

Supplementary Materials

Supplementary materials are provided below for “Quantifying the Vestibulo-ocular reflex with Video-Oculography: Nature and Frequency of Artifacts” (Mantokoudis et al., *Audiology & Neurotology*, 2014). Appendix A describes additional data collection details for video-oculography (VOG) based head impulse tests (HIT), while Appendix B (structured coding manual) describes additional data analysis details.

Appendix A. VOG-Based HIT VOR Data Collection

Head Impulse Test

The vestibulo-ocular reflex (VOR) can be assessed using a brief, high-acceleration head impulse at the bedside. The horizontal head impulse test (h-HIT) is used to assess the lateral canals, while impulses in the ‘RALP’ (right-anterior, left-posterior) and ‘LARP’ (left-anterior, right-posterior) planes assess vertical canal function. When the test is performed non-quantitatively, the patient is asked to fixate a target in front of them while the examiner rotates the head rapidly (and unpredictably) in the plane of the canal being tested. If the VOR is intact and properly calibrated by the brain, the eyes rotate in perfect opposition to the head motion (i.e., with equal amplitude and in the same plane, but in the opposite direction – a VOR gain ratio of eye to head movement of 1.0) with an extremely short latency of 5-6ms [1]. If the VOR is not intact, the eyes are pulled by inertial forces in the *same* direction as the head, causing the patient to lose fixation on the target. If the patient is alert and following instructions after they lose fixation, they will make a corrective saccade (fast eye movement) back to the fixation target. This “refixation saccade” is detected qualitatively by expert examiners at the bedside as an *indirect* marker of VOR failure.

When the h-HIT is recorded quantitatively, the examiner may be placed either in front of or behind the patient—since the device records the findings, the examiner need not be directly viewing the eyes.

VOG device

HIT data were collected using a lightweight, portable VOG device (ICS impulse, GN Otometrics, Taastrup, Denmark) designed for quantitative HIT recording. This video-oculography device has been previously validated in laboratory settings for recording head impulse data against gold standard scleral search coils [2]. The VOG is a rigid ‘goggles’ frame with two primary electronic components embedded in the frame—a high-speed video camera to monitor eye movement and an accelerometer to monitor head movement. The VOG device camera is attached via a cable to a laptop computer running software that receives the video signal and uses a pupil-tracking algorithm to monitor eye position. Together with the accelerometer information, this allows quantitative, real-time measurements of eye and head movements, permitting direct assessment of VOR function. The device plots a trace showing head and eye position over time during each HIT and then calculates the VOR gain ratio (ratio of areas under the curve for eye and head velocity). The HIT maneuver is usually repeated 10-20 times to insure a reproducible result for each side. What makes this new device and similar devices [3-6] different than traditional VOG devices is an ultra-lightweight frame essential to assess the high-acceleration HIT VOR without significant goggles slippage that would otherwise make accurate HIT VOR measurements impossible [7].

A built-in software algorithm verifies the accuracy of eye movement tracking during an initial calibration before HIT measurements begin, however, a wrong calibration resulting in falsely elevated VOR gains is still possible. The device software records and plots HIT VOR physiologic traces and mean gains after two automated, proprietary filtering steps that discard any impulse results detected as invalid. The ICS impulse device software has internal rules that discard grossly incorrect HIT recordings and remove intrusive eye movements occurring during the VOR response that might distort measurement of the VOR gain ratio ('de-saccading' algorithms). Nevertheless, noisy measurements still lead to artifacts in some accepted HIT physiologic traces. Raw data from accepted impulses can be exported for offline analysis.

Appendix B. Classification of VOG Results (Structured Coding Manual)

Slow Phase Eye Movements

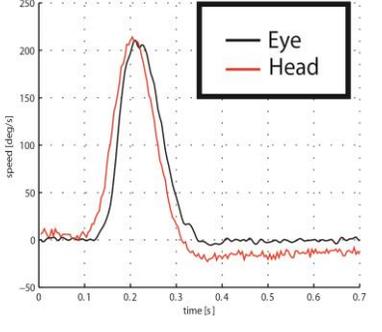
For VOR slow-phase eye movements to be considered 'normal,' we required the following elements:

- (1) peak head velocity during the h-HIT between 100 and 300 °/s;
- (2) no major (disruptive) artifacts during the h-HIT (e.g., no large blinks or loss of pupil tracking);
- (3) normal VOR morphology (bell-shaped curve); and
- (4) peak eye velocity not lower or higher than 20% of the peak head velocity.

