Functional role of plateau potentials in vertebrate motor neurons

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The expression of plateau potentials in spinal motor neurons is regulated by neuromodulatory substances. Recent experiments have shed new light on this regulation at the cellular level. It is now possible to evaluate the existence of plateau potentials in intact organisms, including humans, and to address the functional role of plateau potentials in motor control, as well as in information transfer in the brain.

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Abbreviations

5-HT	5-hydroxytryptamine
GABA	γ-aminobutyric acid
EMG	electromyography
EPSP	excitatory postsynaptic potential
I_{CAN}	calcium-activated nonselective cationic current
I_h	hyperpolarization-activated inward current
I–V	current–voltage
mGlu	metabotropic glutamate (receptor)
NMDA	*N*-methyl-D-aspartic acid
NSR	negative slope conductance region

Introduction

Research over the past 15 years has shown that vertebrate spinal motor neurons in reduced preparations, under certain circumstances, can generate prolonged plateau potentials (reviewed in [1–3]). A plateau potential is a stable membrane potential that is more depolarized than the resting membrane potential. When a plateau potential is initiated, a cell can fire action potentials in the absence of continuous synaptic excitation. This situation is different from the one in which firing is maintained by a summed excitatory drive that is sufficiently large to move the neuron's membrane potential above the threshold for action potentials. In the latter case, sustained synaptic excitation is required for a neuron to maintain continuous firing. The integrative capacity of a motor neuron with or without plateau properties is therefore very different.

In this review, we discuss recent experiments that have increased our knowledge about how plateau properties are regulated at the cellular level, evaluate whether plateau potentials exist in intact organisms (including humans), and examine the functional role of these properties in motor control. We will limit our discussion to the role of plateau potentials in tonic motor output. The involvement of motor neuron plateau potentials and NMDA-induced bursting properties in rhythmic motor output has been reviewed extensively elsewhere [2,4,5] and will not be dealt with here.

Phenomenology and terminology

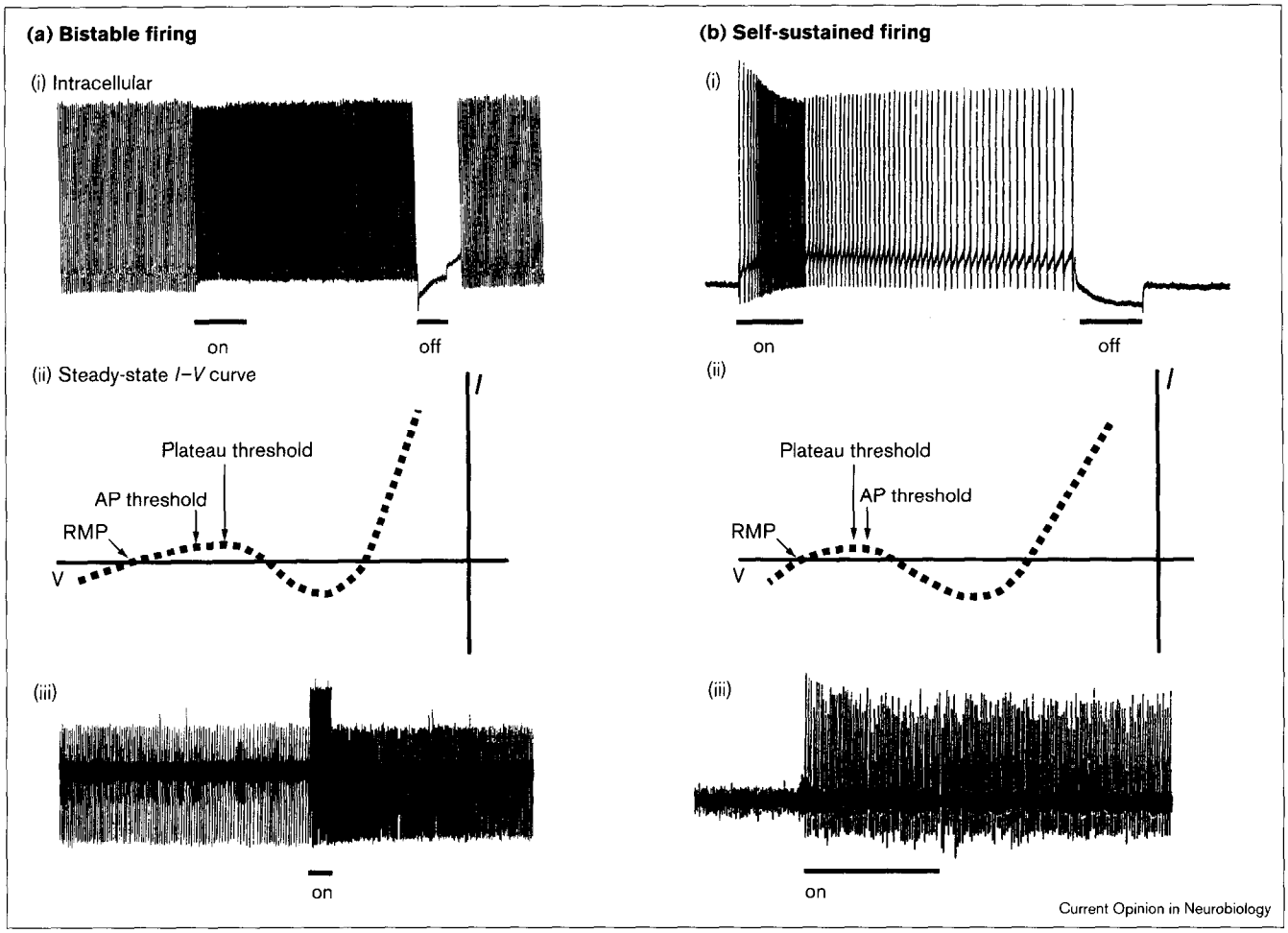
A transient depolarization of sufficient amplitude and duration ('on' stimulus) can initiate a plateau potential. This plateau can persist for minutes before it either terminates spontaneously or is actively turned off by a brief inhibition ('off' stimulus). Therefore, the plateau potential allows a cell to possess two stable membrane potentials: one is at rest and has no spike activity and another at a more depolarized level (i.e. a plateau) that generates sustained firing. This firing behavior is depicted in Figure 1bi. In some motor neurons, it is possible to activate the plateau potential when the cell is already firing (Figure 1ai), and then terminate it again at a later time. This mechanism permits the cell to switch back and forth between two stable modes of firing.

