Meniere’s Disease, Vestibular Migraine & Persistent Postural-Perceptual Dizziness (PPPD)

Do these exit together?
Are they confused?

International Classification of Vestibular Disorders

☐ These three disorders have been defined by Barany Society Consensus documents
☐ Part of the International Classification of Vestibular Disorder by Barany
☐ For Meniere’s Disease this committee was comprised of: Japan Society for Equilibrium Research; AAO-HNS; European Academy of Otology and Neurotology; Korean Balance Society
Case - 49 yr Male

- Began 5 years prior with fluctuant and progressive loss of hearing on the left with tinnitus and aural fullness.
- 1 year after the onset of the auditory symptoms he began with spontaneous spells of vertigo associated with nausea and vomiting lasting 3-8 hours. By day 2 after an event he returned to a fully normal baseline other than auditory symptom.
- The spells of vertigo had been only 2-3 per year until the last 1.5 years and had increased to about 1 per month.
Case - 49 yr Male

- He denied any headache or migraine symptoms with the spells
- Increased tinnitus and reduction in hearing heralded the vertigo events with increased aural fullness
- Controlled spells with Meclizine at first now using Valium with his low sodium diet and diuretic
- Diagnosed with Meniere’s syndrome on the left – temporized with steroid injection in the left – eventually had two injections of Gentamicin – 2 years out and spells have stopped and hearing stabilized.

Meniere’s Disease

- 1995 AAO criteria
  - At least 2 spontaneous spells of vertigo lasting 20 minutes and no longer than 24 hours
  - Documented change in hearing sensitivity
  - Travelers that increase the argument but not required:
    » Aural fullness
    » Tinnitus
- Diagnosis is primarily by history, audiogram and MRI to clear the CPA
- Pathogenesis is unknown and could likely be multifactorial given studies showing that virtually all treatments improve between 80-85% of patients – this is natural history
Meniere’s Disease

- History
  - Can develop Tumarkin Crisis Events – drop attacks no LOC
- Typical Lab findings (including hearing test)
  - Nothing specific – peripheral no CNS
- Prognosis – excellent control with Gent / surg otherwise time typically helps
- Lesion site – Labyrinthine

- Barany Society Consensus document; Japan Society for Equilibrium Research; AAO-HNS; European Academy of Otology and Neurotology; Korean Balance Society
- Part of the International Classification of Vestibular Disorder by Barany

Meniere’s Disease Is

- Multifactorial disorder – combined effect of genetics and environmental factors engender disease onset
- The disease is associated with accumulation of endolymph in the cochlear duct and vestibular organs in histopathological studies
- Endolymphatic hydrops per se does not explain all clinical features – frequency of attacks and progression of hearing loss
Meniere’s Disease Is (2)

- A clinical syndrome of episodes of spontaneous vertigo usually associated with unilateral fluctuant SN hearing loss
- Episodes of vertigo usually more common in the first years of the disease
- Cochlear symptoms can be present between the vertigo spells
- Hearing loss and vestibular hypofunction show great variability resulting in phenotyping of MD difficult

Meniere’s Disease

AKA Meniere’s syndrome And Endolymphatic Hydrops

- Definite MD
  - Two or more spontaneous episodes of vertigo each 20 minutes to 12 hours
  - Audiometrically documented low-to medium-frequency hearing loss in the affected ear on at least one occasion before, during OR after one of the episodes of vertigo
  - Fluctuating aural symptoms (hearing, tinnitus or aural fullness) in the affected ear
  - Not better accounted for by other vestibular diagnosis
Meniere’s Disease

- Probable MD
  - Two or more episodes of vertigo or dizziness, each 20 minutes to 24 hours
  - Fluctuating aural symptoms (hearing, tinnitus or fullness) in the reported ear
  - Not better accounted for by another vestibular diagnosis

MD dx by MRI

- Given the strong association between endolymphatic hydrops and MD can this be diagnosed with MRI
- Lopez-Escamez, J.A. JVR 2019 --- Systematic review of MRI for dx of MD
- Consistently the studies identified the saccule and saccular hydrops as the most involved structure
- Sx started too early for consistent hydrops and the reproducibility of the hydrops protocols is questionable thus limiting the expansion of the techniques into routine clinical practice --- shows promise but not now
Meniere’s Treatment Options

- Conservative – 60-70% long term (2-5 years) success
  - Low Sodium Diet – based on endo hydrops as cause for symptoms
  - Steroid injection – reduction in inflammation
  - Endolymphatic sac decompression / shunt - based on endo hydrops as cause for symptoms
  - Meniett devise - based on endo hydrops as cause for symptoms

- Aggressive – 95+ long term (2-5 years) success
  - These assume that the lesion is in the Labyrinth
  - Gentamicin injections – titrate to effect – used to preserve hearing
  - Vestibular Nerve Section – used to preserve hearing
  - Labyrinthectomy – destroys all vestibular and hearing function

Use of Vestibular and Balance Therapy

- Between spells if symptoms of unsteadiness or head movement provoked symptoms are present
  - Therapy can help the elimination of these symptoms
  - All need to be aware that even if successful in reducing or eliminating the symptoms between spontaneous vertigo spells all resets with each of the spells and therapy needs to start again.
  - Therapy will not prevent the spontaneous spells

