HIGHLIGHTED TOPIC | Neural Changes Associated with Training

Effects of exercise training on α-motoneurons

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Evidence is presented that one locus of adaptation in the “neural adaptations to training” is at the level of the α-motoneurons. With increased voluntary activity, these neurons show evidence of dendrite restructuring, increased protein synthesis, increased axon transport of proteins, enhanced neuromuscular transmission dynamics, and changes in electrophysiological properties. The latter include hyperpolarization of the resting membrane potential and voltage threshold, increased rate of action potential development, and increased amplitude of the afterhyperpolarization following the action potential. Many of these changes demonstrate intensity-related adaptations and are in the opposite direction under conditions in which chronic activity is reduced. A five-compartment model of rat motoneurons that innervate fast and slow muscle fibers (termed “fast” and “slow” motoneurons in this paper), including 10 active ion conductances, was used to attempt to reproduce exercise training-induced adaptations in electrophysiological properties. The results suggest that adaptations in α-motoneurons with exercise training may involve alterations in ion conductances, which may, in turn, include changes in the gene expression of the ion channel subunits, which underlie these conductances. Interestingly, the acute neuromodulatory effects of monoamines on motoneuron properties, which would be a factor during acute exercise as these monoaminergic systems are activated, appear to be in the opposite direction to changes measured in endurance-trained motoneurons that are at rest. It may be that regular increases in motoneuronal excitability during exercise via these monoaminergic systems in fact render the motoneurons less excitable when at rest. More research is required to establish the relationships between exercise training, resting and exercise motoneuron excitability, ion channel modulation, and the effects of neuromodulators.
eral nerve. Early reports on changes in axon diameters in peripheral nerves have shown both increases (29, 60) and decreases (5, 58), with much variability in findings attributable to different species and intensities and types of exercise. With respect to volume of the soma, findings generally indicate that relatively few changes occur as a result of increases, as well as decreases, in chronic neuromuscular activity (45, 61). One study reported a modest (14%) but significant increase in average diameter rat soleus motoneurons following endurance training (53). A more recent electrophysiological study reported that estimated cell capacitance, an index of cell size, was significantly increased for high-threshold fast motoneurons following intense endurance training (10). In contrast to findings at the level of soma and axons, there appears to be an effect of increased activity on dendrites. Lumbar motoneurons of rats subjected to increased activity in voluntary exercise wheels for 5 days had total dendritic arbors that were slightly yet significantly larger, with larger arbors per dendrite (34). Overall, the available literature suggests that changes occurring in motoneuronal morphology with increased activity, if any, are minor (with the exception of changes at the nerve terminal, see below), although the demonstration of dendritic arbor morphology may prove functionally significant with further study.

NEUROMUSCULAR JUNCTION

Motoneuron adaptations also include the dynamics at the site of interaction with its end organ, muscle, at the neuromuscular junction. Endurance training appears to increase nerve terminal branching at the neuromuscular junction (6, 25), although results are equivocal (68). The functional significance of this increased complexity at the neuromuscular junction, other than the demonstration that motoneurons are responsive to increased activity, has not yet been elucidated. What does appear to be consistent is the increased synaptic efficacy due to enhanced neurotransmitter release that occurs with increased activity (7, 24, 27). The increased safety factor and decreased likelihood that neuromuscular propagation is impaired during sustained activation of the neuromuscular junction appear to be consistent with a strengthening of the neuromuscular apparatus as a whole to offset fatigue. It is interesting to note that, while this change is presynaptic, the muscle fiber responds by strengthening the synapse in the form of increased acetylcholinesterase content (38) and acetylcholine receptor number (23). Most likely a significant proportion of these changes is supported by increased motoneuronal synthesis, axon transport, and secretion of trophic substances that influence transcription of subsynaptic myonuclei (see next section, BIOCHEMISTRY/METABOLISM).