We and others previously described, indiscriminately, the firing behaviors depicted in the intracellular traces in Figure 1a,b as 'bistability' or a 'bistable behavior'. As described below, these two firing behaviors most probably reflect different steady-state *I–V* (current–voltage) relationships. Therefore, the terms 'bistability' and 'bistable behavior' as general descriptions of the firing behavior evoked by plateau potentials are imprecise. We suggest it would be better to use the phenomenology based terms 'bistable firing' for when on and off stimuli switch the firing between two stable levels (Figure 1a) and plateau-induced 'self-sustained firing' or 'prolonged firing' when an on stimulus recruits an electrically silent cell to steady firing (Figure 1b). We will use the term 'membrane bistability' to refer to the two stable membrane potentials imparted by the plateau potential.

Plateau properties are regulated by multiple neuromodulators

The expression of plateau potentials in spinal motor neurons is regulated by neuromodulators. This was originally described in cat and turtle motor neurons, where it was shown that the continuous presence of 5-hydroxytryptamine (5-HT) and noradrenaline was necessary for phasic fast synaptic signals to evoke membrane bistability [6–8]. Recent studies by Hounsgaard and colleagues [9•,10••] have shown that plateau properties in turtle motor neurons can also be induced by activation of muscarinic and group 1 metabotropic glutamate (mGlu1) receptors. Moreover, the ability to generate plateaux can be downregulated by $GABA_B$ receptor activation. In an elegant study in which all ionotropic transmission was blocked initially, it was also shown that electrical stimulation of the dorsolateral funiculus could evoke plateau properties by activating 5-HT_{1A}, mGlu1, and muscarinic receptors [10••]. These findings demonstrate a strong

Figure 1



Recordings depicting the relationship between plateau onset threshold, spike threshold, and stimulus-evoked firing behavior. **(a)** Bistable firing. (i) Intracellular recording from a lumbar motor neuron (lateral gastrocnemius–soleus) in a decerebrate cat. The bistable firing was initiated by brief synaptic excitation of the motor neuron pool ('on': medial gastrocnemius nerve stimulated 1.7 × threshold, 300 Hz) and terminated by a brief synaptic inhibition ('off': peroneal nerve stimulated 10 × threshold, 200 Hz). Adapted from [6]. (ii) Theoretical steady-state *I–V* curve that could explain the bistable firing behavior. The plateau onset threshold is above the threshold for spike initiation (action potential [AP] threshold). RMP, resting membrane potential; I, current; V, voltage. Adapted from [22••]. (iii) Bistable firing recorded extracellularly in the soleus muscle of an unrestrained rat. The initial low-frequency firing activity switched to a stable high-frequency firing after a brief excitation of the motor neuron pool ('on': low-threshold stimulation of the tibial nerve, 200 Hz). Adapted from [28]. **(b)** Self-sustained or prolonged firing. (i) Intracellular recording from a lumbar motor neuron in an *in vitro* preparation of the turtle spinal cord. The membrane bistability was induced by 5-HT and initiated by a brief depolarizing current pulse ('on') and terminated by a brief hyperpolarizing current pulse ('off'). Note the sudden jump in firing frequency when the plateau is turned on during the depolarizing pulse. Adapted from [8]. (ii) Theoretical steady-state *I–V* curve that could explain the prolonged firing. The plateau onset threshold is below or only slightly above the threshold for spike initiation. Therefore, a bistable firing pattern is impossible (see text for details). Adapted from [22••]. (iii) Self-sustained or prolonged firing in a human tibialis anterior motor unit initiated by a brief excitation of the motor neuron pool ('on': vibration of tibialis anterior tendon, 100 Hz). Adapted from [31••].

