Unilateral Vestibular loss: Aspects on treatment and compensation mechanisms

Sjögren, Julia

2025

Document Version:
Publisher's PDF, also known as Version of record

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Aspects on treatment and compensation mechanisms

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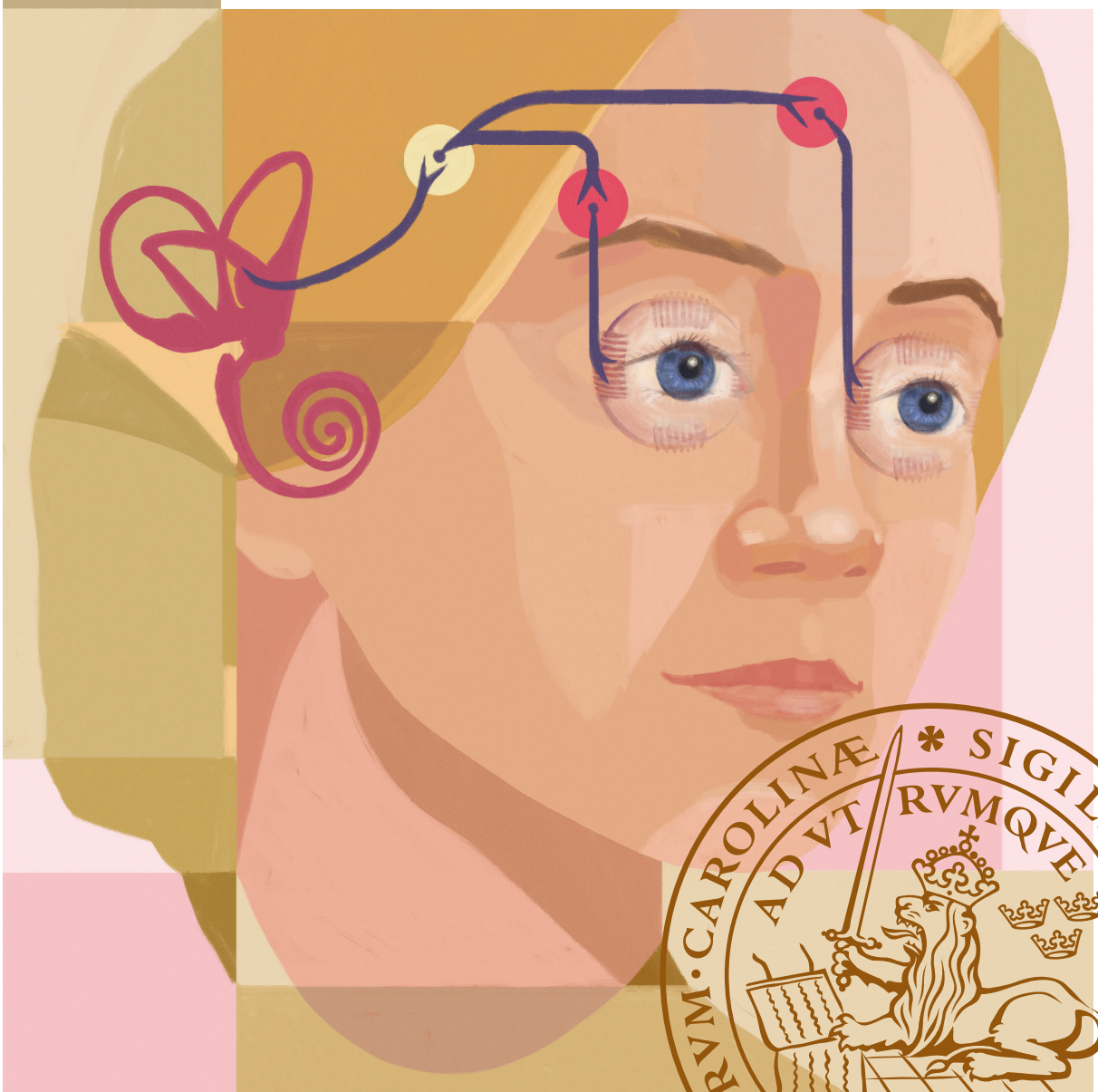

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JULIA SJÖGREN is an otorhinolaryngologist at the Department of Otorhinolaryngology and Head and Neck Surgery at Skåne University Hospital, Sweden. Her doctoral thesis explores the treatment of acute unilateral vestibulopathy and the compensatory mechanisms that follow.

LUND UNIVERSITY

FACULTY OF MEDICINE

Department of Clinical Sciences
Otorhinolaryngology and
Head and Neck Surgery

Lund University, Faculty of Medicine
Doctoral Dissertation Series 2025:73
ISBN 978-91-8021-726-2
ISSN 1652-8220

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Julia Sjögren

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DOCTORAL DISSERTATION

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To be publicly defended at Palaestra et Odeum, Paradisgatan 4, Lund, Sweden, on the 19th of June 2025, 8.15 a.m.

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Organization: LUND UNIVERSITY

Document name: DOCTORAL DISSERTATION **Date of issue:** 19 June 2025

Author(s): JULIA SJÖGREN **Sponsoring organization:**

Title: Unilateral vestibular loss – Aspects on treatment and compensation mechanisms

Abstract:

Background: Acute unilateral vestibulopathy (AUVP) or vestibular neuritis, is a common cause for acute dizziness and entails a sudden loss of vestibular function, leading to vertigo, postural imbalance, and impaired visual stability during movement. The treatment for the condition has not been fully established. Corticosteroids have been widely used to promote recovery but their effectiveness remains controversial. Compensation after a vestibular loss involves both peripheral functional recovery and central compensation processes, including the generation of corrective saccades to improve gaze stability during motion. However, the relationship between these mechanisms and subjective recovery is still not fully understood.

Aims: To investigate the effect of corticosteroid treatment and mechanisms of vestibular compensation

Methods: Paper I was a retrospective case-series comparing caloric recovery when treated within 24 hours versus 25–72 hours after AUVP onset. Paper II was a randomized controlled trial evaluating the effect of corticosteroids on vestibular recovery (caloric test, video head impulse test (vHIT)) and symptoms (Likert scale, Dizziness Handicap Inventory (DHI), Hospital Anexiety and Depression Scale (HADS)) up to one year. Papers III and IV were prospective experimental studies assessing the impact of active versus passive head movements on visual performance and saccadic properties using vHIT and functional Head impulse test (fHIT) in patients with complete unilateral vestibular loss. Paper V was a prospective longitudinal study evaluating vestibular recovery and saccadic characteristics with vHIT from onset to one year after AUVP.

Results: Early corticosteroid treatment within 24 hours of AUVP onset was associated with better caloric recovery ($p<0.05$; Paper I); however, in the randomized controlled trial (Paper II), no significant benefit of corticosteroids over placebo was observed in either vestibular function recovery or symptom relief. Active head impulses improved visual performance ($p=0.002$) and triggered earlier covert saccades ($p=0.004$) compared to passive movements. The eye position error at the time of the visual task was closely associated to the saccade latency ($r=0.915$, $p<0.001$) in patients with complete unilateral vestibular loss (Papers III & IV). Over 12 months, VOR gain improved ($p<0.001$) - most notably within the first 3 months ($p<0.001$) - while both covert ($p=0.005$) and overt ($p<0.001$) saccades decreased. Covert saccade characteristics remained stable and were not associated with subjective symptoms (Paper V).

Conclusions: Vestibular function improved significantly after AUVP, especially within the first three months. Corticosteroid treatment did not improve recovery, nor did it reduce symptoms in the short or long term. Active head movements generated short-latency covert saccades and reduced the positional error between the eye and head, which may explain the near-normal visual performance despite complete unilateral vestibular loss. In contrast, passive head movements triggered covert saccades that did not adapt over time and remained closely associated with persistent vestibular hypofunction up to one year after AUVP.

Key words: unilateral vestibular loss, vestibular neuritis, acute unilateral vestibulopathy, AUVP, corrective saccades, covert saccades, active and passive head movement

Language ENGLISH **Number of pages**:87

ISSN and key title: 1652-8220 **ISBN:** 978-91-8021-726-2

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Cover illustration by Matthew Burne

Illustrations in the thesis by Magdalena Karnebäck

Author portrait by Sabine Swoboda

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Department of Clinical Sciences, Otorhinolaryngology and Head and Neck Surgery

ISBN 978-91-8021-726-2

ISSN 1652-8220

Printed in Sweden by Media-Tryck, Lund University

Lund 2025

Till mamma och pappa

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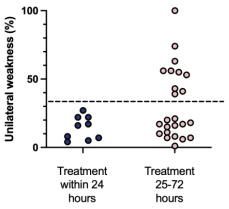
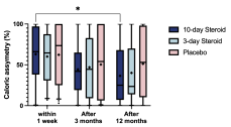
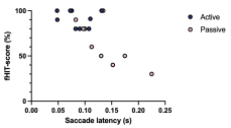
II: Acute unilateral vestibulopathy and corticosteroid treatment - A randomized placebo-controlled double-blind trial. Julia Sjögren, Per-Anders Fransson, Måns Magnusson, Mikael Karlberg, Fredrik Tjernström. Journal of Vestibular Research; 35:91-101, 2025.

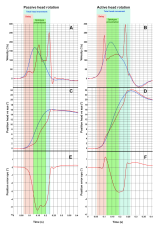
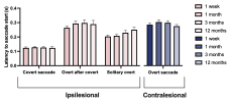
III: Functional Head Impulse Testing Might Be Useful for Assessing Vestibular Compensation After Unilateral Vestibular Loss, Julia Sjögren, Per-Anders Fransson, Mikael Karlberg, Måns Magnusson and Fredrik Tjernström. Frontiers in Neurology; 9:1-7, 2018.

IV: Short-latency covert saccades - the explanation for good dynamic visual acuity after unilateral vestibular loss? Julia Sjögren, Mikael Karlberg, Craig Hickson, Måns Magnusson, Per-Anders Fransson and Fredrik Tjernström. Frontiers in Neurology; 12:1-12, 2021.

V: Vestibular recovery and Central Compensation After Acute Unilateral Vestibulopathy. Julia Sjögren, Per-Anders Fransson, Måns Magnusson, Mikael Karlberg, and Fredrik Tjernström. Manuscript.

Thesis at a glance

	Aim	Method	Main results	Teaser	Conclusion
I	To evaluate if an early start of treatment with corticosteroids in patients with AUVP increases the recovery of vestibular function.	Retrospective cohort of 33 patients with AUVP treated with corticosteroids within 72 hours from disorder onset. Caloric test after 3 months.	All patients treated within 24 hours showed normal caloric test results at 3-month follow-up, compared to 58% of those treated between 25–72 hours ($p < 0.05$).		Treatment within 24 hours in AUVP improves vestibular recovery
II	To evaluate if corticosteroid treatment enhances recovery of vestibular function and reduce symptoms in the acute and chronic phase of AUVP.	A double-blind RCT including 69 AUVP patients randomized to placebo, 3-day, or 10-day corticosteroid treatment. Caloric test (primary outcome), vHIT, vertigo score, DHI, HADS from onset up to 12 months.	All groups showed significant improvement in caloric function over time ($p=0.002$), with no significant differences between groups ($p=0.629$). Secondary outcomes showed no significant group differences.		Corticosteroid treatment does not improve caloric function, vHIT gain, or subjective well-being in patients with AUVP.
III	To evaluate how the VOR, covert saccades and visual performance are influenced by active and passive head movements.	Cross-sectional experimental study on 9 patients with complete unilateral vestibular loss. vHIT and fHIT during both passive and active head movements.	Active ipsilesional head impulses significantly improved visual performance ($p=0.002$) and reduced the latencies of the covert saccades ($p=0.004$).		Active head movements yield near-normal visual performance and reduce latencies of the covert saccades.

IV	To analyze how covert saccades improve visual performance during active and passive head movements.	Cross-sectional experimental study on 8 patients with complete unilateral vestibular loss. vHIT and fHIT during both passive and active head movements.	Active head impulses produced significantly smaller head-eye position errors (p=0.006), which were strongly correlated with shorter latencies of the first corrective saccade (r=0.915, p<0.001).		Active head movements produce position errors within the threshold for brief visual perception due to short-latency covert saccades.
V	To investigate the course of vestibular recovery and the evolution of saccadic behavior - from the onset of AUVP to one year after the onset.	Prospective cohort study of 43 patients with AUVP. vHIT at onset, 1 month, 3 months and 12 months. Self-rated vertigo; Likert scale (first month). DHI at 3 and 12 months.	VOR gain improved significantly over 12 months (p<0.001). Covert (p=0.005) and overt (p<0.001) saccades decreased over time. Covert saccade properties remained consistent and did not correlate with self-reported dizziness.		Covert saccades represent a non-adaptive response and indicate persistent vestibular dysfunction for passive head movements.

Abbreviations

AICA	Anterior inferior cerebellar artery
AUVP	Acute unilateral vestibulopathy
AVS	Acute vestibular syndrome
BPPV	Benign paroxysmal positional vertigo
COR	Cervical ocular reflex
DHI	Dizziness handicap inventory
GABA	Gamma-aminobutyric acid
HADS	Hospital anxiety and depression scale
fHIT	functional head-impulse test
HINTS	Head Impulse, nystagmus, test of skew
HIT	Head-impulse test
HITD-FT	Head impulse test-functional device
LARP	Left anterior right posterior
MLF	Medial longitudinal fasciculus
MRI	Magnetic resonance imaging
PET	Positron Emission Tomography
RALP	Right anterior left posterior
SCC	Semicircular canals
UVL	Unilateral vestibular loss
vHIT	video head-impulse test
VOR	Vestibulo-ocular reflex
VCR	Vestibulo-collic reflex
VNC	Vestibular nuclear complex
VSR	Vestibulospinal reflex

Introduction

The vestibular system was one of the first sensory system to emerge in evolution, with evidence of its presence found in fossils of agnathan fish species dating back 400 million years[1]. The balance organ was first described in the mid-19th century[2]. Robert Bárány developed the caloric test to assess the vestibular function, an achievement for which he was awarded the Nobel Prize in 1909. During 80 years the caloric test was used to assess the function of the lateral semicircular canal, one out of five parts of the vestibular organ[2].

In 1988, Michael Halmagyi and Ian Curthoys introduced the head-impulse test — a simple bedside examination capable of detecting deficits in all three semi-circular canals[3]. In 2009, Halmagyi and Curthoys introduced the video head-impulse test (vHIT), allowing for non-invasive, reliable evaluation of each of the six semicircular canals[4]. Today, vHIT is widely used in specialized clinics around the world, representing a significant advancement in the clinical assessment of vestibular function.

Our capacity to fully evaluate and understand the vestibular function has thus only emerged in recent decades — and the insights gained from these new diagnostic methods continue to reveal complexities that are not yet fully understood. Meanwhile, symptoms of dizziness and vertigo are highly prevalent; 15% of adults report dizziness within the past year[5] and about 3% of all emergency department visits in Sweden and globally by adults are due to dizziness[6, 7].

The need for more effective treatment strategies for vestibular disorders is clear. Vertigo remains the leading cause of sick leave and hospitalization among audiovestibular conditions[8]. In addition, vestibular hypofunction is a major contributor to impaired balance and is a significant risk factor for falls in the elderly[9, 10]. Approximately one-third of individuals aged 65 and older experience at least one fall per year[11] and fall-related injuries are the most common cause of hospital admissions, emergency department visits, and fatalities among older adults in Sweden[12].

The overall aim of this thesis was to enhance the treatment of acute unilateral vestibulopathy and to deepen our understanding of the compensatory mechanisms that occur following unilateral vestibular loss.

Background

What is balance?

Balance refers to the ability to remain in a stable upright position due to an equilibrium between all the forces on the body[13]. Balance is maintained through a sophisticated sensorimotor control system that relies on sensory input from vision, the vestibular system, and somatosensory input from the skin, joints and muscles. The vestibular system detects how the head moves in relation to the space around it, visual input detects head movement relative to the surrounding environment, and somatosensory input registers limb movement relative to the support surface or other body parts. This sensory information is integrated by the nervous system, through a process called multisensory integration, which then sends motor commands to the muscles of the eyes and body to support posture and stability[14]. A disruption to one or several of the sensory cues may impair balance.

The vestibular system

The peripheral vestibular organs, located in each inner ear, consist of five sensory organs: three semicircular canals and two otolith organs (Figure 1). The semicircular canals detect rotational (angular) acceleration/deceleration head movements in three dimensions, triggered by either self-induced movements (active movements) or external forces (passive movements). In contrast, the otolith organs sense linear acceleration and head tilt relative to gravity.

