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Prolonged Firing in Motor Units: Evidence of Plateau Potentials in Human Motoneurons?

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Kiehn, O. and T. Eken. Prolonged firing in motor units: evidence of plateau potentials in human motoneurons? *J. Neurophysiol.* 78: 3061–3068, 1997. Serotonin (5-HT) and norepinephrine-dependent plateau potentials are found in spinal motoneurons in reduced turtle and cat preparations. Triggering the plateau potential by short-lasting synaptic excitation causes a prolonged self-sustained firing, which can be terminated by short-lasting synaptic inhibition. The presence of plateau potentials can also allow neurons to fire in a bistable manner, i.e., shifting between stable low and high firing frequencies. Such a bistable firing behavior has been found in soleus motor units in unrestrained rats. In the present study single motor-unit activity was recorded from low-threshold units in human soleus and tibialis anterior muscles to evaluate whether a bistable firing behavior and/or prolonged firing could be evoked. Vibration of the homonymous muscle tendon (30–100 Hz, 2–10 s) was used as excitatory input to the motoneuron pool. Brief excitation while the muscle was electrically silent induced firing during the vibration and sometimes recruited units into prolonged stable firing outlasting the vibratory stimulus. However, a bistable firing behavior, i.e., vibration-induced maintained shifts between two stable levels of firing, could not be convincingly demonstrated. The reason for this was twofold. First, low-threshold human motor units tended to jump to a “preferred firing range” shortly after voluntary recruitment. This firing range was the same as when units were recruited from silence into prolonged firing by vibration. Below the preferred firing range, maintained firing was unstable and usually only possible when subjects were listening to the spike potentials or had visual force-feedback. Second, vibration when units were firing in the preferred firing range caused a transient increase in firing frequency but no maintained frequency shifts. Recordings from pairs of motor units showed that short-lasting vibration could recruit one unit into prolonged firing, while a second unit, which already fired in its preferred firing range, only transiently increased its firing rate during the vibration. This suggests that the prolonged firing was not the result of an increase in the common synaptic drive to the motoneuron pool. We conclude that a bistable firing behavior as seen in intact rats is probably absent in human low-threshold motor units, but that prolonged firing could be seen in response to short-lasting excitation. This latter phenomenon is compatible with the existence of plateau potentials, which have to have a threshold close to the threshold for sodium spike generation.

INTRODUCTION

The existence of monoamine-dependent motoneuron plateau potentials is well established in reduced turtle and cat preparations (see reviews by Hultborn and Kiehn 1992 and Kiehn 1991a,b). These long-lasting depolarizing potentials can be initiated by sufficiently strong brief depolarizing current pulses or brief barrages of excitatory synaptic inputs

and cause self-sustained firing that outlasts the duration of the excitation (Conway et al. 1988; Hounsgaard et al. 1988; Hounsgaard and Kiehn 1989). The plateau can terminate either spontaneously or in response to a brief inhibition. In turtle and cat motoneurons, activation and deactivation of the plateau potential may therefore switch the motoneuron membrane potential between two stable membrane potentials: one below threshold for firing action potentials and one above threshold. Furthermore, in cat motoneurons, the presence of plateau potentials allow them to display a true *bistable firing behavior*, i.e., shifting between stable low and high firing frequencies by short-lasting excitation and inhibition (Hounsgaard et al. 1988). In this latter situation the low firing frequency was produced by steady depolarizing current injection into the cell.

At present there is no conclusive evidence of motoneuron plateau potentials in intact animals. To obtain such evidence it is necessary to use motor-unit recordings and to look for spontaneous or experimentally induced motoneuron firing behaviors that are compatible with the presence of motoneuron plateau potentials, especially 1) the presence of a bistable firing pattern and/or 2) sustained firing that outlasts an excitatory stimulus (and can be terminated by a brief inhibition). This has previously been done in soleus muscles in unrestrained rats and these studies indicate that plateau potentials are utilized in normal motor behavior (Eken and Kiehn 1989; Eken and Lømo 1993; Kiehn et al. 1996). Thus a bistable firing can be evoked experimentally by short-lasting synaptic excitation and inhibition of the motoneuron pool through peripheral nerve stimulation during quiet standing, when the descending synaptic drive can be assumed to be rather constant (Eken and Kiehn 1989). Furthermore, units can shift spontaneously between low-frequency firing (~10 imp/s) and long-lasting high-frequency firing (~20–25 imp/s). The ability to produce this long-lasting tonic firing develops in parallel with maturation of descending monoaminergic projections (Eken et al. 1990) and disappears after selective depletion of spinal monoamines (Kiehn et al. 1996).

Our experiments with unrestrained rats encouraged us to look for evidence of plateau potentials in human motor units. Baldissera et al. (1991, 1994) already suggested that plateau potentials might be the underlying cause of the sustained muscle contraction seen in some cases of cramps and myokymia. But thus far the many previous studies of normal human motor-unit firing have not specifically tested for the presence of plateau potentials. However, studies in human muscles have shown that weak synaptic excitation of the

motoneuron pool, either by vibration of the muscle tendon or electrical stimulation of Ia afferents, can evoke a sustained muscle contraction that outlasts the excitatory input (Hagbarth 1973; Lance et al. 1966; Lang and Vallbo 1967). This tonic vibration reflex (TVR) is characterized by a prolonged decline in firing after cessation of the stimulus (Lang and Vallbo 1967). This "afterdischarge" can sometimes last for minutes (Lang and Vallbo 1967). As pointed out by Crone et al. (1988) the prolonged decline of the TVR after stimulation might easily be explained by the presence of plateau properties in motoneurons. Reverberating activity in spinal interneuronal networks has also been suggested as a mechanism (Carp and Rymer 1986; Kanda 1972).

