

Proprioceptive Sensory Neurons of a Locust Leg Receive Rhythmic Presynaptic Inhibition during Walking

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Mechanosensory neurons from a proprioceptor (the femoral chordotonal organ) signal the movements and positions of the femorotibial joint of a locust leg. Intracellular recordings from these neurons during walking show that their spikes are superimposed on a depolarizing synaptic input generated near their output terminals in the CNS. The depolarization consists of a rhythmic synaptic input at each step, and a sustained input that begins before walking commences. In different sensory neurons, which signal particular features of the movement, the rhythmic depolarization occurs at distinct times during either the swing or stance phases of the step cycle. The depolarizing input is timed to coincide with the greatest spike response of a sensory neuron. The input is associated with a conductance change, appears to reverse just above resting potential, and thus has similar properties to the presynaptic inhibition in these same neurons during imposed joint movements (Burrows and Laurent, 1993; Burrows and Matheson, 1994). Three sources could contribute to these inputs: (1) interactions between sensory neurons of the same receptor signaling the same movement, (2) signals from different receptors in the same leg and other legs, and (3) outputs of central neurons involved in generating walking. When the leg, whose movements the sensory neurons signal is removed, both the sustained and rhythmic synaptic inputs persist. Sensory neurons in isolated ganglia treated with pilocarpine are also depolarized in phase with a rhythmic pattern expressed in leg motor neurons, indicating that central neurons must contribute.

The maintained synaptic input to the terminals means that the overall effectiveness of the sensory spikes in evoking EPSPs in postsynaptic neurons will be reduced during walking, and the rhythmic component means that the spikes from particular sensory neurons will be further reduced at particular phases of the step cycle that they signal best.

[Key words: grasshopper, presynaptic inhibition, proprioceptor, walking, central pattern generator, primary afferent depolarization]

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Mechanosensory neurons in many animals receive presynaptic inputs close to their output synapses that reduce the effectiveness of their spikes in signaling to postsynaptic neurons. The widespread occurrence of these inputs is probably attributable to the selective control they permit over the action of certain sensory neurons while leaving the excitability of postsynaptic neurons unchanged. These inputs may serve many roles in matching the sensory signals to the particular behavioral context in which movements are performed. Various, they can protect the sensory synapses from habituation so that they are ready to signal stimuli received immediately after a movement that will also have stimulated them (Krasne and Bryan, 1973; Levine and Murphey, 1980); they can sharpen the receptive fields of cutaneous sensory neurons (Janig et al., 1968; Schmidt, 1971), or the response properties of tactile sensory neurons (Blagburn and Sattelle, 1987); they can help to ensure the increased excitation of one set of motor neurons and a reduction of others (Rudomin et al., 1983; Rudomin, 1990); they can act as a gain control mechanism that prevents saturation of the response of postsynaptic neurons when many sensory neurons are active at once (Burrows and Matheson, 1994); and finally, they can reduce hysteresis in the responses of central neurons (Hatsopoulos et al., 1995). These inputs also occur rhythmically during fictive locomotory rhythms in paralyzed cats (Gossard et al., 1990, 1991) and in isolated ganglia of crustaceans (Sillar and Skorupski, 1986; El Manira et al., 1991). They could thus be a part of the mechanisms by which the neurons generating the motor rhythm modify the effectiveness of sensory transmission according to the phase of the movement (Sillar and Skorupski, 1986; Gossard et al., 1990). This means that the reflex responses to the same stimulus have different forms depending on the phase of the step cycle in which they occur (cat, Forssberg et al., 1977; fish, Grillner et al., 1977; lobster, Davis, 1969; crayfish, Skorupski and Sillar, 1986; locust, Pearson et al., 1983). It is assumed that similar inputs occur during normal walking, because the inhibition of Ia sensory neurons of human muscles that are contracting during a particular phase of the movement is reduced while that of the antagonists is increased (Capaday and Stein, 1986, 1987; Hultborn et al., 1987).

To understand more about the role these synaptic inputs play in locomotion, we have recorded intracellularly from proprioceptive sensory neurons of the locust during real, but restrained walking. The locust is alert and only a single thoracic ganglion is exposed to allow access to the CNS (Wolf, 1990, 1992). The movements of the leg joints are monitored by a number of receptors, prominent among which is a chordotonal organ at the

Received Dec. 27, 1994; revised Mar. 7 1995; accepted Mar. 8, 1995.

This work was supported by SFB 156 of the Deutsche Forschungsgemeinschaft and by grants from the NIH (NS 16058-14) and the BBSRC (UK) to M.B. H.W. is a Heisenberg Fellow of the DFG and M.B. was an Alexander von Humboldt awardee during the experimental work in Germany. We thank Prof Werner Rathmayer for the hospitality of his laboratory. We also thank Dr Tom Matheson for the use of his data that are incorporated in Fig. 8, and Dr Gilles Laurent for his help and hospitality during the stay of M.B. in his laboratory that resulted in the data presented in Fig. 9. We also thank U. Bässler, A. Büschges, T. Matheson, P. Newland, A. Norman, and W. Rathmayer for their many helpful comments on the manuscript.

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femorotibial joint. Sensory neurons from this receptor in a hind leg receive depolarizing inhibitory inputs with a reversal potential close to resting potential. These potentials can be mimicked by GABA (Burrows and Laurent, 1993) and many of the input synapses onto the terminals of these neurons also show GABA-like immunoreactivity (Watson et al., 1993). During movements of this joint the synaptic inputs occur when the spike response of a sensory neuron is greatest and are caused by GABAergic interneurons that are excited by other sensory neurons from the same receptor responding to the same stimulus (Burrows and Matheson, 1994). The inputs reduce the excitability of the terminals, and the amplitude of the sensory spikes so that the effectiveness of monosynaptic connections with leg motor neurons is reduced (Burrows and Matheson, 1994).

Intracellular recordings made during walking from sensory neurons of the same receptor of a middle leg now show that each receives a synaptic input that causes a tonic depolarization throughout walking and a rhythmic depolarization in time with a particular phase of the step cycle.

Materials and Methods

Adult male and female locusts, *Locusta migratoria*, from a crowded colony in Konstanz, Germany, were used for analyses of walking as described in detail by Wolf (1990). Briefly the procedure was as follows. A locust was glued with a resin and beeswax mixture by the sides of the thorax to a steel holder. The hind legs were induced to autotomize and the terminal claws of the front and middle pairs of legs were trimmed so that they did not become caught on the treadmill. The locust, with its ventral surface uppermost, was then placed inside a pair of linked treadwheels that were counterbalanced so that the locust had to push against its own body weight to lift and rotate them. The eyes were not covered as in previous experiments by Wolf (1990).

Movements of the right middle leg were monitored by attaching a small piece of foil to the proximal end of the tibia that reflected a light beam that was focused onto a position-sensitive diode (von Helversen and Elsner, 1977). This gave an accurate representation of the swing (protraction) and stance (retraction) phases of the leg movements in the horizontal plane, as determined chiefly by the rotation of the coxa about the body. The leg movements were also recorded by a video camera and the movements of the right middle leg were traced from single frames (40ms intervals) to reveal the sequence of joint movements during the step cycle.

The mesothoracic ganglion was exposed by removing a small portion of the overlying cuticle of the sternum, and was supported on a stainless steel platform fashioned to fit snugly around it and its nerves. A light suction was applied to the dorsal (lower) surface of the ganglion through a hole in the supporting platform to aid stability. Stability was improved further by gluing (Histoacryl blau, Braun Melsungen) nerve 5 of the right middle leg to a small stainless steel hook held in a manipulator and placed about 1 mm from the edge of the ganglion. The whole ganglion was bathed in hemolymph with only occasional supplements of locust saline (based on Clements and May, 1974, but with the sucrose omitted).

Intracellular recordings were made from the axons of sensory neurons from the femoral chordotonal organ just as they entered the mesothoracic ganglion. Electrodes had DC resistances of 40–60 M Ω and were filled with 2 M potassium acetate. The sensory neurons could be identified as being from the femoral chordotonal organ by their responses to imposed movements of the femorotibial joint and by their failure to respond to movements of any of the other joints or to stimulation of exteroceptors. These stimuli were applied before walking sequences were evoked, but in these intact animals give only an approximate picture of the response properties of these sensory neurons. It was, however, possible to determine whether a sensory neuron responded to the position of the femorotibial joint or to the velocity of extension or flexion. In some experiments the neurons were labeled by the intracellular injection of Lucifer yellow. Neurons labeled in this way always had both medially and laterally projecting branches in the neuropil of the mesothoracic ganglion that are characteristic of sensory neurons from the femoral chordotonal organ (Matheson, 1992). Current was injected through the recording electrode to alter the membrane potential

Table 1. Properties of the 42 sensory neurons recorded

Response properties of sensory neuron	Flexion sensitive	Extension sensitive	Extension and Flexion sensitive
Position	2	2	—
Position and velocity	5	5	—
Velocity	6	9	—
Velocity/acceleration	2	1	3
Other sensory neurons	4 from other leg receptors	3 from femoral chordotonal organ that were not characterized fully	

and consequently the amplitude of the synaptic input to the sensory neurons. The current was balanced with a bridge circuit so we do not know to what membrane potential each afferent was shifted by the injected current. Consequently, we do not compare the amplitude of the depolarizing inputs in different neurons. The figure subscripts indicate whether the recordings are at normal or a more hyperpolarized membrane potential, and whether the peaks of the spikes have been truncated so that the underlying synaptic input could be displayed more clearly.

