ANALYSIS OF DENDRITIC DISTRIBUTION OF VOLTAGE DEPENDENT CHANNELS EFFECTS ON EPSP AND ITS RECIPROCAL INHIBITION IN α-MOTONEURONS: COMPUTER MODEL

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Abstract

Modeling of excitation and inhibition of morphologically and physiologically characterized triceps surea motoneuron (MN 42) was executed by a NEURON simulator. The voltage dependent channels of MN 42 were allocated on six dendrites (the rest six dendrites remained passive) according to three types of distribution functions: a step function (SF), an exponential decay (ED, highest density proximally to the soma) and exponential rise (ER, highest density distally to the soma). Maximal densities of the sodium conductance varied between 0.01 and 0.06 S/cm^2. The peak of the EPSP became larger as the maximal density of the voltage dependent channels is increased. In the SF distribution, with the highest total conductance (G, Siemens), the EPSP amplitudes were greater than these in the ER and ED models. The reciprocal EPSP inhibition in the model with the SF was most efficient in comparison to the ED and ER models. EPSP peak inhibition at the ED and ER are similar, despite that the total active conductance in ED is about 10 times smaller than in ER distribution. The dependency of the inhibition on the density of the active conductance in the SF and ED models is not linear. We conclude that in an "ideal neuron" the presence of proximal voltage dependent channels may boost distally located synaptic inputs thus "normalizing" the synaptic responses.

1. Introduction

The location of voltage dependent channels on the different parts of a neuron is fundamental in order to estimate the efficacy of EPSP and its inhibition. Recently we have shown

[1] that reciprocal inhibition located on the dendrites of α-motoneuron (MN) 42 is greatly increased by uniformly distributed active channels on the dendrites (passive soma and axon). The EPSP inhibition is about 10 times more effective than in the case where the voltage dependent channels were placed only on the soma and axon of the same MN. Moreover, the densities of these active dendritic conductances required for this inhibition were about 10 times lower relative to the active somatic channels. The distribution function of the MN's dendritic voltage dependent channels and their maximal specific conductance are not known [2]. In opposite, exponential decay (relative to the soma) densities of the dendritic active channels were described for the pyramidal cortical neurons [3]. Therefore, we asked the following questions: 1. What is the relation between the dendritic voltage dependent channels' density to the EPSP amplitude? 2. How is EPSP inhibition affected by those channels? 3. How are the EPSP and its inhibition affected by the type of the voltage dependent channel distribution?

2. Methods

Modeling of excitation and inhibition of morphologically [4] and physiologically [5] characterized triceps surea MN 42 was executed by a NEURON simulator [6]. The basic parameters of the model (membrane resistance and capacity etc.) and of the excitatory and inhibitory synapses were detailed in our previous publications [7] [1]. The voltage dependent channels of MN 42 were distributed on randomly selected six dendrites at a distance of 0-400 μm [2] from the soma. The rest six dendrites remained passive. Three types of channels distribution were tested: a step function (SF), an exponential decay (ED, highest density proximally to the soma) and exponential rise (ER, highest density distally to the soma). Maximal densities of the sodium conductance (potassium conductance was kept one third of the sodium conductance) varied between 0.01 and 0.06 S/cm^2. Since the postsynaptic inhibition is relatively weak [1], action potentials could not be depressed. Instead, it clearly diminished subthreshold excitatory postsynaptic potentials (EPSPs). Therefore, the soma and the axon remained passive in the model and thus the impact of dendritic-voltage dependent channels on the efficiency of EPSP and its reciprocal inhibition could be distinguished. In the present study we simulated only the reciprocal inhibition (and not recurrent inhibition) since the chosen range of the voltage dependent channels fully overlap the location of the reciprocal inhibitory synapses. The maximal density of these synapses is near the soma and their number decreases distally.

