Top Questions I Get Asked About: Migraine, Movement Disorders, and Dizziness/ Vertigo

Rashmi B. Halker Singh, MD, FAHS, FAAN
Daniel Press, MD
Patricia E. Greenstein, MB.BCh

Disclosures

Rashmi B. Halker Singh, MD, FAHS, FAAN: Advisory Board for Teva and Impel.

Daniel Press, MD: No relevant financial relationships disclosed.

Patricia E. Greenstein, MB.BCh: No relevant financial relationships disclosed.

Pamela Kushner, MD, FAAFP (Moderator): No relevant financial relationships disclosed.

Top Questions I Get Asked About… Migraine

Rashmi B. Halker Singh MD FAHS FAAN

Associate Professor of Neurology

Mayo Clinic

Scottsdale, AZ

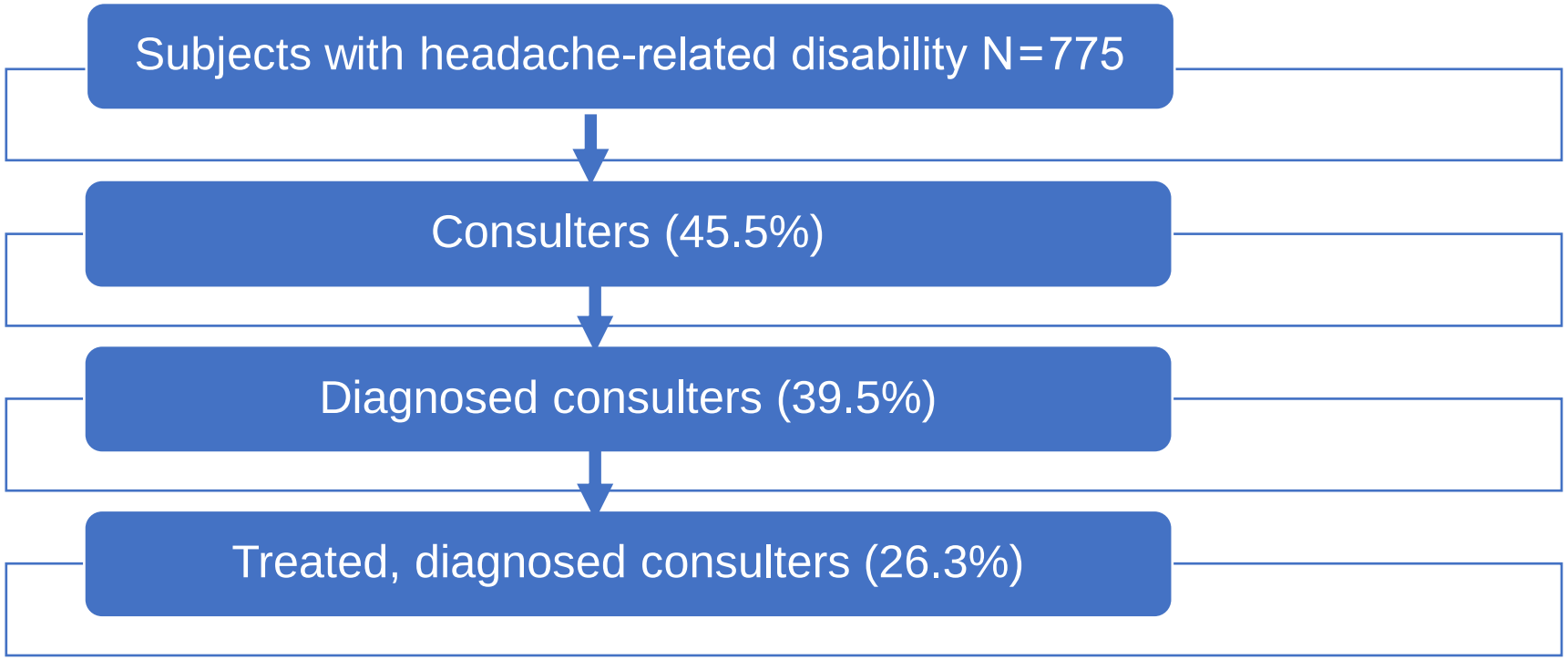
Twitter: @rashmihalker

Is it just a "bad headache" or is it migraine?

