

# March Topic: General Vestibular Knowledge

### March 25, 2021

Casale J, Browne T, Murray I, Gupta G. **Physiology, Vestibular System**. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. 2020 May 24.

The vestibular system is a complex set of structures and neural pathways that serves a wide variety of functions that contribute to our sense of proprioception and equilibrium. These functions include the sensation of orientation and acceleration of the head in any direction with associated compensation in eye movement and posture. These reflexes are referred to as the vestibulo-ocular and vestibulospinal reflexes, respectively. The centrally located vestibular system involves neural pathways in the brain that respond to afferent input from the peripheral vestibular system in the inner ear and provide efferent signals that make these reflexes possible. Current data suggest that the vestibular system also plays a role in consciousness, and dysfunctions of the system can cause cognitive deficits related to spatial memory, learning, and navigation.

PMID: 30422573 Link to free article: <u>https://www.ncbi.nlm.nih.gov/books/NBK532978/</u>

## March 18, 2021

Strupp M, Dlugaiczyk J, Ertl-Wagner BB, Rujescu D, Westhofen M, Dieterich M. **Vestibular Disorders**. Dtsch Arztebl Int. 2020 Apr 24;117(17):300-310. doi: 10.3238/arztebl.2020.0300.

BACKGROUND: Recent research findings have improved the understanding of the diagnosis, pathophysiology, genetics, etiology, and treatment of peripheral, central, and functional vestibular vertigo syndromes.

METHOD: A literature search, with special attention to the current classification, treatment trials, Cochrane analyses, and other meta-analyses.

RESULTS: There are internationally accepted diagnostic criteria for benign positional paroxysmal vertigo, Menière's disease, bilateral vestibulopathy, vestibular paroxysmia, and functional dizziness. Whether an acute vestibular syndrome is central or peripheral can usually be determined rapidly on the basis of the history and the clinical examination. "Cere - bellar vertigo" is a clinically important entity. For bilateral vestibulopathy, balance training is an effective treatment. For Menière's disease, preventive treatment with betahistine (48 mg and 144 mg per day) is not superior to placebo. For vestibular paroxysmia, oxcarbazepine has been shown to be effective. Treatments that are probably effective for functional dizziness include vestibular rehabilitation, cognitive behavioral therapy, and serotonin reuptake inhibitors.



CONCLUSION: The diagnostic assessment of vestibular syndromes is much easier for clinicians now that it has been internationally standardized. There is still a lack of randomized, controlled trials on the treatment of, for example, Menière's disease, vestibular migraine, and "cerebellar vertigo." PMID: 32530417

Link to free article: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7297064/</u>

### March 11, 2021

Dougherty JM, Carney M, Emmady PD. **Vestibular Dysfunction**. 2020 Dec 12. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021

Vestibular dysfunction is a disturbance of the body's balance system. The disorder differentiated into peripheral and central causes. The symptoms of peripheral and central vestibular dysfunction can overlap, and a comprehensive physical examination can often help differentiate the two. Vestibular disorders usually present acutely. The patient's symptom complex typically consists of vertigo, nausea, vomiting, intolerance to head motion, nystagmus, unsteady gait, and postural instability. The most common form of acute peripheral vestibular dysfunction is vestibular neuronitis. The most common cause of severe central vestibular dysfunction is an ischemic stroke of the posterior fossa, which contains the brainstem and cerebellum. An acute ischemic stroke accounts for up to 25% of patients who present as central vestibular function. Since acute stroke is treated differently, it is essential to recognize this disorder. The second common cause of central vestibular dysfunction is a demyelinating disease. Studies have shown there is a small prevalence of vestibular dysfunction in patients with syncope. Syncope is a presentation of vertebral basilar artery disease with a prevalence of five percent of strokes. Symptoms of vestibular dysfunction include a variety of symptoms: vertigo, nausea and vomiting, intolerance to head motion, spontaneous nystagmus, unsteady gait, and postural instability caused by injury to peripheral or central vestibular structures. The prevalence of each of these symptoms varies, and there is no single symptom that helps identify vestibular dysfunction. The predominance of the symptoms listed above as a cluster leads to the suspicion of vestibular dysfunction. The history and physical exam is the way to differentiate peripheral from central vestibular dysfunction. It is necessary to identify which type of vestibular dysfunction a patient has, as this determines the therapeutic approach. The mainstay treatment for peripheral disorders is symptomatic therapy with anticholinergic medications or type 1 antihistamines. The treatment for central vestibular dysfunction caused by an ischemic stroke can include intravenous thrombolytic therapy and interventional clot retrieval in the hyperacute phase and stroke secondary prevention after that. The early identification of demyelinating disorders such as multiple sclerosis is essential so that treatment can be initiated to prevent the rapid decline and development of disabilities. This article will review the epidemiology, history and physical examination, evaluation, differential diagnosis, treatment, complications, and critical points in improving the identification of vestibular dysfunction, and differentiating peripheral from central vestibular disorders.