The femoral chordotonal organ of a middle leg consists of a proximal part containing the cell bodies of about 40 sensory neurons and a distal part containing several hundred smaller cell bodies (Field and Pflüger, 1989). Each part is suspended by a separate strand of connective tissue from the anterior wall of the femur and from the flexor muscle, but both join the same apodeme that runs the length of the femur to insert on the tibia just dorsal to the pivot point of the femorotibial joint. This arrangement means that flexion of the joint will stretch the apodeme and extension will unload it. The anchorage to the flexor tibiae muscle also means that the sensory neurons are excited by isometric contractions of this muscle with their response depending on the position of the joint and hence on the extent to which the muscle is stretched (Burns, 1974). The larger neurons in the proximal part signal movements of the femorotibial joint and control the motor responses to imposed movements of the joint. A few of the smaller proximal neurons also provide this sort of information, but the majority respond to vibrations (Field and Pflüger, 1989).

Extracellular recordings were also made from the anterior coxal rotator muscle (number 92; Snodgrass, 1929) of the right middle leg with 50- μ m-diameter copper wires insulated but for their tips, to give a further stable indication of the swing phase of the stepping cycle. All recordings of electrical activity and leg position were stored on magnetic tape for later analysis and display on a Gould ES 1000 chart recorder.

Locusts from which the recordings are presented walked readily in response to a brief tactile stimulus to the ventral surface of the abdomen that ended before the first step was taken, or sometimes walked when no stimulus had been applied. These walking sequences would typically last for 10–30 steps at stepping frequencies of 0.75–3 Hz, with occasional longer sequences being expressed. Locusts walked repeatedly throughout the 1–3 hr of each experiment. The analysis presented here is based on stable recordings made in 20 locusts from 38 sensory neurons of the femoral chordotonal organ and four other sensory neurons (Table 1). All experiments were performed at temperatures of 28–32°C.

Recordings were also made from sensory neurons of the femoral chordotonal organ in isolated ganglia of *Schistocerca americana* maintained at 20–22°C. The meso- and metathoracic ganglia were dissected out together with the nerve to the femoral chordotonal organ of a hind leg and placed in a small dish of saline. Electrical stimulation of this nerve as it emerged from the organ allowed the impaled sensory neurons to be identified. Slow rhythms in leg motor neurons were induced by introducing 10^{-4} pilocarpine into the saline (Ryckebusch and Laurent, 1993). Some recordings were also made from sensory neurons of the femoral chordotonal organ of the hind leg of *Schistocerca gregaria* (see Burrows and Matheson, 1994, for details) during imposed movements of the different legs. We have observed no differences in the responses of the sensory neurons in the three closely related species that have been used, nor in the responses of the sensory neurons from the middle and hind legs.

Results

Sensory neurons are active at different phases of the step cycle in walking

In upright walking, the femorotibial joint of a middle leg is flexed during the swing phase as the leg is swung forward by rotation at the coxa, and extended during the stance phase when the foot (tarsus) is in contact with the ground and pushing the body forward (Burns, 1973; Burns and Usherwood, 1979). Video analysis of walking in the inverted posture in the apparatus used for the recordings presented in this article indicates a similar relationship between femorotibial movements and the two phases of the step cycle (Fig. 1A). Thus, the femorotibial joint is flexed during the swing phase and extended during the stance phase. The tibia may be extended toward the end of the swing phase if the leg is moved beyond a position perpendicular to the body axis. During the stance phase the tibia is then initially flexed before the main extension movement. As in untethered, upright walking, there is considerable variation in the form of many of the sequential steps.

Sensory neurons of the femoral chordotonal organ signal the movements and positions of the femorotibial joint during imposed changes (Usherwood et al., 1968; Hofmann and Koch, 1985; Hofmann et al., 1985; Zill, 1985; Matheson, 1990). Each sensory neuron codes a particular feature of the movement in its spike discharge, so that some respond to extension and others to flexion. Within these two directions different neurons signal the velocity or acceleration of the movement over particular ranges of joint angles, others signal the position, and others signal combinations of these features.

These neurons also signal the active movements of the joint during walking and their different response properties mean that they are active at different times during the step cycle; three examples are shown in Figure 1B–D. The spikes are initiated at the chordotonal organ as a result of the active movements during walking and are conducted orthodromically toward the CNS where they were recorded at the entrance to the mesothoracic ganglion. The first sensory neuron started to spike during the stance phase when the tibia was extending and reached its highest frequency toward the end of this phase (Fig. 1B). It also produced a brief burst of spikes during the latter part of the swing phase, presumably as the tibia extended, but then was silent. The number and frequency of its spikes during the stance phase and the persistent spikes when the tibia remained in an extended position at the end of the walking sequence indicated that this neuron coded extended positions of the joint and the velocity of extension. These response properties, as for all neurons studied, were verified by imposed movements of the femorotibial joint. By contrast, the second neuron spiked predominantly during the swing phase when the tibia was flexing with a few of its spikes, at lower frequency, extending into the stance phase (Fig. 1C). It responded to the velocity of flexion movements and position over the more flexed angles of the joint. The third neuron spiked only a few times at low frequency during the swing phase and the first part of the stance phase (Fig. 1D). It responded only to high-velocity movements.

Sensory neurons receive sustained and rhythmic depolarizing inputs during walking

At the normal membrane potential of the sensory neurons, the spikes that occurred during walking could often be seen to be superimposed on small fluctuations of the membrane potential

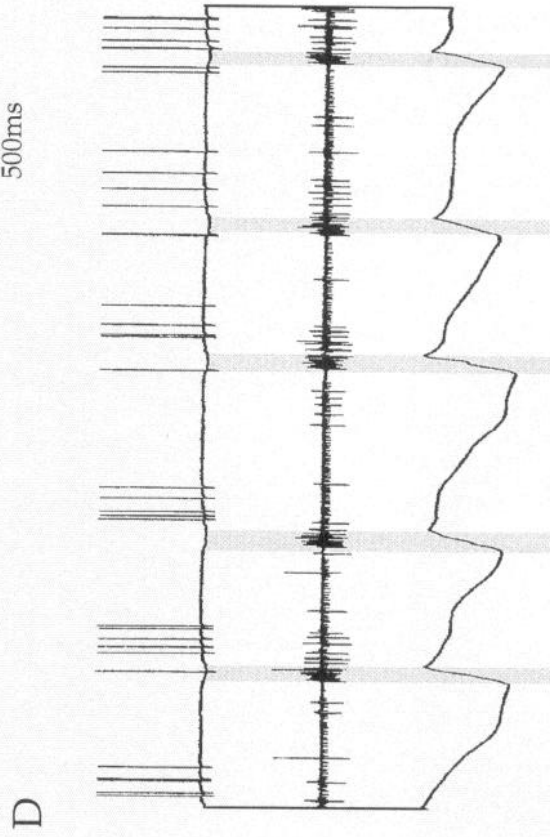
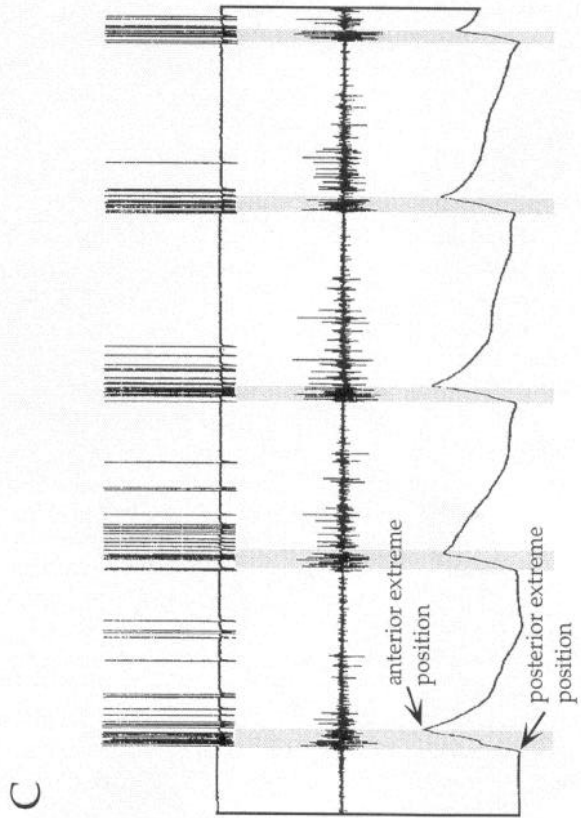
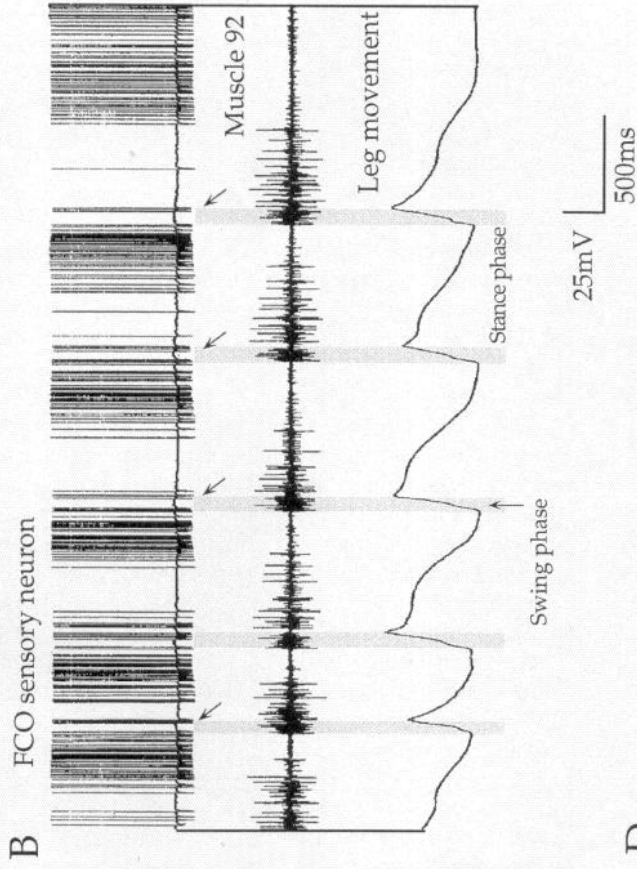
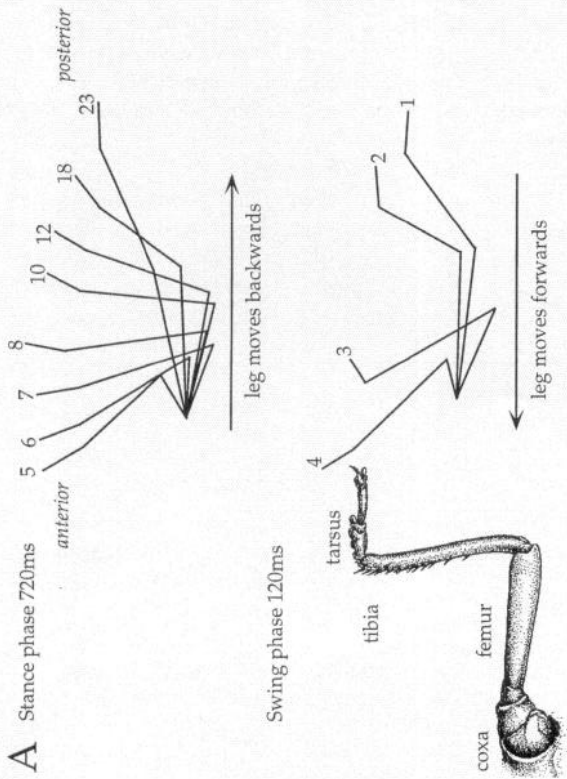
(Fig. 2A; see also Fig. 1B,D). These shifts in potential must result from inputs to the terminals of the sensory neurons within the CNS and close to the recording site. Hyperpolarizing a sensory neuron with a steady current accentuated these shifts in potential (Fig. 2B), and revealed that they were present in all sensory neurons of the femoral chordotonal organ that we recorded. The hyperpolarizing current also revealed that the input was expressed in two ways.

