Analysis of dendritic distribution of voltage dependent channels effects on epsp and its reciprocal inhibition IN α-motoneurons: Computer model

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Introduction

The existence and location of voltage dependent channels on the different parts of a neuron is fundamental in estimating the actual efficacy of the EPSP and its postsynaptic inhibition. Recently we have shown (Gradwohl et al. 2001) that reciprocal inhibition located at the dendrites of simulated **α**-motoneuron (MN '42') is 10 times stronger in depressing the EPSP if voltage dependent channels are uniformly distributed on the dendrites (passive soma and axon) rather than on the soma and axon (passive dendrites). Moreover, the density of active dendritic conductance that required for this inhibition is about 10 times smaller than that required for the active soma model.
The distribution function and maximal conductance of the MN's dendritic voltage dependent channels are not known (Luscher et al., 1998). However, an exponential decay (relative to the soma) density function of the dendritic active channels has been reported for pyramidal cortical neurons (Stuart and Sakmann 1994). Therefore, the following questions were investigated in the present study: 1. How maximal dendritic active conductance affects EPSP amplitude and its depression by reciprocal inhibition? 2. How voltage dependent channels distribution affects EPSP's inhibition?

Methods

Modeling of excitation and inhibition of morphologically (Cullheim et al. 1987) and physiologically (Fleshman et al 1988) characterized triceps surea **α**-MN 42 was executed by a NEURON simulator (Hines et al.1989). The description of the basic parameters of the model (membrane resistance and capacity etc.) and of the excitatory and inhibitory synapses was detailed in our previous publications (Gradwohl et al., 1999; Gradwohl et al., 2001).
The voltage dependent channels of MN 42 were distributed on six dendrites (the other

dendrites remained passive) along 0-400 m distally to the soma (Luscher et al, 1998). Three functions were used to simulate channel density: 1. A uniform step function (SF), 2. An exponential decay (ED)-highest density proximal to the soma, and 3. An exponential rise (ER)-highest density distal to the soma. Maximal density of the sodium conductance (g_{na}) (potassium conductance is kept one third of the sodium conductance) varied between 0.01 and 0.06 S/cm^2. Total conductance (G, Siemens) was calculated for each model by multiplying the compartments area by their designated local conductance (g). Similar to our previous study (Gradwohl et al. 2001), we examined the effects of the dendritic voltage dependent channels distribution only on the inhibition of subthreshold EPSPs. This was accomplished by eliminating action potential generation by the soma and the axon (remained passive). At the present study we modeled the reciprocal inhibition and not the recurrent inhibition since its synapse distribution (proximal to the soma) fully overlap the postulated range of the dendritic voltage dependent channels (in opposite to the recurrent inhibition).

Results

The influence of the dendritic voltage dependent density distribution functions on the amplitude of the EPSP

The peak of the EPSP increased as the maximal density of the voltage dependent channels is raised. However, this boosting was dependent on the type of the distribution function. For the SF, which has the highest G of the dendritic segment, EPSP's amplitude was obviously greater than that of the ER and ED models. EPSP peak ranged between 2 - 51 mV (dependent on the maximal conductance density) compared to 9 - 10 mV and 10 - 13 mV in ED and ER models, respectively. It is important to notice that G in the ED model is larger than that in the ER (since proximal compartments are thicker than the distal ones), yet the magnitude of its EPSPs is smaller.

The efficacy of reciprocal inhibition of the EPSP is dependent on the distribution of the dendritic active conductance

As expected, the reciprocal inhibition of the EPSP in the SF model was most efficient as compared with the ED and ER models and ranged between 18-62% . The inhibition in ED and ER were similar and varied between 30-40%. Unexpectedly, the dependency of the inhibition on the density of the active conductance in the SF and ER models is not linear. Instead, an optimum conductance density of 0.04 S/cm^2 and 0.05 S/cm^2 for the SF and ER models respectively was detected. Namely, an increase or decrease in this critical value reduced the magnitude of the inhibition. In the ED model the magnitude of inhibition increased monotonically with elevated conductance density. As mentioned above, in the three models the

maximal g_{na} varied between 0.01-0.06 S/cm^2. However, similar maximal inhibition (30-40%) was obtained for both ED and ER models although the total G for the ED model was (0.1 x10^{-5} - 0. 5 x 10^{-5} S) 10 times greater than that of the ER model which has an opposite channels distribution function.

Conclusions

This study supports our earlier MN simulation findings (Gradwohl et al. 2001) that voltage dependent conductance on the soma and axon did not influence the EPSP and its reciprocal inhibition, whereas similar conductance on the dendrites was very effective. The present study further indicates the importance of the actual distribution of the voltage dependent channels along the dendrites. The presence of voltage dependent channels distally to the soma, away from the reciprocal synapses' location, is more effective in increasing the EPSP amplitude and its inhibition than overlapping distributions. Under these conditions there is an optimal conductance at which the effect is maximal.