk x 1 hr x 12 wks</td>
<td>Berg balance scale; Sensory organization test; TUG</td>
</tr>
<tr>
<td>Jung, Am J Oto, 200947</td>
<td>Older adults (x=76.5 years); n=153</td>
<td>ENG, rotary chair, MRI</td>
<td>Gaze stability (VORx1 horiz/vert; imaginary target) and walk with head turns vs. usual activity</td>
<td>3x/day x 3 months</td>
<td>ABC, verbal analog scale</td>
</tr>
<tr>
<td>Hall, JNPT, 201048</td>
<td>Older adults (x=years); n=</td>
<td>calories, head thrust test, bedside/ neurological exam</td>
<td>Balance rehabilitation and Gaze stability (VORx1 horiz/vert/checkerboard, eye-head b/t targets) vs. balance rehabilitation only</td>
<td>3x/day x 6</td>
<td>ABC, SOT, gait speed, DGI</td>
</tr>
<tr>
<td>Garg et al, 201552</td>
<td>Relapsing Remitting MS</td>
<td>vHIT</td>
<td>Gaze stability (VOR x 1, seated, standing) Postural stability (standing, walking with head turns)</td>
<td>2-3x/day x 2 weeks</td>
<td>vHIT, FGA, FSST, DHI, ABC</td>
</tr>
</tbody>
</table>

For Vestibular Adaptation

A. Visual input from the Nucleus of the optic tract (NOT) is more critical than occipital lobe function.53, 54
   a. NOT lesions do not enable VOR gain recovery recovery
   b. Occipital lobectomy lesions recover 50-75% VOR gain
   c. Animals restricted to darkness post labyrinthectomy have little/no VOR gain recovery.54,56

B. Head motion is critical
   a. Reduced spontaneous nystagmus in squirrel monkey exposed to rotating chair post labyrinthectomy56
   b. Locomotor recovery in mobile animals is much quicker than restricted animals57

C. Cerebellum
   a. Floccular target neurons and role in VOR gain
   b. Nodular neurons and role in perseverating the duration of nystagmus

D. Brainstem
   a. Vestibular nuclei
References
5. Rigon R1, Rossi AG, Cöser PL. Otoneurologic findings in Type 1 Diabetes mellitus patients. Braz J Otorhinolaryngol. 2007;73(1):100-5.
21. Gawron W1, Pospiech L, Orendorz-Fraczkowska K, Noczynska A. Are there any disturbances in vestibular organ of children and young adults with Type I diabetes? Diabetologia. 2002 May;45(5):728-34.
51. Garg H; Schubert MC; Foreman KB; Sibthorp J; Gappmaier E, Dibble, LE. Test-retest reliability and minimal detectable difference of gaze stability and dynamic balance tests in persons with Multiple Sclerosis and controls. Abstract from 5th International Symposium on Gait and Balance in MS, Portland, OR, September 2015.
52. Garg H; Schubert MC; Foreman KB; Sibthorp J; Gappmaier E, Dibble, LE. Gaze and postural stability training differentially affects vestibular related domains of disability in people with Multiple Sclerosis. Abstract from 5th International Symposium on Gait and Balance in MS, Portland, OR, September 2015.
60. Curthoys I. The interpretation of clinical tests of peripheral vestibular function, Laryngoscope, Vol 12: 1342-1352