3. Results

3.1. Dendritic voltage dependent channel- distribution determines the increase of EPSP amplitude

In general, EPSPs amplitude became larger when the maximal density of the voltage dependent channels increased. However, the EPSP amplitude depends on the type of channel density distribution. Namely, in the SF distribution, with the highest total conductance (G, Siemens), the amplitudes were greater than those in the ER and ED models. The EPSP peak was between 12 and 51 mV corresponding to the maximal conductance density. In the ED model EPSPs peak ranged between 9 and 12 mV and in the ER model between 8 and 10 mV. It is important to notice that G in the ED model is smaller than that in the ER one and yet the magnitude of EPSPs in the ED model is slightly larger (Fig 1 see also Fig 3).

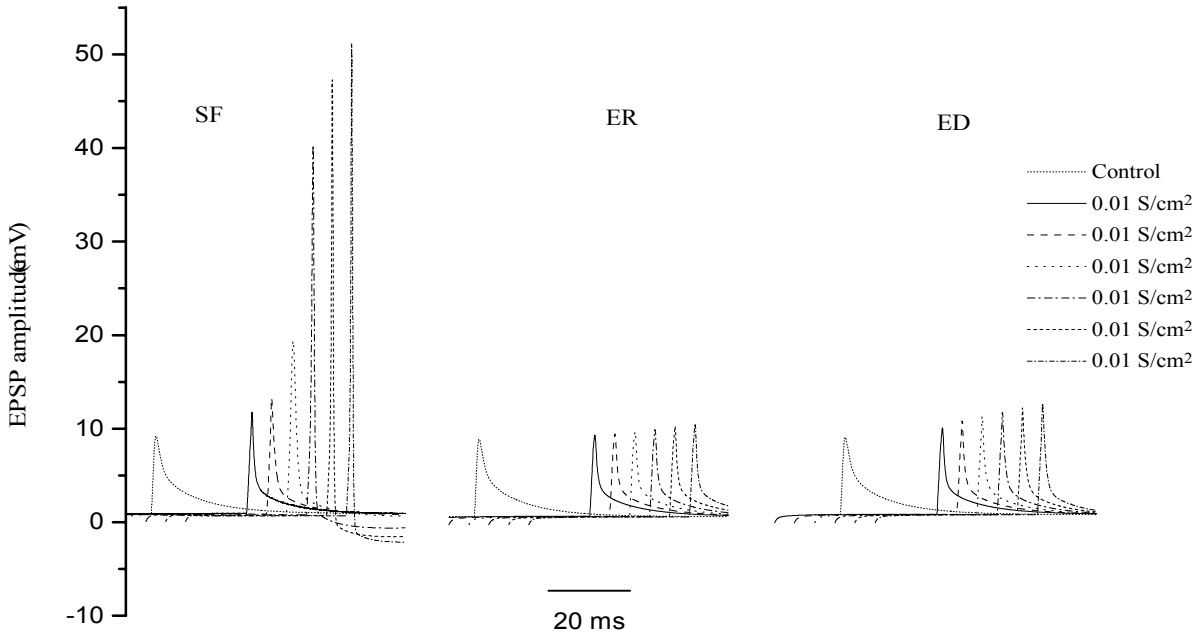

Fig 1: Super positioned EPSPs (artificially shifted to the right for each Na conductance step) simulated by the three models for maximal Na conductance distribution. g_{Na} step varied between 0.01-0.06 S/cm^2. In the control response the dendrite remained passive. The boosting effect in ED is greater than ER despite that the total dendritic voltage dependent conductance (Siemens) is lower.

3.2. The efficiency of reciprocal inhibition of EPSP is dependent on the distribution of the dendritic active conductances

As expected, the reciprocal EPSP inhibition in the SF model distribution was most efficient in comparison to the ED and ER models because of its greatest total conductance. It ranged between 18-62% inhibition, whereas inhibition in ED and ER models, which were similar, varied between 30-40% (Fig 2). Unexpectedly, the dependency of the inhibition on the

conductance density in the SF and ED models is not linear. For example, in the SF model until a critical conductance density of 0.04 S/cm^2 (except 0.02 S/cm^2) EPSP inhibition is enhanced. But at higher conductances (0.05 and 0.06 S/cm^2) this tendency is reversed. Similar behavior, but less prominent, was observed in ED model. In the ER model the magnitude of inhibition increased linearly with increased conductance density (Fig 3).