- After aggressive treatment – now you have a stable unilateral hypofunction
  - Patient needs to understand while the aggressive treatments may bring MD to a stop they are trading spontaneous spells for head movement provoked symptoms and unsteadiness
Intratympanic methylprednisolone versus gentamicin in patients with unilateral Ménière’s disease: a randomised, double-blind, comparative effectiveness trial

Mitesh Patel*, Kiran Agarwal†, Odeer Arshad, Mohamed Hariri, Peter Rea, Barry M Seemungal, John F Golding, Jonny P Harcourt, Adolfo M Bronstein

www.thelancet.com Published online November 16, 2016

30 patients in each group – Methylprednisolone and Gentamicin. Frequency of vertigo events for 6 months prior to injections and then 6 months after injections. Each group were given two injections each 2 weeks apart. All followed for up to two years with the final outcome measure taken at 18-24 months. No difference was found in the effectiveness of the steroid versus the gentamicin.

Barany Meeting 2018

- Bronstein et al: Follow-up of a randomized, double-blind, trial of methylprednisolone vs gentamicin in unilateral MD

- Of the original 60 in the study 1 dropped out, 1 lost to follow up, 2 died of unrelated causes --- total of 46 responded to the survey – 22 with methylprednisolone 24 with gentamicin --- 8 had had further injection treatment due to recurrent symptoms

- # of vertigo attacks in the previous 6 months: ave 1 (SD 2.4) gentamicin, ave .8 (SD 2.6) methylprednisolone
Case - 28 yr Female

- 3 year history of increasing frequency of spontaneous events of vertigo
- Duration of 1-4 hours – started at 4 per year now 1-2 per month
- Between the events she returns to her normal baseline
- Denies any hearing loss but reports tinnitus bilaterally with each of the vertigo events.
- With the events she reports > than 70% occurrence of focal headache with photophobia, phonophobia & osmophobia.

Case - 28 yr Female

- PMH – negative other that onset of headaches well diagnosed as migraine sufferer starting about 13 years old.
- Headaches are 1-2 per week. She uses only Tylenol to control the headaches
- Full work up including VNG, RC, VEMPs, Postural control, Cardiac and Neurology – negative --- ENT tentative diagnosis of developing Meniere’s
- Final Diagnosis Vestibular Migraine– prophylactic medication and diet changes controlled her headaches and her vertigo events stopped
Migraine Events

- Prevalence - Study with 20,000 persons- HA at least once per year
  - 17.6% Adult females
  - 5.7% Adult males
  - 4% children (20% of migraineurs start before age 10, 45% before 20 yrs; risk is 70% if both parents have migraine and 45% if one parent affected)

- 18% HA one or more per month
- Highest prevalence 35-45 years -- 12-30 yrs
- Lowest prevalence > 50 years

- Of 20,000 patients meeting criteria for Dx of migraine only 29% males and 41% females aware.

Migraine Events

- Migraines are Neurological events
- Most common symptom is headache
- Events can range from no pain to severe pain with permanent ischemic damage
- Most common non-pain form of a migraine is visual, but any aura symptom can occur in the absence of pain, including dizziness
International Classification of Headache Disorders, 2nd ed (ICHD-II, 2004)

- Migraine without aura
- Migraine with aura
  - Typical aura with migraine headache
  - Typical aura with non-migraine headache
  - Typical aura without headache
- Familial hemiplegic migraine (FHM)
- Sporadic hemiplegic migraine
- Basilar-type migraine
- Childhood periodic syndromes that are commonly precursors of migraine
  - Cyclical vomiting
  - Abdominal migraine
- Benign paroxysmal vertigo of childhood

The International Classification of Headache Disorders 3rd edition 2018 1st Edition of Cephalalgia
## International Classification of Headache Disorders, 3rd ed (ICHD-III, 2018)

- **1. Migraine**
  - 1.1 Migraine without aura
  - 1.2 Migraine with aura
    - 1.2.2 Migraine with brainstem aura (old Basilar Migraine)
    - 1.2.3 Hemiplegic migraine
    - 1.2.4 Retinal migraine
- **1.3 Chronic migraine
- 1.4 Complications of migraine
- **1.6 Episodic syndromes that may be associated with migraine**
  - 1.6.1 Recurrent gastrointestinal disturbance
  - 1.6.2 Benign paroxysmal vertigo
- **1.5 Probable migraine**
  - 1.5.1 Probable migraine without aura
  - 1.5.2 Probable migraine with aura
  - 1.6.3 Benign paroxysmal torticollis
- **Appendix**
  - A1.6 Episodic Syndromes that may be associated with migraine
    - A1.6.6 Vestibular Migraine

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## Diagnostic criteria: Migraine without Aura

- At least five attacks\(^1\) fulfilling criteria B-D
- Headache attacks lasting 4-72 hr (untreated or unsuccessfully treated)\(^2,3\)
- Headache has at least two of the following four characteristics:
  - unilateral location
  - pulsating quality
  - moderate or severe pain intensity
  - aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)
- During headache at least one of the following:
  - nausea and/or vomiting
  - photophobia and phonophobia
- Not better accounted for by another ICHD-3 diagnosis.
Diagnosis of migraine headache

