

FUNCTIONAL PROPERTIES OF PRIMATE SPINAL INTERNEURONES DURING VOLUNTARY HAND MOVEMENTS

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ABSTRACT

The activity of cervical spinal interneurons (INs) was recorded in monkeys performing alternating hand movements. The contribution of INs to voluntary movement was determined by their response patterns during ramp-and-hold wrist movements and their postspike effects on forelimb muscle activity. Most INs were active during both flexion and extension, in contrast to the unidirectional activity of muscles and corticomotoneuronal cells. When recorded during performance of an instructed delay task, the activity of many INs was modulated during the delay period between the instruction cue and the subsequent go signal. Thus, spinal INs, like cortical neurones, participate in earliest stages of preparation for movement. The modulation of peripheral input to spinal INs was tested during an instructed delay task. The monosynaptic responses to electrical stimulation of a cutaneous nerve decreased during active movement, probably due to presynaptic inhibition. These results provide new insights into the role of spinal INs in preparation and execution of voluntary movement.

INTRODUCTION

The reflex responses of spinal cord interneurons (INs) have been extensively characterized in anesthetized animals (Baldissera et al., 1981; Jankowska, 1992), but little is known about the function of INs in normal voluntary movements. The responses evoked by stimulation of peripheral receptors and nerves as well as descending pathways have served to identify the convergent inputs to INs, but their output effects on different muscle groups remains less well understood. Much of our information derives from studies of lumbar spinal circuits related to the cat hindlimb, and much less is known about segmental circuits controlling forelimb movements in primates. We here review

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briefly some recent work on the role of interneurons in cervical spinal cord of primates in preparation and execution of hand movements.

CONTRIBUTION TO VOLUNTARY WRIST MOVEMENT

To study the contribution of cervical INs to voluntary hand movement we documented their *activity* and their *correlational linkages* to muscles in monkeys performing ramp-and-hold flexion-extension torques about the wrist (Perlmutter et al., 1998; Maier et al., 1998). Single neurones were recorded with movable tungsten microelectrodes in C6-T1 spinal segments, along with EMG activity of multiple forearm muscles, while monkeys generated alternating flexion-extension torques in a step-tracking task. Task-related spinal INs increased their activity during flexion and/or extension, typically with a tonic or phasic-tonic response pattern in their preferred direction (Maier et al., 1998). The tonic components of these responses were usually an increasing function of static torque. Surprisingly, most INs (77%) were active during both flexion and extension, in unexpected contrast to the strictly unidirectional activity of corticomotoneuronal cells (Cheney & Fetz, 1980) and agonist motoneurons and the predominantly unidirectional activity of dorsal root afferents with post-spike effects (Flament et al., 1992). Interestingly, all rubromotoneuronal cells exhibit bidirectional activity (Cheney et al., 1991; Mewes and Cheney, 1994), like most INs.

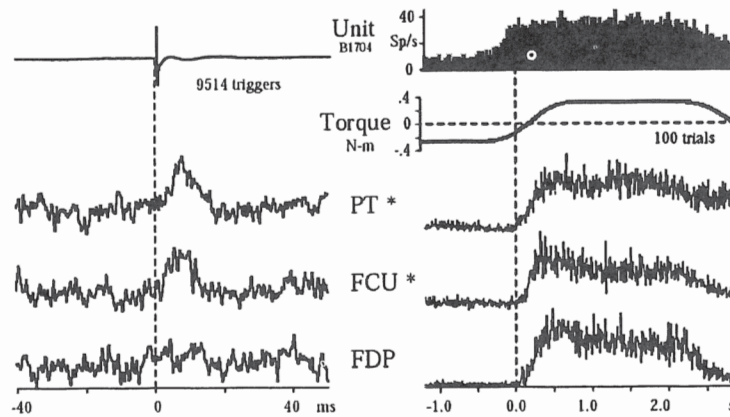


Figure 1. STAs and response averages of a facilitatory PreM-IN located in caudal C8. The STAs (left) show the triggering action potential [top] and average of rectified EMG in 3 independently recorded co-active muscles. Asterisks indicate muscles with significant post-spike effects. The average activity of the neurone during flexion torques is shown in the top right, above the average torque trajectory (positive torque in flexion, negative torque in extension) and average responses of the co-active muscles. This neurone exhibited tonic firing during static torques in both directions, with higher rates for flexion. (From Perlmutter et al., 1998.)