PMID: 32644352

#### March 4, 2021

Kaski D. **Neurological update: dizziness.** J Neurol. 2020 Jun;267(6):1864-1869. doi: 10.1007/s00415-020-09748-w. Epub 2020 Mar 4

The diagnosis and management of vertigo remains a challenge for clinicians, including general neurology. In recent years there have been advances in the understanding of established vestibular syndromes, and the development of treatments for existing vestibular diagnoses. In this 'update' I will review how our understanding of previously "unexplained" dizziness in the elderly is changing, explore novel insights into the pathophysiology of vestibular migraine, and its relationship to the newly coined term 'persistent postural perceptual dizziness', and finally discuss how a simple bedside oculomotor assessment may help identify vestibular presentations of stroke PMID: 32130499

Link to free article: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7293664/</u>

# February Topic: COVID and Dizziness

## February 25, 2021

Correia AO, Feitosa PWG, Moreira JLS, Nogueira SÁR, Fonseca RB, Nobre MEP. **Neurological manifestations of COVID-19 and other coronaviruses: A systematic review.** Neurol Psychiatry Brain Res. 2020;37:27-32. doi:10.1016/j.npbr.2020.05.008

Objective: To describe the main neurological manifestations related to coronavirus infection in humans. Methodology: A systematic review was conducted regarding clinical studies on cases that had neurological manifestations associated with COVID-19 and other coronaviruses. The search was carried out in the electronic databases PubMed, Scopus, Embase, and LILACS with the following keywords: "coronavirus" or "Sars-CoV-2" or "COVID-19" and "neurologic manifestations" or "neurological symptoms" or "meningitis" or "encephalitis" or "encephalopathy," following the Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: Seven studies were included. Neurological alterations after CoV infection may vary from 17.3% to 36.4% and, in the pediatric age range, encephalitis may be as frequent as respiratory disorders, affecting 11 % and 12 % of patients, respectively. The Investigation included 409 patients diagnosed with CoV infection who presented neurological symptoms, with median age range varying from 3 to 62 years. The main neurological alterations were headache (69; 16.8 %), dizziness (57, 13.9 %), altered consciousness (46; 11.2 %), vomiting (26; 6.3 %), epileptic crises (7; 1.7 %), neuralgia (5; 1.2 %), and ataxia (3; 0.7 %). The main presumed diagnoses were acute viral meningitis/encephalitis in 25 (6.1 %) patients, hypoxic encephalopathy in 23 (5.6 %) patients, acute cerebrovascular disease in 6 (1.4 %)



patients, 1 (0.2 %) patient with possible acute disseminated encephalomyelitis, 1 (0.2 %) patient with acute necrotizing hemorrhagic encephalopathy, and 2 (1.4 %) patients with CoV related to Guillain-Barré syndrome.

Conclusion: Coronaviruses have important neurotropic potential and they cause neurological alterations that range from mild to severe. The main neurological manifestations found were headache, dizziness and altered consciousness.

PMID: 33154692

Link to free article: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7261450/</u>

### February 18, 2021

Luís ME, Hipólito-Fernandes D, Mota C, Maleita D, Xavier C, Maio T, Cunha JP, Tavares Ferreira J. A **Review of Neuro-Ophthalmological Manifestations of Human Coronavirus Infection.** Eye Brain. 2020 Oct 30;12:129-137. doi: 10.2147/EB.S268828.

Introduction: Human coronavirus (HCoVs) are a group of viruses with recognized neurotropic and neuroinvasive capabilities. The reports on the neurological and ocular findings are increasing day after day and several central and peripheral neurological manifestations are already described. However, none specifically describes the neuro-ophthalmological manifestation of HCoVs. This is the first article specifically reviewing neuro-ophthalmological manifestations of HCoVs infection.

Methods: PubMed and Google Scholar databases were searched using the keywords: coronaviridae, coronavirus, COVID-19, SARS-CoV-2, SARS-CoV-1, MERS, ocular, ophthalmology, ophthalmological, neuro-ophthalmology, neurological, manifestations. A manual search through the reference lists of relevant articles was also performed. There were no restrictions concerning language or study type and publications not yet printed but available online were considered.

