Canadian Assoc. Emergency Physicians, 2015

H.I.N.T.S. to I.N.F.A.R.C.T.: Recent Advances in Diagnosing Stroke in Acute Dizziness and Vertigo

David E. Newman-Toker, MD, PhD

Associate Professor of Neurology & Otolaryngology
Johns Hopkins University School of Medicine
Johns Hopkins Bloomberg School of Public Health
Work supported by NIH K23 RR17324-01, AHRQ HS017755-01, NIH U01 DC013778-01A1

Devices loaned by GN Otometrics & Autronics-Interacoustics

*Investigational Use – Device*
A Special Word of Thanks To…

- Johns Hopkins…
  - David Zee
  - Daniel Hanley
  - Justin McArthur
  - Yu-Hsiang Hsieh
  - Richard Rothman

- Outside Collaborators
  - Jorge Kattah
  - Jonathan Edlow
  - Kevin Kerber

- Fellows
  - Ali Saber Tehrani
  - Jorgos Mantokoudis
  - Seung-Han Lee
  - Marrylin Zhou
  - Alex Tarnutzer

- Funding agencies
  - NIH (NCRR, NIDCD)
  - AHRQ
  - Foundations (AAN)

…and many, many more
What would you do?

Acute, Continuous Dizziness

- **HPI**: 30 year-old healthy man presents with a 12-hour history of continuous vertigo, nausea, vomiting and gait unsteadiness. He prefers not to move his head and is made worse by any head movement, including rolling in bed. There are no auditory or neurological symptoms.

- **General neuro exam**: gait slightly wide base, cannot tandem walk; otherwise normal

- **Ocular motor exam**: left-beating nystagmus in left gaze; none in primary or right gaze; otherwise normal including vestibular reflexes, ocular alignment, smooth pursuit
Large Cerebellar Infarction

medial PICA-territory stroke, dimensions 3.0 x 5.0 x 4.4 cm
Large Cerebellar Infarction

medial PICA-territory stroke, dimensions 3.0 x 5.0 x 4.4 cm
Learning Objectives

1. Describe clinical presentations and patient profiles at high risk for missed vertebrobasilar stroke in the ED.

2. Distinguish vestibular neuritis from stroke in continuous vertigo or dizziness using bedside eye exams (HINTS).
Lecture Outline

I. Background & Pitfalls in Posterior Stroke

II. Continuous Dizziness/Vertigo (H.I.N.T.S.)

III. Take Home Points
Pitfalls in Posterior Stroke
Dizziness or Vertigo (~4.4 M/yr)

**EAR**
- BPPV
- Neuritis
- Otitis, HZO

**BRAIN**
- TIA-Stroke
- Wernicke’s
- Encephalitis

**HEART**
- BP-Bleeding
- Arrhythmia
- MI, PE, AD

**ENDO**
- Hypoglycemia
- Addison’s
- CO

~1.1 M/yr
~150 K/yr
Pitfalls in Posterior Stroke

Major ED Concern – Missed Strokes

~120,000-200,000 ED dizzy strokes/yr US

#1 Requested Adult EM Decision Rule:
When to image patients with vertigo?

Eagles et al., 2008

Hotson & Baloh, NEJM 1998
Pitfalls in Posterior Stroke
Finding Stroke in Dizziness Isn’t Easy

- ~4 million ED visits/yr US for dizziness (at a total ED cost of $4 billion annually)
- ~3-5% have CVA (~120-200,000/yr) (ischemia of lat. brainstem & inferior cerebellum)
- ~35% are missed (~40-70,000/yr) (versus 4% for those with motor symptoms)
- up to 40% adverse outcomes (~~~10-30,000/yr) (disproportionately affecting those <50yo)
Pitfalls in Posterior Stroke
Missed Stroke in “Benign” Dizziness

Look Back Approach:
Stroke patients more likely to have been discharged from ED with “benign” dizziness prior ~14 days (N = ~180,000 strokes)

Look Forward Approach:
‘Benign’ dizziness sent home from ED more likely to return with a stroke within ~30 days, but not heart attack (N = ~30,000 ED dizzy discharges)

Complaint-Specific ED Treat-and-Release Visits Preceding an Inpatient Stroke Admission

Rate of return to Hospital with a Stroke or Heart Attack after being sent home from ED with “Benign Dizziness or Inner Ear Problems”

- strokes (rate of readmission peaks early on)
- heart attacks (rate of return is a flat ‘base rate’)

Minor strokes initially misdiagnosed as ‘benign dizziness’ returning with major stroke (~20,000 per year in the US)

