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NERVOUS MECHANISMS OF POSTURAL CONTROL

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Cover illustration: A roman bronze reduction of Myron's Discovolos, 2nd century CE. The statue depicts a discus thrower about to release his throw. The moment captured by Myron is an example of rhythmos and balance.

Photo by Matthias Kabel in Glyptothek, Munich.

Στην οικογένειά μου

"I do not know what I may appear to the world; but to myself I seem to have been only like a boy playing on the seashore, and diverting myself in now and then finding of a smoother pebble or a prettier shell than ordinary, whilst the great ocean of truth lay all undiscovered before me."

Sir Isaac Newton (1642-1727)
English physicist and mathematician

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Abstract

Maintenance of body configuration and orientation in space (postural control) is a vital motor function. A general goal of the present study was to analyze nervous feedback mechanisms for the maintenance of posture during different motor behaviors and with different postural perturbations. Different aspects of postural control were considered in this study: (i) the postural motor responses during standing and locomotion, (ii) the role of supraspinal systems (cortico- and reticulospinal), and (iii) the effects of spinal cord injury on postural performance. Three animal models (lamprey, rabbit, cat), most adequate for specific aims, were used.

Control of body orientation in horizontal plane was studied in lampreys. Important elements of the postural system in lamprey are the reticulospinal (RS) neurons. They are driven by vestibular input and transmit commands for postural corrections to the spinal cord. By means of chronically implanted electrodes, responses of RS neurons to lateral turns were studied. It was found that the majority of RS neurons are dynamically activated by a contralateral turn, and these responses are caused mainly by input from the contralateral labyrinth. It was suggested that these RS signals, when arriving to the spinal cord, will cause a turn of the lamprey in the opposite direction and thus will restore the initial orientation of the lamprey in the horizontal plane.

Impairment and recovery of postural control after spinal cord lesions were studied in rabbits. Different damages to the spinal cord at T12 were performed in the rabbit, and their effect on the postural performance was characterized for the task of standing and keeping balance on the tilting platform. It was found that postural control recovered in a few weeks after the lateral and dorsal hemisection, but did not recover after ventral hemisection, suggesting a decisive role of ventral pathways for postural function.

Lateral stability in different motor behaviors was studied in cats. Postural reactions to the same postural perturbation (lateral push) during standing and during walking were compared. It was found that the basic mechanisms for balance control in these two forms of behavior are largely different: this is a re-distribution of muscle activity between the symmetrical limbs (in standing), and a reconfiguration of the base of support due to a lateral step (in walking).

Role of motor cortex in limb coordination during maintenance of equilibrium was studied in cats. The activity of pyramidal tract neurons (PTNs) of the motor cortex is known to strongly correlate with corrective responses to dynamic postural perturbations (lateral tilting of the supporting platform), suggesting that PTNs contribute to formation of these postural corrections. The corrections are caused by tilt-related somatosensory input from limbs. The aim of this study was to reveal a sensory origin of PTNs commands. In chronically instrumented cats, the activity of individual PTNs was recorded during the postural task of standing and keeping balance on the tilting platform. By suspending different numbers and combinations of limbs above the platform (abolishing tilt-related sensory input from them), it was shown that the pattern of PTN responses was determined primarily by the sensory input from the projection limb. These findings suggest that the PTNs are primarily involved in the intra-limb postural coordination, i.e., in the feedback control of the projection limb

and, to a lesser extent, in the coordination of postural activity within a girdle and between the two girdles.

Role of motor cortex in postural adaptations to the environment was studied in cats. When standing or walking on an inclined plane, cats easily adapt their posture to the support inclination, by inducing asymmetry in the configuration of the left and right limbs. The activity of individual PTNs during standing and walking on the inclined plane was recorded. A positional response (i.e., an increase of activity either with ipsi- or with contra-tilt) was observed in many PTNs, either in both tasks, or only in one of them. It was suggested that these PTNs contribute to modifications of the limb configuration necessary for postural adaptation, and there are both common and separate cortical mechanisms underlying this adaptation in the two motor tasks.

List of publications

This thesis is based on the following papers and manuscripts:

I. **Karayannidou A**, Zelenin PV, Orlovsky GN, and Deliagina TG (2006). Responses of reticulospinal neurons in the lamprey to lateral turns. *J Neurophysiol*, 97:512-521.

II. Lyalka VF, Zelenin PV, **Karayannidou A**, Orlovsky GN, Grillner S, Deliagina TG (2005). Impairment and recovery of postural control in rabbits with spinal cord lesions. *J Neurophysiol*, 94:3677-3690.

III. **Karayannidou A**, Zelenin PV, Orlovsky GN, Sirota MG, Beloozerova IN, Deliagina TG (2009). Maintenance of lateral stability during standing and walking in the cat. *J Neurophysiol*, 101:8-19.

IV. **Karayannidou A**, Deliagina TG, Tamarova ZA, Sirota MG, Zelenin PV, Orlovsky GN, Beloozerova IN (2008). Influences of sensory input from the limbs on feline corticospinal neurons during postural responses. *J Physiol*, 586:247-63, 2008.

V. **Karayannidou A**, Beloozerova IN, Zelenin PV, Stout EE, Sirota MG, Orlovsky GN, Deliagina TG (2009). Activity of pyramidal tract neurons in the cat during standing and walking on an inclined plane. (*Submitted*).

The work originates from my years as a PhD student at the Department of Neuroscience at the Karolinska Institute in Stockholm, Sweden. Part of it has been performed in collaboration with my co-supervisor, Dr. Irina Beloozerova, at the Barrow Neurological Institute in Phoenix, USA.

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Finally, my family, for showing me that, when it comes to love and support, distance is just a minor detail. Thank you for all the confidence in me. I dedicate this work to you.

Contents

List of abbreviations

Add Fem	m. adductor femoris
AP	anterioposterior
Bd	body
CCC	corticocortical neurons projecting to the contralateral MC or S1
CC1	corticocortical neurons projecting to the ipsilateral S1
CF5	corticofugal neurons of layer V
CF6	corticofugal neurons of layer VI
CNS	central nervous system
CPG	central pattern generator
DHS	dorsal hemisection
E	eye
EMG	electromyographic
F	force
FO	fiber optic illumination system
Fore	forelimb
Gast	m. gastrocnemius
Glut	m. gluteus
Grac	m. gracilis
Hind	hindlimb
L	left
LHS	lateral hemisection
MC	motor cortex
ME	microelectrode
ML	mediolateral
P	platform
PTN	pyramidal tract neuron
R	right
RF	receptive field
RS	reticulospinal
S	sensor
SCI	spinal cord injury
S1	primary somatosensory cortex
SIN	putative inhibitory interneurons
T12	12th thoracic segment
UL	unilateral labyrinthectomy
V	vestibular organ
Vast	m. vastus
VHS	ventral hemisection
VL	ventrolateral thalamus
VS	vestibulospinal

1. Introduction

1.1 General characteristics of postural system

1.1.1 Significance of postural control

Active maintenance of the basic body posture, upright in bipeds and dorsal-side-up in quadrupeds and other animals, is a vital motor function. Maintenance of this posture is a non-volitional activity based, in many species, on inborn neural mechanisms (Massion, 1998; Vinay et al., 2005). An efficient control of the basic posture is equally important for standing and during walking (Horak & Macpherson, 1995; Macpherson et al., 1997a; Orlovsky et al., 1999), as well as for providing support during voluntary movements of the limbs, trunk, and head (Massion & Duffose, 1988). The postural control system is one of the most complex motor systems, with its nervous mechanisms located in the forebrain, brainstem and spinal cord. Damage to these mechanisms causes a loss of equilibrium during standing and during locomotion, and hampers the performance of voluntary movements that need postural support.

In legged species, the postural system performs two principal functions (Horak & Macpherson, 1996). *First*, it provides a specific body configuration (orientation of body segments with respect to each other). This configuration can be modified depending on the external conditions (such as inclined or narrow support surface under the legs, which require a change of the functional length of the limbs or inter-limb distance) and depending on behavioral tasks (such as standing or walking, bipedal or quadrupedal). *Second*, the postural system maintains equilibrium, i.e., stabilizes a definite position of the body in relation to the environmental factors (gravity vector, position of support surface, etc.). Maintenance of equilibrium during locomotion requires a close interaction between the postural and locomotor systems.

There are two principal modes of operation of the postural system – the feed-back and feed-forward ones. The mode depends on the nature of postural perturbations, i.e, if they are unexpected or expected (Horak & Macpherson, 1996; Gahery et al., 1980).

The feed-back mode of postural control is a compensation for deviations from the desired posture caused by unexpected factors. This mode is performed by a closed-loop control mechanism. Deviation from the desirable body orientation is detected by different sensory systems (somatosensory, vestibular, visual), and their signals cause generation of a corrective movement, which returns the body to the initial position (Horak & Macpherson, 1996; Massion et al., 1997).

The feed-forward mode of postural control is used when postural perturbations are expected. This mode implies a generation of anticipatory postural adjustments. For example, upon initiation of a command for a voluntary movement of the limb, head, or trunk, at the same time (or even earlier) a special command is sent to the postural mechanisms. This command causes a postural response aimed at counteracting the destabilizing effects of the voluntary movement. This mode of operation is based on the activity of an open-loop nervous

mechanism. Normally, the two modes interact. For example, errors in anticipatory adjustments can be compensated by the closed-loop mechanism (Horak & Macpherson, 1996). *The present study was devoted to the feedback mode of postural control.*

1.1.2 Sensory information used for postural control

Sensory information, necessary for the feed-back mode of postural control, is provided by three major systems:

1. Somatosensory system, which includes muscle, joint, and cutaneous afferents. It provides information about the length of individual muscles, about the force they develop, about the joint angles and about the contact force produced by the limb. This information fully characterizes the limb configuration and movement during maintenance of steady posture and during postural corrections.

2. Vestibular system, which comprises two components with specialized receptors located in the inner ear (labyrinth). *First*, the otoliths signal about the head orientation in the gravity field and about the linear acceleration of the head. *Second*, the semicircular canals signal about rotation of the head. Together, they provide full information about the head position and movement.

3. Visual system. There are two types of visual information that contribute to the control of body posture: 1) static visual cues and 2) motion detection cues based on the velocity of the visual field. These visual signals give information about the head position and movement in relation to the environment.

The significance of a particular sensory system depends on a postural task and environmental conditions (Beloozerova et al., 2003b; Deliagina et al., 2000b).

1.1.3 Functional organization of postural system

There are two major concepts about the functional organization of the feed-back mode of postural control:

Non-centralized control. In the classical study by Magnus (1924) performed on quadrupeds, any particular stabilized posture of the animal was considered as a result of interactions between numerous postural reflexes (driven by vestibular, visual and somatosensory inputs); they either supplement or counteract each other. Results of the studies on "simpler animals" – the mollusc *Clione* (Deliagina et al., 1998, 1999, 2000a, 2000d), the lamprey (Deliagina, 1997a; Deliagina & Fagerstedt, 2000c) and the fish (Von Holst, 1935), support the "reflex concept" of postural control.

Centralized control. This concept of postural stabilization was formulated for terrestrial higher vertebrate animals and humans. It suggests that a body posture is characterized by a single "regulated variable" (e.g. position of the center of mass in relation to the support area or orientation of the longitudinal body axis in relation to the gravity vector); a certain value of this variable is stabilized. According to this concept, information about the head and body orientation is delivered by sensory inputs of different modalities (vestibular, visual, and somatosensory). This information is processed and integrated to obtain a current value of the regulated variable. If this value differs from the desired one, a command is sent to the motor centers to elicit a corrective movement (Horak & Macpherson, 1996; Massion & Duffose, 1988; Ghez et al., 1991; Massion, 1994; Massion et al., 1997). It seems likely that

postural control in higher animals is based on both principles, i.e., the central (supraspinal) postural mechanisms operate along with the local (spinal) reflex mechanisms (Deliagina et al., 2006a).

1.1.4 Animal models

In the present study three animal models of different complexity were used: the lower vertebrate animal (lamprey), and two higher vertebrate animals, terrestrial quadrupeds (rabbit and cat).

Lamprey

The lamprey (cyclostome) originates from a group of animals that diverged from the main vertebrate line around 450 million years ago, when ordinary fish had not yet appeared (Forey & Janvier, 1993). The basic organization of the CNS in lamprey is similar to that in higher vertebrates: it has the spinal cord, the telencephalon, diencephalon, mesencephalon and rhombecephalon (Kappers, 1936; Rovainen, 1979; Nieuwenhuys et al., 1998). However, the lamprey CNS contains much fewer neurons than the CNS of higher vertebrates, and therefore allows detailed analytical studies of neuronal networks [for reviews see (Grillner et al., 1983; Grillner & Wallén, 1985; Grillner et al., 1986, 1988, 1990, 1993, 1995, 1997)].

The lamprey is an aquatic animal. It swims due to lateral undulations of the body propagating from the head to the tail. During swimming, the lamprey actively maintains a definite orientation of the body, which is stabilized as one segment. It has two sensory systems, which can be used for the postural control: vestibular system (two vestibular organs) and visual system (two lateral eyes).

Terrestrial quadrupeds

The principal differences of terrestrial quadrupeds (rabbit and cat) from the lamprey are:

1. Their body consists of a number of segments, which can be stabilized in space independently of each other. For example, the cat can maintain the dorsal-side-up orientation of the trunk and, at the same time, move its head, or maintain different head positions (Beloozerova et al., 2005).

2. They can use for postural control not only visual and vestibular information but also somatosensory information from limb mechanoreceptors (skin pressure receptors, muscle spindles and Golgi tendon organs).

3. They can stabilize spatial orientation of the trunk and head during both standing and locomotion.

4. Their CNS contains structures (cerebellum, cerebral cortex) and pathways (e.g. rubrospinal, corticospinal), which are absent in the lamprey.

Studies of the same motor function in different, evolutionary remote species have two advantages. *First*, a comparison across species can help in revealing the common principles underlying this function, as well as in better understanding of the corresponding nervous mechanisms (Orlovsky et al., 1999). *Second*, by using simpler animals, one can address the questions that are difficult to study in higher animals, like the detailed analysis of neuronal networks responsible for motor control. Comparative studies of postural mechanisms are
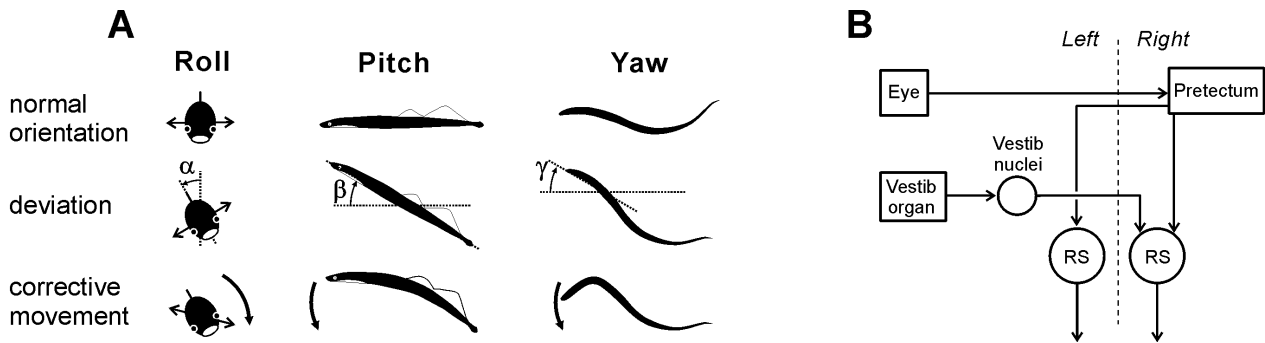
Figure 1.1: *A*. During swimming, the lamprey stabilizes the body orientation in three orthogonal planes – frontal (roll), sagittal (pitch), and horizontal (yaw). A deviation from the stabilized orientation in each of these planes (α,β,γ) evokes a specific corrective movement aimed at restoration of the normal orientation. *B*. Main components of the brain stem postural network. See text for explanations.

based on the assumption that a basic problem such as the nervous control of the antigravity behavior has similar solutions in different species, and thus the results obtained on animal models may have significance for understanding the mechanisms of postural control in humans.