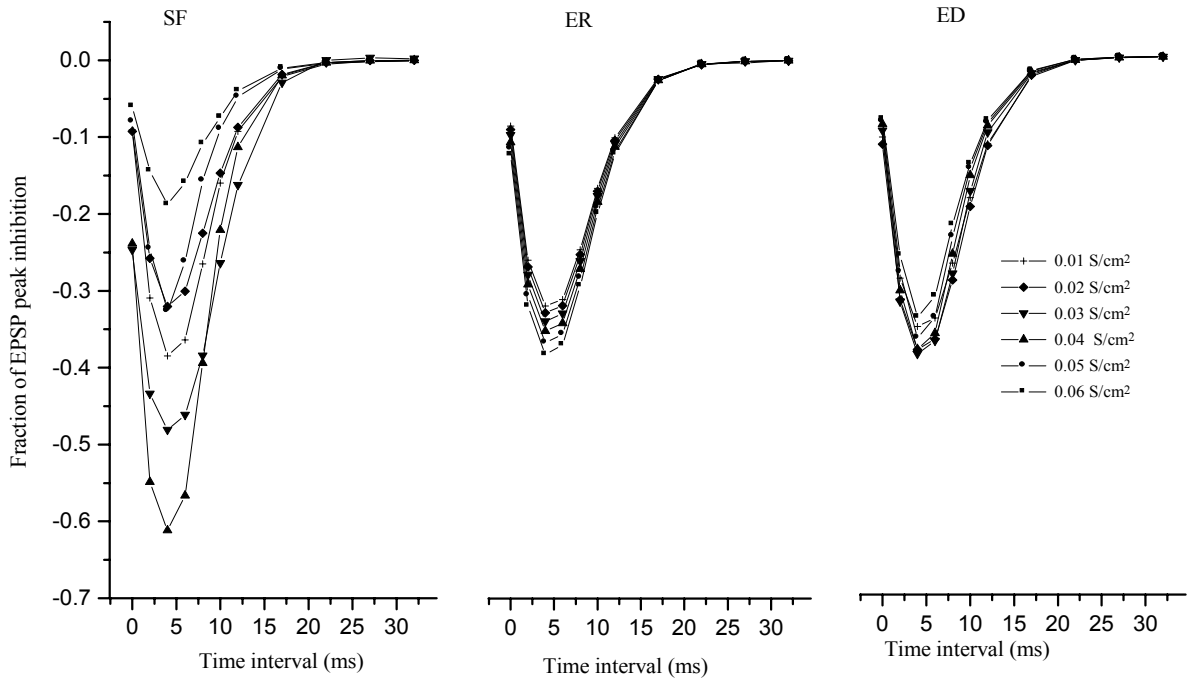

Fig 2: EPSP peak inhibition (PSP), measured at the soma, as a function of time interval at the three types of voltage dependent channels distribution: SF, ED and ER. PSP was simulated at different maximal voltage dependent conductances (0.01-0.06 S/cm^2). Note that at the exponential models only small variations of inhibition is attained by increased g_{Na_step}. Note also that especially in the SF and ED models, inhibition as a function of g_{Na_step} has an optimum; higher values reduce the inhibition efficacy.

As aforementioned, in all types of models the maximal conductance density varied between 0.01-0.06 S/cm^2. However, the total conductance (G, Siemens) for each model varied by a factor of 10 (Fig 3). Despite this difference, maximal inhibition of both ER and ED models was between 30-40%.

4. Discussion and conclusions

Voltage dependent channels, located at the dendrites, may have several functions: enable forward [8] and back propagating spikes [9] and enhancing synaptic inputs, especially distal ones [10] [11]. These functions are dependent on the type of dendritic voltage dependent channels distribution. In the hippocampal pyramidal CA1 neurons, the measured somatic potential of the apical dendrite generated synaptic input is site- independent since mixed

cation I_h inward current (with a reversal potential between -20 and -50 mV) [12], increases with distance from the soma [13]. In the cerebellar Purkinje cell [14] and in the thalamocortical neurons [9] sodium channel current density decreased with distance from the soma. However in the latter, the potassium channels density across the somatodendritic area is uniform [9]. Since the distribution function of the dendritic voltage dependent channels on the motoneuron is not known [2], we evaluated several alternatives of channels dispersions, and the EPSP peak and its inhibition were measured. Locating voltage dependent channels on the soma and axon almost did not influence the EPSP and its reciprocal inhibition [1]. The present study suggests that the efficacy of EPSP peak and its inhibition, as measured at the soma, is improved when the main conductance density of the active channels is located on the

