

Integration of Motor and Visual Information in the Parietal Area 5 During Locomotion

Irina N. Beloozerova and Mikhail G. Sirota

Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, Phoenix, Arizona 85013

Submitted 20 December 2002; accepted in final form 23 April 2003

Beloozerova, Irina N. and Mikhail G. Sirota. Integration of motor and visual information in the parietal area 5 during locomotion. *J Neurophysiol* 90: 961–971, 2003; 10.1152/jn.01147.2002. The parietal cortex receives both visual- and motor-related information and is believed to be one of the sites of visuo-motor coordination. This study for the first time characterizes integration of visual and motor information in activity of neurons of parietal area 5 during locomotion under conditions that require visuo-motor coordination. The activity of neurons was recorded in cats during walking on a flat surface—a task with no visuo-motor coordination required (flat locomotion), walking along a horizontal ladder or a series of barriers—a task requiring visuo-motor coordination for an accurate foot placement on surface that is heterogeneous along the direction of progression (ladder and barriers locomotion), and walking along a narrow pathway—a task requiring visuo-motor coordination on surface homogeneous along the direction of progression (narrow locomotion). During flat locomotion, activity of 66% of the neurons was modulated in rhythm of stepping, usually with one peak per cycle. During ladder and barrier locomotion, the proportion of rhythmically active neurons significantly increased, their modulation became stronger, and the majority of neurons had two peaks of activity per cycle. During narrow locomotion, however, the activity of neurons was similar to that during flat locomotion. We concluded that, during locomotion, parietal area 5 integrates two types of information: signals about the activity of basic locomotion mechanisms and signals about heterogeneity of the surface along the direction of progression. We describe here the modes of integration of these two types of information during locomotion.

INTRODUCTION

Many studies provide evidence that the parietal cortex is involved in the control of limb movements in extrapersonal space (see Andersen et al. 1997; Mountcastle 1995 for review). Visual information and visuo-motor coordination play an important role in this control. Despite the considerable amount of data on the activity of neurons in the parietal cortex during different motor tasks, the neuronal mechanisms by which visual information affects motor commands, as well as the principles of visuo-motor coordination are not well understood. The goal of this study was to characterize the activity of neurons in parietal area 5 during locomotion under conditions that require visuo-motor coordination.

Area 5 is a high-order somato-sensory area, and it receives inputs from various cortical and subcortical visual centers (Avendano et al. 1985, 1988; Hendry et al. 1979; Hyvarinen

1982; Niimi et al. 1983; Symonds et al. 1981). Area 5 provides outputs to the motor cortex, to other cortical and subcortical motor centers, and to the spinal cord (Asanuma 1981; Babb et al. 1984; Ghosh 1997; Groos et al. 1978; Hyvarinen 1982; Kakei et al. 1996; Murray and Coulter 1981; Wiesendanger 1981; Wiesendanger et al. 1979; Yumiya and Ghez 1984). Lesions in area 5 cause difficulties in reaching to visual targets (Fabre and Buser 1980, 1981; Rondot et al. 1977). The activity of neurons in area 5 is correlated with reaching movements (Bioulac et al. 1999; Burbaud et al. 1985; Ferraina and Bianchi 1994; Hyvarinen 1982; Kalaska et al. 1983, 1990; Khitrova-Orlova et al. 1997; Mountcastle et al. 1975; Sakata et al. 1995; Scott et al. 1997; Seal et al. 1982).

It was suggested that neuronal control of natural locomotion with precise stepping uses the same neuronal machinery that is employed during reaching movements (Georgopoulos and Grillner 1989). To walk in natural environments, a subject has to watch the steps because the support surface is usually uneven. Visual information about the surface structure allows the subject to perform necessary adjustments of stepping. Thus natural locomotion involves two essentially different neural mechanisms. First, basic rhythmical pattern of muscle contractions for each limb is generated by the spinal cord (Forssberg et al. 1980 a,b; Grillner and Zangger 1979; Sherrington 1906, 1910; for review, see Orlovsky et al. 1999). Second, the adaptations of this basic pattern to the features of natural supporting surfaces are accomplished by supra-spinal mechanisms. It was shown, for example, that the activity of the motor cortex changes substantially when cats overstep obstacles or place paws precisely on cross-pieces of a horizontal ladder during locomotion (Armstrong and Drew 1984; Beloozerova and Sirota 1993; Drew 1993; Widajewicz et al. 1994).

In the present study, we recorded the activity of neurons in area 5 in cats during three locomotion tasks: walking on a flat surface—a task with no visuo-motor coordination required (flat locomotion), walking on a horizontal ladder or overstepping a series of barriers—a task requiring visuo-motor coordination for accurate foot placement on a surface heterogeneous along the direction of progression (ladder and barriers locomotion), and walking along a narrow pathway—a task requiring visuo-motor coordination for accurate foot placement on a surface homogeneous along the direction of progression (narrow locomotion). Comparison of neuronal discharges during these locomotion tasks provided evidence that neurons in area 5 of

Address for reprint requests: I. N. Beloozerova, Neurobiology, Barrow Neurological Institute, St. Joseph's Hospital and Medical Center, 350 W. Thomas Rd., Phoenix, AZ 85013 (E-mail: ibelooz@chw.edu).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "advertisement" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

parietal cortex receive information about the activity of basic locomotion mechanisms and information about the heterogeneity of the supporting surface along the axis of progression. We describe here the modes of integration of these two types of information in the discharge patterns of area 5 neurons.

Some of the results have been reported in brief (Beloozerova and Sirota 1992).

METHODS

Recordings were obtained from three adult cats (a male and 2 females). Some of the methods have been described (Beloozerova and Sirota 1993; Beloozerova et al. 2003) and will be reported briefly here. All experiments were conducted with the approval of the Barrow Neurological Institute Animal Care and Use Committee.

Experimental design

Positive reinforcement (food) was used to adapt cats to the experimental situation and to induce locomotion (Pryor 1975). A box 2.5 m long and 0.5 m wide served as an experimental chamber. A longitudinal wall divided the box into two corridors that cats passed sequentially and repeatedly. In one of the corridors, the floor was flat, and a horizontal ladder, barriers (Fig. 1A), or longitudinal dividers (Fig. 1B) were placed in the other. The cross-pieces of the horizontal ladder were flat and 5 cm wide. The width of the cross-pieces was chosen to exceed the cat's mean foot length that equals 3.5 mm, so that cats had a full foot support on a crosspiece. Cross-pieces of the ladder were spaced 25 cm apart, that is, at half of the mean step length observed during flat locomotion (Beloozerova and Sirota 1993), and were elevated 8 cm above the ground. Barriers were 7 cm high and 1 cm thick and were also placed 25 cm apart. The width of the narrow walkway was 5 cm. The passage of a cat through the beginning or the end of each corridor was monitored using infrared photodiodes.

Surgical procedures

Surgery was performed under isoflourane anesthesia using aseptic procedures. The skin and fascia were removed from much of the dorsal surface of the skull. At 10 points around the circumference of the head, stainless steel 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. Later, awake cats were rigidly held by this base while searching for neurons before a locomotion test. The base was also used later for fixation of connectors, a miniature microdrive, and a protective and electrically shielding cap. A portion of os parietale and the dura above parietal area 5 over ~1.0 sq cm were removed. The area 5 region was visually identified by the surface features. The aperture was then covered by a 1-mm-thick plastic plate in which holes 0.36 mm in diameter had been drilled and filled by sterile wax. The plate was fastened to the surrounding bone with orthodontic resin (Densply Caulk).

Single-unit recording and neurons sampled

Sampling of neurons began several days after the surgery. The cat was positioned on a table, and the base that was attached to its skull during the surgery was fixed in the frame so that the head was immobilized while the body was put in a comfortable position. Methods ensuring the humane treatment of subjects during immobilization of the head have been described (Beloozerova and Sirota 1993; Beloozerova et al. 2003).

