Modifications of Vestibular Responses of Individual Reticulospinal Neurons in Lamprey Caused by Unilateral Labyrinthectomy

T. G. DELIAGINA AND E. L. PAVLOVA

The Nobel Institute for Neurophysiology, Department of Neuroscience, Karolinska Institute, SE-171 77 Stockholm, Sweden

Deliagina, T. G. and E. L. Pavlova. Modifications of vestibular responses of individual reticulospinal neurons in lamprey caused by unilateral labyrinthectomy. *J Neurophysiol* 87: 1–14, 2002; 10.1152/jn.00315.2001. A postural control system in the lamprey is driven by vestibular input and maintains the dorsal-side-up orientation of the animal during swimming. After a unilateral labyrinthectomy (UL), the lamprey continuously rolls toward the damaged side. Normally, a recovery of postural equilibrium ("vestibular compensation") takes about 1 mo. However, illumination of the eye contralateral to UL results in an immediate and reversible restoration of equilibrium. Here we used eye illumination as a tool to examine a functional recovery of the postural network. Important elements of this network are the reticulospinal (RS) neurons, which are driven by vestibular input and transmit commands for postural corrections to the spinal cord. In this study, we characterized modifications of the vestibular responses in individual RS neurons caused by UL and the effect exerted on these responses by eye illumination. The activity of RS neurons was recorded from their axons in the spinal cord by chronically implanted electrodes, and spikes in individual axons were extracted from the population activity signals. The same neurons were recorded both before and after UL. Vestibular stimulation (rotation in the roll plane through 360°) and eye illumination were performed in quiescent animals. It was found that the vestibular responses on the UL-side changed only slightly, whereas the responses on the opposite side disappeared almost completely. This asymmetry in the bilateral activity of RS neurons is the most likely cause for the loss of equilibrium in UL animals. Illumination of the eye contralateral to UL resulted, first, in a restoration of vestibular responses in the neurons inactivated by UL and in an appearance of vestibular responses in some other neurons that did not respond to vestibular input before UL. These responses had directional sensitivity and zones of spatial sensitivity similar to those observed before UL. However, their magnitude was smaller than before UL. Second, the eye illumination caused a reduction of the magnitude of vestibular responses on the UL side. These two factors tend to restore symmetry in bilateral activity of RS neurons, which is the most likely cause for the recovery of equilibrium in the swimming UL lamprey. Results of this study are discussed in relation to the model of the roll control system proposed in our previous studies as well as in relation to the vestibular compensation.

INTRODUCTION

Ablation of one vestibular organ (unilateral labyrinthectomy, UL) evokes severe motor disorders in all classes of vertebrates. They include abnormal eye positions, spontaneous ocular nystagmus, asymmetry in the head and trunk posture, etc. Over time, these disorders gradually diminish. This process of the recovery of motor functions is usually referred to as "vestibular compensation" and is considered to be one of the most striking examples of CNS plasticity (for a review, see Dieringer 1995; Shaefer and Meyer 1974; Smith and Curthoys 1989; Vidal et al. 1998). Despite extensive studies of vestibular compensation, neuronal mechanisms of the origin of different UL-evoked symptoms and of the recovery of motor functions are still badly understood. The main reason for this is that the corresponding neuronal networks are extremely complex.

We have been investigating the effect of UL on postural stability, as well as the process of recovery of postural function, by using a simple biological model—the lamprey, a lower vertebrate (cyclostome). A reason for this is that the basic design of the lamprey CNS, and especially of the brain stem and spinal cord, is similar to that of higher vertebrates (Nieuwenhuys et al. 1998), but the lamprey presents many more opportunities for analytical studies of the nervous mechanisms for postural control, including studies at the network and cellular levels (Macpherson et al. 1997; Orlovsky 1992).

When swimming, the intact lamprey actively stabilizes the dorsal-side-up orientation of the body due to the activity of the postural control system driven by vestibular input (de Burlet and Versteegh 1930; Deliagina 1995, 1997a,b; Ullén et al. 1995a). Visual input plays only a modulatory role: a unilateral eye illumination evokes a roll tilt toward the source of light–"the dorsal light response" (Ullén et al. 1993, 1995b). Because the postural control system in the lamprey is driven by vestibular input, the effect of UL in this animal is most dramatic. In the swimming lamprey, UL results in a complete loss of postural stability and in continuous rolling toward the damaged labyrinth (de Burlet and Versteegh 1930; Deliagina 1995, 1997a). During a few weeks following UL, the animals gradually recover their capacity to maintain equilibrium (Deliagina 1995, 1997a). The equilibrium can be restored immediately, however, by illuminating the eye contralateral to UL or by electrically stimulating the corresponding optic nerve. The motor behavior of the stimulated animals is not distinguishable from that of well compensated animals (Deliagina 1995, 1997b). This finding suggests that functional changes in postural mechanisms in the stimulated and compensated animals may be similar. In the present study, we examined these changes in the stimulated animals and discuss a possible relevance of our findings for vestibular compensation.

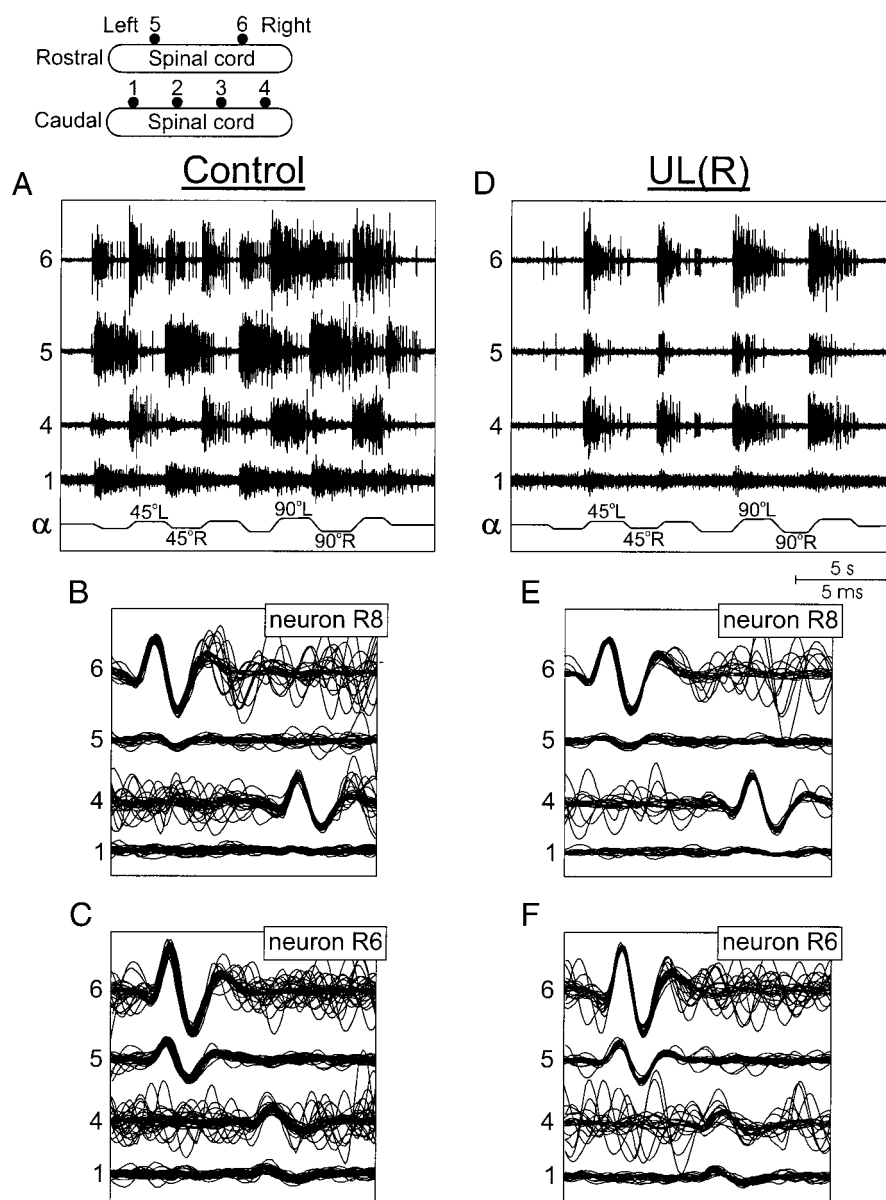0022-3077/02 $5.00 Copyright © 2002 The American Physiological Society

FIG. 1. Vestibular responses in reticulospinal (RS) pathways and in individual RS axons before and after unilateral labyrinthectomy (UL) (*animal G4*). *A* and *D*: mass activity of RS axons elicited by trapezoid roll tilting, α, before (*A*) and after a unilateral (right) labyrinthectomy (*D*). The activity was recorded by 2 electrodes (5 and 6) of the rostral 2-electrode array and by 2 electrodes (1 and 4) of the caudal, 4-electrode array (*inset* in *A*). *B* and *E*, and *C* and *F*: superposition of the activity of 2 individual RS axons (*neurons R8* and *R6*) extracted from the raw data (shown in *A* and *B*) with the spike sorting program, and recorded by 4 electrodes before and after UL (*B, C* and *E, F*, respectively); the display was synchronized by the "event" signal (Deliagina and Fagerstedt 2000).

The postural network in the lamprey has been characterized in considerable detail. Important elements of this network are the reticulospinal (RS) neurons, which transmit commands for postural corrections from the brain stem to the spinal cord. The RS pathways originate from four reticular nuclei of the brain stem: the mesencephalic reticular nucleus (MRN) as well as the anterior (ARRN), middle (MRRN) and posterior (PRRN) rhombencephalic reticular nuclei (Nieuwenhuys 1972). The RS neurons receive vestibular input through interneurons of the vestibular nuclei (Koyama et al. 1989; Northcutt 1979; Rovainen 1979; Rubinson 1974; Stefanelli and Caravita 1970; Tretjakoff 1909). They also receive inputs from other sensory systems as well as from the forebrain, brain stem centers, and spinal cord (Deliagina et al. 1993; Dubuc et al. 1993; Rovainen 1967, 1979; Viana Di Prisco et al. 1995; Wickelgren 1977). In the spinal cord, RS neurons affect motoneurons and different classes of interneurons (Brodin et al. 1988; Ohta and Grillner 1989; Rovainen 1967, 1974, 1979; Wannier et al. 1995; Zelenin et al. 2000b).

In earlier studies (Deliagina et al. 1992a; Orlovsky et al. 1992), responses of RS neurons to natural vestibular stimulation (roll tilt) and unilateral visual input (illumination of 1 eye or electrical stimulation of the optic nerve) were investigated in vitro in a preparation consisting of the brain stem isolated together with the vestibular organs and eyes. It was found that the majority of RS neurons were activated with the contralateral roll tilt due to excitatory input from specific groups of the contralateral vestibular afferents (Deliagina et al. 1992b). They exhibited both dynamic and static reactions within specific angular zones (Deliagina et al. 1992a). A unilateral visual input evoked excitation of the ipsilateral and inhibition of the contralateral RS neurons in MRRN (Deliagina et al. 1993; Ullén et al. 1996).