In this study we used vibration of the homonymous muscle tendon and isometric force ramp contractions to look for evidence of plateau potentials in human leg motor neurons. In an extension of previous studies in unrestrained rats, we have used dual or multiple motor-unit recordings to compare changes in common descending drive to the motoneuron pool and experimentally induced changes in firing frequencies.

Preliminary communications of part of this work have appeared in abstract form (Kiehn and Eken 1992) and in reviews (Hultborn and Kiehn 1992; Kiehn 1993).

METHODS

Single motor-unit and surface electromyographs (EMG) from soleus and tibialis anterior muscles were recorded together with ankle extension force in healthy male ($n = 13$) and female ($n = 11$) volunteers (age, 19–32 yr). All subjects gave informed consent, and all procedures were approved by the local ethics committee.

Single motor-unit recordings were obtained through disposable concentric platinum needle electrodes 0.45×40 mm (surface area, 0.07 mm²; Dantec, Copenhagen) or wire electrodes, which were custom made from three $50\text{-}\mu\text{m}$ -diam Teflon-insulated platinum/iridium wires (surface area, 0.002 mm² each; A-M Systems, Everett, WA) twisted tightly together in a bundle, which was cut transversely and inserted through an intramuscular cannula. For each experiment two needle electrodes or up to four wire electrodes were inserted after the skin was anesthetized with a mixture of lidocaine and prilocaine (Emla cream; Astra, Copenhagen). Wire electrodes could be kept in the muscle for several hours without noticeable discomfort, whereas needle electrodes were withdrawn after each recording. Surface EMG recordings (gross EMGs) from the homonymous muscle and one of its antagonists were obtained through standard electrocardiogram (EKG) electrodes glued to the skin above the muscles. In some instances visual or auditory feedback of single motor-unit activity was given.

Subjects were seated in a comfortable chair during recordings. The knee was flexed ($110\text{--}160^\circ$) and the ankle was dorsiflexed ($95\text{--}105^\circ$). The foot was strapped tightly in a device for measuring isometric force around the ankle joint. To avoid fatigue most experiments were performed with relatively weak sustained-force contractions ($<10\text{--}15\%$ of the maximal dorsi- and plantarflexion force (MVC) that could be sustained for ~ 10 s). Force could be displayed on an oscilloscope in front of the subject.

In the isometric ramp experiments the subject was asked to superimpose the oscilloscope force trace on the output from a waveform generator. The amplitude and speed of the ramp could be varied. Vibratory stimuli were applied through a custom made vibrator or a Vibrator Exciter 4809 (Brüel og Kjær, Copenhagen), which was held firmly against the homonymous muscle tendon.

Stimulus frequency could be varied between 10 and 100 Hz and peak-to-peak amplitude between 0.5 and 1.5 mm.

All signals were taken through preamplifiers and amplifiers and sampled on a frequency-modulation tape recorder (RTP 600B; Kyowa, Japan) or a digital tape recorder (DTR 1801; Biologic, Claix, France; sampling rate 10 kHz). Analyses were performed off-line. Before analysis the single-unit EMGs were high-pass filtered (cutoff frequency usually 40–100 Hz) to obtain maximal signal-to-noise ratio and the filtered signal was fed into spike discriminators (D130, Digitimer, Hertfordshire, UK or Slope/Height Window Discriminator, Frederick Haer). The spike detection pulses triggered an oscilloscope with signal delay circuitry that displayed the unfiltered motor-unit potentials superimposed at high sweep speeds, making it possible to verify visually that the discriminated potentials were of similar shape and hence probably belonged to the same motor unit. EMG signals and single motor-unit spike detection pulses were fed into a computer (Apple Macintosh IIfx or IIfx) equipped with an analog/digital input/output card and a direct memory access (DMA) card (NB-MIO-16H-9 and NB-DMA-8-G; National Instruments, Austin, TX). Applications for data acquisition and analysis were custom made and consisted of "virtual instruments" developed with LabVIEW 2 (National Instruments), with extensions written in a high-level language (THINK Pascal; Symantec Corporation, Cupertino, CA) and assembly language (THINK C; Symantec Corporation). The computer equipment was utilized for analysis and documentation purposes including motor unit identification, spike frequency measurements, signal averaging, and plotting (for more details see Eken and Kiehn 1989). Gross EMGs were root mean square (RMS) processed for illustrations.

RESULTS

Vibration-induced changes in motor-unit firing

In this section we will describe the responses of single motor units to short-lasting vibration of the homonymous muscle tendon. Vibration strongly activates primary muscle spindle afferents (Burke 1978) and is therefore likely to provide an excitatory drive onto the motoneuron pool lasting for the period of the vibration. This stimulation paradigm is analogous to the one used in reduced preparations to test for presence of plateau potentials except that we have not exploited the use of brief inhibitory inputs (Hounsgaard et al. 1988; Hounsgaard and Kiehn 1989; see also Hartline et al. 1988). This section, as well as the rest of RESULTS, is not meant to be an exhaustive description of the recruitment and firing behavior of low-threshold human motor units. Instead, we will provide a description of indirect tests for the presence of plateau potentials in human motoneurons (see INTRODUCTION).