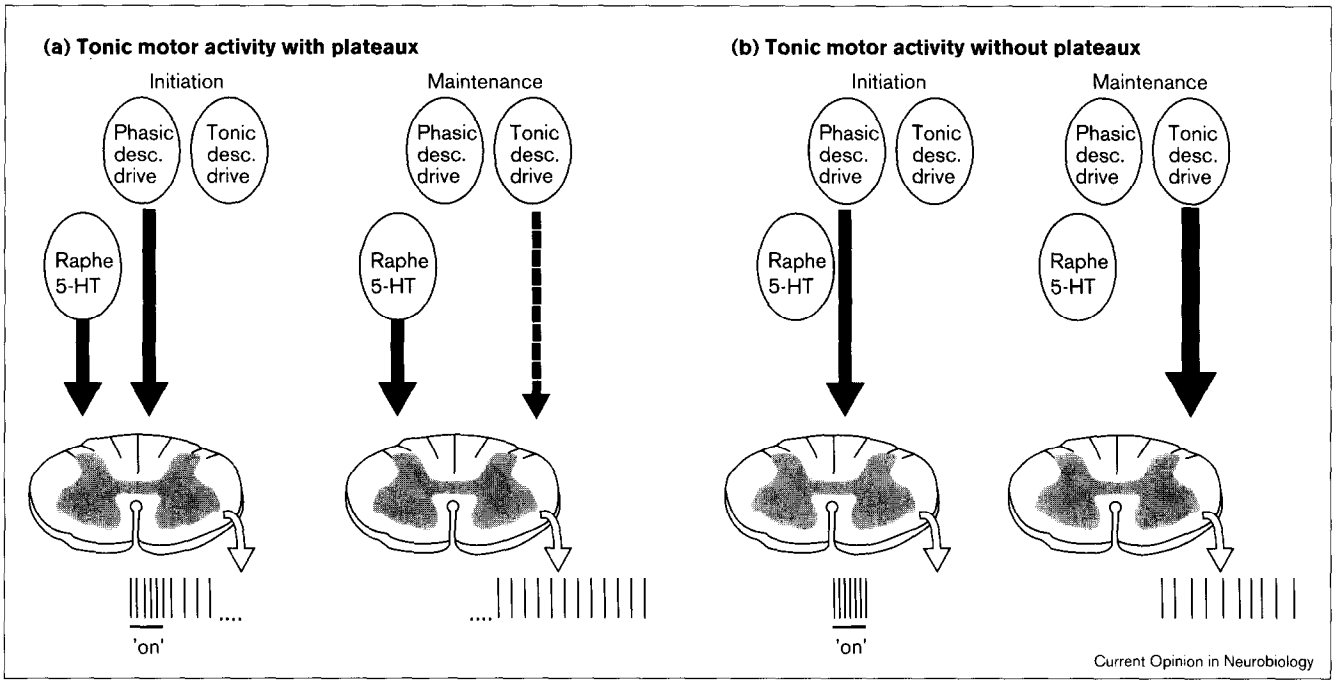
modulatory convergence of various neurotransmitter systems on motor neurons and indicate that plateau potentials in spinal motor neurons are under dynamic regulatory control from several descending fiber systems.

Modulation of ionic conductances underlying motor neuron plateau properties

The modulation of ionic conductances underlying motor neuron plateau properties has been described in detail in previous reviews [2,3]. Here, we shall focus on recent findings.

Plateau potentials are maintained by a non-inactivating or slowly inactivating inward current. In early experiments, Schwindt and Crill [1] suggested that this persistent current was carried by calcium ions and that it normally is counterbalanced by outward conductances. Thus, a pharmacological block of outward potassium conductances or enhancement of inward calcium conductances was required for generating plateaux in cat motor neurons. Later studies of 5-HT-dependent plateau potentials and of plateau potentials induced by inorganic potassium channel blockers in turtle motor neurons complemented this picture by showing that plateaux in the

Figure 2



Schematic to illustrate that the existence of motor neuron plateaux can reduce the need for ongoing conventional synaptic drive during tonic motor activity. **(a)** In the presence of tonic activity (e.g. in raphe–spinal 5-HT fibers), a strong short-lasting barrage of fast EPSPs from the brain ('Phasic descending drive') can trigger plateau potentials in motor neurons ('Initiation'). Because of the plateau potentials, the tonic motor activity can then be maintained ('Maintenance') by less, or no (indicated by broken line), activity in descending tonic motor systems ('Tonic descending drive') than during the phasic activation, except for the activity in the slow modulatory systems ('Raphe 5-HT'). **(b)** In the absence of neuromodulatory inputs from the brain, an increased tonic descending drive is needed to compensate for lack of plateau potentials. desc., descending.

turtle spinal cord also are calcium dependent [8]. As the ability to generate these plateaux is blocked by the organic calcium blocker nifedipine, it suggests that they are mediated by L-like calcium channels [8,11]. The blocking effect of nifedipine has now been shown to include plateaux induced by activation of muscarinic and mGlu1 receptors on motor neurons [9•], as well as spontaneous and transmitter-induced plateau potentials in dorsal horn neurons [12,13]. Using an extracellular electrical field that depolarizes dendrites and hyperpolarizes the soma, Hounsgaard and Kiehn [14] showed in turtle motor neurons that the persistent plateau current is localized mainly to distal dendrites. A similar conclusion was reached when cat motor neuron plateaux were activated with synaptic inputs [15].

