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Stochastic Resonance in the Motor System: Effects of Noise on the Monosynaptic Reflex Pathway of the Cat Spinal Cord

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[1]*Instituto de Fisiología, Benemérita Universidad Autónoma de Puebla, Puebla, Pue., Mexico; and* [2]*Instituto de Física Interdisciplinar y Sistemas Complejos, CSIC-UIB, Campus UIB, Palma de Mallorca, Spain*

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Martinez L, Pérez T, Mirasso CR, Manjarrez E. Stochastic resonance in the motor system: effects of noise on the monosynaptic reflex pathway of the cat spinal cord. *J Neurophysiol* 97: 4007–4016, 2007. First published April 11, 2007; doi:10.1152/jn.01164.2006. In sensory systems, the presence of a particular nonzero level of noise may significantly enhance the ability of an individual to detect weak sensory stimuli through a phenomenon known as stochastic resonance (SR). The aim of this study was to demonstrate if such phenomenon is also exhibited by the motor system; in particular, in the Ia-motoneuron synapse of the cat spinal cord. Monosynaptic reflexes elicited by periodic electrical stimulation to the medial gastrocnemius nerve were recorded in the L_7 ventral root (or in single motoneurons) of decerebrated cats. Random stretches (mechanical noise) were applied to the lateral gastrocnemius plus soleus muscle by means of a closed-loop mechanical stimulator-transducer. In all cats, we observed the SR phenomenon. The amplitude of the monosynaptic reflexes (or number of action potentials recorded in the motoneurons) evoked by the weak electrical stimuli applied to the medial gastrocnemius nerve were an inverted U-like function of the mechanical noise applied to the lateral gastrocnemius plus soleus muscle. A significant maximum value in the amplitude of the monosynaptic responses was reached with a particular noise amplitude value. Numerical simulations on a model of the monosynaptic reflex pathway qualitatively reproduce this stochastic resonance behavior. We conclude that the monosynaptic reflex response elicited by Ia afferents is optimized by the noisy stretching of a synergistic muscle. Our study provides the first direct demonstration that the motor system, and not only the sensory systems, exhibits the SR phenomenon.

INTRODUCTION

Stochastic resonance (SR) is commonly understood to be the enhancement, by noise, of the response of a nonlinear system to a weak input signal (Anishchenko et al. 1999; Ando and Graziani 2000; Gammaitoni et al. 1998; Moss et al. 2004; Wiesenfeld and Moss 1995). The stochastic resonance is a counterintuitive phenomenon in which the response of the system develops an inverted U-like function versus the input noise level; the maximal enhancement of the response values occurs at an intermediate noise amplitude value. This phenomenon has been demonstrated in the CNS (Gluckman et al. 1996; Manjarrez et al. 2002b; Stacey and Durand 2000, 2001). In sensory systems, several SR type effects have been demonstrated in terms of the response amplitude or the signal-to-noise ratio of the output (Ando 2006; Bahar and Moss 2004; Collins et al. 1996, 1997; Dhruv et al. 2002; Hanggi 2002; Ivey et al. 1998; Liu et al. 2002; Manjarrez et al. 2002a, 2003, 2007; Mori and Kai 2002; Moss et al. 2004; Richardson et al. 1998; Russell et al. 1999; Ward et al. 2002; Winterer et al. 1999); however, there is no direct evidence about the existence of this phenomenon in the motor system.

The SR has been shown in electrophysiological experiments of human muscle spindles (Cordo et al. 1996) or in tendon organs and primary and secondary endings of cat muscle spindles (Fallon et al. 2004). Cordo et al. (1996) demonstrated that the sensitivity of muscle-spindle receptors to a weak movement signal is enhanced by introducing a particular level of noise through the tendon of the parent muscle. This means that a particular level of mechanical noise added to muscle spindles could enhance the muscle spindle sensory output. However, because experiments in humans offer certain limitations, it is not clear from these experiments whether the electrical activity of the motor spinal neurons also exhibits the SR behavior. In this context, the purpose of the present study was to extend the observation of Cordo et al. (1996) to the monosynaptic reflex actions of muscle spindle afferents on motoneurons of the cat spinal cord; i.e., to explore the presence of SR in the motor system counterpart. In the experiments reported here, we studied the effects of continuous noisy stretches (input noise) to the lateral gastrocnemius-soleus (LGS) muscle on the amplitude of monosynaptic reflexes (MSR) elicited by periodic stimuli to the medial gastrocnemius (MG) nerve. Thus the signal and the noise were not applied to the same muscle receptors. This protocol allowed that the signal and the noise were mixed not in the muscle spindle but in the motoneurons. In this context, the purpose of the present study was to substantiate whether SR occurs in the synaptic integration when two convergent synaptic inputs, one for the signal and another for the noise, are summated in the motoneurons of the monosynaptic reflex pathway. Disclosure of this phenomenon in the motor system is important because it shows that the motor system, and not only the sensory systems, also exhibits the SR phenomenon. Furthermore, our study shows that synaptic noise could be beneficial to enhance or to depress the monosynaptic reflexes, thus suggesting that the CNS could employ internal noise sources to modulate complex motor tasks.