Subjects were asked to perform a weak contraction of the muscle to keep a level of force or integrated EMG activity just below the threshold for the unit under study. To help the subjects in this task they were often given a visual feedback of force or rectified gross EMG. When a short vibration was provided under those conditions most units could be recruited to firing that only lasted during the vibration. However, some units could also continue firing at a steady level after termination of the vibratory stimulus, despite the subject's effort to keep the force or gross EMG constant. Fig. 1a illustrates this in a tibialis anterior motor unit (*top trace*; instantaneous spike frequency plotted above the recording) with simultaneous recordings of RMS-processed gross EMG

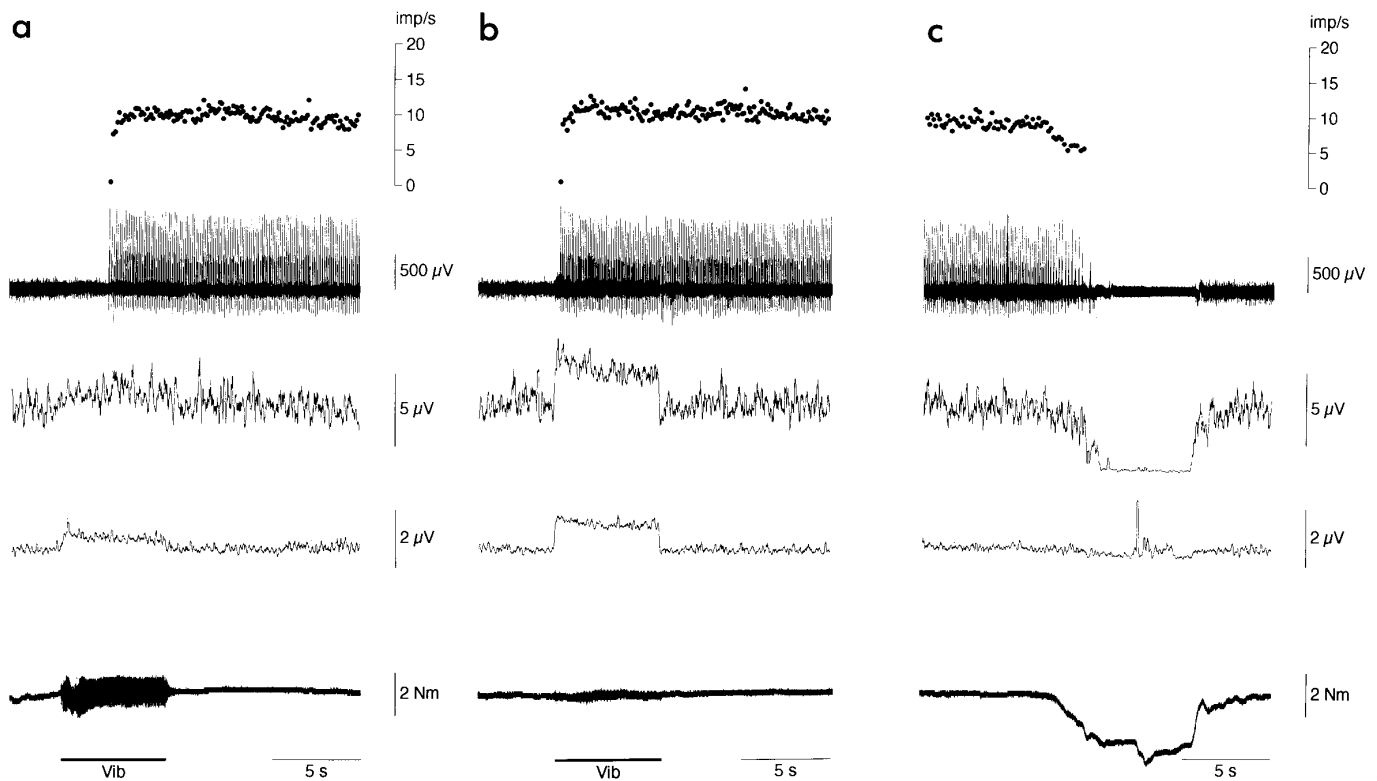


FIG. 1. Prolonged motor-unit discharge induced by short-lasting vibration; single-unit recordings from tibialis anterior (*top traces*) with root mean square (RMS)-processed gross electromyographs (EMGs) from tibialis anterior (*2nd traces*) and soleus (*3rd traces*), and ankle force (*bottom traces*). Instantaneous firing frequency for the motor unit is plotted above single-unit traces. First dot in this and all following figures represents the 1st action potential in the corresponding single-unit trace and is arbitrarily set to 0 imp/s. *a*: the tibialis anterior unit was activated from 0 into prolonged firing by a short-lasting vibration (50 Hz, 3 s; bar below force trace: duration of the vibration) applied to tibialis anterior muscle tendon. Because of electrical interference, the vibration induced a stimulus artifact in both the soleus and tibialis gross EMGs. *b*: successive vibration of same amplitude but at a higher frequency (100 Hz, 3 s) caused the unit to start firing earlier during the vibration and induced a prolonged firing at similar firing frequency as in *a*. After vibration-induced recruitment the unit could only be decruited voluntarily when the force level was below the level of recruitment (*c*).

in tibialis anterior (*2nd trace*) and soleus (*3rd trace*), and ankle force (*bottom trace*). The recruitment of the unit under study was not reflected in any major change in overall motoneuronal pool activity as indicated by the gross-EMG signals. However, a small shift in gross-EMG activity after the vibration was usually seen (see also Fig. 2). This is to be expected because of the recruitment of new units. Note also the late onset of the firing during the vibratory stimulus.