The general goal of the study was, by using three animal models, to analyze the nervous mechanisms responsible for stabilization of the basic body posture. Only the feedback mode of postural control was considered.

1.2   Postural control in lamprey

1.2.1   General characteristics

During swimming, the lamprey actively maintains a definite body orientation in the sagittal (pitch), in the frontal (roll), and in the horizontal (yaw) planes (Fig. 1.1*A*). A deviation from the stabilized orientation in each of these planes (α,β,γ) evokes a specific corrective movement aimed at restoration of the normal orientation. During long-distance swimming, the longitudinal body axis is normally oriented horizontally (β=0), while the dorsal side is directed upward (α=0).

The postural control system in the lamprey is driven by vestibular input. After a bilateral labyrinthectomy, the animals with intact vision cannot maintain a definite orientation in space and are continuously looping in different planes (De Burlet & Versteegh, 1930; Ullén et al., 1995a). On the contrary, blind animals and intact animals in darkness maintain the normal body orientation perfectly well with the help of vestibular organs. However, the visual input can exert modulatory effects on the body orientation. *First*, illumination of one eye evokes a roll tilt towards the source of light (Ullén et al., 1995b, 1997). This postural reflex was termed the dorsal light response (Von Holst, 1935; Platt, 1983). *Second*, illumination of one eye evokes a lateral turn away from the source of light, i.e., the negative phototaxis (Ullén et al., 1993, 1995b). The visual input for these reflexes is transmitted to the contralateral pretectum and is relayed bilaterally to the reticular formation. The dorsal light response is thought to be mediated by crossed pretectum projections, while negative phototaxis – by non-crossed projections (Fig. 1.1*B*) (Ullén et al., 1997).
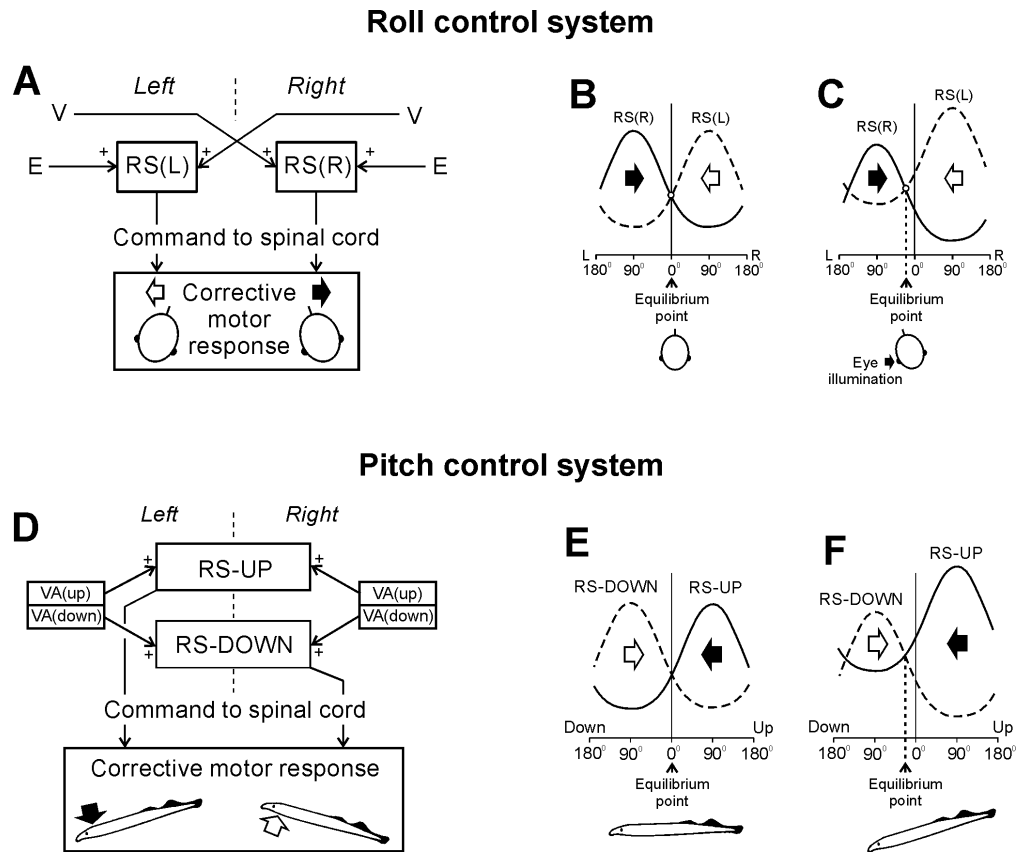
Roll control system

Pitch control system

Figure 1.2: Roll (*A*) and pitch (*D*) control systems. Two antagonistic groups of RS neurons are important elements of each of the two systems. Driven by vestibular inputs, the two groups cause rotation of the animal to opposite directions (arrows). Each of the systems stabilizes the orientation at which the activities of the groups are equal to each other (*B,E*). However, a tonic drive to one of the groups will cause a shift of the equilibrium point and a change of the stabilized orientation (*C,F*).

1.2.2 Stabilization of body orientation in roll and pitch planes

The principal elements of the network for spatial orientation in the lamprey are shown in Fig. 1.1*B*. Deviation of the body orientation from the desirable one in a particular plane activates a specific group of vestibular afferents (Rubinson, 1974; Koyama et al., 1989), which through neurons of vestibular (octavomotor) nuclei affect reticulospinal (RS) neurons (Wickelgren, 1977; Rovainen, 1979). These neurons constitute the main descending pathway in the lamprey, and transmit commands for changing the body orientation. The vestibulospinal (VS) pathway is poorly developed in the lamprey and most likely makes no significant contribution to the control of posture. It projects only to the rostral part of the spinal cord (Rovainen, 1979; Bussières & Dubuc, 1992) and has weak effect on the spinal cord output (Zelenin et al., 2003). The commands for postural corrections transmitted by RS neurons can be modified by ipsilateral visual input through pretectal neurons (Zompa & Dubuc, 1996; Ullén et al., 1997). In response to RS commands the spinal cord generates the corrective movement (Zelenin et al., 2007).

Operation of the postural control systems, stabilizing orientation of the lamprey in roll and pitch planes, is based on the interactions between two antagonistic vestibular reflexes, mediated by two groups of RS neurons causing rotation of the animal in the opposite directions (Deliagina, 1997a, 1997b; Deliagina & Fagerstedt, 2000c; Deliagina et al., 1992a, 1992b, 1993; Pavlova & Deliagina, 2002; Zelenin et al., 2000; Zelenin, 2005). This is il-

lustrated schematically for the roll control system in Fig. 1.2*A-C*. Due to the vestibular input, the activity of each group of RS neurons depends on the orientation of the animal in the roll plane (Fig. 1.2*B*). Each group, due to specific influences on the spinal mechanisms, elicits a motor response that counteracts a deviation from the stabilized orientation. The system has an equilibrium point: it stabilizes the orientation at which the antagonistic vestibular reflexes compensate for each other. Normally, this occurs at the dorsal-side-up orientation. Not only static but also dynamic components of vestibular responses (since they are position-dependent) contribute to postural stabilization (Zelenin et al., 2000). Unilateral eye illumination affects differently the two antagonistic groups of RS neurons and causes a shift of the equilibrium point of the system, which results in a change of the stabilized orientation (Fig. 1.2*C*). In the pitch control system, the stabilized orientation also corresponds to the equal activities in the two antagonistic groups of RS neurons sensitive to the nose-up and nose-down tilt, respectively (Fig. 1.2*D,E*). The stabilized angle can be changed by raising the water temperature, which affects differently the two groups and thus shifts the equilibrium point towards the nose-down orientation (Fig. 1.2*F*).

In the lamprey, a command system for orientation in the roll and pitch planes was analyzed in detail, with characterization of both sensory inputs and motor effects of individual command neurons (Zelenin et al., 2001, 2003, 2007). The effects of signals transmitted from the brain stem to the spinal motor networks by a population of RS neurons depend on motor effects (functional projections) of individual neurons. It was found that individual RS neurons exert a uniform effect on the segmental motor output along the whole extent of their axons (Zelenin et al., 2001, 2003). A strong correlation was found between (i) vestibular inputs to individual RS neurons, and (ii) the effects on efferent spinal output exerted by the same RS neurons (Zelenin et al., 2007). As a rule, if a neuron was activated by a turn in a given plane, its motor effect resulted in a torque opposing the turn. Thus, transformation of the spatial information into the corrective motor response has two steps. *First*, a population of RS neurons, with specific spatial sensitivity, is activated by sensory signals. *Second*, these neurons, due to their spinal functional projections, activate a specific group of muscles that cause correction of orientation.

1.2.3 Stabilization of body orientation in yaw plane

Swimming along a rectilinear trajectory in the horizontal (yaw) plane is often observed in the lamprey. Changes of the direction of swimming occurs in different forms of behavior – during escape reaction, negative phototaxis, steering towards a prey, etc. (McClellan & Grillner, 1983; McClellan, 1984; Ullén et al., 1993, 1997; McClellan & Hagevik, 1997). In contrast to turns in the roll and pitch planes, turns in the yaw plane do not affect the animal's orientation in relation to the gravity vector. Therefore, gravity cannot be used as a reference direction for the system stabilizing the yaw orientation. The question arises then if the vestibular reflexes play a role in the maintenance of body orientation in the horizontal (yaw) plane.

In the study by Zelenin (2005), the population of RS neurons responding to yaw turn was revealed. Most of them were activated by the contralateral turn. However, in that study the vestibular responses of yaw-related RS neurons were not characterized in any detail. Also, the data were obtained on the *in vitro* preparation, in which a number of inputs to RS neurons, like those from the forebrain, from the cranial nerves and from the caudal part of the spinal cord were abolished, and therefore did not allow to characterize the RS activity in normal animals.

One of the aims of the present study was to characterize, in the intact lamprey, the supraspinal commands for stabilization of body orientation in the horizontal plane.

1.3 Postural control in quadrupeds

1.3.1 Maintenance of lateral stability during standing

When standing, cats and rabbits maintain the dorsal-side-up orientation of their trunk (basic posture) due to the activity of the postural system. This closed-loop control system stabilizes the body orientation in the frontal plane, and thus secures lateral stability of the animal. Any deviation from the basic posture elicits a corrective motor response. The pattern of this response depends on the type of postural perturbation. In this study, two types of postural perturbation were employed: (i) the lateral tilt of the supporting surface, and (ii) the lateral force applied to the body. Corrective motor responses in these two postural tasks were different.

Postural reactions to tilts of the support surface during standing

Both cats and rabbits easily solve the postural task of counteracting the destabilizing influences of lateral tilts of the support surface. Operation of the postural system in this task is similar in these two species (Beloozerova et al., 2003b; Deliagina et al., 2006b). A lateral tilt of the platform causes extension of the limbs on the side tilted down and flexion of the limbs on the opposite side. These limb movements are caused by a specific pattern of muscle activity: activation of extensor muscles in the limbs ipsilateral to the side of the platform moving down and reduction of the extensor activity and activation of some flexor muscles in the opposite limbs (Beloozerova et al., 2003b; Deliagina et al., 2006b; Matsuyama & Drew, 2000). Due to these compensatory limb movements, the dorso-ventral axis of the trunk moves towards the vertical. Simultaneously one can observe movement of the dorso-ventral head axis towards the vertical. However, the postural corrections do not compensate fully for the platform tilt, and after their execution the dorso-ventral axis of the head and trunk remain deviated from the vertical (Deliagina et al., 2006b).

The postural control system usually operates as a functional unit and stabilizes both head and trunk orientation. Under certain conditions, however, the system clearly dissociates into the systems controlling independently the head and the trunk (Barberini & Macpherson, 1998; Beloozerova et al., 2005; Berthoz & Pozzo, 1988; Boyle, 2001; Deliagina et al., 2000b). These systems are driven by sensory signals of different modalities: the head orientation is stabilized mainly on the basis of vestibular and visual information; for trunk stabilization, somatosensory inputs from limbs are most important (Beloozerova et al., 2003b; Deliagina et al., 2000b).

It was found that cats and rabbits are able to keep equilibrium in complicated postural tasks, when the anterior and posterior parts of the body are supported by two separate platforms tilted in anti-phase (Beloozerova et al., 2003b; Deliagina et al., 2006b). To explain these results, it was suggested that the system stabilizing the trunk orientation in the frontal plane in quadrupeds consists of two relatively independent sub-systems, stabilizing the anterior and posterior parts of the trunk, respectively. Each sub-system is driven by somatosensory input from the corresponding limbs.

To characterize the functional organization of these sub-systems and their interactions, experiments were carried out in which one, two, or three limbs were suspended and thus were excluded from maintenance of body posture. By recording responses to tilt in such a "reduced" postural system, different components of the system were determined, and influences between them were evaluated (Fig. 1.3) (Deliagina et al., 2006b). These experiments have shown that: (i) Each sub-system is capable to fully compensate for the lateral platform tilt when the limbs of another girdle do not participate in trunk stabilization. (ii) Coordination between the
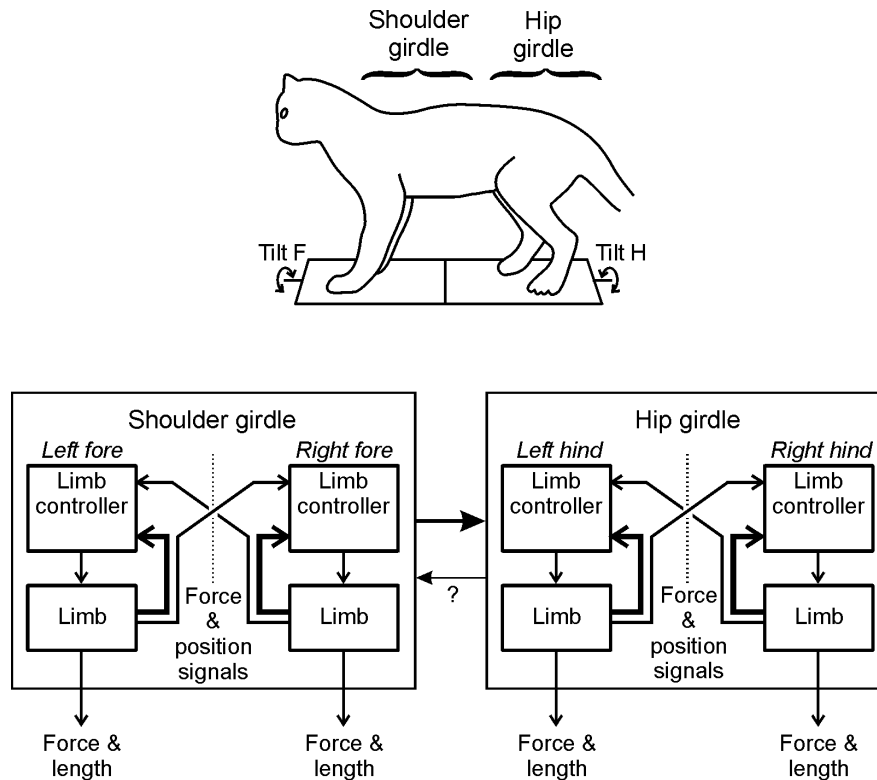
Figure 1.3: Scheme for sensorimotor processing in the postural system stabilizing the dorsal-side-up orientation of the trunk. See text for explanations.

two sub-systems is based primarily on the influences of the forelimbs' sub-system upon the hindlimbs' sub-system. However, these influences do not necessarily determine the responses to tilt in the hindlimbs. In case of mismatch between the somatosensory input from hindlimbs and forelimbs, corrective movements are generated in response to somatosensory input from the hindlimbs. (iii) Each sub-system contains the mechanisms (limb controllers), which generate a part of the corrective movement of an individual limb in response to the tilt-related somatosensory information from the same limb. For the generation of corrective movement of full amplitude, the tilt-related somatosensory input from the contralateral limb of the girdle is necessary.