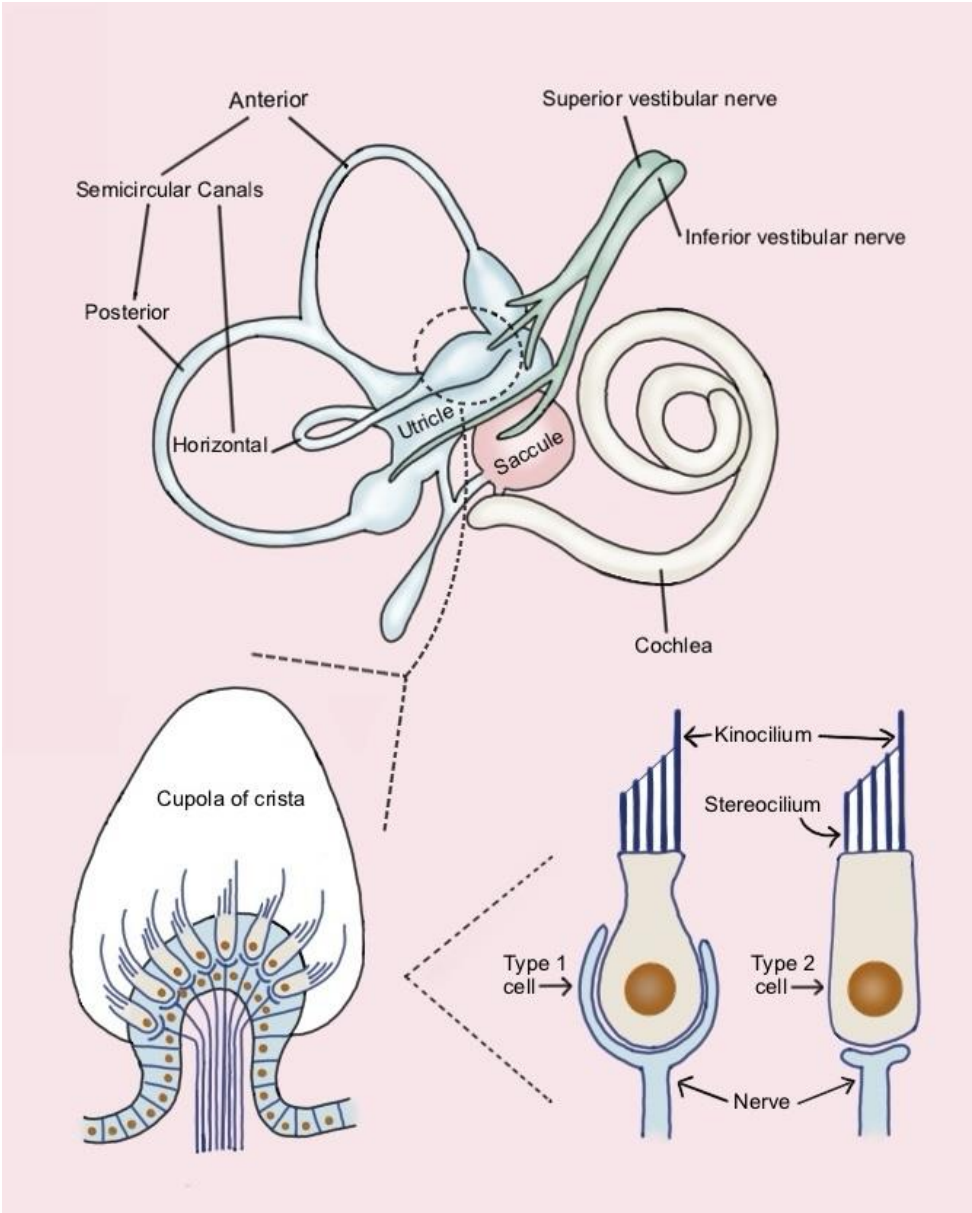


Figure 1. The inner ear; the cochlea and the vestibular system, which includes five sensory organs: three SCCs (anterior, horizontal, posterior) and two otolith organs (utricle and saccule). Vestibular sensory input is transduced by type I and type II hair cells located in the cristae. These cells convert mechanical displacement into electrical signals through deflection of stereocilia relative to the kinocilium.

The three SCCs; the anterior canal (or superior), the lateral (or horizontal) and the posterior (or inferior) canal act like miniature gyroscopes. Because of their orthogonal orientation to each other, they register motion in three dimensions and thereby provide the brain with sensory feedback about the head's rotation. The six semicircular canals make up three functional pairs; the lateral canal pair that detect acceleration in the yaw plane, turning the head from side to side. The right anterior canal and the left posterior canal (RALP) and the left anterior and the right posterior canal (LARP) detect acceleration in planes, which are approximately 45° to the sagittal plane of the head[15] (Figure 2). A displacement of the endolymph within a semicircular canal (SCC) occurs during head rotations in a specific plane that closely aligns with, but is not necessarily identical to, the anatomical plane of the SCC[16]. When one canal is maximally stimulated on one side of the head, the matching canal in the pair on the other side of the head is maximally inhibited. The acceleration of a rotation in any plane is perceived by the sensory epithelium in the cristae, located in the ampullae of the three semicircular ducts.

Vestibular hair cells are the primary motion sensors of the vestibular system, converting mechanical displacement into electrical signals. There are two types: goblet-shaped type I cells, surrounded by a large calyx nerve terminal, and columnar type II cells, connected via smaller bouton-shaped terminals. Type I cells respond to stronger stimuli, while type II cells are more sensitive to weaker inputs, though both share similar response mechanisms[17]. Each hair cell has a bundle of 40–200 stereocilia and one taller kinocilium, embedded in the cupula or otolithic membrane (Figure 1). Deflection of stereocilia toward the kinocilium depolarizes the cell, increasing glutamate release and stimulating vestibular afferents; deflection away causes inhibition. Hair cells also exhibit spontaneous activity, modulated by sensory input[18].

Vestibular nerve

The vestibular nerve, together with the auditory nerve, forms the 8th cranial nerve (n. vestibulocochlearis) and connects the vestibular organs to the brain. Its axons synapse at the bases of hair cells in the cristae of the semicircular canals (SCC) and the maculae of the otolith organs. These fibers pass through the internal acoustic meatus and enter the brainstem at the pontomedullary junction, primarily projecting to the ipsilateral vestibular nuclei, with some projections to the cerebellar flocculo-nodular lobe and vermis. The cell bodies reside in Scarpa’s ganglion, located near the fundus of the internal auditory meatus, and are divided into superior and inferior branches. The superior branch innervates the lateral and anterior SCC ampullae and the utricle, while the inferior branch serves the posterior SCC and the saccule[19]. The bony canals carrying the superior branch are longer and narrower than those of the inferior branch[20]. The vestibulocochlear nerve primarily consists of afferent fibers forming two main pathways: a regular (tonic) pathway, mediated by type II hair cells, which encodes eye velocity via slow-conducting, regularly discharging axons;

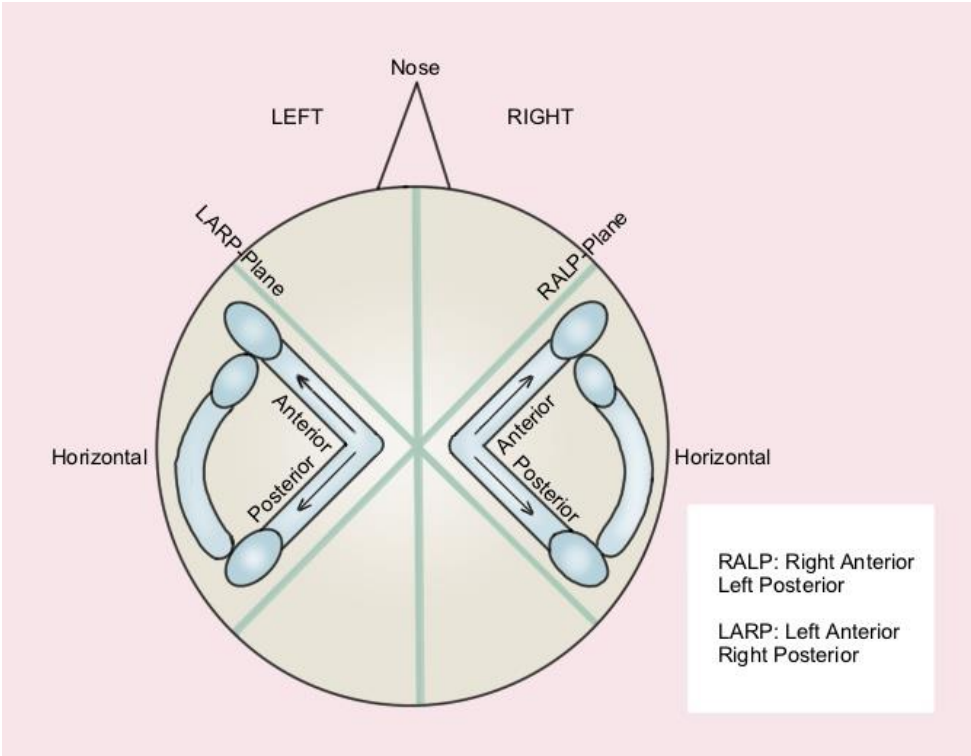


Figure 2. The six SCCs form three functional pairs: the lateral canals detect yaw plane acceleration (side-to-side head turns), while the right anterior–left posterior (RALP) and left anterior–right posterior (LARP) pairs detect rotational acceleration in planes approximately 45° to the sagittal plane of the head.

and an irregular (phasic) pathway, mediated by type I hair cells, characterized by fast-conducting, irregularly discharging axons sensitive to head acceleration, enabling rapid responses[21, 22]. A small portion of the vestibular nerve consists of efferent fibers originating in the brainstem, their role is not yet fully understood. It is generally believed that both animals and humans must differentiate between sensory input generated by their own movements and sensory signals originating from external stimuli. This distinction is thought to be achieved through an efference copy mechanism, in which a duplicate of the motor command is transmitted to sensory structures, allowing the brain to predict and filter out self-generated motion signals[23].

The inner ear's blood supply comes solely from the labyrinthine artery, typically branching from the Anterior inferior cerebellar artery (AICA) or directly from the Basilar artery, it has no collateral circulation[24] and is highly susceptible to ischemia; blood flow interruption for more than eight minutes can cause permanent nerve damage[25].

Central processing of vestibular information

Vestibular afferents primarily project to the vestibular nuclear complex (VNC) and the cerebellum. The VNC serves as the main integrator, rapidly processing vestibular signals for motor output such as eye movements, while the cerebellum acts as an adaptive processor, recalibrating vestibular responses. Both structures integrate vestibular, somatosensory, and visual input to maintain spatial orientation and coordinated movement[26].

The VNC comprises four main nuclei—medial, superior, lateral, and inferior—extending from the caudal pons to the rostral medulla in two columns beneath the fourth ventricle[27]. The medial vestibular nucleus receives input from the horizontal semicircular canals and projects via the medial longitudinal fasciculus (MLF) to ipsilateral and contralateral extraocular motor nuclei, supporting the vestibulo-ocular reflex (VOR), as well as to the spinal cord for vestibulospinal reflexes. The superior vestibular nucleus receives input from the superior and posterior canals and also projects via the MLF to extraocular muscles, contributing to VOR control. The lateral nucleus integrates input from all vestibular organs and the cerebellum, with descending projections forming the lateral vestibulospinal tract, essential for regulating trunk posture and limb extension. The inferior nucleus receives input from the utricle and saccule and projects to other vestibular nuclei and the cerebellum[27, 28]. Commissural fibers connect the vestibular nuclei bilaterally, enabling integration across hemispheres.

The oculomotor system and the vestibulo-ocular reflex

The oculomotor system maintains visual stability and directs eye movements, especially toward the fovea, the retina's high-acuity region. It involves six extraocular muscles controlled by three cranial nerves, which connect to brainstem nuclei and premotor circuits. These circuits coordinate five eye movement systems: optokinetic, smooth pursuit, saccadic, vergence, and the VOR. The optokinetic reflex stabilizes vision during sustained motion; smooth pursuit tracks slow-moving targets; saccades produce rapid, voluntary gaze shifts; vergence adjusts eye alignment for depth; and the VOR uses vestibular input to maintain fixation during head movements.

The VOR stabilizes gaze during head rotations by generating compensatory eye movements in the direction opposite to the head movement. When the head rotates, the endolymph within the SCCs is displaced, deflecting the cupula. This stimulates the hair cells embedded within the cupula. It is likely the activation of the very fast type I receptors that triggers action potentials in the irregular, excitatory afferents, which project to the vestibular nuclei in the brainstem[29]. From the vestibular nuclei, excitatory and inhibitory signals are transmitted to the oculomotor and abducens

nuclei, which then activate and inhibit the appropriate extraocular muscles, generating an eye movement in the opposite direction of the head movement[26] (Figure 3). This three-neuron arc allows for an exceptionally fast response, where the eyes begin to move approximately 8 ms after the head starts to rotate, ensuring visual stability even during rapid and unpredictable head movements[30]. Additionally, neurons from one vestibular nucleus project across the vestibular commissure, delivering inhibitory signals to the contralateral vestibular nucleus during ipsilateral rotations. This reciprocal inhibition amplifies excitatory drive on the stimulated side while suppressing activity on the opposite side, enhancing directional signal clarity[31].

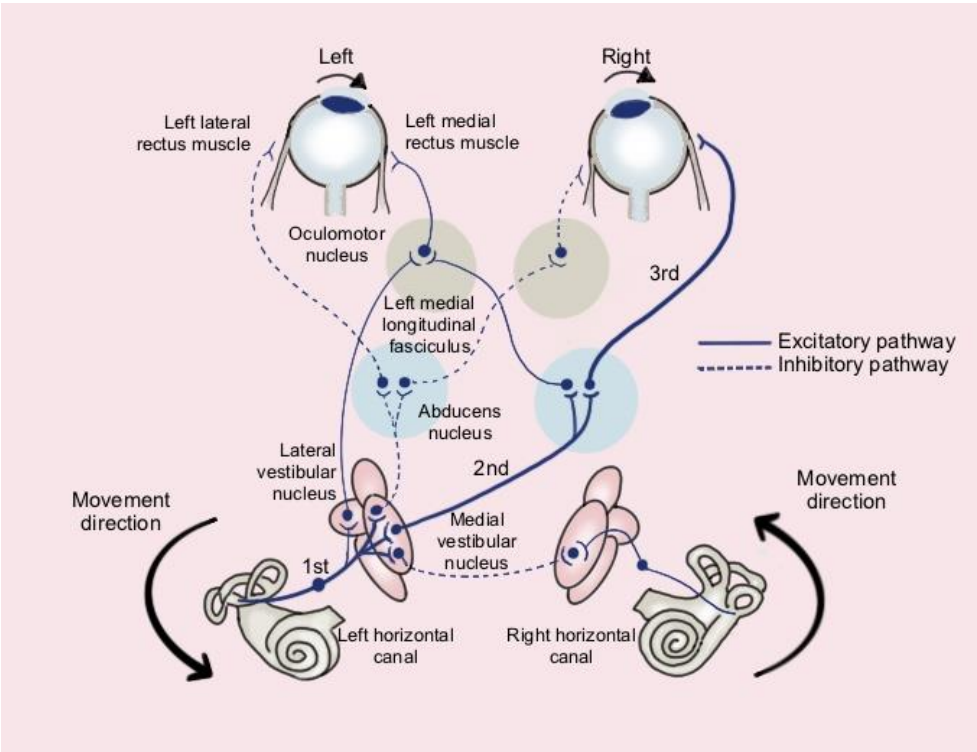


Figure 3. Overview of the vestibulo-ocular reflex (VOR) and its three-neuron arc. Head movement displaces endolymph in the semicircular canals, stimulating hair cells and triggering rapid signals via irregular afferents to the vestibular nuclei (first-order neuron). These signals are relayed to the oculomotor and abducens nuclei (second-order neurons), which then activate the appropriate extraocular muscles (third-order neurons) to generate compensatory eye movements.

Acute unilateral vestibulopathy

Acute unilateral vestibulopathy (AUVP), also known as vestibular neuritis, is a sudden loss of function in the peripheral vestibular system, affecting either the vestibular organs or the vestibular nerve, without any indications of central vestibular dysfunction, such as ischemic stroke or another lesion in the central nervous system.

Terminology

The first description of acute unilateral vestibulopathy (AUVP) was presented by B. Ruttin in 1908, who termed it "Neuritis vestibularis" based on a presumed inflammatory cause[32]. The terminology evolved over time: Nylén introduced "vestibular neuritis" in 1924, and Hallpike proposed "vestibular neuronitis" in 1949 to describe an inflammation that spares the cell bodies in the ganglia, affecting only the axons of the nerve cells. Both terms were based on an assumed inflammatory aetiology, which was later supported by histopathological studies. However, as definitive evidence of inflammation remained inconclusive, a more neutral terminology emerged, including “vestibular neuropathy,” “vestibular failure,” and ultimately “acute unilateral vestibulopathy”. In April 2022, the Bàràny Society formally established the diagnostic criteria for AUVP, standardizing its classification[33].

Epidemiology

Due to inconsistent classification across countries and the recent establishment of international criteria in 2022, existing AUVP incidence data lack standardized epidemiological quality. Prior to standardization, reported annual incidence rates ranged from 3.5 to 15.5 per 100,000[34, 35]. Post-2022 studies still rely on retrospective data not fully aligned with the new criteria. However, a Japanese study using vHIT reported an annual incidence of 7.05 per 100,000[36], while a Norwegian study found a similar rate of 11.2 per 100,000[37].

AUVP is the sixth most common cause of vertigo/dizziness and the third most prevalent peripheral vestibular disorder[38]. There is no gender difference and it can develop at any age[36], though its peak incidence is around 40-50 years[34, 35]. The hypothesis of neuritis or inflammation as the underlying cause of AUVP led to speculation about a seasonal correlation linked to viral spread within the population[39]. However, more recent studies have failed to establish a clear association[40-42]. Reports on AUVP recurrence vary widely, with estimates ranging from 1.9%[43] to 10.7%[44] and up to 23%[45]. However, accurately measuring recurrence rates is challenging, as recurrent vertigo episodes may represent the first mono-

symptomatic manifestation of another peripheral vestibular disorder, such as Menière's disease or vestibular migraine. Additionally, the prevalence of BPPV following AUVP is elevated[46, 47] and can mimic AUVP symptoms and clinical findings, particularly in cases of canalith jam, where otoconia obstructs the entire semicircular canal, causing a blockage of the endolymphatic flow[48].

Etiology

Three main hypotheses have been proposed for the cause of AUVP: viral reactivation, ischemia, and autoimmune response.