For about a fifth of the task-related INs spike-triggered averages (STA) of rectified EMG revealed significant spike-related features suggesting correlational linkages with forelimb muscles (Perlmutter et al., 1998). Some INs were identified as excitatory or inhibitory “premotor INs” (PreM-INs) on the basis of post-spike facilitation or

suppression with appropriate onset latencies after the trigger spike (>3.5 ms, consistent with the latencies of post-stimulus facilitation evoked by single intraspinal microstimuli). Figure 1 illustrates an excitatory PreM IN that was more active during flexion and produced post-spike facilitation in two flexor muscles. The STAs of some INs showed broad peaks or troughs beginning earlier than 3.5 ms (usually before the trigger), attributed to synchronous firing of other PreM neurones. STA features were predominantly facilitatory (85%) and occurred twice as often in flexor muscles as in extensors. The muscle fields of PreM-INs (defined as the set of muscles showing postspike effects) were somewhat smaller than those of supraspinal PreM cells in cortex and red nucleus, and rarely involved reciprocal effects on antagonist muscles. In general the muscle fields of PreM-INs were functionally consistent with their firing properties: for example, excitatory PreM-INs were typically most active in movements that activated their target muscles (Fig. 1). However, many excitatory PreM-INs also fired when their facilitated muscles were silent. Some inhibitory PreM-INs were activated with antagonists of their suppressed target muscles, a pattern of reciprocal inhibition expected of Ia inhibitory INs. Other inhibitory PreM-INs were coactivated with the muscles they suppressed, a pattern expected of Renshaw cells.

These observations indicate that cortical and spinal PreM neurones represent movements and muscles in different ways. Corticomotoneuronal cells represent functional muscle synergies more distinctly than spinal INs: they produce postspike effects in larger muscle groups, including postspike suppression of antagonists of their facilitated target muscles (Kasser and Cheney, 1985), and they fire more specifically during particular movements (Cheney et al., 1991). In contrast, spinal PreM-INs affect one or a few particular muscles, and are broadly activated over a wider range of movements (Maier et al., 1998; Perlmutter et al., 1998). Thus, during normal voluntary movements motoneurones receive superimposed excitation and inhibition from populations of simultaneously active spinal PreM-INs. Excitation from these INs outweighs inhibition when the motoneurones are activated as agonists of a movement, and the balance drops below threshold when they become inactive as antagonists of the movement. In contrast, motoneurones receive more specific commands from corticomotoneuronal cells that are strictly consistent with their recruitment and inhibition.

INVOLVEMENT OF INs IN MOTOR PREPARATION

To document the role of spinal INs in *preparation* for voluntary movement we trained three monkeys to perform instructed delay tasks. Two monkeys performed isometric wrist flexion or extension after a visually cued delay period (Prut and Fetz, 1999; Perlmutter and Prut, 2001). During such instructed delays between a transient cue and a go signal many cortical neurones have been shown to change their activity as the monkey prepares for the subsequent movement. Figure 2 illustrates our instructed delay task and shows the activity of an IN that was inhibited during the delay period. About one third of the tested INs showed modulation of firing rate during the delay period following the visual cue, relative to the pre-cue rate. These *significant delay modulations* (SDM) were never accompanied by any EMG activity, and often differed from the INs' responses during the subsequent active torque period (Fig. 2). SDMs occurring during correct trials were usually absent when the monkey made directional errors. Many INs with SDM showed changes in firing during the delay period with the same polarity

(increase or decrease) as the cell's activity during the active hold period, consistent with a subthreshold priming of INs in the direction they must fire during the subsequent movement. About two-thirds of the SDM were inhibitory, suggesting a global suppression of activity during the delay, preventing the overt expression of the movement.