This vibration-induced prolonged EMG activity is similar to that described in the TVR (Hagbarth 1973; Lance et al. 1966; Lang and Vallbo 1967). In the TVR the latency to onset of muscular activity was shorter with higher stimulus frequencies. A similar relationship between stimulus strength and delay to onset of activity is also observed in motoneurons possessing the ability to generate plateau potentials (Hounsgaard and Kiehn 1989, Fig. 2). In the latter case it is caused by the voltage dependency characteristics of the plateau potential itself. We typically found that the delay to onset of motor-unit firing decreased when the stimulus intensity was increased by increasing the frequency. This is shown in Fig. 1*b* (stimulus frequency, 100 Hz) for the same unit as in Fig. 1*a* (stimulus frequency, 50 Hz). After the stimulation the unit fired at the same frequency as when it was recruited into prolonged firing by the lower stimulus

frequency in Fig. 1*a*. When the unit was voluntarily decruited it stopped firing at a much lower force level than at recruitment (Fig. 1*c*; final part of the same activity period). This difference in recruitment and decruitment threshold was a common phenomenon (see also Fig. 5) and has been described previously by other investigators (Denier van der Gon et al. 1985; Milner-Brown et al. 1973; Romagure et al. 1993). The cause of this phenomenon is unknown (see Van der Linden et al. 1991), but does not seem to have an obvious relation to the presence of plateau potentials in motoneurons.

We noted that it was relatively easy to activate units from silence into prolonged firing by short-lasting vibration. An important question was, however, whether a bistable firing behavior as observed in rat motor units (Eken and Kiehn 1989), i.e., vibration-induced frequency jumps from one stable firing frequency to another, could be induced in human motor units. Such a bistable firing behavior could not be demonstrated. Even with careful gradation of the voluntary force production, most subjects tended to recruit their low-threshold units directly into a stable firing range (Figs. 2, 4, and 5), which was similar to that obtained when units were activated from silence into prolonged firing by vibration. We will call this firing range the *preferred firing range*. Only if

subjects were allowed to listen to the spike potentials or visually follow a set level of integrated-EMG output, could they force the units to fire with a lower but unstable firing frequency. In this situation it was sometimes possible to evoke a sudden change in firing to the preferred firing range by short periods of vibration. These frequency jumps were usually small and not the 70–100% increases in firing frequency observed in unrestrained rats (Eken and Kiehn 1989). When the units were already firing in their preferred firing range, a second vibratory stimulus would cause a transient increase in the firing rate of the unit, although a maintained change was not induced (see Figs. 2 and 3).

Vibration-induced frequency jumps from zero to prolonged firing as described in Fig. 1 were observed in 18 of 24 soleus units (7 subjects) and in 31 of 42 tibialis anterior units (21 subjects).

We concluded from the experiments presented in this section that brief excitation of the motoneuron pool could evoke prolonged changes in motor-unit firing when the units were activated from silence. By contrast, in our study a clear, bistable firing behavior could not be demonstrated.

Paired recordings: using one unit as a monitor of the general excitability of the motoneuron pool

In cases where the vibration-induced prolonged firing occurred in one or several units simultaneously, it cannot be excluded that the prolonged firing was caused by an increase in the common synaptic drive onto the motoneuron pool.

