DYNAMICS OF ADAPTIVE CHANGE IN HUMAN VESTIBULO-OCULAR REFLEX DIRECTION

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Abstract - Adaptive modification of vestibulo-ocular reflex (VOR) direction was characterized in humans by recording vertical and horizontal VOR eye movements during horizontal rotations in darkness at frequencies of 0.05 to 1 Hz before and after exposure to a VOR direction adaptation procedure. This procedure paired yaw horizontal vestibular rotation at 0.25 Hz with synchronous pitch vertical optokinetic motion. Saccades were removed from eye position records and VOR gain and phase were recorded. With an onset time constant of 36 min, the VOR measured during horizontal rotation in complete darkness acquired a vertical component in phase with the optokinetic stimulus presented during adaptation. The amplitude of this newly acquired vertical VOR component was maximal during rotation at the frequency of adaptation; at other frequencies, the amplitude was lower, but still significant. Unlike VOR direction adaptation in cats, the phase of the adaptive VOR component in humans did not show significant leads or lags at test frequencies below or above the adaptation frequency. These data suggest that, like the cat, the human VOR can be directionally adapted, and the pathways involving the adaptive component of the VOR are frequency specific.

Keywords — vestibulo-ocular reflex; adaptation; vestibulo-ocular reflex plasticity; optokinetic reflex.

Introduction

The vestibulo-ocular reflex (VOR) helps maintain a stable image on the retina by sensing head rotation of a certain direction and amplitude and producing a compensatory eye rotation of equal and opposite angular displacement. If the VOR did not have a gain close to unity, the resulting retinal slip of an image would cause that image to be blurred. Developmental change, calibration errors in neural circuitry, or damage to the vestibular or oculomotor apparatus can all alter the VOR output and precipitate retinal slip. This retinal slip provides a neural signal that is used to modify the VOR output and recalibrate the VOR gain (6,7,16). Once adaptation is complete, clear vision is restored, in either the short term (4,8,12) or the long term (5,9,14–16).

Errors in VOR direction can be caused by changes in the direction of visual field motion with respect to the direction of head motion. For example, the VOR direction will be erroneous if the visual field moves vertically every time the subject's head moves horizontally. VOR direction adaptation has been clearly shown to exist in cats, and can change the direction of eye movement produced by activation of the horizontal (10) or vertical semicircular canals, or the otolith organs (1). Study of the directional adaptive component of the human VOR has included the torsional VOR (2) or the vertical VOR (3), but adaptive change in human VOR direction has never been characterized across time and frequency as in cats (10). The experiments reported here are a description of an adaptive component of the human VOR. We show that this reflex dem-
prostrates frequency selectivity and time course response similar to the corresponding reflex of the cat.

**Methods**

Surface electro-oculographic (EOG) recordings were taken from 4 human males (ages 19-35) in 6 separate experimental sessions. Subjects were seated in a chair connected to a computer-controlled servomotor apparatus that could produce sinusoidal oscillations about the earth vertical axis, as illustrated in Figure 1. Their heads were fixed to the headrest of the chair, using a clamping device whose pads were placed securely on the subjects' temporal bones. The apparatus was enclosed in a light-proof room, which had a featureless screen 1.7 m in the front of the subject, upon which an optokinetic stimulus could be projected. Subjects were dark-adapted for a minimum of 30 min prior to each experiment in order to stabilize EOG.
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gain and minimize EOG drift. EOG electrodes were placed as illustrated in Figure 1 so that each eye's pair recorded approximately equal proportions of both horizontal and vertical components of eye movement. An electronic circuit was used to make a weighted sum and difference of the signals from the electrode pairs in order to produce pure vertical signals during optokinetic rotation, and pure horizontal signals during chair rotation with a stationary optokinetic stimulus. On the assumption that pure horizontal chair rotation resulted in no vertical eye motion, and that pure vertical optokinetic stimulation caused no horizontal eye motion, EOG crosstalk was minimized. The horizontal EOG signal was calibrated by instructing the subject to fixate on a stationary object on the screen while the chair was oscillated at a known amplitude in the horizontal plane. The vertical EOG signal was calibrated by instructing the subject to fixate on an object that was vertically oscillated on the screen at a known amplitude. After all EOG data had been collected, saccades were removed by computer-assisted manual editing of EOG records. The remaining slow phase velocities were fitted to sine waves in order to obtain a gain and phase value for each trial. Vertical gain was defined as vertical eye velocity divided by optokinetic stimulus velocity.