First, the depolarizing input began before the walking movements commenced and before the sensory neuron had started to signal the movement of the femorotibial joint by its spikes (Fig. 3A*i,ii*; B). The depolarizing input accompanied the first increase in the activity of the coxal muscle that was used as an indicator of the swing phase, and often preceded the movements of the leg that were recorded. Sometimes the input would even drive the membrane to a maintained level before the sensory spikes began (Fig. 3A). This depolarization was maintained for the duration of walking so that all the spikes that the sensory neuron produced were superimposed on this plateau of depolarizing input. Only at the end of walking did the membrane potential of the sensory neuron return to its original level (Fig. 2B), often taking as long as 2 sec to recover fully.

Second, the depolarization also occurred rhythmically in phase with each step (Figs. 2B, 3B,C). It is upon the depolarizing phase of this rhythmic depolarization that most of the spikes, and all of those that occurred at the highest frequencies were superimposed. Some of the depolarization was undoubtedly caused by the spikes themselves, especially when these occurred at high frequencies, and was also accentuated by the injection of hyperpolarizing current. Nevertheless, even in neurons that spiked many times at high frequency during a step, the membrane was maintained at a depolarized level during pauses between the spikes and did not repolarize as would be expected if the spikes themselves were the only cause of the depolarization (Fig. 2B). In neurons that spiked less often, the rhythmic depolarization clearly preceded and often outlasted their spikes (Fig. 3B). The rhythmic input occurred during every step cycle of the leg movements and without any failures. The tight coupling between the input and the step cycle was particularly well illustrated whenever a swing phase was interrupted and was then followed rapidly by another, smaller swing movement, as might be expected if the leg had encountered an obstacle (Fig. 3C). On such occasions the sensory neuron received an extra wave of depolarizing input but did not always spike, presumably because the movement was not of the right form.

The rhythmic input occurs at different times in the step cycle in different sensory neurons

In general there was a good correlation between the response properties of the neurons as determined by imposed movements of the tibia, the timing of their spikes during the step cycle, and the timing of the depolarizing inputs. These inputs usually occurred during the phase when the sensory neuron was signaling a movement or position with its highest frequency of spikes, so that they occurred at different times during the step cycle in different neurons. Four examples illustrate the different times during a step cycle when inputs were most frequently observed (Fig. 4). First, in some neurons the depolarizing input occurred during the stance phase (Fig. 4A). It began at the start of stance, or just before the end of the preceding swing, and reached its peak in the first half of the stance phase when most of the spikes also occurred. The swing phase therefore corresponded to the



troughs between the rhythmic depolarizations. Second, in other neurons the depolarizing input also occurred during stance, beginning at the start of this phase but then declining only slowly (Fig. 4B). The swing phase again corresponded to the troughs in the depolarization. In a third group of sensory neurons, the rhythmic depolarizations occurred during the swing phase when a sensory neuron produced a high-frequency burst of spikes (Fig. 4C). The input preceded the bursts of spikes and declined during the first part of the stance phase, so that most of the sensory spikes that occurred during this phase were not superimposed on a rhythmic input. In a fourth group of sensory neurons, the rhythmic depolarizations spanned part of both the stance and the swing phase (Fig. 4D). The input began gradually during the middle part of a stance phase, continued into the swing phase to reach a peak at the end of this phase, and then declined abruptly at the start of the next stance phase. The maximum frequency of spikes preceded the peak of the depolarizing input, and the few spikes at the beginning of the stance phase occurred in the absence of the rhythmic depolarizing input. If the swing movement paused with the leg in a less anterior position than usual, then the rhythmic input stopped, the sensory neuron repolarized, and the spikes also stopped.

The input is associated with a conductance change

An explanation of the depolarizations that occurred during walking that is consistent with previous studies (Burrows and Laurent, 1993) is that they are caused by synaptic inputs to the terminals of the sensory neurons. The amplitude of the depolarizations was dependent on the membrane potential of a sensory neuron, but at the usual resting potential of -70 to -75 mV (see Burrows and Laurent, 1993) the inputs were always depolarizing. Hyperpolarizing a sensory neuron increased the amplitude of the inputs, whereas depolarizing it from normal resting potential reduced their amplitude. These observations suggest the potentials are caused by a change in ionic conductance that has a reversal potential more positive than resting potential. To test if the inputs were associated with a conductance change, brief repetitive pulses of hyperpolarizing current were injected into sensory neurons before, during, and after walking movements (Fig. 5). The current/voltage relationship of these sensory neurons is linear at potentials negative to resting potential (Burrows and Laurent, 1993). In the absence of a movement, the membrane showed only slight fluctuations in resistance associated with the low level of small depolarizations that probably were caused by a synaptic input. When walking started, the resistance of the membrane fell by up to 50% during the swing phase, as indicated by the smaller voltage changes caused by

the injected pulses of current (Fig. 5A). These resistance changes were detected in sensory neurons held at their normal membrane potential, but could be more easily associated with the depolarizing inputs when these were accentuated by the injection of a steady hyperpolarizing current. The resistance of the membrane fluctuated in time with the step cycle and with the concomitant rhythmic synaptic input; the resistance was lowest when the depolarization was greatest, and highest when the membrane was at its most repolarized level. This is illustrated by a quantitative evaluation of recordings from one sensory neuron during 54 step cycles (Fig. 6). Thus, for a sensory neuron that was depolarized during every stance phase and whose membrane repolarized during every swing phase, the resistance of its membrane was between 40% and 50% lower during the stance phase than during the swing phase (Figs. 5B, 6). This indicates that the rhythmic depolarizations are caused by inputs associated with a conductance increase, and that the repolarizations most likely result from a transient cessation of these inputs that allows the membrane to repolarize.

All of these observations are consistent with the depolarizations being caused by synaptic inputs to the terminals of the sensory neurons that are associated with a conductance change and with a reversal potential close to normal resting potential (Burrows and Laurent, 1993). The spikes that invade the terminals of a sensory neuron during walking will thus be superimposed on this synaptic input and will have to invade terminals whose resistance has been lowered and whose membrane is shunted close to normal resting level. Nevertheless, neither the sustained nor the rhythmic input were associated with a reduction in the amplitude of the sensory spikes, other than that which can be explained by the occurrence of high instantaneous frequencies of spikes. The recordings are, however, made in the axons as they enter the ganglion at sites some 400–600 μm away from where the terminals of the sensory neurons make output synapses with other neurons. In previous recordings made closer to the terminals of these neurons, a clear reduction in spike amplitude does accompany the depolarizing inputs (Burrows and Matheson, 1994).