Hounsgaard and Kiehn [8] originally suggested that 5-HT induces membrane bistability in turtle motor neurons by removing an opposing outward current, because 5-HT reduces a calcium-dependent potassium current; however, effects on other conductances, such as the L-like calcium current, were not excluded. This issue has not yet been addressed further for 5-HT, but in recent experiments, Svirskis and Hounsgaard [9•] showed that activation of muscarinic and mGlu1 receptors still enhances nifedipine-sensitive plateau properties when several of the outward potassium conductances are blocked. These receptor agonists also reduce the resting input conductance, suggesting that transmitter induction of plateau properties in spinal motor neurons involves regulation of multiple conductances, including enhancement of the L-like calcium conductance, as well as reduction of one or more outward conductances. Such multiple effects of transmitters on single-cell properties are well known, and recent studies of membrane bistability in a crustacean motor neuron [16,17] and in rat trigeminal motor neurons [18•] have shown that 5-HT regulates a hyperpolarization-activated inward current (I_h) that is open at rest, calcium- and non-calcium-dependent resting outward currents, and a persistent calcium current. More extended voltage-clamp studies are needed to clarify whether similar mechanisms lie behind plateau induction in spinal motor neurons.

Another issue that requires further consideration is the plateau current itself. Two recent studies have shown that plateaux can be generated either by a calcium-activated voltage-independent cation-selective current [19] or by a calcium-activated voltage-dependent sodium current [20•]. These inward currents are activated by calcium entering the cell and are referred to as I_{CAN}. Currently, it has not been excluded that I_{CAN} contributes to plateau generation in spinal motor neurons.

Relationship between plateaux and firing threshold

The plateau current in spinal motor neurons is voltage dependent, with a threshold 10–20 mV above resting levels [1,8]. Lee and Heckman [21••,22••] have made a detailed analysis of the relationship between the threshold for spike generation and the plateau threshold in cat motor neurons. A cell that possesses plateau potentials necessarily expresses a negative slope conductance region (NSR), and three crossings of zero current in the steady-state *I–V* relationship (Figure 1aii and bii). The plateau threshold corresponds to the point of zero slope at the inflection that initiates the NSR. Lee and Heckman [22••] measured the plateau thresholds in different motor neurons and compared them with the threshold for spike initiation. They found that in some motor neurons, the plateau onset threshold is below or close to the spike threshold, whereas in others, it is above the spike threshold. They also found a strong correlation between the type of motor neurons and this plateau/spike relationship. Thus, slow motor neurons, which have the lowest recruitment threshold during movements, tend to have a plateau onset threshold below or at the action potential threshold (Figure 1bii), whereas, fast motor neurons, which usually are recruited later in a movement, have a plateau onset threshold above the action potential threshold (Figure 1aii).

These two different *I–V* profiles result in dramatically different motor neuron firing behavior. A cell with a plateau onset threshold above the action potential threshold will be able to demonstrate true bistable firing (Figure 1ai); this is because spiking can be initiated without activating the plateau. In contrast, a cell with a plateau onset threshold below or at the action potential threshold will jump into plateau-induced self-sustained firing at or shortly after recruitment (Figure 1bi); this type of cells will not, therefore, be able to demonstrate true bistable firing.

The relationship between plateau and spike thresholds in a given motor neuron is probably dynamically modulated. For example, recent data obtained in a model of membrane bistability in vertebrate motor neurons have shown that the amount of block of outward currents and/or enhancement of an L-like inward calcium current will determine the plateau onset threshold [23•]. Varying these parameters can thus move the plateau voltage threshold towards or away from the spike threshold. Experimentally, this manipulation would correspond to changes in the concentration of one or several neuromodulators.

The plateau threshold can also be influenced by preceding depolarization. This was discovered by Russo and Hounsgaard [24] in turtle dorsal horn cells. They found that long-lasting near-activation of the plateau would lower its voltage threshold, possibly because of the depolarization-induced potentiation of the L-like calcium channel opening probability. The authors called this effect warm-up of the plateau and demonstrated that in the near-threshold voltage range, the warm-up effect had a time course of 2–3 s. Repetitive short-lasting depolarization (e.g. subthreshold EPSPs) will therefore tend to lower the plateau onset threshold over time. The warm-up effect has also been demonstrated in turtle [25•] and cat [26] motor neurons.