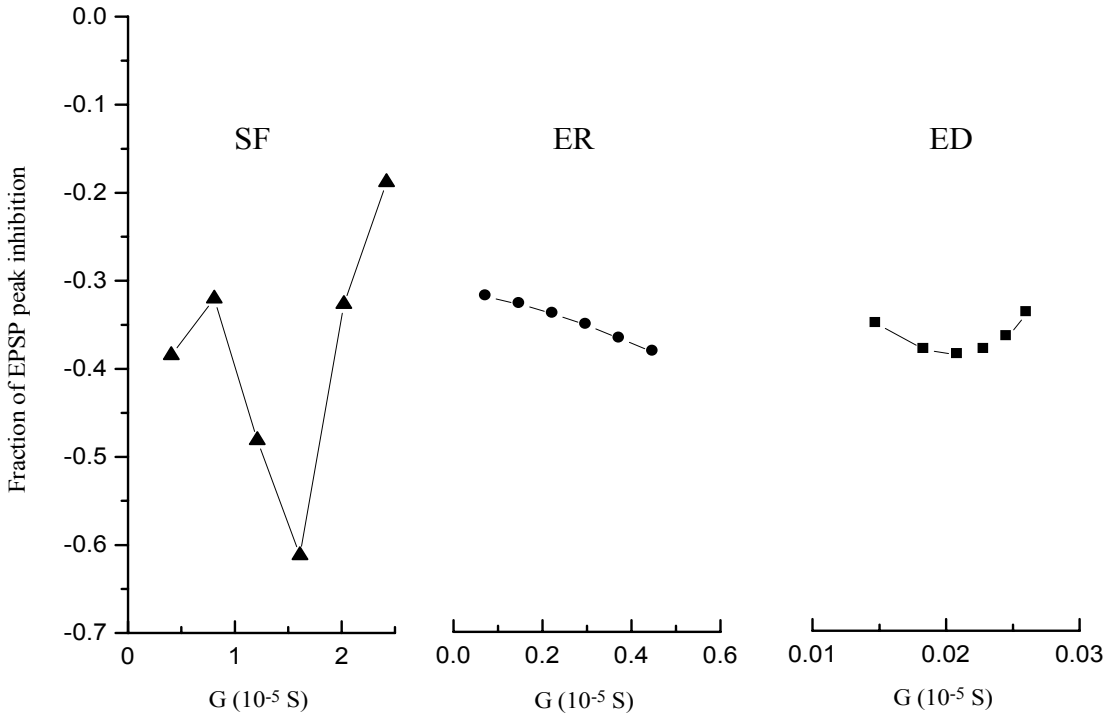

Fig 3: Reciprocal inhibition of EPSP peak at ED, ER and SF models is dependent on dendritic voltage dependent channel distribution. The specific active conductance density (g_{Na_step}) ranges at all models between 0.01-0.06 S/cm^2, but the total conductance (G- Siemens) is different since the surface area of the dendrites is increased distally due to branching. Note the different scales for the three models. The total density is 10 times smaller in ED model than in the ER model. Nevertheless, the maximal inhibition of both models was between 30-40%.

dendrites proximally to the soma (ED distribution). Note that for the same total conductance (see 0.05 x 10^{-5} S at Fig 3.) SF and ER distribution similarly decrease EPSP amplitude. The relation between the increased conductance and enhanced EPSP modulation is non-linear. The efficacy of EPSP amplitude and EPSP inhibition increased until an optimal conductance value, beyond which the efficacy of the inhibition is decreased. We conclude that in an "ideal

neuron" the presence of proximal active conductances may boost distally located synaptic inputs to "normalized" synaptic responses. Yet, over compensation (higher channels densities) may interfere with other integration process such as postsynaptic inhibition.

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