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Research Report

Gain of spinal motoneurons measured from square and ramp current pulses

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ABSTRACT

The gain of motoneurons (MNs) characterizes how variations in synaptic input are transformed in to variations in output firing and muscle contraction. Experimentally gain is often defined as the frequency–current relation observed in response to injected suprathreshold square current pulses or current ramps during intracellular recording. The gain of MNs is strongly affected by adaptation: transient gain in response to depolarization is usually higher than steady state gain measured during sustained depolarization. The transient and the stationary gain of neurons are separate entities that can be selectively modified. Here we investigated how the transient and the stationary gain of spinal MNs obtained from responses to square current pulses are related to gain estimated from the responses to the current ramps. We found, that the gain in response to current ramps is identical to the steady state gain during sustained depolarization. Therefore, gain modulation is more fully characterized with square current pulses than with current ramps.

1. Introduction

The firing pattern of motor units differs during ballistic and slow voluntary movements. Tonic low frequency firing is observed during slow voluntary movement, while phasic high frequency firing characterize ballistic movements (Desmedt and Godaux, 1977a, 1977b; Duchateau and Enoka, 2011). Initially it was thought that there were separate phasic and tonic motor units (Granit et al., 1956, 1957; Tokizane and Shimazu, 1964), but subsequently tonic and phasic firing modes were observed in the same motor unit (Freund, 1983). This is compatible with adaptation in motoneurons during maintained activity (Powers et al., 1999; Sawczuk et al., 1995, 1997). During a suprathreshold depolarizing current pulse motoneurons adapt from a higher frequency at the unset to a lower steady state frequency (Granit et al., 1963; Kernell, 1965a; Kernell and Monster, 1982; Sawczuk et al., 1995, 1997). More importantly, adaptation affects not only frequency but also the gain of motoneurons (Powers et al., 1999; Sawczuk et al., 1995). Gain measured at the beginning of a stimulus (transient gain) is usually higher than gain measured in steady state adaptation (steady gain). Adaptation decreased the gain of rat MNs (Granit et al., 1963; Sawczuk et al., 1995), cat MNs (Kernell, 1965b) and turtle spinal cord motoneurons (Hounsgaard et al., 1988b).

The gain of motoneurons is determined experimentally by injecting suprathreshold currents through microelectrode, measuring the neuron's firing rate and estimating steepness

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of frequency–current (f–I) relation obtained (Granit et al., 1963; Kernell, 1965a). MNs can be stimulated with square current pulses of increasing amplitude (Granit et al., 1963; Ito and Oshima, 1965) or slow triangular current ramps (Bennett et al., 2001b; Button et al., 2006; Hounsgaard et al., 1984, 1988a; Lee and Heckman, 1998). The ramp stimulus is more convenient to use, however the value of gain estimated may be affected by adaptation.

Apart from spike frequency adaptation (Powers et al., 1999; Sawczuk et al., 1995), signal processing in motoneurons is influenced by a number of another nonlinearities mediated by ion conductances and described as the postspike afterhyperpolarization (AHP) (Granit et al., 1963; Kernell, 1965a; Vervaeke et al., 2006; Vogalis et al., 2003) and the persistent inward currents (Heckman et al., 2008; Rekling et al., 2000; Schwindt, 1973). Response properties of the motoneurons can be dramatically altered during spinal network activity by activation of metabotropic receptors for glutamate (Svirskis and Hounsgaard, 1998), serotonin (5-HT) (Heckman et al., 2003; Hounsgaard et al., 1988a; Hultborn et al., 2004; Perrier and Cotel, 2008; Perrier and Hounsgaard, 2003; Perrier et al., 2003), acetylcholine (via muscarinic receptors) (Alaburda et al., 2002; Miles et al., 2007) or dopamine (Clemens and Hochman, 2004). This may alter the gain by adjusting the response properties of MNs to the behavioral needs (Button et al., 2006; Harvey et al., 2006; Hounsgaard and Mintz, 1988; Hultborn et al., 2004; Kernell, 1965a; Lee and Heckman, 2001; Powers and Binder, 2001). More importantly, intrinsic properties of motoneurons may selectively affect transient and stationary gain (Gabrielaitis et al., 2011). For instance the persistent sodium current not only increases excitability (Gabrielaitis et al., 2011; Kuo et al., 2006; Lee and Heckman, 2001; Li and Bennett, 2003) and amplifies synaptic input in motoneurons (Manuel et al., 2007), but can decrease transient gain in MNs, while stationary gain is not affected (Gabrielaitis et al., 2011). However, blocking the persistent sodium current by riluzole (Harvey et al., 2006) did not change the gain measured from responses to current ramps.