- A neurological disorder with a genetic basis
- > 47 million Americans, 10% of school-age children
- 7% have chronic migraine (>15 headache days/month)
- More than "just a headache" - with neurological, sensory, autonomic, vestibular, cognitive, and gastrointestinal symptoms
- The leading cause of years lived with disability in people under the age of 50 worldwide

Global Burden of Disease 2016.

Assessing Barriers to Care in Episodic Migraine: AMPP Study



Lipton RB et al. AMPP Study. *Headache*. 2013;53:81–92

Red Flags in Headache: “SNOOP4”

		Notes
 S	**S**ystemic symptoms, signs, disease	Fever, weight loss, malignancy
 N	**N**eurologic symptoms, signs	Papilledema, sensory, motor, diplopia, bulbar
 O	**O**nset	Abrupt / thunderclap
 O	**O**lder	New headache at age ≥50
 P	**P**attern change **P**recipitation **P**ostural **P**regnancy and postpartum	Loss of pain free periods Valsalva, exertion Orthostatic

So how do we make the diagnosis of migraine?

ICHD-3: 1.1 Migraine

A. At least 5 attacks
B. Headache lasts 4-72 hours
C. 2 of the following 4:
    A. Unilateral location
    B. Pulsating quality
    C. Moderate or severe intensity
    D. Aggravation by or causing avoidance of routine physical activity
D. At least 1 of the following:
    A. Nausea and/or vomiting
    B. Photophobia and phonophobia
E. Not better accounted for by another ICHD-3 diagnosis

ID-Migraine

- P – photophobia
    - *Does light bother you when you have a headache?*
- I – impairment
    - *Do you feel impaired or avoid activities when you have a headache?*
- N – nausea
    - *Do you have nausea when you have a headache?*

2/3 symptoms = 93% PPV
3/3 symptoms = 98% PPV

Cephalalgia 2018.
Lipton RB et al. Neurology 2003.

Great! I've diagnosed migraine! Now how do I choose the best acute treatment?

The Triptans: What are the Options?

- **Fast Onset**
- Eletriptan (PO)
- Rizatriptan (PO, MLT)
- Sumatriptan (PO, SQ, NS)
- Zolmitriptan (PO, NS)
- Almotriptan (PO)
- **Slower Onset:**
- Frovatriptan (PO)
- Naratriptan (PO)

- Side note - Comments from the Choosing Wisely Campaign:

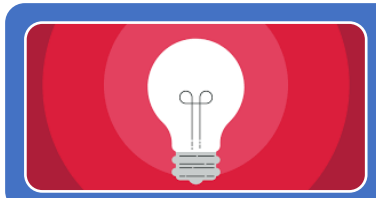
1. Don’t prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders.
2. Don’t recommend prolonged or frequent use of OTC pain medications for headache.

http://www.choosingwisely.org/wp-content/uploads/2015/02/AHS-Choosing-Wisely-List.pdf

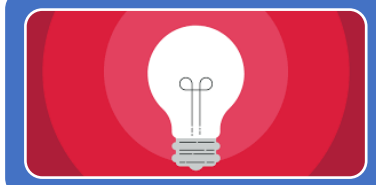
Acute Treatment: Troubleshooting Triptans

Headache recurrence
- Treat early, repeat dose
- Consider combination tx or long-acting triptan

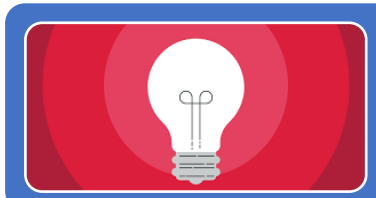
Partial response
- Increase triptan dose
- Repeat dose, consider combination tx