Several findings support the viral hypothesis. MRI has been demonstrated to show isolated vestibular nerve enhancement, suggesting inflammation in the affected nerve[49]. A post-mortem study demonstrated inflammatory degeneration of the vestibular nerve[50], while Herpes Simplex Virus type-1 (HSV-1) RNA has been detected in approximately two-thirds of autopsied human vestibular ganglia, along with activated immune cells (CD8+ T cells)[51, 52]. Additionally, two genome-wide association studies identified a higher prevalence of genetic variants linked to HSV-1 replication[53] and a high-risk allele for herpes labialis severity[54] in AUVP patients compared to the general population. These findings suggest that HSV-1 remains latent in the vestibular ganglia and can be reactivated by external or systemic triggers, leading to viral replication. This process induces inflammation, oedema, and secondary cell damage in the vestibular nerve, ultimately triggering the sudden onset of AUVP symptoms.

The labyrinthine artery, which supplies the vestibular system, lacks collateral circulation, making it highly susceptible to ischemic events. The superior vestibular artery, which supplies the horizontal and anterior semicircular canals and the utricle, is believed to be more vulnerable to ischemia than the inferior vestibular artery[55], potentially explaining why AUVP more often affects the superior division of the vestibular nerve while sparing the posterior canal[56]. Additionally, some studies[57, 58] have reported a higher prevalence of cardiovascular risk factors in AUVP patients, with poorer recovery observed in those with hypercholesterolemia [59], suggesting a potential vascular mechanism. However, findings remain inconclusive due to contradictory reports[60, 61].

An autoimmune mechanism is suggested by elevated proinflammatory markers (CRP, IL-1, TNF-α)[62], and increased activation of peripheral blood mononuclear cells[63]. These findings imply that immune-mediated inflammation may contribute to AUVP in some cases, potentially independent of viral or ischemic causes.

Diagnosing acute unilateral vestibulopathy

Acute Vestibular Syndrome (AVS) is characterized by the sudden onset of continuous vertigo, accompanied by nausea, vomiting, and intolerance to head movements. The most common cause of AVS is AUVP, while the second most frequent cause is an ischemic stroke affecting the cerebellum or brainstem, accounting for approximately 10-25% of AVS cases[64]. Given the potential severity of a central cause, stroke should always be considered in the differential diagnosis. No single test can differentiate AUVP from stroke with absolute certainty. Instead, the correct diagnosis relies on a combination of clinical assessments. In 2009, the HINTS acronym was introduced—standing for Head Impulse, Nystagmus, and Test of Skew.

The head impulse test (HIT) was introduced in 1988 by Curthoys and Halmagyi[3] and evaluates the VOR. The patient is instructed to maintain visual fixation on a target straight ahead while an examiner rotates the patients head in the plane of a SCC pair. The head rotations have to be fast (>100 degrees/second) in order to assess the function of the vestibular system only on one ear, and not include responses evoked by oculomotor systems such as optokinetic, cervico-ocular and smooth pursuit[3] or responses evoked by the vestibular system on the other ear[65]. In a patient with a normally functioning VOR, a rapid, passive head movement triggers an equal and opposite eye movement of the same magnitude, allowing the patient to keep their eyes fixed on the target. In cases of AUVP, where the primary VOR pathway is disrupted, the acceleration signal necessary for eye movement is impaired, which results in the eyes drifting away from the target in the direction of the head movement. Once the head stops, the patient must make a corrective saccade to refocus on the target. The presence of a corrective saccade indicates a compromised VOR, meaning the lesion must be located somewhere along the three-neuron arc responsible for the reflex[3]. All three semicircular canal (SCC) pairs can be assessed using the head impulse test (HIT). However, since isolated dysfunction of the inferior vestibular nerve—resulting in posterior canal hypofunction—is rare, HIT is most commonly performed in the plane of the horizontal canals. If no corrective saccade is observed, the findings are inconsistent with AUVP and warrant evaluation for a central vestibular lesion[66]. The bedside HIT is reported to have a sensitivity of 35-66% and specificity of 86-95%[67, 68], and its reliability varies depending on the examiner [69]. Consequently, if the bedside HIT yields inconclusive results, further evaluation with video head impulse test (vHIT) and/or caloric testing is recommended[33].

AUVP predominantly affects the superior vestibular labyrinth, which includes the superior and horizontal semicircular canals, the utricle, and their afferent pathways, collectively forming the superior division of the vestibular nerve[56, 70]. Patients with superior AUVP exhibit nystagmus with the fast phase beating away from the affected ear, with its direction corresponding to the involved semicircular canals.

This typically presents as a horizontal nystagmus with a slight upward torsional component, indicating dysfunction of the lateral and superior semicircular canals. Isolated inferior vestibular nerve involvement is rare, accounting for only 1% of all AUVP cases[71]. In such cases, nystagmus appears as downbeating with a torsional component, indicating posterior semicircular canal involvement. The nystagmus in AUVP decreases in amplitude with visual fixation and intensifies when the patient looks in the direction of the fast phase. It is never purely vertical or direction-changing, as these features are indicative of a central vestibular lesion[72].

Skew deviation is a vertical misalignment of the eyes caused by disruption along the vestibulo-ocular pathway[73]. Patients with normal ocular alignment do not exhibit refixation movements when one eye is alternately covered and then uncovered while the patient focuses on a fixed target. In contrast, those with an impaired otolith-ocular pathway display disconjugate vertical refixation saccades to maintain fixation on the target, indicating skew deviation. While a minor misalignment can occasionally occur in AUVP, skew deviation is more commonly associated with brainstem or cerebellar pathology, such as stroke, multiple sclerosis, or trauma, where the misalignment typically exceeds 3°[74]. It often presents alongside ocular torsion, abnormal head tilt (torticollis), and a distorted perception of vertical orientation, collectively known as the ocular tilt reaction.

The HINTS assessment method was found to enhance diagnostic accuracy, being even better than MRI for detecting stroke during the first 48 hours[75]. A Cochrane review estimated HINTS to have a sensitivity of 94% and a specificity of 87%[76].

Measuring vestibular function

The caloric test

The caloric test, introduced in the early 19th century by Robert Bárány, has remained the gold standard for assessing vestibular function throughout the decades[77] (Figure 4).

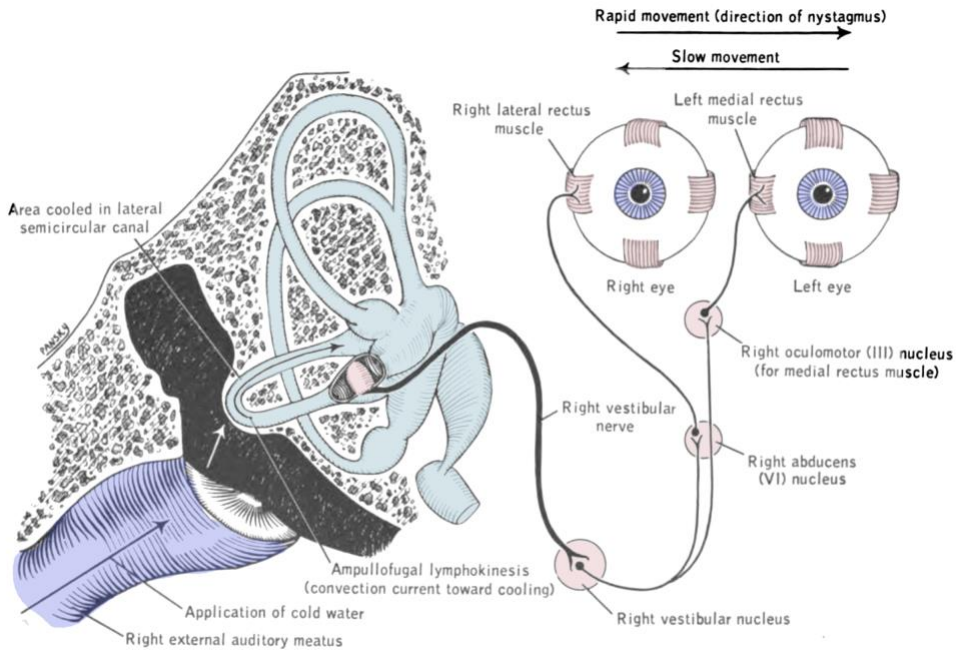


Figure 4. The external auditory canal is irrigated with cold (30°C, as shown) or warm (44°C) water (or air), creating a temperature gradient that induces convective endolymph currents in the lateral semicircular canal. Cold irrigation causes endolymph to sink, deflecting the cupula away from the utricle and inhibiting neural firing. This imbalance in vestibular input produces a sensation of rotation toward the non-irrigated ear and triggers nystagmus with slow phases toward and fast phases away from the irrigated ear. Warm irrigation has the opposite effect. Caloric-induced nystagmus is quantified by measuring peak slow-phase velocity using video-oculography.

Advantages and limitations

The key advantage with the caloric test lies in its ability to evaluate each vestibular organ individually. The caloric test has several limitations. Firstly, it assesses the responses from of the lateral semicircular canal to a stimulation simulating an extremely slow head movement (i.e., a movement frequency of 0.003–0.008 Hz)[77],

which does not reflect the often more straining motion stimuli encountered in daily life. A lack of response to caloric stimulation indicates an inability to detect these artificially induced low-frequency movements but does not provide insight into the semicircular canal's ability to perceive real-world head movements. Additionally, there is considerable variability in individual responses to caloric stimulation, both between ears and among different individuals. These fluctuations arise from anatomical differences, whether congenital or acquired through surgery, infection, or trauma. Additionally, local blood flow variations can influence heat conduction—increased by inflammation or reduced due to vasoconstriction caused by anxiety or pain—leading to either an enhanced or diminished caloric response[78]. To address this limitation, a comparative approach using Jongkees's formula was introduced, assessing the relative response between the left and right ears rather than relying on absolute values:

$$\frac{(\mathrm{R30°} + \mathrm{R44°}) - (\mathrm{L30°} + \mathrm{L44°})}{(\mathrm{R30°} + \mathrm{R44} + \mathrm{L30°} + \mathrm{L44°})} X100$$

The maximum slow-phase velocities from warm (44°C) and cold (30°C) stimulation are summed separately for each ear (R denotes right and L denotes left). The difference between these summed values is then calculated and normalized by dividing it by the total magnitude of all four responses. This quotient is then multiplied by 100, providing a percentage-based measure of vestibular asymmetry and reduced vestibular function[79].

There is no international consensus on the cutoff value for asymmetry to define unilateral vestibulopathy, nor any standardized age-related correction values in the literature. However, an asymmetry greater than 25% (±5) between the two ears has long been regarded as pathological[79] and is widely used as a diagnostic threshold by vestibular labs worldwide. Despite its widespread adoption, this cutoff has not been validated in modern studies that account for patients' clinical signs and symptoms[80]. The caloric test is also a lot more time consuming and unpleasant for the patients compared to vHIT.

The video head impulse test

The VOR can be assessed using the bedside head impulse test, in which the clinician observes how the eyes move in the opposite direction to the head when the patient is asked to maintain fixation on a target during brisk head rotations. In patients with unilateral vestibular loss, a corrective saccade is triggered at the end of each head rotation to realign the gaze with the earth-fixed target[3]. A corrective saccade occurring after the head has stopped moving is visible to the naked eye to the clinician and therefore called overt saccade, and thus, serves as a key clinical sign of canal paresis[33]. However, corrective saccades can also be triggered during the head movement, which makes them difficult to detect with the naked eye. Since these saccades occur during head motion and is not detectable in bedside examination, they are referred to as covert saccades[81] (Figure 5).

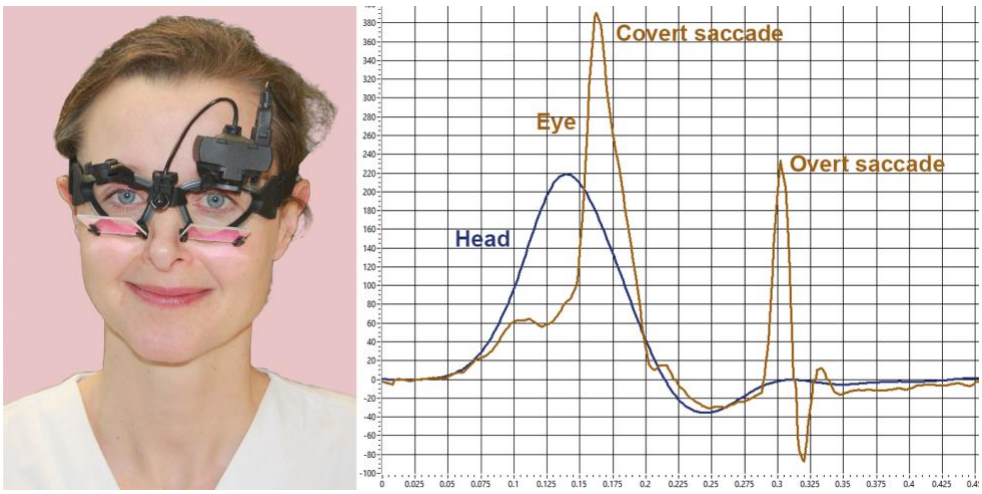


Figure 5. The vHIT goggles use a gyroscope to measure head movements and a high-speed camera to track eye movements, providing an assessment of the VOR. The vHIT procedure is largely the same as the Head Impulse Test (HIT). During the test, the examiner applies small, unpredictable head thrusts in the plane of the semicircular canal to be investigated, while the patient maintains fixation on a stationary target. The system then analyzes whether the eyes accurately compensate for the head movement. A normal VOR results in stable gaze (head and eye movement are of the same size), whereas a reduced VOR (as presented in the figure) leads to the eye position lagging behind the head position. This is addressed by making fast eye movements to catch up, in the form of one covert and one overt saccade.

Quantification of eye movements relative to head motion was historically achieved using the scleral search coil technique, in which magnetic lenses tracked eye movements with high precision[82]. While this method was long considered the gold standard, its semi-invasive nature, complexity, and time-consuming procedure prevented its widespread clinical use. In 2009, the video head impulse test (vHIT)

was introduced[4]. Importantly, vHIT has been demonstrated to be as effective as scleral search coils in detecting vestibular loss in the horizontal canal, both in the acute and chronic phases of dysfunction[4] and in the vertical canals[83].

There are three main methods for quantifying VOR performance, with no universally accepted gold standard: (1) velocity gain - the ratio of eye to head velocity at specific times during the head acceleration phase; (2) regression gain - the slope ratio of eye and head velocity during the head acceleration phase; and (3) position gain - the ratio of areas under the eye velocity and head velocity curves after any saccades has been removed[84]. A normal VOR gain is typically close to 1.0 or at least above 0.8[85]. In unilateral vestibular loss (UVL), gain typically falls below 0.7 during head thrusts toward the lesioned side[86]. Since vHIT measurements are still evolving and no universally accepted method for calculating gains exists, there is a potential for variability in results. Therefore, VOR gains derived from vHIT should be considered estimates influenced by the specific equipment and methodology employed[87].

Advantages and limitations with the test

vHIT is a non-invasive and rapid assessment tool that evaluates the function of all six semicircular canals (SCCs) by measuring VOR performance in the high-frequency range. This range, approximately 0.1 to 10 Hz and peak velocities at about 250 degrees/second, closely aligns with the frequencies detected of the semicircular canals and compensated for by the VOR[88]. Thus, the vHIT tests evaluate the performance when making head movements encountered in daily life[89, 90], making the collected data highly functionally relevant. Furthermore, vHIT provides an objective and quantitative assessment of vestibular function, making it a valuable tool for monitoring recovery and tracking changes over time.

Despite its advantages, vHIT has several limitations. It evaluates at least one pair of semicircular canals at a time. To assess the function in only one semicircular canal, high-acceleration head thrusts are required, as low-velocity head thrusts allow the semicircular oriented in the same plane in the other ear to contribute to the eye movement response[4]. Individual and interindividual anatomical differences in canal plane orientation[91] can further contribute to variability in VOR gain values, as head thrusts intended to stimulate only one canal may simultaneously also stimulate and evoke responses from other semicircular canals[15]. Another limitation is that vHIT reduces the complex three-dimensional eye movement response to a one-dimensional measurement, preventing the detection of torsional movements. This effect is most apparent when testing the vertical canals[92].

Additionally, artifact susceptibility remains a significant issue, with artifacts reported in approximately 30–55% of vHIT[93]. These artifacts can originate from technical errors, including incorrect goggle placement[92], goggle slippage[94], or goggle bounce[93]. Recording issues, such as head thrust oscillations, data recording

loss, or equipment miscalibration, can also compromise data quality[93]. Furthermore, participant-related factors, such as neck rigidity, low eye lid recording artifacts[95] and loss of the patients attention to focus the gaze[93], can contribute to measurement errors, leading to artificially high or low VOR gain values.

The functional Head impulse test

The Functional Head Impulse Test (fHIT) or Head Impulse Testing Device-Functional Test (HITD-FT) is a clinical tool designed to assess how well the VOR performs in respect to its goal of stabilizing gaze and improving visual performance. Early attempts to evaluate this concept involved presenting a stationary optotype during head rotations[96]. However, these approaches were often considered to have limited validity, as they could not account for the contribution of pursuit eye movements that occur when head velocity decreases during sinusoidal motion. A major advancement in functional VOR testing came with the development of computerized systems, which allowed visual acuity to be tested dynamically as a function of head velocity[97]. fHIT is a modern dynamic visual performance test. fHIT measures the head movement with a gyroscope but unlike the vHIT, which measures VOR gain using high-speed eye tracking, fHIT directly tests functional vision by requiring patients to identify a visual symbol while performing rapid head movements (Figure 6). The percentage of correctly recognized optotypes provides a functional measure of how well the VOR functions can provide visual stability during movements[98].

Figure 6. The test starts with an assessment of static visual acuity. The subsequent fHIT is then performed using an optotype size calculated from the size of the smallest correctly detected optotype multiplied by a factor of 0,8logMAR.The examiner then delivers unpredictable, passive head impulses in the plane of the semicircular canals. During the test, the patient wears a headband equipped with a gyroscope that measures the head movement. During each head impulse, a random optotype consisting of a small circle with an opening in eight different directions, appears briefly on a screen, which the patient must identify by pressing the correct key on a keyboard.