The results of these in vitro experiments were recently confirmed in experiments on intact lampreys. The activity of RS neurons was recorded from their axons in the spinal cord by means of implanted electrodes (Deliagina and Fagerstedt 2000; Deliagina et al. 2000). It was found that the majority of
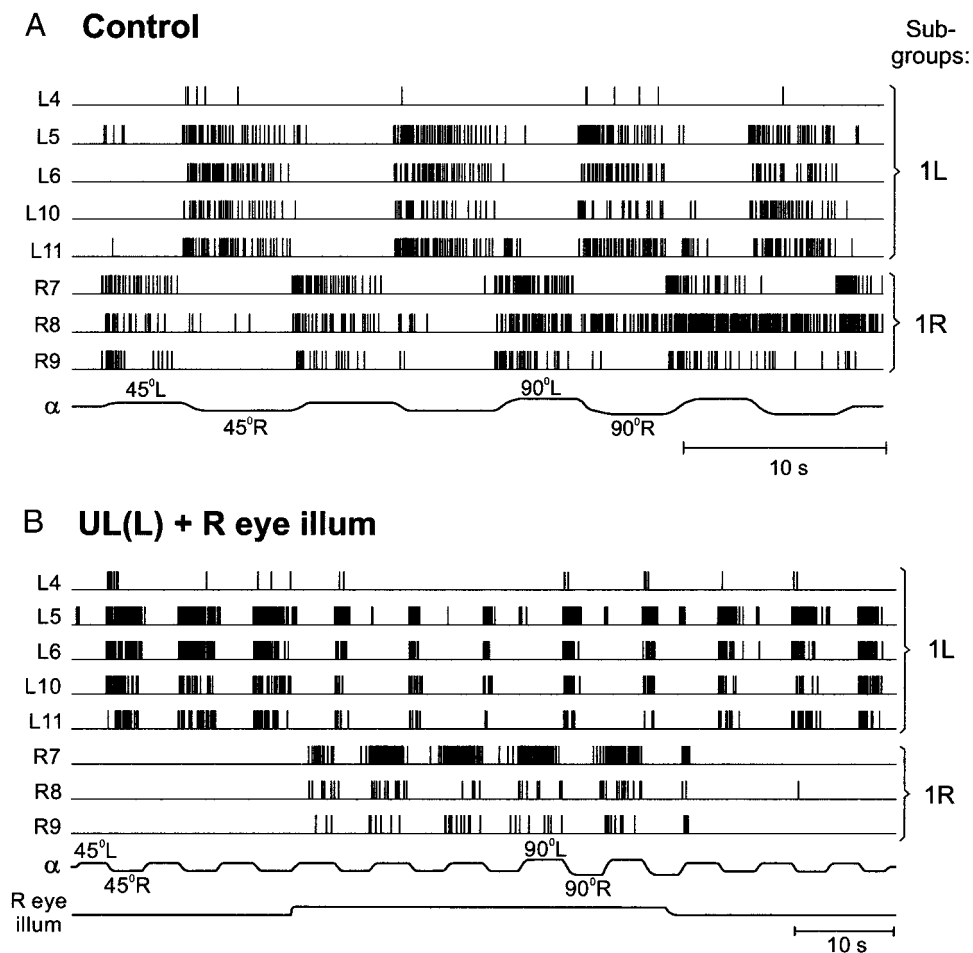
FIG. 2. Responses to trapezoid roll tilts in 8 RS neurons of group 1 (*animal Ch23*). Neurons of subgroups 1L and 1R had their axons located on the left and right side of the spinal cord, respectively. The responses were recorded before UL (*A*) and after UL (*B*). In *B*, a period of right eye illumination is indicated (upward deviation of the *R eye* trace). The database of this paper overlaps considerably with that of the previous paper. In particular, Figs. 2*A* and 3*A* are the modifications of Fig. 5, *A* and *B*, respectively, from Deliagina and Fagerstedt (2000).

recorded neurons (group 1) exhibited vestibular responses (activation with contralateral tilt) similar to those observed in the in vitro experiments. Visual responses, that is activation with illumination of the ipsilateral eye and inhibition with illumination of the contralateral eye, were also similar.

After the commands for postural corrections transmitted by the RS system have been characterized in sufficient detail in intact animals, we can address the question of how these commands are modified in the animals subjected to UL. In the present study, we examined the vestibular responses in individual RS neurons before and after UL. We also analyzed the effect on these responses produced by unilateral eye illumination, that is by the factor that causes immediate restoration of postural control in UL animals.

A brief account of this study has been published in an abstract form (Deliagina 1997c).

METHODS

Experiments were carried out on 12 adult (25–35 cm in length) intact lampreys (*Lampetra fluviatilis),* which were kept in an aerated freshwater aquarium at 7°C, with a 12 h:12 h light:dark cycle.

Electrodes

The activity of RS neurons was recorded from their axons in the spinal cord by means of chronically implanted macroelectrodes as described in detail in the previous papers (Deliagina and Fagerstedt 2000; Deliagina et al. 2000). In short, the electrodes (silver wires 75

μM in diameter and 3 mm in length) were oriented in parallel to the long spinal axons. They allowed an almost exclusive recording of the spike activity from larger fibers that have a conduction velocity of more than 2 m/s. In the lamprey, only RS pathways contain fibers with such a high conduction velocity. The electrodes were glued to a plastic plate (6 mm long, 2 mm wide, and 0.25 mm thick). Three different designs of the electrode array were used: four electrodes, two electrodes, and two electrodes separated by an isolating wall. The wall was then positioned in an incision between the two halves of the spinal cord to record separately from the left and right RS pathways.

Surgery

The effect of UL was studied in eight animals, which were operated on two times under MS-222 (Sandoz) anesthesia (100 mg/l). During the first surgery, implantation of the electrodes was performed as described in detail by Deliagina et al. (2000) and by Deliagina and Fagerstedt (2000). In five of these eight animals, two plates with electrodes were implanted at different rostrocaudal levels. The plate with two electrodes was implanted at the level of the third gill and the plate with four electrodes 20–30 mm more caudally. The electrodes were facing the dorsal aspect of the spinal cord (see Fig. 1*A, inset*). In three of these eight animals, only one plate with two electrodes separated by a longitudinal wall was implanted at the level of the last gill.

The UL was performed 2–3 days after implantation of the electrodes as described in detail earlier (Deliagina 1995, 1997a). In short, the hole was made in the dorsolateral aspect of the vestibular capsule, and the labyrinth was removed with a pair of fine forceps under visual control. After removal, the intact medial wall of the
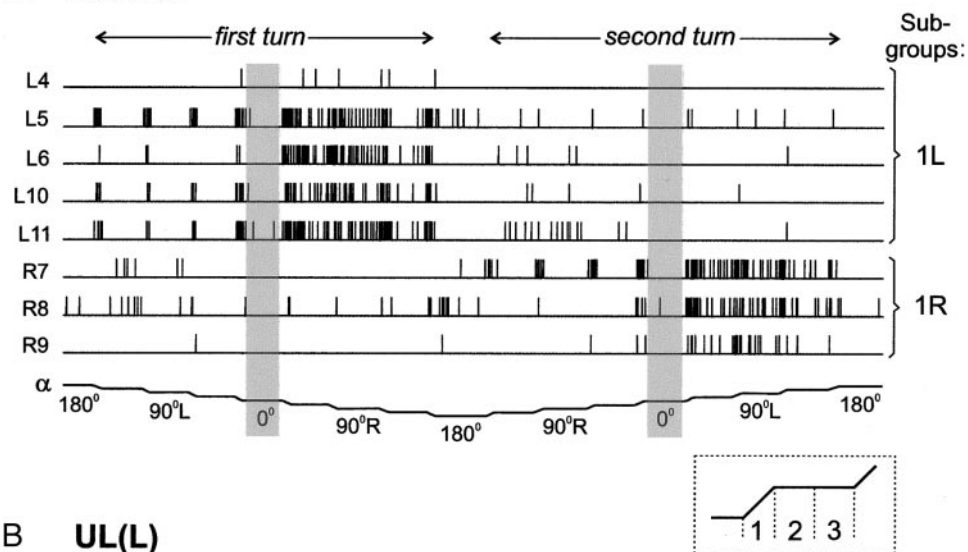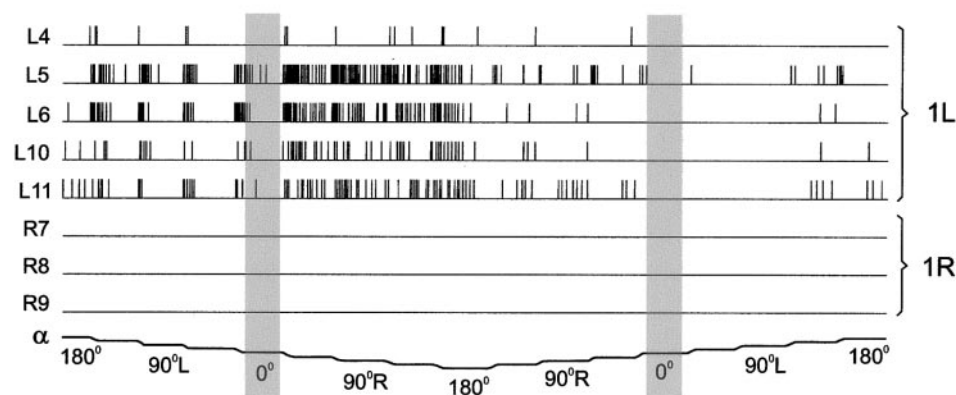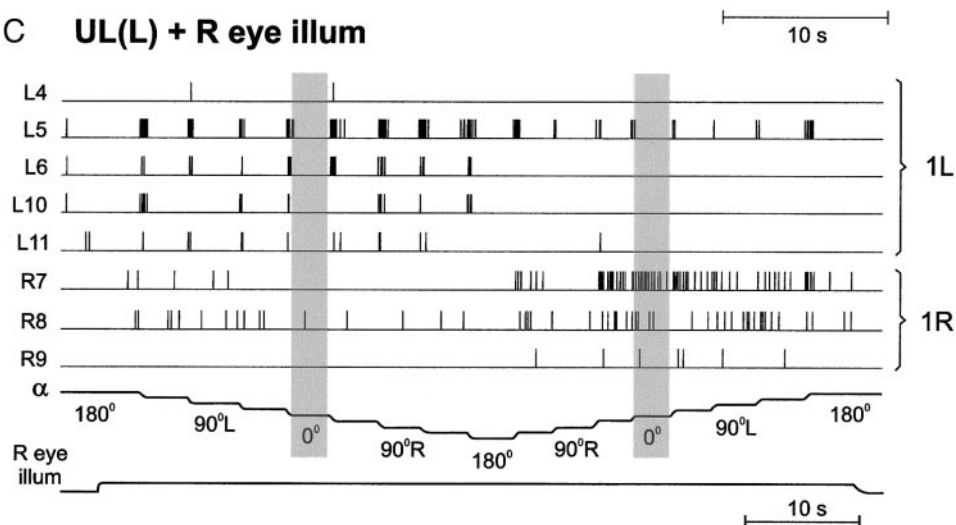
FIG. 3.   Responses of the same neurons as in Fig. 1 to stepwise rotation. Two full turns in opposite directions were performed sequentially (*1st turn* and *2nd turn*). Shaded columns (0°) indicate the normal (dorsal-side-up) orientation of the animal. The responses were recorded before UL (*A*) and after UL (*B* and *C*); in *C*, the right eye was continuously illuminated.

vestibular capsule and a stump of the eighth nerve could be seen. Post mortem investigation showed that, in all cases, removal of the vestibular organ was complete, and the medial wall of the capsule was undamaged.