A change in the plateau threshold in relation to the spike threshold has also been demonstrated in cat motor neurons when current ramps were injected into cell bodies with superimposed tonic dendritic synaptic excitation [27••]. In this situation, the motor neuron jumped to the plateau at a significantly lower firing frequency than when tonic excitation was absent. In contrast, if a tonic inhibitory synaptic input was produced, the threshold for plateau activation could be moved to a more depolarized level and allowed the motor neuron to fire at a lower frequency for a longer time before recruitment of the plateau. These observations are compatible with a dendritic localization of plateaux in cat motor neurons. Bennett *et al.* [27••] suggest that the lowering of the plateau threshold is only apparent because less current is needed in the soma to activate the plateau when (dendritic) synaptic excitation is present. Another possible explanation is that the plateau onset threshold is reduced in response to warm-up caused by the barrage of synaptic excitation. In this way, the plateau threshold can be changed by both fast synaptic excitatory and slow modulatory inputs.

Evidence for motor neuron plateau potentials in intact animals

The first evidence of plateau potentials in intact animals came from recordings in the soleus muscle of unrestrained rats [28,29,30••]. In these animals, a bistable firing pattern (Figure 1aiii) can be evoked experimentally by short-lasting excitation and inhibition of the motor neuron pool by peripheral nerve stimulation. Motor units also shift abruptly between stable low-frequency and long-lasting high-frequency firing in response to spontaneous short-lasting activity episodes. Abrupt stimulus-evoked or spontaneous shifts in frequencies can take place without any change in firing frequency of other simultaneously active motor units, suggesting that the long-lasting changes are not caused by an increase in activity in descending fibres. This behavior causes an apparent dissociation of activity between different motor neurons, which is particularly striking during long-lasting low-amplitude activity, as measured by EMG. Typically, this kind of activity is caused by a small number of motor neurons firing at stable high frequencies (20–30 Hz) for extended periods of time while other motor neurons are silent. There appears to be no fixed order of recruitment and de-recruitment; in contrast, there is a cycling of activity from one tonic period to another between motor neurons. This suggests that individual motor neurons in the soleus pool have rather similar plateau thresholds, but that their ability to generate a plateau varies over time. Thus, at least during tonic activity, plateau mechanisms supplement the classical concepts of a simple motor-unit recruitment hierarchy.

The ability to produce long-lasting tonic activity in the soleus develops in parallel with the maturation of descending

monoaminergic projections (T Eken *et al.*, *Soc Neurosci Abstr* 1990, 16:331) and is strongly reduced after selective depletion of spinal monoamines [29]. All these observations are compatible with the notion that some spinal motor neurons in the intact rat have monoamine-dependent plateau potentials with a steady-state *I–V* relationship, as shown in Figure 1aii, where the threshold for spike activity is lower than the plateau threshold.

We have looked for evidence of plateau potentials in human tibialis anterior and soleus motor neurons and have found that brief excitation of the motor neuron pool by vibrating the homonymous muscle while it is electrically silent could induce motor unit firing during the vibration as well as prolonged firing, which sometimes outlasted the stimulus for many seconds to minutes [31••]. Recordings from pairs of motor units showed that the prolonged firing was not attributable to a systematic change in the common drive to the motor neurons. Similar observations have been made by Gorassini *et al.* [32••]. However, a bistable firing pattern could not be convincingly demonstrated [31••]. This is because these low-threshold neurons most often jumped into what we have called their 'preferred firing range' shortly after recruitment, when activated voluntarily or by vibration. Steady-state firing was not easily obtained below the 'preferred firing range', and neurons already firing in this range were only transiently affected by vibration. This abrupt recruitment pattern was seen, for example, in slow isometric ramp contractions, where neurons would increase their firing frequency very steeply over a few interspike intervals and then fire with a much slower rate during the remaining part of the ascending ramp [31••]. This sudden jump in firing frequency during ramp contractions is a general phenomenon and had previously been described by other investigators in a range of muscles [33–36].

We conclude from our experiments that human ankle motor neurons are unable to display a bistable firing pattern similar to that seen in rat ankle motor units. As discussed above, however, this is not incompatible with the existence of motor neuron plateau potentials in humans. The vibration-induced prolonged firing can be explained by human low-threshold ankle motor neurons having a steady-state *I–V* relationship, as shown in Figure 1bii, where the threshold for spike activity is close to or above the plateau onset threshold.

Why plateau potentials?

As discussed above, the existence of motor neuron plateau potentials reduces the need for steady on-going synaptic drive during maintained muscle contractions [2,3]. Such a mechanism might be useful in postural muscles, where part of a continuous descending synaptic drive could be replaced by self-supporting membrane properties. This concept is illustrated in Figure 2. Thus, in the presence of tonic activity in neuromodulatory systems, such as the raphe–spinal 5-HT system, a strong short-lasting barrage of EPSPs from other supraspinal sources could trigger plateau potentials and thereby prolong tonic motor activity. This prolonged motor activity could then be maintained by less descending tonic activity than during phasic activation (Figure 2a), or possibly by no tonic activity at all. The firing behavior of 'phasic-tonic' corticomotoneuronal cells, which fire with a burst on the onset of a movement and then level off to a much lower steady-state firing during static contraction, fits into this scheme [37]. By contrast, in the absence of supraspinal neuromodulatory inputs, a continuous tonic descending drive is needed to compensate for the lack of plateau potentials (Figure 2b).