Advantages and limitations

The advantages and limitations of fHIT are similar to those of vHIT, with some notable differences. fHIT tests may be more comfortable to perform for patients, as it does not require goggles - only a lightweight headband. Additionally, since fHIT does not rely on pupil tracking, it is not directly affected by artifacts related to eye movement recording, such as goggle slippage or reflections. A key benefit is its educational value for patients, as it provides a clear, visual representation of their functional improvement following vestibular loss. However, fHIT has low specificity, meaning it cannot differentiate between peripheral and central vestibular disorders, often necessitating further diagnostic testing for a more precise diagnosis.

Self-perceived dizziness

Subjective dizziness and well-being after vestibular loss can be assessed using self-reported questionnaires that evaluate the impact of dizziness, imbalance, and vestibular dysfunction on daily life.

The Dizziness Handicap Inventory (DHI) is the most widely used questionnaires for evaluating the impact of dizziness on quality of life[99]. It consists of 25 questions, categorized into three subscales: functional, emotional, and physical. The functional subscale assesses how dizziness affects daily activities such as walking, driving, and social participation. The emotional subscale evaluates the psychological impact of dizziness, including frustration, fear of falling, and anxiety. The physical subscale measures dizziness-related symptoms triggered by head movements or environmental factors. Each item is scored as Yes (4 points), Sometimes (2 points), or No (0 points), with a total possible score ranging from 0 to 100[100]. The questionnaire has been translated into Swedish, validated in the Swedish population[101], and is widely used in clinical practice.

The Hospital Anxiety and Depression Scale (HADS)[102] is a self-assessment questionnaire designed to detect symptoms of anxiety and depression in patients. It consists of 14 items, divided into two subscales: 7 for anxiety (HADS-A) and 7 for depression (HADS-D). Each item is scored from 0 to 3, a higher score depicts a worse condition, giving a maximum score of 21 for each subscale. HADS is widely used for evaluating psychological distress and has been translated and validated in Swedish[103].

A Likert scale is a discrete, ordinal scale commonly used to assess the severity or impact of different symptoms, amongst other dizziness and vertigo. Patients rate their symptoms on a scale with a fixed number of response options, typically ranging from 1 = No dizziness to 10 = Worst dizziness imaginable. The advantage of a Likert scale is its simplicity and ease of interpretation, though it may be less sensitive to small changes in symptom severity[104].

Advantages and limitations

DHI, HADS and Likert scales are non-invasive, quick tools to evaluate how well a patient is doing after AUVP. One could argue that the results only represent the overall outcome of vestibular recovery and compensation. However, how a patient rates their well-being or handicap after AUVP is also strongly influenced by psychological factors and personality traits, particularly an individual's ability to cope with challenges. These factors will also be reflected in self-reported assessments[105].

Vestibular recovery and compensation

AUVP initially induces nystagmus, severe dizziness, postural instability, ocular head tilt reaction and nausea due to the asymmetry in vestibular signaling between the two vestibular organs. This persistent imbalance is disruptive to normal neural processing, prompting the brain to rapidly initiate compensatory mechanisms to adapt to the loss of sensory input from one vestibular organ. This is a complicated and multimodal process occurring both in the periphery (the vestibular organ, hair cells and vestibular nerve) but mostly centrally (vestibular nuclear complex, cerebellum, brain)[106]. Different compensatory processes are initiated at the same time but for simplistic reasons they are often described in relation to the stages of symptom relief.

Vestibular recovery

It is important to note that most studies on vestibular compensation have been conducted using an idealized model of complete permanent unilateral vestibular loss, typically induced through surgical labyrinthectomy or vestibular nerve section. In contrast, AUVP, which is thought to result from viral reactivation or ischemia, could in theory cause reversible and partial rather than total and permanent destruction of the vestibular organ or nerve. Full recovery of vestibular function, as indicated by restoration of VOR gain measured with vHIT, has been observed[107]. Such recovery may be attributed to regeneration of peripheral sensory hair cells, sprouting of new afferent terminals from remaining vestibular nerve fibers, or increased synaptic weighting of residual vestibular inputs, enabling functional restoration despite initial damage[108]. Recovery of vestibular function in long term follow ups (1-10 years post lesion) as measured by the caloric responsiveness has been reported to be in the range of 40-80 %[109-111] and as measured by vHIT 6 months after the onset to be about 80%[112]. If a patient's vestibular function is fully restored, this should be regarded as recovery rather than compensation. However, throughout the healing process, the patient will likely have relied on compensatory mechanisms to maintain balance and gaze stability in parallel with physiological restoration.

Compensation of static symptoms

AUVP disrupts vestibular signaling on one side, leading to an imbalance in neural activity between the two vestibular nuclei. The static symptoms experienced while sitting or lying still - spontaneous nystagmus, head tilt, ocular tilt, and postural imbalance - are a direct result of this asymmetry. However, these symptoms typically diminish within the first few days to a week after the onset as the brain begins to compensate[108].

Following vestibular injury, specific genes are upregulated within hours, initiating a cascade of molecular and cellular events over the following days. A microglial and an astroglial response emerges as early as one day post-lesion, persisting for several weeks in animal models[113-115]. This response correlates with elevated inflammatory markers, indicating neuroinflammation[116]. Simultaneously, levels of neuroprotective and neurotrophic factors increase, along with proteins involved in axonal growth, suggesting that neural protection and structural reorganization occur in parallel within the vestibular nuclear complex[108].

During the initial phase of vestibular compensation, cerebellar inhibition of the vestibular nuclei was traditionally believed to play the primary role[117]. However, more recent studies[118, 119] suggest that it is rather the commissural vestibular system—which connects the vestibular nuclei on both sides of the brainstem through reciprocal inhibitory pathways—that plays the main part. By modulating neural activity through GABA-mediated inhibition, the commissural vestibular system plays a key role in restoring balance between the vestibular nuclei, thereby alleviating the static symptoms of AUVP. These early neuroplastic adaptations and the rebalancing of neural activity within the vestibular nuclei have been demonstrated using functional-PET imaging, which measures regional glucose metabolism in the brain[120]. However, the cerebellum plays a crucial role in recovery after AUVP, as studies have shown that cerebellar lesions can delay or impair the resolution of static symptoms and hinder the initiation of behavioral recovery[121, 122]. It is also thought that the vestibulocerebellum plays a crucial part in consolidating vestibular compensation[123].

Compensation of dynamic symptoms

Dynamic symptoms, meaning those that occur during movement due to a disrupted VOR, tend to persist longer and are often not fully compensated[124]. The compensation of dynamic deficits involves a combination of neural[125] and behavioral compensation[26, 108]. The shared characteristics of these mechanisms are that they involve an active learning process, that inquire the patient to interact with the environment to recalibrate the vestibular system.

Synaptic alterations

Synaptic alterations may play a crucial role in stabilizing and reinforcing early functional recovery following vestibular loss. One key mechanism involves the sprouting of intact vestibular nerve fibers, which form new synaptic connections in the deafferented vestibular nuclei, a process observed within weeks in animal models[126]. Additionally, an increase in post-synaptic receptor density enhances the sensitivity of remaining vestibular inputs, thereby amplifying neural responses[127]. Given the widespread connectivity of central vestibular networks, it is likely that synaptic plasticity extends beyond the vestibular nuclei, influencing multiple brain

regions and contributing to the broader compensatory process and functional recovery[120].

Behavioral vestibular compensation

Behavioral vestibular compensation refers to the adaptive strategies and motor adjustments individuals develop to cope with vestibular dysfunction, allowing them to regain postural stability, gaze control, and spatial orientation. Unlike neural compensation, which involves plasticity within the vestibular pathways, behavioral compensation encompasses both conscious and unconscious modifications in movement patterns, sensory strategies, and motor planning to reduce dizziness and imbalance. However, one could argue that all forms of compensation ultimately involve changes at the synaptic or even gene expression level, suggesting that the distinction between neural and behavioral compensation may be somewhat obsolete. Instead of viewing them as separate processes, it may be more accurate to consider behavioral adaptations as an outward manifestation of underlying neural plasticity. Sensory reweighting, also known as sensory substitution, refers to the replacement of lost vestibular information with sensory input from another functioning sensory system. For example, it is well established that patients with vestibular loss that compensate by relying more on visual information have a better balance[128, 129]. Similarly, minimizing postural challenges helps reduce the risk of falls or missteps, allowing for greater stability. For instance, studies have observed that individuals with vestibular injuries tend to walk and move slower[130].

As previously described, corrective saccades—considered a cardinal sign of AUVP—are generated to redirect the eyes back to the visual target, compensating for impaired gaze stability[131]. When corrective saccades occur after the head movement has ceased, they are visible to the naked eye and are known as overt saccades, forming the basis of a clinically positive head impulse test[3]. In contrast, saccades that occur during the head movement are most often not visible without recording equipment and are therefore termed covert saccades[81]. Covert saccades are initiated during head movement[81, 131], significantly faster than volitional saccades i.e. conscious saccades directed toward a new target[132].

Previous research has demonstrated that actively generated head movements can trigger covert saccades with shorter latencies[133] and that active movements improve dynamic visual performance, compared to passive movements[134] This would in turn suggest that rehabilitation strategies should be designed to promote the generation of covert saccades[135]. Additionally, it has been proposed that covert saccades with short latencies help reduce oscillopsia and enhance visual performance even during passive/unpredictable head movements[136]. It has also been suggested that the initial saccade responses may transition from overt to covert saccades over time[137] and that the latency of covert saccades may progressively decrease - even during passive, unpredictable movement. Such evolution in saccadic behavior could serve as an indicator of successful central compensation following vestibular loss[107, 138].

What triggers covert saccades is not known. The error signal induced by retinal slip i.e. the motion of a visual image across the retina when the eyes fail to stabilize a target effectively during a head movement has been put forward as a possible trigger[139]. Somatosensory signals from the neck muscles via the COR or efference copy has been suggested[138, 140]. Other potential sources of activation may include residual vestibular function[81].

Treatment of Acute unilateral vestibulopathy

Antiemetic treatment

Antiemetic treatment, including antihistamines and serotonin receptor antagonists (5HT3-blockers), is frequently prescribed in the first few days to relieve nausea and vomiting in patients with AUVP. However, its use should be restricted, as many of these medications—particularly antihistamines—have sedative properties that may impede early patient mobilization[141], delaying the initiation of vestibular rehabilitation and hindering the compensatory process.

Corticosteroid treatment

Due to their anti-inflammatory properties, corticosteroids have been the reference treatment for various inflammatory diseases and brain injuries for many years[142, 143]. Their use in AUVP is based on the premise that they may reduce inflammation in the vestibular nerve, thereby preventing nerve swelling, reducing the risk of entrapment and fiber necrosis, and potentially increasing the chance of recovery[20]. While viral reactivation as the cause of AUVP is not yet fully established, evidence indicates that it triggers a neuroinflammatory response, characterized by an increase in microglia, astroglia, and associated inflammatory proteins[113-115]. AUVP has additionally been shown to activate the hypothalamo-pituitary-adrenal axis or the stress axis, leading to a strong release of endogenous corticosteroids within the deafferented vestibular nuclei[144], reenforcing a neuroinflammatory process. The activation of the stress axis and the modulation of the neuroinflammatory process have been identified as potential therapeutic targets for corticosteroid treatment. Several animal studies have reported beneficial effects of corticosteroids on vestibular compensation[145, 146]. However, more recent research suggests that acute endogenous neuroinflammation may play a positive role in facilitating neuroplasticity mechanisms, ultimately enhancing functional recovery after AUVP, and that a inhibition of this process would be directly harmful for the vestibular compensation process[147].

In humans, the effects of corticosteroid treatment on vestibular function have been inconsistent. Some studies have demonstrated that corticosteroids improve vestibular function, as measured by caloric responsiveness, both in the acute phase (<3 months)[111, 148] and in the chronic phase (6-24 months after AUVP onset) [110, 149-151]. However, other studies have found no significant effect on caloric responsiveness in either the acute[112, 152] or chronic phase[111, 112, 152, 153]. Similarly, while some studies suggest corticosteroids reduce symptoms in the acute phase[149, 154-156], others report no significant difference in vertigo or nausea symptoms during this period[157, 158].

Studies have varied in their inclusion criteria, corticosteroid dosage, and treatment duration, while many other studies lack randomizations, placebo control, or blinding, which may contribute to inconsistent findings. Importantly, the timing of treatment initiation has also differed significantly across studies, ranging from within 48 to 72 hours to up to one week after symptom onset, with some not specifying the time frame at all. In Bell's palsy, an idiopathic facial nerve palsy with a suspected viral reactivation etiology similar to AUVP[159], corticosteroid treatment has been shown to be effective [159] with the greatest recovery of nerve function when administered within 48 hours from onset[160], emphasizing the potential importance of early intervention.

Corticosteroids are associated with several side effects, including hyperglycemia, hypertension, gastric ulcers, insomnia, temporary immunosuppression, confusion, irritability, and psychiatric disorders such as depression or mania[161].

Six meta-analyses[162-167] have concluded that there is insufficient evidence to recommend corticosteroid treatment for AUVP. However, the most recent meta-analysis contradicts these findings, advocating for corticosteroid treatment in AUVP[168]. Despite mixed evidence, corticosteroids remain the most used treatment for AUVP worldwide[169].

Vestibular rehabilitation

Vestibular rehabilitation is designed to enhance central compensation following vestibular dysfunction. A Cochrane review concluded that there is moderate to strong evidence supporting vestibular rehabilitation for unilateral peripheral vestibular dysfunction, including AUVP[170]. It reduces symptom intensity and duration[171, 172] with long-term effectiveness comparable to corticosteroids[148, 152], and greater short-term benefit within the first month[173].

Some knowledge gaps and research questions

Studies in both animals and humans have produced contradictory results regarding the efficacy of corticosteroids promoting vestibular recovery. In the largest double-blind RCT, Strupp et al[110]. demonstrated improved vestibular function recovery with corticosteroid treatment. However, several other studies have failed to do the same. While corticosteroids often cause discomfort due to their side effects, they also carry the risk of potentially severe adverse reactions.

Are corticosteroids effective for recovery of vestibular function recovery or reduced symptoms in the acute and in the chronic phase?

The initiation of treatment has varied among studies. Notably, research on Bell's palsy has shown that nerve function recovery is significantly improved when treatment is initiated within 48 hours.

Is there an optimal timing of corticosteroid administration in AUVP, specifically does early intervention play a critical role in its potential efficacy?

Vestibular compensation is a complex, multimodal process, vHIT has become a valuable tool to analyze one aspect of this process—the VOR and the corrective saccades that occur when VOR function is impaired. However, the mechanisms underlying the generation of corrective saccades and their exact role in compensation remain incompletely understood.

Are covert and overt saccades functionally relevant for gaze stabilization?

Currently, no objective measure can definitively determine whether a patient has fully compensated after AUVP. The pattern of corrective saccades, particularly the transition from a mix of covert and overt saccades to predominantly covert saccades, has been suggested as a potential indicator of successful compensation.

Should covert saccades be recognized as a reliable marker of successful vestibular compensation?

Aims

The overall aims of this thesis were to enhance the treatment for patients with AUVP and to gain a better understanding of compensational mechanisms after AUVP.

The specific intentions for the conducted studies were:

Paper I
To evaluate if an early start of treatment with corticosteroids in patients with AUVP enhances the recovery of vestibular function.

Paper II
To prospectively evaluate if corticosteroid treatment enhanced recovery of vestibular function and reduce symptoms in the acute and chronic phase of AUVP.

Paper III
To assess whether VOR gain, the presence and latencies of covert saccades in patients with complete unilateral vestibular loss are influenced by self-generated versus passive head movements, and to determine how these factors impact visual performance.

Paper IV
To analyze how covert saccades improve visual performance during self-generated and passive movements in patients with a complete unilateral vestibular loss.

Paper V
To investigate the course of vestibular recovery and the development of compensatory strategies - particularly the evolution of saccadic behavior - from the onset of AUVP to one year after the onset.

Methods

Study populations

In Paper I, a retrospective analysis was conducted on 33 patients diagnosed with acute total unilateral vestibulopathy (AUVP). All patients had been treated with corticosteroids within three days of symptom onset and closely monitored by the Department of Otorhinolaryngology, Skåne University Hospital, Lund, between July 2004 and December 2005.

In Papers II and V, patients aged 18–80 years with AUVP were prospectively recruited from the Emergency Departments and the Departments of Otorhinolaryngology at three sites in southern Sweden: Skåne University Hospital Lund, Kristianstad Hospital, and Helsingborg Hospital, between December 1, 2015, and March 1, 2021. Eligibility required fulfillment of criteria consistent with the Bárány Society diagnostic criteria for AUVP[33], except for the 24-hour symptom duration criterion. Instead, patients were categorized as having "AUVP in evolution" within the same classification system. Participants had to be capable of providing informed consent and were excluded if they had a history of vertiginous disease or if symptom onset occurred more than 48 hours before possible inclusion. A total of 75 patients were randomized into one of three groups: placebo, 3-day corticosteroid treatment, or 10-day corticosteroid treatment. Of these, 69 patients were included in the final modified intention to treat analysis in Paper II.

In Paper V, 43 patients from study II were included in the final analysis. Twenty-six were excluded due to the use of non-Interacoustics equipment or technical issues transferring vHIT data from the Interacoustics system to the custom-made LabVIEW software.

In Papers III and IV, patients with complete unilateral vestibular loss were included. This cohort consisted of eight individuals who had undergone translabyrinthine schwannoma surgery (mean time since surgery: 8 years; range: 1–16 years) and one patient with unilateral congenital vestibular loss, likely resulting from an intrauterine cytomegalovirus infection. Due to technical issues, in Paper IV data from one schwannoma patient could not be analyzed, resulting in a total of eight patients in the final analysis. Complete vestibular loss was confirmed by bi-thermal caloric testing, video head impulse testing (vHIT) of all six semicircular canals, and cervical vestibular evoked myogenic potentials (cVEMP).