Neuronal activity was recorded extracellularly using either a conventional tungsten-varnish-insulated (50–125 μm OD) microelectrode or a quartz-insulated microelectrode with platinum-tungsten core (40 μm OD) (Reitboeck 1983). The electrode was advanced into

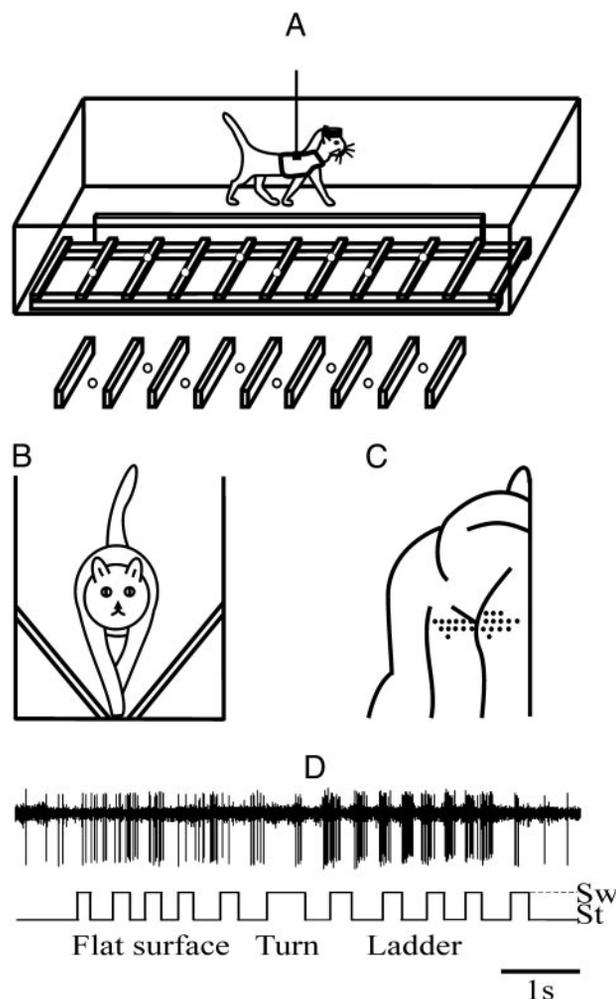


FIG. 1. Experimental design. A: the experimental box was divided into two corridors each 2.5 m long and 0.5 m wide. A horizontal ladder or longitudinal dividers were placed in 1 corridor. Cats were trained to pass sequentially and repeatedly through the corridors. \circ on the cross-pieces of the ladder and in between the barriers schematically show placements of cat forelimbs. B: placement of feet while walking along the narrow walkway. C: positions of tracks from which the activity of neurons was sampled is shown by dots on a schematic drawing of the brain (dorsal view). D: a sample record of a neuron's discharge during flat and ladder locomotion. Bottom: the swing (Sw, deflection up) and stance (St, deflection down) phases of the step cycle of the forelimb contralateral to the recording site in the cortex recorded by an electrical sensor.

cortical tissue through holes in the plastic plate above area 5. A miniature manual single-axis micromanipulator, rigidly fixed to the base, was used to lower the electrode. Positions of tracks from which the activity of neurons was sampled, is schematically shown on Fig. 1C. After amplification and filtering (0.3- to 10-kHz band-pass; Power1401/Spike2 system, Cambridge Electronic Design, Cambridge, UK), unitary activity was displayed on an oscilloscope and archived on a computer disk. A representative record of a neuron discharge is shown in Fig. 1D. To aid in the identification of single neurons, the waveform analysis was employed to discriminate and identify the spikes of the neuron using the Power1401/Spike2 system waveform-matching algorithm.

Receptive field testing

The somatic receptive fields were determined in resting animals by manual application of stimuli to the skin and hair, by palpation of muscles and their tendons, and by passive movements of joints. The

responses to visual stimulation were tested with the head restrained by switching the lights ON-OFF by presenting stable and moving stimuli: two-dimensional circles 2.5 cm in diameter, stripes 5 cm wide and 100 cm long, fields 50 × 50 cm, and complex three-dimensional stimuli: bars as those that were used for cross-pieces on the ladder, toys, pieces of food, hands. Two-dimensional stimuli were black and were presented against a white screen that was positioned 50 cm in front of the animal. Stripes and fields were oriented horizontal, vertical, or diagonal. Eight directions of planar movements were tested: left-right, up-down, and four diagonal directions. In addition, while an object was inside the receptive field of a neuron, the screen was moved back and forward in the range of 25–75 cm in front of the animal. Complex three-dimensional stimuli were presented against the natural laboratory background and were moved in different directions in the frontal plane at the distance of ~50 cm in front of the animal and also toward the animal and away from it. Speed of all stimuli movements was in the range of 0.5–1.0 m/s, which is in the range of the speed of locomotion that cats used inside the experimental chamber.

Processing of neuronal activity

The position and size of receptive fields was determined by listening to the audio monitor and measuring the entire area from which action potentials could be elicited. A directional selectivity was accessed by comparing the number of spikes elicited by stimulation in different directions. During locomotion, the duration of swing and stance phases of each step of the forelimb contralateral to the cortical area under study was recorded using an electrical sensor (Beloozerova and Sirota 1993). To accomplish this, a thin rubber sack was placed on the cat's forelimb, a thin metal electrode was attached to the external surface of the sack under the foot, and a voltage of 2–5 mV was applied to the electrode. The floor of the experimental box was covered by a cloth moistened with 0.1% sodium chloride to make the surface electrically conductive. A wire, sewn into the cloth along the length of the box, was connected to the common ground. The fall of voltage resulting from contact of the foot with the floor was recorded. The start and finish of electrical contact was taken as the start and finish of the stance phase of a step and, in selected experiments, was verified using simultaneous video recording. The onset of the swing phase was taken as the beginning of the step cycle. The duration of each step cycle was divided into 10 equal bins, and the number of spikes in each bin was counted. The discharge frequency in a bin was derived according to the method of Udo et al. (1982) that averages the instantaneous frequency of inter-spike intervals that fall within the bin and also accounts for those intervals that overlap with bin's beginning and end. The frequency histograms were smoothed using moving filter with a span of three bins. The following parameters were calculated for each neuron: the mean discharge frequency; the coefficient of modulation (M) defined as

$$M = (1 - F_{\min}/F_{\max}) \times 100\%,$$

where F_{\min} and F_{\max} are the minimal and the maximal frequencies of discharge in the histogram; and the position of the burst of activity, which was defined as the portion of the cycle where the activity exceeded the minimum by 25% of the difference between the maximal and minimal frequencies in the histogram. The beginning and end of a burst was rounded to the nearest bin beginning/end.

Statistical procedures

Parametric tests were used when possible for comparisons between groups. Unless noted otherwise, for all mean values, the SE is given. The discharge frequency and modulation of neurons during different tasks was compared using paired samples t -test. When data were categorical, nonparametric χ^2 or Mann-Whitney U tests were used.

Histological procedures

At the termination of the experiment, cats were deeply anesthetized with pentobarbital sodium and several reference electrolytic lesions were made in the area of recording. Cats were perfused with isotonic saline followed by a 10% Formalin solution. Frozen sections of 50- μ m thickness were cut in the recording region. The tissue was stained for Nissl substance with cresyl violet. Positions of tracks in the cortex were estimated in relation to the reference lesions.

RESULTS

Role of vision in locomotion tasks tested

We evaluated the involvement of vision in performance of locomotion tasks that we used for our experiments by testing the ability of cats to do these tasks in the complete darkness. Figure 2A shows the stepping pattern of a cat during walking along the horizontal ladder (ladder locomotion) and then during walking on the flat surface (flat locomotion) in an illuminated room. During the passage, the cat walked faster on the flat surface than on the ladder; however, the stepping patterns of each walk were rather regular. In the second trial (Fig. 2B), the lights were turned off when the cat entered the corridor with flat surface. On the flat surface, the cat stepped regularly in the dark and successfully reached the feeding rack. Thus vision was not necessary for flat locomotion. In contrast, when the lights were turned off while the cat was on the ladder in the third trial (Fig. 2C), locomotion was arrested: the cat did not place the foot on a support until after the lights were back on. Thus ladder locomotion required visual control of stepping. A cessation of locomotion was also observed in the fourth trial when the lights were turned off while the cat was in the corridor with barriers (Fig. 2D). Barriers locomotion did also require visual control of stepping. Walking along a narrow pathway (narrow locomotion) was possible, although irregular and greatly slowed in the dark (Fig. 2E). Thus narrow locomotion was dependent on visual control, but a partial compen-

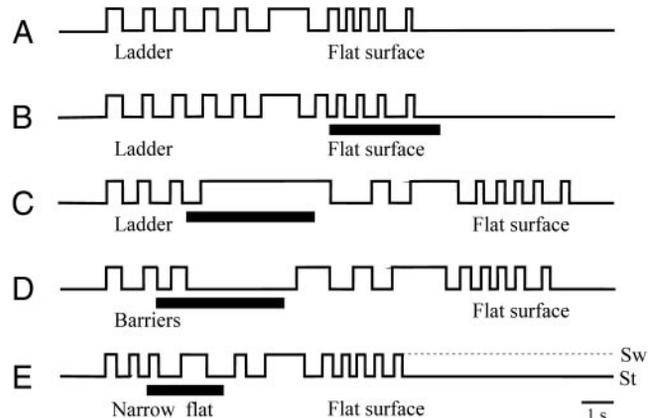


FIG. 2. Cat locomotion abilities in the dark. Five complete rounds made by a cat inside the experimental box are shown (A–E). Top: swing (Sw) and stance (St) phases of steps of 1 forelimb. ■, the time periods when lights were turned off. A: a control passage in the illuminated room. B: lights were turned off when the cat was walking on the flat surface; there was no disturbance of locomotion. C: lights were turned off when the cat was walking along the ladder; locomotion was arrested and resumed only when the lights were back on. D: lights were turned off when the cat was overstepping series of barriers; after 1 step in the dark only locomotion was arrested and resumed only when the lights were back on. E: lights were turned off when the cat was walking along the narrow walkway; locomotion was slowed down.

sation for the loss of vision was possible, probably by the use of somatosensory cues.