Results: Coronavirus eye involvement is not frequent and includes mostly a typical viral follicular conjunctivitis. Recently, retinal anatomical alterations were described using optic coherence tomography. Neuro-ophthalmological symptoms and signs can appear isolated or associated with neurological syndromes. The manifestations include headache, ocular pain, visual impairment, diplopia, and cranial nerve palsies secondary to Miller Fisher syndrome, Guillain-Barré syndrome, or encephalitis, and nystagmus.

Conclusion: Neurological and neuro-ophthalmological syndromes, symptoms, and signs should not be neglected and a complete ophthalmological examination of these patients should be performed to fully describe ocular manifestations related to HCoVs. We believe that major ocular and neuro-ophthalmological manifestations reports lack due to safety issues concerning detailed ophthalmological examination; on the other hand, in a large number of cases, the presence of life-threatening coronavirus disease hinders ocular examination and ophthalmologist's visit to the intensive care unit PMID: 33154692

Link to free article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7608548/



February 11, 2021

Saniasiaya J, Kulasegarah J. **Dizziness and COVID-19.** Ear Nose Throat J. 2021;100(1):29-30. doi:10.1177/0145561320959573

Coronavirus 2019 or COVID-19 is a novel entity which had led to many challenges among physicians due to its rapidly evolving nature. Vertigo or dizziness has recently been described as a clinical manifestation of COVID-19. Countless studies, emerging daily from various parts of the world, have revealed dizziness as one of the main clinical manifestation of COVID-19. This is not surprising as dizziness has historically been associated with viral infections.

An earlier published study from China found dizziness to be the most common neurological manifestation of COVID-19.1 Dizziness was proposed to occur ensuing the neuroinvasive potential of severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2 virus which causes COVID-19. Baig et al postulated that the virus enters the neural tissue from circulation and binds to the angiotensin-converting enzyme 2 receptors found in the capillary endothelium.2 Apart from that, direct invasion, hypoxia, hypercoagulopathy, as well as immune-mediated insult were among the postulated mechanism of neuroinvasion leading to dizziness.3

A literature search was performed using articles published in PubMed on August 1, 2020, to identify dizziness as a clinical manifestation of COVID-19. The keywords used for the article search include giddiness, dizziness, vertigo, COVID-19, SARS CoV 2, Coronavirus disease. To our knowledge, this is the first article that outlines the association between dizziness and COVID-19.

We obtained 14 articles, which include 3 case reports and 11 studies (Table 1). A total of 141 patients were pooled from this review. All patients included in this review had dizziness/vertigo as a presenting symptom. Dizziness was the initial presentation of COVID-19 in 3/141 patients (2.13%),9,11,13 whereby in 2 of these patients, dizziness was later followed by respiratory symptoms.9,13 Most of the studies reporting on dizziness as a clinical manifestation hails from China (11/14), the epicenter which gave rise to the pandemic. Of the 14 studies included, dizziness was specifically investigated and treated only in 2 studies9,11 as dizziness was not the highlight in most studies, it was not investigated and described thoroughly. Additionally, the outcome of dizziness was mentioned only in 1 study by Malayala et al,11whereby vestibular rehabilitation was carried out for the patient successfully.

Dizziness, albeit a nonspecific COVID-19 symptom, requires thorough investigation notably to determine its leading cause including, acute labyrinthitis, vestibular neuritis, acute otitis media, or secondary to stroke following COVID-19.

We would like to emphasize that dizziness should not be taken lightly as it has been proven to be a notable clinical manifestation among COVID-19 patients. Parallel to that, association with other audiovestibular manifestations such as hearing loss and tinnitus ought to be determined. Persistent dizziness posttreatment from COVID-19 requires referral to the Otorhinolaryngology Department for thorough examination and investigation. Additionally, we recommend vestibular rehabilitation therapy, which has revealed promising results, to be carried out for stable COVID-19 patients with dizziness. Lastly, it is imperative that attending physicians remain vigilant, especially when managing nonspecific symptoms such as dizziness, as it can be easily overlooked.