The caloric test

Vestibular function was assessed using the caloric test in Paper I and II. Patients were positioned in a supine posture with the head elevated at a 30° angle to align the horizontal semicircular canals vertically. Infrared video oculography goggles (Interacoustics, VisualEyes), which eliminated visual fixation by blocking all external light, were used to record eye movements. Caloric stimulation was performed using water at 30°C and 44°C in both ears, and the mean peak slow-phase velocity of the induced nystagmus was measured for each irrigation. Vestibular asymmetry was calculated using Jongkees's formula (see section Measuring vestibular function) for vestibular paresis. An interaural difference exceeding 32%[174] in Paper I and 22% in Paper II (normative value at the Department of Otorhinolaryngology, Skåne University Hospital, Lund) was considered indicative of abnormal vestibular function.

video Head Impulse Test

Vestibular function was also evaluated using the video Head Impulse Test (vHIT) in Papers II-V. In Paper II, vHIT was performed using a combination of systems: Interacoustics EyeSeeCam (version 1.2, Interacoustics A/S, Middelfart, Denmark)[175], ICS Impulse video goggles (Otometrics, Taastrup, Denmark)[65], and SYNAPSIS[176]. In Papers III–V, the Interacoustics EyeSeeCam system (version 1.2) was consistently used to assess VOR gain in all six semicircular canals. However, as the vHIT provides the highest precision in assessing the horizontal (lateral) semicircular canals, only data from the lateral canals are presented in all papers. In the final gain analysis (Paper II), regression-based gain was used for patients assessed with the Interacoustics software, while area-under-the-curve gain was used for those examined with the Otometrics and SYNAPSIS systems. In Paper III, regression-based gain was also utilized. In Paper V, both regression-based gain and gain values at 40, 60, and 80 ms are presented.

The vHIT procedure was the same (Paper II-V); the subject was seated in an armless chair positioned 1.5 meters in front of a white wall, fixating on a 3 × 3 cm blue marker placed at eye level, which served as the visual target throughout the test. Subjects were instructed to maintain fixation on the target at all times. All tests were conducted by two different examiners (Paper II and V) and by the same examiner (Paper III and IV), who stood behind the subject and manually applied rapid, passive horizontal head impulses. These movements had peak velocities exceeding 150°/s, accelerations/decelerations typically between 3,000 and 8,000°/s², and amplitudes of approximately 10–20°. Testing continued until the Interacoustics software had accepted the characteristics of at least 10 performed head impulses in each direction.

In Paper III and IV, patients performed active horizontal head movements adhering to the same criteria of peak velocity, acceleration, and amplitude as was used during the trials with passive head movements. Participants were allowed to make practice attempts before the actual recording. Testing proceeded until the software had accepted the characteristics of at least10 active head movements per direction.

functional Head Impulse Test

In Papers III and IV, vestibular function was assessed using a functional test of visual performance - the Head Impulse Testing Device - Functional Test (HITD-FT), also known as the fHIT (Beon Solutions Srl, Zero Branco (TV), Italy)[98, 177]. Participants were seated 1.5 meters in front of a full HD fHIT monitor (1920 × 1080 resolution, 60 Hz refresh rate), wearing a head-mounted accelerometer and holding a keyboard. Before initiating the functional test, static visual acuity was assessed. During this pre-test, the participant viewed scaled Landolt C optotypes, starting at a size corresponding to 1.0 logMAR (logarithm of the Minimum Angle of Resolution). The optotype size decreased progressively across 20 trials, based on the participant's error rate. The smallest correctly identified optotype size was used to determine the stimulus size for the fHIT trials, calculated as 0.8 logMAR of that baseline size.

During the first fHIT session, the examiner manually applied horizontal head impulses until the software had accepted 10 impulses in each direction. A valid head impulse was defined by the software as having an acceleration between 3,000–6,000°/s². The subject was instructed to fixate on a central dot on the screen. As soon as the angular head velocity exceeded 10°/s and acceleration surpassed 300°/s², the software triggered a Landolt C optotype (in one of eight orientations) after a delay of approximately 62 ms. The optotype remained visible for 83 ms. The participant was then prompted to identify the orientation of the symbol by pressing the corresponding button on the keyboard. In the second fHIT session, the same testing procedure was followed, but the head impulses were performed actively by the participants themselves. Participants were allowed a brief familiarization period and typically required only a few trials before performing consistent and reliable self-generated head thrusts.

fHIT performance was expressed as the percentage of correctly identified optotypes, as calculated by the fHIT 1.0 software system.

Self-rated symptoms and questionnaires

In Papers II and V, subjective well-being was assessed from the onset of AUVP through one year post-onset. During the acute phase (the first month), vertigo severity was self-rated daily using a Likert scale ranging from 1 (no symptoms) to 10 (worst possible symptoms). In the chronic phase—specifically at the 3- and 12-month follow-ups - self-perceived disability related to dizziness was measured using the Dizziness Handicap Inventory (DHI)[100], while psychological distress was assessed with the Hospital Anxiety and Depression Scale (HADS)[102]. The DHI consists of 25 items evaluating the frequency of dizziness-related difficulties or distress in everyday situations. Each item is rated on a 5-point scale from 0 (no distress) to 4, with total scores ranging from 0 (no perceived handicap) to 100 (maximum perceived handicap). The HADS is a 14-item questionnaire comprising two subscales—Anxiety and Depression—each with seven items. Responses are scored from 0 (no symptoms) to 3 (severe symptoms), yielding subscale scores between 0 and 21. Validated Swedish versions of both the DHI[101] and HADS[103] were used.

Adverse events

In Paper II all patients received written information regarding the potential adverse effects of corticosteroid treatment. They were instructed to record any side effects or adverse events in a diary throughout the study period. Adverse effects were systematically assessed during follow-up visits at 1 month, 3 months, and 1 year post-treatment initiation. Treatment was discontinued if a patient chose to withdraw from the study at any point.

Data analysis in custom-made Labview software

In Papers III-V the vHIT recordings were analyzed by a custom-made Labview software. Initially, the recordings were screened for artifacts in the eye position trace. This included removing trials affected by eye blinks, noise due to failed pupil detection or segmentation by the recording software, anticipatory eye movements, and slippage of the goggles, as indicated by eye movements occurring before the head movement onset.

In Papers IV and V, the error between eye and head movements was analyzed. As a first step, the correspondence between eye and head movement amplitudes was verified for each trace, acknowledging that the Interacoustics vHIT system records these signals via different techniques - eye movements through video tracking and

head movements via an accelerometer. Positional data for both eye and head movements were computed over a 700 ms window, including ~50 ms prior to head movement onset, by integrating the recorded velocity signals. Total displacement was determined by identifying stable start and end points and calculating the difference between them. To ensure accurate comparison, eye position data were corrected at the sample level using head position data as a reference, aligning the overall movement amplitude of both signals. These normalized position traces were then used for further analysis. When required, corresponding velocity and acceleration values were derived from the normalized position data.

The software automatically analyzed eye velocity data to detect the presence of corrective saccades (Paper II-V). Detected saccades were classified as covert if initiated during the head movement and as overt if initiated after the head movement had ceased. A saccade was considered present - either toward the lesioned or contralesional side - if it occurred in more than one head impulse in the same patient (Paper III and V).

In Paper III-V; for each first covert and overt saccade, the software measured the peak latency, defined as the time (in seconds) from head movement onset to the peak saccade velocity, and recorded the peak velocity (°/s). Head movement onset was defined as the point at which head velocity exceeded 30°/s. Corrective saccades were identified based on three criteria: a peak velocity greater than 80°/s, acceleration and deceleration phases exceeding 3,000°/s², and a duration between 10 and 80 milliseconds.

In Paper IV, the software calculated the absolute mean error between eye and head position across three defined time windows. The first window covered the entire head movement, beginning when head velocity exceeded 10°/s and ending when it dropped below that threshold. The second window represented the delay period, spanning from the moment head velocity surpassed 10°/s to 62 milliseconds later - reflecting the delay used in the fHIT test. The third window corresponded to the optotype presentation period in the fHIT test, starting 62 ms after head velocity first exceeded 10°/s and lasting for 80 ms.

In Paper V the software also calculated the amplitude (°) of each saccade and the gaze error at both the onset and completion of the saccade movement. Gaze error at the onset was defined as the positional difference between the head and eye at the start of the saccade, while gaze error at the end was defined similarly at the point of saccade completion.

Statistical methods

Across the five studies, data distribution was assessed visually and, when skewness was suspected, verified using the Shapiro-Wilk test. If data were not normally distributed, log-transformation was applied (Paper II – DHI and HADS scores). Group comparisons and within-group changes were primarily analyzed using repeated measures GLM ANOVA or Friedman's test (Paper V). Due to relatively small sample sizes and occasional non-normality, non-parametric post hoc tests (Mann-Whitney U and Wilcoxon signed-rank tests) were used. Fisher's exact test and chi-square were applied for categorical comparisons. Bonferroni correction was used to adjust for multiple comparisons. Spearman correlation was used to examine associations between variables. In Paper II power calculations were made for the primary end point (caloric responsiveness) and based on Strupp et al.[110]. The mean (±SD) difference requirements were set to 25 ±26% (calculated with Jongkees's formula)[79]. The power analysis yielded an effect size of 0.96 and a sample size requirement of 18 patients in each group, assuming a t-test for difference between two independent means (two groups), a two-sided alpha level of 0.05 and a statistical power of 0.80. In Paper III and IV the sample size analyses were performed on the parameters used that were unaffected by boundaries (i.e., the f-HIT-score and the frequency of covert saccades parameters could only assume values within the range of 0–100). The sample size analysis of the vHIT gain parameter revealed an effect size of 1.8, which shows that with the p-value set to 0.05 (2-tailed), our study would require n = 5 subjects to reach a power value of 0.8 for this parameter. The sample size analysis of the saccade peak latency parameter revealed an effect size of 2.2, which shows that with the p-value set to 0.05 (2-tailed), our study would require n = 4 subjects to reach a power value of 0.8 for this parameter.

All statistical analyses were performed using IBM SPSS Statistics (versions 24–28) and power calculations were made in GPower software (versions 3.1 – 3.1.9.7).

Ethical considerations

All studies were approved by the regional ethics board, Etikprövningsmyndigheten, Lund, Sweden; DNR 2017/400 for Paper I, DNR 2015/5 for Paper II and V, DNR 2016/32 for paper III and IV. In the prospective studies (Paper II-V) all patients gave their written and informed consent prior to participation.

Investigations and results

Paper I

Study population: Thirty-three patients (17 men, 16 women), aged 17–85 years (mean 57), diagnosed with AUVP and treated with corticosteroids within 72 hours of symptom onset.

Study design: Retrospective analysis of caloric asymmetry after 3 months. All patients received oral prednisolone (50 mg/day for 5 days, followed by a tapering regimen of 10 mg/day over the next 5 days). Intravenous betamethasone was used if the patients were unable to tolerate oral medication the first days. Patients treated within 24 hours (n=9) were compared to those treated between 25 and 72 hours after symptom onset (n=24).

Results: All patients treated within 24 hours showed normal caloric test results at 3-month follow-up, compared to 58% of those treated between 25–72 hours ($p<0.05$).

Conclusion: Early steroid treatment within 24 hours of symptom onset in AUVP improves vestibular recovery, as measured by caloric test normalization. The results suggest a time-sensitive therapeutic window, thus supporting an early intervention with glucocorticoids for better vestibular restitution.

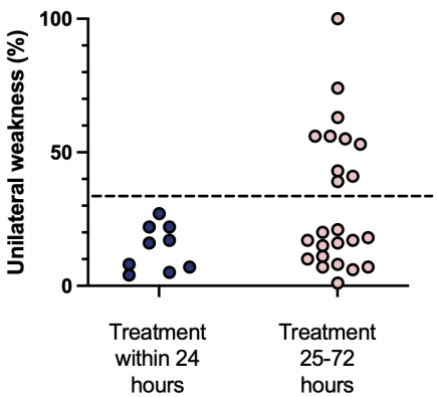


Figure 7. Caloric responses at follow-up after 3 months for treatment within 24 hours versus after 24 hours. Dashed line indicates cutoff for normal caloric response (32%).

Paper II

Study population: a modified intention to treat population of 69 patients (mean age =55 years, range 22–78 with AUVP recruited within 48 hours of symptom onset from emergency departments at three sites in southern Sweden between 2015 and 2021.

Study design: A randomized, placebo-controlled, double-blind trial comparing three groups: placebo, 3-day corticosteroid treatment, and 10-day corticosteroid treatment. The primary outcome was canal paresis (caloric asymmetry) after 12 months. Secondary outcomes included caloric asymmetry after 3 months, VOR gain measured by vHIT at onset, 1 month, 3 months, and 12 months; daily vertigo severity recorded over the first month using a Likert scale; and self-reported measures of dizziness-related handicap (DHI) and psychological distress (HADS) evaluated at 3 and 12 months.

Results: All groups demonstrated a significant decrease in caloric asymmetry over time ($p=0.002$), with no significant differences between treatment groups at any time point ($p=0.629$). In the 10-day steroid group, caloric asymmetry significantly decreased from 63±35% at one week to 37±35% at 12 months ($p=0.014$). The 3-day steroid group showed a non-significant trend toward improvement, with asymmetry decreasing from 60±33% to 41±34% ($p=0.039$), while the placebo group showed minimal change, from 64±38% to 54±38% ($p=0.496$). Corticosteroid treatments were well tolerated, with no safety concerns observed.

All groups exhibited progressive improvement in ipsilesional vHIT gain over time ($p < 0.001$); however, no significant treatment effect was observed ($p = 0.687$).

Vertigo symptoms, measured on a Likert scale, decreased significantly in all groups during the first month ($p < 0.001$); however, no significant differences were found between the corticosteroid-treated groups and the placebo group ($p = 0.524$). Self-perceived dizziness handicap, assessed with the DHI, showed significant improvement between the 3- and 12-month follow-ups ($p=0.006$), but again, no differences were observed between treatment groups ($p=0.454$). Scores on the HADS remained low for both anxiety and depression, with no significant change between the 3- and 12-month follow-ups, and no differences between the treatment groups.

Conclusion: The findings indicate that corticosteroid treatment does not improve symptoms in either the acute phase or in the long-term phase of AUVP, nor does it lead to substantial recovery of vestibular function.

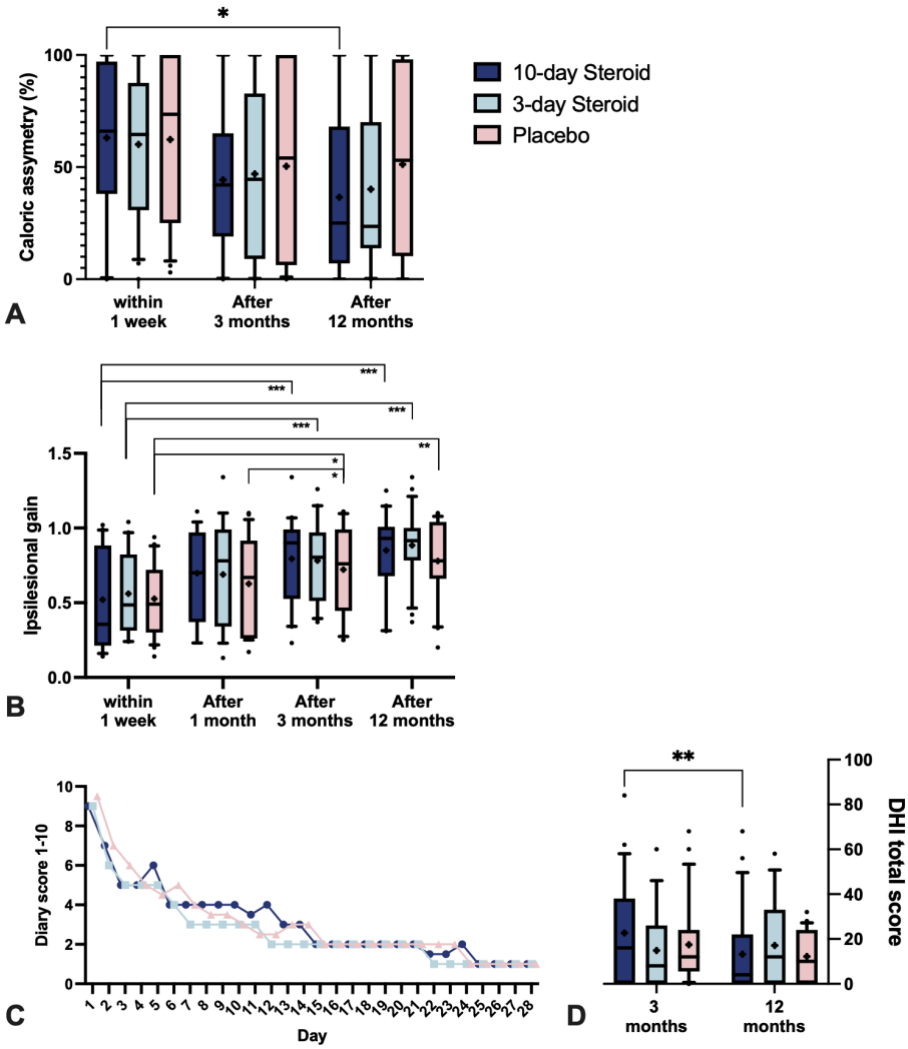


Figure 8. Outcomes from Paper II comparing caloric function, vHIT gain, and subjective symptoms across treatment groups. A) Caloric asymmetry with Bonferroni-corrected significance levels (*p < 0.025). B) Ipsilesional vHIT gain with Bonferroni correction (*p < 0.0125; **p < 0.01; ***p < 0.001). C) Median vertigo scores (Likert scale) from day 1 to 28. D) DHI scores (**p < 0.01). In panels A, B and D, boxes represent treatment groups; "x" marks the mean; horizontal lines show the 25th, 50th (median), and 75th percentiles; and whiskers indicate the 10th and 90th percentiles.