Activity of neurons during locomotion on the flat surface

The activity of 137 neurons was recorded during locomotion on the flat surface (flat locomotion). The mean speed of flat locomotion across the cats was 0.65 ± 0.14 (SD) m/s, and the step coefficient (the portion of swing phase in the step cycle) was $42 \pm 1\%$. On transition from standing to locomotion, the discharge rate of many neurons increased, so the mean discharge rate for the whole population during locomotion was higher than that during standing (21.6 ± 1.7 vs. 16.3 ± 1.2 imp/s; $P < 0.01$, paired-samples *t*-test). During flat locomotion, the activity of 66% of all recorded neurons was modulated in the stepping rhythm; that is, the activity was higher in one phase of the step and lower in another phase (Fig. 3, A and B). The coefficient of modulation (*M*) was on average $58 \pm 2\%$. Three patterns of modulation were observed. Among all recorded neurons, 27% had one peak of activity during step cycle (as the neuron in Fig. 3A), 19% had one trough (as the neuron in Fig. 3B), and 20% had two peaks (as the neuron in Fig. 3C). The neurons with one peak and one trough will be considered together in this paper and will be referred to collectively to as "one-peak" neurons (Fig. 3D). The bursts of activity of different neurons were distributed slightly unevenly over the step cycle. The bursts of some more neurons started around the beginning of swing and were well aligned to it (Fig. 3E). The mean duration of the bursts in this group was $30 \pm 1\%$ of the cycle. The bursts of somewhat smaller fraction of neurons started later in the cycle and were distributed with a more variable onset throughout the late swing and stance phases (Fig. 3E). In contrast to the bursts of neurons from the first group, the duration of bursts in these neurons on average was longer ($55 \pm 3\%$ of the cycle; $P < 0.001$, *U* test). The histogram of the mean frequencies of all step-related neurons had a weak peak during the swing phase (Fig. 3F).

Activity of neurons during locomotion on the ladder

On the horizontal ladder the surface was significantly heterogeneous along the direction of progression. During walking along the ladder (ladder locomotion), each limb overstepped two gaps and every other cross-piece of the ladder. The footprints of the two forelimbs are schematically shown in Fig. 1A as open circles on the cross-pieces of the ladder. The mean speed of ladder locomotion was 0.58 ± 0.07 (SD) m/s, and the step coefficient was $39 \pm 1\%$.

All 137 neurons that were studied during flat locomotion were also studied during ladder locomotion. Three typical examples of the activity of neurons during flat and ladder locomotion are presented in Fig. 4. The activity of the neuron shown in A was not step-related during flat locomotion but had a double-peak discharge pattern during ladder locomotion. The neuron shown in B had one peak of activity during flat locomotion and two peaks during ladder locomotion, with each of the peaks being higher than that during flat locomotion. The neuron shown in C had two peaks during flat locomotion, and this discharge pattern became even more pronounced during ladder locomotion.

The discharge rate of 55% of neurons increased on transition

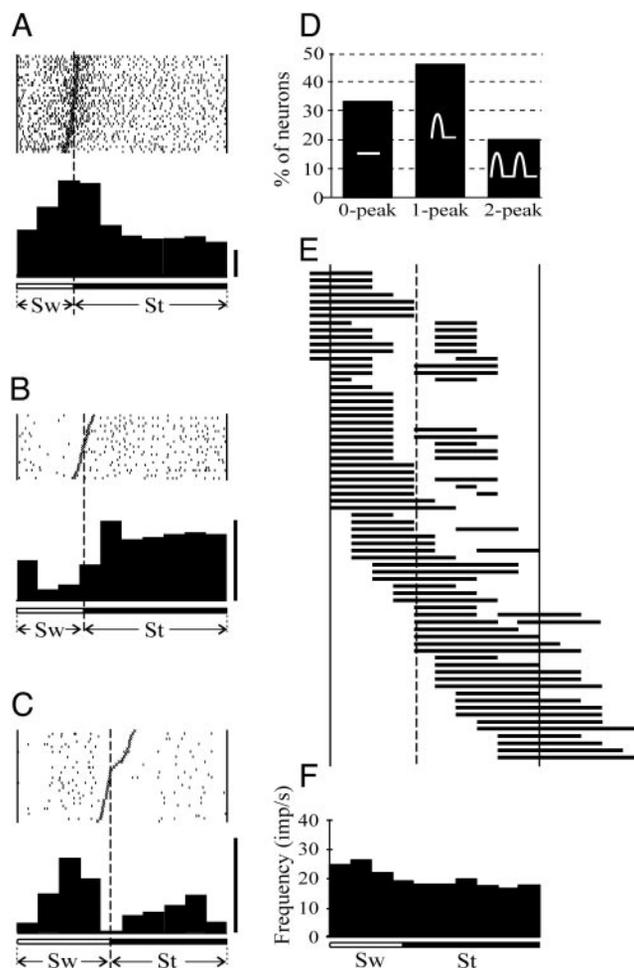


FIG. 3. Activity of neurons during locomotion on the flat surface (flat locomotion). A: the activity of a neuron was step-related during locomotion. It had 1 peak of activity at transition from swing to stance of the contralateral forelimb. In the raster, the duration of the step cycle is normalized to 100%, and the raster is rank-ordered according to the duration of the swing phase. Swing is separated from stance by a cross. Beneath the histogram, swing is indicated by the white (\square) and stance by the black (\blacksquare). ---, the mean beginning of the stance phase. B: the activity of another neuron was also step-related. This neuron discharged at a rather constant rate through the duration of the stance phase and had a sharp decrease in the activity during swing phase. C: the activity of this neuron had 2 peaks during the step cycle: one in swing and the other one in stance phase. In A–C, vertical scale bar equals 20 imp/s. D: percentages of neurons with activity that was not step-related, had 1 peak per step cycle, or had 2 peaks. E: phase distribution of bursts of individual neurons in the step cycle. Each trace represents a burst (bursts) of 1 neuron. Neurons are rank ordered so that those bursting earlier in the cycle are plotted on the top of the graph. F: phase distribution of the mean frequencies of the step-related neurons in the step cycle.

from flat to ladder locomotion, and the mean discharge rate of the whole population was higher during ladder locomotion as compared with flat locomotion (29.1 ± 2.6 vs. 21.6 ± 1.7 imp/s; $P < 0.01$, *U* test). The fraction of modulated neurons was larger during ladder than during flat locomotion (93 vs. 66%; $P < 0.01$, χ^2 test). The average *M* also increased (82 ± 2 vs. $58 \pm 2\%$; $P < 0.001$, *U* test), as did the proportion of the double-peak neurons (84% vs. 20%; $P < 0.001$, χ^2 test; Figs. 3D and 5A). In the double-peak neurons, one peak usually occurred in swing, and the other one in stance phase (Fig. 5B). The two bursts of activity were on average of an approximately similar duration, occupying $30 \pm 1\%$ of the step cycle each. In

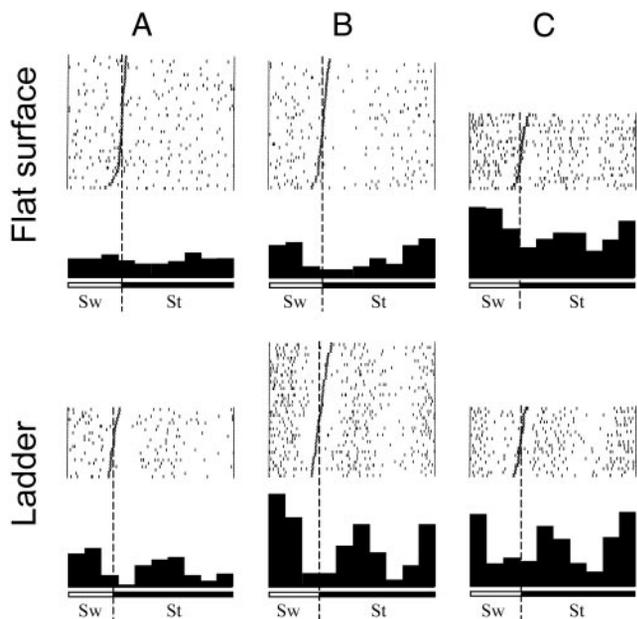


FIG. 4. Examples of activity changes on transition from flat to ladder locomotion in neurons with different discharge patterns during flat locomotion. A: the activity of this neuron was not step-related during flat locomotion but was with two clear-cut peaks during ladder locomotion. B: the activity of this neuron was step-related during flat locomotion with 1 activity peak at the transition phase from stance to swing. There were 2 peaks in the activity of the neuron during ladder locomotion, each of which was stronger than the peak observed during flat locomotion. C: the activity of this neuron was step-related during flat locomotion with two weak peaks per step cycle. The two peaks of activity became stronger during ladder locomotion, but the step phase position of them did not change. Vertical scale bar equals 20 imp/s. Designations as in Fig. 3.

contrast to flat locomotion, there were much more cells the first burst of activity in which started around the beginning of swing and much less of those whose first bursts started later in the cycle (Figs. 3E and 5B). In 68% of the double-peak neurons, the activity peak in swing was higher than that in stance. This was not due to a better alignment of the histogram to the beginning of swing because when aligned to the beginning of stance, the histograms of the same portion of neurons still had the highest peak in swing phase. The predominantly double peak pattern of the discharge was reflected in the histogram of the mean frequencies of all step-related neurons that had two peaks: one in the swing and another one in the stance phase (Fig. 5C). The peak in the swing phase was the stronger one.