Figures 2A and 2B show two examples of normal HIT traces with equal head and eye velocity and a calculated gain of 1.0, but at different HIT peak head velocities.

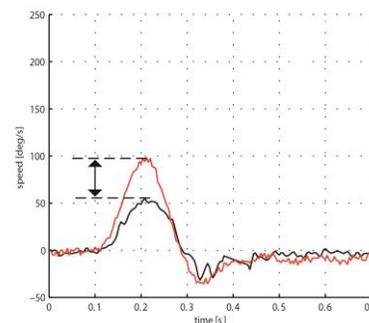
For VOR slow-phase eye movements to be considered (correctly recorded yet) 'abnormal,' we required the same velocity, absence of major artifacts, and normal morphology, but a peak eye velocity at least 20% lower than the head velocity (Figure 2C), with or without nystagmus or corrective refixation saccades [8]. Traces with an initial normal slow phase VOR (0-60ms) followed by an abrupt decline of eye velocity (Figure 2D) were classified as an abnormal HIT with 'abrupt decline' of gain [9, 10].

Coding options (mutually exclusive and jointly exhaustive):

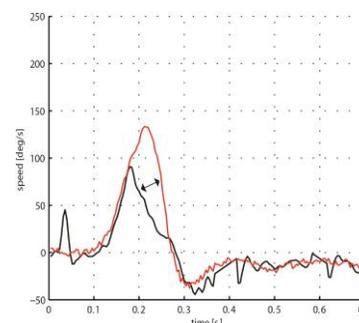
Normal HIT	Exemplar
<ul style="list-style-type: none"> • Normal morphology with symmetric, bell-shaped curves. Eye and head velocity traces are ideally overlaid (gain 1.0). • Peak eye velocity is not more than 20% lower or 20% higher than peak head velocity. These cutoffs have been chosen considering previous works which measured VOR gain using scleral search coils and a video-oculography device [2]. • Minor (non-disruptive) artifacts (e.g., head bounce) or non-disruptive fast phases are allowed if a bell-shaped morphology is still recognizable and key VOR landmarks are not obscured. 	

Abnormal HIT (without abrupt decline)

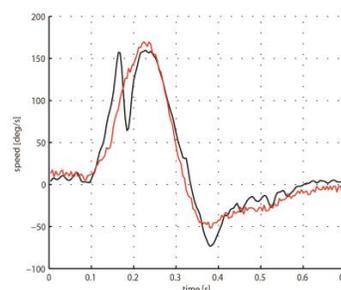
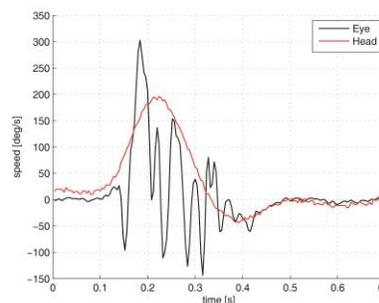
- Normal morphology with symmetric, bell-shaped curves, despite the abnormal (reduced) VOR response.
- Peak eye velocity is more than 20% lower than peak head velocity (if eye velocity exceeds head velocity by more than 20% it is considered an artifact, not an abnormal HIT).
- Minor (non-disruptive) artifacts (e.g., head bounce) or non-disruptive fast phases are allowed if a bell-shaped morphology is still recognizable and key VOR landmarks are not obscured.

Exemplar**Abnormal HIT (with abrupt decline)**

- Abnormal morphology (not symmetric, bell-shaped curve) with initial normal rising slope of eye velocity, then sudden decline almost linearly to zero baseline before the head stops. This trace could either be considered as a true physiologic result [9] or as what has been called 'bump' artifact [10].
- This trace is classified as an abnormal head impulse whether or not the peak eye velocity is less than 20% of head velocity.
- Minor (non-disruptive) artifacts (e.g., head bounce) or non-disruptive fast phases are allowed if a bell-shaped morphology is still recognizable and key VOR landmarks are not obscured.

