Predictive Action of the Vestibulo-Ocular Reflex

Jun Maruta
Brain Trauma Foundation*

Abstract
The vestibulo-ocular reflex (VOR) is a fast reflex with machine-like features that stabilizes vision during head movement. The fact that even a reflex as simple and fundamental as the VOR involves a neural delay may imply that we are at least a step behind the reality. However, the VOR is equipped with mechanisms that anticipate the visual consequence of the reflex action to produce appropriate responses in various contexts. That is, the brain maintains a predictive state even at the reflex level. This perspective may lead to further understanding of brain functions.

Introduction
Do we live in the past? We know that neural processing requires time. Simply put, the existence of processing delays implies that, by the time neurons transmit signals triggered by the external events, the events themselves have already taken place. The reflex eye movement that stabilizes vision during head movement, namely the vestibulo-ocular reflex (VOR), is one of the fastest outputs the brain can generate from sensory input. Nevertheless, the latency of the VOR is in the order of 10 ms. The upshot of visual stabilization, i.e., visual perception, may require an additional 80 ms. It may thus appear that the information the brain receives from sensory organs is only a reflection of the past. However, the statement would be true only if the brain were to just passively receive and process information. This paper will re-examine this assumption in light of various aspects of the VOR. Based on the evidence of proactive characteristics of the VOR, a conclusion will be drawn that the brain maintains a predictive state even at the reflex level.

Orienting vs. compensatory VOR
Vestibularly evoked eye movements can be classified as compensatory or orienting regardless of whether they are induced by angular acceleration (mediated by the semicircular canals) or linear acceleration (mediated by the otoliths). Compensatory eye movements support maintenance of a fixed gaze direction or gaze point in space and can be produced by the angular VOR or the high frequency linear VOR (Fig. 1A). On the other hand, orienting eye movements have been variously described as goal-directed gaze shifts toward a real or fictive self-motion, changes in the center of interest, a tendency to align the eye vertical with the spatial reference vector of the gravito-inertial acceleration (GIA), displacement of the reference eye position of the planar field of eye movement, and so on.

A generalized definition of orienting eye movements may be given as purposive changes in the center of action, about which compensatory, pursuit, and localizing eye movements take place. With this definition, the essential nature of orienting eye movements embodies anticipation that facilitates early visual processing, i.e., predicting where visually interesting features are going to be found. Orienting eye movements may be voluntary or reflexive, but only those related to the VOR will be...
Fig. 1 Response to head rotation. A. The point of gaze is stabilized in space against the head rotation with a compensatory eye movement. The movement may be considered to be reactive in this context. B. The point of gaze is directed into the direction of the head rotation. This movement is proactive because it prepares the eyes to receive new information.

Efficiency of these other eye movements is promoted because counter rotation redefines the way the dimensionality of motion is reduced. Efficient eye movements in turn will promote visual processing.

Besides tilt-induced responses, ocular roll and pitch during selective otolith stimulation of low to mid-band frequencies also strongly orient the vertical axis of the eyes toward the spatial reference vector of the GIA in the rabbit. Furthermore, even though the orienting response to linear acceleration in the rabbit declines with an increase in the stimulus frequency, simultaneous stimulation of semicircular canals during dynamic tilting expands the frequency range of response and increases the gain of ocular-counter rotation. Since the expanded responsiveness makes the orientation dynamics also appropriate for active motion, ocular orientation can be regarded as part of the inherent process built into the vestibular system.

During orienting reflexes in the rabbit, eyes rotate about axes that do not compensate head movements despite the importance of aligning the head and eye movements to stabilize vision. In particular, there is a prominent yaw vergence effect that accompanies ocular pitch. A possible functional significance of the concurrent ocular pitch and yaw vergence is to modulate binocular vision. At rest, the largest binocular overlap occurs in the rostrodorsal visual field. While ocular counter-roll and -pitch that stabilize the position of the eyes relative to the gravity are both compensatory and orienting, the orienting property supports visual responsiveness during head tilts by holding the retina to align the visual streak with the spatial horizontal defined by gravity.

Rats and monkeys also produce similar non-compensatory yaw vergence during otolith stimulation by off-vertical axis rotation. The commonality of the behavior among different species and the range of stimuli that produce changes in the binocular field with concurrent ocular pitch and yaw vergence imply that anticipatory facilitation of binocular vision is directly influenced by vestibular input during various types of normal head move-
ments as the organism navigates in the natural environment.