All these eight animals, prior to the present study, had been also used in other studies: the animals with two implanted electrode arrays (*n* = 5) had been used for collecting data on the vestibular and visual responses in RS neurons (Deliagina and Fagerstedt 2000) and the animals with a single array (*n* = 3) for collecting data on the activity of RS neurons during locomotion (Deliagina et al. 2000).

In addition to the main group of eight animals, in four animals, UL and implantation of electrodes (the 4-electrode array at the level of the last gill) were performed during one surgery. These animals were not used to characterize the effect of UL but rather to characterize the ipsi- and contralateral influences of the labyrinth on RS neurons (see RESULTS).

Experimental protocol

In eight animals, vestibular and visual responses of RS neurons were examined two times—on the next day after implantation of the electrodes and on the next day after UL. In the four animals subjected to a single surgery, the responses were examined only after UL. The arrangement for vestibular and visual stimulation, and the characteristics of stimuli have been described in the previous paper (Deliagina and Fagerstedt 2000). Two patterns of vestibular stimulation were used: alternating trapezoid tilts to the left and to the right (see e.g., Fig. 2) and two full turns about the longitudinal axis (by 45° steps); the rotation in the first and in the second turn being performed in opposite directions (see e.g., Fig. 3). Illumination of each of the eyes could be performed either separately or in combination with vestibular stimulation.

Data processing

Signals from the electrodes were amplified by conventional AC amplifiers, digitized with a sampling frequency of 10 kHz and stored on the hard disk of an IBM AT compatible computer by means of data-acquisition software (Digidata 1200/Axoscope, Axon Instruments, Union City, CA). The recorded multiunit spike trains were separated into unitary waveforms, representing the activity of individual axons, by means of data analysis software ("spike sorting," Datapac III, Run Technologies, Laguna Hills, CA). The mediolateral position of individual axons in the spinal cord was estimated by comparing the amplitudes of the same spike recorded by electrodes of the same array differing in their lateral position. In animals with the electrodes implanted at two rostrocaudal levels ($n = 5$), the conduction velocity in individual axons could also be measured using the time delay between spikes from the same axon recorded by rostral and caudal electrodes.

All the analytical procedures and possible sources of errors during the spike sorting have been described in detail in a previous paper (Deliagina and Fagerstedt 2000) and are briefly summarized in DISCUSSION. Besides the possible errors introduced by spike sorting, an additional possible source of errors in the present study could have been a change in the recording conditions caused by displacement of the electrode arrays during the second surgical intervention (UL). However, there were no marked changes in spike waveforms following UL in any of eight experiments, as illustrated for *animal G4* in Fig. 1. Figure 1, *A* and *D,* shows the mass activity in RS pathways caused by trapezoid tilts and recorded by the rostral and caudal electrodes (*5* and *6* and *1* and *4,* see Fig. 1*A, inset*), before and after UL, respectively. These raw data were then analyzed by the spike sorting procedure (Deliagina and Fagerstedt 2000). Eight neurons with their axons on the right side of the spinal cord, and 11 neurons with left-side axons, were identified in control. After UL, all 11 left-side axons and 3 of the 8 right-side axons had not been identified. The remaining five right-side axons were identified both before and after UL. Two of them, *R8* and *R6,* are illustrated in Fig. 1, *B* and *C* and *E* and *F,* respectively, where the display was synchronized by the "event" signal (Deliagina and Fagerstedt 2000). One can see that for each of the neurons the shape and absolute value of spike waveform in individual electrodes, the ratio between the spike amplitudes in different electrodes, and the time delay between the spikes in the rostral and caudal electrodes, were not changed after UL (compare Fig. 1, *B* and *E,* as well as *C* and *F*).

RESULTS

In eight animals, the activity in RS pathways was recorded both before and after UL. The activity of individual axons was then separated from the mass activity, and all neurons were divided into two groups according to the criteria formulated earlier (Deliagina and Fagerstedt 2000). Group 1 neurons ($n =$ 47) were activated by the contralateral tilt and by the illumination of the ipsilateral eye. Group 2 neurons ($n = 8$) were activated by tilt in any direction, and they could also respond to illumination of the ipsi- and/or contralateral eye. It seems most likely that the neurons of group 1, with clear-cut vestibular responses, carry information about spatial orientation of the animal, and play the major role in postural control (Deliagina and Fagerstedt 2000). The role of a small group 2, whose neurons' activity did not correlate with spatial orientation, is less clear. Evidently, neurons of this group cannot directly participate in stabilization of any particular spatial orientation. However, the presence of weak and unspecific vestibular responses in these neurons suggests that they may slightly affect the level of excitability in spinal networks. Only group 1 neurons will be considered in the following text.

Of the 47 group 1 neurons, 23 neurons were located on the side ipsilateral to the subsequent UL, and 24 neurons on the opposite side. From 3 to 11 neurons were recorded in individual animals. For the cases when an axon was recorded by both rostral and caudal electrodes ($n = 22$), the conduction velocity was calculated. The velocity ranged from 2.6 to 4.2 m/s.

Modifications of vestibular responses of individual RS neurons caused by UL and eye illumination

Data from the *animal Ch23* is used to illustrate the modifications of vestibular responses in individual group 1 neurons caused by UL as well as the effect of contralateral eye illumination. In this animal, 8 of 11 recorded neurons belonged to group 1.

Figure 2*A* shows the responses to trapezoid tilts in RS neurons of group 1 recorded before UL. Typically, these neurons were silent before the stimulus was applied. The neurons of subgroup 1R (R7–R9), with their axons located on the right side of the spinal cord, were excited with the contralateral (left) tilt. Their responses contained both a dynamic component (activity during movement) and a static component (discharge
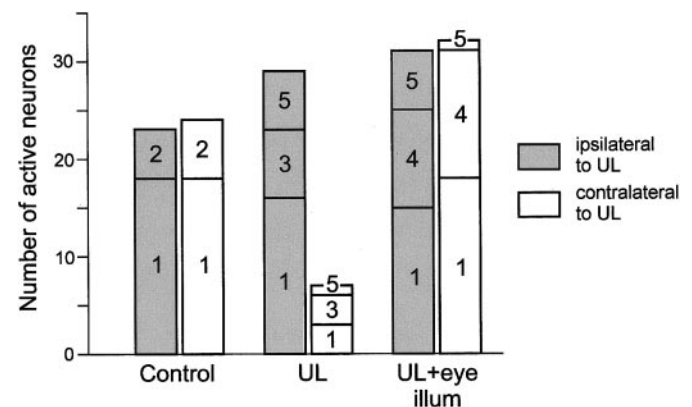

FIG. 4. Number of neurons (bar height) on the 2 sides (ipsilateral and contralateral to UL) that were activated by contralateral tilt under different conditions—before UL (control), after UL without eye illumination (UL), and after UL during illumination of the eye contralateral to UL (UL + eye illum). Five populations of neurons could be distinguished (*1–5*); their numbers are shown as subdivisions of the bars: *1,* neurons were present before UL as well as after UL under one or both lighting conditions (eye illuminated/not illuminated); *2,* neurons were present only before UL; *3,* neurons were present only after UL and only without eye illumination; *4,* neurons were present only after UL and only with eye illumination; *5,* neurons were present only after UL under both lighting conditions.

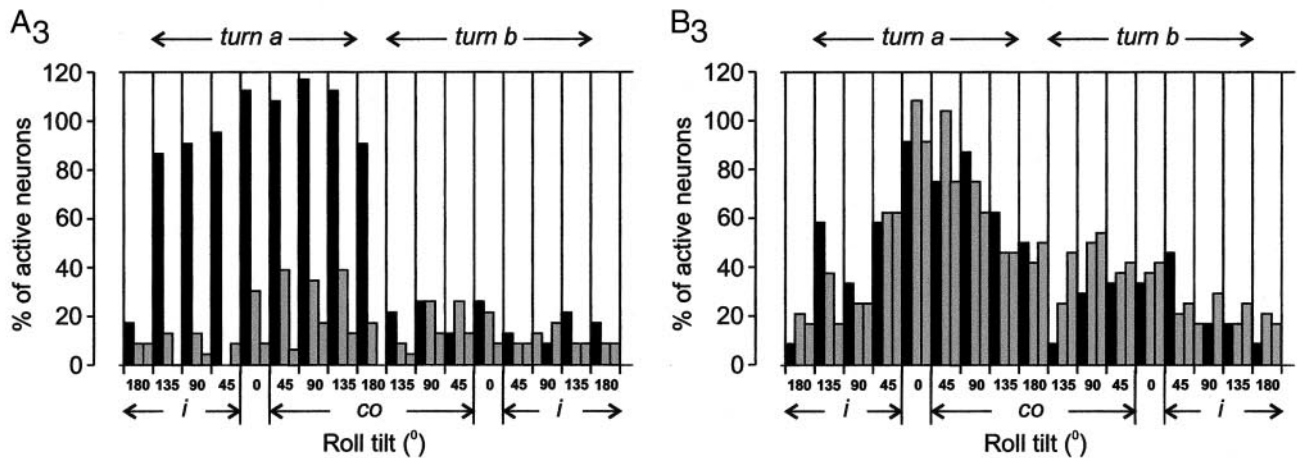# RS neurons ipsilateral to UL   RS neurons contralateral to UL