Kim et al., 2010
California OSHPD database analysis
Pitfalls in Posterior Stroke
Missed Stroke in “Benign” Dizziness

Misdiagnosis More Frequent in Women & Minorities (~20-30%)
Young 18-44yo (~7x vs. >75yo)
(Newman-Toker et al, Diagnosis 2014)
**Imaging Misuse:**
CT does not “rule out” stroke in dizziness…
*negative CT predicts* future stroke (OR 2.3)

N = 8,596

Grewal et al., 2015
Pitfalls in Posterior Stroke

False Negative MRI in Dizzy Strokes

False negative initial MRI in ~50%
Large artery (high risk) lesion in ~50%
Acute Vestibular Syndrome (AVS)

High-risk-for-stroke Group

(~400-800,000 per year in US)
Acute, Continuous Dizziness (days)

Definition of Acute Vestibular Syndrome

- acute, continuous dizziness, vertigo, or gait ataxia lasting days to weeks with nausea or vomiting, head motion discomfort, nystagmus

- ‘Post-Exposure’ and ‘Spontaneous’ forms
  - Post-Exposure: anti-epileptic drugs, TBI, etc.
  - Spontaneous: vestibular neuritis, stroke, MS

This is NOT episodic, positional vertigo, even if the patient gets worse with changes in position
Acute, Continuous Dizziness (days)
Spontaneous AVS

- Peripheral and central vestibular causes
  - ~75% peripheral (vestibular neuritis/labyrinthitis)
  - ~25% central (80% stroke, almost all ischemic)

- ~10-20% of all ED dizziness, ~80-90% of strokes

- ~80% no focal neurologic signs ('isolated' AVS)

- fraction of isolated AVS with stroke ~15-20%

- co-morbid auditory symptoms increase risk (AICA)
H.I.N.T.S.
3 bedside oculomotor findings: H.I.N.T.S.

- Head Impulse
- Nystagmus
- Test of Skew
Acute, Continuous Dizziness (days)

H.I.N.T.S. to I.N.F.A.R.C.T.

AVS EXAM: 3-component “H.I.N.T.S.” Battery
- Head Impulse
- Nystagmus
- Test of Skew

STROKE FINDINGS: “I.N.F.A.R.C.T.”
- Impulse Normal
- Fast-phase Alternating
- Refixation on Cover Test

Any ONE of these points to stroke in AVS
H.I.N.T.S.
Acute Vestibular Syndrome

Head Impulse
(H.I.N.T.S.)
h-HIT **ABNORMAL** is usu. PERIPHERAL

Video shows Normal R, Abnormal L HIT

Courtesy of David Zee, MD (video from Leigh & Zee, Neurology of Eye Movements)
Vestibulo-ocular reflex

6th & 3rd ‘Out’

8th ‘In’
Vestibulo-ocular reflex

cerebellar stroke

lat. pons stroke

vestibular neuritis
H.I.N.T.S.
Acute Vestibular Syndrome

Nystagmus

(H.I.N.T.S.)
Direction-Changing Nystagmus is CENTRAL Acute Vestibular Syndrome

Vestibular-Type Nystagmus

- persistently present (at least s visual fix.)
- horizontal > torsional
- damps when looking towards slow phase and vice-versa
- never changes direction (e.g. always leftward, not rightward)
Peripheral Vestibular Nystagmus
Direction-Changing Nystagmus is CENTRAL

Mixed Vestibular/Gaze-Holding

- Vestibular
  (usually peripheral, typical of neuritis)

- Gaze-Holding
  (central, most typical of cerebellar degeneration)
Direction-Changing Nystagmus is CENTRAL
Acute Vestibular Syndrome

The ‘Tell’

Acute, unilateral cerebellar or brainstem strokes may look like neuritis, but sometimes declare themselves with direction-changing nystagmus
Direction-Changing Nystagmus is CENTRAL
Acute Vestibular Syndrome
H.I.N.T.S.
Acute Vestibular Syndrome

Test of Skew
\[\text{H.I.N.T.S.}\]
Skew Deviation (vertical dev.) is CENTRAL
Acute Vestibular Syndrome

Courtesy of Jorge Kattah, MD; from Kattah, et al. Stroke, 2009
H.I.N.T.S. to
I.N.F.A.R.C.T.
H.I.N.T.S.
Acute Vestibular Syndrome

Impulse Normal (I.N. F.A.R.C.T.)