- Diagnosis is based on history (ICHD-III criteria)
- No tests for migraine
- Physical examination and imaging are used to exclude other causes of headache (e.g., tumor, hemorrhage)

Clinical clues that raise suspicion for migraine
- Young/middle age, female
- History of motion sickness and / or sleep walking especially pre-puberty
- Family history of migraine or vertigo
- Hormonal and / or Migraine triggers

Dietary triggers - Partial list – Those with casual exposure several times per month

- Alcohol with color
- MSG
- Chocolate
- Caffeine
- Processed (Packaged) meats
- Processed (Packaged) Cheese
- Artificial sweeteners
Vestibular migraine: Diagnostic criteria

Consensus document of the Bárány Society and the International Headache Society

Thomas Lempert1,*, Jes Olesen2, Joseph Furrman3, John Waterston4, Barry Seemungal4, John Carey5, Alexander Bisdorf5, Maurizio Versino6, Stefan Evers7 and David Newman-Tasker8

1Department of Neurology, Schlusspark-Klinik, Berlin, Germany
2Danish Headache Center and Department of Neurology, University of Copenhagen, Copenhagen, Denmark
3Departments of Otolaryngology and Neurology, University of Pittsburgh, Pittsburgh, PA, USA
4Department of Neurology and Monash University Department of Medicine, Alfred Hospital, Melbourne, Australia
5Department of Clinical Neuroscience, Charing Cross Hospital, London, UK
6Department of Otolaryngology, Head and Neck Surgery, Johns Hopkins University School of Medicine, Baltimore, MD, USA
7Department of Neurology, Centre Hospitalier Emile Mayrisch, Esch-sur-Alzette, Luxembourg
8Department of Neurological Sciences University of Pavia, HSC and BCC National Neurological Institute IRCCS C. Mondino Foundation, Pavia, Lombardy, Italy

From the ICHD –III – Diagnostic Criteria VM

- A- At least five episodes fulfilling criteria C and D
- B- A current or past history of 1.1 Migraine without aura or 1.2 Migraine with aura1
- C- Vestibular symptoms2 of moderate or severe intensity3, lasting between 5 minutes and 72 hours4
- D- At least half of episodes are associated with at least one of the following three migrainous features5:
  - headache with at least two of the following four characteristics:
    - a) unilateral location
    - b) pulsating quality
    - c) moderate or severe intensity
    - d) aggravation by routine physical activity
    - photophobia and phonophobia6
    - visual aura7
- Not better accounted for by another ICHD-3 diagnosis or by another vestibular disorder8.
From the ICHD –III – Diagnostic Criteria

- Vestibular symptoms, as defined by the Bárány Society’s Classification of Vestibular Symptoms and qualifying for a diagnosis of A1.6.6 Vestibular migraine, include:
  - a) spontaneous vertigo:
    - internal vertigo (a false sensation of self-motion);
    - external vertigo (a false sensation that the visual surround is spinning or flowing);
  - b) positional vertigo, occurring after a change of head position;
  - c) visually-induced vertigo, triggered by a complex or large moving visual stimulus;
  - d) head motion-induced vertigo, occurring during head motion;
  - e) head motion-induced dizziness with nausea (dizziness is characterized by a sensation of disturbed spatial orientation; other forms of dizziness are currently not included in the classification of vestibular migraine).

- Vestibular symptoms are rated moderate when they interfere with but do not prevent daily activities and severe when daily activities cannot be continued.

- Duration of episodes is highly variable. About 30% of patients have episodes lasting minutes, 30% have attacks for hours and another 30% have attacks over several days. The remaining 10% have attacks lasting seconds only, which tend to occur repeatedly during head motion, visual stimulation or after changes of head position. In these patients, episode duration is defined as the total period during which short attacks recur. At the other end of the spectrum, there are patients who may take 4 weeks to recover fully from an episode. However, the core episode rarely exceeds 72 hours.

- One symptom is sufficient during a single episode. Different symptoms may occur during different episodes. Associated symptoms may occur before, during or after the vestibular symptoms.

Migraine prevention - Behavioral
(Tusa, 1994)

- Stress reduction
  - Aerobic exercise - for balance disorders Tai-Chi
  - Regular meals
  - Stable sleep schedule

- Avoid nicotine

- Hormone replacement (variable response)

- Migraine diet
Migraine - Pharmacological Rx

- Prophylactic agents
  - Tricyclic Antidepressants (nortriptyline, amitriptyline, others)
  - Beta Blockers (propranolol, others)
  - Ca++ Channel Blockers (verapamil, others)
  - Antiepileptic Drugs (topiramate, divalproex, others)
  - Special situations
    » Acetazolamide – for channelopathies associated with migraine [e.g., familial episodic ataxia II, familial hemiplegic migraine, spinal cerebellar ataxia 6, which all have calcium channel gene mutations on chromosome 19]
  - OTCs (aspirin)
  - Supplements (riboflavin, magnesium oxide)
  - Other classes (little research support)
    » SSRIs – largely negative results
    » SNRIs – some positive data, but may also worsen headache in 10% of patients