No response
- After 2 adequate trials, switch to different triptan or different class



Inconsistency
- Switch route, change to different drug, increase dose, add prevention



Overuse
- Set limits and add prevention

New non-vasoconstrictive acute treatments

Class	Drug	Route	Form	Max 24 hr Dose	Common AEs
Gepant (CGRP small molecule antagonist)	Rimegepant	ODT	75 mg ODT	75mg	Nausea
Gepant (CGRP small molecule antagonist)	Ubrogepant	Oral	50mg, 100mg	200 mg	Drowsiness, Nausea
Ditan (serotonin 1F agonist)	Lasmiditan* **Scheduled drug – patients may not drive for 8 hours post dose!*	Oral	50mg, 100mg, 200mg	1 dose per 24 hours (regardless of dose)	Dizziness, Fatigue/somnolence, Paresthesia, Nausea/vomiting


When should I start preventive therapy?

Significant interference with activities despite acute treatment

Attack frequency > 1 per week

Elevated risk: medication overuse or daily headache

Acute meds: ineffective, contraindicated, used >2x/week

Patient preference

Uncommon migraine types (brainstem, hemiplegic, prolonged aura, migrainous infarct)

Important to also consider attack-related disability..

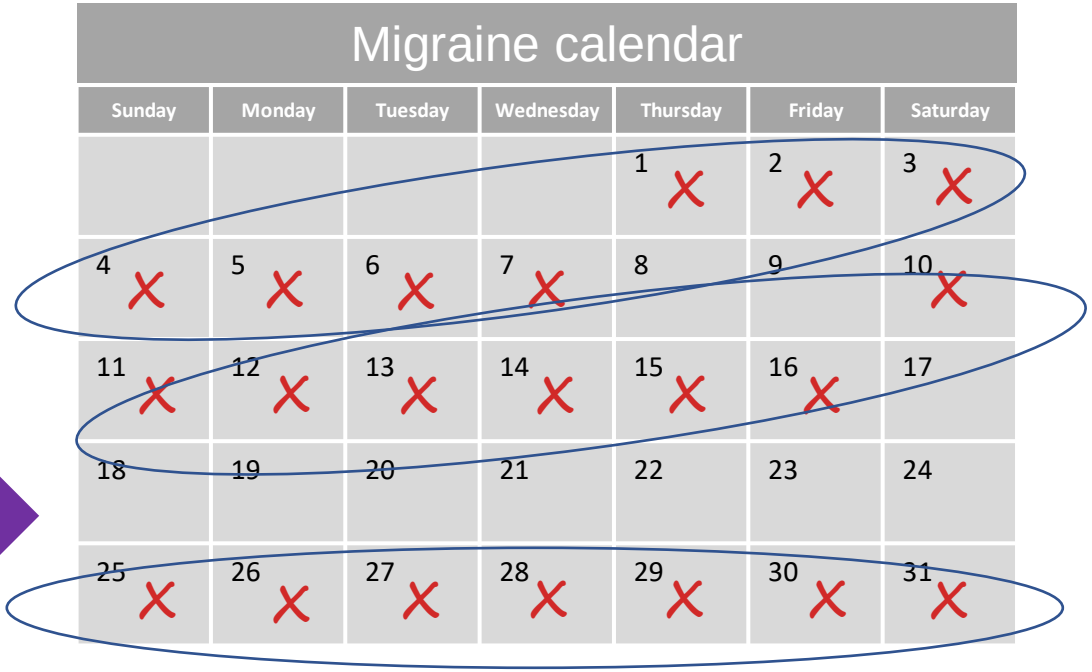
Prevention should be…	Headache days/month	Degree of disability*
Offered	≥ 6	None
	≥ 4	Some
	≥ 3	Severe
Considered	4 or 5	None
	3	Some
	2	Moderate

The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice. Headache. 2019 Jan;59(1):1-18.