Changes in the discharge pattern of individual neurons on transition from flat to ladder locomotion

NEURONS UNMODULATED DURING FLAT LOCOMOTION, $N = 47$ (34% OF THE TOTAL SAMPLE). The activity of 79% (37/47) of these neurons became modulated in the rhythm of stepping during ladder locomotion. Sixty-six percent of them had a double-peak pattern (as the cell in Fig. 4A), and 13%, a single-peak one.

NEURONS WITH ONE PEAK OF ACTIVITY PER CYCLE DURING FLAT LOCOMOTION, $N = 63$ (46% OF THE TOTAL SAMPLE). In 90% (57/63) of these neurons there appeared a second peak of activity during ladder locomotion (as in cell in Fig. 4B). In addition, in one half of these neurons (28/57), the first peak

changed its position in the step cycle on transition from flat to ladder locomotion (not illustrated). The two peaks always were approximately one half the duration of the cycle away from each other.

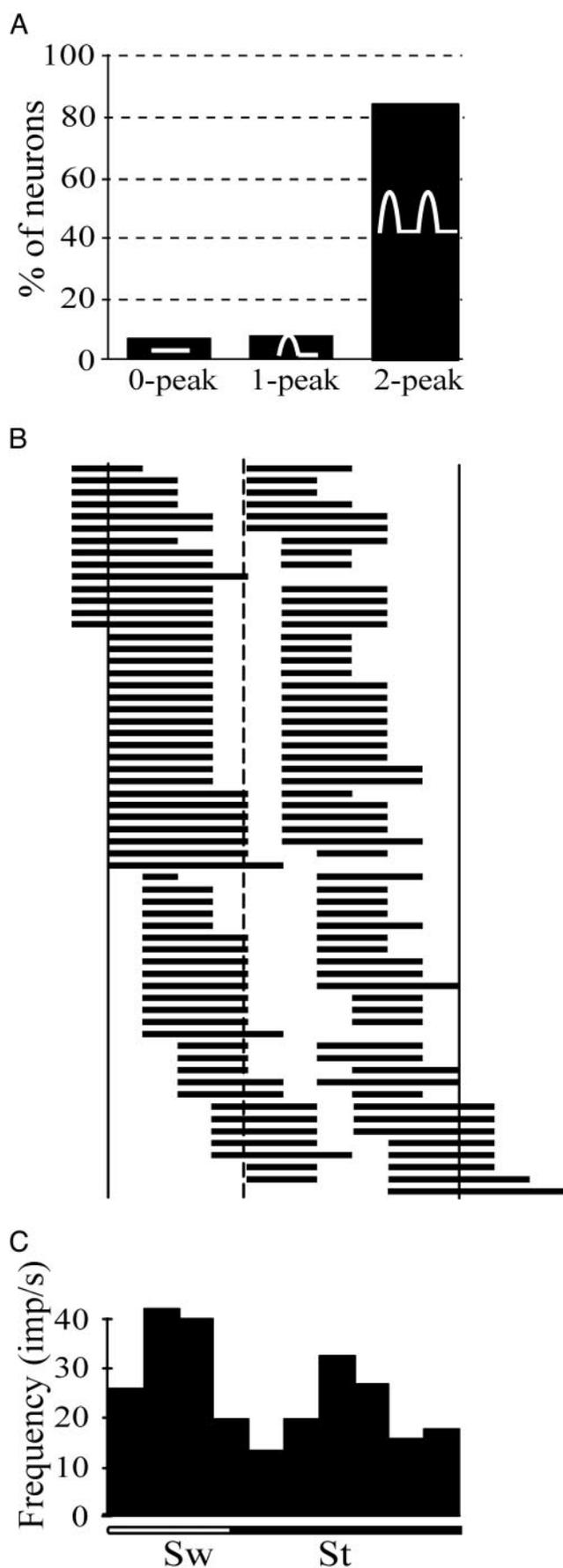
NEURONS WITH TWO PEAKS OF ACTIVITY PER CYCLE DURING FLAT LOCOMOTION $N = 27$ (20% OF THE TOTAL SAMPLE). All these neurons retained their double-peak discharge pattern during ladder locomotion as did the cell in Fig. 4C. The phase positions of the peaks in all but one of these cells remained unchanged.

Activity of neurons during stepping over a series of barriers

Although the width of the cross-pieces of the ladder exceeded the length of cat's foot by ~ 1.5 cm, we did an experiment to find out whether the differences in activity of the neurons during flat and ladder locomotion were due to the different requirements for the body stabilization during these two locomotion tasks. We presented cats with a walkway partitioned with a series of barriers. With the barriers, the surface of the corridor was significantly heterogeneous along the direction of progression, as it was on the ladder; however, the supporting surface was very wide (25 sq cm), thus the requirement for the body stabilization was similar to that during flat locomotion. During walking through a series of barriers (barriers locomotion), each limb overstepped two successive barriers and every other gap between them (Fig. 1A). The mean speed of barriers locomotion was 0.65 ± 0.15 (SD) m/s, and the step coefficient was $44 \pm 1\%$.

Of 137 neurons recorded during flat and ladder locomotion, the activity of 47 neurons was also recorded during barriers locomotion. Figure 6, A–D, shows two typical examples of the activity of neurons during flat and barriers locomotion. The activity of the first neuron (A and B) was not step-related during flat locomotion (A) but had a clear-cut modulation with a two-peak pattern during barriers locomotion (B). The activity of the second neuron (C and D) had one peak per cycle during flat locomotion (C), and two peaks during barriers locomotion, each of which being higher than that during flat locomotion (D).

On transition from flat to barriers locomotion, the discharge rate of a large number of neurons (43%) increased as it did on transition to ladder locomotion, although in this case the mean activity increase for the whole population did not reach the level of statistical significance (24.4 ± 3.0 imp/s as compared with 21.6 ± 1.7 imp/s during flat locomotion). The fraction of modulated neurons was larger during barriers than during flat locomotion (87 vs. 66%; $P < 0.01$, χ^2 test). The average M was also larger (83 ± 2 vs. $58 \pm 2\%$; $P < 0.001$, U test), as was the proportion of the double-peak neurons (70 vs. 20%; $P < 0.001$, χ^2 test; Figs. 6E and 3D). All the preceding parameters were similar to those found during ladder locomotion. Although the beginnings of the activity bursts were more variable during barriers than during ladder locomotion, the predominantly double peak discharge pattern during barriers locomotion was also reflected in the histogram of the mean frequencies of the step-related neurons (Fig. 6G). That histogram had two peaks: one in the swing and another one in the stance phase.



Activity of neurons during locomotion along the narrow walkway

In contrast to ladder and barriers locomotion, during walking along the narrow walkway (narrow locomotion), the surface on which cats stepped was homogeneous along the direction of progression. However, as during ladder and barriers locomotion, the feet had to be placed accurately on the narrow supporting surface. Thus using narrow locomotion task we could further test if the activity of area 5 neurons during locomotion depended on the precision of stepping or did it depend on irregularities in the visual scene. The mean speed of narrow locomotion was 0.57 ± 0.08 (SD) m/s, and the step coefficient was $43 \pm 1\%$.

Of 137 neurons recorded during flat and ladder locomotion, the activity of 45 neurons was also recorded during narrow locomotion. Figure 7, A–C, gives a typical example of the activity of a neuron in 40 steps during each flat, narrow, and ladder locomotion. The discharge frequency of the neuron during flat locomotion (A) was low, but the activity did show a step-related modulation (the cell discharged more spikes at the end of stance phase than in any other portion of the step cycle). The discharge frequency of the neuron during narrow locomotion (B) was also low, and the step-related modulation was absent. When tested during ladder locomotion (C), however, the neuron demonstrated much higher activity and a clear-cut modulation that had two peaks: one approximately coinciding with the peak observed during flat locomotion and a newly formed one in early stance.