Exemplar**Uninterpretable HIT (incorrect morphology)**

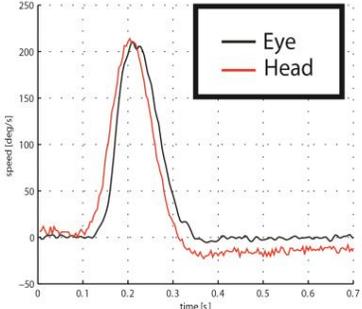
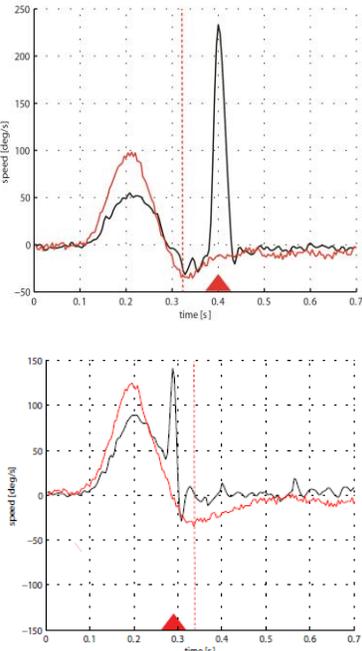
- Every HIT which does not qualify as normal or abnormal HIT.
- This generally implies a major (disruptive) artifact occurring during the HIT head movement (e.g., pseudo-saccades [first exemplar], 'two-peaks' artifact [second exemplar]).
- *NOTE: Some uninterpretable traces may be due to disruptive saccades occurring during the HIT head movement, rather than disruptive artifacts. Typical covert refixations associated with an abnormal VOR, however, occur late enough to be non-disruptive (see Suspected Corrective Refixation Saccade).*

Exemplars

Fast Phase Eye Movements

Fast phase eye movements occurring during or after the VOR were classified as suspected corrective saccades, spontaneous nystagmus, or unclassifiable. If an isolated saccade occurred during or shortly after an abnormal slow phase VOR, we considered it a corrective, refixation saccade. Corrective saccades occurring during an abnormal HIT, generally towards the end of the head movement, were labeled *covert saccades* (Figure 2F); those occurring shortly after HIT completion were labeled *overt saccades* (Figure 2E), in accordance with standard convention [8]. Spontaneous nystagmus could be visually differentiated from refixation saccades by the presence of one of two distinctive patterns: (1) a constant and regular nystagmus frequency with at least three consecutive rhythmic ‘beats’ (roughly evenly spaced saccades) in the trace (Figure 2G); or (2) at least two consecutive ‘beats’ (appropriately spaced saccades) directed opposite to the VOR eye movement and any corrective saccade (Figure 2H).

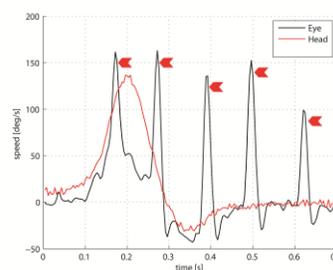
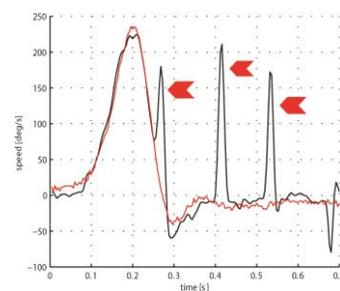
Coding options (mutually exclusive and jointly exhaustive):

<p>No Refixation Saccades or Nystagmus</p> <ul style="list-style-type: none"> No fast phase eye movements visible at any direction. 	<p><i>Exemplar</i></p> 
<p>Suspected Corrective Refixation Saccade</p> <ul style="list-style-type: none"> Saccade morphology (spike) with peak eye velocity of 60 °/s or greater eye velocity. This cutoff was chosen by considering the main sequence of saccades [1]. Same direction as slow phase VOR (eye trace in HIT). Abnormal HIT slow phase, as defined above. One or two saccades present (if more than two are present, then saccades are considered unclassifiable). Further classified as either <i>overt</i> (onset of saccade after head movement, as in first exemplar) or <i>covert</i> (onset of saccade during head movement, as in second exemplar) (also Fig. 1). 	<p><i>Exemplars</i></p> 