Paper III

Study population: 9 individuals (5 women, 4 men; mean age 47 years) with complete unilateral vestibular loss were included. Eight participants had undergone translabyrinthine surgery for vestibular schwannoma (mean time since surgery: 8 years, range 1–16), and one had congenital vestibular loss likely due to intrauterine cytomegalovirus infection.

Study design: Cross-sectional experimental study evaluating vestibular function using vHIT and fHIT during both passive and active head movements.

Results: Active head impulses toward the lesioned (ipsilesional) side resulted in significantly better visual performance compared to passive impulses, as reflected by higher fHIT scores (91.2% vs. 64.4%, p=0.002). VOR gain also increased significantly during active movements (p=0.006), with the most pronounced improvement observed toward the lesioned side (p=0.005). Covert saccades during active movements demonstrated significantly shorter latencies overall (p=0.048), particularly for ipsilesional movements (p=0.004).

Conclusions: active head movements lead to near-normal dynamic visual performance, even toward the side with complete vestibular loss. This improvement could be due to the presence of short-latency covert saccades.

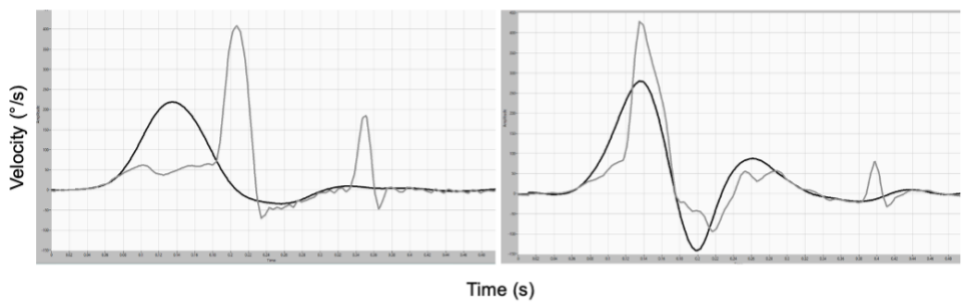


Figure 9. Eye and head velocity traces from a representative subject during head impulses toward the ipsilesional side. Left figure: Passive head impulse showing reduced eye velocity during head movement, followed by a late covert saccade (~135 ms) and an overt compensatory saccade. Right figure: Active head rotation in the same subject demonstrating an early covert saccade (~60 ms) occurring during the head movement.

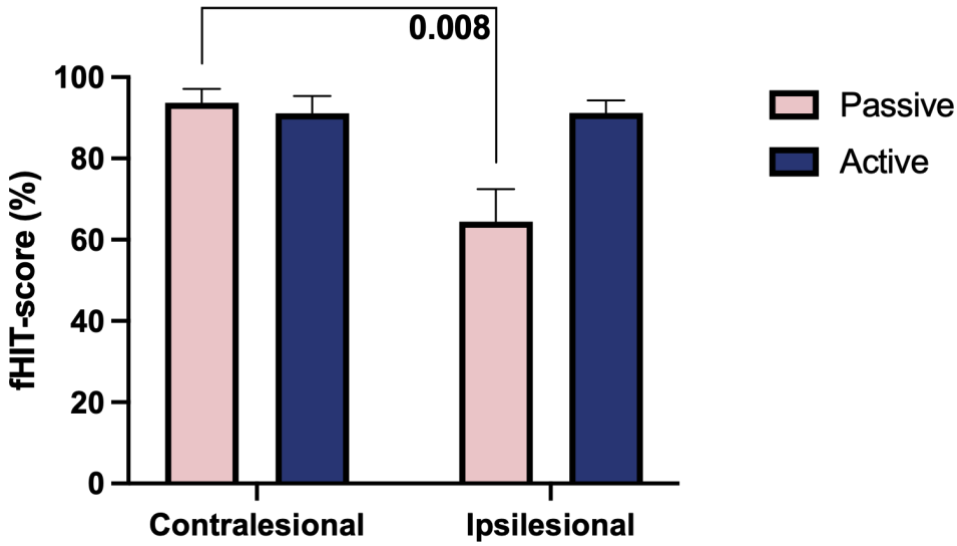


Figure 10. Percentage of correctly identified optotypes in the fHIT test during passive (pink) and active (blue) head impulses toward the ipsilesional and contralesional sides.

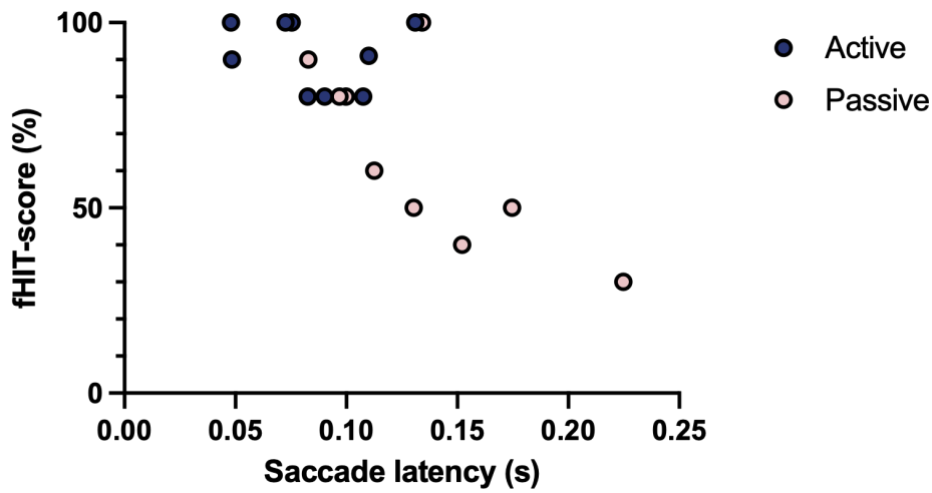


Figure 11. Graphic illustration of the relationship between fHIT-scores and corrective saccade latencies during passive and active ipsilesional head impulses.

Paper IV

Study population: 8 individuals (4 women, 4 men; mean age 47 years) with complete unilateral vestibular loss were included. 7 participants had undergone translabyrinthine surgery for vestibular schwannoma (mean time since surgery: 8 years, range 1–16), and one had congenital vestibular loss likely due to intrauterine cytomegalovirus infection.

Study design: cross-sectional experimental study evaluating vestibular function using vHIT and fHIT during both passive and active head movements.

Results: Active head impulses resulted in significantly smaller position errors between head and eye during the time frame corresponding to the visual perception task (fHIT), compared to during passive impulses ($p=0.006$). Furthermore, reduced position errors during this period were strongly associated with shorter latencies of the first corrective saccade ($r=0.915$, $p<0.001$).

Conclusions: active head impulses even toward the side with complete vestibular loss results in position errors that remain within or near the threshold required for brief visual perception in patients with chronic unilateral vestibular loss. This effect appears to be attributed by the occurrence of short-latency covert saccades, which help position the eyes more effectively during head movements.

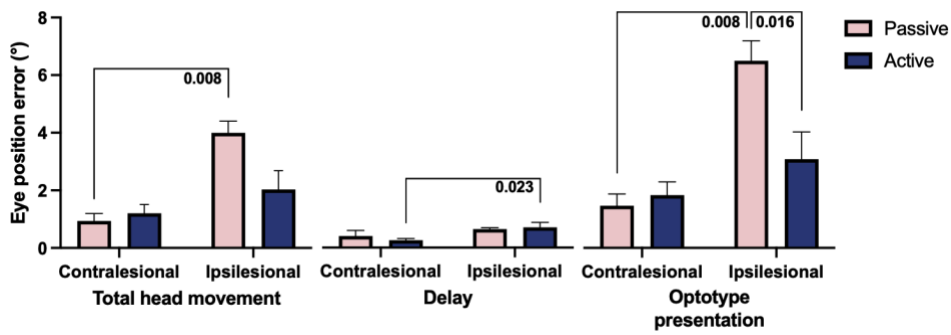


Figure 12. Absolute eye-head position errors, reflecting deviation from the visual target during head movement. Errors are shown for three time frames: the total head movement, the 62 ms delay, and the 80 ms optotype presentation window. Data are presented for both ipsilesional and contralesional directions during active and passive head impulses. Bars represent group mean values; error bars indicate standard error of the mean (SEM). Bonferroni-corrected post-hoc p-values are shown numerically.

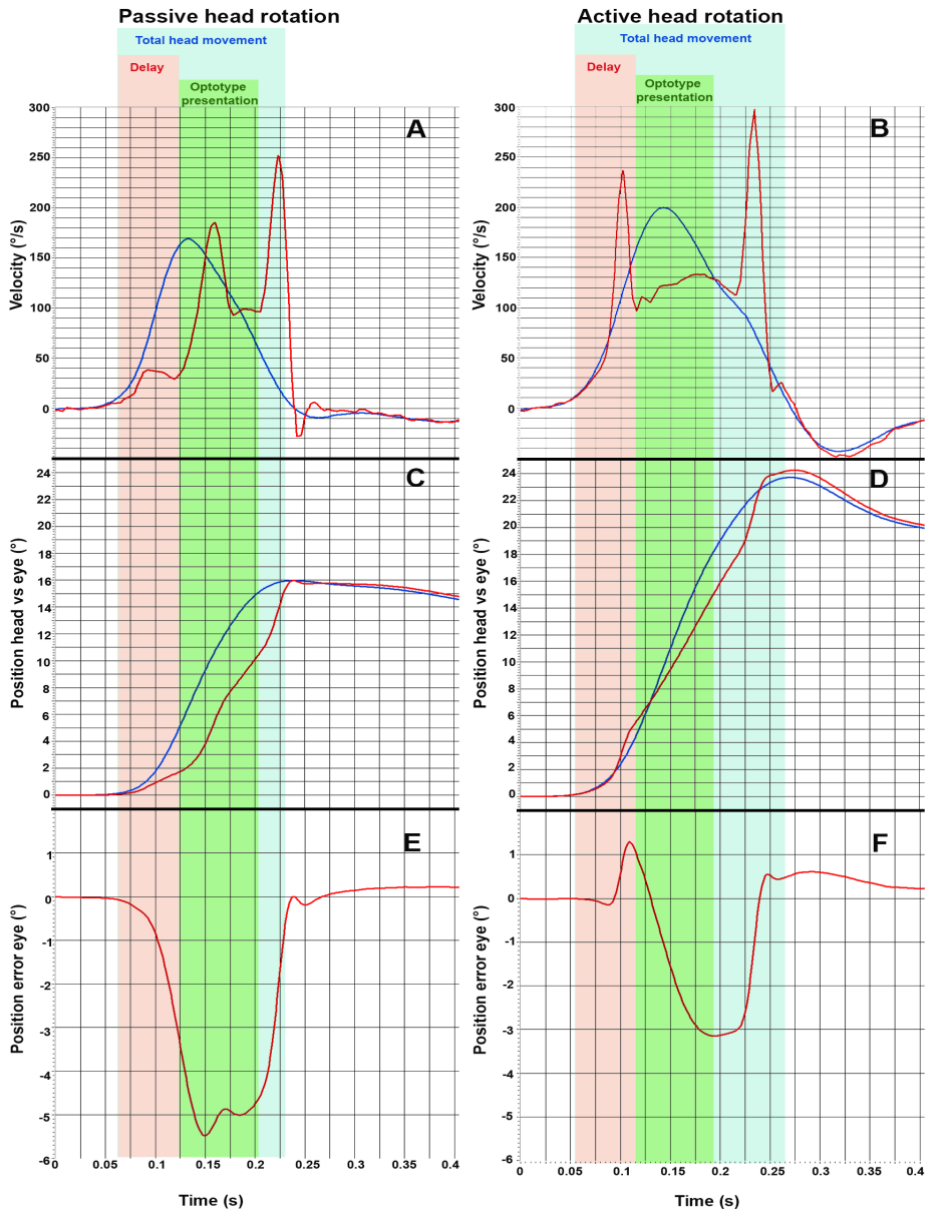


Figure 13. vHIT traces from a representative subject during passive (A, C, E) and active (B, D, F) ipsilesional head impulses. Panels A and B display head velocity (blue) and eye velocity (red) during the head thrust. Panels C and D show angular head and eye positions. Panels E and F illustrate the angular position error between eye and head, where negative values indicate that the eyes lag behind head movement. Shaded areas indicate the analyzed time frames: light blue represents the total head movement, orange marks the 62 ms delay, and green highlights the 80 ms optotype presentation window used in the fHIT test.

Paper V

Study population: 43 patients (27 male, 16 female; mean age 55, rang 41-69) diagnosed with AUVP.

Study design: A prospective longitudinal study that assessed vestibular recovery and central compensation from the onset of acute unilateral vestibulopathy (AUVP) through one year. Vestibular function was evaluated using vHIT at four time points: within the first week of symptom onset, and at 1, 3, and 12 months. The study included a detailed analysis of covert and overt saccades - examining their latency, velocity, amplitude, and gaze error - to explore their role in the compensation process. Subjective well-being was assessed using daily vertigo ratings on a Likert scale during the first month and the Dizziness Handicap Inventory (DHI) at 3 and 12 months.

Results: Following AUVP, VOR gain improved significantly over 12 months ($p<0.001$), with the most substantial recovery observed within the first 3 months ($p<0.001$). The presence of both covert ($p=0.005$) and overt ($p<0.001$) saccades decreased over time. A low VOR gain (<0.6) was associated with covert saccades, intermediate gain (0.8-1.0) with overt saccades, and normal gain (>1.0) with the absence of corrective saccades. The properties of covert saccades remained unchanged over time and demonstrated no correlation with self-reported dizziness.

Conclusion: Following AUVP, vestibular function improves over time, accompanied by a gradual reduction in both covert and overt saccades. VOR recovery varies between individuals, with covert saccades emerging at lower VOR gain and overt saccades emerging till at very high gains. The properties of covert saccades - latency, amplitude, and velocity - remain stable during passive head movements, suggesting they function as a reflexive, ballistic response rather than an adaptable mechanism. Thus, while covert saccades are not reliable indicators of compensation progress, their presence indicates persisting vestibular dysfunction.

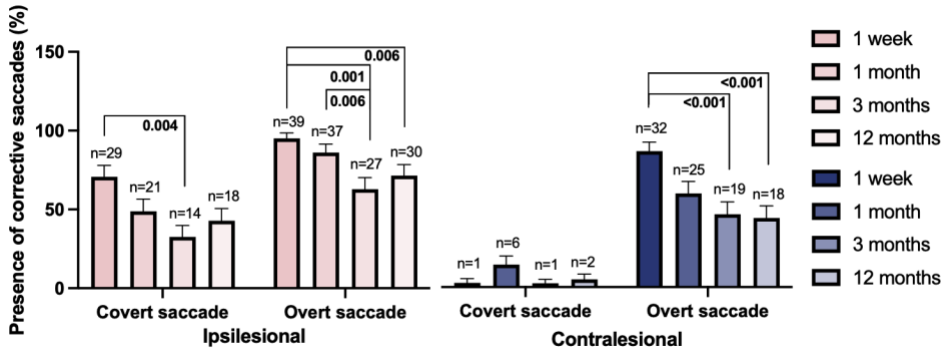


Figure 13. Presence of corrective saccades during ipsilesional (pink) and contralesional (blue) head impulses from the first week to 12 months after AUVP onset. Bars represent mean values; error bars indicate standard error of the mean (SEM). The number of patients (n) exhibiting corrective saccades at each time point is shown above each bar. Bonferroni-corrected post-hoc p-values are reported numerically.

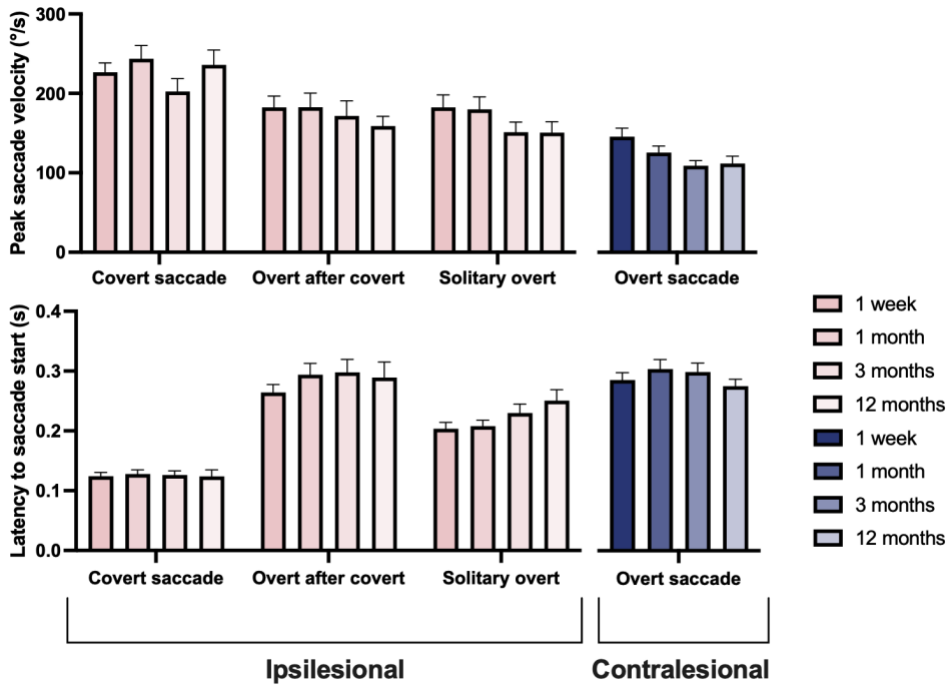


Figure 14. Evolution of saccadic properties from AUVP onset to 12 months post-diagnosis for ipsilesional (pink) and contralesional (blue) saccades. The top graph shows peak saccade velocity, and the bottom graph displays peak saccade latency. Bars represent mean values, and error bars indicate the standard error of the mean (SEM).