During narrow locomotion, the mean discharge rate of the neurons was similar to that during flat locomotion (25.0 ± 3.2 as compared with 21.6 ± 1.7 imp/s). The activity of 64% of neurons was modulated in the locomotion rhythm: 47% of them having single-peak pattern and 17% the double-peak pattern (proportions that were close to those found during flat locomotion, Figs. 7D and 3D). The average M was also similar to that during flat locomotion (57 ± 3 compared to $58 \pm 2\%$). There were slightly more cells that had bursts in swing phase of the contralateral forelimb (Fig. 7E). The histogram of the mean frequencies of the step-related neurons had one peak in the swing phase (Fig. 7E). The bursts and the mean frequency distributions both were similar to those observed during flat locomotion (Fig. 3, E and F).

Activity of neurons with somato-sensory receptive fields

Somato-sensory receptive fields were found in 22% (14/64) of the neurons tested. The different receptive fields are summarized in Table 1.

During flat locomotion, the activity of only seven (50%) neurons with somatosensory receptive fields was step-related (Table 1), and there were five single-peak and two double-peak neurons. The mean frequency (19.0 ± 4.9 imp/s) and the average M ($59 \pm 5\%$) of these neurons were similar to those of the nonsomatosensory responsive ones (20.3 ± 1.7 imp/s and $58 \pm 2\%$, respectively). In six neurons, a peak of activity

FIG. 5. Discharge patterns and phases of neuronal activity during ladder locomotion. A: percentages of neurons whose activity was not step-related, had 1 or 2 peaks per step cycle. B: phase distribution of bursts of individual neurons in the step cycle. C: phase distribution of the mean frequencies of the step-related neurons in the step cycle. Designations as in Fig. 3.

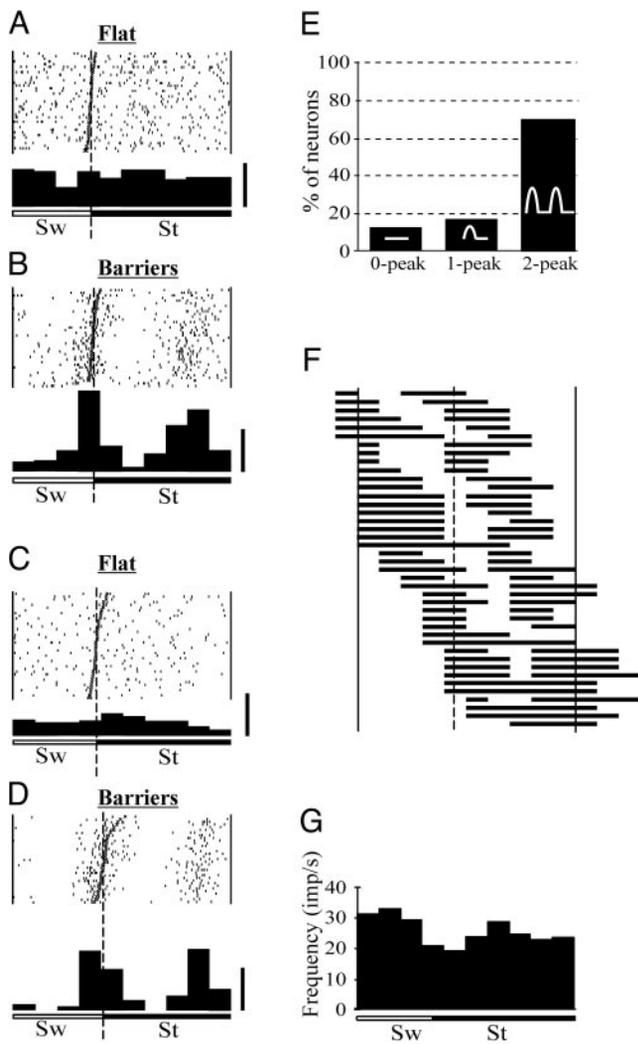


FIG. 6. Activity of neurons during barriers locomotion. *A–D*: examples of the activity of 2 neurons during flat (*A* and *B*) and barriers (*C* and *D*) locomotion. *A*: during flat locomotion the activity of this neuron was not step-related. *B*: in contrast, during barriers locomotion, the activity of the neuron had 2 clear peaks per cycle. *C*: the activity of the second neuron had 1 peak during flat locomotion. *D*: during barriers locomotion, however, the neuron discharged with 2 clear peaks per cycle. In *A–D*, vertical scale bar equals 20 imp/s. *E*: percentages of neurons the activity of which was not step-related, had 1 or 2 peaks per step cycle. *F*: phase distribution of bursts of individual neurons in the step cycle. *G*: phase distribution of the mean frequencies of the step-related neurons in the step cycle. Designations as in Fig. 3.

occurred during swing phase of the contralateral forelimb. The activity of more than half of the neurons with receptive fields on the forelimb as well as both neurons with receptive fields on the neck was not step-related (Table 1).

During ladder locomotion, the activity of 12 (86%) neurons with somatosensory receptive fields was step-related (Table 1), and there were three single-peak and nine double-peak neurons. The mean activity (23.9 ± 4.8 imp/s) and the average M ($87 \pm 4\%$) of these neurons were again similar to those of the nonsomatosensory responsive ones (26.8 ± 2.5 imp/s and $82 \pm 2\%$, respectively). In nine neurons, a peak of activity occurred during swing phase of the contralateral forelimb, and if there were two peaks, the one in the swing phase was the strongest one. The activity of one neuron with receptive field on the forelimb was still not step-related (Table 1).

Activity of neurons with visual receptive fields

Visual receptive fields were found in 20% (17/83) of the neurons tested. In all of these neurons, responses to lights ON-OFF and to stationary stimuli were weak or absent, however, all of the neurons responded well to moving stimuli. The receptive fields of all cells were excitatory and were located in the lower portion of the visual field in front of the animal. Except for three, all neurons responded to simple stimuli (black circles, stripes, or fields) moving in the frontal plane. Most neurons showed little or no directional selectivity in the frontal plane; however, all of them discharged more vigorously in response to approaching stimuli as compared with receding ones. All neurons responded to complex stimuli (bars, hands, toys, or food) with the approaching direction of their movement being the strongest stimulus.

At rest the activity of the visually responsive neurons was similar to that of the nonvisually responsive ones. With the start of locomotion, however, the activity of the visually responsive neurons decreased and during flat locomotion was

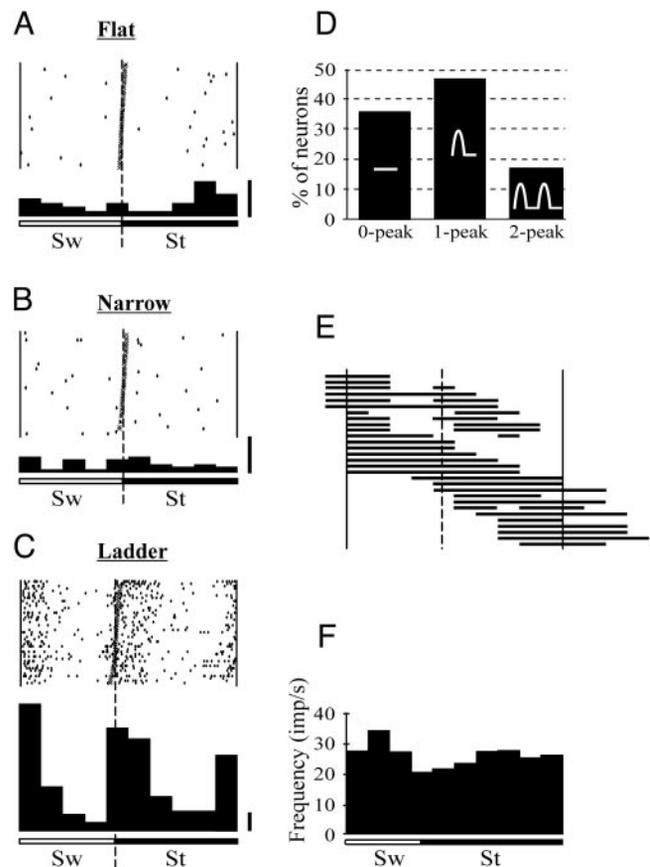


FIG. 7. Activity of neurons during narrow locomotion. *A–C*: examples of the activity of the same neuron in 40 steps during each flat (*A*), narrow (*B*), and ladder (*C*) locomotion. *A*: during flat locomotion, the activity of the neuron was low but step-related with 1 weak peak at the transition phase from stance to swing. *B*: during narrow locomotion the activity of the neuron was also low and not step-related. *C*: during ladder locomotion the neuron discharged very differently from its discharge both during flat and narrow locomotion: the discharge rate was much higher and there were two peaks in the activity of the neuron. In *A–C*, vertical scale bar equals 10 imp/s. *D*: percentages of neurons the activity of which was not step-related, had 1 or 2 peaks per step cycle. *E*: phase distribution of bursts of individual neurons in the step cycle. *F*: phase distribution of the mean frequencies of the step-related neurons in the step cycle. Designations as in Fig. 3.