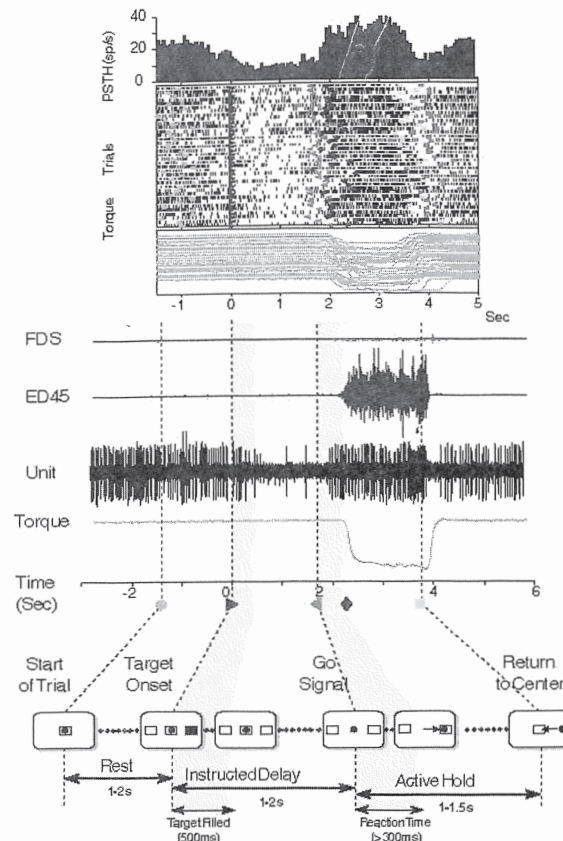


Figure 2. Activity of spinal IN during instructed delay task. Components of the behavioural task are schematically shown at bottom. Filled circle represents a cursor whose position is controlled by the monkey's wrist torque; squares represent targets. The instructed delay period begins with a transient visual cue (right target filled for 500 ms) and ends with a go signal (extinguishing of center hold target). Middle traces show activity of flexor digitorum sublimis (FDS) and extensor digitorum 4 & 5 (ED45) muscles and the IN, and isometric torque about the wrist. Top portion of figure shows responses during successive extension trials, aligned on cue onset (at time 0). From top down, peristimulus histogram (PSTH) of IN firing rate, rasters of IN spikes in successive trials and traces of torque trajectories. (Adapted from Prut and Fetz, 1999.)

A third monkey learned to interpret transient visual or proprioceptive cues to perform appropriate delayed wrist movements against an elastic load. The proprioceptive cue was a brief wrist perturbation whose direction and amplitude indicated the subsequent required movement. The perturbation evoked characteristic short-latency sensory responses in many INs that revealed two major groups of INs. Some INs gave bidirectional excitatory responses at the onset and offset of the perturbation pulses. These INs often fired transiently and bidirectionally with active movements, consistent with responses from cutaneous receptors. Other INs exhibited biphasic responses to

perturbation pulses, being activated by the flexion component and inhibited by the extension component (or vice versa), consistent with proprioceptive input from muscle or joint receptors. These INs tended to exhibit sustained activity during the active hold in their preferred direction.

Excluding any brief response to the perturbation, the delay period activity for many INs was similar in visual and perturbation trials, consistent with motor preparation that is independent of the cue modality. However, other INs exhibited different SDM in the visual trials and the perturbation trials, similar to modality-specific SDM seen in cortical areas. These results suggest that segmental INs are involved, with cortex, in the earliest stages of movement preparation instructed by various cue modalities. The appearance of instructed delay period activity at spinal levels similar to that documented in motor cortical areas indicates a widely distributed network for movement preparation, mediated by the numerous descending and ascending pathways between cortex and spinal cord.