The transient and the stationary gain of the neurons are not only different but can be selectively modified. Here we investigated how the transient and stationary gain of spinal MNs obtained from responses to square current pulses are related to the gain estimated from the responses to current ramps.

2. Results

2.1. Intrinsic properties of MNs estimated by a square and ramp current pulses

The input conductance of MNs recorded was 0.11 ± 0.01 μS and threshold current for action potential initiation measured from square current pulses was 1.40 ± 0.25 nA (n = 9). It was the strong positive correlation (R^2 = 0.97) between the threshold current and input conductance, as reported in cat MNs (Gustafsson and Pinter, 1984). There was no significant difference in threshold current for spike initiation measured from square and slow (1 nA/s) ramp stimulus. The ramp speed did not affect the threshold current too.

The voltage threshold for action potential initiation was −42.7 ± 1.6 mV (square pulse), −39.1 ± 1.9 mV (0.5 nA/s ramp), −39.6 ± 1.8 mV (1 nA/s ramp), 40.9 ± 1.7 mV (5 nA/s ramp), −41.9 ± 1.7 mV (10 nA/s ramp) and −42.1 ± 1.6 mV (20 nA/s ramp). The voltage threshold was significantly higher when measured from responses to 0.5 nA/s and 1 nA/s ramps than from square pulses. The voltage threshold measured from faster ramps did not differ significantly from the one measured by square pulses. It was the negative correlation between ramp speed and action potential voltage threshold.

2.2. f–I relation of spinal motoneurons measured from responses to square current pulses

We measured the gain of spinal MNs from response to square current pulses (Fig. 1A) of increasing amplitude and current ramps of increasing speed (Fig. 1B). The frequency of action potentials decreased due to adaptation during square current pulses in all MNs tested (Fig. 1A, upper trace). The transient firing frequency (first two APs) was significantly higher by 24.7 ± 2.9% (n = 9) than early firing frequency (first four APs) and significantly higher by 71.2 ± 3.2% than the steady state frequency during a depolarizing square current pulse with an amplitude of 2.9 nA. To estimate the influence of adaptation on the gain of MNs we measured the steepness of f–I relation at different stages of adaptation (see Experimental procedures). An example is shown in Fig. 1C. The steepness of transient f–I (transient gain) was 56.3 ± 6.9 Hz/nA, the steepness of early f–I (early gain) was 43.0 ± 2.8 Hz/nA and the steepness in steady state (steady gain) was 16.5 ± 1.1 Hz/nA (n = 9) (Fig. 1D). The transient gain was 19.2 ± 5.9% higher than early gain, and 68.1 ± 3.7% higher than the gain in steady state. The steepness of early gain was 60.9 ± 2.9% higher than in steady state.

2.3. f–I relation of spinal motoneurons measured from responses to current ramps

Current ramps (0.4–6 nA/s) have also been used to estimate the gain of MNs (Bennett et al., 2001b; Button et al., 2006; Harvey et al., 2006; Hounsgaard et al., 1984, 1988a; Lee and Heckman, 1998, 2000). We compared the gain measured by square current pulses and slow (1 nA/s) ramp from the same MNs (Fig. 1C, D). The steepness of f–I relation measured from responses to a slow current ramp (1 nA/s) was 15.9 ± 1.5 Hz/nA (n = 9) and did not differ significantly ($P < 0.05$) from steepness of the f–I relation in steady state (16.5 ± 1.1 Hz/nA) determined with square current pulses (Fig. 1D). The transient and the early gain were 68.1 ± 4.9% and 62.2 ± 3.8% respectively higher than the gain measured from slow (1 nA/s) current ramp (n = 9) (Fig. 1D). This shows that slow current ramps provide the steady state gain but not the transient or the early gain in MNs.

2.4. Influence of ramp speed on f–I estimation

The gain of spinal MNs decreases with adaptation (Powers et al., 1999; Sawczuk et al., 1995). Therefore the speed of ramp could be an important factor influencing the estimated gain. We measured the gain of the same spinal MNs