The subjects were adapted by exposing them to a visuo-vestibular stimulus which consisted of sinusoidal horizontal oscillation about an earth vertical axis at 0.25 Hz with a peak velocity of 19°/s, combined with a phase synchronized sinusoidal vertical optokinetic stimulus with a 26°/s peak velocity. The optokinetic stimulus was a full field (180° of visual angle) pattern of projected small spots. The axis of rotation of the spherical projection system was aligned parallel to the subject’s interaural axis when the chair was centered at rest.

As a control, we measured the baseline horizontal and vertical VOR eye movements in an unadapted state by rotating the subjects horizontally in complete darkness at 0.05 Hz, 0.1 Hz, 0.25 Hz, 0.5 Hz, and 1.0 Hz. There were 4 trials at each frequency (8 trials at 1.0 Hz), and each trial consisted of 5 sinusoidal cycles (one cycle at 0.05 Hz). The data acquisition system sampled 1024 points of data for each trial, resulting in sample rates of 51.2 Hz, 20.5 Hz, 51.2 Hz, 102.4 Hz, and 204.8 Hz for the 5 respective rotation frequencies. The inputs to the data acquisition system were all filtered with 8 pole Bessel filters set to cut off at 10 Hz. Rotations had a constant peak velocity of 19°/s at all frequencies. Subjects were instructed to fixate on an imaginary object 1.7 m in front of them in order to elicit robust VOR responses. After a 2-h adaptation period, interrupted every 15 min by shutting off the optokinetic projector and measuring the horizontal and vertical VOR at the adaptation frequency, the subject underwent a series of tests identical to those in the unadapted state, again in complete darkness. Three of our subjects were subsequently “de-adapted” by rotating them in a stationary visual field; the optokinetic projector was turned on but remained immobile. Every 5 min throughout this “de-adaptation” period, the VOR was measured at 0.25 Hz in complete darkness, again while the subject was attempting to fixate on an imaginary object. Alertness was maintained by talking to the subject during the testing sessions. During the training sessions, different diversions such as music, murder mystery recordings, or humorous recordings were used to maintain alertness. Horizontal and vertical VOR gains and phases measured in the unadapted or adapted state were vectorially averaged together across multiple runs at the same test frequency. The preadaptation vertical VOR averages were then vectorially subtracted from the postadaptation vertical VOR averages to obtain the gain and phase of the adaptively generated changes in the VOR.

Results

Figures 2A and 2B depict the preadaptation and postadaptation vertical VOR induced by horizontal rotation at 0.25 Hz. After adaptation, when the subject was exposed to a horizontal vestibular stimulus in
Figure 2. Horizontal head position and vertical eye position during yaw rotation before adaptation (A), after adaptation (B), and after "de-adaptation" (C). Vertical eye velocity and vertical eye velocity fit were computed for each trial taken, after saccades were removed. There is little vertical VOR during yaw before adaptation and after "de-adaptation," but vertical eye movement is clearly evident 2 h after adaptation. (The small vertical VOR responses in columns (A) and (C) are due to the limitations of the horizontal and vertical calibration procedure, and the expanded scale of the velocity fit records.) All data sets were taken from the same experiment.

complete darkness, the VOR showed a vertical component that was not seen prior to adaptation. The phase of the acquired response was the same as that of the adapting optokinetic stimulus. This additional component of the VOR was present throughout the postadaptation testing period. Figure 2C shows the vertical VOR response in complete darkness 10 min after "de-adaptation" by rotation in a stationary visual field for a period of 20 min. Clearly, the response that was present throughout the postadaptation test interval diminished back to baseline.