**Beating field of nystagmus (schlagfeld)**

Nystagmus is a repetitive eye movement consisting of alternating slow and quick phases. During the VOR, the slow phases counter the head movement, which would support stable vision. The quick phases may be regarded as saccadic resetting movements that keep the eye position in the oculomotor range. Visual perception is suppressed during saccades. Nystagmus may be accompanied by a positional offset that shifts its field of motion known as the beating field or schlagfeld.

The modulation of the beating field may be considered to be a specialized function of ocular orientation that changes the center of interest. In humans, the immediate action of the angular VOR during a sharp head turn is a saccade toward the direction of head rotation, which is an anti-compensatory response, rather than a movement that opposes the head rotation. In humans, cats, and rats, the beating field of nystagmus of the VOR tends to occur in the side of the quick phase direction, i.e. in the direction of the rotation; thus, the source of the visual input is anticipated. Correspondingly, the modulation of the beating field of optokinetic nystagmus (OKN) in humans is closely related to the perceived self-rotation, even as the perception can be erroneous and can be periodically switched in direction independently of the stimulus.

Specific functional demands likely guide the beating field. For example, the directional preponderance of the beating field modulation is reversed in foveal and peripheral visions in humans. Consistent with this observation with peripheral vision, the shift of the beating field of VOR nystagmus in the rabbit is in the direction of the slow phases and thus compensatory, highlighting the importance of orienting to the stable visual surroundings in this lateral eyed animal. Thus, the directional preponderance of the beating field is also likely to be determined by variations in species-typical visual exploratory behavior and strategies. It is also known that regulation of the beating field is acquired through visual experiences.

The neural substrates of beating field modulation are not well understood, but there are some clues. The magnitude of the shift in the beating field is influenced by the frontal eye field, a locus of selective visual attention. A loss of the post-saccadic gaze-holding ability, which is implemented by the neural integrator in the brain stem, is also associated with a disruption of the normal beating field regulation. In cerebellarized rabbits, saccades during OKN are diminished in amplitudes and thus fail to reset the eye position offsets generated during the slow phases. This reduction in saccade amplitudes exaggerates the directional preponderance of the beating field shift toward the slow phase side that is observed in normal rabbits. In examples from human patients with a cerebellar degenerative disease or lesion, the beating field appears to shift toward the side of the slow phases during the VOR, which is opposite from normal people, but similar to rabbits. Damage in the cerebellum reduces the gaze-holding ability at eccentric positions, presumably by influencing the time constant of the neural integrator, but centripetal post-saccadic drifts associated with this condition cannot explain a beating field shift toward the side of the slow phases; thus the exact contribution of the cerebellum to the beating field modulation is unclear.

**Gain adaptation**

Plasticity in the VOR is a well-known phenomenon. As the VOR compensates for head motion with eye rotation, the system constantly calibrates itself to ensure stability of vision by reducing the mismatch between the input and output. The VOR performance is typically expressed in terms of gain, which is defined as the ratio between the eye and head rotation speeds in the angular VOR. Changes in visual-vestibular interactions, induced with optical or mechanical manipulations, can drive the VOR gain up or down, and such gain adaptation paradigms have provided a useful model to study the neural mechanism of memory formation.

An important realization relevant to the discus-
sion at hand is that learning is not a passive storage mechanism. Instead, the goal of learning is to optimize the outcome of a particular action that has yet to take place. That is, memory is an internal representation of what the world should be in the future; when an organism learns, it is already predicting what is likely to occur in the future. That VOR gain adaptation can occur far more efficiently during active head movements than passive ones \(^{42}\) implies that learning is a proactive rather than reactive process whereby an error signal (retinal slip) is compared to prediction. VOR gain adaptation may be better described as a prospective process that checks the difference between the expected and the experienced so as to update the expectation, rather than a process that retrospectively corrects for errors.

VOR gain adaptation can be general or context-specific \(^{43}\). When generalized adaptation takes place, the system is predicting a global change in the outcome of the VOR, whereas context-specific adaptation suggests associative learning, or a context-specific prediction. Generalized and context-specific adaptations are necessarily implemented by different neural loci and modules, but the cerebellum appears to provide an ideal substrate for relevant courses of action in both cases \(^{39–41, 43}\).