Headache Frequency: Questions to Ask

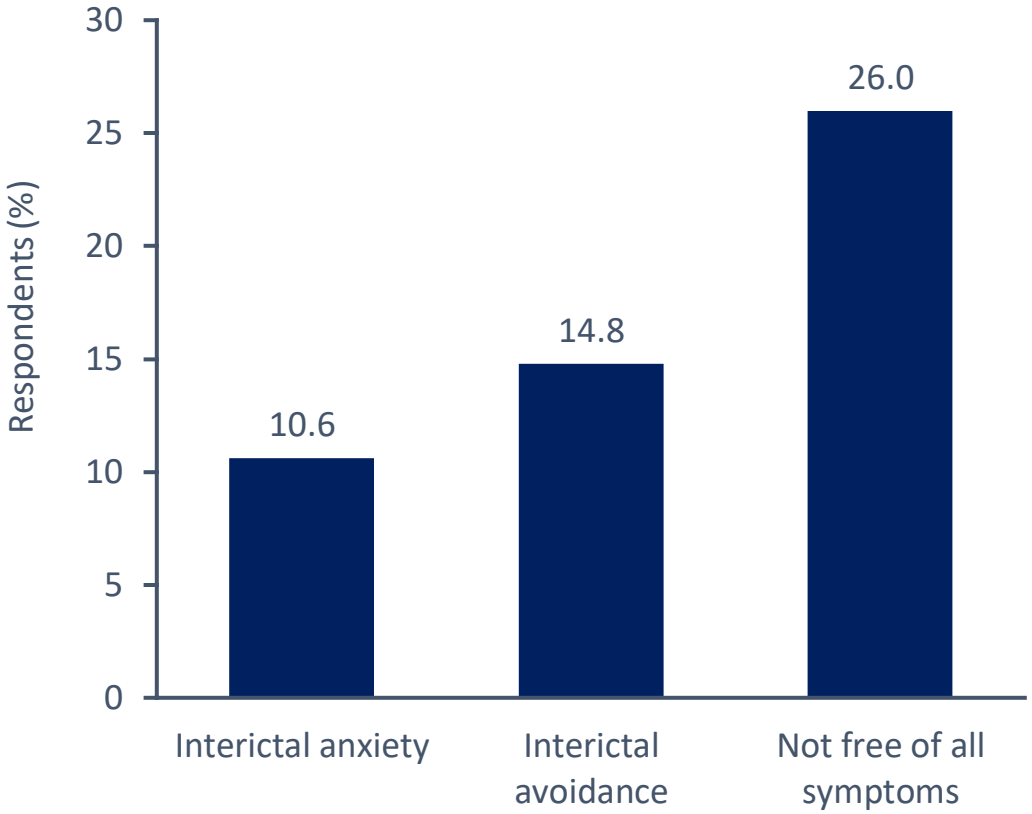
- Determine headache frequency:
  days with headache in the last month + days completely headache free
  - Discuss any days that are unaccounted for
  - Important to distinguish between headache days vs headache/migraine attacks
  - Gives you the most complete picture

Patient may have 3 attacks per month, with each lasting for 7 days = ***21 days***, 3 attacks ➔ chronic migraine!



Migraine-Associated Disability

- Interictal burden is the impairment ***between*** migraine attacks
  - Anxiety about the next attack
  - Avoidance: fear of making plans (professional, social, etc.)
  - Persistence of symptoms
- ***Total migraine burden*** = ictal + interictal burden
  - Both are targets of preventive treatment
- Important to ask about impact of migraine on QoL to help guide need for prevention



Lampl C et al. *J Headache Pain*. 2016;17:9. Bryson J et al. *Neurology*. 2010;16:254–261.