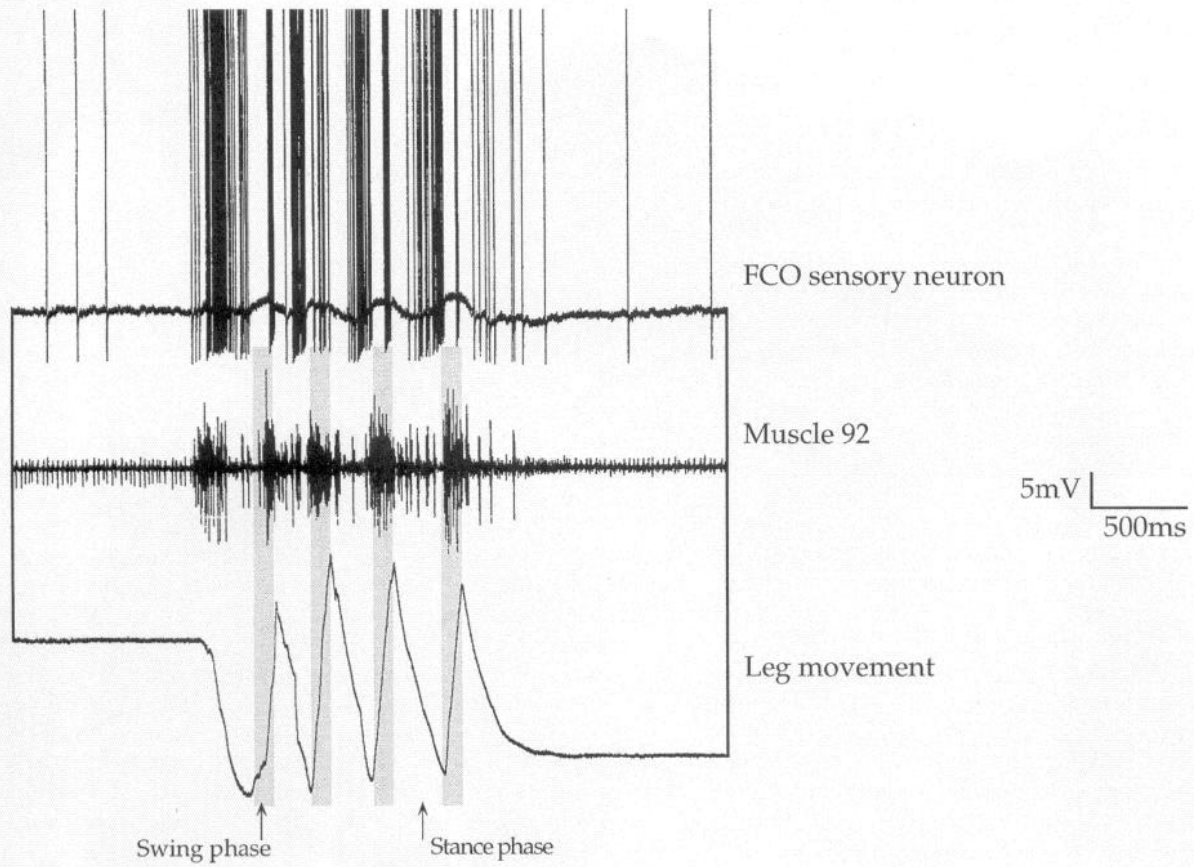
What is the source of the synaptic input?

The sustained and the rhythmic depolarizing inputs that occur during walking may be derived from at least three sources: (1) from interactions that are initiated by spikes in other sensory neurons of the same receptor responding to the same movements (Burrows and Laurent, 1993; Burrows and Matheson, 1994)—these potentials are generated by interneurons that are excited by the other sensory neurons; (2) from sensory signals generated

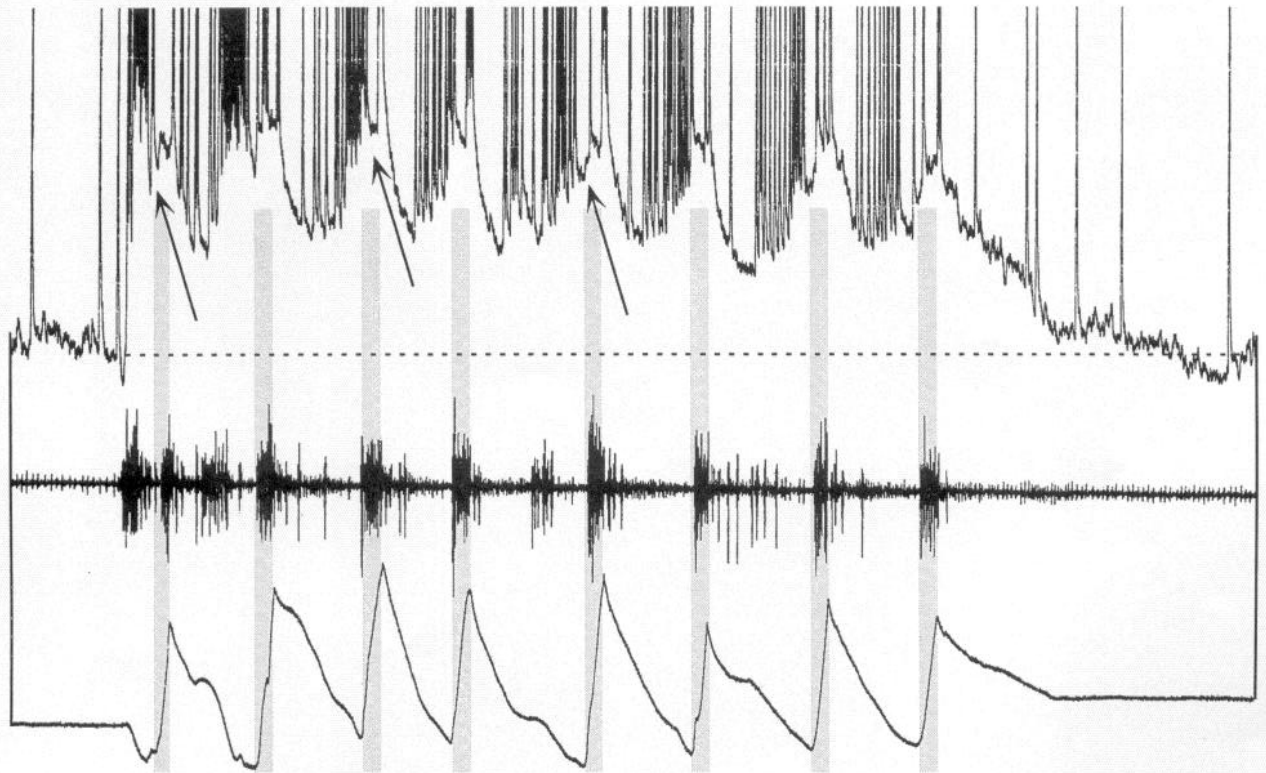
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Figure 1. Sensory neurons from the femoral chordotonal organ with different response properties spike at different times during a step cycle of walking. *A*, Movements of the leg during one cycle of walking to show that the femorotibial joint is flexed during the swing phase and extended during the stance phase. The tracings of the leg movements were made from a video recording with the camera positioned at right angles to the right side of the locust. The numbers indicate the frame numbers from the video and are thus separated by 40 msec. *B* and *C*, Extracts of intracellular recordings from sensory neurons during sequences of forward walking. The sensory neurons from the femoral chordotonal organ (*FCO* sensory neuron) are all recorded at their normal membrane potential and their spikes are displayed at full amplitude. The movements of the right middle leg in the horizontal plane are shown on the first traces; during forward walking an upward deflection indicates that the leg is lifted from the ground and moved forward relative to the body (*Swing phase*), and a downward deflection when it is in contact with the ground and moved backward relative to the body (*Stance phase*). *B*, A sensory neuron (*second trace*) that spikes during the stance phase, coding both the velocity and position of extension of the tibia. It also produces a brief burst of spikes during the end of the swing phase (*arrows*) when the tibia may extend. *C*, A neuron recorded sequentially from the same animal that spikes phasically during the swing phase, and codes for velocity of flexion movements and position over the more flexed angles of the joint. *D*, A neuron in a different locust that spikes only a few times during each step, preferentially at the start of swing and during early stance. *I* spikes during both flexion and extension movements. The middle traces show the extracellularly recorded activity in the right anterior coxal rotator muscle of the right middle leg (muscle 92), which begins to spike at the start of the swing phase. These conventions are also used in subsequent figures.