TABLE 1. *Task relation of somato-sensory responsive neurons*

Receptive Field	Cell Count	Flat Locomotion	Ladder Locomotion
All body	3	3	3
Forelimb	7	3	6
Neck	2	0	2
Vibrissae	2	1	1
Total	14	7	12

lower than that of the nonvisually responsive ones (8.5 ± 2.0 vs. 21.3 ± 1.7 imp/s; $P < 0.0001$, U test). The activity of 60% of the visually responsive neurons was related to the locomotion cycle with an average M of $59 \pm 6\%$, a value similar to that of the nonvisually responsive neurons ($59 \pm 3\%$). All of the visually responsive neurons had one peak of activity per step cycle, and in all of them, that peak occurred in the swing phase of the contralateral forelimb.

During ladder locomotion, the visually responsive neurons retained their low activity. The activity of 80% of them was modulated in the locomotion cycle; however, the average M was lower than that of the nonvisually responsive neurons (78 ± 4 vs. $82 \pm 2\%$; $P = 0.05$, U test). Like the nonvisually responsive neurons, the great majority of the visually responsive neurons had two peaks of activity per step cycle. The phase distribution of the peaks of activity of the neurons with visual receptive fields was similar to that of the nonvisually responsive neurons.

DISCUSSION

Activity of neurons during flat locomotion—the roles of internal and peripheral information

The first finding of the present study is that the activity of many neurons in parietal area 5 was step-related during locomotion on the flat surface, when visual control of stepping was not necessary. It can thus be concluded that area 5 receives movement-related information not only during the “high-order” arm reaching movements, but also during the “lower-order” spinally organized locomotion.

Is the step-related activity of area 5 neurons during flat locomotion driven by somatosensory stimulation or is it driven by inputs from other motor centers? At least three facts suggest that the activation of somatosensory receptors does not importantly contribute to modulation of activity of neurons in area 5 during locomotion. First, most of the neurons with the step-related modulation of activity had no somatosensory receptive fields, at least those that we could reveal with our testing technique in resting condition. Second, the activity of four of seven neurons with somato-sensory receptive fields on the forelimb was not step-related (Table 1). Third, an extra flexion of the limbs and thus an additional activation of somatosensory receptors during overstepping series of barriers as compared with that during ladder locomotion had little effect on the activity of the neurons as they were rather similarly active and modulated during both locomotion tasks (Figs. 6 and 5). Therefore it seems probable that much like during arm reaching movements (Bioulac et al. 1999; Mountcastle et al. 1975; Seal et al. 1982, 1983), activity of area 5 during flat locomotion to a significant extent depends on the status of other motor-related brain centers and not on the status of

peripheral receptors. The similarity between phase distribution of the activity of neurons in area 5 (Fig. 3E) and spinal interneurons (Orlovsky and Feldman 1972; Baev et al. 1979) suggests that spinal locomotion generator could be a source of such internal information and thus be primarily responsible for modulation of the activity of 66% of the neurons in area 5.

Activity of neurons during ladder locomotion—the roles of surface heterogeneity, precision of stepping, body stabilization, and direct visual stimulation

Visuo-motor coordination and, therefore supraspinal control of locomotion was required during ladder locomotion. The second finding of the present study was that the activity of neurons in area 5 was dramatically different during ladder locomotion as compared with flat locomotion. That difference was found in all of the measured parameters of the activity of most of the neurons: in the discharge rates, the coefficients of modulation, and the discharge patterns. Such pronounced differences strongly suggest that area 5 participates in visuo-motor coordination during ladder locomotion. The question arises as to with what aspects of the coordination area 5 is concerned.

Unlike the flat surface, the horizontal ladder required precise placing of feet on the support. From our previous work in the motor cortex, we know that the requirement for precise feet placing may cause a dramatic change in the activity of neurons (Beloozerova and Sirota 1993). However, for area 5, we have earlier found that this cortical area is not involved in the control of accuracy of stepping (Beloozerova and Sirota 1992). Indeed, in a test that involved overstepping a series of barriers spaced progressively more closely to each other, thus gradually imposing more strict requirements for precision of stepping, the neurons of area 5 failed to correspondingly increase their discharges.

The potentially enhanced requirements for the body stabilization during ladder locomotion comparing to those during flat locomotion were also not responsible for the difference in the neuronal activity during the two locomotion tasks. In the control barriers locomotion test, the body stabilization requirements were close to those in the flat locomotion test; however, the discharges of the neurons were very different in these two tasks (Figs. 6 and 3); in contrast, they closely resembled the ones found during ladder locomotion (Figs. 6 and 5). The body stabilization was clearly compromised during narrow locomotion due to the unusual placing of right and left feet along a single line; however, the neuronal discharges during narrow locomotion were very similar to those during flat locomotion.

We hypothesized that during ladder locomotion, the activity of area 5 is primarily concerned with the visual heterogeneity of the supporting surface rather than with the motor aspects of locomotion. To test this hypothesis, we have constructed a locomotion task that required precise placing of feet on the support but in a pathway that was visually homogeneous along the direction of progression—the task of narrow locomotion. It was found that during narrow locomotion the activity of neurons was similar to that during flat locomotion (Figs. 3 and 6). Therefore we concluded that the visual heterogeneity of the surface along the direction of progression was the main factor that modulated the activity of neurons during ladder locomotion in addition to their motor related modulation. The sub-

stantially different phase distributions of neuronal activity during ladder and flat locomotion (Figs. 5B and 3E) also suggest the very different driving forces for the activity modulation during these two tasks.

On the other hand, we have to conclude that the visual responsiveness of area 5 neurons, at least that that we could reveal with our testing technique in the resting conditions, was not responsible for modulation of neuronal activity during ladder locomotion. In our sample, there were a number of neurons that had visual receptive fields in the front of the animal. However, even the highly sensitive to incoming stimuli neurons, which seemed to be well situated to detect an approach of a transverse target during locomotion (a cross-piece of the ladder), demonstrated below the average levels of activity and step-related modulation during ladder locomotion. In contrast, neurons with no visual receptive fields at rest displayed a high involvement in visuo-motor coordination during locomotion. Although visual responsiveness of the neurons may be different during locomotion as compared with resting conditions, our findings allow to hypothesize that the visual *peripheral* information does not play much role in modulation of the activity of neurons of area 5 during locomotion, that it is the *processed* visual information that affects it in this situation.

Modes of integration of motor and visual information

The influence of visual information on the basic locomotion rhythm during ladder locomotion was exerted on the activity of the great majority of neurons. This influence was rather diverse, however.

For 37 neurons (27% of the total sample), the activity of which was not step-related during flat locomotion but was during ladder locomotion, visual information was the main modulator of their activity on the ladder (Fig. 8A). In addition, there were 28 neurons (20% of the total sample) in which visual information during ladder locomotion caused a change in the phase position of the activity peak observed during flat locomotion (Fig. 8B).

In contrast, visual information about the support surface during ladder locomotion had a relatively small effect on the discharge pattern of 27 neurons (20% of the total sample) the activity of which had two peaks per step cycle during flat locomotion (Fig. 8C). In the activity of these cells, the movement-related pattern was the dominant one. The role of visual information was to increase the activity levels and the efficacy of the step-related modulation (the coefficient of modulation, *M*).

There were also 29 neurons (21% of the total sample) in which the peak of discharge remained in place during transition from flat to ladder locomotion while the second peak emerged in the opposite phase of the step cycle (as in the cell shown in Fig. 4B). That group of neurons can be regarded as a group of "an equal representation," because in the activity of these neurons the motor-related modulation was present along with the visually driven modulation (Fig. 8D).