NOTE THIS IS COUNTERINTUITIVE
H.I.N.T.S.
Acute Vestibular Syndrome

One Impulse ABNORMAL = Neuritis
(or occasionally AICA-territory stroke)

Both Impulses NORMAL = Stroke

SO CASE SELECTION IS CRITICAL
H.I.N.T.S.
Acute Vestibular Syndrome

Fast-phase Alternating

(I.N.F.A.R.C.T.)
H.I.N.T.S.
Acute Vestibular Syndrome

Refixation on Cover Test
(I.N.F.A.R.C.T.)

(vertical skew only… horizontal does not count)
ROC Analysis: Expert HINTS vs. Neuroimaging for Stroke in Acute, Continuous Dizziness/Vertigo

HINTS 'plus'
HINTS
HIT alone
MRI <24hr
CT <24hr

Sensitivity (True Positive Rate)

1 - Specificity (False Positive Rate)

ROC for Any Central Cause (n=190)
HINTS AUC 0.995
Acute, Continuous Dizziness (days)
H.I.N.T.S. vs. MRI within 48hrs of Onset

HINTS – any one of the three bedside oculomotor findings predict stroke with pooled…

- sensitivity 99.2%, specificity of 97.0%
- negative likelihood ratio (NLR) “rule out power” of HINTS vs. acute brain MRI DWI <24-48 hrs

<table>
<thead>
<tr>
<th>Test</th>
<th>NLR</th>
<th>(95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HINTS bedside</td>
<td>0.01</td>
<td>(0.00–0.06)</td>
</tr>
<tr>
<td>Acute MRI DWI</td>
<td>0.21</td>
<td>(0.16-0.26)</td>
</tr>
</tbody>
</table>

If the patient has a 50% chance of stroke…
Benign HINTS = <1% vs. Negative MRI = 17%
**Acute, Continuous Dizziness (days)**

**Acute Vestibular Syndrome**

<table>
<thead>
<tr>
<th>Impulse Test</th>
<th>Nystagmus</th>
<th>Skew</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Present</td>
<td></td>
</tr>
</tbody>
</table>
## Acute, Continuous Dizziness (days)

### Acute Vestibular Syndrome

<table>
<thead>
<tr>
<th>Impulse Test</th>
<th>Nystagmus</th>
<th>Skew</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td>Neuritis</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Present</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Present</td>
<td></td>
</tr>
</tbody>
</table>
### Acute, Continuous Dizziness (days)
#### Acute Vestibular Syndrome

<table>
<thead>
<tr>
<th>Impulse Test</th>
<th>Nystagmus</th>
<th>Skew</th>
<th>DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td>Neuritis</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Unidirectional</td>
<td>Present</td>
<td>Stroke</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td>Stroke</td>
</tr>
<tr>
<td>Abnormal</td>
<td>Bidirectional</td>
<td>Present</td>
<td>Stroke</td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Absent</td>
<td>Stroke</td>
</tr>
<tr>
<td>Normal</td>
<td>Unidirectional</td>
<td>Present</td>
<td>Stroke</td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Absent</td>
<td>Stroke</td>
</tr>
<tr>
<td>Normal</td>
<td>Bidirectional</td>
<td>Present</td>
<td>Stroke</td>
</tr>
</tbody>
</table>
Acute, Continuous Dizziness (days)
Acute Vestibular Syndrome

Benign HINTS+ (neuritis)…

- **Straight Eyes** (normal eye alignment, esp. vertical)
- **No Deafness** (no moderate to severe hearing loss)
- **Head Impulse Misses** (unilaterally abnormal h-HIT)
- **One-way Nystagmus** (unidirectional, horizontal)
- **Healthy Otic and Mastoid Examination** (pearly; no pimples, pus, perforation, or pain on palpation)

S.E.N.D.  H.I.M.  O.N.  H.O.M.E.
Conclusions

Take Home Messages
Take Home Messages

Common Misconceptions…

1) Ongoing vertigo with nl neuro exam is not stroke
2) A normal CT scan rules out stroke
3) A normal MRI scan rules out stroke
4) Young people with dizziness don’t have stroke
5) Hearing loss indicates a benign peripheral problem
6) Exacerbation by head movement = benign peripheral
Take Home Messages

The Big Picture

1) Focus on timing and triggers, not type

2) Segregate new dizziness/vertigo into EVS & AVS

3) For AVS, think neuritis vs. stroke, focus on exam (HINTS to INFARCT, no hearing loss, can walk)

4) When you’re not sure, ask for help or get an MRI (don’t bother with the CT unless lethargic or focal)

5) VOG may help in future with these distinctions
A New Technology: The “Eye ECG”
The “Eye ECG”
Portable Video-Ocululography (VOG)

Expertise in a box

Newman-Toker
The "Eye ECG"
Portable Video-Ocululography (VOG)
The “Eye ECG”
Vestibular Neuritis vs. Stroke