Migraine - Pharmacological Rx - New

- A protein call calcitonin gene-related peptide (CGRP) is released during a migraine attack
- 2018 FDA approved 3 similar medications that inhibit this protein
- Each is injected under the skin monthly / quarterly
- Erenumab (Aimovig), fremanezumab (Ajovy), galcanezumab (Emgality) – are for persons with frequent migraine events and limited treatment option
- Studies show 50% of persons in trials have a 40-50% reduction in the monthly frequency of headaches
- Important to remember this only has an effect on one of several complex pathways that produce migraines
Migraine - Pharmacological Rx

- Abortive agents
  - Triptans (sumatriptan, rizatriptan, others)
  - NSAIDs (ibuprofen, ketoprofen, naproxen, others)
  - Combination products
    » Caffeine (Cafergot, Excedrin)
    » Isometheptene (Midrin)
  - Older anti-emetics (prochlorperazine)
  
- Not preferred (but still used)
  » Narcotics
  » Barbiturates (Fiorinal)

Vertigo, migraine and vestibular migraine

- General population
  - German National Health Survey (Neuhauser et al 2006)
- Life time prevalence of migraine ~16%, vertigo ~7%
- Concurrence of the two by chance ~ 1.1%
- Actual concurrence ~ 3.2%
Migraine Events & Dizziness

- Clinical populations
  - In migraineurs:
    » the prevalence of non-specific dizziness is up to 54% versus 10-15% in the general population (>3x).
  - In patients with dizziness:
    » the prevalence of migraines is up to 38% compared to 16% in the general population (2.4x).
  - In patients with Meniere’s
    » The prevalence of migraine is 56% compared to 16% in the general population (3.5x).

Treatment for VM

- One controlled trial to guide medication options
  - One prophylactic trial
  - No abortive trials
  - Expert consensus: treat as other migraine

- Controversy regarding vestibular habituation
  - Medication first (no vestibular rehab to start)
  - Gentle, but persistent habituation (with or without meds)
  - Especially for those with head or visual motion provoked symptoms
Is there a drug with effectiveness VM?

Propranolol and Venlafaxine for Vestibular Migraine Prophylaxis: A Randomized Controlled Trial

Mehti Salvis, MD; Turgut Yuce, MD; Hurtan Acar, MD; Abdullah Karatas, MD; R. Murat Acikalin, MD

Propranolol vs Venlafaxine

- Finding suggest both drugs are equally effective in the prophylaxis treatment of Vestibular migraines

- Venlafaxine performed better at control of depression symptoms
Vestibular Migraine and Meniere’s

*Mutually Exclusive??*

Prosper Meniere in 1861; Radtke et. al Neurology 59, 2002

<table>
<thead>
<tr>
<th>Migraine</th>
<th>Meniere’s</th>
</tr>
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<tbody>
<tr>
<td>- Spontaneous Vertigo</td>
<td>- Spontaneous Vertigo</td>
</tr>
<tr>
<td>- Unilateral tinnitus and fluctuant hearing</td>
<td>- Unilateral tinnitus and fluctuant hearing</td>
</tr>
<tr>
<td>- Unlikely permanent progressive hearing loss</td>
<td>- Likely permanent progressive hearing loss</td>
</tr>
<tr>
<td>- Mild ENG findings including mild asymmetry</td>
<td>- Mild to significant ENG findings - mild to significant asymmetry</td>
</tr>
<tr>
<td>- Duration of vertigo seconds to days</td>
<td>- Duration &gt;20 min &lt;24 hours</td>
</tr>
</tbody>
</table>

When MD and VM exist together

- It may be difficult to sort which disorder is the primary source of the symptoms
- You can treat VM aggressively without burning any bridges
- Aggressive treatment of MD causes further damage
- Start with conservative measures for MD and aggressive VM treatment – If headaches come under control than the spells left are assumed to be MD
Persistent Postural-Perceived Dizziness (PPPD)
Chronic Subjective Dizziness Syndrome (CSD)

Case Example - 47 yo WF

- Sudden onset of vertigo awakening her from sleep 1.5 years ago.
- The vertigo with nausea and vomiting was constant independent of position but worsened with head movement.
- Symptoms continued in a constant manner for 2 days – was hospitalized and medication was of assistance in blunting the intensity of the symptoms.
- By day 3 if she was holding still the vertigo was absent but she continued with general unsteadiness and mild feeling of vague self-motion.
Case Example - 47 yo WF

- Work up in the hospital including non-contrasted MRI of the brain was all normal
- Discharged day 3 to follow up with primary care physician – diagnosis of possible inner ear virus – sent home on Meclizine
- She denied any change in hearing and reported that the symptoms of head movement provoked vertigo finally stopped after about 1 week but she was left with a sensation of vague self movement and unsteadiness
- She continued to use Meclizine but that was just causing drowsiness
- She reports that the onset of the symptoms provoked significant fear reaction

Over the next month symptoms seem to improve very slowly but did not resolve

- She was tried on Valium, Xanax and Zoloft without any help but was on the medications only for 1-2 weeks each
- After about 6-8 weeks the symptoms seem to plateau with 24/7 vague sensation of self motion, unsteadiness improved with sitting and lying worse when standing and walking
- Symptoms were exacerbated with head movements and she began to notice that visual motion, visual complexity and visual patterns would also worsen the symptoms
- PMH was negative other than on and off mild anxiety difficulties in the past
Case Example - 47 yo WF