Figure 3 shows the time course of adaptation of the vertical VOR. Adaptation initially occurs rapidly, first appearing after about 15-30 min, but the increase in vertical VOR gain rapidly tapers off. When modeled by a simple exponential, the time constant obtained by fitting the average of all six sets of time course data was 36 min, which is remarkably close to the value of 35 min obtained for the cat (10). When the subjects were rotated in a stationary visual environment after adaptation, all reported a sensation of visual field movement which was in the opposite direction of spot motion during training. In other words, when leftward vestibular stimulation had been coupled with upward optokinetic stimulation, the subjects reported a downward movement of the visual field when they were rotating leftward, even though the visual field was stationary. No subject, however, reported a sensation of body axis tilt. "De-
adaptation" time course was measured in 3 of the 6 cases. In each of these cases, the acquired vertical VOR response in complete darkness had clearly diminished in amplitude within 5 to 10 min, and had returned completely to baseline within 15 to 25 min.

As shown in Figure 4A, the greatest postadaptation vertical VOR response to yaw movements occurred at the 0.25 Hz training frequency. At test frequencies lower and higher than the training frequency, the response was smaller, but still significantly greater than in the pretraining condition. This effect is similar to what happens in the cat. Surprisingly, the phase of the acquired response across all frequencies, showed little deviation from 0°. This is in contrast to VOR direction adaptation in the cat, which shows a significant phase lag at high frequencies, and a phase lead at the lower frequencies.

There was no consistent difference in the horizontal VOR after the adaptation period, as shown in Figure 4B. Some of our subjects showed an increase in gain, and some showed a decrease in gain. (A gain was assigned a negative value if its corresponding phase value was >90°, or <−90°.)

Discussion

Several studies in recent years have demonstrated a broad range of adaptive capability of the VOR. The gain, phase, and direction of the VOR have been shown to be modifiable in animals from goldfish (19,20) to rabbits (11) to monkeys (15) to humans (2,3,8,9). Adaptation of the VOR has been induced by altering visual input during vestibular stimulation produced by passive head rotation (12,17). Passive sinusoidal rotation has been used to study the frequency selectivity of VOR adaptation. All animals tested have shown selectively greater adaptation gain near the training frequency (6,10), with the broadest tuning reported in monkeys (13). Our results suggest that human VOR adaptation to sinusoidal rotation produces even broader frequency tuning than found in monkeys.

The time constant of 36 min that we obtained was very similar to the time constant obtained in comparable studies on the cat. Previous human studies have also shown that human time course of adaptation can have a short time constant, on the order of minutes (4,8), in addition to intermediate and long
Figure 4. Dynamics of induced vertical eye movement at a training frequency of 0.25 Hz. (A) Differential band-pass characteristics of vertical eye movements in the dark. Data in this plot display the postadaptation responses with the preadaptation responses vectorially subtracted from them. Vertical gain was defined as the ratio of eye velocity to optokinetic stimulus velocity. (B) Differential characteristics of horizontal eye movements in the dark. As above, the preadaptation horizontal eye responses were vectorially subtracted from the postadaptation responses and displayed. Note that vertical data show a stereotypically shaped curve, but horizontal data are not reproducible from subject to subject. Each symbol type represents data from a single experiment. Symbols connected by solid lines indicate the vectorial mean of all data at each particular frequency.

time constants that can be as long as a few days (9). This evidence supports the idea that there may be more than one adaptive process going on in the brain: one that may react quickly, but not have a very strong effect, and others that may have a slower onset, but a more robust impact on VOR gain. Other possibilities that may account for different
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Time constants include strength of the adaptation stimuli, both visual and vestibular, and state of awareness of the subject.

The broad frequency response we observed, with nearly constant phase across the spectrum from 0.05 to 1.0 Hz, could be attributed to either a species difference or to our use of a VOR direction adaptation paradigm. A comparison of cat and human VOR studies pairing yaw vestibular rotation to pitch optokinetic stimulation supports the idea of a species difference. Using the same bandpass filter model that we applied to our cat VOR direction adaptation data, we obtained time constants of 0.11 and 2.9 s for the human data, as compared to 0.14 and 1.1 s in cats (10). The more widely spaced time constants for the human data indicate that the human curve has a much broader tuning than the similarly shaped cat curve. The bandpass filter model provided a good fit to the adaptive VOR phases in the cat, but does not predict the nearly constant phase of adaptive human VOR (see Figure 2B). This apparent species difference suggests that human VOR modification involves more complex mechanisms than in lower animals.

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