Because the activity of a majority of the neurons had two peaks per step cycle during ladder locomotion, we believe that there were two visual messages reflected in the activity of the neurons. These messages probably corresponded to the results of the visual inspection of the two successive cross-pieces of the ladder. Studies show that although humans and cats usually

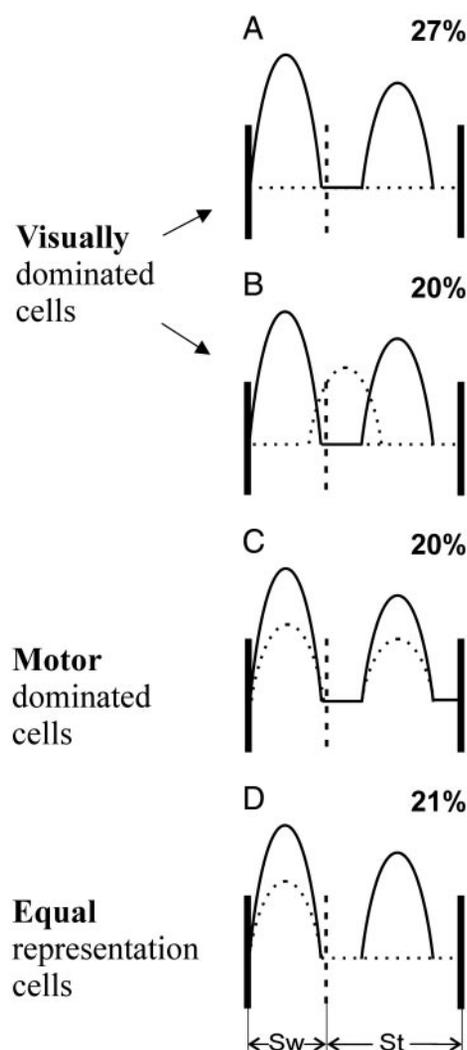


FIG. 8. A schematic presentation of the changes in the discharge patterns of the neurons on transition from flat to ladder locomotion. In A–D, \cdots , the activity during flat locomotion; —, activity during ladder locomotion. A: neurons with activity mostly dominated by visual input during ladder locomotion. B: neurons with activity mostly dominated by visual information in which there was a shift of the "motor" peak observed during flat locomotion. C: neurons with activity dominated by motor information, but with modulation added by visual information. D: neurons in which both visual and motor information was represented during ladder locomotion. Neurons with the activity unrelated to steps and those with one peak of activity per cycle during ladder locomotion are not shown in this scheme.

do not look constantly at the landing targets when they walk with an accurate stepping (Patla et al. 1996; Patla 1997; Sherk and Fowler 2000, 2001), they do make short-lasting visual inspection of them approximately two steps ahead (Patla and Vickers 2003). When the stepping task is challenging enough, however, saccades are almost always made to the next footfall target (Hollands and Marple-Horvat 2001). Obtained ahead of the time or immediately before the step, information about positions of the targets on the surface reaches area 5 and modifies activity of its neurons. The fact that the area 5 populational peak of activity during all locomotion tasks occurred during swing phase of the contralateral forelimb suggests that area 5 was more concerned with the position of the footfall target for that limb than with the one for the ipsilateral limb. It remains unclear, however, if visual and motor infor-

mation are originally integrated on the neurons of area 5 or if area 5 receives this information already integrated from another motor center, for example as an “efference copy” of a motor command.

How is the integrated visual and motor information used?

In the activity of area 5 neurons, visual information was integrated with locomotor rhythmicity by enhancing it and, in many instances, by adjusting its pattern. A question arises as to how this combined information is used for control of the limbs. To answer this question, recordings from identified efferent neurons of area 5 are required. At present we can only stress that it does not seem likely that parietal area 5 exerts its influence on the peripheral apparatus during locomotion via the motor cortex. There are at least three major features in the activity of area 5 and the motor cortex that argue against this route.

First, one of the major changes in the activity of area 5 on transition from flat to ladder locomotion is the change in the pattern of activity of most neurons from a single-peak to a double-peak pattern. As a result, the majority of neurons in area 5 have two peaks of activity per step cycle during ladder locomotion. During the same time, the predominant pattern of activity of neurons in the motor cortex is the single-peak pattern (Beloozerova and Sirota 1993; Drew 1993; Widajewicz et al. 1994). It does not seem likely that the single-peak pattern of neurons in the motor cortex is formed from the double-peak pattern of neurons in area 5.

Second, in a considerable number of neurons in area 5 the change in the pattern of activity was accompanied by a change in its phase distribution. In contrast, the characteristic feature of the activity of neurons in the motor cortex during transition from flat to ladder locomotion is the rather stable phase distribution of the activity in spite of a dramatic change in its magnitude (Beloozerova and Sirota 1993). It seems unlikely that a stable phase distribution is constructed out of a flexible one.

Finally, the activity of neurons in area 5 is not related to the precision of stepping, while the activity of neurons in the motor cortex clearly is (Beloozerova and Sirota 1993).

It seems most likely that area 5 acts independently of motor cortex imposing its direct control on spinal cord and/or other subcortical motor centers to which it projects (Asanuma 1981; Groos et al. 1978; Leichnetz et al. 1984; Murray and Coulter 1981; Wiesendanger 1981; Wiesendanger et al. 1979). For example, it was shown that the movements of the face musculature evoked by microstimulation of area 5 are independent on the motor cortex (Waters and Asanuma 1983). Thus visual information about heterogeneity of the support surface in the direction of progression that is incorporated into step-related discharges of neurons of area 5 promotes appropriate adjustments of stepping on uneven support surfaces.

There were several hypotheses proposed for the role of area 5 in the control of limb movements including the “sensory” hypothesis (Hyvarinen 1982), the “command” hypothesis (Mountcastle et al. 1975), the “planning action” hypothesis (Andersen et al. 1998), the “attention” hypothesis (Colby and Goldberg 1999), the “decision” hypothesis (Shadlen and Newsome 2001), the “reference frames transformation” hypothesis (Cohen and Andersen 2002), and others. To a large extent, the

diverse roles of area 5 may be complementary to each other (Kalaska 1996) or they may depend on the behavioral task. Our findings extend knowledge about area 5 of the parietal cortex by showing for the first time how the neuronal activity of this area reflects the process of integrating information about the limb movements and the heterogeneity of the support surface during goal directed stepping.

We thank P. Wettenstein for exceptional engineering assistance. We also thank Drs. Gregory Orlovsky and Alan Gibson for critical review of the manuscript.

DISCLOSURES

The research reported in this paper was supported by National Institute of Neurological Disorders and Stroke Grant R01 NS-39340 to I. N. Beloozerova.

REFERENCES

- Andersen RA, Snyder LH, Batista AP, Buneo CA, and Cohen YE.** Posterior parietal areas specialized for eye movements (LIP) and reach (PRR) using a common coordinate frame. *Novartis Found Symp* 218: 109–122, 1998.
- Andersen RA, Snyder LH, Bradley DC, and Xing J.** Multimodal representation of space in the posterior parietal cortex and its use in planning movements. *Annu Rev Neurosci* 20: 303–330, 1997.
- Armstrong DM and Drew T.** Discharge of pyramidal tract and other motor cortical neurons during locomotion in the cat. *J Physiol* 346: 471–496, 1984.
- Asanuma H.** The pyramidal tract. In: *Handbook of Physiology*, Bethesda, MD: Am Physiol Soc, 1981, sect 1, vol. II, p. 703–733.
- Avendano C, Rausell E, Perez-Aguilar D, and Isorna S.** Organization of the association cortical afferent connections of area 5: a retrograde tracer study in the cat. *J Comp Neurol* 278: 1–33, 1988.
- Avendano C, Rausell E, and Reinoso-Suarez F.** Thalamic projections to areas 5a and 5b of the parietal cortex in the cat: a retrograde horseradish peroxidase study. *J Neurosci* 5: 1446–1470, 1985.
- Babb RS, Waters RS, and Asanuma H.** Corticocortical connections to the motor cortex from the posterior parietal lobe (Areas 5a, 5b, 7) in the cat demonstrated by the retrograde axonal transport of horseradish peroxidase. *Exp Brain Res* 54: 476–484, 1984.
- Baev KV, Degtiarenko AM, Zavadskaia TV, and Kostiuk PG.** Activity of interneurons of the lumbar region of the spinal cord during fictive locomotion of thalamic cats (in Russian). *Neirofiziologija* 11: 329–338, 1979.
- Beloozerova IN and Sirota MG.** Activity of neurons in area 5 of the cerebral cortex during locomotion in awake cats (Abstract). *J Physiol* 45: 291P, 1992.
- Beloozerova IN and Sirota MG.** The role of the motor cortex in the control of accuracy of locomotor movements in the cat. *J Physiol* 461: 1–25, 1993.
- Beloozerova IN, Sirota MG, and Swadlow HA.** Activity of different classes of neurons of the motor cortex during locomotion. *J Neurosci* 23: 1087–1097, 2003.
- Bioulac B, Seal J, Guehl D, Burbaud P, and Gross C.** Reorganization of area 5 neuron activity in trained deafferented monkeys. *Brain Res* 835: 266–274, 1999.
- Burbaud P, Gross C, and Bioulac B.** Peripheral inputs and early unit activity in area 5 of the monkey during a trained forelimb movement. *Brain Res* 337: 341–346, 1985.
- Cohen YE and Andersen RA.** A common reference frame for movement plans in the posterior parietal cortex. *Nat Rev Neurosci* 3: 553–562, 2002.
- Colby CL and Goldberg ME.** Space and attention in parietal cortex. *Annu Rev Neurosci* 22: 319–349, 1999.
- Drew T.** Motor cortical activity during voluntary gait modifications in the cat. I. Cells related to the forelimbs. *J Neurophysiol* 70: 179–199, 1993.
- Fabre M and Buser P.** Structures involved in acquisition and performance of visually guided movements in the cat. *Acta Neurobiol Exp* 40: 95–116, 1980.
- Fabre M and Buser P.** Effect of lesioning the anterior suprasylvian cortex on visuo-motor guidance performance in the cat. *Exp Brain Res* 41: 81–88, 1981.
- Ferraina S and Bianchi L.** Posterior parietal cortex: functional properties of neurons in area 5 during an instructed-delay reaching task within different parts of space. *Exp Brain Res* 99: 175–178, 1994.