- At about the 6 week point she was evaluated by ENT with normal hearing and vestibular testing showing a right mild (45% by caloric water irrigations) hypofunction with no ongoing nystagmus
- She was diagnosed with Vestibular Neuronitis and recommend to begin VBRT
- After 3 months of vestibular rehab she reports that the head movement sensitivity did decrease but she continued with the 24 / 7 vague movement sensation and unsteadiness and the visual sensitivity to motion, complexity and patterns
- She was then seen by a variety of specialists (neurology, cardiology, endocrinology, ophthalmology) tried on a variety of medication over the next year – no firm diagnosis – meds no help and tried VBRT again – no help

Case Example - 47 yo WF

- Was seen by a Neurotologist and was given the diagnosis of Vestibular Neuronitis with failure to compensate – REC either vestibular nerve section OR Gentamicin injections in the right
- Referred to Mayo for second opinion
  - Full laboratory work showed a right hypofunction with horizontal, anterior canal and utricular / saccular involvement in a physiologically compensated state but with functional difficulty with postural control yet completely normal gait – pattern suggestive of anxiety reaction to testing
  - Hospital Anxiety Depression Scale (HADS) was highly positive for anxiety and negative for depression
Case Example - 47 yo WF

- Final Diagnosis – Right vestibular neuronitis cause for initial symptoms but the perpetuation of symptoms and development of the visual sensitivities was suggestive of Persistent Postural-Perceived Dizziness (Chronic Subjective Dizziness Syndrome)

Diagnostic Criteria for PPPD

A. Dizziness, unsteadiness, or both are present on most days for 3 months or more.\(^1,2\)

- Symptoms are persistent, but wax and wane.
- Symptoms tend to increase as the day progresses, but may not be active throughout the entire day.
- Momentary flares may occur spontaneously or with sudden movements.
  » 1. present for more than 15 of every 30 days. Most, every day or nearly every day.
  » 2. Symptoms need not be continuous, but must be present for prolonged (hours-long) periods throughout the day. Momentary symptoms alone do not fulfill this criterion.
Diagnostic Criteria for PPPD

B. Symptoms are present without specific provocation, but are exacerbated by:
   - Upright posture,
   - Active or passive motion without regard to direction or position, and
   - Exposure to moving visual stimuli or complex visual patterns.

   » 3. The three provocative factors of criterion B must be discernable in the clinical history, but do not have to be equally troublesome.

Diagnostic Criteria for PPPD

C. The disorder begins shortly after an event that causes acute vestibular symptoms or problems with balance.
   - Precipitating events include acute or episodic vestibular syndromes, other acute neurologic or medical illnesses, and acute or episodic psychological distress.
   - Symptoms usually settle into the pattern of criterion A as precipitants resolve, but may occur intermittently at first, and then consolidate into a persistent course.
   - A slow, gradual onset is uncommon.

   » common events: acute / episodic peripheral / central vestibular, attacks of vestibular migraine, panic attacks / generalized anxiety, concussion / whiplash injuries, orthostatic intolerance.
Diagnostic Criteria for PPPD

- These three factors may not be equally provocative.
- Symptoms cause significant distress or functional impairment.
- Symptoms are not better attributed to another disease or disorder.\(^5\)

\(^5\) PPPD may co-exist with other diseases or disorders. Evidence of another active illness does not necessarily exclude a diagnosis of PPPD.

Posturographic profile of patients with persistent postural-perceptual dizziness on the sensory organization test

Eliane Söhsten\(^a,4\), Roseli S.M. Bittar\(^b\) and Jeffrey P. Staab\(^c\)

\(^a\)Department of Otorhinolaryngology, Division of Oto-neurology, Hospital das Clínicas, Medical School, Universidade de São Paulo (USP), São Paulo, SP, Brazil

\(^b\)Department of Otorhinolaryngology, Division of Oto-neurology, Medical School, Universidade de São Paulo (USP), São Paulo, SP, Brazil

\(^c\)Department of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA
SOT patterns in PPPD

- Purpose of the work:
  - Expand on the number of subjects for comparison
  - Use age as a stratifying variable
  - Investigate the combined effect of vestibular hypofunction + PPPD
  - Can the profile be used as more than a descriptor – i.e. used to identify PPPD?

- Methods
  - Retrospective study of consecutive patients seen at Mayo Rochester OCT 2016 – APR 2017 in order to find the following groups of patient – total N=221
  - Patients were divided into groups by diagnostic category
    » Dx Cat 1 = PPPD (the final and only diagnosis for the patient) – N=96
    » Dx Cat 2 = > 25% unilateral vestibular hypofunction without any central system indications and no other secondary diagnosis – N=72
    » Dx Cat 3 = > 25% unilateral vestibular hypofunction AND PPPD – N=53
  - Patients were divided into groups by age category
    » Grp 1 = 20-59 years of age – N=108
    » Grp 2 = 60-69 years of age – N=50
    » Grp 3 = 70 and above – N=63

Study repeated with 96 PPPD, 72 UVH and 53 PPPD+UVH divided by age
SOT patterns in PPPD

Discussion

- There is a pattern for the SOT in patients with PPPD and PPPD+UVH that shows poorer performance on the easiest conditions (1-3) and improvement at the more difficult condition to equal a UVH patient alone.
- The larger numbers help to confirm this as a valid pattern.
- As the patients age above 69 it is age that produces significant difference not the diagnostic category.
- While demonstrating a pattern that expands the overall profile for the PPPD patient it is not sufficiently effective in identification of the PPPD to be used as a bio-marker for the disorder.
- Adds evidence to the concept that this pattern is not Aphysiologic - There is a physiologic explanation – anxiety reaction