Postural reactions to lateral pushes

Freely behaving animals are often subjected to lateral forces in their natural habitats, when colliding with obstacles or when interacting with other animals. To ensure the lateral stability, the postural system has to compensate for the body displacements in the frontal plane caused by lateral forces applied to the body. Cats and rabbits easily solve this postural task. In the study by Kato et al. (1985) it was shown that standing cats can oppose lateral pushes and do not fall even with application of forces up to 0.5-1 kg in the hip region. Rabbits also oppose lateral pushes (Musienko et al., 2008). These findings suggest that the postural system can efficiently compensate for such disturbances. However, any analysis of the postural reactions to pushes, which counteract their destabilizing influences on the body posture, was lacking. *One of the aims of the present study was to characterize postural reactions to lateral pushes during standing.*

1.3.2 Interaction of postural and locomotor systems

During locomotion, the postural system has the same function as during standing – stabilization of the head and trunk orientation in space. In both motor behaviors, postural mechanisms compensate for all destabilizing influences, both expected and unexpected (see e.g. Horak & Macpherson, 1996; Nashner & Forssberg, 1986; Misiaszek, 2006a). However, the postural control (maintenance of equilibrium) during walking has an important distinctive feature; it requires close interaction between the postural and locomotor control systems.

The stepping movements of limbs are controlled by the spinal central pattern generator (CPG), which determines the rhythm of stepping and the alternating activity of limb muscles. It was shown that postural corrections during walking are well incorporated into the basic locomotor pattern, both in the feed-forward mode of postural control (compensation for destabilizing effects of voluntary movements, see Nashner and Forssberg, 1986) and in the feed-back mode [compensation for lateral and downward displacements of the support surface and its tilts (Misiaszek, 2006a; Marple-Horvat et al., 1993; Matsuyama & Drew, 2000)]. Also, in both modes, the pattern and magnitude of postural reactions during stepping were phase-dependent. *One of the aims of the present study was to characterize the postural reactions to lateral pushes during walking, and to compare them with the reactions during standing.* This contributed to the understanding of the differences between the postural control strategies in these two motor behaviors.

1.3.3 Distribution of postural functions:
spinal and supraspinal mechanisms

Animals decerebrated at the precollicular-premammillary level can maintain equilibrium during standing and during locomotion. When positioned on its side, the animal exhibits a set of righting reflexes and assumes the normal, dorsal side-up posture (Bard & Macht, 1958; Magnus, 1924; Musienko et al., 2008). Decerebrated rabbits produce postural corrections in response to push and to lateral tilt of the supporting platform. The EMG pattern of these corrections is similar to that observed in intact animals, though the magnitude of corrections is reduced as compared to normal animals (Musienko et al., 2008). These findings indicate that an essential part of the nervous mechanisms responsible for postural control are located below the level of decerebration, i.e. in the cerebellum, brain stem and spinal cord.

Participation of the brain stem and cerebellum in the control of posture was also shown in the following experiments. *First*, electrical stimulation of two areas in the brain stem, the dorsal and ventral portions of the caudal tegmental field, as well as stimulation of the hook bundle in the cerebellum, strongly modified the extensor muscle tone, which is a necessary condition for the control of body posture (Mori, 1987, 1989; Asanome et al., 1998; Musienko et al., 2008). These effects are thought to be mediated by reticulospinal and vestibulospinal pathways. *Second*, single neuron recordings in intact cats walking on the treadmill have shown that brain stem neurons (giving rise to the vestibulospinal and reticulospinal descending tracts) were modulated with a tilt of the treadmill, in both sagittal and frontal plane (Matsuyama & Drew, 2000).

One important question regarding postural control is related to the interactions between spinal and supraspinal postural mechanisms (for discussion see Deliagina & Orlovsky, 2002b; Horak & Macpherson, 1996). Presumed interactions between the spinal and supraspinal levels of the postural system stabilizing trunk orientation are shown in Fig. 1.4. For each of the girdles (shoulder and hip), there are two closed-loop nervous mechanisms (shown for the hindlimbs in Fig. 1.4). One of the mechanisms (Short loop) resides in the spinal cord.
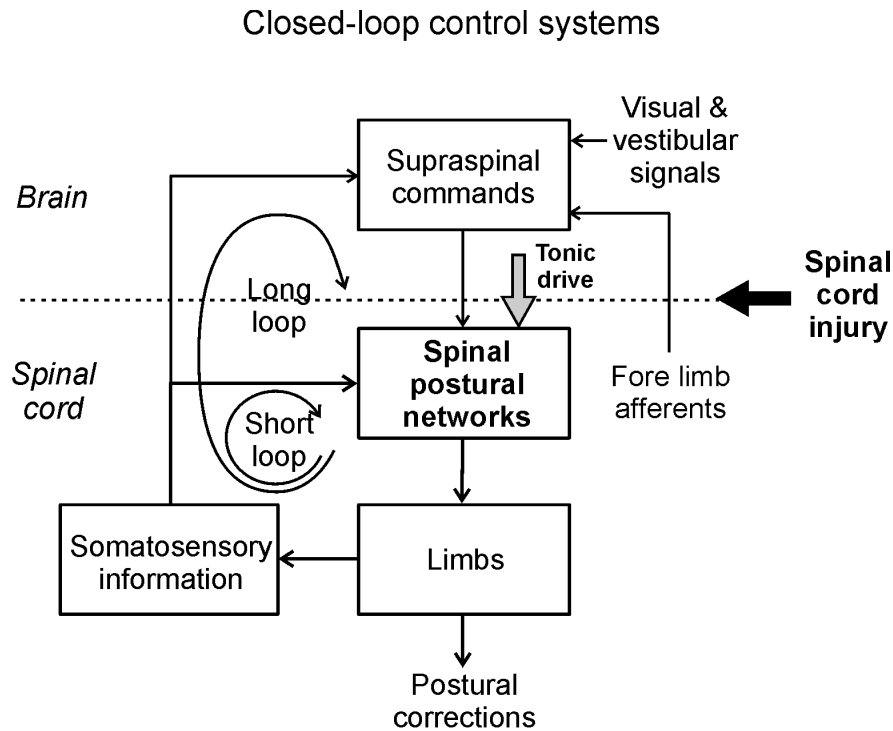
Closed-loop control systems

Figure 1.4: Spinal and supraspinal levels of postural system operating in the feedback mode. Two closed-loop mechanisms (Short-loop and Long-loop) participate in stabilization of trunk orientation in the frontal plane.

It is driven by input from limb mechanoreceptors, and contributes to generation of postural corrections in response to postural disturbances.

The other mechanism contributing to generation of postural corrections contains a "long" reflex loop (Long loop in Fig. 1.4) involving supraspinal centers. This mechanism receives sensory signals from hindlimb mechanoreceptors and, in addition, information about head orientation from visual and vestibular systems, as well as signals from forelimb mechanoreceptors. The output of this mechanism represents the phasic corrective signals, which are sent to the spinal cord via different descending pathways (reticulospinal, vestibulospinal, rubrospinal, corticospinal). These commands, along with spinal reflexes, contribute to corrections of posture.

However, a relative contribution of the spinal and supraspinal closed-loop mechanisms to the generation of postural corrections is not clear. On one hand, the animals with a complete transection of the spinal cord in the lower thoracic region exhibit very poor postural responses and, as a rule, are not able to maintain the dorsal-side-up orientation of their hindquarters (Macpherson et al., 1997b; Macpherson & Fung, 1999). These results were interpreted as evidence to suggest a minor role for spinal reflexes (Short loop in Fig. 1.4) in postural control (Horak & Macpherson, 1996). However, some elements of postural control (like weight-bearing standing episodes) in spinal animals may remain (Giuliani & Smith, 1985; Grillner, 1973; Kellog et al., 1946), and they can be improved by training (De Leon et al., 1998; Edgerton et al., 2001, 2004; Pratt et al., 1994).

Inability of spinal animals to counteract postural disturbances can be caused by two reasons. *First*, one can suggest that, in terrestrial quadrupeds, the spinal mechanisms do not generate postural corrections, and as in lamprey, their main function is a transformation of the specific supraspinal commands to the motor pattern of postural corrections. If so, they are not sufficient for doing this in spinal animals. *Second*, one can suggest that the

spinal postural reflexes play an important role in the generation of postural corrections. However, the reflex mechanisms need supraspinal drive to be activated, and loss of this drive dramatically reduces the reflexes (see Fig. 1.4).

Indirect support of the second hypothesis came from lesion experiments, in which animals with a lateral hemisection of the spinal cord, after some period of recovery, were able to maintain equilibrium during both standing and locomotion (Kuhtz-Buschbeck et al., 1996; Helgren & Goldberger, 1993). Similar results were obtained with two lateral hemisections performed on the opposite sides at different levels (Kato et al., 1985). Since the lateral hemisection impaired the transmission of both ascending signals and descending commands in a hemicord, and thus severely damaged the long-loop (supraspinal) mechanism, one can suggest that the recovery of postural reactions after the lateral hemisection was due to the activation of spinal postural mechanisms. However, in these studies a quantitative analysis of postural deficits caused by spinal lesions was lacking. *One of the aims of the present study was to characterize the impairment and subsequent recovery of postural control after different partial lesions to the spinal cord.*

1.3.4   Role of motor cortex in control of equilibrium

A participation of the motor cortex in postural control was directly demonstrated by recording of different classes of motor cortex neurons (Fig. 1.5*A*) in the rabbit maintaining balance on the platform that was periodically tilted in the frontal plane. It was found that the activity of corticofugal neurons of layer 5 (projecting to the subcortical motor nuclei and the spinal cord) and the activity of putative GABA-ergic fast-spike inhibitory interneurons strongly correlated with the corrective movements of the limbs caused by platform tilts (Beloozerova et al., 2003a). In the cat performing a similar postural task, the activity of pyramidal tract neurons (PTNs) from the limb representation of the motor cortex was profoundly modulated by tilts (Fig. 1.5*B*) (Beloozerova et al., 2005). It was shown, that GABA-ergic interneurons of the motor cortex reduce their posture-related responses, but have a little role in determining their response timing (Tamarova et al., 2007).

The low activity and weak modulation of other classes of cortical neurons (CCI, CCC and CF6 neurons, Fig. 1.5*A*) during the postural task (Beloozerova et al., 2003a) suggests that these neuronal populations do not have any significant role in the control of posture. The inactivity of callosal neurons suggests that coordination between the two symmetrical limbs during postural corrections does not require interaction of the two hemispheres, and is achieved at the brainstem-spinal level. The low activity of CF6 neurons, which are essential part of the thalamo-cortical loop (Sherman & Guillery, 2001), suggests that functioning of this loop during postural corrections is based mostly on the feedback signals that are transmitted to the thalamus by CF5 neurons.

The functional significance of profound modulation of PTNs during postural corrections was not quite clear, however. On one hand, the integrity of the motor cortex is not necessary for the generation of postural corrections and for maintenance of the basic body posture, as demonstrated, e.g., in decerebrated animals. On the other hand, the magnitude of reactions in these animals was smaller than in the intact animals (Musienko et al., 2008). To understand the cortical contribution to postural control, it is necessary to determine cortical participation in the intra-limb and inter-limb coordination (Fig. 1.4) by analyzing the sensory origin of corticospinal commands. This can be done by studying the contribution of somatosensory inputs coming from individual limbs to the tilt-related modulation of PTNs. *One of the aims of the present study was to analyze the role of the motor cortex in postural limb coordination in the standing cat during maintenance of equilibrium.*
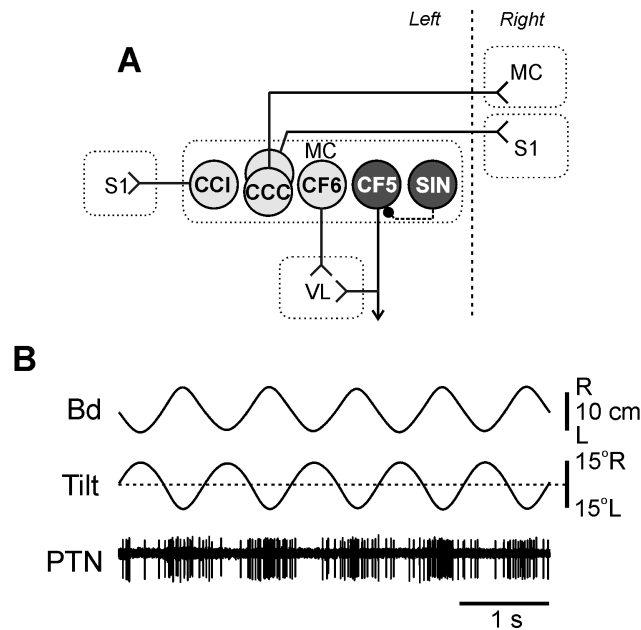
Figure 1.5: *A*: Different classes of motor cortex neurons studied during postural corrections. CC1, Corticocortical neurons projecting to the ipsilateral primary somatosensory cortex (S1); CCC, Corticocortical neurons projecting to the contralateral MC or S1; CF6, Corticofugal neurons of layer VI projecting to the ventrolateral thalamus (VL); CF5, Corticofugal neurons of layer V with collaterals projecting to the VL; SIN, Putative inhibitory interneurons. Of these types, CF5 and SIN were profoundly modulated by tilts. *B*: Responses of a PTN to platform tilts (Tilt) recorded along with corrective movements of the body (Bd).

1.3.5   Role of motor cortex in postural adaptations to environment

In addition to its main function (maintenance of equilibrium), the postural control system in quadrupeds is also responsible for adaptation of the animal's posture to the environment, which requires modifications of the body configuration (Horak & Macpherson, 1996). One of these adaptive changes is observed during standing or walking on an inclined plane. As shown by Matsuyama and Drew (2000), the walking cat easily adapted to these new conditions by acquiring a specific body configuration: the functional length of the limbs in the stance part of the step (when they support the body) increased on the side tilted down, and decreased on the opposite side. Corresponding postural adaptations were also observed in the task of standing on a laterally inclined platform, both in cats (Beloozerova et al., 2005) and in rabbits (Beloozerova et al., 2003a).

There are data suggesting that a number of supraspinal motor centers participate in postural adaptations performed when standing and walking on an inclined plane. As demonstrated by Matsuyama and Drew (2000), the activity of vestibulospinal and reticulospinal neurons in the cat is modulated in the rhythm of stepping, and the magnitude of this activity depends on the value of the stationary lateral tilt. Involvement of other descending systems (corticospinal, rubrospinal) was not investigated. *One of the aims of the present study was to characterize the role of the motor cortex in postural adaptations to the environment (tilt of support surface) during standing and walking.*

Specific aims of the study

1. To characterize supraspinal commands for stabilization of body orientation in the horizontal plane in the lamprey. *(Paper I)*

2. To characterize impairment and subsequent recovery of postural functions after different partial lesions of the spinal cord. *(Paper II)*

3. To characterize postural reactions to lateral pushes during standing and walking. *(Paper III)*

4. To analyze the role of motor cortex in the limb coordination in standing during maintenance of equilibrium. *(Paper IV)*

5. To study the role of motor cortex in postural adaptations to the environment during standing and during walking. *(Paper V)*

2. Methods

Four major types of experiments in these studies were performed on different animal models: the lamprey (a lower vertebrate), the rabbit, and the cat.

1. The *in vivo* studies of vestibular and visual responses in reticulospinal neurons during lateral turns were carried out on the river lampreys (*Lampetra fluviatilis*) (*Paper I*).

2. The studies of the effects of different spinal cord lesions on postural performance were carried out on New Zealand rabbits (*Paper II*).

3. The behavioral experiments for studying postural reactions during standing and walking were carried out on cats (*Papers III, IV, V*).

4. The experiments with *in vivo* recording of pyramidal tract neurons from the motor cortex were also carried out on cats (*Papers IV, V*).

Studies 1 and 2 were performed with the approval of the local ethical committee (Norra Djurförsöksetiska Nämnden) in Stockholm. Studies 3 and 4 were approved by the Barrow Neurological Institute Animal Care and Use Committee.

In this section, only the main methodological approaches are briefly described. Specific details of methodologies can be found in the corresponding papers.