Control
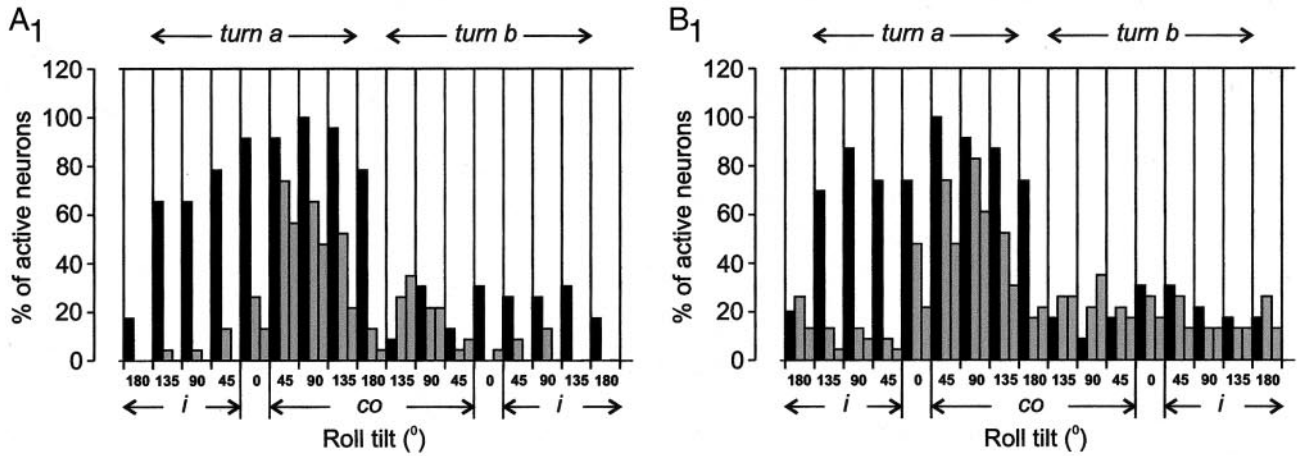
UL
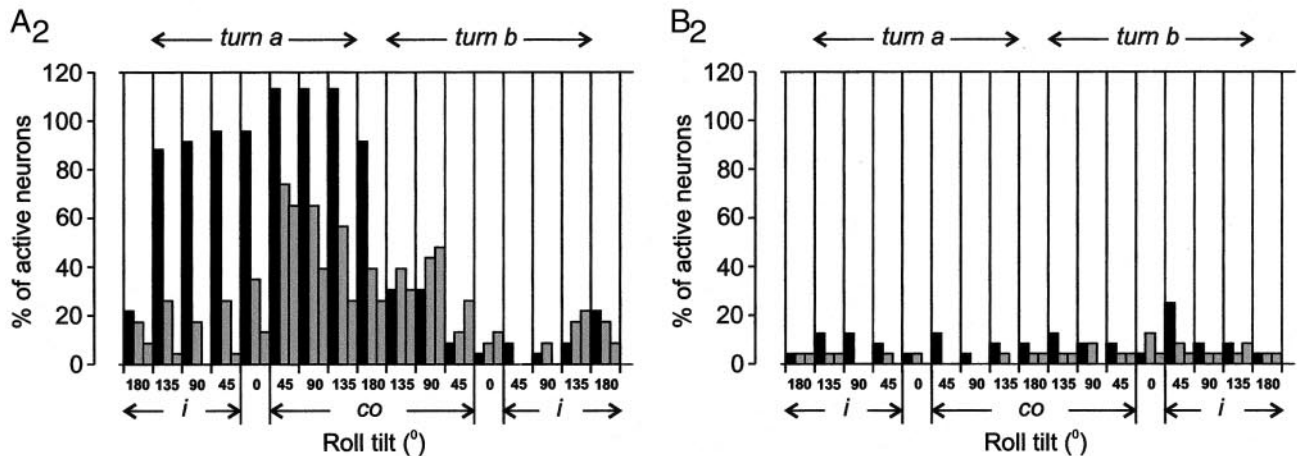
UL + eye illum

when a new position was maintained). The subgroup 1L neurons (L4–L6, L10, L11), with their axons on the left side, were excited with the right tilt.

Activity of the same neurons during two full turns is shown in Fig. 3A. In the first turn (rotation toward the contralateral labyrinth), most subgroup 1L neurons exhibited a dynamic response with any change in position. In addition, a static response was observed within the zone between 45°R and 135°R. In the second turn (rotation toward the ipsilateral labyrinth), the subgroup 1L neurons exhibited almost no activity. The activity of the subgroup 1R neurons mirrored that of the subgroup 1L neurons: they responded in the second turn, both statically (in the zone between 45°L and 135°L) and dynamically. In the first turn, the activity of subgroup 1R neurons was much weaker than in the second turn. Thus the two subgroups respond to rotation in opposite directions and have different spatial zones of sensitivity.

Figure 2B shows responses to trapezoid tilts in the same neurons recorded 1 day after the left labyrinth had been removed (see the 3 initial and 3 last tilt cycles performed in the absence of visual stimulation). Responses in the subgroup 1R neurons (located on the undamaged side) disappeared after UL. In subgroup 1L, the responses remained unchanged: the neurons were excited with the contralateral tilt, and their responses contained both dynamic and static components.

Activity of the same neurons during two full turns is shown in Fig. 3B. The 1R neurons were not active at any position, whereas responses in the subgroup 1L neurons remained almost unchanged if compared with the test before UL (Fig. 3A). The only difference was a slight prolongation of the dynamic responses, and a slight widening of the zones of static responses (45–180° against 45–135° before UL).

Illumination of the eye contralateral to UL strongly affected the vestibular responses in RS neurons. As shown in Fig. 2B, illumination of the right eye caused a re-appearance of the responses to trapezoid tilts in the previously silent subgroup 1R neurons. By contrast, the responses in the subgroup 1L neurons were considerably reduced, and their static component was almost completely inhibited.

When tested by two full turns combined with right eye illumination (Fig. 3C), the responses of the subgroup 1R neurons were also restored. As in the control before UL, the neurons were activated in the second turn. However, their spatial sensitivity zones became wider (45°R–135°L against 45°L–135°L before UL). Also the magnitude of the response, and especially of its dynamic component, was smaller than before UL. Eye illumination also led to a reduction of the response magnitude in the subgroup 1L neurons; especially affected was the static component of the response.

Quantitative characteristics of the modifications of vestibular responses caused by UL and eye illumination

Because RS neurons were normally silent prior to stimulation, the effect of stimulation could be roughly evaluated by simply counting the number of activated neurons. In Fig. 4, the compounded height of the bars indicates the total number of neurons on each of the two sides (ipsilateral and contralateral to UL) that were activated by contralateral tilt under three conditions—before UL, after UL but without eye illumination, and after UL during illumination of the eye contralateral to UL.

By tracking the activity of individual neurons under the three conditions, five populations of neurons (1–5) could be distinguished (Fig. 4). Neurons of *population 1* were present before UL as well as after UL with or without eye illumination. Neurons of *population 2* were present only before UL. Neurons of *population 3* were present only after UL and only without eye illumination. Neurons of *population 4* were present only after UL and only with eye illumination. Finally, neurons of *population 5* were present only after UL in both lighting conditions. This analysis has shown that *1*) about 70% of the neurons that were activated before UL were also activated after UL when the eye was illuminated and *2*) about a half of the neurons that were activated after UL were not activated before UL. *3*) The UL caused a threefold reduction in the number of responding neurons on the contralateral side and a slight increase of this number on the ipsilateral side. Eye illumination caused a fourfold increase of the number of responding neurons on the contralateral side that resulted in a restoration of "symmetry" in the ipsilateral and contralateral responses.

To describe spatial zones of activity for the whole population of group 1 neurons under different conditions, we used two characteristics (Deliagina and Fagerstedt 2000): the percent of simultaneously active neurons as a function of the tilt angle and the frequency curve, that is, the average discharge frequency of the responding neurons as a function of the tilt angle. Each step of the angular change was divided into three intervals (*inset* in Fig. 3A). *Interval 1* corresponded to a movement from the preceding position to a new one, and *intervals 2* and *3* to a period when the new position was maintained. Both functions were calculated separately for each of the three intervals of each step and then averaged over all neurons activated in a given test in all eight animals. The activity in the *interval 1* was considered as a dynamic response, and the activity in the *intervals 2* and *3* as an early and late static responses, respectively (Deliagina and Fagerstedt 2000).

Figure 5, A_1 and B_1, shows the histograms of the relative number (percent) of simultaneously active neurons recorded before UL on the side ipsilateral to a subsequent UL (A_1) and on the opposite side (B_1). Along the horizontal axis the successive angles of roll tilt during 2 turns (a and b), performed in opposite directions in relation to the recorded neuron, are

FIG. 5. Summary of responses to full turn rotation in 2 subgroups of RS neurons—ipsilateral to UL (A_1–A_3) and contralateral to UL (B_1–B_3). The responses were characterized by the relative number (percent) of active neurons as a function of roll angle. The angle of 0° corresponds to the dorsal-side-up orientation of the lamprey. The angular zones where the ipsilateral (i) or contralateral (co) labyrinth is facing downward are indicated. Rotation was performed toward the contralateral labyrinth in turn a and toward the ipsilateral labyrinth in turn b. In each of the angular steps, the dynamic response (activity during rotation) is shown by a black bar, the early and late static responses—by 2 successive shaded bars. A_1 and B_1: responses before UL; A_2 and B_2: responses after UL without eye illumination; A_3 and B_3: responses after UL during illumination of the eye contralateral to UL. The responses were averaged over 8 tested animals and normalized to control. (Occurrence of responses exceeding 100% was due to an increase of the number of responding neurons after UL.)