- Forssberg H, Grillner S, and Halberstma J.** The locomotion of the low spinal cat. I. Coordination within a hindlimb. *Acta Physiol Scand* 168: 269–281, 1980a.
- Forssberg H, Grillner S, Halberstma J, and Rossignol S.** The locomotion of the low spinal cat. II. Interlimb coordination. *Acta Physiol Scand* 168: 283–295, 1980b.
- Georgopoulos AP and Grillner S.** Visuomotor coordination in reaching and locomotion. *Science* 245: 1209–1210, 1989.
- Ghosh S.** Comparison of the cortical connections of areas 4 γ and 4 δ in the cat cerebral cortex. *J Comp Neurol* 388: 371–396, 1997.
- Grillner S and Zangger P.** On the central generation of locomotion in the low spinal cat. *Exp Brain Res* 34: 241–261, 1979.
- Groos WP, Ewing LK, Carter CM, and Coulter JD.** Organization of corticospinal neurons in the cat. *Brain Res* 143: 393–341, 1978.
- Hendry SHC, Jones EG, and Graham J.** Thalamic relay nuclei for cerebellar and certain related fiber systems in the cat. *J Comp Neurol* 185: 679–714, 1979.
- Hollands MA and Marple-Horvat DE.** Coordination of eye and leg movements during visually guided stepping. *J Mot Behav* 33: 205–216, 2001.
- Hyvarinen J.** *The Parietal Cortex of Monkey and Man. Studies of Brain Function.* Berlin: Springer-Verlag, 1982, vol. 8.
- Kakei S, Futami T, and Shinoda Y.** Projection pattern of single corticocortical fibers from the parietal cortex to the motor cortex. *Neuroreport* 7: 2369–2372, 1996.
- Kalaska JF.** Parietal cortex area 5 and visuomotor behavior. *Can J Physiol Pharmacol* 74: 483–498, 1996.
- Kalaska JF, Caminiti R, and Georgopoulos AP.** Cortical mechanisms related to the direction of two-dimensional arm movements: relations in parietal area 5 and comparison with motor cortex. *Exp Brain Res* 51: 247–260, 1983.
- Kalaska JF, Cohen DA, Prud'homme M, and Hyde ML.** Parietal area 5 neuronal activity encodes movement kinematics, not movement dynamics. *Exp Brain Res* 80: 351–364, 1990.
- Khitrova-Orlova TV, Sidiyakin VG, Kulichenko AM, and Pavlenko VB.** Pre-movement activity of neurons in the parietal associative cortex of the cat during different types of voluntary movement. *Neurosci Behav Physiol* 27: 82–86, 1997.
- Leichnetz GR, Smith DJ, and Spencer RF.** Cortical projections to the paramedian tegmental and basilar pons in the monkey. *J Comp Neurol* 228: 388–408, 1984.
- Mountcastle VB.** The parietal system and some higher brain functions. *Cereb Cortex* 5: 377–390, 1995.
- Mountcastle VB, Lynch JC, Georgopoulos A, Sakata H, and Acuna C.** Posterior parietal association cortex of the monkey: command functions for operations within extrapersonal space. *J Neurophysiol* 38: 871–908, 1975.
- Murray EA and Coulter JD.** Organization of corticospinal neurons in the monkey. *J Comp Neurol* 195: 339–365, 1981.
- Niimi K, Matsuoka H, Yamazaki Y, and Katayama T.** Thalamic afferents to the anterior and middle suprasylvian gyri in the cat traced with horseradish peroxidase. *J Hirnforsch* 24: 173–187, 1983.
- Orlovsky GN, Deliagina TG, and Grillner S.** *Neuronal Control of Locomotion. From Mollusc to Man,* Oxford, UK: Oxford Univ. Press, 1999.
- Orlovsky GN and Feldman AG.** Classification of lumbosacral neurons according to their discharges during evoked locomotion (in Russian). *Neurophysiologia* 4: 410–417, 1972.
- Patla AE and Vickers JN.** How far ahead do we look when required to step on specific locations in the travel path during locomotion? *Exp Brain Res* 148: 133–138, 2003.
- Patla AE.** Understanding the roles of vision in the control of human locomotion. *Gait Posture* 5: 54–69, 1997.
- Patla AE, Adkin A, Martin C, Holden R, and Prentice S.** Characteristics of voluntary visual sampling of the environment for safe locomotion over different terrains. *Exp Brain Res* 112: 513–522, 1996.
- Pryor K.** *Lads Before the Wind.* New York: Harper & Row, 1975.
- Reitboeck HJ.** Fiber microelectrodes for electrophysiological recordings. *J Neurosci Methods* 8: 249–262, 1983.
- Rondot P, de Recondo J, and Dumas JL.** Visuomotor ataxia. *Brain* 100: 355–376, 1977.
- Sakata H, Taira M, Murata A, and Mine S.** Neural mechanisms of visual guidance of hand action in the parietal cortex of the monkey. *Cereb Cortex* 5: 429–438, 1995.
- Scott SH, Sergio LE, and Kalaska JF.** Reaching movements with similar hand paths but different arm orientations. II. Activity of individual cells in dorsal premotor cortex and parietal area 5. *J Neurophysiol* 78: 2413–2426, 1997.
- Seal J, Gross C, and Bioulac B.** Activity of neurons in area 5 during a simple arm movement in monkeys before and after deafferentation of the trained limb. *Brain Res* 250: 229–243, 1982.
- Seal J, Gross C, Doudet D, and Bioulac B.** Instruction-related changes of neuronal activity in area 5 during a simple forearm movement in the monkey. *Neurosci Lett* 36: 145–150, 1983.
- Shadlen MN and Newsome WT.** Neural basis of a perceptual decision in the parietal cortex (area LIP) of the rhesus monkey. *J Neurophysiol* 86: 1916–1936, 2001.
- Sherk H and Fowler GA.** Optic flow and the visual guidance of locomotion in the cat. *Int Rev Neurobiol* 44: 141–170, 2000.
- Sherk H and Fowler GA.** Neural analysis of visual information during locomotion. *Prog Brain Res* 134: 247–264, 2001.
- Sherrington CS.** *The Integrative Action of the Nervous System.* New Haven, CT: Yale Univ. Press, 1906.
- Sherrington CS.** Flexion-reflex of the limb, crossed extension reflex, and reflex stepping, and standing. *J Physiol* 40: 28–121, 1910.
- Symonds LL, Rosenquist AC, Edwards SB, and Palmer LA.** Projection of the pulvinar lateral posterior complex to visual cortical areas in the cat. *Neuroscience* 6: 1995–2020, 1981.
- Udo M, Kamei H, Matsukawa K, and Tanaka K.** Interlimb coordination in cat locomotion investigated with perturbation. II. Correlates in neuronal activity of Deiter's cells of decerebrate walking cats. *Exp Brain Res* 46: 438–447, 1982.
- Waters RS and Asanuma H.** Movement of facial muscles following intracortical microstimulation (ICMS) along the lateral branch of the posterior bank of the ansate sulcus, areas 5a and 5b, in the cat. *Exp Brain Res* 50: 459–463, 1983.
- Widajewicz W, Kably B, and Drew T.** Motor cortical activity during voluntary gait modifications in the cat. II. Cells related to the hindlimbs. *J Neurophysiol* 72: 2070–2089, 1994.
- Wiesendanger M.** The pyramidal tract. Its structure and function. *Handb Behav Neurobiol* 5: 401–491, 1981.
- Wiesendanger R, Wiesendanger M, Ruegg DG.** An anatomical investigation of the corticopontine projection in the primate (*Macaca fascicularis* and *Saimiri sciureus*). II. The projection from frontal and parental association areas. *Neuroscience* 4: 747–765, 1979.
- Yumiya H and Ghez C.** Specialized subregions in the cat motor cortex: anatomical demonstration of differential projections to rostral and caudal sectors. *Exp Brain Res* 53: 259–276, 1984.