The mechanism by which these neuromuscular junction changes occur has been elucidated to some degree by experiments with crayfish (51). In crayfish neuromuscular junctions, 14 days of electrical stimulation produce an adaptation in neuromuscular transmission (smaller decrease in end-plate potential amplitude during sustained excitation) similar to that found following endurance training, which is independent of transmitter release and muscle fiber contraction and is evoked by depolarization of the neuron alone (51). It appears that metabolic events in the motoneuron soma related to depolarization produce this change in synaptic efficacy that occurs with increased usage.

BIOCHEMISTRY/METABOLISM

Contrary to the lack of evidence of significant morphological adaptations in motoneurons to increased activity, several indexes of the metabolic state of motoneurons are altered. Motoneurons of treadmill-trained rats possess nucleoli that are increased in area and surrounded by basophilic particles and have an increased staining intensity for glucose-6-phosphate dehydrogenase, suggesting increased protein synthesis (30, 35). Trained motoneurons appear to possess the capability to transport larger amounts of protein in their axons, in both orthograde and retrograde directions (21, 48–50). This transport is most likely important for the delivery of substances to and from the periphery that are important for adaptation of the motor unit as a whole. For example, the synaptosome-associated protein SNAP25, an important protein for docking of the synaptic vesicle to the presynaptic membrane, is selectively transported in higher quantities in axons of trained motoneurons (50).

Some proteins are present in higher quantities in trained motoneurons. The enzyme malic dehydrogenase and the trophic factor calcitonin gene-related peptide are present in higher amounts in the somata of trained motoneurons (35, 36). It seems that the increased malic dehydrogenase, which exists in mitochondrial and cytoplasmic isofoms, does not indicate an increased mitochondrial content, since the mitochondrial enzyme succinic dehydrogenase (SDH) is not responsive to endurance training or even decreased usage (53, 61). Although SDH activity appears to vary inversely with soma size (26, 45, 63), the functional significance of this relationship has yet to be determined. The lack of responsiveness of this enzyme to variations in chronic activity, which is contrary to the relationship seen in muscle, probably indicates the lack of stress to the mitochondrial energy-producing system that increased activity imposes. It is worth noting that electrical stimulation of motor axons for 50% of the total time per day for 8 wk in cats also failed to evoke changes in SDH measured in somata, despite dramatic changes in the same enzyme in the stimulated muscles. Since the motoneurons in that study were deprived of peripheral afferent input, and thus action potential development was antidromic during the chronic stimulation, one can conclude that the number of action potentials per day generated...
by a motoneuron (calculated from stimulation frequency and time and pattern of stimulation) does not constitute a metabolic stressor significant enough to evoke a mitochondrial enzyme response. Similar conclusions were arrived at by Jasmin et al. (48), who found that increased orthograde axon transport did not occur with swimming training, despite the fact that weight-supported running training, which did result in an adaptive response, involved approximately one-half of the total number of extra action potentials per day.

The rate of regeneration and sprouting in response to a given stimulus has been used experimentally to determine the effects of activity on motoneuron metabolism, since these events involve alterations in protein synthesis and axon transport. Endurance-trained motoneurons appear to sprout more robustly when given the stimulus (i.e., signals emanating from denervated fibers following partial denervation) to do so (31). However, sprouting and regeneration capacities are reduced when chronic activity is increased during the regenerative/reinnervation process (33, 62).

More recently, emphasis has been placed on possible activity-mediated neurotrophic effects on motoneurons, since the repeated demonstrations of exercise-induced increased neurotrophin expression in hippocampus (54). In hippocampus, brain-derived neurotrophic factor (BDNF) increases are important for synaptic plasticity, learning, and memory (67). Hippocampal BDNF also increases robustly with exercise, and exercised animals show enhanced cognitive function because of this (67). BDNF regulates the mRNA levels of itself, its receptor trkB, the transcription factor cyclic AMP-responsive element binding protein, and synapsin I, which affects synaptic transmission. These changes in protein transcriptional activity are intimately linked to receptor activation, intracellular calcium levels, and activation of signaling pathways, such as mitogen-activated protein kinases (66).