Suspected Nystagmus

- Saccade morphology (spike) with peak eye velocity of 60 °/s or greater eye velocity. This cutoff was chosen by considering the main sequence of saccades [1].
- At least three consecutive fast phases with an approximately regular pattern (i.e., direction, velocity, and frequency).
- Normal (first exemplar) or uninterpretable (second exemplar) HIT slow phase VOR, as defined above.
- *Note: Multiple fast eye movements seen in association with an abnormal HIT slow phase were considered ‘unclassifiable’ because multiple saccades with a reduced VOR gain might have been either nystagmus or ‘stair-step’ refixations (i.e., multiple hypometric refixations to return to the visual target).*

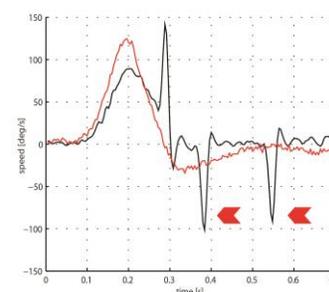
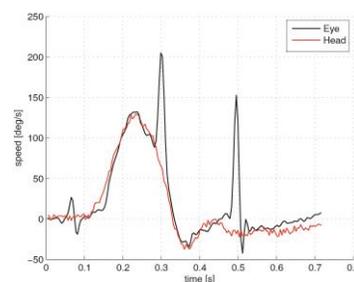
Exemplars



Unclassifiable Saccades

- Saccade morphology (spike) with peak eye velocity of 60 °/s or greater eye velocity. This cutoff was chosen by considering the main sequence of saccades [1].
- Does not meet criteria for suspected corrective saccades or nystagmus, as above. Generally this includes traces with only one or two saccades and a normal slow-phase VOR during the HIT (first exemplar). Alternatively, there could have been ≥ 3 saccades in the context of an abnormal slow-phase VOR.
- We also classified as a special sub-type *wrong-way saccades* (second exemplar) with two or more saccades oppositely directed from the slow phase VOR. Although this special pattern was an unusual finding (~1%)* it could have been due to ‘wrong-way nystagmus’ (beating towards a deficient VOR), corrective refixations following overshoot (e.g., due to head bounce or a miscalibrated refixation saccade), or random, extraneous saccades (e.g., fixation losses).

Exemplars

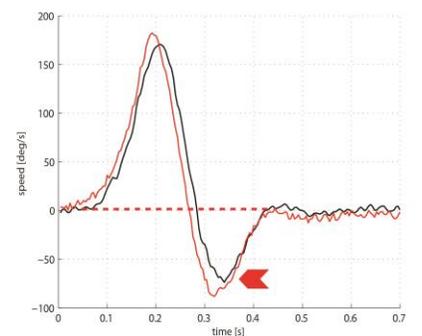
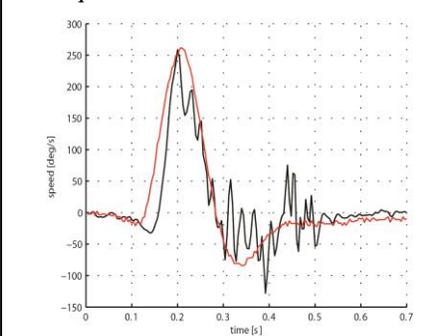


* One patient in our series with wrong-way saccades had a right AICA stroke—the patient had an asymmetric bilateral VOR gain deficit (worse on the right) with spontaneous left-beating nystagmus that changed to right-beating in right gaze. The right-sided VOR deficit with HIT, leftward covert corrective saccade, and (presumed) right-beating nystagmus were all evident on the HIT trace. This pattern might also be expected in some cases of bacterial labyrinthitis with initial *irritative* nystagmus [11] or post-treatment nystagmus reversal days to weeks after an initial *destructive* nystagmus beating away from the lesion side [12]. It is also theoretically possible in cases of Menière’s disease during the *recovery* nystagmus phase [13], but it is unclear whether this actually occurs, since few patients have been systematically tested with quantitative HIT during attacks and at least some of those who have been tested do not have unilaterally deficient VOR responses by this test method [14]. Thus, although this finding is probably non-specific vis-à-vis the underlying etiology, a preponderance of HIT traces with this ‘wrong-way’ pattern should at least spark consideration of a possible central lesion, given its relative rarity in neuritis.