2.1 Experiments on lampreys

In these *in vivo* experiments, the stabilization of lamprey's orientation in the horizontal plane was investigated. Vestibular and visual responses of reticulospinal neurons (RS) during lateral turns were analyzed. The activity of RS neurons was recorded from their axons in the spinal cord by means of four macroelectrodes chronically implanted at the level of the third gill (Fig. 2.1*A,B*). The electrodes were oriented in parallel to the long spinal axons, allowing recording the spike activity from larger RS axons (Deliagina & Fagerstedt, 2000c). By comparing the spike amplitude recorded by different electrodes, one could determine the axon's position and its conduction velocity (Deliagina & Fagerstedt, 2000c).

For vestibular and visual stimulation, the lamprey was positioned in a special setup (Fig. 2.1*C*)) that consisted of a tube fastened to a small platform. After having been positioned into the tube, the lamprey attached to the platform with its sucker mouth. The setup allowed rotating the animal in the horizontal (yaw) plane by 60° peak-to-peak. Periodical turns were used (sinusoidal T=4 s or trapezoidal T=12 s, Fig. 2.1*D,E*)). Illumination of the left or the right eye was done by the fiber optic system attached to the turning platform.

The recorded multiunit spike trains were separated into unitary waveforms, representing the activity of individual axons ("spike sorting"), by means of data analysis software (Spike 2, CED). The requirements for suggestion that activity is generated by the same individual RS neuron were the following: (i) the constant shape and value of spike waveform recorded
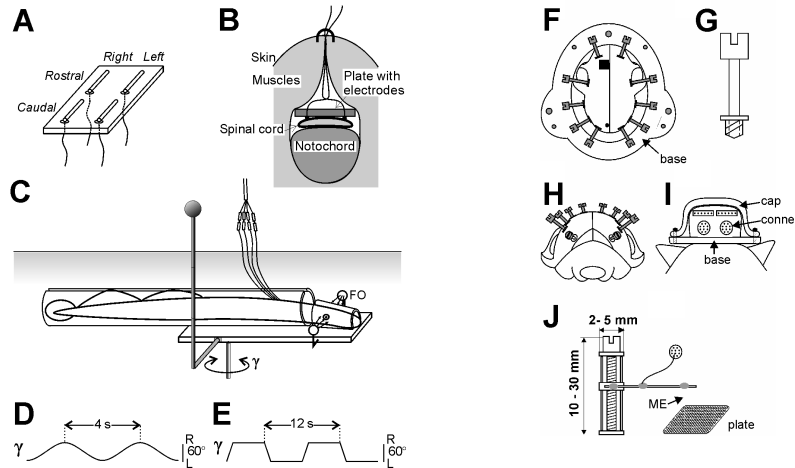
Figure 2.1: Methods for *in vivo* recording of neuronal activity. *A-E*. Methods for recording vestibular and visual responses in reticulospinal (RS) neurons in lamprey. *A*. Design of the electrodes. *B*. Position of the plate with electrodes as seen in the transverse section of the lamprey's body. *C*. Experimental device for vestibular and visual stimulation (γ, yaw angle; FO, fiber optic illumination system). *D,E*. Patterns of vestibular stimulation. *F-J*. Method for recording PTNs with movable microelectrode in cat. *F*. View of dorsal surface of the skull with screws inserted into the bone and attached to the plastic circular base (base) used for rigid fixation of the head during searching for neurons, for fixation of connectors, and protective and electrically shielding cap. *G*. A view of the screw. *H*. Dorso-caudal view of screws inserted in skull. *I*. The position of the base with attached connectors (connec) and a protective cap (cap) on cat's head, view from behind. *J*. A miniature micro drive moving a microelectrode (ME) through the hall in plastic plate (plate) covering the hall in bone above the motor cortex (indicated by a black square in *F*).

by individual electrodes, (ii) the constant ratio between the spike amplitudes recorded by different electrodes, and (iii) the constant time delay between the spikes recorded by the rostral and caudal electrodes. The activity of a population of RS neurons was presented in a form of histograms. The cycle of platform turns was divided into bins, and the frequency of individual neurons was measured for a given bin and then averaged for each bin over sequential cycles and over all neurons.

2.2 Experiments on rabbits

In these experiments, the effects of different spinal cord lesions on postural performance were investigated in the rabbit keeping balance on the tilting platform. The rabbits did not need any special training to perform this task. Each animal was subjected to two surgeries. During the first surgery, EMG electrodes were implanted bilaterally into selected limb muscles. When the animal had recovered from the first surgery (in 3-4 days), its postural responses to tilts were tested, and afterwards a second surgery was performed, i.e., a lesion of the spinal cord in the lower thoracic region (dorsal, ventral, or lateral hemisection).

Postural corrections were tested regularly after the spinal cord lesion. The rabbit was positioned on two platforms, P1 under the forelimbs and the P2 under the hindlimbs (similar to the position of the cat shown in Fig. 2.2*A*). The two platforms were tilted together (*B*), or only P2 was tilted while P1 was kept horizontal. The latter test allowed postural disturbances to be applied primarily to the hindquarters. Periodical tilts ($\pm 20^o$) were used (sinusoidal or trapezoidal). Lateral displacements of the rostral and caudal parts of the trunk in relation to the corresponding platform (postural corrections) were monitored separately by sensors

S1 and S2 (Fig. 2.2*A,B*). Video recording was used to characterize the body configuration in the standing animal.

2.3 Experiments on cats

In these experiments we studied (i) reactions of the cat to different perturbations of its posture during standing and during walking, and (ii) responses of pyramidal tract neurons (PTNs) of the motor cortex to some of these perturbations. Initially the cats were habituated to the experimental setup (up to 6 weeks). Usually they were easily engaged in all postural tests. Afterwards, the surgery was performed.

2.3.1 Surgical procedures

Surgery was performed under isoflurane anesthesia using aseptic procedures.

The cat was instrumented for recording and antidromic identification of individual PTNs. The skin and fascia were removed from the dorsal surface of the skull. At 10 points around the circumference of the head, screws were screwed into the skull and connected together with a wire; the screw heads and the wire were then inserted into a plastic cast to form a circular base (Fig. 2.1*F-H*). Later, while searching for neurons before behavioral tests, awake cats were rigidly held by this base. The base was also used to fixate connectors, a miniature microdrive, a pre-amplifier, contacts for stimulating electrodes, and a protective cap (Fig. 2.1*I-J*). A portion of the skull and dura above the left motor cortex were removed. The aperture was then covered by a plastic plate with many small holes (Fig. 2.1*J*). Two guide tubes were implanted vertically above the medullary pyramids, for subsequent insertion of stimulating electrodes into the pyramidal tract. The EMG electrodes were implanted bilaterally into the selected limb muscles.

2.3.2 Postural tests

Five postural tasks were employed in our studies on cats (Fig. 2.2):

1. Standing on the tilting platform with all four limbs. The cat was positioned on two platforms, P1 under the forelimbs and the P2 under the hindlimbs (*A*). The two platforms were tilted in-phase (*B*), or in anti-phase (*C*). Periodical tilts ($\pm15^o$) were used (sinusoidal or trapezoidal). Lateral displacements of the rostral and caudal parts of the trunk in relation to the corresponding platform (postural corrections) were monitored separately by mechanical sensors S1 and S2. The contact force under each foot was measured by a force sensor (F in Fig. 2.2*B*).

2. Standing on the tilting platform with a reduced number of limbs, while other limbs were suspended (examples are shown in *D,E*).

3. Walking on the moving treadmill (v=0.5 m/s), which was subjected to tilts around the longitudinal axis (*F,G*). Stepping movements of limbs were monitored by sensors (one of them, AP, is shown in *F*).

4. Walking on the moving treadmill with only hindlimbs (*F*), or with only forelimbs. Lateral pulses of force (pushes) were applied to the body in the hip (Push in *F*) or shoulder region.
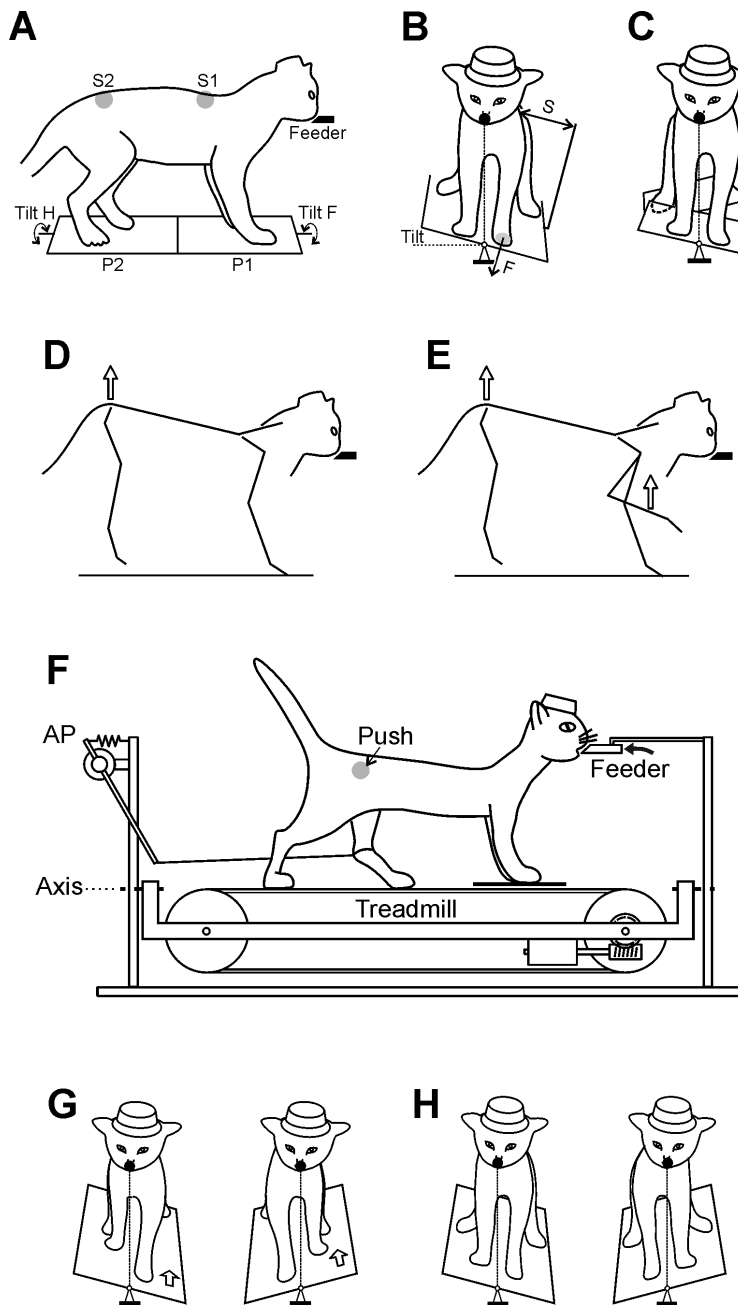
Figure 2.2: Postural tests in the standing (A-E,H) and walking (F,G) cat. See text for explanations.

5. Tests 3 and 4 (H) were performed also during standing. Movements of the animal were monitored by mechanical sensors, by video recording, and by Visualeyez system, which detects the positions in 3D space of light-emitting photodiodes attached to the skin projections of the main limb joints. Positive reinforcement was used in all postural tests. Both during standing and during walking, the cat continuously licked food from a feeder positioned in front of the animal (Fig. 2.2F).

2.3.3   Activity of pyramidal tract neurons

Each PTN was identified by its antidromic response to stimulation of pyramids, using the test for collision of spikes (Bishop et al., 1962; Fuller & Schlag, 1976). Then the activity of the PTN was recorded during postural tests. We suggested that the PTN was involved in the postural control if its activity contained a significant periodical component, which was phase-locked to the tilt cycle. To reveal this component in postural tests on standing animals, we used the first harmonic of Fourier image of the spike sequence (see *Paper IV* for details). Since the walking animals have a step-related modulation of PTNs [see e.g., Drew (1993); Beloozerova and Sirota (1993a, 1993b)], we used the tilt-caused change of the magnitude of this modulation as indicative of postural involvement (see *Paper V* for details).

3. Results and Discussion

3.1 Stabilization of body orientation in horizontal plane in lampreys

3.1.1 Yaw-related RS neurons

The yaw control system was investigated in *Paper I*. For this purpose responses of RS neurons to natural vestibular stimulation, that is rotation of the animal in the horizontal (yaw) plane, were recorded in intact lampreys using chronically implanted electrodes. Two patterns of vestibular stimulation were used: 1) sinusoidal turns (Fig. 2.1*D*), to simulate the vestibular stimuli caused by head undulations during swimming, and 2) trapezoidal turns (Fig. 2.1*E*), to simulate the vestibular stimuli caused by sudden lateral turns.

It was found that two groups of RS neurons showed directional specificity of responses to the turns and, therefore, could participate in the control of body orientation in the yaw plane: *group 1* neurons (71%) were activated by the contralateral turn; *group 2* neurons (9%) - by the ipsilateral turn. Figure 3.1 shows the summary of responses of all *group 1* neurons to sinusoidal (*A*) and trapezoidal turns (*B*). The majority of *group 1* neurons had their axons located laterally in the spinal cord, and had a conduction velocity >2 m/s, which characterizes the large- and middle-sized RS cells (Ohta & Grillner, 1989; Rovainen, 1967, 1978).

To determine the contribution from the ipsi- and contra-lateral labyrinths to the yaw responses of RS neurons, experiments with unilateral labyrinthectomy (UL) were performed. The UL resulted in a significant reduction in the responses of RS neurons on the contralateral side, and only in a slight reduction on the ipsilateral side. Thus, the yaw responses in the majority of RS neurons are driven mainly by input from the canal afferents of the contralateral labyrinth. These influences seem to be transmitted by the afferents in the posterior branch of the contralateral vestibular nerve (Lowenstein et al., 1968; Lowenstein, 1970; Pflieger & Dubuc, 2004). Persistence of weak vestibular responses in some RS neurons on the side contralateral to UL suggests that the excitatory input to RS neurons from the ipsilateral labyrinth supplements the main input from the contralateral labyrinth. These influences are most likely transmitted by the afferents in the anterior branch of the ipsilateral vestibular nerve (Lowenstein et al., 1968; Lowenstein, 1970; Pflieger & Dubuc, 2004).

3.1.2 Operation of yaw control system

A conceptual model of the yaw control system, based on the data of the present study and the study by Zelenin et al. (2007), is shown in Fig. 3.1*C,D*. If an external force causes a passive turn of the lamprey to the left, the right sub-population of RS neurons is activated by the vestibular input (mainly from the left labyrinth). This sub-population, by causing the ipsilateral (rightward) body flexion (Zelenin et al., 2007), will elicit a corrective turn of the
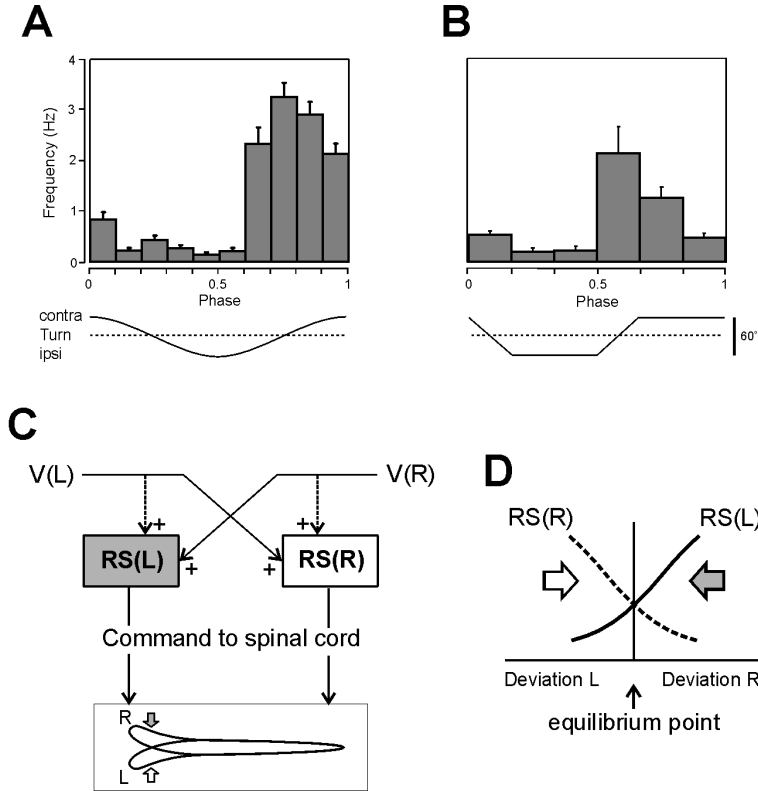
Figure 3.1: *A,B.* Summary of responses of group 1 neurons in the lamprey to sinusoidal (*A*) and trapezoidal (*B*) yaw turns. Histograms show the mean frequency (±SE) in different phases of the turn cycle. The turn was performed towards the side of RS neuron (ipsi) in the first half of the cycle and in the opposite direction (contra) in the second half. *C.* A conceptual model of the yaw control system in the lamprey. Two sub-populations of RS neurons, RS(R) and RS(L), are driven by vestibular inputs from the left, V(L) and right, V(R) vestibular organs, and respond to the left and right yaw turn, respectively. The RS neurons affect the spinal network and cause right and left turning of the lamprey, respectively (white and gray arrows). Solid and interrupted lines indicate the major and minor vestibular inputs, respectively. *D.* Operation of the system during swimming. The two curves represent the activity of RS(R) and RS(L) sub-populations caused by a dynamic deviation of the head. The motor effect of each sub-population is proportional to its activity. The direction of turning caused by RS(R) and RS(L) is indicated by the gray and white arrows, respectively. The system has an equilibrium point, where the effects of RS(R) and RS(L) are equal to each other.

animal to the right via the spinal mechanisms, and restoration of the initial orientation in the yaw plane. *Group 2* neurons, responding to ipsi-turn, could supplement *group 1* by activating contralateral myotomes, although these effects have not been demonstrated (Zelenin et al., 2007). Thus, the yaw control system, based on vestibular reflexes, counteracts any deviations from the rectilinear swimming caused by external factors.