Although these relationships have not been worked out in motoneurons, we have evidence that they may be similar to those seen in hippocampus. Expression of BDNF, trkB, synapsin I, growth-associated protein-43, and cyclic AMP-responsive element binding protein are all increased in lumbar spinal cord with voluntary exercise and decreased with muscle paralysis (40). Following spinal isolation (transection of the cord above and below the motoneuron cell bodies, and section of peripheral afferents to these motoneurons), expression of BDNF and synapsin I, which is regulated by BDNF, is reduced in the lumbar cord, but increased in the cervical cord, the latter response presumably a forelimb overload effect (39). Evidence of neurotrophin-related changes in motoneurons that are similar to those in hippocampus has led to the idea that motoneurons may be “learning” physical activity during the training process (32).

**MOTOR UNIT RECRUITMENT BEHAVIOR**

Although we can obtain some insight into motoneuron adaptations to training from human studies, this information is, of course, limited by the complexities of voluntary movement and of its integration in the spinal cord. However, some observations are strongly suggestive of motoneuron adaptations; a few examples are cited below.

In motor units of the first dorsal interosseus, recruitment thresholds, average firing rates, initial firing rates, and firing rate discharge variability are all significantly lower for the dominant as opposed to the nondominant hand. All of these changes would be consistent with an increased excitability (lower, more clustered thresholds) and increased afterhyperpolarization (AHP) amplitudes and/or durations of motoneurons (lower initial firing rates, and less firing rate variability) with increased usage (1). This observation is consistent with that of Cracraft and Petajan (19), who showed that 6 wk of low-intensity, moderate-duration endurance exercises of the tibialis anterior resulted in less variable firing rates of motor units.

Interestingly, ballistic-type training of the tibialis anterior also resulted in a decrease in the recruitment thresholds of motor units. Also, the authors contended that there was some evidence that the increased presence of doublet discharges following ballistic training might be due to changes in biophysical properties of the motoneuron, perhaps at the level of delayed depolarization (65).

On the other hand, force-modulation or force-tracking training, which involves more skill than the training modes mentioned above, results in increased recruitment thresholds and reduced firing frequencies of motor units at percentages of maximal voluntary contraction (55). Such an adaptation would allow more precise and accurate control of increments in muscle force (12).

Although some reflex studies have suggested that motoneurons might have increased excitabilities following training, this interpretation is tenuous, given the many caveats in interpreting the H reflex (70). Although reflex responses evoked during voluntary contractions are potentiated following strength training, the corresponding H reflexes and F responses at rest are not, suggesting that changes in intrinsic motoneuronal excitability are not involved in this response (59).

**ELECTROPHYSIOLOGY**

Measurements of the biophysical properties of motoneurons have been a fairly recent development, and some consistent adaptations have been noted with increased activity (9, 10). Evidence from recruitment studies referred to above might lead us to expect changes with endurance training in measurements of basic excitability, such as rheobase and input resistance, and in properties such as the duration of the AHP, which is known to influence firing rates. Intense endurance training for 16 wk in rats resulted in hyperpolarized resting membrane potentials (RMPs), hyperpolarized voltage thresholds (VT), faster action potential rise times, and, in fast motoneurons, increased estimated capacitance in those motoneurons innervating the ankle extensors/toe flexors (10). These measurements were made 24–48 h following the last training session and were, therefore, adaptations to the resting state of the motoneuron. When exercise was of milder intensity, intermittent, and of longer daily duration, in the form of continuous access to voluntary exercise wheels, similar adaptations were found in RMP and VT, with the added increase in the AHP amplitude, and these adaptations were isolated to those motoneurons innervating slow-twitch fibers.
These observations allow us to make several statements. First, motoneurons are sensitive to increased chronic activity and respond with phenotypic changes. This adds to the evidence from biochemical and neuromuscular junction adaptations referred to above, that the motoneuron responds to a change in its normal activity level. Second, it appears that some properties are more sensitive to the intensity and/or the daily duration of the overload (action potential rise time, AHP) than others (RMP, VT). Third, it seems that motoneurons can adapt in several functionally significant properties, without changes in its signature properties that designate it as a fast or slow motoneuron (such as AHP duration, rheobase, and input resistance) and that would be expected to change to explain recruitment behavior changes referred to in the previous section. In the studies described above, properties that normally covary significantly with the type of muscle fiber innervated (slow fibers are innervated by motoneurons possessing longer AHPs, lower rheobase currents, and higher input resistances) showed no adaptations to training: the proportions of slow and fast motoneurons were not influenced by training (not even any tendencies in this direction were present).