RS neurons ipsilateral to UL   RS neurons contralateral to UL

Control
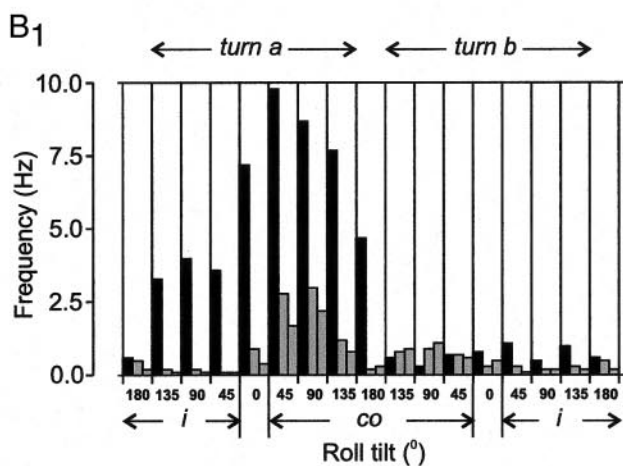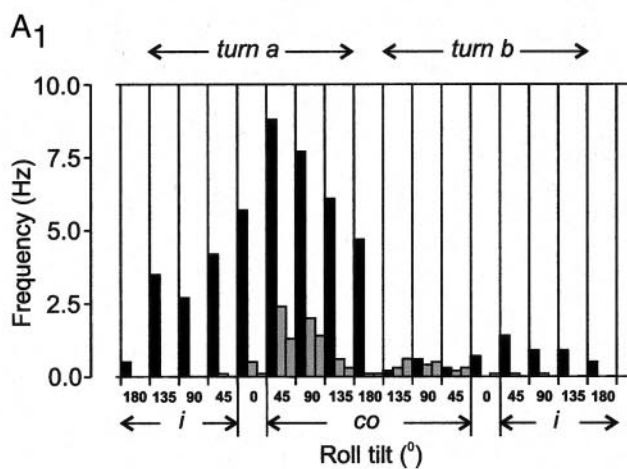
UL
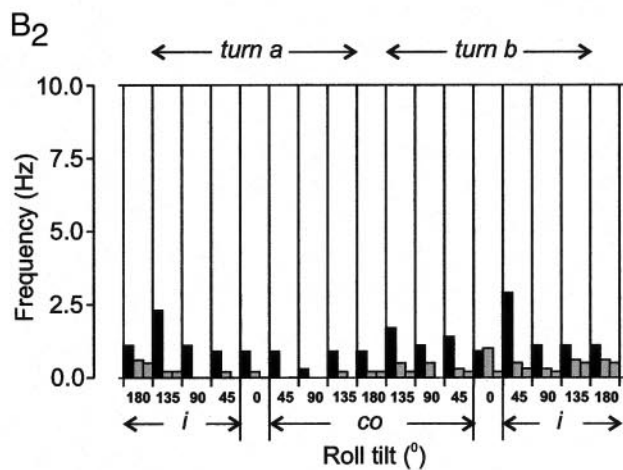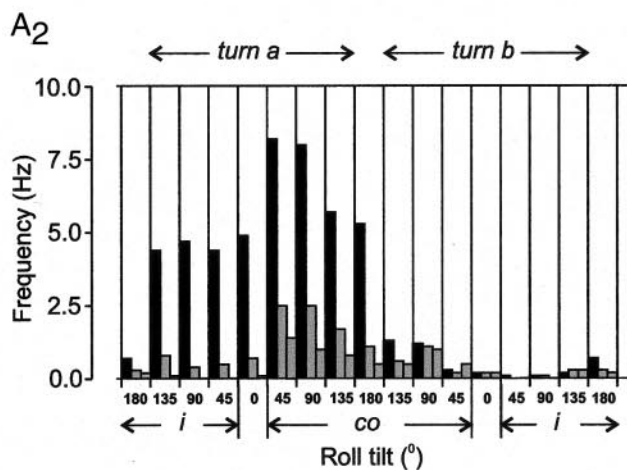
UL + eye illum
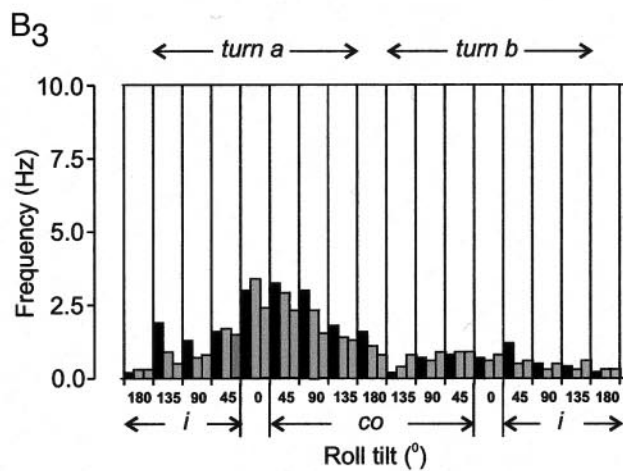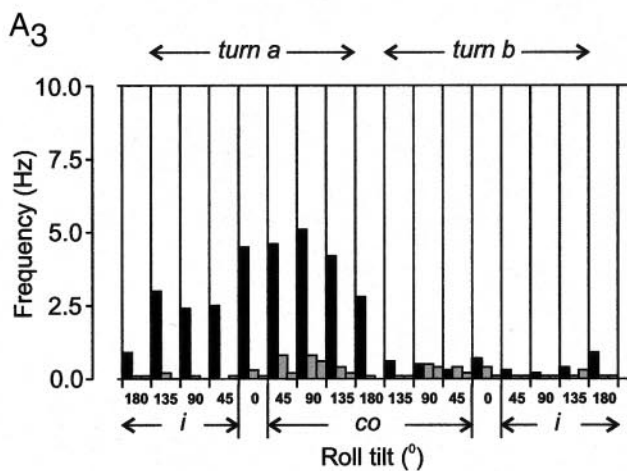
indicated. From these graphs, one can see that the responses recorded before UL on the 2 sides were similar to each other; they were also similar to the responses described in a previous paper (see Fig. 7A in Deliagina and Fagerstedt 2000). During turn a, with rotation toward the contralateral labyrinth, any change of orientation evoked a dynamic response in most RS neurons. During turn b, with rotation toward the ipsilateral labyrinth, the dynamic responses were much weaker than in turn a. Static responses were most pronounced in turn a, in the positions 45°_{co} and 90°_{co} where up to 70% of the neurons were activated. When the same positions were reached by rotation in the opposite direction (turn b), only a small proportion of neurons was activated.

Figure 6, A_1 and B_1, shows the frequency curves for the same populations of neurons recorded before UL on the side ipsilateral to a subsequent UL (A_1) and on the opposite side (B_1). The frequency curves were similar to each other; they were also similar to the curve obtained for group 1 neurons in a previous study (see Fig. 7D in Deliagina and Fagerstedt 2000). The dynamic responses were much stronger than the static responses. Within the zone of maximal activity (turn a, 45°_{co}–135°_{co}), the frequency in the dynamic responses exceeded 8 Hz, whereas that in the static responses was only 1–2.5 Hz.

After UL, vestibular responses on the UL side, when characterized by the number of active neurons, slightly increased (compare Fig. 5A, 1 and 2). However, the firing frequencies of active neurons remained unchanged (compare Fig. 6A, 1 and 2). On the side contralateral to UL, vestibular responses dramatically decreased. The number of responding neurons reduced several times (compare Fig. 5B, 1 and 2) as well as the firing frequencies of active neurons (compare Fig. 6B, 1 and 2).

Illumination of the eye contralateral to UL evoked substantial changes in the vestibular responses on both sides. On the UL side, the responses were reduced. When characterized by the number of active neurons, a reduction of the static component can be seen (compare Fig. 5A, 2 and 3). When characterized by the firing frequency of active neurons, a reduction of both components is evident (compare Fig. 6A, 2 and 3). On the side contralateral to UL and ipsilateral to the stimulated eye, illumination of the eye led to a partial restoration of vestibular responses, especially of their static component. Spatial zones of the restored responses were similar to those observed before UL (compare Fig. 5B, 1 and 3, as well as Fig. 6B, 1 and 3).

The major effect of UL, i.e., a dramatic reduction of vestibular responses in the contralateral neurons, and the major effect of eye illumination, i.e., restoration of these responses, were robust and were observed in all eight animals. To evaluate these effects, we calculated a mean value of the response within the zone of maximal sensitivity (45–135°) under different conditions. The UL led to a reduction in this value by a factor of 23 in the number of active neurons, and by a factor of 17 in firing frequency. Eye illumination led to 100 or 51% restoration of the response when it was characterized by the number of active neurons or firing frequency, respectively.

Similar effects of UL and eye illumination were revealed when vestibular stimulation was performed by periodical trapezoid roll tilts. To characterize the responses, the cycle of simulation was divided into six intervals (1–6 in Fig. 7), and the activity of neurons was calculated separately for each of the intervals and then averaged (as described in the preceding text for the full-turn rotation). In intact animals, RS neurons exhibited both dynamic and static excitatory responses to contralateral tilt, as characterized by both the percent of active neurons (control in Fig. 7, A_1 and B_1) and by their firing frequency (control in Fig. 7, A_2 and B_2). UL caused moderate changes in the responses on the side ipsilateral to UL (UL in Fig. 7A, 1 and 2), but a dramatic reduction in magnitude of the response on the contralateral side (UL in Fig. 7B, 1 and 2). Illumination of the eye contralateral to UL led to a considerable increase in the responses on the side contralateral to UL (UL + eye illum in Fig. 7B, 1 and 2). On the side ipsilateral to UL, eye illumination caused some decrease of the response (UL + eye illum in Fig. 7A, 1 and 2).

Comparison of inputs to RS neurons from ipsilateral and contralateral labyrinths

Input from the contralateral labyrinth was considered in earlier studies as the major source of roll-dependent drive to RS neurons (Deliagina 1997a; Deliagina and Fagerstedt 2000; Deliagina et al. 1993). This input is shown by solid lines in the conceptual model of the roll control system (Fig. 9A). The present study has demonstrated that input from the ipsilateral labyrinth can also play a role under certain conditions (Figs. $5B_3$ and $6B_3$), thus confirming the earlier finding by Rovainen (1979) that RS neurons respond to electrical stimulation of both ipsi- and contralateral vestibular nerves. Experiments were performed to estimate a contribution of the two inputs to the roll-dependent activity of RS neurons. In the UL-lamprey, RS neurons were tonically activated by illuminating the ipsilateral eye (up to a firing frequency of 3–5 Hz), and then a 90° tilt was performed. This test was done for the RS neurons on the side contralateral to the intact labyrinth to examine their contralateral vestibular input and also on the side ipsilateral to the intact labyrinth to examine their ipsilateral input. The responses were normalized to the background firing rate induced in the neurons by eye illumination. When the input from the contralateral labyrinth was examined, the contralateral tilt (in relation to RS neurons) evoked an increase in activity up to 250% as compared with the background (Fig. $8A_1$). With the ipsilateral tilt, the activity decreased down to 20% (Fig. $8A_2$). When the input from the ipsilateral labyrinth was examined, the contralateral tilt caused an increase of the activity up to 150% (Fig. $8B_1$); with the ipsilateral tilt the activity decreased down to 20% (Fig. $8B_2$).

Thus the two labyrinths supplement each other: each of them causes an increase of RS activity with contralateral tilt (Fig. 8, A_1 and B_1), and a decrease with ipsilateral tilt (Fig. 8, A_2 and B_2). The main action of the contralateral labyrinth is excitatory