A Normal membrane potential



B Hyperpolarised



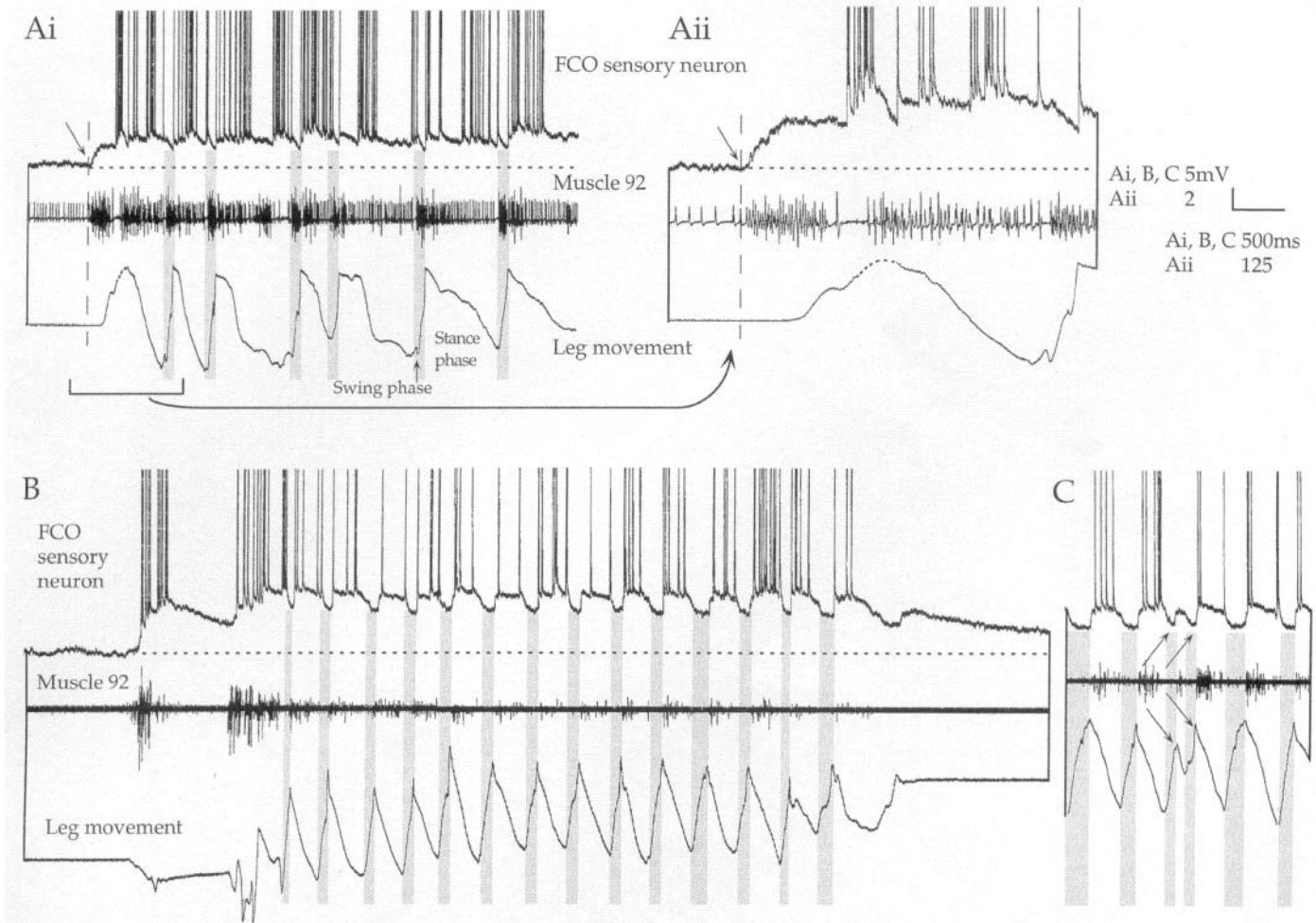


Figure 3. The depolarization of sensory neurons during walking consists of a sustained and a rhythmic input. *Ai*, When walking starts and before the sensory neuron has begun to spike, it receives a depolarizing synaptic input (arrow) that is maintained throughout the walking sequence. *Aii*, An expanded portion of *Ai* shows that the initial depolarization of the sensory neuron occurs before a change in the activity of a coxal muscle and before any movement of the leg is recorded. *B*, Another sensory neuron recorded in another locust is also depolarized at the start of walking, but superimposed on this sustained input are clear rhythmic depolarizations during each stance phase of the step cycles. *C*, A section of another walking sequence from the same neuron in which one swing phase was terminated prematurely and was then quickly followed by a second swing phase movement. The synaptic input to the sensory neuron matched this pattern of leg movement, but the additional swing movement was not now signaled by spikes. The neurons in *A–C* were from two locusts, were both held hyperpolarized by a steady current, and their spikes have been truncated.

in other receptors of the same or different legs—the signals from the legs of other segments must be conveyed to the ganglion controlling the middle legs by intersegmental interneurons; (3) from central interneurons that are involved in generating some aspects of the walking motor pattern—to assess the contribution of these different possible sources of inputs we carried out the following experiments.

Synaptic inputs when a leg is removed. To test whether the synaptic inputs could arise from spikes in other sensory neurons of the femoral chordotonal organ itself, or from other receptors

in the same leg, the leg was removed at the coxa (Fig. 7). A sensory neuron was first recorded with the right middle leg intact to determine its response properties, the pattern of its spikes and its synaptic inputs during walking. This leg was then removed and the remaining pattern of synaptic inputs that the sensory neuron received during walking was recorded. Two examples are illustrated in Figure 7. In the first, the sensory neuron was depolarized rhythmically during each stance phase of walking (Fig. 7*Ai*). When the leg had been removed, rhythmic depolarizations persisted during walking and could be seen to occur at

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Figure 2. Sensory neurons receive a depolarizing input during walking. *A*, A short walking sequence in which a sensory neuron that responds to extension movements of the tibia spikes toward the end of the stance phase and at the end of the swing phase. A depolarizing input is apparent at each step cycle even though the sensory neuron is recorded at its normal membrane potential. *B*, The same neuron is now held hyperpolarized by a steady current during another short walking sequence. At the start of walking the membrane depolarizes and stays depolarized throughout, only subsiding to its original potential (indicated by horizontal dashed line) when walking ceases. At each step the membrane depolarizes. The arrows point to some of the pauses between spikes where the membrane remains at a depolarized level. The peaks of the spikes have been truncated.

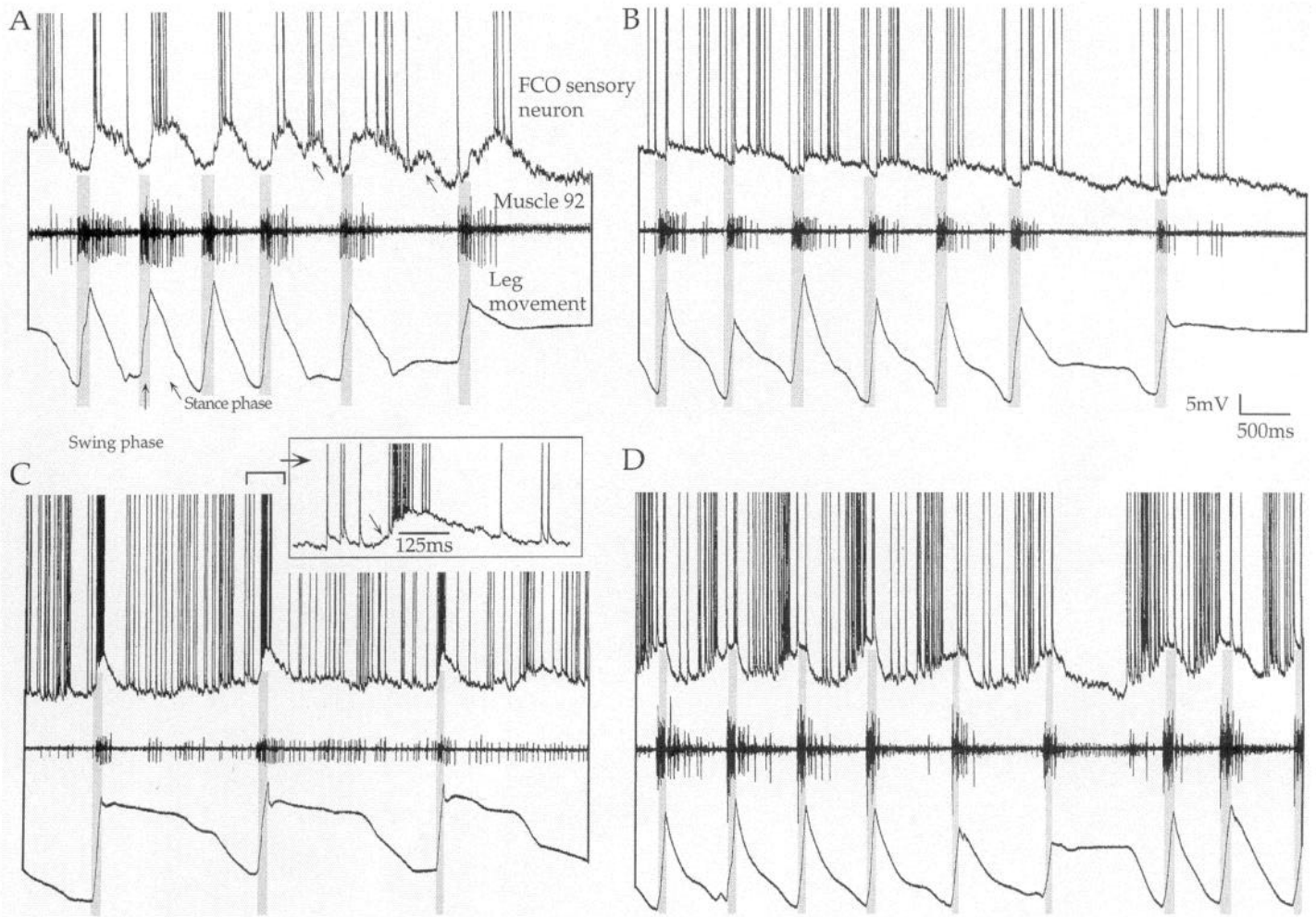


Figure 4. The rhythmic depolarizing input to sensory neurons that signal different features of tibial movement occurs at different times during the step cycle. *A*, The rhythmic input to one sensory neuron occurs during the stance phase, beginning at the transition from the swing to the stance phase and ending before the transition to the swing phase. The neuron spikes during the stance phase and codes extension movements of the tibia. Arrows indicate extra waves of depolarization associated with slow flexion movements of the leg. *B*, The rhythmic depolarizations in a second sensory neuron begin at the start of the swing phase and decline gradually during the stance phase. The neuron codes the velocity of extension movements over a restricted range of femorotibial angles. *C*, The rhythmic depolarizations in a third sensory neuron occur during the swing phase when the sensory neuron spikes most rapidly in coding the velocity of tibial flexion movements and more flexed tibial positions. The inset shows that the depolarization precedes the burst of spikes. *D*, The rhythmic depolarizations in a fourth sensory neuron begin toward the end of the stance phase, reach a peak during the swing phase but end before the next stance phase begins. The neuron codes the velocity of tibial extension movements. The four neurons were recorded in different locusts, each is held hyperpolarized by a steady current, and their spikes have been truncated.

a similar phase of the step cycle by reference to the activity in a coxal muscle (Fig. 7*Aii*) and were associated with rhythmically changes in the conductance of the membrane (Fig. 7*Aiii*). The amplitudes of these rhythmic depolarizations were similar to those when the leg was intact and each was associated with a reduction in the resistance of the membrane. In the second example, the sensory neuron was depolarized before walking began and then received a rhythmic synaptic input during each stance phase (Fig. 7*Bi*). When the leg was removed, the sustained input still occurred at the onset of walking, and continued throughout it, and the rhythmic depolarizations at each step cycle, though less pronounced, were still present (Fig. 7*Bii*).