These adaptations with increased activity are given more credence by the finding that many of these changes occur in the opposite direction when activity is reduced by hindlimb unweighting (17) and spinal cord transection (11). In the latter model, changes in the depolarizing direction of RMP and VT, as well as a shift in the frequency/current relationship to one of reduced excitability, were prevented by daily passive exercise of the paralyzed hindlimbs.

Interestingly, Cleary et al. (16) reported that motoneurons of Aplysia involved in long-term behavioral training of the siphon withdrawal reflex adapted with a hyperpolarization of the RMP of ~4 mV and of the VT of ~2 mV. Similarly, VT changes measured from motoneurons in situ have been proposed as possible mechanisms for the effects of operant conditioning on H-reflex amplitudes in primates (14). For this reason, the adaptive electrophysiological changes of motoneurons in response to increased activity may arguably be considered, to some extent, learning (32). Carroll et al. (15), using transcranial magnetic and electrical stimulations to determine the effects of strength training in neural pathways, concluded that changes in intrinsic properties of motoneurons, similar to those summarized above, were consistent with their results.

In summary, changes to motoneurons with exercise training appear to include functional changes at the neuromuscular synapse, alterations in protein synthesis, gene expression, and axon transport, and some biophysical properties, which will influence the manner in which these cells behave during voluntary recruitment. In the next section, we present a modeling exercise to attempt to reproduce the biophysical changes described above, by selectively altering ionic conductances. In this way, we may have some insight into the ion channels that are involved and perhaps that are modulated chronically with increased activity.

**MODELING MOTONEURONAL ELECTROPHYSIOLOGICAL ADAPTATIONS**

Since the electrophysiological changes with endurance training described above involve changes in ion conductances, we proceeded to attempt to reproduce these changes in a mathematical model. Two motoneuron models (S and F type) were built with GENESIS. The structure of the models was based on the previous five-compartment models (22). The passive properties of the models were based on the data from rat lumbar motoneurons (17, 52). The 10 active conductances included in the models are fast sodium ($g_{Na}$), persistent sodium ($g_{NaP}$), delayed rectifier ($g_{Kdr}$), calcium-dependent potassium ($g_{KCa}$), A-current ($g_{A}$), H current ($g_{H}$), T-type calcium ($g_{CaT}$), N-type calcium ($g_{CaN}$), L-type calcium ($g_{CaL}$), and leak conductances, which were mediated by potassium ($g_{leak}$) and passive membrane current ($g_{p}$). The distribution of the conductances was the same as that described in the previous models (22). The Hodgkin-Huxley equations for the ionic currents are written as