---

FIG. 6. Summary of responses to full-turn rotation in 2 subgroups of RS neurons—ipsilateral to UL (A_1–A_3) and contralateral to UL (B_1–B_3). The responses were characterized by the average discharge frequency of active neurons as a function of roll angle. A_1 and B_1: responses before UL; A_2 and B_2: responses after UL; A_3 and B_3: responses after UL and during illumination of the eye contralateral to UL. The average frequency was calculated as the number of spikes generated by all active neurons in each of the intervals of the step and then divided by the number of active neurons and by the interval duration.
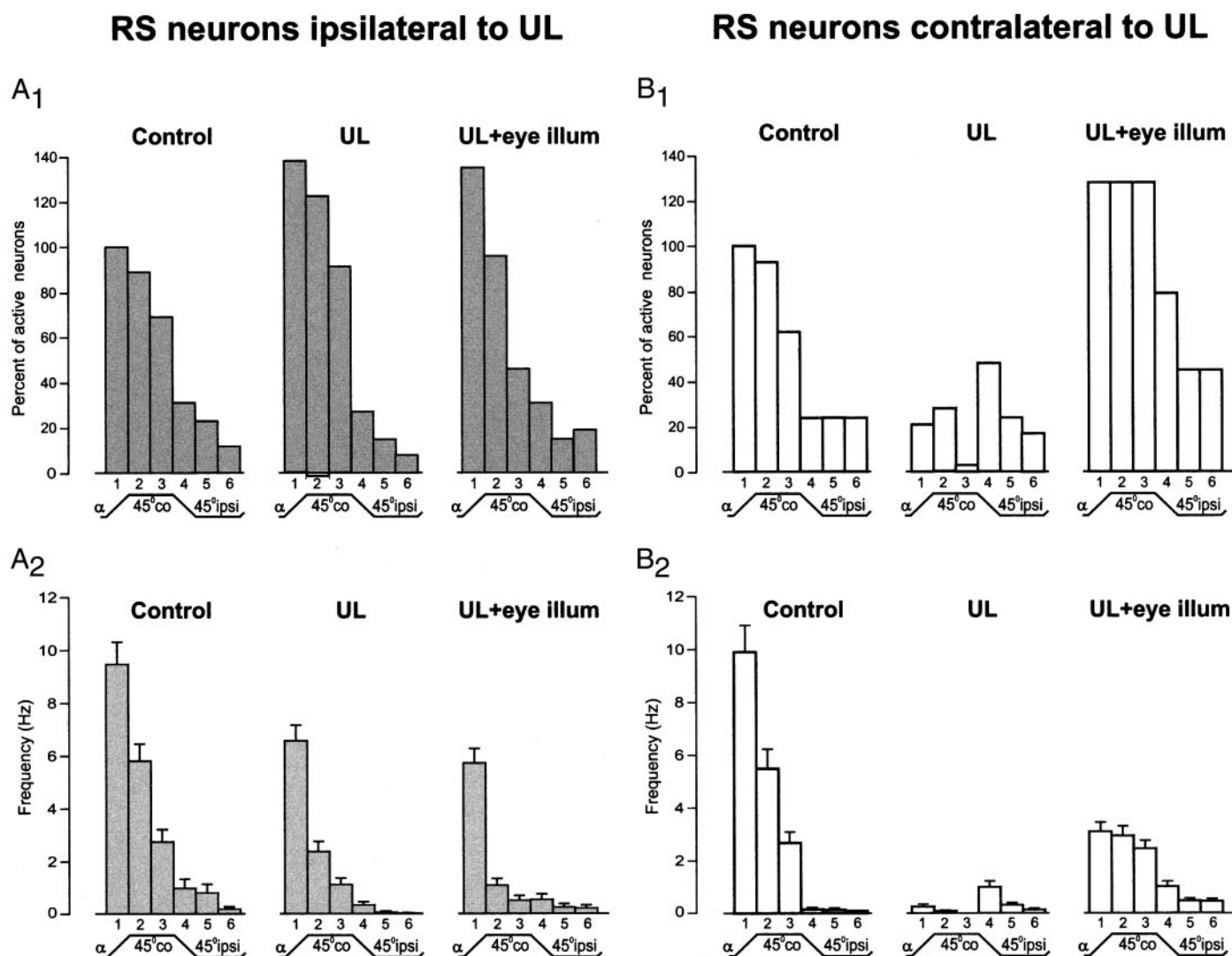
RS neurons ipsilateral to UL

RS neurons contralateral to UL

FIG. 7.   Summary of responses to periodic trapezoid tilts in 2 subgroups of RS neurons—ipsilateral to UL (A_1 and A_2) and contralateral to UL (B_1 and B_2). The responses were characterized by the relative number (percent) of active neurons (A_1 and B_1) and by the average discharge frequency ($\pm$SE) of active neurons (A_2 and B_2). The responses were recorded before UL (control), after UL with no eye illumination (UL), and after UL during illumination of the eye contralateral to UL (UL + eye illum).

in the sense that an increase of RS activity with contralateral tilt (Fig. $8A_1$) is larger than a decrease of this activity with ipsilateral tilt (Fig. $8A_2$). The main action of the ipsilateral labyrinth is inhibitory in the sense that a decrease of RS activity with ipsilateral tilt (Fig. $8B_2$) is larger than an increase of this activity with contralateral tilt (Fig. $8A_2$).

From Fig. 8 it can also be seen that the excitatory action of the contralateral labyrinth on RS neurons is much stronger than that of the ipsilateral labyrinth. The inhibitory actions of the two labyrinths are similar in strength, i.e., they cause a three- to fourfold decrease in the background activity.

DISCUSSION

Possible errors caused by spike sorting and by instability of recording conditions

A detailed analysis of possible errors caused by the spike sorting procedure was given in the previous paper (Delia-

gina and Fagerstedt 2000). In brief, discharges in individual axons were separated (clustered) on the basis of multiple criteria: simultaneous occurrence of spike in all electrodes of the array, constancy of the spike waveform in each electrode, constancy of the axon position in the spinal cord, and constancy of the axonal conduction velocity. Due to the multitude of criteria, both possible types of errors in clustering, i.e., misidentification and loss of spikes, were reduced considerably. An estimate for these errors was obtained when the same cluster of units was separated on the basis of inputs from different combinations of electrodes and even the electrodes from the rostral and caudal arrays. It was found that the difference in the number of spikes in a cluster was always less than 20%. These errors might lead to the corresponding errors in the mean firing frequency of RS neurons. However, such small errors in frequency could not affect any principal conclusions of the present study, that is a disappearance of the response to tilt in one sub-
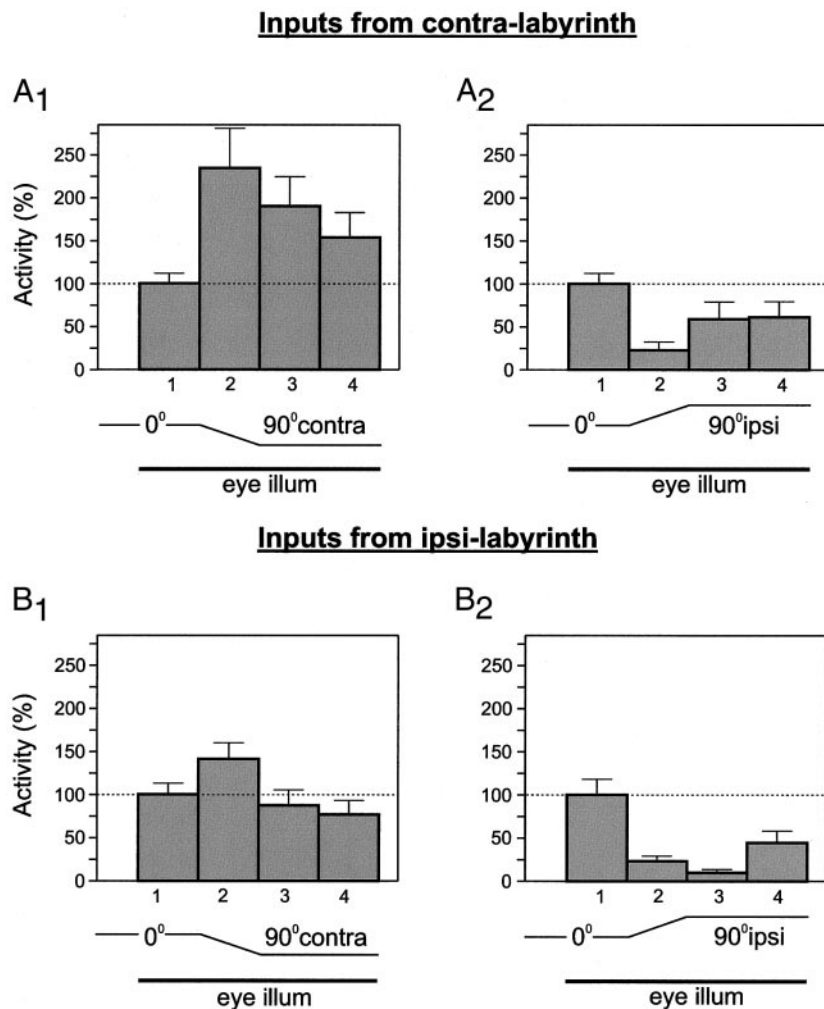
Inputs from contra-labyrinth

Inputs from ipsi-labyrinth

FIG. 8. Vestibular inputs to RS neurons revealed in UL-lamprey. A_1 and A_2: inputs from the contralateral labyrinth revealed by tilts contralateral (A_1) and ipsilateral (A_2) to the recorded neurons. B_1 and B_2: inputs from the ipsilateral labyrinth revealed by tilts contralateral (B_1) and ipsilateral (B_2) to the recorded neurons. In all the tests, the neurons were initially activated by a continuous illumination of the ipsilateral eye; this activity was taken as 100% (controls, bar 1). The activity during tilt (dynamic component of the response, bar 2), and during maintenance of a new position (early and late static components, bars 3 and 4, respectively) was normalized to the control activity. The responses were averaged over 14 (A_1 and A_2) and 12 (B_1 and B_2) RS neurons recorded in 4 animals; mean values $\pm$ SE are shown.

group of RS neurons caused by UL, and its restoration when the eye was illuminated (see RESULTS).

As judged from minor changes of the spike waveform in the RS neurons identified both before and after UL (Fig. 1), the surgical intervention had practically no effect on the recording conditions for these neurons and, most likely, for other neurons. Therefore it is very unlikely that the UL-caused disappearance of the activity in the contralateral RS neurons was caused by deterioration of recording conditions, especially when taking into account that, in most of these neurons, the activity could be restored by ipsilateral eye illumination. Similarly, the appearance of activity in "new" RS neurons after UL can hardly be attributed to the improvement of recording conditions specifically for these axons without affecting the recording conditions for the neighboring axons.

Modification of vestibular responses in RS neurons caused by UL and eye illumination: functional implications

Previous studies on in vitro preparations (Deliagina et al. 1992a,b, 1993) and intact animals (Deliagina and Fagerstedt 2000; Zelenin et al. 2000) led to formulation of a conceptual model of the roll control system in the lamprey (Fig. 9A, connections shown by solid lines). The model was discussed in detail by Deliagina (1997a). In brief, the key elements of the model are the two subgroups of RS neurons, the left [RS(L)] and the right [RS(R)]. The main input to these neurons is the excitatory one from the contralateral labyrinth. Because of this input, the activity of RS neurons is orientation dependent with its peak at approximately 90° of contralateral roll tilt (Fig. 9B_1). The two subgroups also receive an excitatory input from the ipsilateral eye and an inhibitory input from the contralateral eye. It was suggested that each of the subgroups, via spinal mechanisms, elicits ipsilateral rotation of the lamprey (Fig. 9, A and B_1, arrows). The system will stabilize an orientation in space with equal activities of RS(L) and RS(R), that is, the dorsal-side-up position (equilibrium point in Fig. 9B_1).