Once a leg is removed all spikes from receptors distal to the cut are abolished. The persistence of the synaptic inputs in the absence of these sensory signals indicates they must be initiated by sensory signals from the stump of the right middle leg, from the remaining legs, or from central neurons controlling the walk-

ing rhythm (sources 2 and 3 above). Inputs from other sensory neurons from the same chordotonal organ, or other receptors, could contribute during normal walking when the leg is intact, and could explain the changes in the inputs when the leg is removed.

Synaptic inputs caused by stimuli to the other legs. In a locust that is not walking, stimulation of one leg leads to synaptic inputs to sensory neurons of the femoral chordotonal organ of another leg (Fig. 8). Most of these observations were made with the locust immobilized on its back, but similar effects were also observed when a locust was mounted in the apparatus where walking was studied. None of the sensory neurons of the distal joints of a leg project to the ganglia of other segments, so these signals must be conveyed by intersegmental interneurons. Recordings from a sensory neuron of the chordotonal organ of a hind leg showed that it received a synaptic input when any of the other five legs were stimulated mechanically (Fig. 8*A–E*).

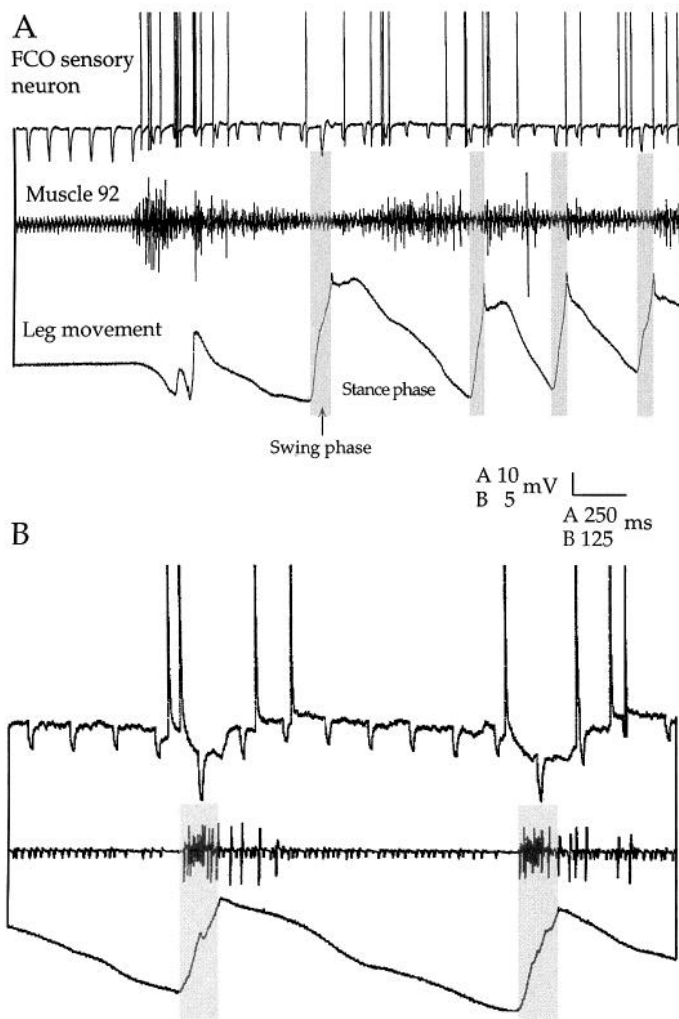


Figure 5. Conductance changes occur in the membrane of a sensory neuron during the depolarizing inputs. *A*, Repetitive pulses of hyperpolarizing current are injected into a sensory neuron at its normal resting potential before the locust begins to walk. During walking the membrane resistance falls as indicated by the smaller voltage deflections caused by the injected current. *B*, Hyperpolarizing current is injected into the sensory neuron, and an expanded record shows that the conductance change rises during the stance phase and falls during the swing phase. All recordings were from the same sensory neuron in the same locust and their spikes have been truncated.

Thus, during normal walking these inputs could contribute to the depolarization of a sensory neuron from a proprioceptor of a different leg.

Synaptic inputs in an isolated ganglion that expresses a rhythm in leg motor neurons. All contributions of sensory feedback to the synaptic inputs were eliminated by isolating the meso- and metathoracic ganglia from the rest of the CNS and from any effectors and sensory neurons in the periphery. Such ganglia isolated in a dish of saline express a slow motor rhythm when treated with the muscarinic agonist pilocarpine (Ryckebusch and Laurent, 1993). The motor pattern is recorded in the motor neurons that innervate the muscles of a leg and that are activated in similar phase relationships to those that occur during walking. Intracellular recordings were made from 10 sensory neurons of the femoral chordotonal organ in such rhythmically active preparations but their response properties could not be

determined as the leg was no longer present. They were identified by their spikes that were evoked by electrical stimulation of the nerve supplying the chordotonal organ, which had been dissected from the leg to the point where it enters the organ itself. Recordings from such identified chordotonal sensory neurons showed that they were depolarized at the same time as a flexor tibiae motor neuron (Fig. 9*A,B*). Recordings over a longer period than shown in Figure 9 revealed that the depolarizations occurred rhythmically and that they were always linked in the sensory and motor neurons. The synaptic inputs in these isolated ganglia could only have come from central neurons that participate in generating the motor rhythm. This experiment demonstrates that central interneurons can provide a synaptic drive to the sensory neurons that is in time with the rhythm that they generate in the motor neurons.

Discussion

During walking, we have been demonstrated that synaptic inputs are generated in sensory neurons from the femoral chordotonal organ close to their terminals. These inputs began at the time when walking started, held the sensory neurons depolarized throughout walking and were modulated rhythmically at a particular phase of the step cycle. In different sensory neurons the rhythmic depolarizations occurred at different phases of the step cycle but always corresponded with the greatest spike response of these sensory neurons. The synaptic inputs in all these types of sensory neuron should alter the efficacy of their spikes in transmitting signals to postsynaptic neurons. This will mean that the overall effectiveness of the sensory spikes will be reduced as soon as walking starts, and then reduced further at a particular phase of each step cycle.

The source of the input to the sensory neurons

Three possible sources for the synaptic inputs that occur during walking are implicated.

First, they could result from the activation of interneurons by spikes in other sensory neurons from the femoral chordotonal organ responding to the same movements (Burrows and Matheson, 1994). These interneurons appear to mediate their effects by the release of GABA. Inputs generated by these interactions are prominent during both active and passive movements of a joint. When the leg that contained the chordotonal organ whose sensory neurons were recorded was removed, both sustained and rhythmic synaptic inputs were still present during walking and these could not therefore have been caused by spikes in other chordotonal sensory neurons. There were, however, some differences in the inputs with the leg removed as compared to those with the leg intact. In one sensory neuron the sustained component was absent, and in a second the rhythmic component was reduced. These differences could be attributed to the absence of other sensory spikes, and to possible alterations in the walking pattern due to removal of a leg. It is likely therefore that in walking the spikes in other chordotonal sensory neurons do contribute to synaptic inputs in others.

Second, the inputs could be caused by intersegmental interneurons signaling the movements of the other legs. Mechanical stimulation of the other legs did result in inputs to the sensory neurons in quiescent animals. This indicates that during normal walking the sensory signals from one leg can result in inputs to sensory neurons of other legs.

Third, the inputs could be caused by central neurons involved in generating the motor rhythm. When the ganglia controlling

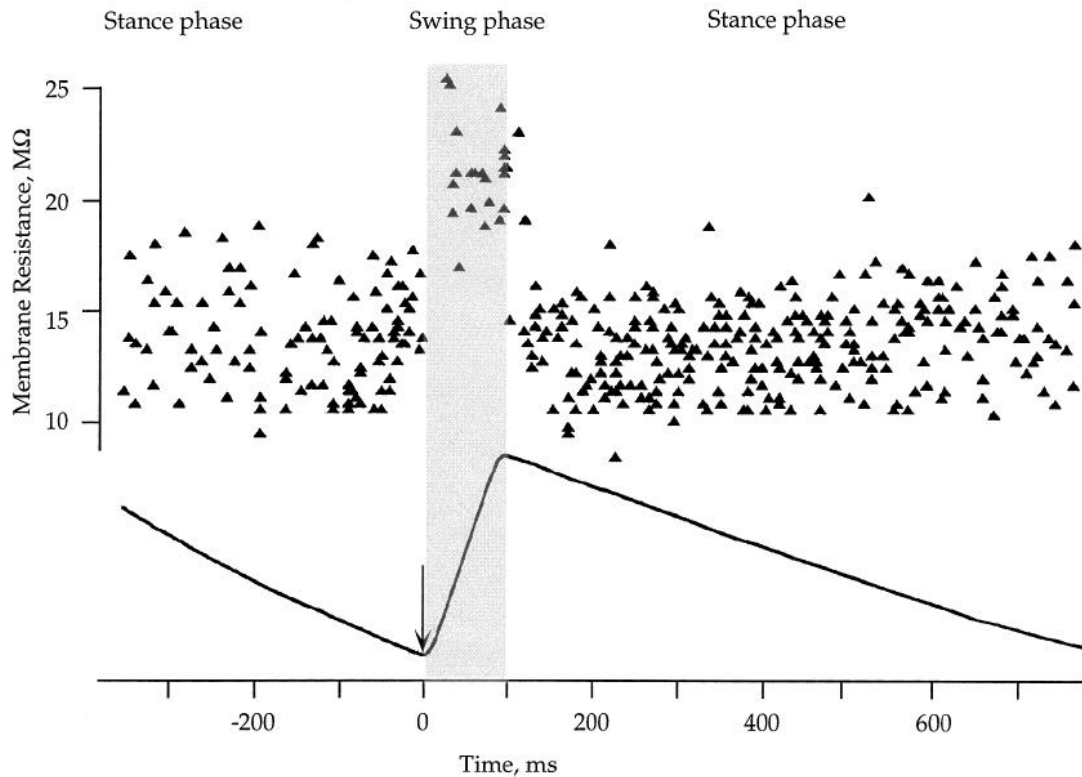


Figure 6. Conductance changes in sensory neurons occur in time with particular phases of the step cycle. The input resistance of a sensory neuron (see also Fig. 5B) was determined by the injection of brief pulses of current and plotted against the time of the step cycle. The resistance was low during the stance phase when the membrane was depolarized and rose during the swing phase when the membrane repolarized. Fifty-four cycles of leg movement were evaluated, and each were aligned at the start of the swing phase (*arrow*). Pulses were injected every 100 msec but those that coincided with spikes were not measured. The duration of the stance phase was variable and thus explains the different density of data points.

the middle and hind legs are isolated in a dish from all sensory feedback and are treated with pilocarpine, the sensory neurons are still depolarized in time with the rhythmic motor pattern that is produced. This indicates that central inputs must be expected to contribute to the depolarization of sensory neurons during walking.

