THE INFLUENCE OF VISUAL AND SOMATOSENSORY INPUT ON THE VESTIBULO-OCULOMOTOR REFLEX OF PIGMENTED RATS

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Abstract—Eye movements were recorded in the pigmented rat during vestibular, optokinetic and combined visual-vestibular stimulation. The dominant time constant in pigmented rats, tested during angular vestibular stimulation in darkness, is about two times longer than the cupular time constant. The gain and the duration of nystagmus, achieved by angular vestibular stimulation, can be enhanced by visual impulses. This is most evident during an optokinetic temporonasal stimulation, but is also seen with a nasotemporal stimulation. A mere optokinetic monocular stimulation without a synchronous vestibular excitation causes nystagmus only when the stimuli has a temporonasal direction. The duration of nystagmus, achieved by angular vestibular stimulation, is prolonged by disturbances of the neck proprioceptive system. This is more evident during a simultaneous visual input than in darkness. The ability to cancel nystagmus during conflicting vestibular and optokinetic impulses is well developed in the pigmented rat.

Keywords—rat; eye movements; vestibulo-oculomotor reflex; optokinetic nystagmus; visual suppression; neck muscle lesion; velocity storage.

Introduction

Gaze stabilization is performed by the interaction of inputs from the vestibular, visual, and somatosensory systems to the nuclei for the eye muscles and to motor command centers regulating head and body position. The basic mechanism for this complicated system of gaze stabilization has been extensively investigated in man and in the monkey, cat, and rabbit (1). The main interest has been focused on the opto- and vestibulo-oculomotor systems, including the vestibulo-oculomotor reflex (VOR), optokinetic nystagmus (OKN), visual suppression, and smooth pursuit eye movement.

The laboratory rat is a standardized animal with well-known basic data concerning physiology, biochemistry, and pharmacology, which are useful in vestibular research. The availability and low costs of this animal enable large series of experiments. A recently described method of recording eye movements in small laboratory animals has further facilitated vestibular experiments on rats (2). The usefulness of this species has been illustrated in experiments with lesions in the vestibular pathways (3,4,5) and in neuropharmacological research concerning solvent toxicity in the vestibular system (6). For the further use of rats in this field of research, it seems urgent to investigate how the basic mechanisms of gaze stabilization, studied by recording of eye movements, correlate with those of previously used species. Such a comparison has been performed concerning the optokinetic system (7). The purpose of the present investigation was to clarify how visual impulses in conflict or in agreement with the vestibular stimuli will affect the time course of the VOR in the pigmented rat. Another purpose was to determine how disturbances of the neck proprioceptive input might influence the same parameter. We will also discuss
how our findings fit into a previous mathematical model for gaze stabilization, mainly based on experiments on monkeys and rabbits.

**Methods**

Pigmented rats (DA-HAN), aged 4 to 9 months, weighing 175-350 g, were used. The rats were placed in a stereotactic instrument under general anesthesia. A nut was attached to the skull by dental cement and six metal screws to allow proper fixation of the head during the subsequent tests. The rats were given a recovery period of one week after the surgery before recordings were made. During this period the animals were put 2 to 3 times into the fixation device for 1 h in order to get them used to the experimental situation. The head was restrained within a plastic frame that also had side walls for the body.

Recordings of horizontal eye movements were made by a magnetic search coil system, described by Kasper and colleagues, 1987 (2). For details concerning the application of the method to rats, see Hess and colleagues, 1985 (7). The coil was glued to the cornea under topical local anesthesia. The eye position signal and the eye velocity signal, obtained by differentiation of the position signal, were registered on a linear recorder (Linearcorder Mark VII, Graphtec Corp., Tokyo). Vestibular stimulation was performed by angular acceleration/deceleration of a turntable. The slow phase velocity (SPV) was measured every other second from the differentiated curve. The SPV$_{eos}$ was defined as the SPV at the end of the acceleration/deceleration stimulation period. The duration of nystagmus upon vestibular stimulation was defined as the time from the onset of turntable acceleration/deceleration until the eye velocity signal equaled zero or was reversed. The dominant time constant (Tv) was calculated by dividing the integrated area under the SPV envelope by the peak SPV (8). For optokinetic stimulation, a pattern of vertical ribs and random spots was projected on a cylindrical screen surrounding the animal (9).