The yaw control system differs substantially from the roll and pitch control systems (see Introduction and Fig. 1.1*A*). In the roll and pitch systems, the RS neurons receive vestibular signals about orientation of the lamprey in the gravity field, which allow the animal to maintain a definite orientation in these planes (Deliagina et al., 2006a). By contrast, turns in the yaw plane do not affect the animal's orientation in relation to the gravity vector, and the yaw control mechanism receives vestibular signals only about dynamic changes of the yaw orientation, but not about the orientation itself (Fig. 1.1*A*). As a result, this mechanism can reduce rapid but not slow deviations from the rectilinear swim trajectory. Thus, maintenance of a certain direction of swimming in the yaw plane requires participation of other sensory

inputs (e.g. visual, olfactory) signaling the absolute value of the yaw angle. Under the conditions of our experiments, however, lampreys did not demonstrate any goal-directed (steering) and navigation behavior.

3.1.3   RS neurons mediating negative phototaxis

It is known that unilateral eye illumination in the lamprey elicits a contralateral turn in the yaw plane (negative phototaxis, Ullén et al. (1993, 1995b, 1997)). One of the aims of the present study was to reveal the RS neurons presumably involved in initiation of this response. For this purpose, we studied responses of RS neurons to unilateral eye illumination, as well as interactions of vestibular and visual inputs to these neurons. We found that only a small part of RS neurons (27% of *group 1* neurons and some neurons of *group 4*) was activated by the contralateral eye illumination and could thus mediate the negative phototaxis.

3.1.4   Future studies

1. Data obtained in the present study suggest that the lamprey stabilizes orientation of its body in the horizontal plane on the basis of interaction of antagonistic vestibular reflexes. One can expect that during swimming vestibular reflexes caused by external factors and by undulatory head movements (Wallén & Williams, 1984; Williams et al., 1989), interact. Vestibular reflexes can also be rhythmically modulated by the spinal locomotor CPG via two routes: (i) the RS neurons themselves are modulated by efference copy signals (Kasicki et al., 1989), and (ii) the efficacy of vestibular input to these neurons is rhythmically gated (Bussières & Dubuc, 1992b; Pflieger & Dubuc, 2004). To study this problem, recording of the activity of RS neurons during swimming, and correlation of this activity with passive head movements in yaw plane (caused by external force) should be carried out.

2. Does the yaw control system operate also in the cases when the lateral turns are initiated by the lamprey itself as, e.g., during the negative phototaxis? Our experiments have shown that unilateral visual input did not change the basic pattern of responses of RS neurons to yaw-turns: they were activated during the contralateral rotation. This finding suggests that the yaw stabilizing system counteracts not only passive but also active turns of the head. One can suppose that the commands for active turn, addressed to RS neurons, overcome the action of vestibular reflexes, or the efficacy of vestibular input to these neurons decreases when the lateral turn is initiated by the lamprey itself. To test this hypothesis, recording of the activity of yaw-related RS neurons during negative phototaxis should be carried out.

3.2   Impairment and recovery of postural control after spinal cord lesions

The impairment and recovery of postural control after different partial lesions to the spinal cord were characterized in *Paper II*. For this purpose, the postural performance in rabbits with three types of lesion – the lateral, dorsal or ventral hemisection (LHS, DHS and VHS) performed at lower thoracic level were analyzed. Two principal functions of the postural control system were considered – the control of body (limb/trunk) configuration and the maintenance of equilibrium (see Introduction).
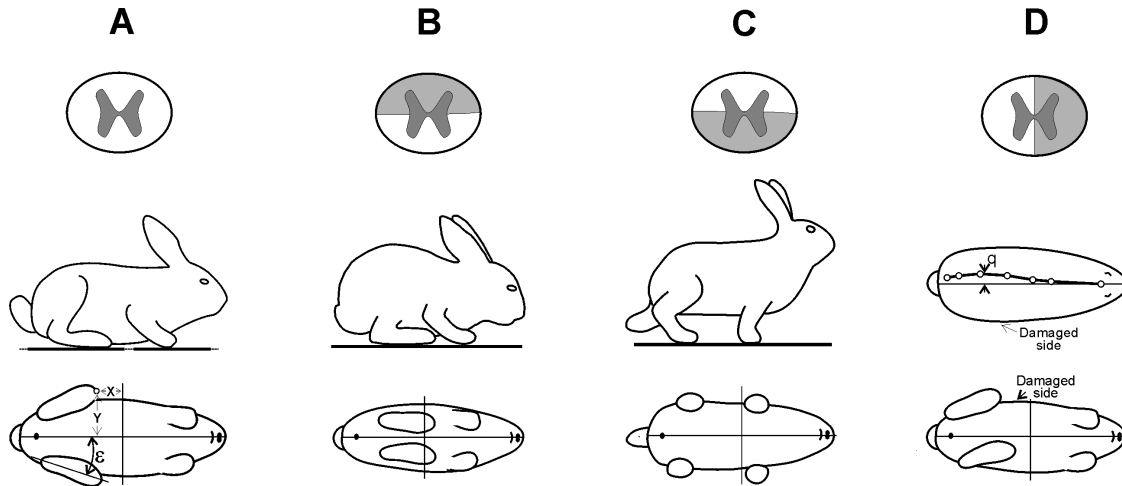
Figure 3.2: The basic body configuration of rabbit (A) and its distortions caused by dorsal (B), ventral (C) and lateral (D) hemisection.

3.2.1 Control of body configuration in SCI subjects

When standing, rabbits, like other quadrupeds (Lacquaniti et al., 1984; Maioli & Poppele, 1991), can assume a number of body configurations, differing in the interlimb distance, in the degree of limb extension, and even in the number of supporting limbs (quadrupedal *versus* bipedal standing). Apparently, the postural control system selects the appropriate body configuration on the basis of environmental conditions and behavioral state of the animal. However, when standing on the horizontal surface in a quiescent state, the rabbit usually maintains a basic body configuration (Fig. 3.2A).

It was found that different types of SCI caused different distortions of the basic body configuration (Fig. 3.2B-D):

i. The DHS led a decrease in the distance and angle between the left and right feet, and to a more rostral position of the feet (B) as compared to control (A). These distortions were very slowly compensated or not compensated over time.

ii. The effects of LHS were asymmetrical: the limb on the damaged side was positioned more caudally than in control, whereas the opposite limb was turned inward; the trunk was bent and twisted (D). The distortions of limb configuration slowly decreased over time, while the body bending and twisting increased.

iii. In VHS rabbits, the main deficit was a gradual development of the extensor tone (C), which became so strong that the animals were not able to position their hindlimbs under the trunk for body support when standing.

Thus, different types of SCI resulted in the specific distortions of body configuration, which were badly compensated over time. This finding suggests that supraspinal control of body configuration is mediated by a number of different descending pathways (reticulospinal, vestibulospinal, rubrospinal etc.), which cannot substitute one another. In addition, an interruption of descending pathways, not related directly to the induction of postural configuration, may cause an imbalance in supraspinal tonic drive to different components of the spinal postural network (Fig. 1.4), which will also result in a distortion of the body configuration.

3.2.2 Control of equilibrium in SCI subjects

The maintenance of equilibrium on the tilting platform is achieved due to corrective motor responses to perturbation of posture (postural reflexes). In DHS, LHS, and VHS rabbits, we tested the dynamic and static postural reflexes by application of sinusoidal and trapezoidal tilts, respectively. It was found that the initial effect of all three types of lesion was similar – when positioned on the tilting platform, the animals were not able to stand on their hindlimbs and to maintain equilibrium of their hindquarters.

In DHS and LHS rabbits, this ability reappeared in 1.6±0.2 and 4.7±1.0 days, respectively, and then gradually improved over time, so that the gain of dynamic postural reflexes approached the control value within 1-2 wk and 1-5 wk, respectively. The reflexes were well pronounced with tilting of only the hindquarters, suggesting that they were due to the activity of the hindlimbs postural mechanisms (Fig. 1.3). Timing of EMG responses was very similar to that in control. However, there was a significant decrease in the gain of static reflexes attributed to a gradual decay of the corrective postural responses to stationary tilts, which lasted for the whole period of observations (1-2 months).

In VHS rabbits (in contrast to DHS and LHS ones), the ability for standing and keeping balance in the hindquarters did not recover during the period of observations. When positioned on the platform, the hindquarters passively swayed towards the side tilting downwards although small EMG responses with normal phasing could be observed in some muscles during the first few days postlesion. The complete loss of postural functions in VHS animals, as well as their recovery in DHS and LHS animals suggest the critical role of the ventral spinal pathways (reticulo- and vestibulospinal) in postural control.

The data obtained in the present study represent some indirect evidences in favor of the hypothesis about a substantial contribution of the spinal postural networks in generation of postural corrections. The animals subjected to DHS and LHS exhibited a rapid recovery of postural corrections and the temporal characteristics of their EMG patterns were similar to those in intact rabbits. Since these lesions evidently cause dramatic changes both in the ascending sensory signals and in the descending commands, it would be very difficult to explain the persistence of the principal features of postural responses in DHS and LHS animals by the operation of severely damaged long-loop mechanisms (Long loop, Fig. 1.4). It seems more likely that the spinal postural networks contribute substantially to the generation of postural corrections in both intact, DHS and LHS rabbits. After these lesions, the spinal circuits could be activated by a tonic drive through the remaining ventral descending pathways. We suggest that the recovery of postural reflexes in DHS and LHS animals is associated with an increase in efficacy of the activating drive.

Recently it was shown that in acute spinal rabbits, the EMG pattern of postural limb reflexes could be restored by tonic electrical stimulation of the spinal cord below the lesion and further enhanced by its pharmacological stimulation (Musienko et al., 2007). This finding suggests that the spinal cord contains neuronal networks underlying the spinal postural limb reflexes, which are activated by the supraspinal tonic excitatory drive and contribute to trunk stabilization in intact animals.

3.2.3 Future studies

To test further the hypothesis proposed in the present study one should: (i) try to substitute the tonic supraspinal drive in chronic spinal subjects by electrical or pharmacological stimulation of the cord below the lesion; (ii) record the activity of ventral descending pathways in intact animals maintaining equilibrium on the tilting platform, and compare this activity

with that recorded in LHS and DHS animals in the acute state and after recovery of postural corrections.

3.3 Maintenance of lateral stability during standing and walking

The aim of the present study was to characterize the postural reactions to lateral pulses of force (pushes) in the cat during standing and walking (*Paper III*). Such postural perturbations are very frequent in natural habitats, when animals collide with obstacles during locomotion or are affected by other animals.

3.3.1 Postural reactions during standing

It was found that a lateral push applied to the caudal trunk during standing caused a lateral displacement of the caudal part of the body, and evoked a postural corrective movement towards the initial position. The postural response included (i) an initial activation of the extensor muscles (Gast and Vast) in the hindlimb on the side contralateral to push, and (ii) inhibition of the corresponding muscles on the side of push application. Excitation of the contralateral extensors allowed the limb to support an additional load, which was caused by the displacement of the center of mass towards this limb, and to provide the support necessary for the body to return to its initial position (with equal loading of the limbs). The hip abductor (Glut) and the hip adductor (Grac) of the contralateral limb were also activated, suggesting an increase of stiffness in the hip joint when postural corrections take place. Similar responses to push were observed in the rabbit, both intact or decerebrated at precollicular-premammillar level (Musienko et al., 2008). A similar pattern of extensor activity was also observed in response to lateral translation of the supporting platform (Macpherson, 1988b).

3.3.2 Postural reactions during walking

During stationary walking on the treadmill, as well as on the ground (Misiaszek, 2006b), landing of the foot at the end of the swing phase in sequential steps occurs at approximately the same medio-lateral (ML) position (*Cycle –1* in Fig. 3.3*B,D*). It was found that a lateral push caused a lateral body displacement, and a specific corrective motor response, i.e., appearance of a lateral component in the limb transfer trajectory in the current step. Due to this component, the foot of the corrective limb was transferred and landed at a ML position differing from that in normal steps. The rightward displacement of the trunk caused the rightward lateral step and the leftward displacement caused the leftward step. This pattern of response was observed both when walking with hindlimbs and when walking with forelimbs. The choice of the corrective limb depended on the phase of the locomotor cycle when the push was applied – the corrective function was performed by the limb that was close to the end of its stance phase or was performing the swing phase. Thus, each limb could perform either outward step (if it was contralateral to the side of push application, Fig. 3.3*A,B*) or inward step (if it was ipsilateral to the push Fig. 3.3*C,D*). The magnitudes of outward and inward steps on average were similar (see Figs. 3.3*B* and *D* for the hindlimbs).