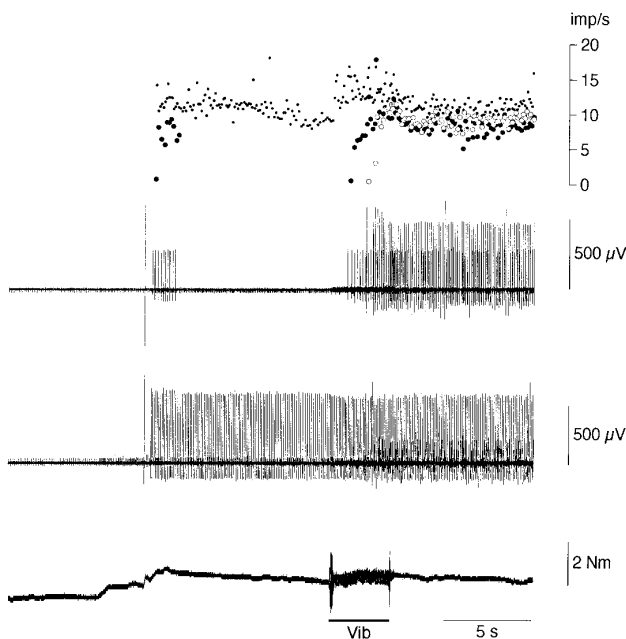


FIG. 2. Vibration-induced recruitment investigated with paired-unit recordings. Parallel single-unit recordings from 2 electrodes in tibialis anterior (*top* and *2nd* traces) with ankle force (*bottom* trace). Here and in Fig. 3, one unit was used to monitor common synaptic drive to motoneuron pool before and after the vibration. Instantaneous firing frequencies of 3 motor units are plotted above the single-unit EMG in *top* trace. *Units* 2 (●) and 3 (○) in single-unit *top* trace were activated from zero to ~8–10 imp/s by the vibration (34 Hz, 3.4 s). By contrast, *unit* 1 (high-amplitude spikes in *2nd* trace), which was already recruited voluntarily into its preferred firing range (see RESULTS) ~11 imp/s, only increased its firing frequency during the vibration.

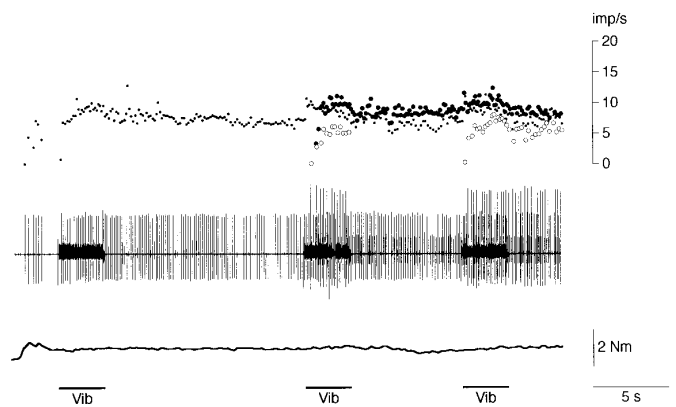


FIG. 3. Sequential vibration-induced recruitments in 3 soleus units. Same paired-unit paradigm as in Fig. 2; all vibrations 71 Hz, 3 s. *Unit* 1, *top* (middle-amplitude unit, ●) was used to monitor the common synaptic drive. It was recruited into prolonged firing by the 1st vibration. *Unit* 2 (small amplitude, ●) was recruited into prolonged firing by the 2nd vibration. *Unit* 3 (large amplitude, ○) was transiently recruited by 2nd vibration and fully recruited by 3rd vibration. After 2nd and 3rd vibrations, firing frequency of *unit* 1 remained stable or was even slightly lower than after the 1st vibration. *Unit* 2 also served as a monitor unit for *unit* 3 after the last vibration. Single-unit recording was enhanced according to Edin et al. (1988).

However, if the synaptic drive only increases during the vibration and remains the same after the vibration as before, then the vibration-induced prolonged firings are more likely to be ascribed to intrinsic self-sustaining motoneuronal mechanisms, like plateau potentials. To have a monitor of the common synaptic drive onto the motoneuron pool, we analyzed the firing behavior in several units recorded from the homonymous muscle in parallel, by the same or different electrodes (see also Eken and Kiehn 1989; Eken and Lømo 1993). We then looked for cases where only one or two units jumped from zero to their preferred firing ranges whereas the frequency of others, which were already recruited into their preferred ranges, remained unchanged except for the period of vibration. Such an example is illustrated in Fig. 2, which shows frequency versus time plots for three tibialis anterior units together with ankle force recordings. In this case the larger unit in the single-unit *bottom* trace (*unit* 1; ●) serves as a *monitor* or control of the common drive to the motoneuron pool. This unit, which had already been recruited voluntarily into its preferred firing range (10.62 ± 1.54 imp/s, mean \pm SD) at the beginning of the trace, was strongly activated during the vibration but returned to the same range as before the vibration (11.00 ± 1.15 imp/s, 1st s after stimulation excluded to include only stable firing). By contrast, *units* 2 and 3 (● and ○, respectively; single-unit *top* trace) were activated from 0 to ~8 and ~10 imp/s by the same short-lasting vibration. The prolonged changes in firing frequencies in *units* 2 and 3 cannot be the result of a persistent increase in the common drive onto the motoneuron pool, because the changes in firing frequency of *unit* 1 did not persist after the vibration (see DISCUSSION). In fact the firing frequency of *unit* 1 and the force output were slightly decreased just before the vibration (see frequency plot).

Figure 3 shows another example of this paired-recording paradigm in three soleus units recorded by the same electrode and followed through three consecutive vibration peri-

ods of the same frequency, amplitude, and duration. *Unit 1* (●) was recruited into prolonged firing by the first period of vibration. It then served as a monitor for *unit 2* (●), which was recruited into prolonged firing by the second vibration, and for *unit 3* (○), which was transiently recruited by the second period of vibration and fully recruited into its preferred firing range by the third period of vibration. Note that *unit 2* also served as a monitor for *unit 3* when it was recruited by the last vibration. The firing of both *unit 1* (7.44 ± 0.94 imp/s between stimuli 1 and 2, 6.81 ± 0.90 between stimuli 2 and 3, and 6.71 ± 1.16 after stimulus 3) and *unit 2* (8.54 ± 0.73 between stimuli 2 and 3; 8.58 ± 0.68 after stimulus 3) remained stable after recruitment, suggesting that the common drive onto the motoneuron pool was relatively constant throughout the recording period.