**Stimulation**

a) **Vestibular stimulation in darkness.** Velocity trapezoids were performed with an initial acceleration of 13 or 1000°/s$^2$ up to a constant velocity of 40 or 120°/s. After a constant velocity period of 90 s, deceleration of 13 or 1000°/s$^2$ followed.

b) **Vestibular stimulation with an illuminated earth-fixed surrounding.** Velocity trapezoids were performed as described above, but a still-standing pattern was projected on the surrounding screen.

c) **Vestibular stimulation with an illuminated head-fixed surrounding.** Velocity trapezoids were performed as described above. The rat was surrounded by a screen, mechanically coupled to the turntable. The screen had the same appearance as the projected optokinetic pattern.

d) **Vestibular stimulation in darkness, followed by illumination of a head-fixed surrounding.** Velocity trapezoids were performed as described above. The period of acceleration/deceleration was performed in darkness. At the end of stimulation a head-fixed pattern was illuminated.

e) **Optokinetic stimulation.** A moving optokinetic pattern was projected on the screen around the animal. The movement was presented as a constant velocity between 20 and 80°/s or as a velocity trapezoid with an initial acceleration of 13°/s$^2$, followed by a constant velocity of 120°/s, followed by deceleration of 13°/s$^2$.

f) **Monocular stimulation.** The left eye was covered with a dark rubber cone. The coil was placed on the uncovered eye. Vestibular and optokinetic stimulation was performed as described above.

**General Time Schedule of Each Experiment**

In each experiment the vestibular stimulation was repeated with an interval of 5 min.
every other time clockwise (Clw) or counterclockwise (CClw). Usually two different types of vestibular stimulations as described above were compared. The time schedule of a typical experiment is demonstrated in Figure 1.

Lesion of the Neck Muscles

Under general anesthesia the posterior straight neck muscles were cut at the attachment to the occipital bone and the skin was sutured. Vestibular testing was performed before and one week after surgery. In a control group, a vertical incision of the skin without damaging the muscles was carried out.

Statistical Evaluation

In each experiment the mean value of Clw and CClw stimulation was calculated (see Figure 1). In the experiments with one eye covered, Clw and CClw values were separated.

SPV, based on mean values from several rats, as a function of time after onset of vestibular stimulation are presented in the figures. The mean duration of nystagmus, the mean SPVecs, and the number of rats participating in the experiments are also presented in the figures.

For estimation of the statistical significance, Student's t test was used. If nothing else is stated, the test was paired. A difference of $P \leq 0.05$ was considered to be statistically significant.

Results

VOR in Darkness versus with an Illuminated Earth-Fixed Surrounding

VOR response to angular acceleration/deceleration was tested in darkness by using two different velocity trapezoids (13 or 1000°/s²) with a maximal velocity of 120°/s (Figure 2). There was no difference in the shape of SPV between postacceleratory and postdeceleratory nystagmus. The mean dominant time constant ($T_v$), calculated as described in methods, after acceleration and deceleration was 4 to 7 s (Table 1). The SPV reached a maximum at a lower level during a continuous stimulation of 9 s than during a short lasting stimulation of 0.1 s ($P \leq 0.001$ both for acceleration and deceleration, unpaired t test).

The SPVecs increased when angular acceleration up to a constant velocity of 120°/s was performed with an illuminated earth-fixed surrounding, compared with experiments in darkness (Figure 2). The duration of nystagmus was also prolonged. If the constant velocity level was limited to 40°/s, the nystagmus was permanent until the deceleration started. The SPVecs decreased during deceleration in an illuminated earth-fixed surrounding, compared with darkness, when the deceleration rate was 13°/s². The SPVecs was unchanged when the deceleration rate was 1000°/s². The duration of nystagmus was shortened at both rates of deceleration tested.