Postural corrections during walking were well incorporated into the basic locomotor pattern: (i) The abnormal ML position of the corrective limb was maintained during only one stance period. Within the next swing period the limb returned to its usual ML position, and
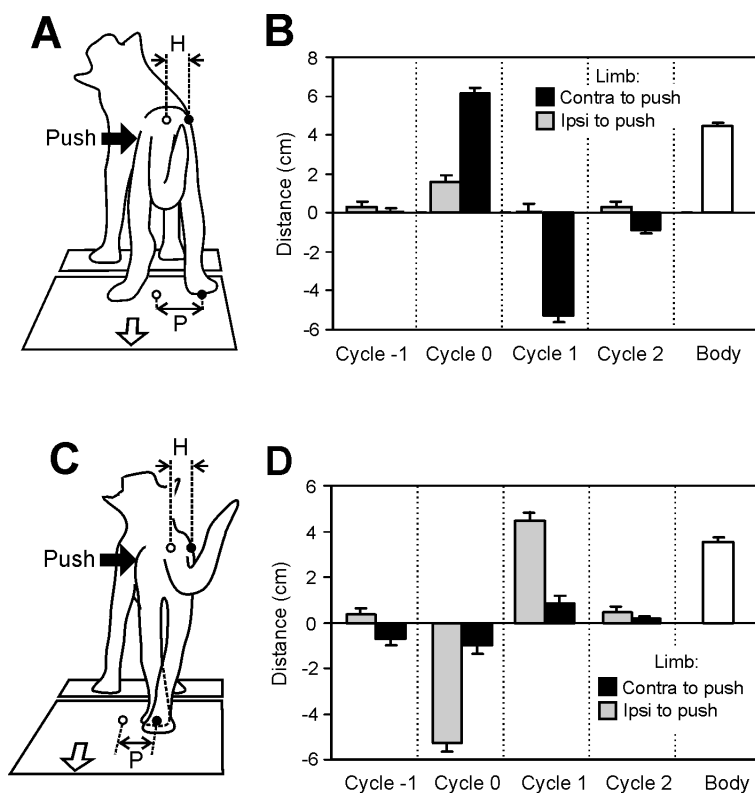
Figure 3.3: Corrective motor responses to push during locomotion: outward (*A,B*) and inward (*C,D*) steps. *A,C*. Characteristic position of the walking cat resulting from the push applied in the hip region towards the right. The push caused a rightward displacement of the trunk and landing of the foot at a more lateral position (outward step, *A*) or more medial position (inward step, *C*) than during unperturbed locomotion. Positions of the trunk and foot in unperturbed and perturbed cycles are shown by unfilled and filled circles, respectively. The values of their lateral displacements are indicated (H and P). *B,D*. Mean values (± SE) characterizing the lateral component of step in sequential cycles of the hindlimbs. Positive and negative values correspond to outward and inward displacement of the limb, respectively. Designation of cycles: (–1): the cycle before push; (0): the cycle including push; (1): the cycle next to the affected cycle; (2): the cycle next to (1). The mean value of push-caused trunk displacement is also presented (Body).

the normal locomotor pattern was restored. (ii) Changes in the duration of the locomotor cycle associated with postural corrections were relatively small (10-15%). Corrections for other types of postural perturbations during walking in cats (lateral translation or dropping of the supporting platform) are also completed in 1-3 step cycles (Misiaszek, 2006b; Marple-Horvat et al., 1993). By contrast, humans require multiple steps to regain medial-lateral stability during walking (Maki et al., 2000; Oddsson et al., 2004).

It was found that abductors and adductors are strongly involved in generation of corrective lateral steps. In the effective limb, the adductors (Grac and Add fem), significantly increased their activity in the inward step, which accounted for the limb adduction in this step. In the outward step, an increase of activity was observed not only in the abductor (Glut), but also in the adductors (Grac and Add fem). It is likely that the net effect of these muscles co-activation is an increase of stiffness during the abduction of the limb. A considerable activation of the adductor (Grac) during the outward step was observed in the limb supporting the body during correction of posture. This could generate a torque counteracting the effect of push. Abductors and adductors are strongly involved also in generation of postural corrections caused by other disturbances in the frontal plane, such as lateral translation of the walkway

(Misiaszek, 2006b), and lateral tilts of the supporting surface during standing and walking (*Paper V*).

To conclude, comparison of postural reactions in the cat to the same destabilizing stimulus (lateral push) during standing and during walking has shown that the basic mechanisms for balance control in these two forms of behavior are largely different. They perform a re-distribution of muscle activity between symmetrical limbs during standing and a reconfiguration of the base of support due to a lateral step in walking.

3.3.3 Future studies

Lateral steps are observed in a number of motor behaviors, e.g., with a high risk of a loss of equilibrium during standing (Beloozerova et al., 2003b, *Paper IV*), during circling in the animals with vestibular deficits (Deliagina et al., 1997c; Magnus, 1924), and during placing and hopping reactions (Bard, 1933; Brooks, 1933; Rademaker, 1931). However, the mechanisms of sensory elicitation of lateral steps, as well as the contribution of spinal and supraspinal motor centers to their generation are not clear.

The ability of animals deprived of the forebrain (decerebrated at the premammillary level) to keep balance during walking (Bard & Macht, 1958; Musienko et al., 2008) suggests that they can perform postural corrections during locomotion, but the presence of corrective lateral steps has not been documented. On the other hand, it was reported that damage to the sensory-motor cortical areas deprived the standing animal of the ability to make compensatory lateral steps during placing and hopping reactions (Bard, 1933; Brooks, 1933). However, it remains unclear if the cortical lesions affected also the corrective lateral steps during walking.

In future studies, it is interesting to examine the ability of the animal to perform lateral steps after damage or inactivation of the motor cortex, and to study supraspinal commands causing lateral steps in response to push.

3.4 Role of motor cortex in postural limb coordination

It was shown that the activity of pyramidal tract neurons (PTNs) in the cat correlates with postural corrections elicited by periodical tilts of the supporting platform (Beloozerova et al., 2005). These postural corrections are caused by tilt-related somatosensory inputs from the limbs. The aim of the present study was to reveal the contribution of sensory inputs from individual limbs to the posture-related modulation of PTNs. For this purpose, we used the experimental design shown in Fig. 2.2*A-E*, and recorded responses to periodical lateral tilts in PTNs. We manipulated the peripheral sensory inputs to PTNs by suspending some of the limbs and thus eliminating the tilt-related sensory inputs from these limbs. The magnitude and phase of tilt-related modulation of the PTN activity was used as a characteristic of sensory influences.

3.4.1 Role of sensory information from different limbs in posture-related PTN activity

It was found that the tilt-related modulation of the activity in a given PTN was mostly caused by the sensory signals coming from its own, target limb (contralateral to the PTN). This conclusion was based on the following findings: (i) the pattern of modulation (its magnitude and phase) did not change significantly when the cat was standing on the target limb alone, in
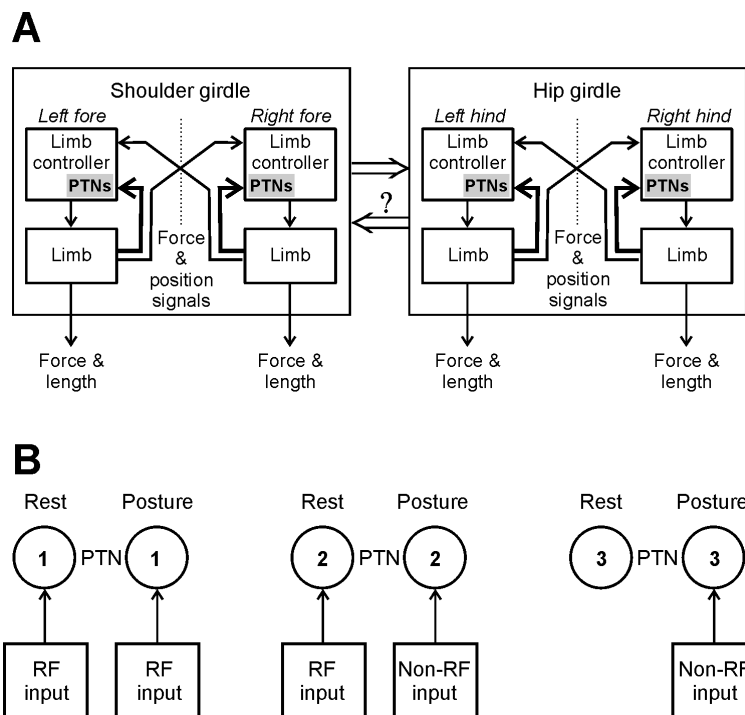
A

B

Figure 3.4: Role of PTNs in postural system stabilizing the dorsal-side-up trunk orientation. (For description of the system, see Introduction and Fig. 1.3). *A*. The PTNs constitute a part of each limb controller; they are primarily involved in the control of their own limb on the basis of sensory feedback. (See text for explanations). *B*. Role of signals from the receptive field in modulation of PTNs. Three types of PTNs are shown: 1 - in this PTN, the receptive field input (RF input) controls the activity both at rest and in the postural task. 2 - in this PTN, the receptive field input controls the activity only at rest; the activity in the postural task is controlled by a different sensory input (Non-RF input). 3 - in this PTN, the receptive field input is absent; the activity in the postural task is controlled by a special sensory input (Non-RF input).

spite of the dramatic reduction of sensory inputs from the three other limbs. For the majority of PTNs – 83% of forelimb PTNs and 75% of hindlimb PTNs – the phase shift was less than 0.2 as compared to control; (ii) lifting of the target limb strongly reduced the magnitude of tilt-related PTN modulation and changed the phase of this modulation (as compared to those observed when the limb was standing). In this test, 56% of the forelimb PTNs and 49% of the hindlimb PTNs, showed a shift of preferred phase more than 0.2 as compared to control. These results strongly suggest that, *first*, in the postural task, the PTNs constitute a part of the limb controller, and they are primarily involved in the feed-back control of postural responses in their own limb ("intra-limb coordination"). The corresponding sensory influences are shown by thick black arrows in the scheme of sensorimotor processing in the postural system (Fig. 3.4*A*). *Second*, in the postural task, the PTNs are much less involved in the coordination of activity between the two limbs within a girdle, and between the two girdles. The corresponding influences are shown by thin black and empty arrows in Fig. 3.4*A*.

The whole population of PTNs, however, was not homogeneous in respect to the relative role of the three sensory inputs. *First*, the input from the foreign girdle was usually much weaker in the forelimb PTNs than in the hindlimb PTNs. When the cat was standing on the hindlimbs only, there was a significant decrease in the magnitude of modulation of forelimb PTNs as compared to control and a phase shift more than 0.2 in the majority of them (67%). *Second*, for a portion of hindlimb PTNs (56%), the tilt-related modulation was mainly caused by sensory influences from the hindlimbs while, in another portion (44%), sensory influences

from the forelimbs noticeably contributed to the modulation.

3.4.2   Sensory origin of PTN responses

It is known that the limb areas of the motor cortex have specific afferent projections from the corresponding limbs ("peripheral receptive fields"), which can be revealed in the quiescent state of the animal (Asanuma, 1989; Armstrong & Drew, 1983a). This input comes from different groups of muscle, joint and cutaneous afferents (Oscarsson & Rosén, 1966a, 1966b; Landgren & Silfvenius, 1971; Duysens et al., 2000) and seems to be important for the control of posture and locomotion (Welt et al., 1967).

In the present study, after revealing the receptive field of a PTN at rest, one could speculate what afferent signals the PTN would receive from its receptive field during tilts, and what will be a pattern of PTN modulation. In a portion of PTNs (34%), the response pattern well corresponded to the pattern expected if the PTN was driven solely by its receptive field input. These PTNs were presumably controlled by their receptive field inputs (PTN 1 in Fig. 3.4B).

In the majority of PTNs (66%), however, the input from the receptive field could not be responsible for the PTN reactions to tilts. One can suggest that, in these neurons (PTN 2 in Fig. 3.4B), the somatosensory input from the receptive field (RF input) is replaced by another input (Non-RF input) when an active behavior is taking place. In the neurons with no receptive field at rest (PTN 3 in Fig. 3.4B), the response to tilts is due to a newly formed afferent input. This hypothesis could be further supported by the view that the somatosensory signals from limb mechanoreceptors are processed in the spinal and brainstem networks before they reach the motor cortex (see e.g. Asanuma, 1989; Landgren & Silfvenius, 1971). Also rather weak correlation was found between the locomotor-related neuronal discharges and peripheral receptive fields in the cat motor cortex (Armstrong & Drew, 1984a, 1984b).

3.4.3   Future studies

To understand the functional role of cortical activity, one has to answer two questions: (1) What is the origin of posture-related cortical activity? (2) What are the motor effects of this activity? The present study gave answer to the first question. The second one needs further studies.

3.5   Role of motor cortex in postural adaptations to the environment

Freely behaving animals have to adapt their posture to different features of the terrain on which they are standing or walking. One of these is inclination of the support surface. The aim of the present study (*Paper V*) was, *first*, to analyze the motor pattern of postural adaptations in the cat during two motor tasks (i.e., standing and walking on the surface inclined in the roll plane), and, *second*, to assess the motor cortex participation in postural adaptations in these tasks. For this purpose, we recorded the activity of individual pyramidal tract neurons (PTNs) during standing and walking on the treadmill subjected to trapezoidal tilts (Figs. 2.2*F-H*, 3.5*A,B,E*).

3.5.1   Postural adaptations to inclination of support surface

To analyze the motor pattern of postural adaptations in the cat standing and walking on the inclined surface, kinematical and EMG pattern analysis was performed.

Both standing and walking on the inclined plane require specific modifications of the body configuration, with asymmetry in the functional length of the opposite limbs, as illustrated in Fig. 3.5*C,D*. It was shown that these changes in the limb configuration are caused by specific modifications of the EMG pattern. During standing, the extensor activity increased when the ipsi-side was tilted down and the limb was extended, and decreased when the ipsi-side was tilted up and the limb was flexed (*Standing* in Fig. 3.5*E*). During walking, these changes were incorporated into a step cycle, so that the extensor bursts in the stance part of the step increased when the ipsi-side was tilted down, and decreased when it was tilted up (*Locomotion* in Fig. 3.5*E*). These changes did not perturb the basic pattern of stepping, with rhythmical alternation of its swing and stance phases (Orlovsky et al., 1999). The obtained results confirm data reported earlier for the terrestrial quadrupeds standing (Beloozerova et al., 2005) and walking (Matsuyama & Drew, 2000) on inclined surface.

3.5.2   Reflection of stationary tilts in PTN activity

To assess the motor cortex participation in postural adaptations, the activity of individual pyramidal tract neurons (PTNs) during standing and walking on the treadmill subjected to trapezoidal tilts (Figs. 2.2*F-H*, 3.5*A,B,E*) were analyzed.

The main result of this study was that, both during standing and during walking, many PTNs had a positional response to tilt, that is, their activity depended on the value of stationary tilt of the support surface.

In the standing cat, in 46% of forelimb PTNs and in 47% of hindlimb PTNs, their frequencies during ipsi-side down tilt and during contra-side down tilt were significantly different. On average, this difference was more than two-fold. We suggest that this population of PTNs, by sending the tilt-related commands to the spinal cord, contributes to modifications of the motor pattern necessary for standing on an inclined plane. If this is a case, the main pattern of the corrective motor response, that is, activation of extensors on the side tilted down (Fig. 3.5*E*), requires an excitatory action upon the extensor motoneurons from the sub-group of PTNs activated with contra-tilt (taking into account crossed PTN projections). The sub-group activated with ipsi-tilt should have an inhibitory action on the extensors, or no action.