The above description of the involvement of motor neuron plateaux in tonic motor output is a natural extension of the plateau phenomenology. In addition to this, we would like to propose that plateau potentials are superior to continuous steady synaptic activity for the maintenance of steady prolonged motor neuron firing. This is because synaptic transmission is a probabilistic process, which is believed to be the main source of the irregular spiking that has been observed in all areas of the central nervous system. Activation of a long-lasting plateau will tend to uncouple spike generation from the variability in synaptic input, as well as from the effects of nonlinear synaptic summation of excitatory synaptic potentials, and will thereby favor a more steady and predictable firing. Moreover, during the plateau, the input conductance increases two to three times compared to resting membrane potential [8]. Synaptic inputs arriving when the plateau is activated will therefore be less effective because of the shunting effect. For motor units, these factors will thus give a more stable force output. Finally, the dendritic localization of plateau potentials optimizes information flow as slow DC potentials spread towards the soma with less attenuation than fast EPSPs [38••].

In the rat soleus muscle, the sigmoid shape of the tension–frequency curve further attenuates firing frequency variations. Simulation of motor neuron tension output after plateau activation predicts that muscle fibers contract at more than 80% of maximal tetanic tension with only minute variability [28]. Stable tension production is important in order to avoid oscillations in the tension-producing system, and stability in individual motor neurons becomes all the more important when the number of active neurons is small. Thus, we propose that motor neuron plateau potentials play an essential part in the generation of stable postural activity.

Conclusions

The preceding years have brought significant advances in our understanding of the regulation of plateau potentials in spinal motor neurons. One of the most important advances at the cellular level is a precise analysis, both from actual experiments and from modeling, of the relationship between plateau onset threshold and spike threshold, which predicts the firing pattern caused by plateau activation. These results support the idea that the differences between firing behavior in tonic ankle motor units in intact rats and humans can be ascribed to the existence of motor neuron plateau potentials with different onset thresholds.

Researchers are already addressing how preceding depolarization can change the plateau onset threshold. It will be important to elaborate this theme further in future experiments by investigating how different neuromodulators in varying concentrations affect the plateau onset threshold. Experiments with denervated descending monoaminergic fibers suggest that these systems play an important role in tonic motor output, presumably because they control plateau expression in motor neurons. We need to find out more about the firing of descending monoaminergic neurons innervating spinal motor neurons during tonic motor output [39] and how the activity in these neurons is associated with activity in well-known descending motor systems.

Finally, the expression of plateau potentials in a neuron probably reduces the stochastic nature of spike activity that is otherwise imposed by steady synaptic potentials. We suggest that this general hypothesis should be tested also in other areas of the brain in which plateau potentials interact with synaptic activity (e.g. in the cortex and cerebellum).

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Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

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5-HT has previously been shown to induce plateau properties in turtle motor neurons [8]. Using voltage-clamp experiments with triangular voltage ramp commands, the authors show that activation of mGlu1 and muscarinic receptors also promotes the generation of plateau potentials, possibly by increasing an L-like inward current and by decreasing the resting conductance. $GABA_A$ receptor activation suppresses the generation of plateau potentials by decreasing the L-like calcium current and increasing the input conductance. These results show that multiple transmitters control the expression of plateau potentials in turtle motor neurons and that the effects are mediated through the modulation of several conductances.

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This study investigates the ionic basis for 5-HT-induced bistable membrane properties in guinea pig trigeminal motor neurons (TMNs). It is found that 5-HT induces a region of negative slope conductance region (NSR) in the steady-state current–voltage (I–V) relationship, which allows the cells to generate plateau potentials. The NSR was strongly reduced by an L-type calcium channel antagonist. A remaining inward rectification in the I–V relationship was linearized by tetrodotoxin (TTX), suggesting that L-type calcium and persistent sodium currents mediate the bistable membrane properties in TMNs. In other experiments by the same group, it was shown that 5-HT had multiple effects on TMNs, including a reduction of a leakage potassium current, a reduction in a calcium-dependent potassium current ($I_{K(Ca)}$), and an enhancement of an inwardly rectifying mixed cationic current (I_h). As pharmacological suppression of the leakage potassium and $I_{K(Ca)}$ did not elicit robust membrane bistability in TMNs, the authors propose that 5-HT, in addition to reducing outward currents, enhances inward current(s), in particular the L-like calcium current.