<table>
<thead>
<tr>
<th>Stimulation</th>
<th>13°/s²</th>
<th>1000°/s²</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_v$ (acceleration)</td>
<td>4.6 s ± 1.5</td>
<td>6.2 s ± 1.5</td>
</tr>
<tr>
<td>$T_v$ (deceleration)</td>
<td>4.4 s ± 1.5</td>
<td>5.8 s ± 1.6</td>
</tr>
<tr>
<td>$n$</td>
<td>53</td>
<td>20</td>
</tr>
</tbody>
</table>
Turntable Duration of nystagmus (s) SPV_{ecs} (deg/s) n
Acc.darker 15 ± 2 45 ± 16 8
Acc.lighter 41 ± 7 88 ± 15 8
Dec.darker 15 ± 2 46 ± 20 8
Dec.lighter 9 ± 2 9 ± 12 8

Turntable Duration of nystagmus (s) SPV_{ecs} (deg/s) n
Acc.darker 14 ± 3 85 ± 6 10
Acc.lighter 55 ± 29 92 ± 5 10
Dec.darker 12 ± 4 80 ± 6 10
Dec.lighter 6 ± 1 74 ± 8 10

Figure 2. Y-axis: SPV of nystagmus during turntable rotation, presented as acceleratory and deceleratory steps of 13 (left) and 1000 (right) deg/s^2 in darkness or with an illuminated earth-fixed surrounding. X-axis: time after onset of stimulation. The periods of acceleration/deceleration of the turntable are indicated by horizontal bars. Error lines indicate 1 SD. *P: ≤ 0.05, **P: ≤ 0.01, ***P: ≤ 0.001.

OKN-Monocular Testing

Optokinetic stimulation with constant velocity between 20° and 80°/s was presented to rats with one of the eyes covered. The stimulation caused a nystagmus each with a gain near unity when stimuli were presented in the temporonasal direction relative to the uncovered eye. No nystagmus was seen when stimuli were presented nasotemporally.

Optokinetic stimulation with a trapezoid velocity profile (acceleration of 13°/s^2, constant velocity of 120°/s and deceleration of 13°/s^2), presented in temporonasal direction relative to the uncovered eye, caused a short-lasting nystagmus with a low gain during acceleration (Figure 3, left). No nystagmus was seen during the period of constant velocity or deceleration. The same kind of stimulation in nasotemporal direction did not elicit nystagmus at all (Figure 3, right).

VOR in Darkness versus with an Illuminated Earth-Fixed Surrounding-Monocular Testing

With the left eye covered, turntable rotation with a trapezoid velocity profile was performed with an illuminated earth-fixed surrounding, giving simultaneous vestibular and optokinetic stimulation, and in darkness, giving only vestibular stimulation (Figure 3). The SPV_{ecs} and the duration of postacceleratory nystagmus were increased in light, as compared to darkness (Figure 3, left). The in-
Figure 3. Y-axis: SPV of nystagmus with left eye covered, a) during optokinetic stimulation by pattern rotation, presented as acceleratory (left) and deceleratory (right) steps of 13 deg/s² (Clw or CClw), b) during vestibular stimulation by turntable rotation (Clw or CClw), presented as acceleratory (left) and deceleratory (right) steps of 13 deg/s² in darkness or with an earth-fixed illuminated surrounding. X-axis: time after onset of stimulation. The periods of acceleration/deceleration of the turntable or the optokinetic pattern are indicated by horizontal bars. Error lines indicate 1 SD. *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001.
crease of SPV$_{ecs}$ and duration was more evident during Clw rotation of the rat, causing temporonasal optokinetic stimulation of the uncovered eye, than during CClw rotation, causing nasotemporal optokinetic stimulation. During deceleration, the results were reversed (Figure 3, right). There was a decrease in SPV$_{ecs}$ and duration in light compared to darkness during Clw as well as during CClw rotation. The decrease in duration was more evident during Clw than during CClw rotation, but there was no corresponding difference in SPV$_{ecs}$.