\[ I_{Na} = g_{Na} \cdot m^3 \cdot h \cdot (V_m - E_{Na}); \]
\[ I_{NaP} = g_{NaP} \cdot m^3 \cdot h \cdot (V_m - E_{Na}); \]
\[ I_{Kdr} = g_{Kdr} \cdot n^4 \cdot (V_m - E_{K}); \]
\[ I_{Kap} = g_{Kap} \cdot q \cdot (V_m - E_{K}); \]
\[ I_{CaT} = g_{CaT} \cdot m_T \cdot h_T \cdot (V_m - E_{Ca}); \]
\[ I_{CaN} = g_{CaN} \cdot m_N \cdot h \cdot (V_m - E_{Ca}); \]
\[ I_{CaL} = g_{CaL} \cdot m_L \cdot (V_m - E_{Ca}); \]
\[ I_{leak} = g_{leak} \cdot (V_m - E_L); \]
\[ I_p = g_p \cdot (V_m - E_{rest}); \]

where $I_{Na}$ is the current for fast Na$^+$ channels; $I_{NaP}$, persistent sodium; $I_{Kdr}$, delayed rectifier K$^+$; $I_{Kap}$, Ca$^{2+}$-dependent K$^+$; $I_{K}$, A current; $I_H$, H current; $I_{CaT}$, T-type Ca$^{2+}$; $I_{CaN}$, N-type Ca$^{2+}$; $I_{CaL}$, L-type Ca$^{2+}$; $I_{leak}$, leak current mediated by potassium; and $I_p$, leak current mediated by passive membrane. $E_{Na}$, $E_K$, $E_{Ca}$, and $E_L$ are equilibrium potentials for Na$^+$, K$^+$, Ca$^{2+}$, and H currents and equal to 55, −70, 80, and −55 mV, respectively. $E_{rest}$ is RMP and set to −60 mV. $V_m$ is membrane voltage. Letters $m$, $h$, $n$, and $q$ (with or without subscripts) are membrane state variables that are defined by the Hodgkin-Huxley type equation:

\[ \frac{dX}{dt} = \alpha (1 - X) - \beta X \]

where steady-state value $X_\infty = \alpha / (\alpha + \beta)$ and time constant $\tau = 1 / (\alpha + \beta)$.

The intracellular calcium concentration ([Ca$^{2+}$]$_{in}$) in the soma and dendrite compartments satisfy the following equation (64).

\[ \frac{d[Ca^{2+}]_{in}}{dt} = BI_{CaN} - \frac{[Ca^{2+}]_{in}}{\tau_{Ca}} \]

where $B$ is a scaling constant in arbitrary units and set to −50 in the soma compartment and −40 in the dendrite compart-
EFFECTS OF EXERCISE TRAINING ON α-MOTONEURONS

Table 1. The structure of the S- and F-type models

<table>
<thead>
<tr>
<th>Compartment</th>
<th>Diameter, μm</th>
<th>Length, μm</th>
<th>Rm, gcm²</th>
<th>Ra, gcm</th>
<th>Cm, μF/cm²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axon</td>
<td>6</td>
<td>400</td>
<td>5,400‡, 4,500*</td>
<td>20</td>
<td>1.0</td>
</tr>
<tr>
<td>IS</td>
<td>4</td>
<td>50</td>
<td>5,400‡, 4,500*</td>
<td>20</td>
<td>1.0</td>
</tr>
<tr>
<td>Soma</td>
<td>8</td>
<td>200</td>
<td>5,400‡, 4,500*</td>
<td>20</td>
<td>1.0</td>
</tr>
<tr>
<td>P dendrite</td>
<td>20</td>
<td>300†, 500*</td>
<td>5,400‡, 4,500*</td>
<td>40</td>
<td>1.0</td>
</tr>
<tr>
<td>D dendrite</td>
<td>15</td>
<td>400†, 600*</td>
<td>5,400‡, 4,500*</td>
<td>40</td>
<td>1.0</td>
</tr>
</tbody>
</table>

IS, initial segment; P, proximal; D, distal; Rm, specific membrane resistance; Ra, specific axial resistance; Cm, specific membrane capacitance. *Parameters for F-type model only. †Parameters for S-type model only.

ment. τCa is a time constant, the rate of decay of [Ca²⁺]_{in}. It is set to 20 ms for both soma and dendrite compartments. ICa_N is the N-type Ca²⁺ current.