Results similar to those described in Figs. 2 and 3 were observed in paired recordings (>2 units) from tibialis anterior units in seven subjects and from soleus units in four subjects.

Firing behavior during isometric ramp contractions

To further investigate the firing behavior of low-threshold soleus and tibialis anterior motor units, subjects were asked to perform isometric ramp contractions. In these experiments we found a consistent discrepancy between the linear force development and the changes in firing frequency.

Figures 4 and 5 show examples from three tibialis anterior units (Fig. 4) and four soleus units (Fig. 5). The units increased their firing frequencies steeply after recruitment and then with a much slower rate during the remaining part of the ascending ramps (force: Figs. 4 and 5, *bottom traces*; instantaneous frequency plotted above the single-unit recordings in *top traces*, Figs 4 and 5). The de-recruitment threshold was usually lower than the recruitment threshold

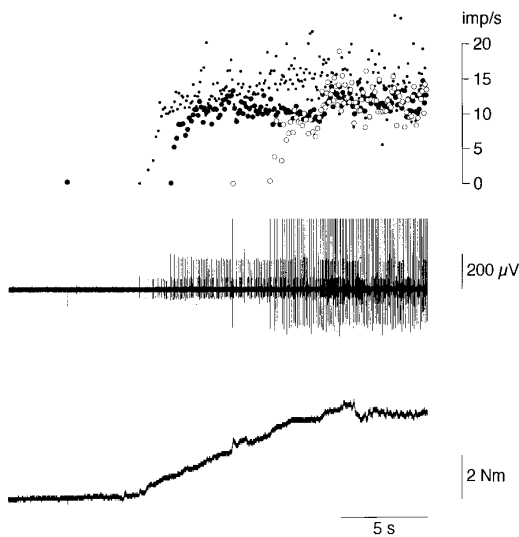


FIG. 4. Firing behavior during isometric ramp contractions. Characteristically, firing frequency increased steeply shortly after recruitment and then at a slower rate during the remaining part of the ascending phase of the ramps. This phenomenon is illustrated in 3 tibialis anterior motor units. Single-unit signal with instantaneous frequency above and force ramp below.

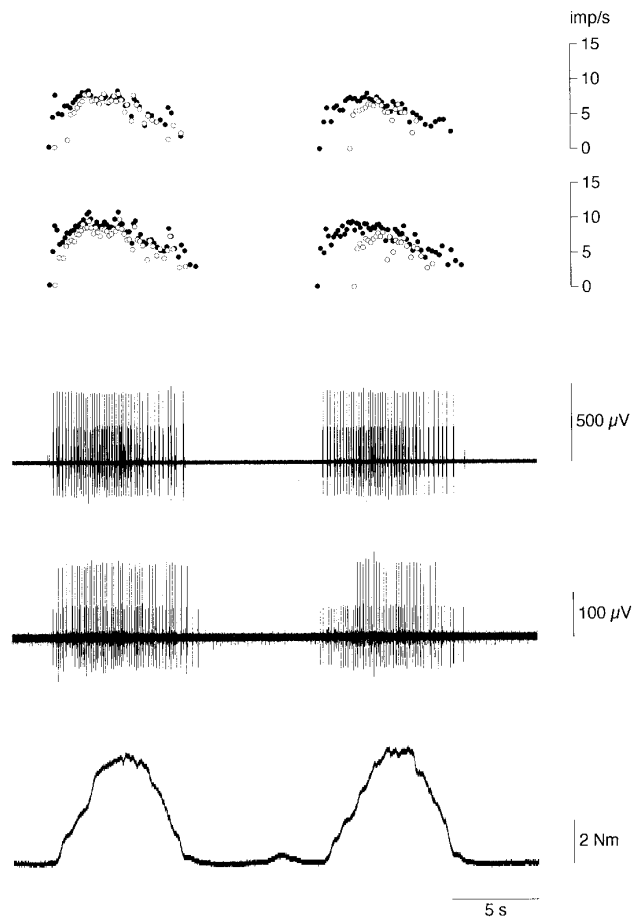


FIG. 5. Firing behavior during isometric ramp contractions in 4 soleus motor units. See Fig. 4 for description. Single-unit traces with instantaneous frequencies plotted above and force ramps below.

(see Fig. 5). A similar firing behavior on the ascending phase of the ramps was found in all subjects tested (soleus, $n = 6$; tibialis anterior, $n = 17$).

DISCUSSION

In this paper we have described prolonged firing in human leg motor units in response to short-lasting excitation of the motoneuron pool by vibration of the homonymous muscle tendon. Such a prolonged firing can be evoked in spinal motoneurons from cats and turtles by a short-lasting synaptic excitation or a brief depolarizing current pulses after monoaminergic receptor activation (Conway et al. 1988; Hounsgaard et al. 1988; Hounsgaard and Kiehn 1989) or pharmacological blockage of outward potassium currents (Hounsgaard and Mintz 1988; Schwindt and Crill 1980a–c). In these cases, the prolonged firing is caused by activation of a calcium-dependent depolarizing plateau potential, which is uncovered by decreasing outward and/or increasing inward currents (Hounsgaard and Kiehn 1985, 1989; Hounsgaard and Mintz 1988; Schwindt and Crill 1980a). The plateau potential can persist for minutes before it terminates spontaneously or is terminated prematurely by a short-lasting inhibition. Furthermore, the presence of plateau potentials in cat motoneurons allows them to fire in a bistable manner, i.e., shifting between stable low and high firing frequencies.