Interaction between anxiety and vestibular symptoms has been thought to be either one effects the other. This paper presents the view that Threat assessment is an inherent part of spatial perception and locomotion in both well and ill states – not a reaction of the vestibular system to an exogenous stimulus. Anxiety is not the cause or the consequence of spatial perception or locomotion disturbance but one manifestation of the threat perception system which is an integral part of mobility.
## Threat and Balance Function

<table>
<thead>
<tr>
<th>Challenge</th>
<th>Effect</th>
</tr>
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<tbody>
<tr>
<td>Fall from bed or height</td>
<td>Slower gait, shortened stride, co-contraction of tibialis anterior with gastrocnemius</td>
</tr>
<tr>
<td>Walking on a tilted platform</td>
<td>Slower, shorter gait, increased effort</td>
</tr>
<tr>
<td>Walking on a windy day</td>
<td>Slower, shorter gait, increased effort</td>
</tr>
<tr>
<td>Walking on a narrow walkway</td>
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Adkin, et al., 2002; Brown, et al., 2002; Ohno, et al., 2004; Carpenter, et al., 2004; Viaud-Delmon, et al., 2000

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## Threat Assessment

- Threat Assessment – especially misinterpretations of the risk of a particular threat have been shown to be part of the mechanism behind the development of:
  - Fear-of-Falling – the reactions to this in the form of slower gait, shortened stride length, co-contraction of tibialis anterior with gastrocnemius actually increase the actual risk for falls.
    Vestibular symptoms increased by factor of > 2 the report of fear of falls in older adults compared to those of the same age without vestibular symptoms.
  - Primary and secondary anxiety disorders that may be the cause or consequence of the development of vestibular symptoms.
  - PPPD
What Lasts?

*VN, BPPV, Dizziness & Anxiety in 43 Patients*

- Prospective study of physical outcomes

Acute VN or BPPV (N=43)

- Recovered (N=30)
- BFTs
  - Compensated (N=9)
  - Non-compensated (N=4)

Chronic dizziness (N=13)

Fear of body sensations

$R^2 = 0.91$

3 months


This tells it all
This tells it better

Even though the review was of a small # of articles (15) selected that addressed the full disorder and treatment—they conclude that this is currently a clinical diagnosis with no tests for PPPD and in general the treatment is a combination of Patient Ed, Vestibular Rehab therapy, SSRI/SNRI, and CBT. Their view of the process in the development of PPPD is shown next.
Neuroticism Modulates Brain Visuo-Vestibular and Anxiety Systems During a Virtual Rollercoaster Task

Roberta Riccelli,1 Iole Indovina,2,3 Jeffrey P. Staab,4 Salvatore Nigro,5 Antonio Augimeri,7 Francesco Lacquaniti,2,5,6 and Luca Passamonti5,7

1Department of Medical and Surgical Sciences, University “Magna Gracia,” Catanzaro, Italy
2Laboratory of Neuromotor Physiology, IRCCS Santa Lucia Foundation, Rome, 00179, Italy
3Centre of Space Biomedicine, University of Rome Tor Vergata, Rome, 00173, Italy
4Department of Psychiatry and Psychology, Mayo Clinic, Rochester, Minnesota
5Institute of Brain Imaging and Molecular Physiology, National Research Council, Catanzaro, 88100, Italy
6Department of Systems Medicine, University of Rome Tor Vergata, Rome, 00133, Italy
7Department of Clinical Neurosciences, University of Cambridge, Cambridge, United Kingdom
Personality Traits and Anxiety

- fMRI was used to investigate the effects of neuroticism and introversion – key traits related to anxiety with presentation of virtual reality motion
- Comparing the horizontal and vertical motions a positive correlation was seen between the level of neuroticism and the left Parieto-insular vestibular cortex and the right amygdala in vertical movements
- Patients with PPPD have been shown to have higher trait anxiety, neuroticism and introversion compared to those without indications of PPPD.
Barany 2018

  - 10 Patients with visually induced dizziness (VID) and 10 age and gender matched controls underwent function MRI in a resting state.
  - The findings showed the VID patients had stronger connectivity within visual areas and weaker connectivity in the primary vestibular area. The findings are in line with the behavioral profile of the VID patients, i.e. increased reliance on visual cues for spatial perception.
  - This could well apply to our PPPD patients.