Migraine Prevention: Level A Recommendations

- **Antiepileptics:**
  - Divalproex/sodium valproate 400-1000mg/day*
  - Topiramate 25-200mg/day
- **Beta blockers:**
  - Metoprolol 47.5-200mg/day
  - Propranolol 120-240mg/day
  - Timolol 10-15mg BID
- **CGRP mAbs:**
  - Erenumab
  - Gacanezumab
  - Fremanezumab
  - Eptinezumab

- **Chronic migraine*:**
  - OnabotulinumtoxinA

- **Antidepressants are level B:**
  - Amitriptyline 25-150mg/day
  - Venlafaxine extended release 150mg/day

Chronic migraine:
- *Headache > 15 days/month*
- *Meets migraine criteria 8 days/month*

Silberstein et al. *Neurology* 2012
Holland et al. *Neurology* 2012

Pearls

- Remember to *"PIN" the diagnosis* – even in patients who have a bilateral moderate to severe recurrent headache, consider migraine as it remains underrecognized
- Most patients need to be able to use the highest dose of a triptan at onset with the option to repeat it
- Remember troubleshooting tricks to triptans, including that patients who wake up with migraine attacks or have early N/V may do better with a non-oral choice
- Consider gepants or lasmiditan in patients with comorbid vascular diagnoses
- Ask patients how many days (per week/per month, etc) they are *completely headache free* to ensure you have a complete picture of their problem
- Ask about headache-related disability to help determine the need for prevention

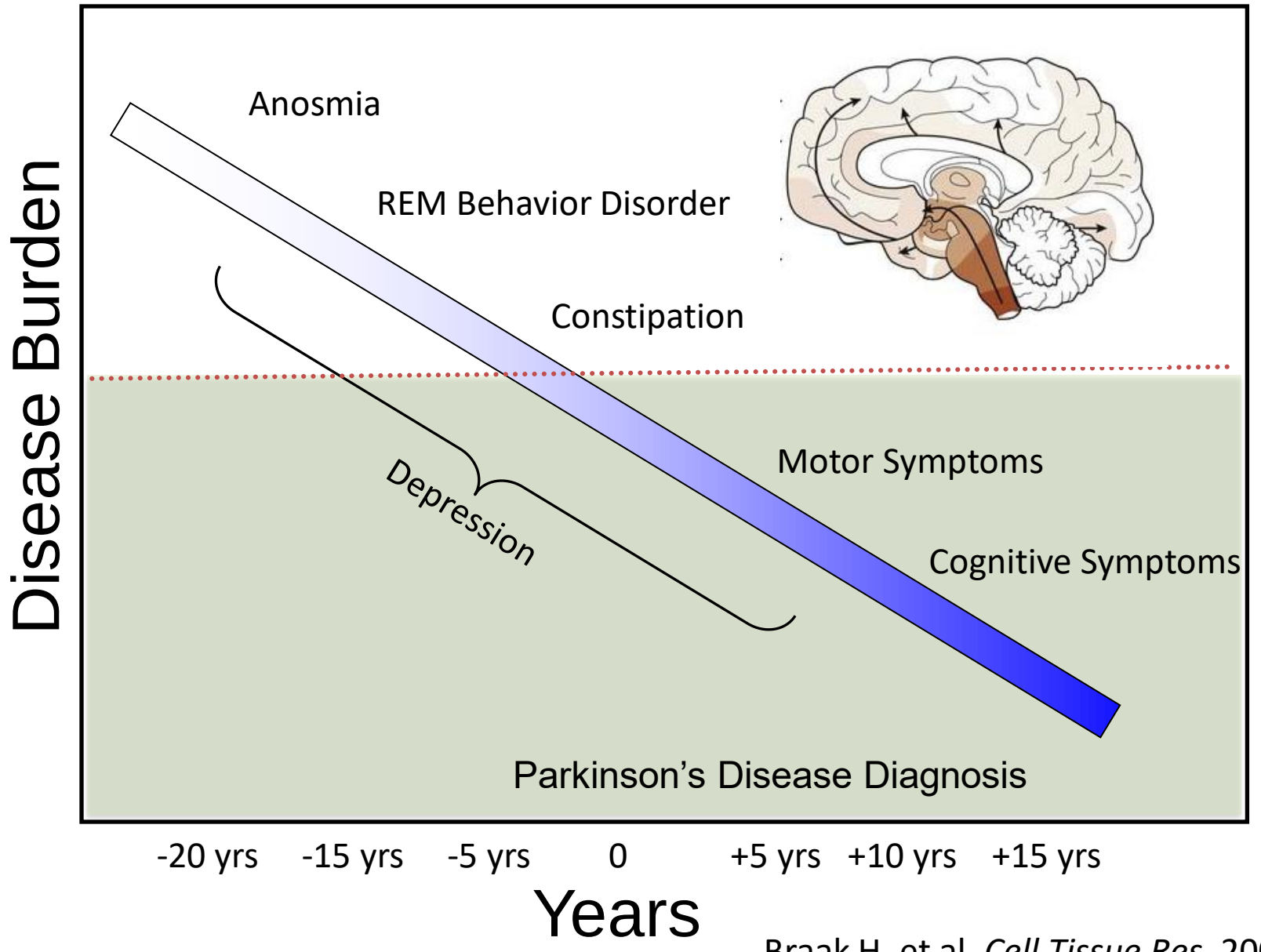
Top Questions I Get Asked About: Movement Disorders