**Velocity storage**

The vestibular organ in the inner ear is a set of biomechanical accelerometers. However, during rotation at a constant velocity in the absence of persistent acceleration, the sensation of rotation continues beyond the initial acceleration. One explanation for this observation is in the fluid inertial consequence within the peripheral vestibular organ that prolongs the signals \(^{44}\). Yet, the sensation of rotation still outlasts the peripheral input. The velocity storage integrator is the central mechanism that stabilizes eye velocity during rotation and extends the time over which the VOR can compensate for head movement \(^{45, 46}\).

Velocity storage may be thought of as a short-term memory of an ongoing rotation. The velocity storage mechanism can be activated by input from the semicircular canal or otolith components of the vestibular organ \(^{46, 47}\), or visual \(^{45}\) or somatosensory \(^{48}\) input.

Remarkably, the stored velocity-related information can undergo transformation, which results in a shift of the eye rotation axis toward the at-the-moment inertial reference, i.e. the GIA, when the axis of the stimulus is different from the orientation of the GIA. For example, in the monkey, optokinetic stimulation about the animal’s vertical axis given while the animal is in a tilted position induces OKAN whose axis tends toward the spatial vertical instead of the original axis along the animal’s vertical \(^{49}\), and off-centered rotation, that is centrifugation, of a monkey induces nystagmus that tends toward the combined vector of the centripetal and gravitational accelerations instead of the axis of the applied angular acceleration \(^{50}\). Existence of similar cross-coupling phenomena has been demonstrated in the rabbit during centrifugation \(^{45}\) and during secondary after-nystagmus following long-term optokinetic stimulation \(^{51}\). These shifts in the axis of eye rotation show that velocity storage is amenable to real-time adjustment.

Although the velocity storage integrator is at least partially implemented in the brain stem \(^{52, 53}\), the cerebellum, in particular the nodulus along with the adjoining uvula, plays a critical role in the control of the stability of the velocity storage mechanism \(^{54}\), and influences the dynamics of the VOR in three dimensions \(^{55}\). The nodulus and uvula are also involved in generation of cross-coupling between eye rotation axes \(^{50, 51, 56}\), presumably by inhibiting one axis of eye movement while disinhibiting another \(^{50, 56}\). Thus, during cross-coupling, the nodulus and uvula appear to transfer the stored velocity-related information about one axis to another axis.

Velocity storage can be regarded as an active working memory system that provides an expectation of head and body orientation in space. This formulation is also the basis of a theory of motion sickness \(^{57–59}\). The purpose of motion sickness is unknown but it has long been postulated that a sensory conflict causes motion sickness. However, it should be noted that a sensory conflict arises pre-
cisely because there is an internal prediction of the external input\textsuperscript{60}. The velocity storage theory proposes that the critical component of the sensory conflict is the misalignment between the expected spatial vertical and the detected inertial reference, which can be measured in terms of the orientation of the axis of eye rotation and the GIA. Taken together, the velocity storage mechanism is closely tied to spatial orientation and serves as an important element of predictive behavior.

**Role of cerebellum**

The VOR is a phylogenetically old, predominantly di-synaptic reflex arc. Nevertheless, prediction is actually a basic feature of the VOR as reviewed above. The close relationships between the vestibular and cerebellar functions, with the cerebellar circuit forming a side-loop to the direct VOR pathway, are well recognized, and the role of the cerebellum is implicated in many of the predictive aspects of the VOR. Formulation of internal prediction per se may be so basic a requirement for survival of an organism that it may not necessarily involve the cerebellum\textsuperscript{60}. However, predictive mechanisms are likely to be implemented by multiple layers of neural substrates, and better understanding of the functional role of the cerebellum may be obtained when neural predictions are considered\textsuperscript{61}.

**Conclusion**

That the information processed by the brain is only of a time past is hardly true. The orienting and adaptive properties of the VOR actively prepare an organism to acquire visual information by foreseeing the optimal placement of the eyes. Thus, we are not only reactive but also proactive even at the level of a reflex. Foreseeing the future is not just a cognitive ability.

A broad implication of the present proposition is that our past, present, and future simultaneously exist in the now. It is only that the connection to the reality may have some time shift. The purpose of this connection is literally a “reality check” just so one is prepared to respond to a stimulus with the best educated guess for the moment. When the stability of the best educated guess can be supported by a set of computational rules within some time window, a slight time shift in the connection to the reality is not critical. Nor is it essential that the connection is maintained continuously.

**References**

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