VOR in Darkness versus with an Illuminated Head-Fixed Surrounding

Eye movements were recorded during acceleration/deceleration of the rat when surrounded by an illuminated head-fixed visual pattern. With a stimulation of 13°/s$^2$, the nystagmus was almost completely suppressed when the pattern was illuminated as compared to in darkness (Figure 4). With a stimulation of 1000°/s$^2$, nystagmus was not suppressed.

When angular vestibular stimulation of

<table>
<thead>
<tr>
<th>Turntable</th>
<th>Duration of nystagmus (s)</th>
<th>SPV$_{ecs}$ (deg/s)</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acc, dark</td>
<td>17±3</td>
<td>53±16</td>
<td>14</td>
</tr>
<tr>
<td>Acc.conflict</td>
<td>2±2</td>
<td>1±3</td>
<td>14</td>
</tr>
<tr>
<td>Dec, dark</td>
<td>17±2</td>
<td>58±19</td>
<td>14</td>
</tr>
<tr>
<td>Dec.conflict</td>
<td>1±2</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
</table>

Figure 4. Y-axis: SPV of nystagmus during turntable rotation, presented as acceleratory and deceleratory steps of 13 deg/s$^2$ in darkness or with an illuminated head-fixed environment (conflict). X-axis: time after onset of stimulation. The periods of acceleration/deceleration of the turntable are indicated by horizontal bars. Error lines indicate 1 SD. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. 

13 deg/s$^2$
13°/s² was performed in darkness and an illuminated head-fixed surrounding was presented by the end of the stimulation period, the duration of nystagmus decreased as compared to tests in continuous darkness. This was evident during acceleration as well as deceleration ($P \leq 0.001, n = 9$).

**VOR before versus after Lesion of Posterior Neck Muscles**

The eye movement response to an angular acceleration/deceleration of 13°/s² was investigated in rats after surgical sectioning of the posterior neck muscles at the occipital bone (Figure 5). The duration of nystagmus upon an acceleratory angular stimulation was prolonged by the lesion. This was more evident when stimulation was performed with an earth-fixed illuminated background (Figure 5, right) than in darkness (Figure 5, left). The duration of nystagmus upon a deceleratory angular stimulation, performed in darkness, was also prolonged postoperatively as compared to preoperative values (Figure 5, left). The $SPV_{es}$ was mostly uninfluenced by the lesion. A sham operation changed neither the $SPV_{es}$ nor the duration of nystagmus.

**Discussion**

**Mathematical Modelling and Velocity Storage**

Results from recording of horizontal eye movements upon vestibular and/or visual stimulation have been explained by referring to a mathematical model, originally proposed by Robinson (10). New findings have continuously led to different modifications of this model but the basic principle has not been changed (1). In the model, vestibular nystagmus is induced by stimulation of the semicircular canals. Visual input to the eye movement system is induced by a retinal slip signal, integrated with the VOR signals. The visual as well as the vestibular stimulations cause eye movements through direct and indirect pathways. The direct pathways, dependent on a normal function of the flocculus, are characterized by fast dynamics and are responsible for the fast changes in SPV of OKN and vestibular nystagmus. The smooth pursuit system and visual suppression are closely connected to these pathways. The indirect pathways comprise a velocity storage mechanism, represented by a "leaky integrator." They are responsible for a slow buildup of steady state SPV of OKN, optokinetic after-nystagmus, and per- and postrotatory nystagmus. The activity of the velocity storage mechanism may be "dumped" by visual impulses, induced by full-field fixation. This phenomenon is connected to the nodulus (11).

How do the findings obtained from pigmented rats fit to the principle of this model for visual-vestibulo-oculomotor control? What are the relative strengths of the direct and indirect mechanisms in the rat as compared to other species?