Artifacts

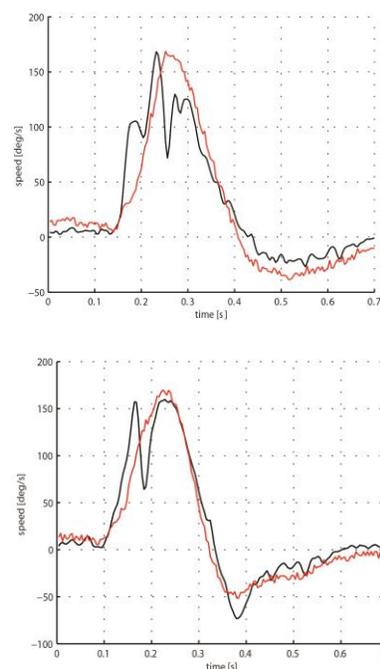
Any HIT eye movement trace morphology that did not fall into a known physiologic category (i.e., slow phase or fast phase, as described above) was considered an artifact. Artifacts were further classified based on morphologic similarity to deliberately induced artifacts in a single normal subject (manuscript author GM). Although artifacts were, by their nature, inconsistent, there were general morphologic patterns that emerged as reproducible, described below; for the most part, these were reliably coded (see Table 1). All HIT traces were classified as having artifacts ‘absent’ or ‘present’ and, if ‘present’, major (disruptive) or minor (non-disruptive). A ‘disruptive’ artifact was an artifact in the eye movement trace occurring during the HIT and likely to affect VOR gain measures by distorting key landmarks for VOR gain calculation. Beyond ‘absent’ vs. ‘present’ (mutually exclusive and jointly exhaustive – i.e., one and only one code per HIT), multiple artifact types could be coded for a single HIT trace (e.g., ‘bounce’ AND pseudo-saccades). Note that for grossly distorted traces (e.g., ‘wrong-way’ VOR), additional artifacts were not coded. Specific artifact types listed below are in order of descending frequency identified in our series (Table 2).

Coding options (artifact types are jointly exhaustive but not mutually exclusive):

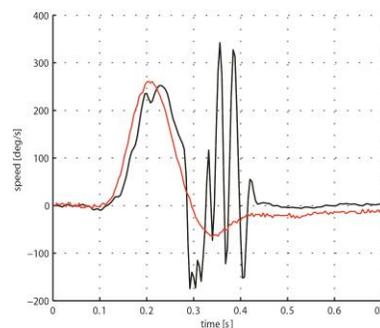
<p>Head bounce (improper HIT technique)</p> <ul style="list-style-type: none"> • Head velocity traces overshoot in the opposite direction after the head stops, before returning back to baseline (this head reversal following deceleration is known as ‘bounce’) • Small amounts of bounce are unavoidable; to code this error, we required an oppositely-directed peak head velocity ≥ 50 °/s • <i>NOTE: This is an error in technique, but not an artifact, per se (it represents an examiner-induced overcorrection at the termination of the impulse, with an oppositely-directed, appropriate physiologic VOR eye movement response). Excessive bounce could lead to false VOR gain estimates.</i> 	<p><i>Exemplar</i></p> 
<p>Trace oscillations (suspected pupil tracking loss)</p> <ul style="list-style-type: none"> • Any discontinuity (break) of the eye trace (<i>rarely seen</i>) OR • Continuous oscillations at baseline with amplitudes $< 75\%$ of peak eye velocity OR total duration > 150 milliseconds • Magnitude of oscillations > 20 °/s eye velocity • Should cross the baseline at least twice • Subcategories: occurring <i>during</i> or <i>after</i> HIT (or both) 	<p><i>Exemplar</i></p> 

Multiple peaks (suspected touching of the goggles)