Discussion

Corticosteroid treatment for AUVP?

The main finding in our material is that corticosteroids do not enhance recovery as measured by a caloric test or vHIT. Neither does it reduce symptoms in the acute or chronic phase of AUVP.

The findings of Paper I and II are contradictory, reflecting the overall uncertainty surrounding the efficacy of corticosteroid treatment in AUVP. The largest RCT[110] exploring the effect of corticosteroids in AUVP demonstrated a significant effect on caloric responsiveness. Other studies reported enhanced vestibular recovery, as measured by caloric responses, following corticosteroid treatment[150, 178]. However, these studies were not randomized, nor blinded. Two randomized controlled studies [111, 148] found that corticosteroids may accelerate an early caloric recovery, but did not demonstrate superior long-term outcomes. Other RCTs of similar size failed to show any effect on caloric responsiveness[112, 152].

One potential factor influencing the caloric test outcomes in Paper II was the relatively broad inclusion criteria. Inclusion was based on clinical symptoms and bedside examination protocols recommended by the Bárány Society, without requiring a pathological caloric asymmetry. As a result, some patients had only mild asymmetries at baseline, leaving limited room for measurable improvement. In contrast, a recent double-blind randomized controlled trial from Switzerland not yet published but criteria available at clinical trails.com (NCT05024448) presented at the Bárány Society meeting[179] required a caloric asymmetry of greater than 70% for inclusion, yet still failed to demonstrate any significant effect of corticosteroid treatment. This suggests that even in patients with pronounced vestibular deficits, corticosteroids may not provide a measurable benefit.

Another possible explanation for the beneficial effect on caloric responsiveness reported in some previous studies is the potential influence of corticosteroids on vestibular hydrops. Corticosteroids have been shown to affect water channel regulation in the inner ear[180] potentially influencing endolymphatic hydrops, and have also been reported to reduce vertigo and hearing symptoms in patients with Ménière's disease[181]. The observed effect may therefore be attributable to a subset of patients misclassified as having AUVP who were, in fact, experiencing a first episode of Ménière's disease, which can present with similar clinical features. We

attempted to analyze outcomes in patients with a pathological caloric test but a normal vHIT at the first examination - an indicator that may suggest Ménière's disease - but the sample size was too small to allow for meaningful statistical analysis. Furthermore, all patients that evolved episodic vertigo during the study were excluded. Another differential diagnosis is canalith jam, a rare form of Benign paroxysmal positional vertigo (BPPV) caused by complete obstruction of the lateral canal with otoconia. This condition can mimic AUVP both symptomatically and clinically. Some patients - particularly those with symptom onset in the morning (a common feature in BPPV) and rapid recovery - may have had canalith jam. A retrospective analysis exploring these diagnostic subgroups within the study population would be of interest.

Another factor that may influence the effectiveness of corticosteroid treatment is the timing of its initiation. Studies on Bell's palsy have shown that corticosteroids are most effective when administered within 48 hours of symptom onset , with even greater benefits observed when treatment begins within 24 hours [182]. This finding formed the basis for the hypothesis explored in Paper I, which suggested a similar time-dependent effect in patients with AUVP. As a result, early intervention - defined as initiating treatment within 48 hours—was established as a key inclusion criterion in the study presented in Paper II. However, no significant effect of corticosteroid treatment was observed, despite all patients receiving treatment within 48 hours. Further subgroup analyses of patients who began treatment within 24 hours—and even within 12 hours - also failed to demonstrate any measurable benefit. Most previous studies have used a broader inclusion window of up to 72 hours, with mixed results as stated above. Notably, Goudakos et al.[148] initiated corticosteroid treatment within 48 hours and observed an accelerated recovery in caloric function; however, this effect did not persist at long-term follow-up, with no sustained advantage over placebo.

One could argue that post-hoc analysis revealed a significant reduction in caloric asymmetry over time only in patients treated with corticosteroids, suggesting a potential therapeutic effect. However, whether corticosteroids influence caloric function appears to have limited clinical relevance, as no differences - not even a trend - were observed in self-perceived symptoms or dizziness-related handicap between the treatment and placebo groups, either in the acute phase or at long-term follow-up in our study. This finding aligns with several other studies that have similarly reported no long-term benefit of corticosteroids on self-rated symptoms or dizziness-related disability[111, 112, 148, 152, 157, 179]. Corticosteroids are widely used in clinical practice for the prevention and management of postoperative nausea and vomiting[183, 184], and this effect may potentially offer short-term relief for patients with AUVP. Indeed, one study have shown that corticosteroids provide better symptom relief from vertigo and nausea in the first few days after onset compared to placebo[156] and a retrospective cohort found that it reduced perceived dizziness-related handicap during the first week[155]. However, two more studies have failed to

demonstrate a significant effect on vertigo or nausea in the acute phase of AUVP[157, 158].

While the largest RCT to date[110] did demonstrate a positive effect of corticosteroids on caloric responsiveness, it is important to note that caloric testing evaluates vestibular function at low frequencies[77] - levels not typically engaged in daily life[89, 90] - and correlates poorly with subjective symptoms and functional handicap[185-188]. Furthermore, in our study, corticosteroids showed no beneficial effect on vestibular function as measured by vHIT, which evaluates high-frequency responses more representative of real-life movements. This finding aligns with the results of Yoo et al.[112], who also found no significant improvement in VOR recovery among corticosteroid-treated patients. Therefore, even if corticosteroids influence caloric outcomes, their overall impact on meaningful clinical recovery remains questionable.

On the other hand, placebo interventions generally have no major physiological effect. Placebo can influence patient-reported outcomes, particularly in the short term[189]. For the questionnaires administered at 3 and 12 months, the placebo effect is expected to be minimal. However, the close monitoring of patients during the first four weeks may have amplified the placebo response. Additionally, the experience of receiving a treatment - compared to not receiving one - is inherently different and may further enhance perceived improvement due to psychological and contextual factors.

In our study, no serious adverse events were observed; however, analyses of private insurance claims involving 1.5 million individuals have shown significantly increased rates of sepsis, venous thromboembolism, and fractures associated with systemic steroid therapy - even for short treatment durations[190]. We did not see any psychiatric side effects but they can arise at any point during treatment, most commonly early in the course of therapy[191].

Despite a substantial body of evidence questioning the efficacy of corticosteroids, they remain the most used treatment for AUVP[169]. This may, in part, reflect the limited availability of alternative treatment options. In contrast, there is moderate to strong evidence supporting the effectiveness of vestibular rehabilitation[170], which should ideally be initiated as early as possible. However, for many patients, the idea of performing movement-based exercises in the first days following AUVP can feel overwhelming or even intolerable.

Antiemetic medications are frequently prescribed to alleviate nausea and prevent vomiting, but their sedative properties may inadvertently delay the start of vestibular rehabilitation and interfere with central compensatory mechanisms[141]. Animal studies have shown that suppressing vestibular symptoms too early can reduce the physiological drive for central compensation, potentially prolonging imbalance and delaying recovery[192]. More recent human studies support this notion, suggesting that early symptom suppression may indeed hinder the natural compensatory process[193].

In Paper II, patients reported whether they used antiemetic medications. We analyzed differences in antiemetic use between the corticosteroid and placebo groups and found no significant difference. However, we did not assess whether antiemetic use was associated with prolonged symptoms and elevated handicap - a question that warrants further investigation.

The most effective long-term approach may be to allow patients to experience discomfort in the acute phase. Encouraging early mobilization and rehabilitation—despite the initial distress - will ultimately lead to better recovery outcomes. In other words, helping patients understand the importance of pushing through the acute symptoms may be the most compassionate and effective strategy.

Corrective saccades compensate for a disrupted VOR in self-generated movements

In patients with complete vestibular loss due to deafferentation - such as following translabyrinthine schwannoma surgery - the VOR is abolished, resulting in an inability to stabilize gaze during head movements. In our studies (Papers III and IV), these patients demonstrated covert saccades in response to passive head impulses, with an even higher frequency observed during active head movements. In Paper III, we found that active head movements toward the lesioned side elicited covert saccades with shorter latencies. These results align with previous studies showing that covert saccades occur during both passive and active movements[194] but are more frequent and exhibit shorter latencies when the movements are active[133, 195] or predictable[196, 197]. Furthermore, active head movements improved visual performance compared to passive movements, resulting in visual performance comparable to head rotations toward the intact side—an effect also reported in earlier research[134]. In Paper IV, we demonstrated that during active head rotations toward the lesioned side, the position error between the eye and head remained within - or close to - the threshold required for brief visual perception. We also found a strong correlation between the position error and the latency of the covert saccade. Subsequent research has since confirmed this observation[198]. Given that visual input is suppressed during saccadic eye movements due to saccadic suppression[199], the improvement in visual performance cannot be attributed solely to the presence of saccades. Rather, it depends on their timing - they must be initiated early enough to effectively substitute for the deficient VOR. The extremely short latencies of these covert saccades during self-generated movements suggest they are unlikely to be driven by feedback reflexes, which would be too slow to account for such rapid responses.

Vestibular recovery and compensation after AUVP

Following AUVP, recovery on the lesioned side - as assessed by both caloric responsiveness and vHIT gain - can be observed over the course of the first year. These findings are consistent with previous studies reporting improvements in caloric function[200-202] and vHIT gain[203, 204]. In our study, the most pronounced recovery occurred within the first three months, after which the results plateaued - an observation also reported by Yoo et al.[112]. This early improvement likely reflects restorative processes in the VOR, including the sprouting of intact vestibular nerve fibers and the formation of new synapses in the deafferented vestibular nuclei[126]. Additionally, increased post-synaptic receptor density may enhance the responsiveness of remaining vestibular inputs[127, 205]. The critical window for these adaptive changes appears to be within the first few months following the lesion, resembling the neuroplasticity observed during post-stroke rehabilitation[206]. Importantly, these compensatory mechanisms are highly dependent on sensory input - particularly movement - underscoring the critical role of early vestibular rehabilitation in promoting recovery[207, 208]. Notably, studies have shown that initiating vestibular rehabilitation within two weeks of symptom onset can reduce dizziness and improve VOR gain [209] and may also have a positive impact on caloric responsiveness and overall balance function[210].

Corrective saccades compensate for the disrupted VOR, bringing the eyes back on target, making them part of the compensational process. Previous studies have suggested that the initial saccade response may shift from overt to covert saccades over time[137] and that covert saccade latencies may shorten as compensation progresses - even during passive, unpredictable movements - potentially reflecting successful vestibular adaptation[107, 138]. However, our findings did not support this pattern of transition. At disorder onset covert saccades and overt saccades were present in the majority of patients, but as they recovered the presence of both covert and overt saccades decreased which is in concordance with other studies evaluation the presences of corrective saccades post AUVP[211, 212]. In our study, the properties of covert saccades - latency, velocity, and amplitude - remained stable over time, regardless of the position error between the eye and head at saccade onset. Clustering of saccades during passive head movements has also been proposed as a marker of successful vestibular compensation[213-215]. We did not specifically assess clustering but the narrow variation in saccade latency suggests that such clustering was not present in our cohort. These findings align with previous studies in patients with complete vestibular loss following translabyrinthine surgery[216] and in individuals with AUVP assessed before and after vestibular rehabilitation[217]. Both studies reported no major temporal changes in covert saccade properties. The consistency of these properties implies that covert saccades are not subject to adaptation over time, despite evident clinical compensation.

Moreover, the presence of covert and overt saccades did not significantly correlate with subjective vertigo symptoms or self-perceived handicap over time. This suggests that while saccadic compensation mechanisms are activated following vestibular dysfunction, their presence alone is not a reliable predictor of symptom severity as experienced by the patient. No association was found between the specific properties of covert saccades and self-rated well-being. In contrast, adaptive changes were observed in the characteristics of overt saccades which also showed a correlation with subjective well-being at the one-month follow-up in concordance with previous research[218], indicating that these may play a more meaningful role in perceived recovery.

Rather than representing an adaptive response to gaze position error, covert saccades may function as ballistic reflexes triggered by insufficient vestibular input. Although they serve a compensatory role by reducing eye–head position error, their occurrence appears to reflect low VOR gain (in our study, <0.6) and persistent vestibular hypofunction. If covert saccades indeed operate as ballistic reflexes, their capacity for adaptation - such as through clustering - seems unlikely. In a clinical setting the presence of covert saccades should not be interpreted as a sign of successful compensation but rather as evidence of a persistently hypo-functioning VOR.

What triggers covert saccades?

Corrective saccades are typically categorized as covert if they occur during head movement, and overt if they are triggered after the head has stopped moving. This terminology is widely used in clinical practice due to its simplicity and intuitive nature. An alternative classification describes saccades based on their order of appearance - first, second, third, and so on. Both approaches are commonly used in research, each with its own advantages and limitations. The covert/overt distinction relies solely on the timing of the saccade relative to head movement, not on its underlying neurophysiological mechanism. For example, a saccade occurring just milliseconds after the head stops will be labelled as overt, despite likely sharing the same neural origin as a covert saccade. Conversely, classifying saccades by their sequence can group together saccades with fundamentally different physiological origins. For instance, a patient who initially exhibits only overt saccades may, following vestibular deafferentation, begin to generate both covert and overt saccades. In this scenario, the overt saccade that was previously labelled as the "first saccade" would now be classified as the "second saccade," simply because a covert saccade has emerged. Thus, while both classification systems provide useful insights, neither is without limitations, and this should be kept in mind when interpreting or analyzing corrective saccades.

Visual information - particularly retinal slip, or the movement of an image across the retina that results in blurred vision - has been proposed as a primary trigger for saccades. Van Nechel et al demonstrated that the presence of covert saccades doubled when patients with bilateral vestibular loss were tested in a well-lit room compared to complete darkness but found no effect on the latency to the first saccade [139]. Pogson et al. demonstrated that in patients with bilateral vestibular loss, testing in complete darkness - i.e., in the absence of visual cues - led to a shorter latency of the first saccade and a reduced frequency of second saccades. This suggests that only covert saccades were triggered, and inspection of raw data traces indicated that they were consistently triggered at the same time point. Moreover, in patients with complete unilateral vestibular loss, the frequency and characteristics of the first saccade remained unchanged regardless of the presence or absence of visual input[219]. Further, Hermann et al demonstrated that patients with bilateral vestibular loss triggered covert saccades in the compensatory direction despite conflicting or misleading visual cues[220].

Iwasaki et al[221] investigated the role of neck proprioception in triggering corrective saccades in patients with unilateral and bilateral vestibular loss. They applied horizontal head impulses and whole-body rotations with the neck fixed to suppress sensory input from the neck. Their results showed that overt saccades were reduced by 50% when neck input was blocked, while covert saccades remained unaffected, suggesting different triggering mechanisms for the two. Supporting this, studies in rhesus monkeys have shown that within one day of vestibular loss, neurons in the vestibular nuclei begin responding strongly to neck proprioception - a phenomenon absent in healthy animals[140]. The same study also concluded that active movements resulted in eye movements that compensated better for the insufficient VOR compared to passive movements. This suggests that when the VOR is disrupted the brain relies more on the cervical-ocular reflex (COR) and uses motor efference copy information to maintain a stable gaze during head movements. Further supporting the efference copy theory, several human studies, including ours, have demonstrated that active or predictable head movements enhance VOR gain and improve gaze stabilization more effectively than passive movements following a complete vestibular loss due to translabyrinthine surgery[222-224]. For passive movements there is a very moderate VOR improvement in both the acute and chronic phase[216, 225]. However if covert saccades are triggered by motor efference copy—a feedforward signal representing the intended cortical motor command it raises the question of why some saccades have latencies at all and why some head impulses trigger more than one saccade.

Residual or contralateral vestibular input has also been proposed as a possible trigger for covert saccades[81]. When input from one vestibular organ is lost, the inhibitory commissural signal to the contralateral vestibular nucleus is disrupted. The lost “off-signal” could be a potential trigger of covert saccades. Horizontal saccades generated while the head is stationary are initiated by excitatory burst

neurons located in the paramedian pontine reticular formation[199]. It has been shown that vestibular input can enhance the firing of these burst neurons via projections from the superior colliculus, with latencies as short as 2–4 ms[226]. Notably, burst neuron activity increases during contralateral horizontal head rotation and decreases during ipsilateral rotation, indicating modulation by vestibular signals. Theoretically, if the inhibitory commissural signal ("off-signal") to the contralateral vestibular nucleus is lost—as in unilateral vestibular loss—this disinhibition could further enhance burst neuron excitability, potentially facilitating the generation of short latency covert saccades. Covert saccades for passive, unpredictable movements are triggered within 150 ms from when the head starts to move, the typical duration of a head impulse, but latencies can be as low as ~70 ms[81, 131]. Given that saccades are elicited roughly 50 ms after superior colliculus activation[199], the full vestibular-to-saccade pathway would remain within the latency window of covert saccades. However, covert saccades are triggered in patients with bilateral vestibular loss[219], where no off-signal from either ear should exist. The explanation may lie in minimal residual vestibular function, which is often present even in cases of presumed complete bilateral vestibular loss. In rare cases of surgical bilateral deafferentation—where no residual vestibular function remains—corrective saccades occur with longer latencies, typically after head movement has stopped[219], suggesting they may instead be triggered by visual or somatosensory input.

This interplay between vestibular input and saccade generation highlights the complexity of covert saccade initiation. Building on this, the role of vestibular input in suppressing reflexive eye movements—such as saccades and blinks—during head motion may be another explanation why covert saccades emerge when vestibular function is compromised.