Unlike in motoneurons in decerebrated cats and intact rats (Eken and Kiehn 1989; Eken and Lømo 1993), a bistable firing behavior could not be convincingly demonstrated in humans. Thus during voluntary contraction, subjects quickly recruited their motor units into a relatively narrow frequency range, which we have called the preferred firing range, similar to that obtained when motor units were recruited into prolonged firing by a short-lasting vibration of the homonymous muscle tendon. Stable firing was not easily obtained below the preferred range and vibration when units were already firing in the preferred range caused only a transient increase in the firing rate (Figs. 2 and 3). Thus with the experimental paradigm used in this study we could not convince ourselves that the motor units showed a bistable firing in the same way as has been demonstrated in motor units in unrestrained rats and in cat motoneurons.

The lack of a bistable firing behavior of human tibialis anterior and soleus motor units might of course be that the motoneurons do not possess the ability to generate plateau potentials and that the preferred firing range corresponds to a state with no plateau potentials. However, in the next section we will argue that the sudden and prolonged change in firing frequency after short-lasting vibration seen in this study can be explained by the activation of plateau potentials in motoneurons. This discussion should not be seen as an attempt to provide a conclusive proof for the existence of plateau potentials in human motoneurons, but rather as a possible way of interpreting the available data.

Comparison of firing in human motor units with firing in motoneurons with plateau properties

If the recruitment of motoneuronal plateau potentials is the explanation for the prolonged firing, how then do we explain the difficulties in obtaining a bistable firing behavior in human motor units? An obvious possibility is that the threshold for triggering a sustained plateau in human motoneurons is close to the threshold for generating sodium spiking. This is the case for plateau potentials in turtle motoneurons (Hounsgaard and Kiehn 1989; Fig. 2), which in contrast with cat motoneurons do not display a true bistable firing behavior, but merely prolonged firing that outlasts a short-lasting excitatory stimulus (Hounsgaard and Kiehn 1989; J. Hounsgaard, personal communication). Changes in the threshold for the plateau potential and the consequences for firing were simulated in a mathematical model of vertebrate motoneurons with calcium-dependent plateau potentials (Booth and Rinzel 1995; Booth et al. 1997). When the amount of block of outward currents and/or enhancement of inward currents was increased in this model, the membrane potential where the plateau potential is activated during the ascending phase of a slow current ramp is moved closer to the threshold for initiation of sodium spikes. This change causes the cell to jump to a high-frequency firing shortly after recruitment. Similar changes were seen in actual experiments when a tonic dendritic synaptic excitation was superimposed on slow current ramps in motoneurons in decerebrated cats (Bennett et al. 1995). Conversely, if a tonic inhibitory synaptic input was produced, the threshold for plateau activation could be moved to a more depolarized level that allowed the motoneuron to fire at low frequencies

for a longer time during the ascending phase of a current ramp. These theoretic and experimental studies show that when the plateau threshold is close to the threshold for the sodium action potentials the motoneuron firing will be shifted to higher frequencies shortly after recruitment, when the plateau potential is triggered. In other words, in this situation the motoneurons will not display a bistable firing behavior even though they have the ability to generate plateau potentials. Therefore the absence of a bistable firing behavior in human tibialis anterior and soleus motor units does not exclude the presence of plateau potentials in the motoneurons. In fact, the firing behavior described in the present experiments could be interpreted as if the membrane potentials of low-threshold motoneurons will jump to the plateau shortly after firing a few action potentials as seen, for example, in turtle motoneurons and in invertebrate motoneurons (Hartline et al. 1988). This interpretation implies that the action potentials are riding on a plateau potential when the motoneurons are firing in what we have called the preferred firing range. Or, in other words, the maintained firing is supported by the presence of a plateau potential. In future studies it will clearly be of interest to investigate the effects of brief inhibitory inputs on the prolonged firing.

A consistent finding in reduced preparations was that the plateau potential is a threshold phenomenon; i.e., when the amplitude of the excitatory ON signal reaches a certain threshold the plateau is triggered in an all-or-none fashion and will persist for a prolonged time until it terminates spontaneously or is terminated by a short inhibitory input (see Fig. 3 in Hounsgaard and Kiehn 1989). After triggering the plateau it reaches a constant amplitude at a given holding membrane potential. A similar all-or-none behavior for the vibratory-induced changes in human motor unit firing behavior was seen (Fig. 1), but there was often a variability in the firing frequency reached after vibration. Studies using the model of vertebrate motoneurons mentioned previously have shown that the amplitude of the plateau will vary as a function of concentration of the plateau-inducing transmitter [e.g., serotonin (5-HT)] (Booth et al. 1997). Thus an increased 5-HT concentration, mimicked as an increased block of outward currents or increased inward currents, will beyond a certain threshold value increase the amplitude of the plateau potential. As a consequence high 5-HT concentrations will enable plateau potentials giving rise to higher firing frequencies than do low 5-HT concentrations. Unlike in the *in vitro* experiments where the monoamine concentration can be clamped by extrinsic drug application and in the decerebrated cat where the descending monoaminergic drive, at least in the serotonergic fibers, seems to be high (see Crone et al. 1988 and Hounsgaard et al. 1988 for references), little is known about the normal moment-to-moment variation in monoamine concentration in the spinal cord in intact organisms. Furthermore, the synaptic background activity will impose a positive or negative bias on the motoneurons. Being unable to control these factors in intact animals and humans, one would expect some variability in the size of vibration-induced frequency jumps over time in individual motoneurons even in the presence of plateau potentials. We have, therefore, refrained from a systematic quantification of the size of the frequency jumps.