The model could also explain the loss of equilibrium after UL. The model implies that UL causes inactivation of RS neurons on the contralateral side (Deliagina 1997a) as illustrated for the right side labyrinthectomy in Fig. 9B_2. Because of the inactivation of RS(L), the two activity curves no longer intersect, the system has no equilibrium point, and the dominating RS(R) will cause the main postural deficit—rolling of the lamprey to the right. This prediction of the model has been confirmed in the present study. It was found that the two activity curves, which intersected in intact animals (Fig. 9C_1), did not intersect after UL (Fig. 9C_2). A divergence of the curves was caused not only by inactivation of RS(L) (as was predicted by the model) but also by some increase of the response in RS(R).
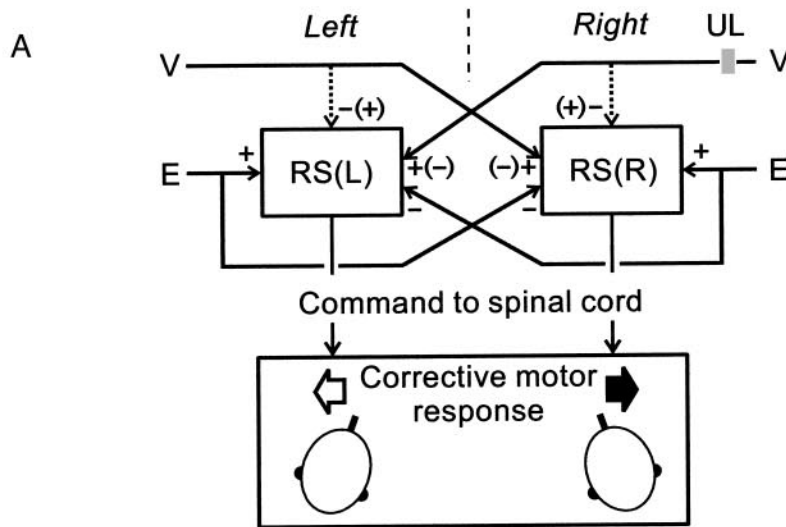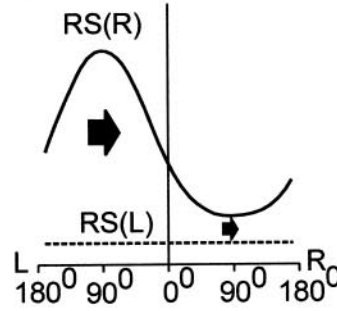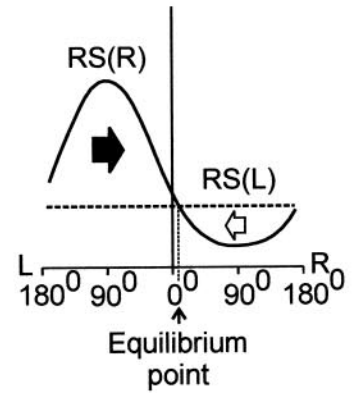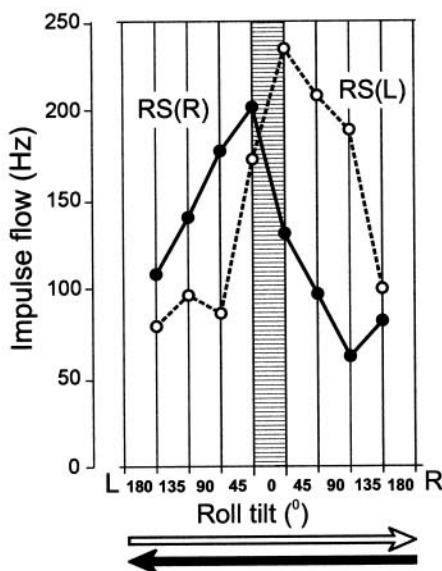
Model
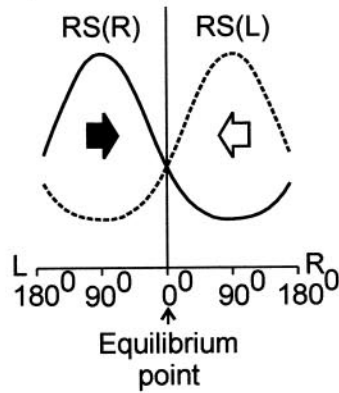
Experiment
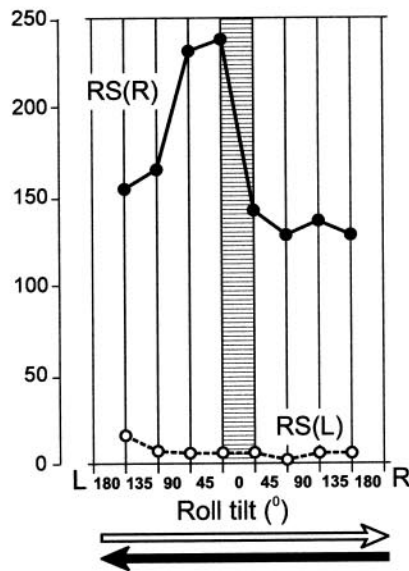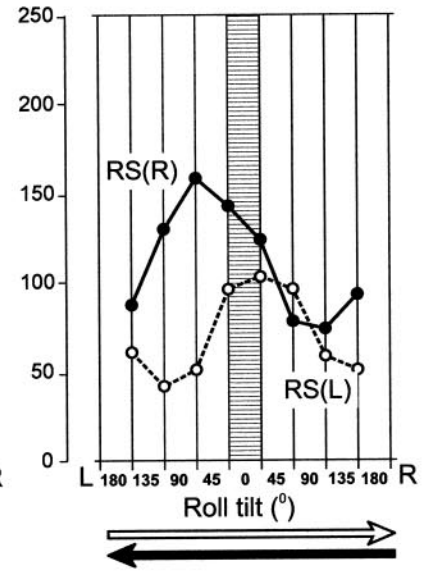
The model could also explain the restoration of postural equilibrium with eye illumination. The model implies that an excitatory input from the eye contralateral to UL (Fig. 9A) can compensate for the lacking vestibular input. This is illustrated in Fig. 9B_3, where an upward translation of the RS(L) curve is due to an excitatory input to RS(L) from the illuminated left eye, and a downward translation of the RS(R) curve is due to an inhibitory input to RS(R) from the same eye. These modifications of the responses will lead to a recreation of the equilibrium point in the system and to a termination of rolling. This prediction of the model has also been confirmed in the present study. It was found that the two activity curves, which did not intersect without eye illumination (Fig. 9C_2), did intersect during continuous eye illumination (Fig. 9C_3). A convergence of the curves was caused both by the upward translation of the RS(L) curve and by the downward translation of the RS(R) curve.

In contrast to the prediction of the model, however, the RS(L) activity not only increased under the effect of visual input but also appeared to be roll-dependent. This finding indicates that RS neurons receive input not only from the contralateral labyrinth but also from the ipsilateral one, thus confirming the earlier finding by Rovainen (1979). The latter input was not incorporated in the initial version of the model. It has been characterized in detail in the present study (Fig. 8) and is shown by the dotted lines in Fig. 9A. The input from the ipsilateral labyrinth supplements the main input from the contralateral labyrinth, and causes the roll-dependent changes in RS activity similar to those caused by the contralateral input, but of a smaller magnitude [compare RS(L) curves in Fig. 9C, 1 and 3].

Relevance of present results to vestibular compensation: comparison to other species

Experiments on mammals have shown that removal of a labyrinth has two major consequences. First, UL leads to elimination of a tonic excitatory inflow from vestibular afferents on the damaged side to their brain stem targets, the neurons of the ipsilateral vestibular nuclei. Deprived of this input, these neurons reduced or even completely lose their tonic activity (Chen et al. 1999; Hamann and Lannou 1988; Precht 1974; Ris et al. 1997; Smith and Curthoys 1988a,b). This causes a imbalance between the activity levels in the vestibular nuclei on the two sides as well as in their targets in the brain stem and in the spinal cord, which is probably the main factor responsible for postural disturbances (for discussion, see Deliagina et al. 1997; Smith and Curthoys 1989). The present study has shown that, in the lamprey, UL also results in a dramatic central asymmetry as monitored by the difference in the excitability levels of RS neurons on the two sides

(see Fig. 9C_2). In the previous section, the arguments where presented that this asymmetry is the major cause for a loss of postural equilibrium.

Another consequence of UL is a considerable reduction of the sensory inflow signaling head orientation; this inflow comes from one labyrinth in UL animals versus two labyrinths in intact animals (Chen et al. 1999; Pompeiano et al. 1984; Xerri et al. 1983). This will lead to a decrease of the gain in the postural control circuits and, consequently, to a reduction of postural stability (for discussion, see Deliagina et al. 1997; Zennou-Azogui et al. 1993). A similar effect of UL was observed also in the lamprey. When the central symmetry was restored by eye illumination, vestibular responses in RS neurons (characterizing the gain in the brain stem circuits) were considerably smaller than in intact animals (compare Fig. 9C, 1 and 3).

Studies on mammals have shown that compensation of the UL-induced motor deficits is associated with a restoration of the central symmetry as monitored by the recovery of activity in the deafferented vestibular nuclei (Chen et al. 1999; Hamann and Lannou 1988; Precht 1974; Ris et al. 1997; Smith and Curthoys 1988a,b). It seems most likely that restoration of the central symmetry is the main factor responsible for the vestibular compensation (see, however, Ris et al. 1997). In the UL lamprey, a unilateral eye illumination is an experimental tool to immediately and reversibly restore postural equilibrium (Deliagina 1997b). In the present study, we have found that eye illumination results in a restoration of the central symmetry (Fig. 9C_3). This finding strongly suggests that it is the restoration of the central symmetry, and the symmetry in RS commands addressed to the spinal cord in particular, that is, responsible for postural recovery in the lamprey. To directly test this hypothesis, however, recordings from RS axons during the period of compensation are necessary. This is the focus of ongoing investigations.

The method of recording the activity of RS neurons by means of implanted macroelectrodes, used in the present study, allowed us to track the activity of individual neurons under different conditions, i.e., before UL, after UL, and also during restoration of the central symmetry caused by eye illumination. We have found that the populations of neurons responding to vestibular stimuli under these different conditions overlap only partly (Fig. 4). In particular, under the two conditions when the lamprey can maintain a postural equilibrium (control and UL + eye illum in Fig. 4) the populations of active neurons strongly differed from each other. This finding suggests that the recovery of postural control after UL is not necessarily related to the recovery of activity in the same population of RS neurons that was involved in postural control before UL.

FIG. 9. Impairment of postural system caused by UL, and restoration of postural function caused by unilateral visual input. *A*: conceptual model of the roll control system as proposed earlier (solid lines) (see Deliagina and Fagerstedt 2000), and its modifications based on the present study (interrupted lines). The signs (+ and −) indicate the major effects on RS neurons produced by sensory inputs, the signs in brackets indicate the minor effects. B_1–B_3: operation of the initial model under different conditions. The curves represent activity of the left and right subgroups of RS neurons as a function of roll angle. The presumed directions of rolling caused by RS(R) and RS(L) are indicated by the black and white arrows, respectively. B_1: control (intact lamprey). The 2 curves intersect, and the system has an equilibrium point at 0° (dorsal-side-up orientation). B_2: the right labyrinth removed (shown by a shaded rectangle in *A*). The system has no equilibrium point. B_3: effect of the left eye illumination. Visual input causes tonic activation of RS(L), and re-creation of the equilibrium point. C_1–C_3: activity of RS neurons on the 2 sides under different conditions as established experimentally in the present study. The curves represent the flow of impulses (the mean frequency multiplied by the number of active neurons) in the right and left subgroups of RS axons during the dynamic component of the vestibular response. C_1: control; C_2: the right labyrinth removed; C_3: effect of the left eye illumination. Graphs C_1–C_3 are based on Fig. 6. See text for further details.