The activity of the velocity storage mechanism in the indirect pathway is often characterized by the "dominant time constant" ($T_c$), calculated from the shape of the SPV after an angular vestibular stimulation. From a mathematical point of view such a calculation requires an exponential decay curve, as seen in experiments on monkeys (12). However, the use of time constants has also been extended to linear decay curves as seen in rabbits (13). The difference between the $T_c$ and the long time constant of the first vestibular neuron ($T_c$) represents the prolongation of nystagmus induced by velocity storage. The $T_c$ for monkeys, cats, and rabbits are 5 to 6 s (14), 4 s (15,16), and 3 s (17) respectively. The corresponding $T_{vs}$ for these animals are at least a factor of 3 times (12), 5 times (18), and 3 times (13) higher.

The $T_c$ of albino rats is 3 s (19). It should be the same in pigmented rats, assuming a similar anatomy of the labyrinths in the two species (20). The $T_c$, calculated in the present investigation from a velocity step of 1000°/s², was 6 s. Hess (4), using another model for calculation, reported a $T_c$ of 7.5 s. Regarding these figures, it seems that the velocity storage
Figure 5. Y-axis: SPV of nystagmus during turntable rotation, presented as acceleratory and deceleratory steps of 13 deg/s² in darkness (left) or with an earth-fixed illuminated surrounding (right), before (preop) and after (postop) lesion of the posterior neck muscles. X-axis: time after onset of stimulation. The periods of acceleration/deceleration of the turntable are indicated by horizontal bars. Error lines indicate 1 SD. *P ≤ 0.05, **P ≤ 0.01, ***P ≤ 0.001.
activity is less developed in pigmented rats than in the other species mentioned above. This is in accordance with the fact that the occurrence of optokinetic afternystagmus in pigmented rats is often sparse and irregular and without an exponential type of decay (7,9).

Although the mean SPV upon an acceleratory or deceleratory stimulation showed an exponential decay phase in the present investigation, there was a high degree of variability. In many experiments, the individual decay curves are better fitted to a linear representation or showed a biphasic appearance. Therefore, instead of time constants, the duration of nystagmus was used to express velocity storage activity throughout this paper. Repeated angular stimulation caused a higher degree of habituation at 1000°/s² than at 13°/s². Therefore, in order to avoid habituation the lower figure of acceleration/deceleration was used in the present work to evaluate the influence of different sensory inputs on the velocity storage network.

SPVecs during angular stimulation of rats in darkness did not reach the stimulus velocity of 120°/s. Thus the nystagmus was not completely compensatory; the gain was below unity. The compensation was more insufficient during a long-standing acceleration/deceleration (9 s) than during a short one (0.1 s) (Figure 2). This phenomenon is also reported to occur in monkeys (21) and is thought to represent some kind of peripheral adaptation during long-standing continuous cupular stimulation (16).

**Enhancement of the VOR by Visual Input**

In different experimental situations, the VOR was enhanced or suppressed by a visual input. When the rat was accelerated to a constant velocity of 120°/s with an illuminated earth-fixed environment, the SPV was enhanced (Figure 2), even though a pure optokinetic stimulation of the same magnitude did not elicit nystagmus. In spite of this enhancement, the SPV did not match the velocity of stimulation; the gain was still below unity. In the rhesus monkey, combined visual-vestibular stimulation of the same magnitude gave a gain near unity (21). In the rabbit a vestibular angular step stimulation up to 60°/s gave a gain of about 0.9 with an illuminated surrounding (22). The enhancement in light is generally explained by a retinal slip signal (17) that develops when the SPV of nystagmus does not match the vestibular stimulation. The signal improves the compensatory eye movements through a mossy and a climbing fiber input to cerebellar Purkinje cells, representing the direct pathway in the model described above.

Not only the SPV but also the duration of nystagmus was increased during angular acceleration of rats with a visual earth-fixed surrounding compared to darkness (Figure 1). This fact indicates that the velocity storage mechanism of rats was enhanced by the visual input. However, this mechanism is not capable to maintain ocular compensatory movements during continued relative rotation of the head and the surroundings at 120°/s, which is a velocity well above the optokinetic threshold of rats. In comparative experiments with monkeys, the postacceleratory nystagmus continued as long as a constant rotation of 120°/s was sustained (21). During deceleration of the rats in the earth-fixed visual surrounding, the duration was decreased compared with experiments in darkness. This reaction was seen also in monkeys (12) and could be explained in the model by a fixation-suppression mechanism, represented by a switch, which discharges the velocity storage activity.