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This paper demonstrates that newborn mouse ambiguus neurons, which control the esophageal phase of swallowing, display calcium-dependent plateau potentials in response to brief excitation. The plateau potentials were expressed in the absence of neuromodulatory substances, and were blocked completely by intracellular injection of the fast calcium chelator bis-(*O*-aminophenoxy)-*N*,*N*,*N*',*N*'-tetraacetic acid (BAPTA). The plateau potentials persisted in the presence of tetrodotoxin (TTX) but were blocked when extracellular sodium was replaced with choline. This suggests that the plateau potential in ambiguus neurons are generated by a calcium-activated inward current carried by sodium. This current shares similarities with the calcium-activated inward unspecific cationic current (I_{CAN}) present in many invertebrate and vertebrate neurons.

While many CAN channels are voltage insensitive, the calcium-activated plateau current in ambiguus neurons is very sensitive to voltage.

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This interesting paper assesses the ability of spinal motor neurons in decerebrated cats to produce long-lasting firing in response to brief excitation from muscle spindle Ia afferents. To enhance plateau properties, the authors exposed the spinal cord to a noradrenergic α_1 agonist. Under those conditions, 35% of the recorded cells produced steady firing, out-lasting the stimulus for more than 3 s. This group of cells was classified as 'fully bistable', and probably innervates fatigue-resistant muscle fibers. 65% of the motor neurons produced prolonged firing lasting less than 3 s. This group of cells was classified as 'partially bistable' and probably innervates fast-fatigable muscle fibers. The 'fully bistable' motor neurons displayed a jump in firing frequency immediately upon initiation of rhythmic firing, while a similar frequency jump in 'partially bistable' motor neurons appeared later after recruitment. The relationship between the persistent inward plateau current and the firing characteristic of 'fully bistable' and 'partially bistable' neurons was investigated in an accompanying paper [22••]. Both types of cells displayed a region of negative slope conductance region in the steady state *I–V* relationship. The activation and deactivation of the inward plateau current occurred at a significantly more hyperpolarized level in 'fully bistable' cells than in 'partially bistable' cells. Thus, the onset threshold for the plateau current in 'fully bistable' motor neurons was close to or below the action potential threshold, while it was above the threshold for action potential generation in 'partially bistable' motor neurons. These fundamentally different types of *I–V* relationships are schematically illustrated in Figure 1 of this review (Figure 1aii and bii) and may serve to explain the difference in firing behavior between motor neurons with a 'bistable firing behavior' (Figure 1a) and motor neurons with 'self-sustained firing' (Figure 1b; see text for further explanation).

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See annotation [21••].

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The authors used a quantitative two-compartment motor neuron model in which the soma compartment contained ionic conductances that generated sodium action potentials (I_{Na}, $I_{K\text{-}dr}$, $I_{Ca\text{-}N}$, $I_{K(Ca)}$), the dendrite compartment contained conductances responsible for plateau generation ($I_{Ca\text{-}N}$, $I_{K(Ca)}$, $I_{Ca\text{-}L}$), and the current spread between the two compartments through a relatively weak coupling conductance. This is the first motor neuron model to address the systematic development of complex and bistable firing patterns by appropriate simulation of multiple ion channel blockers and neurotransmitters that account for a variety of complex firing behaviors experimentally observed in turtle motor neurons.

24. Russo RE, Hounsgaard J: **Short-term plasticity in turtle dorsal horn neurons mediated by L-type Ca^{2+} channels.** *Neuroscience* 1994, **61**:191-197.

25. Svirskis G, Hounsgaard J: **Depolarization-induced facilitation of**
• **plateau-generating current in ventral horn neurons in turtle spinal cord.** *J Neurophysiol* 1997, **78**:1740-1742.

This paper shows that all ventral horn interneurons and motor neurons that are able to generate plateau potentials show depolarization-induced facilitation of the underlying inward current, possibly as a result of a use-dependent facilitation of the persistent L-like calcium current. This effect corresponds to the previously described 'warm-up' effect on the plateau potential [12,24].

26. Bennett DJ, Hultborn H, Fedirchuk B, Gorassini M: **Short-term plasticity in hindlimb motoneurons of decerebrate cats.** *J Neurophysiol* 1998, **80**:2038-2045.

27. Bennett DJ, Hultborn H, Fedirchuk B, Gorassini M:
•• **Synaptic activation of plateaus in hindlimb motoneurons of decerebrate cats.** *J Neurophysiol* 1998, **80**:2023-2037.

The authors injected current into motor neuron cell bodies through a recording electrode and found that the threshold for plateau activation under resting conditions is significantly above the threshold for recruitment of action potentials. The plateau threshold could be lowered by tonic Ia afferent excitation, and raised by tonic reciprocal Ia inhibition. Both effects were graded. Strong tonic synaptic excitation lowered the threshold sufficiently to activate the plateau at or before recruitment of action potentials. The plateau threshold was affected in a similar fashion when action potentials were inactivated. The results are consistent with a dendritic localization of the plateaux, and point to a possibly important role for plateaux in securing effective recruitment.

28. Eken T, Kiehn O: **Bistable firing properties of soleus motor units in unrestrained rats.** *Acta Physiol Scand* 1989, **136**:383-394.