During rapid head movements, such as those elicited during the head impulse test, healthy individuals typically maintain gaze stability, either by blinking or initiating compensatory eye movements in the direction opposite to head motion, unless instructed otherwise[227]. The ability to maintain clear vision during head movements relies on suppression of reflexive eye movements, such as blinks and saccades, and also requires a suppression of the head turn-evoked vestibular-ocular reflex. Vestibular input plays a crucial role in this process[228]. Given the physiological similarities between the blink reflex and saccades in visual perception, it is postulated that vestibular stimulation may inhibit saccades as well. Therefore, in the presence of a vestibular deficit, the reduced vestibular input may compromise the ability to suppress reflexive eye movements. Consequently, the absence of suppression of saccades during head turns would lead to the appearance of covert saccades. These covert saccades, if present, should have a latency similar to that of blinks. Furthermore, catch-up saccades following the covert saccade should appear after approximately 100 milliseconds plus the latency of the saccade[229]. The automatic nature of the reflex-like behaviour suggests that the amplitude of the saccades might be relatively stimulus-independent.

In summary, overt saccades appear to be influenced by both visual and somatosensory input, while covert saccades during active head movements are likely driven by efference copy mechanisms. In contrast, the triggers for covert saccades during passive, unpredictable movements remain poorly understood. Visual input is an unlikely factor, as covert saccades occur with similar timing even in complete darkness. Somatosensory cues from the neck also appear insufficient, given that covert saccades persist with the same latency and frequency when the neck is immobilized. One hypothesis is that residual vestibular input—or the loss of the vestibular "off-signal" from the intact ear—may serve as a trigger. However, this fails to fully explain the presence of covert saccades in patients with bilateral vestibular loss. It is possible that, in non-surgically deafferented cases, minimal residual input continues to reach the vestibular nuclei. Alternatively, the absence of vestibular input may unmask a phylogenetically older, latent saccadic system but this remains to be further studied. Ultimately, the precise trigger for covert saccades remains unknown and warrants further investigation.

Methodological considerations

In addition to the method-specific limitations discussed in the background section, there are also some general methodological considerations that warrant attention.

Study I was a retrospective analysis of patients treated with corticosteroids. Compared to the randomized controlled design of Study II, its methodology was less robust, and the use of a 32% cut-off for pathological caloric asymmetry is not the most widely accepted threshold but was presented by Herzog et al[174]. Cut-off values for unilateral vestibulopathy up to 40% is still used at some centers[169]. The study was included in this thesis to illustrate the conflicting evidence surrounding corticosteroid use in AUVP and to highlight why a symptom duration of less than 48 hours became a key inclusion criterion in Study II. Notably, in Study II, no effect of corticosteroids was observed—even when treatment was initiated within 24 or 12 hours of symptom onset. The results of Study I should therefore not be interpreted as conclusive evidence for corticosteroid treatment, but rather as part of the research rationale that formed the design of the subsequent, more rigorous Study II.

In Paper II, only 72 out of 350 assessed patients were included in the study. The majority were excluded for not meeting inclusion criteria (n=92), most commonly due to symptom duration exceeding 48 hours (n=68), meeting exclusion criteria (n=54), or being treated at another clinic (n=82). Additionally, 45 patients (13%) declined participation. It is possible that those who declined experienced more severe vestibular loss and symptoms, which may introduce selection bias. However, no baseline differences were observed between the treatment groups, and only three patients were lost to follow-up, supporting the study's high internal validity. The

large proportion of eligible but ultimately excluded patients highlights the reality that many individuals seek medical care later than 48 hours after symptom onset and illustrates the practical challenges of conducting high-quality research in acute clinical settings, where time pressure and the need for written informed consent may hinder inclusion.

The sample size in Papers III and IV was relatively small, which increases the risk of Type II errors - that is, failing to detect a true significant effect. However, power calculations confirmed that the sample was sufficient, and several significant differences between active and passive head movements were identified. While small samples can also raise the risk of Type I errors (false positives), the consistency of our findings with those reported in other studies strengthens their validity[133, 195].

In Study III and study IV, eye-tracking during vHIT and functional performance during fHIT were not measured simultaneously and by the same measurement devices, which complicates direct comparisons between vHIT metrics like position error and fHIT outcomes such as perceptual accuracy. However, both measurement devices applied the same inclusion criteria for accepting a head thrust as correctly performed, e.g., that it had the same minimum peak head velocity, meaning the assessment procedure and the definitions of time phases analyzed during the head thrusts were consistent across the vHIT and fHIT assessments.

Future perspectives

Although a single study is not sufficient to definitively rule out the effectiveness of corticosteroids in treating acute unilateral vestibulopathy (AUVP), it contributes to the growing body of evidence questioning their clinical utility. Future research should aim to strengthen this evidence. By incorporating a third study arm with randomization to no pharmacotherapy the role of the placebo effect—particularly in relation to patient-reported outcomes should be further evaluated.

A cornerstone of high-quality research is comparability; thus, future studies should standardize treatment protocols by initiating corticosteroid therapy within the same time window, using consistent dosing regimens, and assessing both functional recovery and subjective well-being.

A standardized terminology for corrective saccades would simplify comparison of results.

Simultaneously performing vHIT and a dynamic visual task such as fHIT could strengthen the observed relationship between corrective saccades and visual performance, while also providing deeper insight into the mechanisms that trigger these saccades. Further exploration of saccadic behavior in patients with complete or incomplete, unilateral or bilateral vestibular loss - particularly when combined with cerebellar dysfunction and particularly if the assessments both were performed in light and completely dark environment - could provide a more comprehensive understanding of the multisensory and contextual factors involved in saccade generation.

Given the limited correlation between caloric test results, vHIT gain, and patients perceived recovery, covert saccades have been considered a promising indicator of vestibular compensation. Our findings suggest they may instead reflect persistent dysfunction. Importantly, most head movements in daily life are self-generated, yet current vestibular testing relies almost exclusively on passive stimulation. The neural mechanisms engaged during active head movements likely differ from those during passive motion, in both healthy and vestibular-impaired individuals. Therefore, future studies should also evaluate vestibular compensation during active movements following AUVP, which may offer a more realistic and functionally meaningful measure of recovery.

Conclusions

- After AUVP there is significant recovery of vestibular function as measured by both caloric responsiveness and vHIT, with the greatest recovery seen during the first three months.
- Corticosteroid treatment does not improve symptoms in either the acute or chronic phase of AUVP, nor does it enhance vestibular function as measured by caloric responsiveness or vHIT. However, the standard corticosteroid regimen used in southern Sweden and applied in this study was safe, with no serious adverse events reported.
- Self-generated head movements towards the ear with a complete vestibular loss trigger short-latency covert saccades that reposition the eyes more effectively during head motion, allowing gaze stability comparable to that achieved when moving toward an intact vestibular organ.
- Following AUVP, vestibular function improved over time, accompanied by a gradual reduction in both covert and overt saccades. VOR recovery displayed a variable pattern, with the degree of VOR gain deficit influencing the type of compensatory saccades: covert saccades were linked to lower gain values, while overt saccades appeared with higher gains.
- For passive head movements the properties of covert saccades - latency, amplitude, and velocity - remained stable over time, suggesting they function as a ballistic, reflexive response rather than an adaptable mechanism. Therefore, while covert saccades may not be helpful for monitoring vestibular compensation, their presence remains a strong indicator of persistent vestibular dysfunction.

Populärvetenskaplig sammanfattning

Bakgrund

Vestibularisneurit – ofta kallad "virus på balansnerven" – är en vanlig orsak till akut yrsel och drabbar cirka 1 000 personer per år i Sverige. Tillståndet orsakas troligen av att ett vilande herpesvirus (Herpes simplex typ 1) reaktiveras och orsakar en inflammation i balansnerven, vilket leder till svullnad, inklämning och funktionsförlust. Vid insjuknandet får hjärnan bara signaler från det friska balansorganet, vilket hjärnan tolkar som en kraftig rörelse mot den friska sidan, ofta med intensiv yrsel och illamående som följd. De akuta symtomen avtar vanligtvis inom några veckor, men många patienter upplever kvarstående yrsel och suddig syn vid huvudrörelse. Balansorganen står i nära förbindelse med ögonens muskler genom en reflexkedja – den vestibulo-okulära reflexen (VOR) – som håller blicken kvar på den punkt vi fokuserar på när vi rör på huvudet. När denna reflexkedja inte fungerar som den ska glider blicken med huvudrörelsen, och synen blir suddig. Hjärnan försöker kompensera för detta genom att ögonen gör snabba korrigerande rörelser (sackader) tillbaka till den punkt som man försökte fokusera på. Om dessa korrigerande ögonrörelser sker efter huvudrörelsen avstannat kallas de overta sackader, och om de sker under huvudrörelsens gång kallas de coverta sackader. Det är fortfarande oklart hur effektiv kompensationen med snabba ögonrörelser är, och om förekomsten och egenskaperna hos av dessa ögonrörelser kan användas som ett mått på grad av återhämtning efter en skada på balansorganen.

Vissa studier har visat att behandling med kortison kan göra att funktionen i balansorganen återkommer bättre och att man känner mindre symptom i den akuta fasen. Andra studier har inte visat på samma goda effekt. Behandling med kortison under en kort tid kan medföra biverkningar, som oftast inte är farliga, men som kan vara besvärliga för patienterna.

Syfte

Det övergripande målet med avhandlingen var att utvärdera om kortisonbehandling förbättrar återkomsten av balansorganens funktion efter vestibularisneurit samt att öka kunskapen om de kompensationsmekanismer som träder i kraft efter en ensidig förlust av balansfunktion.

Studie I-V

Studie I, inkluderade en retrospektiv analys som utvärderade om en tidig behandlingsstart med kortison inom 24 timmar efter ett insjuknande i vestibularisneurit ledde till bättre återkomst av balansorganens funktion, uppmätt med kalorisk spolning, jämfört med om man fick kortisonbehandling först mellan 25–72 timmar efter ett insjuknande. Studien indikerade att så var fallet; alla patienter som fick kortisonbehandling inom 24 h efter symptomdebut hade normala resultat i det kaloriska testet vid uppföljning. Detta resultat låg till grund för inklusionskriterierna i studie II.

Studie II, var en dubbelblind, randomiserad och placebokontrollerad studie som utvärderade om kortisonbehandling förbättrade återkomsten av balansorganens funktion och förbättrade måendet hos patienter som insjuknat med vestibularisneurit. Subjektivt välbefinnande och balansfunktion, mätt med både kalorisk spolning och vHIT utvärderades från vid initialt insjuknande och upp till ett år efter insjuknandet. Vi fann att kortisonbehandling inte hade någon effekt på vare sig subjektivt mående eller återkomst av balansorganens funktion. Återhämtningen skedde successivt hos alla, oavsett behandling, med störst förbättring under de första tre månaderna.

Studie III utvärderade hur huvudrörelser initierade av patienterna själva (aktiva rörelser) eller av en undersökare (passiva rörelser) påverkade synförmågan under huvudrörelse hos patienter med en ensidig total förlust av balansorganens funktion. Bakgrunden är att en ensidig totalförlust alltid leder till en ofullständig VOR vilket i sin tur leder till att blicken ej kan stabiliseras perfekt vid rörelser mot sidan med funktionsförlust. Vi fann att aktiva rörelser gav en nästan normal synförmåga under huvudrörelse medan passiva rörelser resulterade i en kraftig nedsättning av synförmågan. Aktiva rörelser skapade coverta sackader som kom mycket tidigare under huvudrörelsen jämfört med passiva rörelser.

Studie IV utvärderade varför synförmågan var bättre vid aktiva jämfört med passiva huvudrörelser hos patienter med en ensidig total balansorgansförlust. Vi fann att vid aktiva huvudrörelser låg ögat närmare fokuseringsmålet vid den tidpunkt då synförmågan mättes, så pass nära att en avläsning skulle ha varit möjlig. Vid passiva huvudrörelser låg ögat långt ifrån fokuseringsmålet vid samma tidpunkt. Förklaringen tycks vara att när patienten själv vrider huvudet så skapas coverta sackader så pass tidigt under huvudrörelsen att ögat ligger på rätt plats när synförmågan testas.

Studie V utvärderade återkomsten av balansorganens funktion, utvecklingen av korrigerande sackader och subjektivt mående från insjuknandet i vestibularisneurit upp till ett år efter skadan. Vi fann att förekomsten av och styrkan hos korrigerande sackader minskade parallellt med att balansfunktionen återkom. Coverta sackader var associerade med betydande funktionsnedsättning och dess egenskaper förblev

oförändrade över tid. Det fanns ingen korrelation mellan coverta sackader och subjektivt mående.

Sammanfattning

Kortisonbehandling verkar inte förbättra återkomsten av balansorganens funktion eller förbättra mående vid vestibularisneurit. Återkomsten av balansorganens funktion sker spontant, med störst förbättring under de första tre månaderna. Förekomsten av coverta sackader skapade av passiva rörelser verkar inte var ett mått på en framgångsrik kompensation utan är snarare ett tecken på kvarstående funktionsförlust. Men coverta sackader skapade under aktiva rörelser förbättrar tydligt synförmågan vid huvudrörelser och kompenserar för en utslagen VOR.

Acknowledgements

Först och främst vill jag rikta ett innerligt tack till alla patienter som deltagit i våra kliniska studier och därigenom gjort detta arbete möjligt. Ett stort tack riktas också till Lunds universitet och Region Skåne för att ha möjliggjort denna avhandling.

Vidare vill jag även tacka alla skattebetalare som via skattemedel finansierar forskning, i mitt fall via **ALF-medel** och **Regionalt forskningsstöd**. Jag vill även tacka stiftelsen **ACTA Otorhinolaryngologica** för de forskningsmedel jag tilldelats. Denna avhandling hade inte blivit till utan sammanhängande perioder av arbete på dagtid.

Att få doktorera har varit en sann ynnest och jag är djupt tacksam för denna möjlighet. Det finns många som jag vill tacka:

Fredrik Tjernström, min huvudhandledare – tack för att du både introducerade mig till forskning i allmänhet och den vestibulära forskningen i synnerhet. Tack för allt du lärt mig, för alla dörrar du öppnat och för ditt orubbliga stöd. Jag har verkligen känt att du trott på mig hela vägen.

Per-Anders Fransson, min handledare – tack för ditt stora engagemang, din uppmuntran, din ovärderliga hjälp med statistiken och för att du alltid funnits där med snabba svar och kloka råd.

Mikael Karlberg, handledare – tack för dina kloka tankar och fina formuleringar.

Måns Magnusson, professor och inofficiell handledare – tack för alla inspirerande idéer och den värdefulla vägledning du bidragit med.

Karin, Dan och **Anastasia** på balanslabbet – tack för alla snygga vHIT-kurvor, er stora hjälpsamhet och alla trevliga samtal.

Alla kollegor på ÖNH-kliniken SUS, Helsingborg och Kristianstad – tack för ert tålamod och er insats med att inkludera patienter i kortisonstudien, även när det var kämpigt. Ert arbete har haft stor betydelse.

Ett alldeles särskilt tack till **alla kollegor på ÖNH-kliniken SUS** – världens finaste kollegor – för all er värme, all den kunskap ni delat med er av, och för att ni stöttat mig genom att ta mina jourer och ta hand om mina patienter när jag varit iväg och forskat.

Pernilla Björnberg – tack för att du friställt mig från kliniken och gjort det möjligt för mig att få längre sammanhållna forskningsperioder, något som varit avgörande för att kunna komma vidare.

Peter White och **Arni Örnolfsson** – tack för förståelse, flexibilitet och kontinuerlig och lågmäld psykoterapi i from av kaffebryggning och generell omtanke.

Eva Nero – tack för all hjälp med dechiffreringen av det ekonomiska systemet, hade inte klarat av det utan dig.

Johannes Ehinger – tack för de avgörande råden som ledde till ALF-finansiering för ST-läkare. Utan din hjälp, ingen forskningstid – och därmed ingen avhandling.

Magdalena Karnebäck – tack för de vackra illustrationerna i avhandlingen och för din kärlek och vänskap. Du är en sann konstnär och en sann vän.

Matthew Burne – tack för den vackra framsidan till min avhandling.

Kristina Nordenson – tack för korrläsning, kärlek och allmän psykisk grundning.

Ett stort tack för all uppmuntran till **mina vänner från norr till söder** och **öster** till **väster**. Jag är lyckligt lottad som har de smartaste, roligaste, varmaste och vackraste vännerna i hela världen.

Ann-Christine och Janne, mina svärföräldrar – tack för all hjälp och allt stöd. Anki du är en sann inspiration!

Familjen Nystedt – tack för att ni underhållit och tagit hand om min familj när jag suttit framför datorn.

Tack till mina fantastiska kollegor och innerliga vänner **Franzi, Sabine, Emma, Emma och Johanna** – tack för att ni gör varje dag på jobbet till en glädje, för alla era kloka tankar om allt från himmel till jord och för allt roligt vi gjort tillsammans. Vad skulle jag göra utan er?

Min älskade bror **Viktor** och världens bästa svägerska **Maria** – tack för allt stöd och kärlek. Jag är så glad och stolt att just ni är en del av min familj.

Mamma och pappa – tack för att ni har givit mig allt. Jag vore inte den jag är utan er och skulle aldrig ha kommit någon vart utan er som inspiration, ert stöd och framförallt all den kärlek som ni marinerat mig i.

Louise och **Selma** – min största prestation, min stora lycka! Tack för er oändliga kärlek och för att ni sätter mig på plats på kontinuerlig basis.

Och slutligen, älskade **Andreas**. Utan dig hade denna avhandling aldrig blivit verklighet. Tack för allt ditt stöd, all tid du ordnat för mitt skrivande och i synnerhet din matematiska expertis. Tack för att du är du – och för att du är min!

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