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METHODS

Preparation

Experiments were performed in seven adult cats (weight range, 2.0–3.5 kg). Guidelines contained in the National Institutes of Health *Guide for the Care and Use of Laboratory Animals* (85–23, revised in 1985) were followed throughout. For surgery, gaseous anesthesia was induced and maintained with halothane (5%) delivered in a mixture of 30% oxygen and 70% nitrous oxide. Atropine (0.05 mg/kg) and dexamethasone (2 mg/kg) were given at the beginning of the surgery. The radial vein was canulated to administer fluids, and blood pressure was monitored from the carotid artery. A bicarbonate and glucose (5%) solution was delivered intravenously through the experiment at a rate of 5 ml/h. A mechanical precollicular-postmammillary decerebration was performed with removal of both cortices and all tissue rostral to the transection. Dextran and saline solutions were given to maintain blood pressure between 80 and 120 mmHg. After decerebration the anesthetic was discontinued. Animals were paralyzed with pancuronium bromide (Pavulon, Organon) and artificially ventilated.

The lumbo-sacral and low thoracic spinal segments were exposed and the dura mater removed. After the surgical procedures, the animal was restrained in a stereotaxic apparatus using spinal and pelvic clamps. The ventral roots L_4–S_2 were dissected and sectioned. The L_7 ventral root was placed in a pair of electrodes for recording. Pools were made with the skin around the exposed tissues and filled with mineral oil (after placement of the electrodes). The animal was maintained at a constant temperature (37°C) by means of a heating pad and radiant heat. The left MG nerve was cut and placed in pair of electrodes for stimulation. With the LGS nerves intact, the left LGS muscles were freed from the skin and surrounding tissue as completely as possible without disturbing their blood supply. The tendon of Achilles was longitudinally attached to the mechanical stimulator-transducer. Transmission of mechanical noise through the bone was avoided by removing a 1-cm section of the left femur.

Test stimuli (input signal)

Test stimuli (electrical pulses) were applied on the MG nerve (Fig. 1*A*). Such stimuli consisted of single pulses with a total duration of