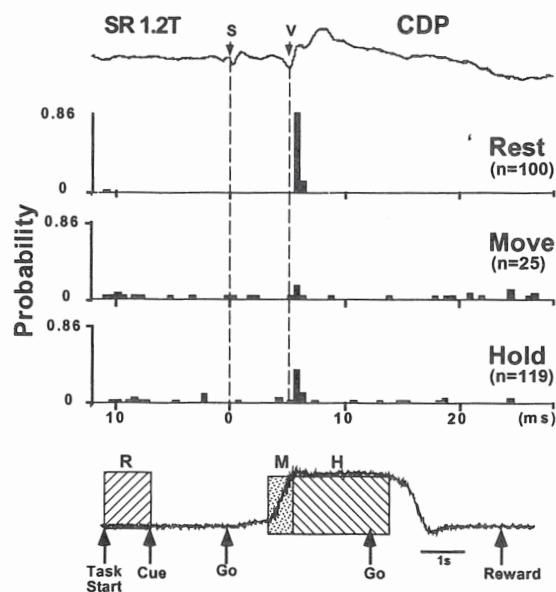


Figure 3. Modulation of monosynaptic response of cervical IN during task. Response to electrical stimulation of superficial radial nerve during performance of instructed delay task. Histograms show responses to electrical stimulation of nerve cuff compiled during task periods schematized at bottom: rest prior to cue (R), dynamic active movement (M) and static hold (H). Top trace shows cord dorsum potential (CDP) indicating time of stimulus (S) and afferent volley (V). The short latency of histogram peaks indicates a monosynaptic response, which is reduced during Move and Hold. Histograms plot probability of action potentials per stimulus per bin (0.5 ms).

MODULATION OF SENSORY INPUT DURING MOVEMENT

In other experiments we investigated the *task-dependent modulation* of neural responses to peripheral input. In a monkey performing wrist flexion/extension movements in a visually cued instructed delay task, cutaneous responses were evoked by

electrical stimulation of the superficial radial (SR) nerve through a cuff electrode. SR stimulation of low-threshold afferents produced excitatory responses in many INs, sometimes at monosynaptic latencies from the afferent cord dorsum volley (<1.5 ms). Post-stimulus histograms compiled separately for different phases of the task (intertrial rest, instructed delay, dynamic movement and active hold period) revealed that the SR-evoked responses were typically suppressed or abolished during the dynamic movement phase (Fig. 3). In most cases the monosynaptic excitation from the SR was suppressed at the same time that task-related activity of the INs increased, indicating that the suppression was mediated by presynaptic rather than postsynaptic inhibition. The amplitudes of evoked monosynaptic field potentials in dorsal horn were also reduced during the dynamic movement period. Preliminary evidence from antidromic volleys in the nerve cuff evoked by intraspinal stimulation suggests that the excitability of SR afferents increased transiently during the dynamic component of active movement, consistent with primary afferent depolarization (Wall, 1958). These results indicate that presynaptic inhibition of cutaneous input increases significantly during the dynamic phase of active movement. This could function to gate out inappropriate reflex responses from peripheral receptors and is consistent with increased perceptual thresholds during active movement.

BEHAVIOURAL FUNCTIONS OF SPINAL INs

The observations summarized here suggest that under normal behavioural conditions many spinal INs have response properties similar to those previously documented for cortical neurones in behaving animals. The notion that cortical cells are involved in "higher order" behavioural functions while spinal INs are merely involved in transmitting sensory input or motor commands is based on a history of research involving fundamentally different experimental conditions. The reflex responses of spinal INs have been documented extensively in anaesthetized or decerebrate animals, while the activities of cortical cells have been documented during behavioural tasks that test their involvement in voluntary movement and cognitive functions. We suspect that examining spinal INs under appropriate behavioural conditions in awake animals will reveal that INs are also involved in many functions beyond simple sensory or motor relays (Fetz et al., 2000).

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