Previous investigators have shown that optokinetic nystagmus in nonfoveate animals like rabbits and rats can only be elicited by temporonasal stimulation (23,7). This was evident also in the present investigation of rats with one eye covered. No nystagmus was seen during nasotemporal optokinetic stimulation, neither with a constant velocity of the pattern nor with a trapezoid velocity profile (Figure 3). An enhancement of nystagmus during vestibular angular acceleration with an earth-fixed illuminated surrounding occurred as ex-
pected when the turntable rotation caused a simultaneous temporonasal optokinetic stimulation of the uncovered eye. However, a smaller but still highly significant increase of the gain was also seen during a reverse direction of the turntable rotation, which caused a nasotemporal optokinetic stimulation (Figure 3). Thus, there is a discrepancy between the results from a pure optokinetic stimulation as compared to a combined vestibular-optokinetic stimulation. One explanation may be the occurrence of bidirectional retinal slip pathways, giving rise to compensatory eye movements only during a simultaneous vestibular stimulation. In fact, there are neurophysiological correlations in the pigmented rat to such a hypothesis. Floccular Purkinje cell units that respond bidirectionally to monocular optokinetic stimulation have been demonstrated (24). Vestibular neurons that are dependent on coactivation by optokinetic and cupular inputs have also been reported (25).

**Suppression of the VOR by Visual Input**

A visual-vestibular conflict situation was performed by acceleration/deceleration of rats with a visual head-fixed environment. Vestibular nystagmus was almost completely suppressed at turntable acceleration of 13°/s² but not at 1000°/s². Almost complete suppression was evident up to an angular velocity stimulation of 10°/s² in monkeys (26) and up to a maximal acceleration of 5°/s² during an oscillatory vestibular stimulation in rabbits (17). In the model, the visual conflict signal developed by the retinal slip and/or other factors should oppose vestibular compensatory movements through the direct pathway and through the fixation-suppression switch as mentioned above. A similar conflict situation was presented by exposing the rats to a head-fixed visual full-field at the end of an acceleration/deceleration in darkness. The duration of nystagmus compared to experiments in continuous darkness is thereby reduced. This finding is more apparent in the monkey, probably because of the longer postacceleratory/deceleratory nystagmus in darkness in this species compared to the rat (27).

**Enhancement of the VOR by Lesion of Neck Muscles**

Disturbances of the normal function of the neck muscles evidently prolonged the duration of nystagmus after vestibular stimulation. This prolongation was more evident during angular acceleration with an illuminated earth-fixed environment than during vestibular stimulation in the dark. Similar results during combined vestibulo-visual stimulation have previously been reported (28). It is well known that a cervical proprioceptive input interacts with the VOR. Studies of rabbits have implied that stimulation of neck muscles provides a head position signal that is fed to the vestibulo-visual-oculomotor system (29). It is difficult to interpret in what way an unspecific lesion of the posterior neck muscles as performed in the present investigation might change the static inflow of signals to the system for gaze stabilization. Nevertheless, the present results indicate that such a lesion will enhance the velocity storage mechanism, especially during a combined vestibular-optokinetic stimulation. Our findings support a suggestion that the velocity storage mechanism has a broad function "to serve as a focus for superposing a variety of sensory inputs that signal motion" (30).

**Conclusions**

The results of this paper indicate that the velocity storage mechanism, which is a component of the indirect pathway of the model for gaze stabilization, is poorly developed in the pigmented rat as compared to the nonfoveate rabbit and the foveate monkey. However, it can be enhanced by a retinal slip
signal, as in acceleration with a visual earth-fixed surrounding or by a disturbed input from the proprioceptive system. Similar enhancement of the velocity storage mechanism has been demonstrated to occur during the influence of toluene (9). The direct pathway of the model, tested by different visual-vestibular conflict situations, seems to be well developed in the pigmented rat. In some respects it is comparable with that of the monkey.

REFERENCES


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