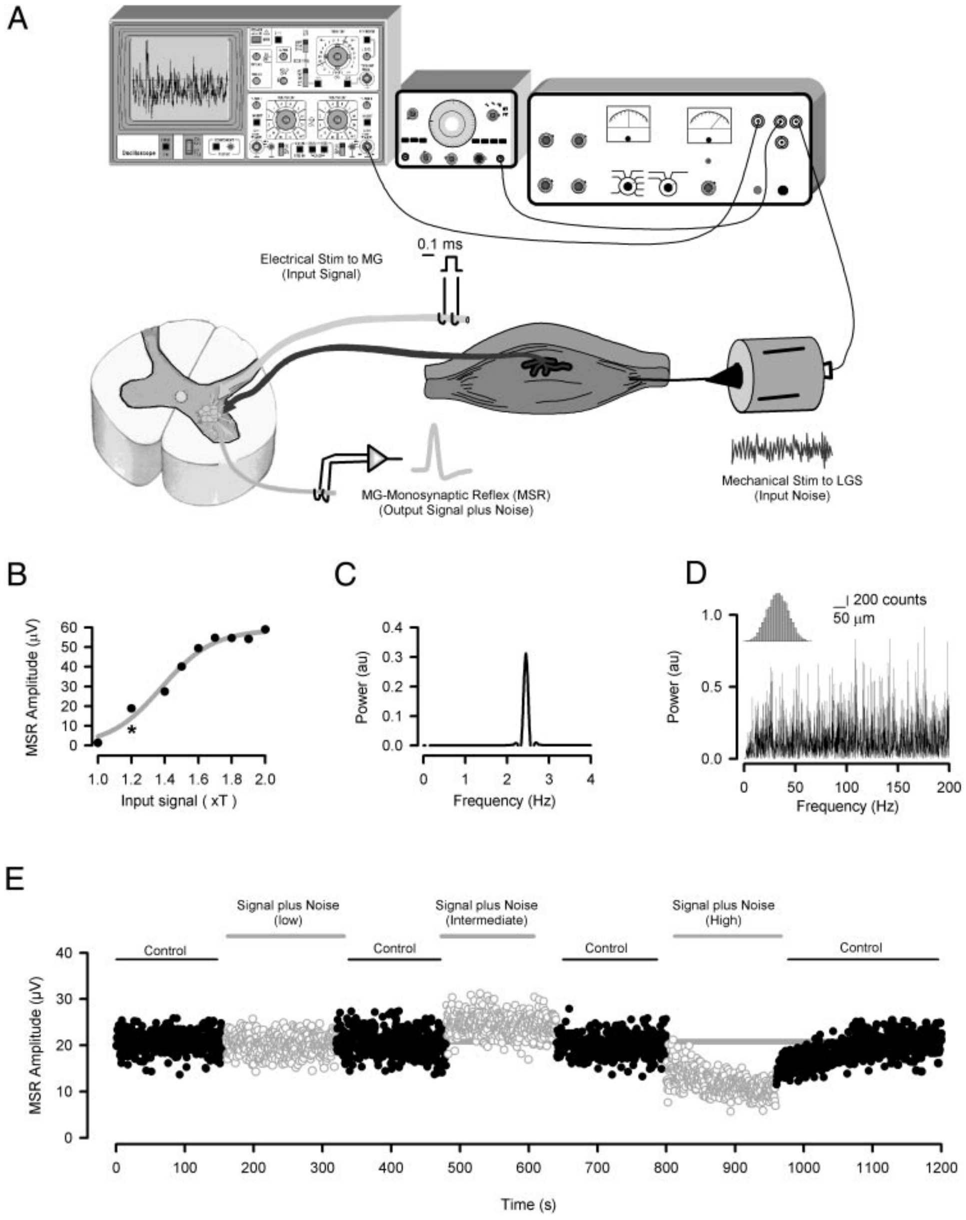

FIG. 1. *A*: scheme of the experimental arrangement. *B*: amplitude of monosynaptic reflexes (MSR) vs. intensity of the electrical stimuli (input signal, expressed as times threshold, ×T) applied to the medial gastrocnemius nerve (MG). *, weak intensity used to produce the MSRs in control conditions and during continuous noise applied to the lateral gastrocnemius plus soleus muscle (LGS). *C*: power spectrum of the MSRs elicited at 2.5 Hz. *D*: power spectrum of the random stretches (mechanical input noise) applied to the LGS muscle by means of a close-loop mechanical stimulator-transducer. All noise applications were made longitudinally with the LGS muscle stretched by 500 μm. *Inset*: amplitude distribution for the random stretches around this 500 μm. *E*: amplitude of successive monosynaptic reflexes in the conditions indicated. Note that the mean amplitude of the MSRs was significantly enhanced ($P < 0.05$, *t*-test) for an intermediate level of mechanical noise.

0.1-ms delivered at a constant frequency of 2.5 Hz. Figure 1*B* shows the input-output curve for the L_7 MSR amplitude versus the test stimulus strength, and Fig. 1*C* shows the power spectrum of the MSRs, indicating a frequency of response of 2.5 Hz. Figure 1*B* (*) indicates the weak intensity of the periodic stimuli used to evoke the MSRs.

Input noise

Mechanical noise was applied with a closed-loop mechanical stimulator-transducer that allowed measures of the displacement. The output of a function generator [Wavetek (San Diego, CA) 132] provided input to the stimulator-transducer and supplied the input noise (Fig. 1*A*). In the protocol of stimulation we employed five or six levels of noise; but because we used a nondigital-Wavetek function generator (Fig. 1*A*), the increments in the intensity level of noise were exactly not equally spaced. Noise with a power spectrum ranging from 0.1 to 200 Hz was applied on the tendon of the LGS muscle (Fig. 1*A*). Figure 1*D* shows the power spectrum of a typical noisy stimulus. The inset in Fig. 1*D* shows the amplitude distribution (Gaussian) of the typical noisy stimulus. The magnitude of the input noise was quantified by means of the SD of the input stretching (σ_n of input noise, displacement expressed in μm). All noise applications were made longitudinally with the LGS muscle stretched by 500 μm.