Abnormal Right Vestibular Function in a 60yo Patient with AVS

Cerebellar stroke

Bilaterally Normal Vestibular Function in a 30yo Patient with AVS
The “Eye ECG”
Vestibular Neuritis vs. Stroke

60yo AVS - Neuritis

30yo AVS - Stroke
The “Eye ECG”
VOG for Neuritis vs. Stroke

![Graph showing VOR (Velocity of Ocular Rotation) gains for different conditions.](image-url)
The “Eye ECG”  
Combined Low- & High- Risk Groups

Table 1. Cost savings of implementing VOG approach nationally using variable projections of effects on physician behavior

<table>
<thead>
<tr>
<th>For All ED Dizziness</th>
<th>Current (2013 US National)</th>
<th>Conservative Projection</th>
<th>Intermediate Projection</th>
<th>Optimistic Projection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED CT Reduction from Current Baseline</td>
<td>0%</td>
<td>50%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>All ED Dizziness CT Rate</td>
<td>41.2%</td>
<td>20.6%</td>
<td>10.3%</td>
<td>4.1%</td>
</tr>
<tr>
<td>ED MRI Increase from Current Baseline</td>
<td>0%</td>
<td>50%</td>
<td>25%</td>
<td>0%</td>
</tr>
<tr>
<td>All ED Dizziness MRI Rate</td>
<td>2.4%</td>
<td>3.6%</td>
<td>3.0%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Anticipated Admit Rate Reduction for Ear Disorders</td>
<td>0%</td>
<td>25%</td>
<td>50%</td>
<td>75%</td>
</tr>
<tr>
<td>All ED Dizziness Admission Rate</td>
<td>18.8%</td>
<td>18.0%</td>
<td>17.2%</td>
<td>16.4%</td>
</tr>
<tr>
<td>Total ED/Hospital Workup Costs</td>
<td>$9,242,624,941</td>
<td>$8,703,997,576</td>
<td>$8,198,729,820</td>
<td>$7,735,623,708</td>
</tr>
<tr>
<td>Total Annual US Healthcare Cost Savings</td>
<td>$0</td>
<td>$538,627,365</td>
<td>$1,043,895,121</td>
<td>$1,507,001,233</td>
</tr>
<tr>
<td>Public (Federal/State) Insurance Cost Savings</td>
<td>$0</td>
<td>$186,903,696</td>
<td>$362,231,607</td>
<td>$522,929,428</td>
</tr>
</tbody>
</table>

Estimated $1B in annual savings in US EDs of the $9B spent on ED dizziness each year

Newman-Toker et al., BMJQS, 2013
The “Eye ECG”
Combined Low- & High- Risk Groups

Table 1. Cost savings of implementing VOG approach nationally using variable projections of effects on physician behavior

<table>
<thead>
<tr>
<th>For All ED Dizziness</th>
<th>Current (2013 US National)</th>
<th>Conservative Projection</th>
<th>Intermediate Projection</th>
<th>Optimistic Projection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ED</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total Annual US Healthcare Cost Savings</td>
<td>$0</td>
<td>$538,627,365</td>
<td>$1,043,895,121</td>
<td>$1,507,001,233</td>
</tr>
<tr>
<td>Public (Federal/State) Insurance Cost Savings</td>
<td>$0</td>
<td>$186,903,696</td>
<td>$362,231,607</td>
<td>$522,929,428</td>
</tr>
</tbody>
</table>

High-risk groups (underuse) – save lives
Low-risk groups (overuse) – save money

(Newman-Toker et al, BMJQS 2013)

Estimated $1B in annual savings in US EDs of the $9B spent on ED dizziness each year

Newman-Toker et al., BMJQS, 2013
STANDARD ED DIAGNOSIS
Non-selective neuroimaging
Many unnecessary admissions

EVIDENCE-BASED ED DIAGNOSIS
Targeted neuroimaging
Few unnecessary admissions

>40% all-dizzy imaging rate (mostly CT)
(none-selective imaging based on age/vascular risks)

~12% inner-ear admission rate
(includes unnecessary stroke ‘rule out’ admissions)

<10% all-dizzy imaging rate (mostly MRI)
(targeted imaging based on bedside eye exams)

~4% inner-ear admission rate
(admissions only for dehydration, severe balance problems)

Abbreviations: ED = Emergency Department; CT = Computed Tomography; MRI = Magnetic Resonance Imaging.
The “Eye ECG”
Novices Trained to Expert in <1Hr

![Graph showing cumulative HIT maneuvers performed by trainees to achieve competence.](image-url)