The experiments suggest that all three sources contribute to the depolarization of the sensory neurons during normal walking, but do not allow the relative contributions of each to be assessed. In most sensory neurons, however, the synaptic input began at about the same time or even before we could detect any leg movement or change in muscle activity. It would therefore seem probable that this initial input must be caused by a central drive and that it does not result from sensory feedback.

The nature of the inputs to the sensory neurons

All the available evidence indicates that the inputs that occur during walking are depolarizing, inhibitory, synaptic inputs. At the normal membrane potential of the sensory neurons the inputs caused only a small depolarization but a large change in conductance. The voltage changes were enhanced by hyperpolarizing currents injected into a sensory neuron and decreased by depolarizing ones, indicating a reversal potential close to the resting membrane potential.

The inputs to the locust sensory neurons during walking have all the characteristics of those previously analyzed in the homologous neurons of a hind leg during imposed movements of its femorotibial joint (Burrows and Laurent, 1993; Burrows and Matheson, 1994). The inputs are initiated by spikes in other

sensory neurons from the same receptor, those from other receptors in this and the other legs, and the inputs from interneurons generating the walking rhythm may converge onto the same sets of presynaptic interneurons or they may each activate parallel sets of presynaptic interneurons. The available evidence suggests that the majority of these presynaptic interneurons act by the release of GABA, which in turn works on receptors linked to chloride channels. Electron microscopy, however, suggests that the presynaptic control of the sensory neurons may be more complicated than this, because it demonstrates the presence of input synapses from some neurons that do not show GABA-like immunoreactivity (Watson et al., 1993).

We did not observe any inputs in the terminals that were able to evoke spikes, as would be expected if they reverse so close to resting potential (Burrows and Laurent, 1993). The inputs thus differ from those in sensory neurons of cats (Gossard et al., 1991) and crayfish (Cattaert et al., 1992) that can evoke antidromic spikes in patterns that reflect the underlying synaptic input. These potentials must therefore exceed the spike threshold in the terminals. Thus, recordings from sensory neurons in paralysed cats are superficially similar to those we present but are in fact very different. The spikes in the cat sensory neurons are antidromic and caused by the underlying synaptic input, whereas in the locust the spikes are orthodromic and are caused by the leg movements during walking. They are then superimposed on the synaptic input delivered to their terminals. The antidromic spikes in cat and crayfish are thought to increase the inhibitory effects of the synaptic input by colliding with the incoming orthodromic spikes activated by movements of the joints. This

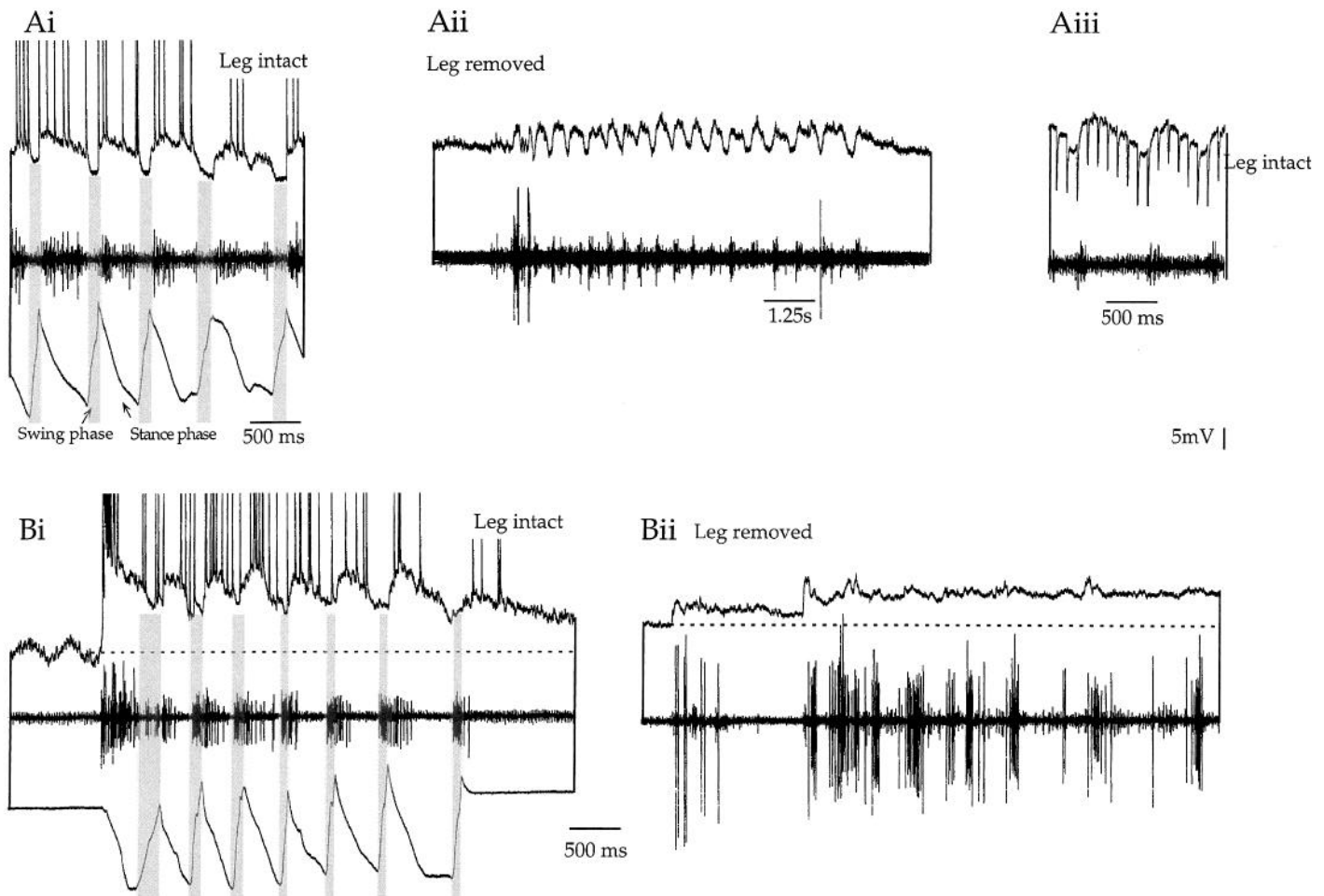


Figure 7. The sensory neurons receive a rhythmic synaptic input in time with the walking rhythm even when the leg whose tibial movements they monitor is removed. *Ai*, In a sensory neuron (same neuron as in Fig. 3*B*) of an intact locust, each step during walking is accompanied by a depolarization. *Aii*, After removal of the leg, the same sensory neuron still receives a rhythmic, but smaller, synaptic input at each step during walking. The neuron no longer spikes because the receptor at which the spikes are generated is removed. *Aiii*, During each depolarizing phase of this input the conductance rises. *Bi*, A sensory neuron from a different locust during a short walking sequence. It receives a sustained input and a rhythmic input in time with each step. *Bii*, A tonic synaptic input during walking persists after the right middle leg is removed. Superimposed on this sustained input are small depolarizations at each step that are correlated with the activity of the coxal muscle.

explanation requires that the antidromic spikes are unable to invade the terminals and evoke transmitter release onto postsynaptic neurons, whereas the orthodromic spikes clearly can.

Timing of the sensory inputs

Each sensory neuron receives a depolarizing synaptic input at a particular phase of the step cycle, so that some are depolarized during the stance phase, some during the swing phase and in some the input occurs during parts of both phases. Our sampling does not reveal any greater number of sensory neurons that are depolarized in one phase rather than the other. In the cat the response properties of the afferents could not be related to their input because the animals were paralyzed (Gossard et al., 1991). Most of the sensory neurons from both the flexor and extensor muscles, however, received a large depolarizing input when the flexors were active with many also receiving a smaller input when the extensors were active, indicating that their sensory signals are likely to be modified most during the flexor (swing) phase.