The passive and active parameters of the models are shown in Table 1 and 2, respectively, and the membrane properties of the real motoneurons and models are presented in Table 3. Rate constants in the Hodgkin-Huxley equations are in the Appendix. Note in Table 3 that the properties of rat motoneurons were fairly well depicted using this model.

The target values obtained from the experiments were set for the modeling with some restrictions. The simulations were performed on the principle that the least number of conductances was altered to achieve the most target values with no or the least breakage of the restrictions. In this study, the VT, RMP, and the maximum rising rate of action potentials were set as the target values, whereas the rheobase, input resistance, and frequency/current relationship were regarded as the restrictions. The AHP was set as both.

Table 4 summarizes our attempts to produce endurance-trained motoneurons using this modeling procedure. The simulation conditions in the far left column in Table 4 are changes made in the model for control rat motoneurons, to simulate training-induced adaptations in motoneuron properties. The conditions are as follows:

1) Sodium conductance in soma and initial segment was increased by 50%, with all other conductances remaining unchanged.

2) Delayed-rectifier potassium conductance in soma and initial segment was decreased by 50%.

3) Combination of conditions 1 and 2.

4) This is condition 1 with the addition of a 100% increase in soma and dendrite leak conductance.

5) Increased sodium conductance as in condition 1, with the addition of a 20% decrease in delayed rectifier potassium conductance.

6) Condition 4, with the addition of a 50% increase in the soma and dendrite potassium conductance associated with the AHP.

Most of the changes involved changes in conductances of the fast sodium and delayed-rectifier potassium conductances in the soma and initial segment, as these conductances are concentrated here. We can make a number of general observations from the data in Table 4. First, increased sodium conductances are most likely involved, as the only condition with no sodium conductance involvement failed to produce the increased maximum rate of rise of the action potential seen with endurance training. Second, an increase in leak conductance may occur with endurance training, as this increase, in combination with an increased sodium conductance, resulted in a hyperpolarized RMP (condition 4). Third, an increased delayed-rectifier potassium conductance is probably not involved, as this resulted in a dramatic increase in AHP half-decay time, which did not occur with endurance training (condition 5). In general, the conditions that seem to best describe endurance training-induced adaptations in motoneurons are conditions 1, 3, 4, and 6, all of which involve at least an increase in sodium conductance. Preliminary results suggest that gene expression of the α-subunit of the fast sodium conductance channel NaV1.6 is significantly upregulated as soon as 5 days following initiation of a daily treadmill training program.

ACUTE CHANGES IN MOTONEURON PROPERTIES DURING EXERCISE

The electrical properties of spinal motoneurons are strongly influenced by synaptic inputs with neuromodulatory actions via G protein-coupled receptors. It is likely that levels of at least some of these neuromodulators are different during exercise than during the resting state. The best studied neuromodulatory input is the monoaminergic system, which originates in the brain stem and includes axons releasing either serotonin (5-HT) or norepinephrine (NE) (13). These two systems arise from different brain stem areas (the caudal raphe nucleus for 5-HT) or norepinephrine (NE) (13). These two systems arise from different brain stem areas (the caudal raphe nucleus for 5-HT or the locus coeruleus for NE), but both project throughout the length of the spinal cord, with branches reaching both dorsal and ventral areas. In the ventral horn, both 5-HT and NE have similar actions on motoneurons,
markedly enhancing their excitability by several mechanisms, including facilitation of persistent inward currents, depolarization of the RMP, hyperpolarization of action potential threshold, and reduction in the amplitude of the AHP (2, 37, 41, 44, 56, 57). The monoaminergic systems are highly state dependent, with the serotonergic system being especially active during tonic motor output (47) and the noradrenergic system varying with state of arousal (8). Thus, during exercise, motoneuron excitability should markedly increase (46, 47).