In the walking cat, the overwhelming majority of PTNs exhibited the step-related modulation of their activity. We approximated this periodic modulation by a two-level fit, characterized by the burst and inter-burst frequencies. When walking on an inclined plane, in 54% of forelimb PTNs and in 63% of hindlimb PTNs, their burst frequencies during ipsi-side down tilt and during contra-side down tilt were significantly different. In the population of responding PTNs, a 30° change in the stationary tilt of the support surface caused (on average) a 10 imp/s change in their burst frequency. The tilts only slightly affected the phase of the step-related modulation in these PTNs. We suggest that this population of PTNs, by sending step-related and tilt-related commands to the spinal cord, can modify the output of the spinal locomotor CPG (by increasing or decreasing the extensor bursts), and thus can contribute to the modifications of stepping movements that are necessary for walking on the inclined plane (Fig. 3.5*D,E*). To increase the extensor bursts on the side tilted down, the sub-groups of PTNs, activated with contra-tilt and with ipsi-tilt, should have an excitatory and inhibitory action on the extensor motoneurons, respectively.
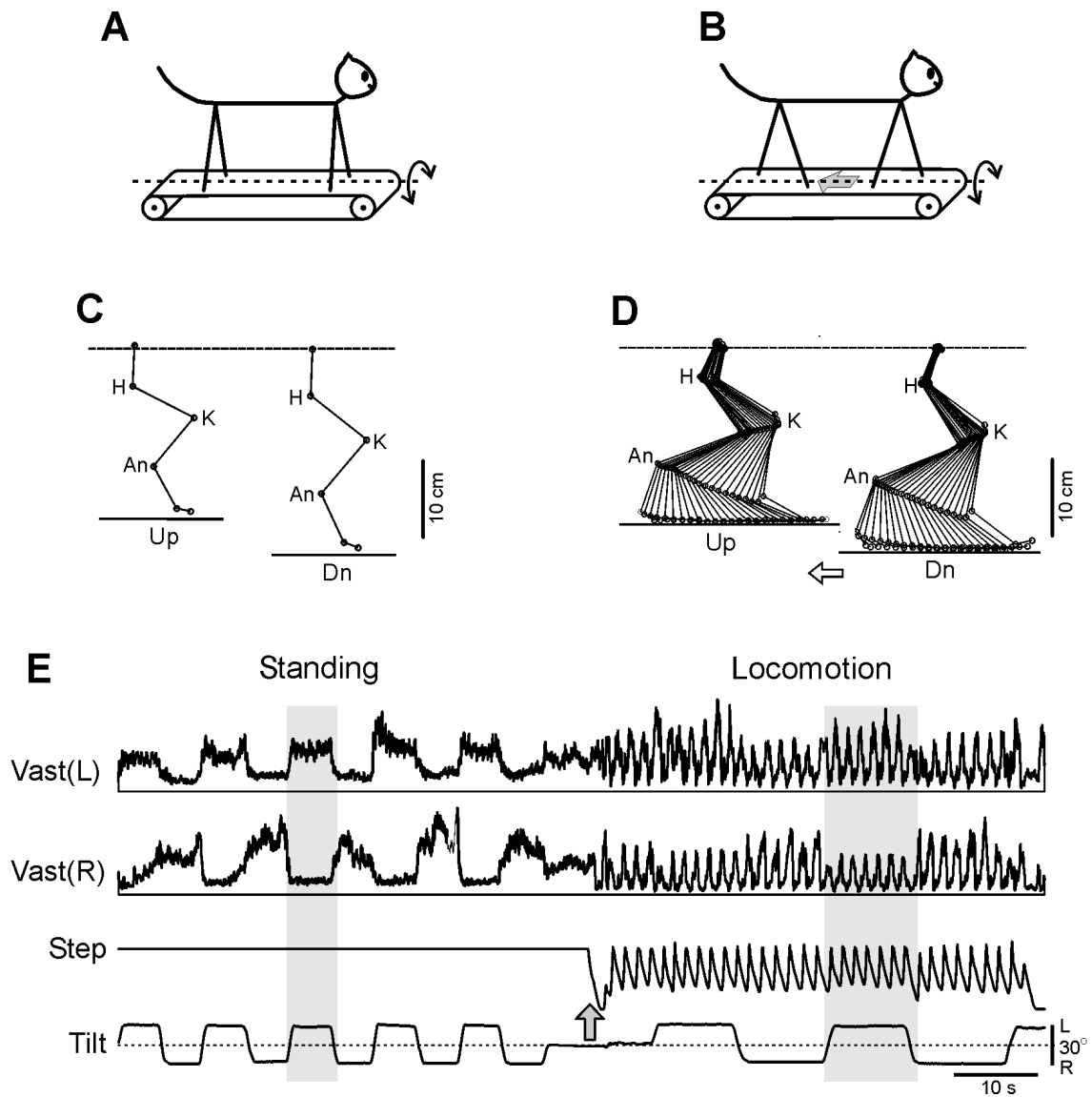
Figure 3.5: *A-E*. Adaptive changes in the hindlimb configuration and in the EMG activity when standing (*A*) and walking (*B*) on treadmill subjected to lateral tilts. *C,D*. Configuration of the right hindlimb (stick diagrams) during standing (*C*) and during walking (*D*) on an inclined plane is shown for two positions of the support under the limb (up and down). In *D*, there are shown sequential limb positions in the stance phase of the step. *E*. Example of EMG responses in the left (*L*) and right (*R*) knee extensors (vastus lateralis, *Vast*) to tilts during standing and during walking.
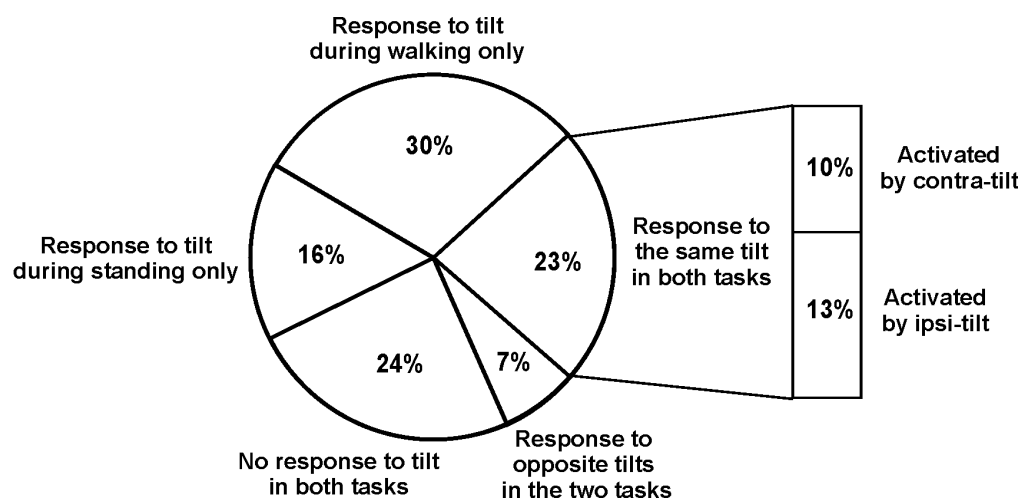
Figure 3.6: Proportions of PTNs, which exhibited different combinations of responses to stationary tilts in the task of standing and in the task of walking.

It should be noted, however, that only a part of PTNs, with their burst located in the stance phase of the step cycle, could participate in the control of extensors. Such neurons constitute from 50% to 71% in different sub-groups of PTNs. Another part of PTNs, which were active in the swing phase of the step cycle, could be responsible for those modifications of the swing motor pattern that were observed during walking on an inclined plane (see Fig. 4B in *Paper V*).

These results suggest that the motor cortex, along with other descending systems, e.g., reticulo- and vestibulospinal ones (Matsuyama & Drew, 2000) sends commands to the spinal cord and medulla that determine a postural body configuration and its adaptive modifications. Thus, the motor cortex participates in the control of both principal postural functions formulated by Horak & Macpherson (1996) – the maintenance of equilibrium (Beloozerova et al., 2003b, 2005) and the maintenance of a definite body configuration.

By comparing the positional responses to tilts in individual PTNs recorded in the two motor tasks (standing and walking), we revealed four groups of PTNs (Fig. 3.6): responding to tilts in both tasks (30%); responding only during standing (16%); responding only during walking (30%); responding in none of the tasks (24%). This striking diversity suggests that both common and separate cortical mechanisms are used in the two motor tasks (standing and walking) for the control of postural adaptations to inclinations of the supporting surface. Among the PTNs responding in both tasks (30%), the majority of neurons (23%) were activated by the same tilt in both tasks, either contra (10%) or ipsi (13%). One can suggest that this group of PTNs performs similar functions during both standing and walking, that is, they affect the value of extensor tone (in standing) in the same way as they affect the value of periodical extensor bursts (in walking). One should note that the diversity of relationships between the activity of cortical neurons on one hand and the variables characterizing the motor pattern on the other is a common finding in many studies of the motor cortex (see e.g. Drew, 1993; Kakei et al., 2003), including those devoted to postural control (Beloozerova et al., 2005).

3.5.3 Future studies

Experiments with partial lesion of the spinal cord (*Paper II*) have shown that supraspinal signals play a crucial role in both the maintenance of basic body configuration on horizontal

surface, and in adaptation of body configuration to the inclined surface. The present study has revealed different populations of PTNs contributing to adaptation of the body configuration to the inclined surface only during standing, only during locomotion, and in both tasks. To reveal the contribution of other descending systems (rubrospinal, reticulospinal and vestibulospinal) to adaptation of body configuration to the environment in the motor tasks of standing and locomotion, future studies are needed.

References

Armstrong, D. M., & Drew, T. (1983a). Topographical localization in the motor cortex of the cat for somatic afferent responses and evoked movements. *J Physiol*, *350*, 33–54.

Armstrong, D. M., & Drew, T. (1984a). Locomotor-related neuronal discharges in cat motor cortex compared with peripheral receptive fields and evoked movements. *J Physiol*, *346*, 497–517.

Armstrong, D. M., & Drew, T. (1984b). Discharges of pyramidal tract and other motor cortical neurones during locomotion in the cat. *J Physiol*, *346*, 471–495.

Asanome, M., Matsuyama, K., & Mori, S. (1998). Augmentation of postural muscle tone induced by the stimulation of the descending fibers in the midline area of the cerebellar white matter in the acute decerebrate cat. *Neurosci Res*, *30*(3), 257–269.

Asanuma, H. (1989). *The motor cortex*. Raven Press.

Barberini, C. L., & Macpherson, J. M. (1998). Effect of head position on postural orientation and equilibrium. *Exp Brain Res*, *122*(2), 175–184.

Bard, P. (1933). Studies on the cerebral cortex i. localized control of placing and hopping reactions. *Arch Neurol Psychiatr*, *30*, 40–74.

Bard, P., & Macht, M. (1958). The behavior of chronically decerebrate cat. In G. Wolstenholme & C. O' Connor (Eds.), *Neurological basis of behavior* (pp. 55–71). Churchill, London.

Beloozerova, I. N., & Sirota, M. G. (1993a). The role of the motor cortex in the control of accuracy of locomotor movements in the cat. *J Physiol*, *461*, 1–25.

Beloozerova, I. N., & Sirota, M. G. (1993b). The role of the motor cortex in the control of vigour of locomotor movements in the cat. *J Physiol*, *461*, 27–46.

Beloozerova, I. N., Sirota, M. G., Orlovsky, G. N., & Deliagina, T. G. (2005). Activity of pyramidal tract neurons in the cat during postural corrections. *J Neurophysiol*, *93*(4), 1831–1844.

Beloozerova, I. N., Sirota, M. G., Swadlow, H. A., Orlovsky, G. N., Popova, L. B., & Deliagina, T. G. (2003a). Activity of different classes of neurons of the motor cortex during postural corrections. *J Neurosci*, *23*(21), 7844–7853.

Beloozerova, I. N., Zelenin, P. V., Popova, L. B., Orlovsky, G. N., Grillner, S., & Deliagina, T. G. (2003b). Postural control in the rabbit maintaining balance on the tilting platform. *J Neurophysiol*, *90*(6), 3783–3793.

Berthoz, A., & Pozzo, T. (1988). Intermittent head stabilization during postural and locomotory tasks in humans. In *Posture and gait: Development, adaptation, and modulation.* (pp. 189–198). New York, NY: Elsevier Science Inc.

Bishop, P. O., Burke, W., & Davis, R. (1962). The identification of single units in central visual pathways. *J Physiol*, *162*, 409–431.

Boyle, R. (2001). Vestibulospinal control of reflex and voluntary head movement. *Ann N Y Acad Sci*, *942*, 364–380.

Brooks, C. M. (1933). Studies on the cerebral cortex ii. localized representation of hopping

and placing reactions in the rat. *Am J Physiol*, 162–171.

Bussières, N., & Dubuc, R. (1992). Phasic modulation of vestibulospinal neuron activity during fictive locomotion in lampreys. *Brain Res*, *575*(1), 174–179.

Bussières, N., & Dubuc, R. (1992b). Phasic modulation of transmission from vestibular inputs to reticulospinal neurons during fictive locomotion in lampreys. *Brain Res*, *582*(1), 147–153.

De Burlet, H. M., & Versteegh, C. (1930). Uber ban und funktion des petromyzon-labyrinthes. *Acta Oto-laringologica (Suppl.)*, *13*, 5–58.

De Leon, R. D., Hodgson, J. A., Roy, R. R., & Edgerton, V. R. (1998). Locomotor capacity attributable to step training versus spontaneous recovery after spinalization in adult cats. *J Neurophysiol*, *79*(3), 1329–1340.

Deliagina, T. G. (1997a). Vestibular compensation in lampreys: impairment and recovery of equilibrium control during locomotion. *J Exp Biol*, *200*(Pt 10), 1459–1471.

Deliagina, T. G. (1997b). Vestibular compensation in lampreys: role of vision at different stages of recovery of equilibrium control. *J Exp Biol*, *200*(Pt 23), 2957–2967.

Deliagina, T. G., Arshavsky, Y. I., & Orlovsky, G. N. (1998). Control of spatial orientation in a mollusc. *Nature*, *393*(6681), 172–175.

Deliagina, T. G., Beloozerova, I. N., Popova, L. B., Sirota, M. G., Swadlow, H. A., Grant, G., et al. (2000b). Role of different sensory inputs for maintenance of body posture in sitting rat and rabbit. *Motor Control*, *4*(4), 439–452.

Deliagina, T. G., & Fagerstedt, P. (2000c). Responses of reticulospinal neurons in intact lamprey to vestibular and visual inputs. *J Neurophysiol*, *83*(2), 864–878.

Deliagina, T. G., Grillner, S., Orlovsky, G. N., & Ullén, F. (1993). Visual input affects the response to roll in reticulospinal neurons of the lamprey. *Exp Brain Res*, *95*(3), 421–428.

Deliagina, T. G., & Orlovsky, G. N. (2002b). Comparative neurobiology of postural control. *Curr Opin Neurobiol*, *12*(6), 652–657.

Deliagina, T. G., Orlovsky, G. N., Grillner, S., & Wallén, P. (1992a). Vestibular control of swimming in lamprey. ii. characteristics of spatial sensitivity of reticulospinal neurons. *Exp Brain Res*, *90*(3), 489–498.

Deliagina, T. G., Orlovsky, G. N., Grillner, S., & Wallén, P. (1992b). Vestibular control of swimming in lamprey. iii. activity of vestibular afferents: convergence of vestibular inputs on reticulospinal neurons. *Exp Brain Res*, *90*(3), 499–507.

Deliagina, T. G., Orlovsky, G. N., Selverston, A. I., & Arshavsky, Y. I. (1999). Neuronal mechanisms for the control of body orientation in clione i. spatial zones of activity of different neuron groups. *J Neurophysiol*, *82*(2), 687–699.

Deliagina, T. G., Orlovsky, G. N., Selverston, A. I., & Arshavsky, Y. I. (2000a). Neuronal mechanisms for the control of body orientation in clione ii. modifications in the activity of postural control system. *J Neurophysiol*, *83*(1), 367–373.

Deliagina, T. G., Orlovsky, G. N., Selverston, A. I., & Arshavsky, Y. I. (2000d). Asymmetrical effect of gaba on the postural orientation in clione. *J Neurophysiol*, *84*(3), 1673–1676.

Deliagina, T. G., Orlovsky, G. N., Zelenin, P. V., & Beloozerova, I. N. (2006a). Neural bases of postural control. *Physiology*, *21*, 216–225.

Deliagina, T. G., Popova, L. B., & Grant, G. (1997c). The role of tonic vestibular input for postural control in rats. *Arch Ital Biol*, *135*(3), 239–261.

Deliagina, T. G., Sirota, M. G., Zelenin, P. V., Orlovsky, G. N., & Beloozerova, I. N. (2006b). Interlimb postural coordination in the standing cat. *J Physiol*, *573*(Pt 1), 211–224.

Drew, T. (1993). Motor cortical activity during voluntary gait modifications in the cat. i. cells related to the forelimbs. *J Neurophysiol*, *70*(1), 179–199.

Duysens, J., Clarac, F., & Cruse, H. (2000). Load-regulating mechanisms in gait and posture: comparative aspects. *Physiol Rev*, *80*(1), 83–133.

Edgerton, V. R., De Leon, R. D., Harkema, S. J., Hodgson, J. A., London, N., Reinkensmeyer, D. J., et al. (2001). Retraining the injured spinal cord. *J Physiol*, *533*(Pt 1), 15–22.

Edgerton, V. R., Tillakaratne, N. J. K., Bigbee, A. J., De Leon, R. D., & Roy, R. R. (2004). Plasticity of the spinal neural circuitry after injury. *Annu Rev Neurosci*, *27*, 145–167.

Forey, P., & Janvier, P. (1993). Agnathans and the origin of jawed vertebrates. *Nature*, *361*, 129–134.

Fuller, J. H., & Schlag, J. D. (1976). Determination of antidromic excitation by the collision test: problems of interpretation. *Brain Res*, *112*(2), 283–298.

Gahery, Y., Ioffe, M., Massion, J., & Polit, A. (1980). The postural support of movement in cat and dog. *Acta Neurobiol Exp (Wars)*, *40*(4), 741–755.