Daniel Press, MD
Associate Professor of Neurology
Harvard Medical School
Chief, Cognitive Neurology Unit
Beth Israel Deaconess Medical Center
Boston, MA

Learning Objectives

- Review current controversies and challenges in movement disorders with a focus on Essential Tremor and Parkinson's disease
- Evaluate treatments for non-motor symptoms in Parkinson's disease, since these symptoms are a major factor in disability
- Discuss the current data for a new non-surgical treatment for essential tremor

How does Parkinson’s disease start?



Braak H, et al. *Cell Tissue Res.* 2004;318(1):121-134.

What are the major non-motor symptoms of PD?

Symptom	Frequency
Cognitive symptoms	31%
Depression	36%
Anxiety	33%
Fatigue	40%
Sleep disturbances	47%
Sensory symptoms	63%

Shulman LM, et al. *Mov Disord*. 2001;16(3):507-510.

PD: Treating Cognitive Symptoms

- Minimize other medications that can worsen cognition (especially anticholinergics)
- Improve sleep to help daytime alertness
- Treat depression and anxiety
- Specific medications (cholinesterase inhibitors): donepezil, rivastigmine, and galantamine

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Rivastigmine for Dementia Associated with Parkinson's Disease

Murat Emre, M.D., Dag Aarsland, M.D., Ph.D., Alberto Albanese, M.D.,

- Placebo-controlled study of cholinesterase inhibitor rivastigmine for treatment of cognitive symptoms in Parkinson's disease dementia
- 541 patients enrolled, 420 completed study
- Alzheimer's scales used for endpoints

Image can be found at:
https://www.nejm.org/na101/home/literatum/publisher/mms/journals/content/nejm/2004/nejm_2004.351.issue-24/nejmoa041470/production/images/img_medium/nejmoa041470_f2.jpeg

Depression in PD

- Incidence approaches 40-50%
- Excessive even when matched for disability
- Global Parkinson's Disease Survey (WHO, 1999)
  - Recognized in as few as 1% of cases
  - Accounts for greatest impairment in quality of life

SAD-PD Trial

A randomized, double-blind, placebo-controlled trial of antidepressants in Parkinson disease

I.H. Richard, M.P. McDermott, R. Kurlan, et al.

Neurology 2012;78;1229; Published online before print April 11, 2012;

- Largest trial of antidepressants in PD
- Three groups: placebo, paroxetine and venlafaxine
- Found both to be better than placebo

New treatments for Essential Tremor?