It is interesting to note that neuromodulatory effects of monoamines and adaptations to exercise have opposite actions on motoneuron resting potential (monoamines depolarize, exercise hyperpolarizes). The increase in AHP amplitude with longer duration exercise in S motoneurons is also opposite of the monoaminergic action. Parallel effects are seen on threshold voltage (hyperpolarized in both cases). Thus, in part, the exercise adaptations may be a response to the increased excitability mediated by the monoaminergic input.

From a functional viewpoint, the key issue is the difference between the RMP and the action potential VT of the motoneuron. This difference can be assessed by measuring the injected current required to initiate an action potential, i.e., the cell rheobase. Because the hyperpolarization of action potential VT and RMP is about equal, rheobase stays about the same (9, 10). Yet neuron excitability is complicated: the exercise-induced hyperpolarizing shift in action potential VT coupled with the increased AHP would tend to hyperpolarize the average membrane potential during repetitive firing. This hyperpolarization may reduce the activation of persistent inward currents and thus generate a lower level of excitability for prolonged inputs. It is thus possible that exercise does adapt motoneurons to a lower state of excitability, but clearly more experiments need to address the interaction between exercise and persistent inward currents.

SUMMARY AND CONCLUSIONS

α-Motoneurons adapt to training by changing several of their properties (Fig. 1). While many of the adaptations seem destined to have functional consequences during endurance exercise (increased capacities for axon transport and for neurotransmitter release), many others do not seem to have obvious functional implications for enhanced neuromuscular performance (hyperpolarization of RMP and action potential threshold, and increased amplitude of AHPs). Future studies will be required to study motoneurons under conditions that are closer to the in vivo situation during endurance exercise, or with model motoneurons, to determine how motoneurons behave during endurance exercise, with and without altered properties.
### Effects of Exercise Training on α-Motoneurons