PPPD without a Bio-Marker

- DRD2 is a gene that encodes the protein that is responsible for a dopamine receptor.
- Polymorphic alleles of this gene are suggested to be the site of psychotropic medications and have been implicated to be involved with many disorder effected by these medications.
- In a study by Cui et al 2019, JVR – suggests an association between the DRD2 Taq IA gene polymorphism and PPPD – one allele could be the susceptibility polymorphism for PPPD and that the alternative allele pair having a protector role.
- Much larger studies are needed to confirm this.
Treatment Options

- There are no large-scale controlled studies of treatments for PPPD.
- Smaller scale studies support 3 interventions
  - Antidepressant medications
  - Vestibular & balance rehabilitation therapy
  - Cognitive behavioral psychotherapy (this has been shown less useful than originally expected)

Medications used in the US

<table>
<thead>
<tr>
<th>Medication</th>
<th>Initial Therapy Daily Dose (mg)</th>
<th>Titration (2 wk) Daily Dose (mg)</th>
<th>Titration (4-6 wk) Daily Dose (mg)</th>
<th>Therapeutic Range Daily Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>5–10</td>
<td>10–20</td>
<td>20–40</td>
<td>20–60</td>
</tr>
<tr>
<td>Sertraline</td>
<td>12.5–25</td>
<td>25–50</td>
<td>50–100</td>
<td>50–150</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>5–10</td>
<td>10–20</td>
<td>20–40</td>
<td>20–60</td>
</tr>
<tr>
<td>Citalopram</td>
<td>5–10</td>
<td>10–20</td>
<td>20–40</td>
<td>20–60</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>2.5–5</td>
<td>5–10</td>
<td>10–20</td>
<td>10–20</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>25</td>
<td>25–50 twice daily</td>
<td>50–100 twice daily</td>
<td>50–100 twice daily</td>
</tr>
</tbody>
</table>

| Serotonin and norepinephrine reuptake inhibitors | | | | |
| Venlafaxine | 25–37.5 | 37.5–50 | 75–150 | 75–225 |
| Milnacipran | 12.5–25 twice daily | 25–50 twice daily | 50 twice daily | 50–75 twice daily |
| Duloxetine | 20–30 | 40–60 | 40–60 | 40–60 |
| Desvenlafaxine | ... | ... | ... | ... |

* The higher initial dose can be prescribed for most patients to start treatment. Those who do not tolerate that dose and those who prefer to start treatment more cautiously may be prescribed the lower initial dose.
* Fluvoxamine is typically started at 25 mg once daily for 1 to 2 weeks and then increased to twice-daily dosing thereafter.
* Milnacipran is typically started at 12.5 mg once daily for 2 to 3 days and then increased to twice-daily dosing thereafter.
* Duloxetine has not been studied in clinical trials for chronic subjective dizziness (CSD), but it is used clinically.
* Desvenlafaxine has not been studied in clinical trials for CSD. It is available only in 50-mg and 100-mg capsules, which does not permit gradual titration; therefore, it is not used commonly in clinical practice for patients with CSD.
Treatment – VBRT

- Enhance central vestibular compensation
  - First several weeks after illness onset
- Provide behavioral habituation exercises for reversing the sensitivities that have developed to the visual stimuli and head movements.
  - Even after months to years of symptoms
  - Outcomes similar for patients with and without identifiable neurotologic pathology.
  - Stepwise approach
    » patience, persistence, creativity
- Reduce anxiety and depression

Jacob, et al., J Anxiety Disord, 2001; Johansson et al., Oto-HNS, 2001; Pavlou, et al., J Neurol 2004; Thompson et al, 2015 to be submitted

Treatment -- Psychotherapy

- Cognitive-behavioral therapy
  » Reframe catastrophic ideas (I’ll crash the car.”)
  » Counteract avoidance
  » Short-term benefits may not be sustained

Holmberg et al., J Neurol, 2006
Case Example - 47 yo WF

**Medications**
- Started on venlafaxine XR (Effexor XR) at low dose -- 37.5 mg/d, increased to 75mg/d
- Low dose clonazepam 0.5mg twice daily.

**VBRT**
- Habituation therapy to reduce her sensitivity to head and visual motion and complex visual environments.
- Taught home CRP maneuvers to manage future recurrences of BPPV.

**CBT**
- Started cognitive behavior therapy near her home.

**Outcome**
- **First return visit (6 weeks)**
  - Function was improving, minimal anxiety
    » Back to shopping mall for short intervals
- **Second return visit (12 weeks)**
  - Cancelled
    » Called to say she was doing well
Outcomes to Date

- Studies conducted to date with medications, CBT, psychoeducation and VBRT show a 78% reduction in dizziness sustainable for 1-3 year [Nada, Ibraheem, & Hassaan, 2019; Schaaf & Hesse, 2015]

- Overall, the use of VBRT is being shown to be a vital component in the treatment of PPPD [Dieterich & Staab, 2017; Dieterich et al., 2016; Popkirov et al., 2018; Seemungal & Passamonti, 2018]

Conclusions

- PPPD (CSD)
  - Common syndrome of persistent dizziness and hypersensitivity to motion stimuli
  - Differential diagnosis
    » Anxiety, migraine, TBI, dysautonomia, dysrhythmia
  - Easily identifiable, stable, reliable concept
    » User-friendly for clinicians
    » Acceptable to patients
  - Causes of PPPD can be treated
    » SSRIs, VBRT, Cognitive therapy
    » Selected medical interventions
Illness Profiles: Vertigo, Unsteadiness, Dizziness

- Ménière’s
- BPPV
- Migraine
- 3PD

Comorbidity affects presentation

- Hours-long vertigo attacks with/without aural symptoms
  - VM and Meniere’s
- Vertigo attacks lasting seconds to days
  - VM alone
  - VM and Meniere’s
  - VM and BPPV
- Episodic vertigo and chronic dizziness
  - VM and CSD
Comorbidity of migraine and other neurotologic conditions in tertiary patients with dizziness

706 diagnoses in 489 patients

- Ménière's
- BPPV
- Peripheral
- Central
- CSD
- Migraine


Vestibular Migraine and Persistent Postural-Perceptual Dizziness:
Pharmacologic Dissection Trial using Verapamil and Sertraline

Do vestibular migraines cause chronic / persistent symptoms?
Hypothesis: VM+3PD

- Probable VM
- Headache with verapamil probe
- 3PD with sertraline probe

Hypothesis: Chronic VM

- Headaches & Dizziness
- In both headache & dizziness with verapamil
- No impact on headache or dizziness with sertraline
Conclusions:

- This is further evidence that chronic vestibular symptoms in patients with VM are due to co-existing PPPD, not a chronic form of VM.