The rhythmic input to a sensory neuron occurs during the phase of the step cycle when it is signaling joint positions and

movements with its greatest spike response. An exact correlation between the response properties of a sensory neuron and the timing of its inputs cannot be made because of two constraints on the way the measurements were made during walking. First, the response properties of the sensory neurons could not be determined with precision because controlled movements of the tibia about the femur could not be applied in a locust that was able to move its legs freely. Only a coarse classification of response properties was possible, but in general this was in good agreement with their actions during walking. Second, the monitor of leg movements gave an accurate measure of movements in the horizontal plane that resulted largely from movements of the coxa about the thorax. The movements of the femorotibial joint were thus not recorded, so that the actions of the sensory neurons cannot be described in relation to the joint movements that they themselves are signaling. We can only describe the spike response of the sensory neurons in relation to the swing and stance phase, to which the femorotibial joint may be making a variable contribution. Despite these limitations it is clear that the sensory neurons receive a depolarizing input at the phase of

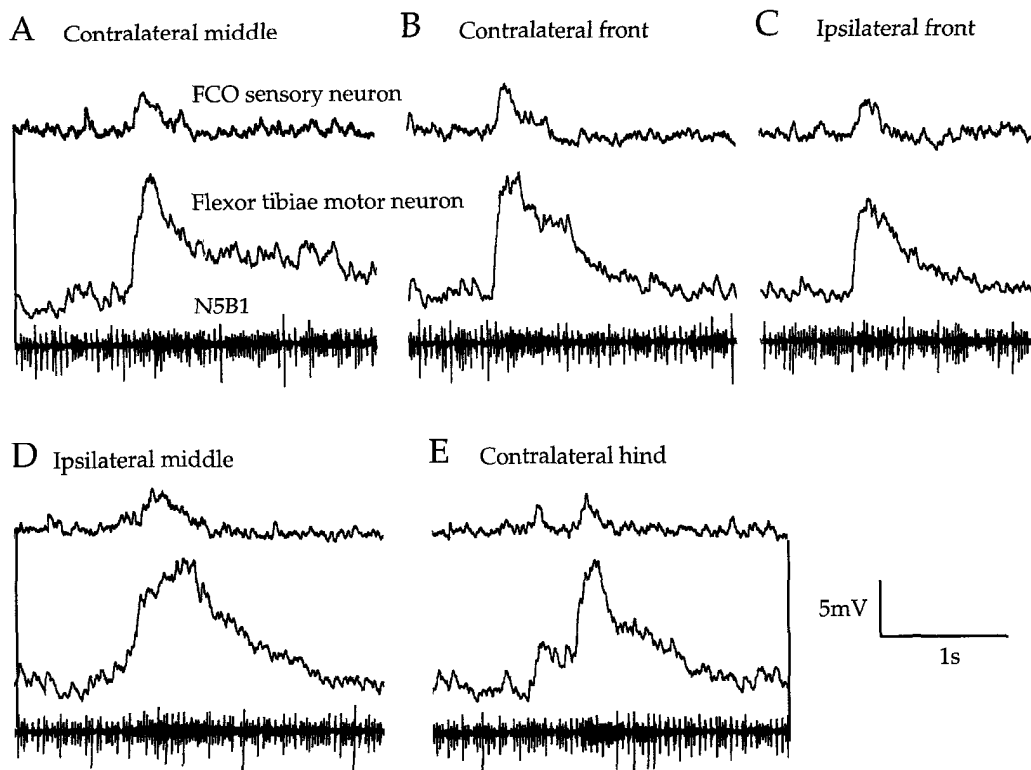


Figure 8. Sensory neurons receive synaptic inputs when other legs are moved or stimulated mechanically. *A–E*, A sensory neuron from the femoral chordotonal of the left hind leg was recorded intracellularly and held hyperpolarized with injected current while the other legs were stimulated mechanically in sequence. The extracellular recording of N5B1, which contains the axons of the sensory neurons from the femoral chordotonal organ, of the left hind leg shows that the stimulation does not lead to increases in the frequency of spikes of other chordotonal afferents in the hind leg. A depolarizing input also occurs at the same time in a flexor tibiae motor neuron that innervates the same hind leg. These recordings were made from *Schistocerca gregaria* reared in Cambridge.

the step cycle which they signal with their greatest spike response.

The effect of the synaptic inputs on sensory signaling during walking

In locusts, intracellular recordings show that the sensory neurons receive a depolarizing input at the start of walking and that it continues for the duration of a walking sequence. In tadpoles, extracellular recordings from the dorsal and ventral roots during fictive swimming also show a sustained depolarization and a rhythmic depolarization in time with each cycle of the motor pattern (Stehouwer and Farel, 1981). The sustained input during both locust walking and tadpole swimming should depress the effectiveness of the sensory spikes in evoking synaptic potentials in their postsynaptic neurons regardless of their response properties and without relation to their timing during the phase of the motor pattern. This may be a mechanism to prevent saturation of the postsynaptic neurons and extend their dynamic range in the anticipation that the movements will excite many sensory neurons at the same time. The result will be that the whole sensory inflow will be downregulated during active walking movements. This role is therefore similar to that proposed to operate during changes in the angle of a joint (Burrows and Matheson, 1994). When only one sensory neuron is active, its spikes have a high gain output to postsynaptic motor neurons, but if many sensory neurons are active together then the gain of the synaptic transmission is reduced. Thus, the actions of an individual sensory neuron from a particular receptor are depen-

dent on the signals from the other sensory neurons from the same receptor that signal the same changes at the joint. The whole operates to control the gain of transmission from the sensory neurons to motor neurons and interneurons.

The rhythmic depolarization at different phases of the step cycle in different sensory neurons may represent a predictive action of the CNS when generating a motor pattern. Proprioceptive feedback is important in establishing the regular and adaptive features of a movement, so that once a regular movement has been established it can then be performed with progressively less reliance on the feedback. There will, however, still be many occasions when feedback is necessary to monitor the unpredictable. For example, during the swing phase spikes of flexion sensitive sensory neurons would be predicted by the central neurons and the effectiveness of their output synapses will be reduced by the rhythmic synaptic input. If, however, a flexion occurs during the stance phase the sensory neurons will respond, but now their signals will be unexpected and will not be reduced by a synaptic input generated by the central neurons. In this scheme the central portion of the walking pattern generator can be regarded as a *predictor* of self-generated events, and can foresee that extension sensitive sensory neurons will be activated at a certain time following the flexion sensitive ones. The time when the regular feedback is expected may thus be represented by the synaptic input to the sensory neurons. The unpredicted feedback which must be heeded, either occurs when there is little synaptic input, or is represented by a different pattern of spikes during the synaptic input. Such a design is faster, more reliable, and

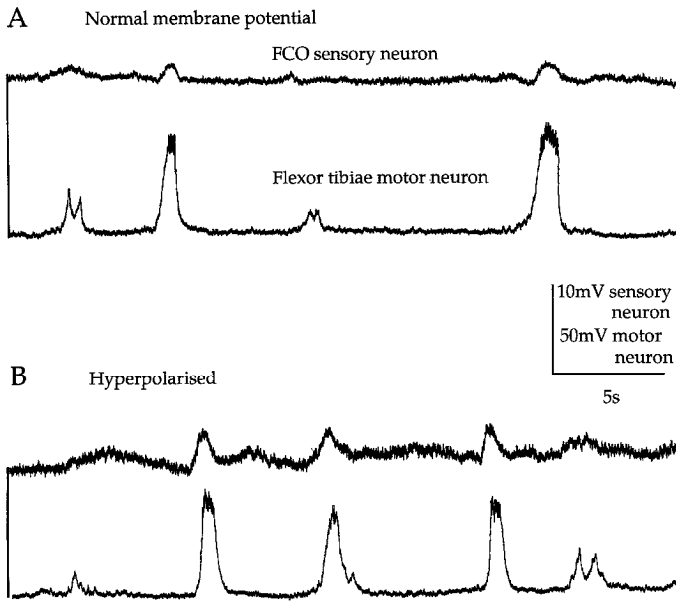


Figure 9. Sensory neurons receive synaptic inputs during rhythmic motor patterns expressed by isolated ganglia. The meso- and metathoracic ganglion were isolated in a dish and bathed in saline containing 5×10^{-5} M pilocarpine. **A**, A sensory neuron from the femorotibial organ of a hind leg is at its normal resting potential and is depolarized each time that a flexor motor neuron, which innervates the same hind leg, is depolarized. **B**, The sensory neuron is hyperpolarized with injected current and the synaptic input is accentuated. These recordings were made from *Schistocerca americana* reared in Caltech, Pasadena, CA.

more robust than if feedback were necessary to control or initiate every movement in a sequence, and could explain why central commands are important for the generation of so many different types of movements.

During imposed extension movements of the femorotibial joint in a quiescent locust, the sensory signals from the chordotonal organ excite flexor tibiae motor neurons and inhibit extensors so that the imposed movement is resisted. Resistance reflexes such as this result from complex patterns of excitatory connections made by the sensory neurons with local interneurons, intersegmental interneurons, and with motor neurons (Burrows, 1987; Laurent and Burrows, 1988; Burrows et al., 1988) and by interconnections among the interneurons themselves. These resistance reflexes to an unpredicted movement can still occur while an insect is walking (Cruse and Pflüger, 1981), and can also vary in gain and may even reverse in sign so that they assist a voluntary movement (Bässler, 1976, 1986; Bässler et al., 1986; Zill and Jepson-Innes, 1990). This variation in gain could be accomplished by mechanisms involving interneurons but could also involve the presynaptic modification of the sensory signaling. For example, the sensory neurons that signal extension of the tibiae during the stance phase receive a depolarizing input that should reduce the effectiveness of their spikes. This in turn should reduce their excitation of the flexor motor neurons and allow the extensors more easily to propel the body forward. This implies that the presynaptic drive is one mechanism for allowing voluntary movements to proceed in the face of circuitry that would otherwise oppose it. Such a mechanism would still allow unexpected movements to be met by an appropriate resistance response.

To understand better the subtleties of the control of the sen-

sory signaling we need now to examine the connections made by the different types of sensory neurons with motor neurons and other neurons of the central circuitry, and during walking relate their synaptic inputs more closely to the actions of the joint they monitor.

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