Characteristics

- Generally an action tremor but in severe cases can continue into rest
- Typically bilateral but is often somewhat asymmetric
- In addition to arms, it can affect head and voice
- Present with posture (outstretched arms) and worsens with goal directed movements such as finger-to-nose, writing, or drinking from a glass
- Exacerbated by stress, anxiety, but not caffeine
- Relieved by small amounts of alcohol

Differential Diagnosis of Tremors

- Enhanced physiological tremor- usually briefer and only obvious under stress
- Metabolic disorders- hyperthyroidism, hypercalcemia
- Drug induced tremors- especially valproic acid, lithium, SSRIs, amiodarone, beta-agonists, steroids
- Parkinson’s disease vs. Essential Tremor

Differentiating ET from PD

Clinical Features	Parkinson's disease tremor	Essential Tremor
Asymmetry	Marked	Minor
Genetics	Weak in 10-15%	Strong, in about 50%
Character	Rest and action	Mainly action
Associated motor features	Bradykinesia, rigidity, gait change, micrographia	Improvement with EtOH
Associated non-motor features	Anosmia, constipation, REMBD	None of these

Treatment of Essential tremor

- Medical treatment- initiate depending on degree of disability
- If intermittent issues (with writing checks, for instance), short acting propranolol (10mg)
- If persistent disability- propranolol XR (60-320mg/d) or primidone (50-750mg/day, starting at 25mg and with slow titration), or combination if needed
- Second line agents: atenolol (if propranolol not tolerated), gabapentin, topiramate
- Third line: deep brain surgery (DBS) and focused ultrasound

Severe ET: Surgical Treatment (DBS)

Ventral Intermediate Nucleus of thalamus (VIM)

<u>Advantages</u>

- Immediate symptomatic improvement of 60-90%
- Adjustable, can be customized
- Lower risk than lesions

<u>Disadvantages</u>

- Batteries require replacement
- Risk of implantation
- Cost/coverage

Severe ET: Focused Ultrasound

- Focused ultrasound creates high temperatures (50-60^{o}c) that creates a permanent lesion
- Long procedure (2-3 hours) but not invasive

Images from Brigham and Women's hospital FUS program

Severe ET: FUS vs. DBS

DBS

Advantages

- Not permanent
- Programmable/modifiable
- Lower risk than lesions

Disadvantages

- Surgery/surgical risks

Focused Ultrasound

Advantages

- No surgery
- Instant effect/no programming

Disadvantages

- Side effects: numbness (38%)
- Gait disturbance (36%)
- Durability isn’t clear

Top Questions I Get Asked About… Dizziness/Vertigo

Patricia E. Greenstein, MB.BCh

What do we mean by dizzy?

- It is a very common experience
- If there are 100 people in a room and you ask who has ever been dizzy, you may get 100 different answers
- Dizziness is a term used to describe a range of sensations, such as feeling faint, woozy, weak, or unsteady
- A detailed expert history-taking and some simple physical signs on examination are required to reach an accurate diagnosis of what a patient is describing
- Dizziness may be caused by both benign and dangerous conditions, so a careful history is important to improve the diagnostic accuracy

3 Important diagnostic considerations in distinguishing dizziness

- What is lightheadedness, presyncope?
- How do we distinguish central from peripheral vertigo?
- What is disequilibrium or unsteadiness?