PMID: 32931322 Link to free article: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7492824/</u>

### February 4, 2021

Malayala SV, Raza A. **A Case of COVID-19-Induced Vestibular Neuritis.** Cureus. 2020;12(6):e8918. Published 2020 Jun 30. doi:10.7759/cureus.8918

The World Health Organization (WHO) declared COVID-19, a novel coronavirus infection, as a pandemic in March 2020. Since the origin of the disease in Wuhan, China, understanding the pathophysiology, clinical presentation, screening guidelines, and management of the disease has been ever-evolving. Though respiratory pathologies have been the major complications of a COVID-19 infection, other presentations like abdominal pain, deep venous thrombosis, cardiomyopathy, and even acute cerebrovascular ischemic attacks have been reported. We present a case of a young patient presenting with vertigo, possibly from COVID-19-induced acute vestibular neuritis. This is a 20-year-old Hispanic female patient presenting with intractable vertigo, nausea, and vomiting but without any typical symptoms like fever, cough, or shortness of breath. Initial examination and imaging ruled out an acute stroke. There was minimal improvement in her vestibular symptoms with the recommended COVID-19 treatment as of March 2020 (hydroxychloroquine and azithromycin) and symptomatic management. Her inflammatory markers were surprisingly normal all through the hospital course. She was then treated with oral prednisone and subsequently discharged home after a prolonged course of eight days. The pathophysiology of COVID-19-induced vestibular neuritis could be similar to any other viral infection. Clinicians should consider COVID-19 in the differential diagnosis for patients presenting with similar symptoms, especially in areas of a high prevalence of this disease. Early diagnosis of COVID-19 in such cases is important for proper isolation, to minimize exposure and avoid further unnecessary investigations. These symptoms will just resolve with symptomatic management like any other case of vestibular neuritis without any further management that is specific for a COVID-19 infection. PMID: 32760619

Link to free article: <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7392187/</u>

# January Topic: Central Vestibular Dysfunction

#### January 28, 2021

Daniel, A, Barker, L, Martini, M. Pain modulation by illusory body rotation: A new way to disclose the interaction between the vestibular system and pain processing. Eur J Pain. 2020; 24: 1119–1129

Background: Clinical and experimental evidence advocates a structural and functional link between the vestibular and other sensory systems. For instance, visuo-vestibular and vestibular–somatosensory



interactions have been widely reported. However, whether visual inputs carrying vestibular information can modulate pain is not yet clear. Recent evidence using natural vestibular stimulation or moving visual stimuli, points at an unspecific effect of distraction.

Methods: By using immersive virtual reality (VR), we created a new way to prompt the vestibular system through the vision of static visual cues, studying the possible interaction with pain. Twenty-four healthy participants were visually immersed in a virtual room which could appear with five different degrees of rotation in the sagittal axis, either towards the right, left or with no rotation. Participants' heat pain thresholds and subjective reports of perceived body rotation, sense of presence and attention were measured.

Results: 'Being' in a tilted room induced the sensation of body rotation in our participants, even though they were always in an upright position. We also found that rotating the visual scenario can modulate the participants' pain thresholds, determining a significant increase when a left tilt is displayed. In addition, a positive correlation between the perceived body midline rotation and pain threshold was found when the virtual room was titled 15 degrees toward the left. Importantly, all VR conditions were found to be equally distractive.

Conclusions: Vestibular information present in static visual cues can modulate experimentally-induced acute pain according to a side-dependent manner and bypassing supramodal attentional mechanisms. These findings may help refining pain management approaches based on multimodal stimulation. Significance: This study explored how the visualization of static environments in immersive virtual reality can lead to pain threshold modulation through the activation of the vestibular system. Immersion into rotated virtual environments led to the illusory sensation of body rotation, and this sensation was found to be related with a modulation of pain perception. Possible analgesic effects due to distraction could be ruled out. These results expand our current knowledge about how the visual, vestibular and somatosensory (pain) systems interact. These findings may influence future pain treatment strategies based on multisensory stimulation.

PMID: 32170809

#### January 20, 2021

Katz-Nave, G., Adini, Y., Hetzroni, O.E. and Bonneh, Y.S. **Sequence Learning in Minimally Verbal Children With ASD and the Beneficial Effect of Vestibular Stimulation**. Autism Research, (2020)13: 320-337