Ghez, C., Hening, W., & Gordon, J. (1991). Organization of voluntary movement. *Curr Opin Neurobiol*, *1*(4), 664–671.

Giuliani, C. A., & Smith, J. L. (1985). Development and characteristics of airstepping in chronic spinal cats. *J Neurosci*, *5*(5), 1276–1282.

Grillner, S. (1973). Locomotion in the spinal cat. In R. Stein, K. Pearson, R. Smith, & J. Redford (Eds.), *Control of posture and locomotion* (pp. 515–535). Plenum, New York.

Grillner, S., Brodin, L., Sigvardt, K., & Dale, N. (1986). On the spinal network generating locomotion in lamprey: transmitters, membrane properties and circuitry. In *Neurobiology of vertebrate locomotion.* (pp. 335–352).

Grillner, S., Buchanan, J., Wallén, P., & Brodin, L. (1988). Neural control of locomotion in lower vertebrates-from behavior to ionic mechanisms. In A. Cohen, S. Rossignol, & S. Grillner (Eds.), *Neural control of rhythmic movements in vertebrates* (pp. 1–40). Wiley New York.

Grillner, S., Deliagina, T. G., Ekeberg, O., El Manira, A., Hill, R. H., Lansner, A., et al. (1995). Neural networks that co-ordinate locomotion and body orientation in lamprey. *Trends Neurosci*, *18*(6), 270–279.

Grillner, S., Georgopoulos, A., & Jordan, L. (1997). Selection and initiation of motor behavior. In P. Stein, S. Grillner, A. Selverston, & D. Stuart (Eds.), *Neurons, networks, and motor behavior* (pp. 3–17). MIT press Cambridge, MA.

Grillner, S., Matsushima, T., Wadden, T., Tegner, J., El Manira, A., & Wallén, P. (1993). The neurophysiological bases of undulatory locomotion in vertebrates. *Seminars in Neuroscience*, *5*, 17–27.

Grillner, S., McClellan, A., Sigvardt, K., & Wallén, P. (1983). On the spinal generation of locomotion, with particular reference to a simple vertebrate: the lamprey. *Birth Defects Orig Artic Ser*, *19*(4), 347–356.

Grillner, S., & Wallén, P. (1985). Central pattern generators for locomotion, with special reference to vertebrates. *Annu Rev Neurosci*, *8*, 233–261.

Grillner, S., Wallén, P., & Prisco, G. Viana di. (1990). Cellular network underlying locomotion as revealed in a lower vertebrate model: transmitters, membrane properties, circuitry, and simulation. *Cold Spring Harb Symp Quant Biol*, *55*, 779–789.

Helgren, M. E., & Goldberger, M. E. (1993). The recovery of postural reflexes and locomotion following low thoracic hemisection in adult cats involves compensation by undamaged primary afferent pathways. *Exp Neurol*, *123*(1), 17–34.

Horak, F., & Macpherson, J. (1995). Postural orientation and equilibrium. In *Handbook of physiology.* Oxford University Press, New York.

Horak, F., & Macpherson, J. (1996). Postural orientation and equilibrium. In *Handbook*

of physiology. exercise: Regulation and integration of multiple systems (pp. 255–292). Oxford University Press, New-York.

Kakei, S., Hoffman, D. S., & Strick, P. L. (2003). Sensorimotor transformations in cortical motor areas. *Neurosci Res*, *46*(1), 1–10.

Kappers, C. U. (1936). The endocranial casts of the ehringsdorf and homo soloensis skulls. *J Anat*, *71*(Pt 1), 61–76.

Kasicki, S., Grillner, S., Ohta, Y., Dubuc, R., & Brodin, L. (1989). Phasic modulation of reticulospinal neurones during fictive locomotion and other types of spinal motor activity in lamprey. *Brain Res*, *484*(1-2), 203–216.

Kato, M., Murakami, S., Hirayama, H., & Hikino, K. (1985). Recovery of postural control following chronic bilateral hemisections at different spinal cord levels in adult cats. *Exp Neurol*, *90*(2), 350–364.

Kellog, W. N., Deese, J., & Pronko, N. H. (1946). On the behavior of the lumbo-spinal dog. *Exp Psychol*, *36*, 503–511.

Koyama, H., Kishida, R., Goris, R. C., & Kusunoki, T. (1989). Afferent and efferent projections of the viiith cranial nerve in the lamprey lampetra japonica. *J Comp Neurol*, *280*(4), 663–671.

Kuhtz-Buschbeck, J. P., Boczek-Funcke, A., Mautes, A., Nacimiento, W., & Weinhardt, C. (1996). Recovery of locomotion after spinal cord hemisection: an x-ray study of the cat hindlimb. *Exp Neurol*, *137*(2), 212–224.

Lacquaniti, F., Maioli, C., & Fava, E. (1984). Cat posture on a tilted platform. *Exp Brain Res*, *57*(1), 82–88.

Landgren, S., & Silfvenius, H. (1971). Nucleus z, the medullary relay in the projection path to the cerebral cortex of group i muscle afferents from the cat's hind limb. *J Physiol*, *218*(3), 551–571.

Lowenstein, O. (1970). The electrophysiological study of the responses of the isolated labyrinth of the lamprey (lampetra fluviatilis) to angular acceleration, tilting and mechanical vibration. *Proc R Soc Lond B Biol Sci*, *174*(37), 419–434.

Lowenstein, O., Osborne, M. P., & Thornhill, R. A. (1968). The anatomy and ultrastructure of the labyrinth of the lamprey (lampetra fluviatilis l.). *Proc R Soc Lond B Biol Sci*, *170*(19), 113–134.

Macpherson, J. M. (1988b). Strategies that simplify the control of quadrupedal stance. i. forces at the ground. *J Neurophysiol*, *60*(1), 204–217.

Macpherson, J. M., Deliagina, T. G., & Orlovsky, G. N. (1997a). Control of body orientation and equilibrium in vertebrates. In P. S. G. Stein, S. Grillner, A. Selverston, & D. G. Stuart (Eds.), *Neurons, networks and motor behavior* (pp. 257–267). Cambridge, MA: MIT Press.

Macpherson, J. M., & Fung, J. (1999). Weight support and balance during perturbed stance in the chronic spinal cat. *J Neurophysiol*, *82*(6), 3066–3081.

Macpherson, J. M., Fung, J., & Jacobs, R. (1997b). Postural orientation, equilibrium, and the spinal cord. *Adv Neurol*, *72*, 227–232.

Magnus, R. (1924). *Korperstellung.* (B. Springer, Ed.).

Maioli, C., & Poppele, R. E. (1991). Parallel processing of multisensory information concerning self-motion. *Exp Brain Res*, *87*(1), 119–125.

Maki, B. E., Edmondstone, M. A., & McIlroy, W. E. (2000). Age-related differences in laterally directed compensatory stepping behavior. *J Gerontol A Biol Sci Med Sci*, *55*(5), M270–M277.

Marple-Horvat, D. E., Amos, A. J., Armstrong, D. M., & Criado, J. M. (1993). Changes in

the discharge patterns of cat motor cortex neurones during unexpected perturbations of on-going locomotion. *J Physiol, 462*, 87–113.

Massion, J. (1994). Postural control system. *Current Opinion Neurobiology, 4*, 877–887.

Massion, J. (1998). Postural control systems in developmental perspective. *Neurosci Biobehav Rev., 22*, 465–72.

Massion, J., & Duffose, M. (1988). Coordination between posture and movement: why and how? *News Physiol Sci, 3*, 88–93.

Massion, J., Popov, K., Fabre, J. C., Rage, P., & Gurfinkel, V. (1997). Is the erect posture in microgravity based on the control of trunk orientation or center of mass position? *Exp Brain Res, 114*(2), 384–389.

Matsuyama, K., & Drew, T. (2000). Vestibulospinal and reticulospinal neuronal activity during locomotion in the intact cat. ii. walking on an inclined plane. *J Neurophysiol, 84*(5), 2257–2276.

McClellan, A. D. (1984). Descending control and sensory gating of 'fictive' swimming and turning responses elicited in an in vitro preparation of the lamprey brainstem/spinal cord. *Brain Res, 302*(1), 151–162.

McClellan, A. D., & Grillner, S. (1983). Initiation and sensory gating of 'fictive' swimming and withdrawal responses in an in vitro preparation of the lamprey spinal cord. *Brain Res, 269*(2), 237–250.

McClellan, A. D., & Hagevik, A. (1997). Descending control of turning locomotor activity in larval lamprey: neurophysiology and computer modeling. *J Neurophysiol, 78*(1), 214–228.

Misiaszek, J. E. (2006a). Neural control of walking balance: if falling then react else continue. *Exerc Sport Sci Rev, 34*(3), 128–134.

Misiaszek, J. E. (2006b). Control of frontal plane motion of the hindlimbs in the unrestrained walking cat. *J Neurophysiol, 96*(4), 1816–1828.

Mori, S. (1987). Integration of posture and locomotion in acute decerebrate cats and in awake, freely moving cats. *Prog Neurobiol, 28*(2), 161–195.

Mori, S. (1989). Contribution of postural muscle tone to full expression of posture and locomotor movements: multi-faceted analyses of its setting brainstem-spinal cord mechanisms in the cat. *Jpn J Physiol, 39*(6), 785–809.

Musienko, P. E., Zelenin, P. V., Lyalka, V. F., Orlovsky, G. N., & Deliagina, T. G. (2008). Postural performance in decerebrated rabbit. *Behav Brain Res, 190*(1), 124–134.

Musienko, P. E., Zelenin, P. V., Orlovsky, G. N., & Deliagina, T. G. (2007). Enhancement of limb reflexes in the spinal rabbit by stimulation of the spinal cord. In *Soc neurosci abstr* (Vol. 33, p. 75.17).

Nashner, L. M., & Forssberg, H. (1986). Phase-dependent organization of postural adjustments associated with arm movements while walking. *J Neurophysiol, 55*(6), 1382–1394.

Nieuwenhuys, R., Donkelaar, H., & Nicholson, C. (1998). *The central nervous system of vertebrates* (Vol. 1). Springer, Berlin.

Oddsson, L. I. E., Wall, C., McPartland, M. D., Krebs, D. E., & Tucker, C. A. (2004). Recovery from perturbations during paced walking. *Gait Posture, 19*(1), 24–34.

Ohta, Y., & Grillner, S. (1989). 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*(5), 1079–1089.

Orlovsky, G. N., Deliagina, T. G., & Grillner, S. (1999). *Neuronal control of locomotion: From mollusc to man.* Oxford UP, Oxford.

Oscarsson, O., & Rosén, I. (1966a). Short-latency projections to the cat's cerebral cortex from skin and muscle afferents in the contralateral forelimb. *J Physiol*, *182*(1), 164–184.

Oscarsson, O., & Rosén, I. (1966b). Response characteristics of reticulocerebellar neurones activated from spinal afferents. *Exp Brain Res*, *1*(4), 320–328.

Pavlova, E. L., & Deliagina, T. G. (2002). Responses of reticulospinal neurons in intact lamprey to pitch tilt. *J Neurophysiol*, *88*(3), 1136–1146.

Pflieger, J., & Dubuc, R. (2004). Vestibulo-reticular projections in adult lamprey: their role in locomotion. *Neuroscience*, *129*(3), 817–829.

Platt, C. (1983). The peripheral vestibular system of fishes. In R. Northcutt & R. Davis (Eds.), *Fish neurobiology. brainstem and sense organs.* (Vol. 1, pp. 89–123). University of Michigan Press, Ann Arbor.

Pratt, C. A., Fung, J., & Macpherson, J. M. (1994). Stance control in the chronic spinal cat. *J Neurophysiol*, *71*(5), 1981–1985.

Rademaker, G. (1931). *Das stehen. berlin, j.* Springer.

Rovainen, C. M. (1967). 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*(5), 1000–1023.

Rovainen, C. M. (1978). Muller cells,"mauthner cells" and other identified reticulospinal neurons in the lamprey. In *Neurobiology of the mauthner cell* (pp. 245–269). Raven New York.

Rovainen, C. M. (1979). Neurobiology of lampreys. *Physiol Rev*, *59*(4), 1007–1077.

Rubinson, K. (1974). The central distribution of viii nerve afferents in larval petromyzon marinus. *Brain Behav Evol*, *10*(1-3), 121–129.

Sherman, S., & Guillery, R. (2001). *Exploring the thalamus.* Academic Press San Diego.

Tamarova, Z. A., Sirota, M. G., Orlovsky, G. N., Deliagina, T. G., & Beloozerova, I. N. (2007). Role of gaba a inhibition in modulation of pyramidal tract neuron activity during postural corrections. *Eur J Neurosci*, *25*(5), 1484–1491.

Ullén, F., Deliagina, T. G., Orlovsky, G. N., & Grillner, S. (1995a). Spatial orientation in the lamprey. i. control of pitch and roll. *J Exp Biol*, *198*(Pt 3), 665–673.

Ullén, F., Deliagina, T. G., Orlovsky, G. N., & Grillner, S. (1995b). Spatial orientation in the lamprey. ii. visual influence on orientation during locomotion and in the attached state. *J Exp Biol*, *198*(Pt 3), 675–681.

Ullén, F., Deliagina, T. G., Orlovsky, G. N., & Grillner, S. (1997). Visual pathways for postural control and negative phototaxis in lamprey. *J Neurophysiol*, *78*(2), 960–976.

Ullén, F., Orlovsky, G. N., Deliagina, T. G., & Grillner, S. (1993). Role of dermal photoreceptors and lateral eyes in initiation and orientation of locomotion in lamprey. *Behav Brain Res*, *54*(1), 107–110.

Vinay, L., Ben-Mabrouk, F., Brokard, F., Clarac, F., Jean-Xavier, C., Perlstein, E., et al. (2005). Perinatal development of the motor systems involved in postural control. *Neural Plast*, *4*, 131–139.

Von Holst, E. (1935). Uber den lichtruckenreflex bei fishen. *Pubbl Staz Zool Napoli*, *15*, 143–158.

Wallén, P., & Williams, T. L. (1984). Fictive locomotion in the lamprey spinal cord in vitro compared with swimming in the intact and spinal animal. *J Physiol*, *347*, 225–239.

Welt, C., Aschoff, J. C., Kameda, K., & Brooks, V. B. (1967). Intracortical organization of cat's motorsensory neurons. In D. P. Purpura & M. D. Yahr (Eds.), *Neurophysiological basis of normal and abnormal motor activities* (pp. 255–293). Raven Press.

Wickelgren, W. O. (1977). Physiological and anatomical characteristics of reticulospinal neurones in lamprey. *J Physiol*, *270*(1), 89–114.

Williams, T. L., Grillner, S., Smoljaninov, V. V., Wallén, P., Kashin, S., & Rossignol, S. (1989). Locomotion in lamprey and trout: the relative timing of activation and movement. *Journal of Experimental Biology, 143*(1), 559–566.

Zelenin, P. V. (2005). Activity of individual reticulospinal neurons during different forms of locomotion in the lamprey. *Eur J Neurosci, 22*(9), 2271–2282.

Zelenin, P. V., Deliagina, T. G., Grillner, S., & Orlovsky, G. N. (2000). Postural control in the lamprey: A study with a neuro-mechanical model. *J Neurophysiol, 84*(6), 2880–2887.

Zelenin, P. V., Grillner, S., Orlovsky, G. N., & Deliagina, T. G. (2001). Heterogeneity of the population of command neurons in the lamprey. *J Neurosci, 21*(19), 7793–7803.

Zelenin, P. V., Orlovsky, G. N., & Deliagina, T. G. (2007). Sensory-motor transformation by individual command neurons. *J Neurosci, 27*(5), 1024–1032.

Zelenin, P. V., Pavlova, E. L., Grillner, S., Orlovsky, G. N., & Deliagina, T. G. (2003). Comparison of the motor effects of individual vestibulo- and reticulospinal neurons on dorsal and ventral myotomes in lamprey. *J Neurophysiol, 90*(5), 3161–3167.

Zompa, I. C., & Dubuc, R. (1996). A mesencephalic relay for visual inputs to reticulospinal neurones in lampreys. *Brain Res, 718*(1-2), 221–227.