Lightheadedness and presyncope

- A sensation of going to pass out: presyncope
- Presyncope occurs more commonly than syncope
- It lasts for seconds to minutes and a patient may report their vision greying out
- They may also report lightheadedness or a feeling of warmth, diaphoresis, and/or nausea
- Ask about a prior history of cardiac disease and hypertension and about new medication, especially in older adults. Ask specifically about chest discomfort, shortness of breath, and palpitations
- Antihypertensives in older adults are frequent culprits of overtreatment
- Remember to measure orthostatics in the office

DISEQUILIBRIUM

- Disequilibrium is a sense of imbalance that occurs primarily when walking. Chronic dizziness or disequilibrium can cause significant impairment of physical and social functioning, particularly in older adults
- Disequilibrium has many causes which include:
  - Peripheral neuropathy
  - Cervical myelopathy with posterior column loss
  - Parkinson's disease with disequilibrium and postural hypotension
  - Visual impairments
  - Cerebellar disorders
- You should inquire about symptoms of neurologic and gait disorders, especially those suggestive of parkinsonism, cerebellar incoordination, or peripheral neuropathy. Patients may not be aware that their symptoms are exacerbated by walking

Vertigo

- Vertigo is a symptom of illusory movement
- Vertigo is the predominant symptom that arises from an acute asymmetry of the vestibular system
- Vertigo is a symptom, not a diagnosis
- The vestibular system includes the vestibular apparatus in the inner ear, the vestibular nerve and nucleus within the medulla, as well as connections to and from the vestibular portions of the cerebellum
- Our first goal is to establish whether there is true vertigo or other causes of dizziness

Clinical features of common causes of vertigo

	Time Course	Clinical Setting	Nystagmus	Other diagnostics
Benign paroxysmal positional vertigo	Recurrent, brief seconds	Predictable movements of the head precipitate symptoms	Always peripheral	Dix-Hallpike maneuver with classic findings
Meniere Disease	Recurrent episodes	Viral syndrome precedes vertigo	Always peripheral	Head impulse test abnormal, hearing loss and or tinnitus
Vestibular Migraine	Recurrent episodes lasting minutes to hours	History of migraine	Peripheral characteristics	Between episodes all tests are normal
Vertebrobasilar TIA	Single or recurrent episode lasting minutes to hours	Older patient, vascular risk factors, or cervical trauma	Central characteristics	MRI/MRA may show a vascular lesion or dissection
Vestibular neuritis	Single episode, lasting days	Viral syndrome precedes vertigo	Peripheral	No brainstem symptoms
Cerebellar infarction or hemorrhage	SUDDEN ONSET	Vascular risk factors, hypertension, cocaine	Central	Urgent MRI/CT

How to distinguish peripheral vs. central nystagmus

	Peripheral	Central
Nystagmus		
Features (direction and type)	Unidirectional, fast component toward the normal ear Horizontal with torsional component, never purely torsional or vertical	Gaze-evoked direction changing nystagmus Remember that purely vertical or purely torsional is a central sign
Postural Instability	Unidirectional instability, walking preserved	Severe instability, patient often falls when walking
Deafness or tinnitus	May be present	Mostly absent
Other neurological signs/symptoms	Absent	Often present (diplopia, ataxia, focal weakness, dysarthria)

What is the difference between Dix-Hallpike and Epley maneuver?

- Dix-Hallpike : Positional maneuvers designed to reproduce vertigo and elicit nystagmus in patients with a history of positional dizziness. These maneuvers are most useful in patients who do not have symptoms or nystagmus at rest. The Dix-Hallpike maneuver tests for canalithiasis of the posterior semicircular canal, which is the most common cause of BPPV
- Epley: A repositioning maneuver to encourage the debris to migrate toward the common crus of the anterior and posterior canals and exit into the utricular cavity

- https://www.youtube.com/watch?v=KLt2LtISPmQ

Home treatment to offer a patient with benign positional vertigo

- Brandt-Daroff Maneuver which can performed at home by a patient
- It is useful when one is uncertain as to the side of the canalithiasis

84-year-old woman with a history of hypertension presented with sudden onset nausea.
She complained of lightheadedness, and she had to hold on to the wall to prevent herself from falling.
She noted that her dizziness got worse with positional change of her head.
There was no nystagmus on examination. There was only nausea when she was asked to walk.


Questions?