29. Kiehn O, Erdal J, Eken T, Bruhn T: **Selective depletion of spinal monoamines changes the rat soleus EMG from a tonic to a more phasic pattern.** *J Physiol* 1996, **492**:173-184.

30. Eken T: **Spontaneous electromyographic activity in adult rat**
•• **soleus muscle.** *J Neurophysiol* 1998, **80**:365-377.

The author studied single-motor-unit and whole-muscle EMG activity in a homogeneous slow hindlimb muscle in unrestrained rats, and found a good correlation of single-unit activity to whole-muscle EMG during locomotion. However, during tonic activity, there was an apparent dissociation between the firing in individual motor neurons, and thus between single-neuron and whole-muscle EMGs. Furthermore, there was a seemingly random recruitment of individual neurons to long-lasting firing, resulting in a cycling of activity between motor neurons over time. The behavior during tonic activity can be fully explained by the existence of motor neuron plateau potentials.

31. Kiehn O, Eken T: **Prolonged firing in motor units – evidence of**
•• **plateau potentials in human motoneurons?** *J Neurophysiol* 1997, **78**:3061-3068.

The authors studied EMG activity in human low-threshold motor neurons. They found that brief excitation of motor neurons by vibration of the homonymous muscle tendon could recruit neurons from silence to long-lasting firing in a 'preferred firing range'. Recordings from pairs of motor neurons showed that vibration-induced recruitment of one neuron to prolonged firing could happen with only transient changes in frequency in a second neuron already firing in its 'preferred firing range' – that is to say, that the prolonged firing in the first neuron was not attributable to increased activation of the whole motor neuron pool. However, unlike in the rat, a true bistable firing (i.e. shifting between two stable frequency levels) could not be demonstrated. On voluntary recruitment, neurons tended to jump directly from silence to the 'preferred firing range', making it very hard, or even impossible, to maintain steady firing at lower frequencies. It is argued that the findings are compatible with the existence of plateau potentials with a threshold close to or below the action potential threshold.

32. Gorassini M, Bennett DJ, Siu M, Yang JF: **Self-sustained firing of**
•• **human motor units.** *Neurosci Lett* 1998, **247**:13-16.

By using paired recordings of motor units, these authors confirm the findings from [31••], showing that vibration-induced prolonged firing can appear in a 'test unit' without change of the firing in a 'control unit', suggesting that the prolonged firing is attributable to activation of plateau potentials rather than changes in descending drive. In addition, the duration of the prolonged firing often increased progressively after each vibration, similar to the 'warm-up' property shown for plateau potentials in turtle dorsal horn neurons and motor neurons [12,24,25•] and cat motor neurons [26].

33. De Luca CJ, Lefever RS, McCue MP, Xenakis AP: **Behaviour of human motor units in different muscles during linearly varying contractions.** *J Physiol* 1982, **329**:113-128.

34. Bawa P, Calancie B: **Repetitive doublets in human flexor carpi radialis muscle.** *J Physiol* 1983, **339**:123-132.

35. Denier van der Gon JJ, ter Haar Romeny BM, van Zuylen EJ: **Behaviour of motor units of human arm muscles: differences between isometric contraction and relaxation.** *J Physiol* 1985, **359**:107-118.

36. Vander Linden DW, Kukulka CG, Soderberg GL: **The effect of muscle length on motor unit discharge characteristics in human tibialis anterior muscle.** *Exp Brain Res* 1991, **84**:210-218.

37. Fetz EE, Cheney PD: **Functional properties of primate corticomotoneuronal cells: comparisons with spindle afferents and motor units.** In *The Segmental Motor System.* Edited by Binder MD, Mendell LM. Oxford: Oxford University Press; 1990:381-392.

38. Thurbon D, Lüscher H-R, Hofstetter T, Redman SJ: **Passive electrical**
•• **properties of ventral horn neurons in rat spinal cord slices.** *J Neurophysiol* 1998, **79**:2485-2502.

Whole-cell tight-seal recordings were made simultaneously with two electrodes from the soma of ventral horn neurons in a transverse spinal cord slice preparation from young rats in order to determine the passive electrical properties of the cells. One electrode could be used for current injection, and the two-electrode configuration minimized the voltage artifact on the recording electrode. The electrical passive responses of the cell were matched optimally to responses of a compartmental model of the same neuron, and specific membrane capacitance (C_m), membrane resistivity (R_m), and cytoplasmatic resistivity (R_i) were determined. A main finding from the analysis was a much higher value of C_m than previously assumed. This implies that distal fast synaptic potentials might be more attenuated when they reach the soma than has previously been anticipated. DC voltages will be much less affected by the large C_m, and the cell will therefore appear more electrotonically compact for distally generated slow potentials than distally generated fast potentials.

39. Jacobs BL, Fornal CA: **Activation of 5-HT neuronal activity during motor behavior.** *Semin Neurosci* 1995, **7**:401-408.