REFERENCES

BRODIN L, GRILLNER S, DUBUC R, OHTA Y, KASICKI S, AND HÖKFELT T. Reticulospinal neurons in lamprey: transmitters, synaptic interactions and their role during locomotion. *Arch Ital Biol* 126: 317–345, 1988.

CHEN YS, SHUM DK, AND LAI CH. Neuronal response sensitivity to bidirectional off-vertical axis rotation: a dimension of imbalance in the bilateral vestibular nuclei of cats after unilateral labyrinthectomy. *Neuroscience* 94: 831–843, 1999.

DE BURLET HM AND VERSTEEGH C. Ueber Bau und Funktion des Petromyzonlabyrinthes. *Acta Oto-laringol (Suppl)* 13: 5–58, 1930.

DELIAGINA TG. Vestibular compensation in the lamprey. *Neuroreport* 6: 2599–2603, 1995.

DELIAGINA TG. Vestibular compensation in lampreys: impairment and recovery of equilibrium control during locomotion. *J Exp Biol* 200: 1459–1471, 1997a.

DELIAGINA TG. Vestibular compensation in lampreys: roll of vision at different stages of recovery of equilibrium control. *J Exp Biol* 200: 2957–2967, 1997b.

DELIAGINA TG. Responses of reticulospinal neurons in intact lamprey to vestibular and visual inputs. Effect of unilateral labyrinthectomy. *Soc Neurosci Abstr* 23: 765, 1997c.

DELIAGINA TG AND FAGERSTEDT P. Responses of reticulospinal neurons in intact lamprey to vestibular and visual inputs. *J Neurophysiol* 83: 864–878, 2000.

DELIAGINA TG, ORLOVSKY GN, GRILLNER S, AND WALLÉN P. Vestibular control of swimming in lamprey. II. Characteristics of spatial sensitivity of reticulospinal neurons. *Exp Brain Res* 90: 489–498, 1992a.

DELIAGINA TG, ORLOVSKY GN, GRILLNER S, AND WALLÉN P. Vestibular control of swimming in lamprey. III. Activity of vestibular afferents. Convergence of vestibular inputs on reticulospinal neurons. *Exp Brain Res* 90: 499–507, 1992b.

DELIAGINA TG, GRILLNER S, ORLOVSKY GN, AND ULLÉN F. Visual input affects the response to roll in reticulospinal neurons of the lamprey. *Exp Brain Res* 95: 421–428, 1993.

DELIAGINA TG, POPOVA LB, AND GRANT G. The role of tonic vestibular input for postural control in rats. *Arch Ital Biol* 135: 239–261, 1997.

DELIAGINA TG, ZELENIN P, FAGERSTEDT P, GRILLNER S, AND ORLOVSKY GN. Activity of reticulospinal neurons during locomotion in the freely behaving lamprey. *J Neurophysiol* 83: 853–863, 2000.

DIERINGER N. "Vestibular compensation": neural plasticity and its relations to functional recovery after labyrinthine lesions in frogs and other vertebrates. *Prog Neurobiol* 46: 97–129, 1995.

DUBUC R, BONGIANNI F, OHTA Y, AND GRILLNER S. Dorsal root and dorsal column mediated synaptic inputs to reticulospinal neurons in lampreys: involvement of glutamatergic, glycinergic, and GABAergic transmission. *J Comp Neurol* 327: 251–259, 1993.

HAMANN KF AND LANNOU J. Dynamic characteristics of vestibular nuclear neurons responses to vestibular and optokinetic stimulation during vestibular compensation in the rat. *Acta Otolaryngol Suppl Stockh* 455: 1–19, 1988.

KOYAMA H, KISHIDA R, GORIS RC, AND KUSUNOKI T. Afferent and efferent projections of the VIIIth cranial nerve in the lamprey *Lampetra japonica*. *J Comp Neurol* 280: 663–671, 1989.

MACPHERSON J, DELIAGINA TG, AND ORLOVSKY GN. Control of body orientation and equilibrium in vertebrates. In: *Neurons, Networks and Motor Behavior*, edited by Stein PSG, Grillner S, Selverston AI, and Stuart D. Cambridge, MA: MIT Press, 1997, p. 257–267.

NIEUWENHUYS R. Topological analysis of the brain stem of the lamprey *Lampetra fluviatilis*. *J Comp Neurol* 145: 165–177, 1972.

NIEUWENHUYS R, DONKELAARTEN H, AND NICHOLSON C. *The Central Nervous System of Vertebrates*. Berlin: Springer, 1998, vol. 1.

NORTHCUTT RG. Central projections of the eight cranial nerve in lampreys. *Brain Res* 167: 163–167, 1979.

OHTA Y AND GRILLNER S. Monosynaptic excitatory amino acid transmission from the posterior rhombencephalic reticular nucleus to spinal neurons involved in the control of locomotion in lamprey. *J Neurophysiol* 62: 1079–1089, 1989.

ORLOVSKY GN. Gravistatic postural control in simpler systems. *Curr Opin Neurobiol* 1: 612–627, 1991.

ORLOVSKY GN, DELIAGINA TG, AND WALLÉN P. Vestibular control of swimming in lamprey. I. Responses of reticulospinal neurons to roll and pitch. *Exp Brain Res* 90: 479–488, 1992.

POMPEIANO O, XERRI C, GIANNI S, AND MANZONI D. Central compensation of vestibular deficits. II. Influences of roll tilt on different size lateral vestibular nurons after ipsilateral labyrinth deafferentation. *J Neurophysiol* 52: 18–38, 1984.

PRECHT W. Characteristics of vestibular neurons after acute and chronic labyrinthine destruction. In: *Handbook of Sensory Physiology. Vestibular System. Psychophysics, Applied Aspects and General Interpretations,* edited by Kornhuber HH. Berlin: Springer, 1974, vol. 6/2, part 2, p. 451–462.

RIS L, CAPRON B, DE WAELE C, VIDAL PP, AND GODAUX E. Dissociation between behavioural recovery and restoration of vestibular activity in the labyrinthectomized guinea-pig. *J Physiol (Lond)* 500: 509–522, 1997.

ROVAINEN CM. Physiological and anatomical studies on large neurons of central nervous system of the sea lamprey (*Petromyzon marinus*). I. Müller and Mauthner cells. *J Neurophysiol* 30: 1000–1023, 1967.

ROVAINEN CM. Synaptic interactions of reticulospinal neurons and nerve cells in the spinal cord of the sea lamprey. *J Comp Neurol* 154: 207–223, 1974.

ROVAINEN CM. Electrophysiology of vestibulospinal and vestibuloreticulospinal systems in lampreys. *J Neurophysiol* 42: 745–766, 1979.

RUBINSON K. The central distribution of VIII nerve afferents in larval *Petromyzon marinus*. *Brain Behav Evol* 10: 121–129, 1974.

SCHAEFER KP AND MEYER DL. Compensation of vestibular lesions. In: *Handbook of Sensory Physiology. Vestibular System. Psychophysics, Applied Aspects and General Interpretations,* edited by Kornhuber HH. Berlin: Springer, 1974, vol. 6/2, part 2, p. 463–490.

SMITH PF AND CURTHOYS IS. Neuronal activity in the contralateral medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 444: 295–307, 1988a.

SMITH PF AND CURTHOYS IS. Neuronal activity in the ipsilateral medial vestibular nucleus of the guinea pig following unilateral labyrinthectomy. *Brain Res* 444: 308–319, 1988b.

SMITH PF AND CURTHOYS IS. Mechanisms of recovery following unilateral labyrinthectomy: a review. *Brain Res Rev* 14: 155–180, 1989.

STEFANELLI A AND CARAVITA S. Ultrastructural features of the synaptic complex of the vestibular nuclei of *Lampetra planeri* (Bloch). *Z Zellforsch Mikrosf Anat* 108: 282–296, 1970.

TRETJAKOFF D. Das nervensystem von Ammocoetes II. *Gehirn Arch Mikrosk Anat Entwicklungsmech* 74: 636–779, 1909.

ULLÉN F, DELIAGINA TG, ORLOVSKY GN, AND GRILLNER S. Spatial orientation of lamprey. I. Control of pitch and roll. *J Exp Biol* 198: 665–673, 1995a.

ULLÉN F, DELIAGINA TG, ORLOVSKY GN, AND GRILLNER S. Spatial orientation of lamprey. II. Visual influence on orientation during locomotion and in the attached state. *J Exp Biol* 198: 675–681, 1995b.

ULLÉN F, DELIAGINA TG, ORLOVSKY GN, AND GRILLNER S. Visual potentiation of vestibular responses in lamprey reticulospinal neurons. *Eur J Neurosci* 8: 2298–2307, 1996.

ULLÉN F, ORLOVSKY GN, DELIAGINA TG, AND GRILLNER S. Role of dermal photoreceptors and lateral eyes in initiation and orientation of locomotion in lamprey. *Behav Brain Res* 54: 107–110, 1993.

VIANA DI PRISCO GV, OHTA Y, BONGIANNI F, GRILLNER S, AND DUBUC R. Trigeminal inputs to reticulospinal neurons in lampreys are mediated by excitatory and inhibitory amino acids. *Brain Res* 695: 76–80, 1995.

VIDAL PP, DE WAELE C, VIBERT N, AND MUHLETHALER M. Vestibular compensation revisited. *Otolaringol Head Neck Surg* 119: 34–42, 1998.

WANNIER T, ORLOVSKY GN, AND GRILLNER S. Reticulospinal neurones provide monosynaptic glycinergic inhibition of spinal neurones in lamprey. *Neuroreport* 6: 1597–1600, 1995.

WICKELGREN WO. Physiological and anatomical characteristics of reticulospinal neurones in lamprey. *J Physiol (Lond)* 279: 89–114, 1977.

XERRI C, GIANNI S, MANZONI D, AND POMPEIANO O. Compensation of central vestibular deficits. I. Response characteristics of lateral vestibular neurons to roll tilt after ipsilateral labyrinth deafferentation. *J Neurophysiol* 50: 428–448, 1983.

ZELENIN PV, DELIAGINA TG, GRILLNER S, AND ORLOVSKY GN. Postural control in the lamprey—a study with a neuro-mechanical model. *J Neurophysiol* 84: 2880–2887, 2000.

ZELENIN PV, GRILLNER S, ORLOVSKY GN, AND DELIAGINA TG. Heterogeneity of the population of command neurons in the lamprey. *J Neurosci* 21: 7793–7803, 2001.

ZENNOU-AZOGUI Y, BOREL L, LACOUR M, EZ-ZAHER L, AND OUAKNINE M. Recovery of head postural control following unilateral vestibular neurectomy in the cat. *Acta Otolaryngol Stockh* 509: 5–19, 1993.