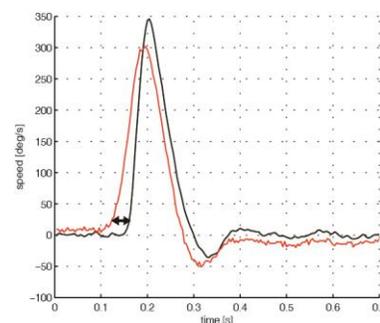
- HIT slow phase with incorrect morphology (i.e., not bell shaped), with two or more ‘peaks’; peaks are differentiated from trace oscillations based on each peak representing at least 25% of the total height of the eye velocity trace
- *NOTE: Although this pattern was typical when goggles were touched during the HIT (first exemplar), a two-peaks artifact could also be due to mini-blinks (second exemplar). Some such traces may also be due to disruptive saccades occurring during the HIT, rather than true artifact.*

Exemplars**Pseudo-saccades (suspected blinks or mini-blinks)**

- One or more oscillations which cross the baseline with high amplitude (amplitude $\geq 75\%$ of peak eye velocity) AND short duration (≤ 150 milliseconds) +/- loss of pupil tracking
- Subcategories: occurring *during* or *after* HIT (or both)

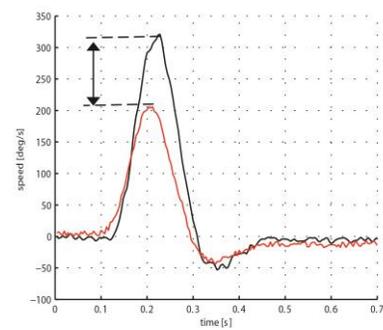
Exemplar**Phase shift (suspected loose strap)**

- Any shift of phase more than 20 milliseconds between the onset of the head movement and onset of the eye movement
- *NOTE: Although the eye can sometimes lead the head if compensation for goggles slippage is not properly calculated [3], phase shifts are generally delays in the eye trace relative to the head trace (exemplar). A normal, physiologic VOR delay is approximately 6 milliseconds [1]. In cases with significantly reduced VOR gain, it may be difficult to differentiate artifact from a true VOR onset lag.*

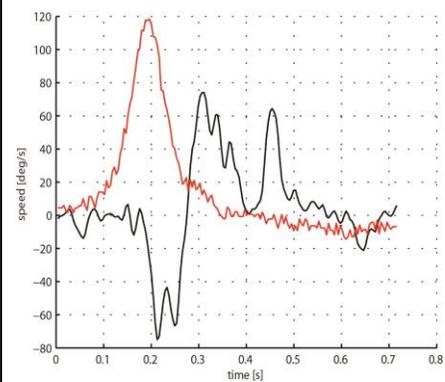
Exemplar

High gain (suspected miscalibration)

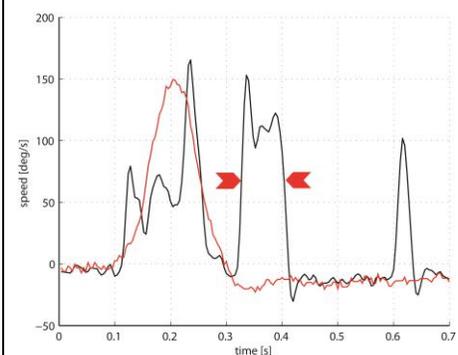
- HIT with peak eye velocity greater than peak head velocity by a margin of more than 20%
- *NOTE: Cerebellar disinhibition or central VOR adaptation to hyperopic spectacle correction [15] could produce a similar pattern, although true VOR gains above 1.2 are very rare.*

Exemplar**Wrong-way VOR (suspected patient inattention)**

- During the HIT VOR, the eye deviates in the incorrect direction (i.e., with, rather than opposite the head... displayed graphically as moving away from [rather than in concert with] the head movement, since the eye trace is reversed for display)
- With this artifact, other types of artifacts were not coded

Exemplar**Unclassifiable artifact (unknown cause)**

- Any other artifact not matching a specific artifact pattern (exemplar, red chevrons)
- When unclassifiable artifacts were present, other types of artifacts, even if recognizable, were not coded

Exemplar

References

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