People with autism spectrum disorder (ASD) and especially the minimally verbal, often fail to learn basic perceptual and motor skills. This deficit has been demonstrated in several studies, but the findings could have been due to the nonoptimal adaptation of the paradigms. In the current study, we sought to characterize the skill learning deficit in young minimally verbal children with ASD and explore ways for improvement. For this purpose, we used vestibular stimulation (VS) whose beneficial effects have been demonstrated in the typical population, but the data regarding ASD are limited. We trained 36 children ages 6–13 years, ASD (N = 18, 15 of them minimally verbal) and typical development (TD, N = 18), on a touch version of the visual-motor Serial-Reaction-Time sequence-learning task, in 10 short (few minutes)



weekly practice sessions. A subgroup of children received VS prior to each training block. All the participants but two ASD children showed gradual median reaction time improvement with significant speed gains across the training period. The ASD children were overall slower (by ~250 msec). Importantly, those who received VS (n = 10) showed speed gains comparable to TD, which were larger (by ~100%) than the ASD controls, and partially sequence-specific. VS had no effect on the TD group. These results suggest that VS has a positive effect on learning in minimally verbal ASD children, which may have important therapeutic implications. Furthermore, contrary to some previous findings, minimally verbal children with ASD can acquire, in optimal conditions, procedural skills with few short training sessions, spread over weeks, and with a similar time course as non-ASD controls. PMID: 31729171

#### January 14, 2021

Lee, J-O, Lee, E-S, Kim, J-S, et al. Altered brain function in persistent postural perceptual dizziness: A study on resting state functional connectivity. Hum Brain Mapp. 2018; 39: 3340– 3353

This study used resting state functional magnetic resonance imaging (rsfMRI) to investigate whole brain networks in patients with persistent postural perceptual dizziness (PPPD). We compared rsfMRI data from 38 patients with PPPD and 38 healthy controls using whole brain and region of interest analyses. We examined correlations among connectivity and clinical variables and tested the ability of a machine learning algorithm to classify subjects using rsfMRI results. Patients with PPPD showed: (a) increased connectivity of subcallosal cortex with left superior lateral occipital cortex and left middle frontal gyrus, (b) decreased connectivity of left hippocampus with bilateral central opercular cortices, left posterior opercular cortex, right insular cortex and cerebellum, and (c) decreased connectivity between right nucleus accumbens and anterior left temporal fusiform cortex. After controlling for anxiety and depression as covariates, patients with PPPD still showed decreased connectivity between left hippocampus and right inferior frontal gyrus, bilateral temporal lobes, bilateral insular cortices, bilateral central opercular cortex, left parietal opercular cortex, bilateral occipital lobes and cerebellum (bilateral lobules VI and V, and left I–IV). Dizziness handicap, anxiety, and depression correlated with connectivity in clinically meaningful brain regions. The machine learning algorithm correctly classified patients and controls with a sensitivity of 78.4%, specificity of 76.9%, and area under the curve = 0.88 using 11 connectivity parameters. Patients with PPPD showed reduced connectivity among the areas involved in multisensory vestibular processing and spatial cognition, but increased connectivity in networks linking visual and emotional processing. Connectivity patterns may become an imaging biomarker of PPPD. PMID: 29656497

Link to free text: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6866559/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6866559/</a>



#### January 6, 2021

Zhe, X., Gao, J., Chen, L., Zhang, D., Tang, M., Yan, X., . . . Zhang, X. (2020). Altered structure of the vestibular cortex in patients with vestibular migraine. Brain and Behavior, 10(4) doi:http://dx.doi.org.augie.idm.oclc.org/10.1002/brb3.1572

Introduction: Previous voxel-based morphometry (VBM) studies have revealed changes in brain structure in patients with vestibular migraine (VM); these findings have improved the present understanding of pathophysiology. Few other studies have assessed the association between structural changes and the severity of dizziness in VM. This study aimed to examine the structural changes and cortical morphometric features associated with migraine and vertigo attacks in patients with VM. Methods: Twenty patients with VM and 20 healthy normal volunteers were scanned on a 3-tesla MRI scanner. The gray matter volume (GMV) was estimated using the automated Computational Anatomy Toolbox (CAT12). The relationship between clinical parameters and morphometric abnormalities was also analyzed in VM.

Results: Compared with controls, VM patients have decreased GMV in the prefrontal cortex (PFC), posterior insula–operculum regions, inferior parietal gyrus, and supramarginal gyrus. Moreover, patient scores on the Dizziness Handicap Inventory (DHI) score showed a negative correlation with GMV in the posterior insula–operculum regions.

Conclusion: These findings demonstrated abnormality in the central vestibular cortex and correlations between dizziness severity and GMV in core regions of the vestibular cortex of VM patients, suggesting a pathophysiological role of these core vestibular regions in VM patients.

PMID: 32157823

Link to free text: <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177586/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177586/</a>