**Invited Review**

#### Table 1A. Rate constants in Hodgkin-Huxley equations (resting membrane equilibrium potential = 60 mV)

<table>
<thead>
<tr>
<th>Conductance</th>
<th>Compartment</th>
<th>Forward (α)</th>
<th>Backward (β)</th>
</tr>
</thead>
<tbody>
<tr>
<td>gNa</td>
<td>Initial segment</td>
<td>S type: $\alpha_n = \frac{-0.4(55 + V)}{\exp\left(\frac{55 + V}{-5}\right) - 1}$</td>
<td>$\beta_n = \frac{0.4(V + 30)}{\exp\left(\frac{V + 30}{5}\right) - 1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = 0.28 \exp\left(\frac{35 + V}{-20}\right)$</td>
<td>$\beta_h = \frac{4}{\exp\left(\frac{35 + V}{-10}\right) + 1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>F type: $\alpha_n = \frac{-0.4(60 + V)}{\exp\left(\frac{60 + V}{-5}\right) + 1}$</td>
<td>$\beta_n = \frac{0.4(V + 35)}{\exp\left(\frac{V + 35}{5}\right) - 1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = 0.28 \exp\left(\frac{40 + V}{-20}\right)$</td>
<td>$\beta_h = \frac{4}{\exp\left(\frac{40 + V}{-10}\right) + 1}$</td>
</tr>
<tr>
<td></td>
<td>Axon and soma</td>
<td>$\alpha_n = \frac{-0.4(42.5 + V)}{\exp\left(\frac{42.5 + V}{-5}\right) - 1}$</td>
<td>$\beta_n = \frac{0.4(V + 15)}{\exp\left(\frac{V + 15}{5}\right) - 1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = 0.28 \exp\left(\frac{35 + V}{-20}\right)$</td>
<td>$\beta_h = \frac{4}{\exp\left(\frac{20 + V}{-10}\right) + 1}$</td>
</tr>
<tr>
<td>gNa,P</td>
<td>Initial segment and soma</td>
<td>$\alpha_n = \frac{-0.4(52.5 + V)}{\exp\left(\frac{52.5 + V}{-5}\right) - 1}$</td>
<td>$\beta_n = \frac{0.4(V + 25)}{\exp\left(\frac{V + 25}{5}\right) - 1}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = 0.25 \exp\left(\frac{60 + V}{-80}\right)$</td>
<td>$\beta_h = \frac{4}{\exp\left(\frac{50 + V}{-80}\right) + 1}$</td>
</tr>
<tr>
<td>gKd</td>
<td>Initial segment</td>
<td>$\alpha_n = \frac{-0.02(50 + V)}{\exp\left(\frac{20 + V}{-10}\right) - 1}$</td>
<td>$\beta_n = \frac{0.25 \exp\left(\frac{60 + V}{-80}\right)}{0.25 \exp\left(\frac{50 + V}{-80}\right) + 1}$</td>
</tr>
<tr>
<td></td>
<td>Axon and soma</td>
<td>$\alpha_n = \frac{-0.02(40 + V)}{\exp\left(\frac{40 + V}{-10}\right) - 1}$</td>
<td>$\beta_n = \frac{0.25 \exp\left(\frac{60 + V}{-80}\right)}{0.25 \exp\left(\frac{50 + V}{-80}\right) + 1}$</td>
</tr>
<tr>
<td>gKs</td>
<td>Soma</td>
<td>$\alpha_n = \frac{0.032(V + 54)}{1 - \exp\left(\frac{V + 54}{-6}\right)}$</td>
<td>$\beta_n = \frac{0.203}{\exp\left(\frac{V + 30}{24}\right) + 0.05}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = \frac{0.05}{1 + \exp\left(\frac{V + 76}{-10}\right)}$</td>
<td>$\beta_h = \frac{0.05}{1 + \exp\left(\frac{V + 76}{-10}\right)}$</td>
</tr>
<tr>
<td>gL</td>
<td>Soma</td>
<td>$\alpha_n = \frac{0.06}{1 + \exp\left(\frac{V + 75}{5.3}\right)}$</td>
<td>$\beta_n = \frac{0.06}{1 + \exp\left(\frac{V + 75}{5.3}\right)}$</td>
</tr>
<tr>
<td>gCaT</td>
<td>Soma</td>
<td>$\alpha_n = \frac{0.02(V + 38)}{1 - \exp\left(\frac{V + 38}{-4.5}\right)}$</td>
<td>$\beta_n = \frac{-0.05(V + 41)}{1 - \exp\left(\frac{V + 41}{4.5}\right)}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = \frac{-0.0001(V + 43)}{1 - \exp\left(\frac{V + 43}{7.8}\right)}$</td>
<td>$\beta_h = \frac{0.03}{1 + \exp\left(\frac{V + 41}{-4.8}\right)}$</td>
</tr>
<tr>
<td>gCaN</td>
<td>Soma and dendrite</td>
<td>$\alpha_n = \frac{0.2}{1 + \exp\left(\frac{V + 20}{6.13}\right)}$</td>
<td>$\beta_n = \frac{0.2}{1 + \exp\left(\frac{V + 20}{-55.2}\right)}$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\alpha_h = \frac{0.05}{1 + \exp\left(\frac{V + 35}{-55.2}\right)}$</td>
<td>$\beta_h = \frac{0.05}{1 + \exp\left(\frac{V + 35}{6.13}\right)}$</td>
</tr>
<tr>
<td>gCaL</td>
<td>Soma and dendrite</td>
<td>$\alpha_n = \frac{0.025}{1 + \exp\left(\frac{V + 30}{7}\right)}$</td>
<td>$\beta_n = \frac{0.025}{1 + \exp\left(\frac{V + 30}{7}\right)}$</td>
</tr>
<tr>
<td>gKd,dep</td>
<td>Soma and dendrite</td>
<td>$\alpha_n = 10^{-3}[Ca^{2+}]_c^2$</td>
<td>$\beta_n = 0.4$</td>
</tr>
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