Perhaps the strongest evidence that the prolonged firing

is the result of plateau potentials comes from the paired-unit recordings. This approach was also used in previous studies (Eken and Kiehn 1989; Eken and Lømo 1993) and the idea is to use one unit as a monitor of the common synaptic drive onto the motoneuron pool. With this set-up it was possible to observe that a short-lasting vibration could recruit units into prolonged firing whereas the frequency in the monitor unit, which already was firing in its preferred firing range, only increased during the vibration. This would suggest that the prolonged firing in the newly recruited units was not caused by increase in the common synaptic drive onto the motoneuron pool, but rather by activation of some intrinsic neuronal mechanism, like plateau potentials. Gorassini et al. (1997) also exploited the paired-unit recording paradigm and obtained similar results. However, for the paired-unit recording paradigm to be useful, it requires that the monitor units are sensitive to small changes in background activity. We have no way of determining this, but it can be seen in Figs. 2–3 that units that were firing in their preferred firing range still showed spontaneous variations as well as vibration-induced increases in firing frequency. Furthermore, at the moment there are only indirect ways of controlling that motoneurons share a common synaptic drive. One measure of the common drive onto pairs of motoneurons is the short-term cross-correlation, where a strong coupling is indicative of a strong common presynaptic drive. In preliminary experiments we have determined the coupling between pairs of units where vibration caused changes in the firing of one or both units (Kiehn, Eken and Conway, unpublished observations). In some of those pairs, where vibration shifted the firing from the unstable, low firing frequency to the preferred firing range, the short-term correlation decreased significantly compared with the previbratory values, which showed strong coupling. This could be interpreted as introduction of an additional intrinsic motoneuronal factor (plateaus). However, to really substantiate such a statement similar cross-correlation experiments in a model with bistable motoneurons would be needed to show how the coupling is influenced by activation of plateau potentials. Furthermore, the coupling could change as a mere consequence of changes in frequency or because new presynaptic cells were active in the postvibratory period. Therefore we do not feel at the moment that cross-correlation techniques can contribute further evidence for or against the plateau hypothesis in humans.

Finally, analogous firing-frequency profiles to those described in Figs. 4 and 5 have previously been described for several types of human muscles (flexor carpi radialis, Bawa and Calancie 1983; deltoid, De Luca et al. 1982; biceps brachii, Denier van der Gon et al. 1985; tibialis anterior, Van der Linden et al. 1991; extensor carpi radialis, Romaguere et al. 1993) and might be a general characteristic for low-threshold tonic motor units. Notably, these motor units steeply increase their firing shortly after recruitment and then at a slower rate during the remaining part of the ascending phase of the ramp. The steeper discharge rate observed during the initial part of the ascending ramp could represent firing in a sub-primary firing range (Kudina and Alexeeva 1992). The interspike interval in this range can be longer than the after-hyperpolarization after an action potential and a small increase in the synaptic drive can produce a large

increase in firing. This explanation does not, however, exclude the possibility that plateau potentials contribute to the nonlinear firing frequency seen in human motoneurons. If this is the case, plateau potentials with thresholds close to the sodium spikes in low-threshold human motoneurons could explain the well-known phenomenon of recruitment being more important than rate modulation at low force levels in many muscles (Basmajian and De Luca 1985).

Functional significance

As previously discussed, motoneuronal plateau potentials provide a mechanism for a short-term memory that could reduce the need for steady ongoing synaptic drive during maintained muscle contraction (Kiehn 1991a,b). Such a mechanism might be useful in postural muscles, for example, where part of a continuous descending synaptic drive could be replaced by self-supporting intrinsic membrane properties. In fact, the firing behavior of the phasic-tonic cortico-motoneuronal cells, which fire with a burst at the onset of a movement and then level off to a much lower steady-state firing during the static contraction (Fetz and Cheney 1990), would fit into that scheme. Furthermore, the decrease in tonic motor output in the rat soleus muscle after selective depletion of spinal monoamines may also suggest that motoneuronal plateau potentials support the muscle activity in the upright position (Kiehn et al. 1996).

We thank H. Hultborn and B. Conway for valuable comments on experiments and data interpretation.

This research was supported by Carl P. Petersens Fond, Fakultetsfonden, Jacob Madsens Fond, Wachterhausens Fond, L'Ége Sofus Carl Emil Friis og Hustru Olga Doris Friis' Legat, and Vera og Carl Johan Michaelsens Fond. T. Eken was supported by the Norwegian Research Council for Science and the Humanities. O. Kiehn is an Associate Research Professor supported by the Novo Foundation.

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Received 23 May 1997; accepted in final form 24 July 1997.

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