- When patients meet criteria for VM together with meeting the criteria for PPPD it is necessary to treat Migraine for control of VM BUT this is not sufficient to treat the chronic dizziness – The 3 PD must be treated separately.

Propranolol vs Venlafaxine

- Finding suggest both drugs are equally effective in the prophylaxis treatment of Vestibular migraines

- Venlafaxine performed better at control of depression symptoms
Retrospective review and telephone follow-up to evaluate a physical therapy protocol for treating persistent postural-perceptual dizziness: A pilot study

Karla J. Thompson,*, Jay C. Goetting, Jeffrey P. Staab and Neil T. Shepard

*Department of Physical Medicine and Rehabilitation, Mayo Clinic, Rochester, MN, USA
bDepartment of Psychiatry and Psychology, Mayo Clinic, Rochester, MN, USA
cDepartment of Otorhinolaryngology, Mayo Clinic, Rochester, MN, USA

Habituation Exercises for PPPD

Visual vertigo exercises

1. Umbrella optokinetics
Use a striped golf umbrella or patterned umbrella as the stimulus. Do twice daily.

In a seated position spin the umbrella in front of you, just fast enough that it is uncomfortable, but so you can tolerate it. Do this for about 30 seconds. Rest until symptoms return to baseline. Repeat 2-3 times. Slowly build up to 2 minutes at this speed and then slowly begin to increase the speed.

Once you tolerate this for 2 minutes at a fairly fast speed, do the exercise while standing. Start with your feet apart. Note: Slow the speed down again until you see how this affects your balance. You may also have to decrease the time. Slowly increase the time and speed again. Once you have increased the speed and time, begin bringing the feet closer and closer together until they are touching.
Habituation Exercises for PPPD

2. VOR cancellation
   Sit in chair. Hold card with letter or short word on it at arm's length
   away from you. Move card, upper body, and head side to side as a unit.
   Keep eyes focused on letter or word. Repeat for 30 seconds to 1 minute.
   Do twice daily. Progress to standing when able. For extra challenge, do
   exercise with a “busy” background about 5 feet in front of you.

Habituation Exercises for PPPD

Store walking program

Do this exercise at a store, mall, or any place that has lots of activity.
1. Walk into store until you notice an increase in your symptoms (1-2
   point increase on 0-10 scale). Stop and rest, noting length of time to
   reach this point. Rest until symptoms return to baseline.
2. Walk the same length of time further into the store, rest again.
3. Turn around and walk the same amount of time, rest again
4. Walk out of the store.
5. Do this 2-3 days/week
6. Every 2 weeks increase the length of the walk by 4 minutes (each
   segment of the walk would be one minute longer)
7. Gradually increase the length of the walk until you are able to walk
   30-45 minutes without increasing symptoms more than 1-2 points on
   0-10 scale.

If you are not able to do this exercise as listed and need to go to store, try to
   take frequent standing breaks to rest, minimizing increase in symptoms. 
   Short shopping trips are better than long trips.

   This exercise can also be done walking outside in a busy neighborhood.
Habituation Exercises General Rules

General rules:
1. Avoid more than 2 point increase in symptoms on 0-10 scale while doing exercise.
2. Symptoms should return to baseline within 15-20 minutes after completing exercise session. If not, do fewer repetitions or for less time.
3. Split up exercises into manageable components if needed.
4. When shopping or in crowds. If symptoms increase, take frequent standing breaks to rest to minimize increase in symptoms. Better to do short shopping trips than long.
5. Any activity that increases symptoms can be made into a habituation exercise by following these general guidelines. (watching television, playing video game, using computer, riding in car)

Effects of clinical state and visual background composition on visual dependence

Jeffrey P. Staab, MD, MS  
Lindzey V. Wheeler  
Neil T. Shepard, PhD  
Adolfo M. Bronstein, MD, PhD
Meniere's Disease, Vestibular Migraine, PPPD

Independent effect: Diagnosis within background

- Normal controls (N=35)
- Patients without PPPD (N=14)
- Patients with PPPD (N=12)

SVV error (deg)

*PPP D ≠ control
*p<0.05

Predictors of visual dependence

- Dizziness Handicap Inventory score
- Diagnostic group
- Multivariate model
  - Age
  - Sex
  - Visual background
  - DHI score (R^2=0.381)
  - Personality traits
    » Neurotic
    » Introverted
    » Low self-efficacy
  - R^2=0.541
  - F=24.8, df=17, p<0.0001

ANOVA F=200.3, df=2, p<0.0001