Protocol of stimulation

To access the effects of mechanical noise (local tendon-displacements) to the LGS muscle on the amplitude of the MG MSRs, 64 periodic pulses were applied to the MG nerve, and the evoked MSRs were averaged. The effects of different levels of noise on the MSR amplitude were measured with respect to averages over 64 MSRs in control conditions. We applied five or six sequences, each with a different mechanical noise intensity level. The presentation order of the different noise levels was varied randomly to remove possible serial effects. We waited a period of ~1 or 2 min to apply a control sequence after every noise level. Because in long-lasting recordings of MSRs we observed stability in the MSR amplitude sequence (see Fig. 1*E*), we used 64 samples of MSRs. We observed that the statistical significance of the data (Student's *t*-test) was successfully accessed with these 64 samples in control conditions versus other 64 samples for each level of noise. Every change in the mean MSR amplitude produced by each level of noise was compared with their own control (i.e., the mean MSR elicited by 64 electrical pulses applied to the MG nerve).

Electrophysiological recordings

Spinal cord potentials (output afferent volleys; see Fig. 2*D*) were recorded from the surface of the L_7 dorsal horn with a silver ball electrode against an indifferent electrode placed on the near paravertebral muscles. Furthermore, dorsal root potentials were recorded with

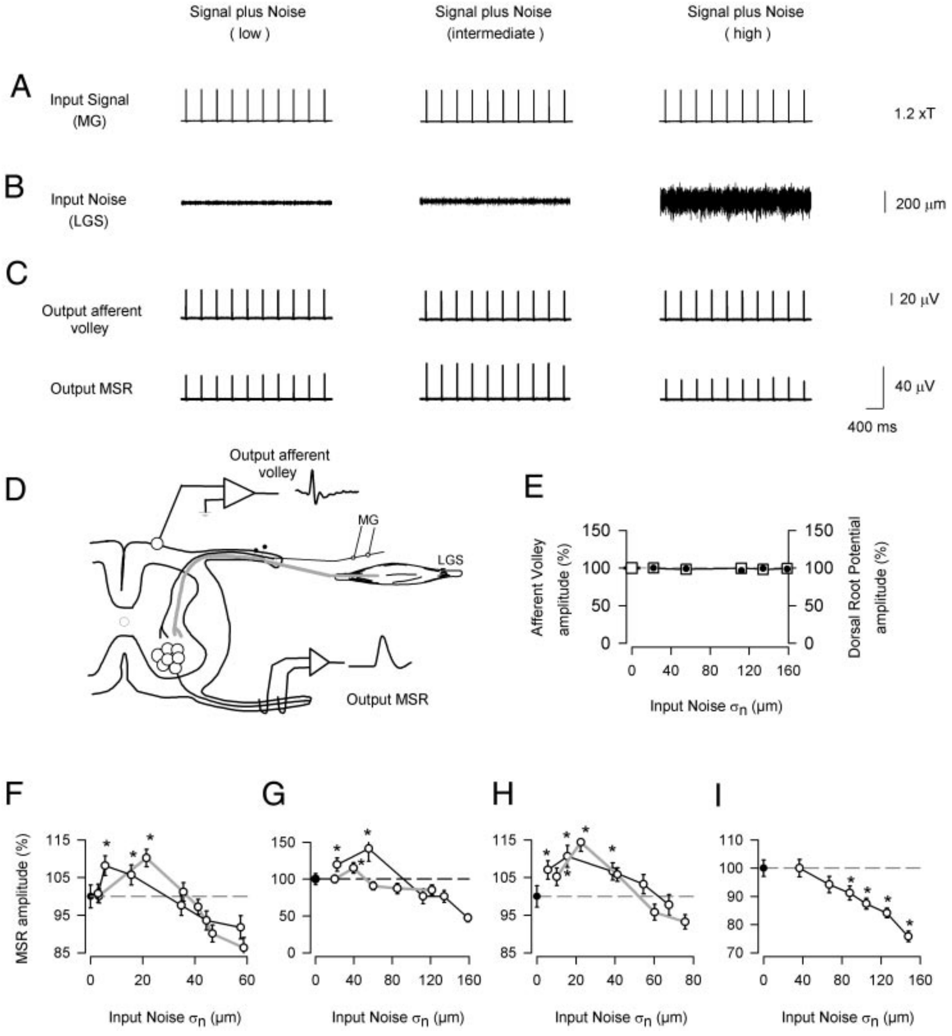

FIG. 2. The amplitude of the monosynaptic reflexes evoked by the electrical stimuli to the MG nerve was an inverted U-like function of the mechanical noise (σ_n) applied to the LGS muscle. *A*: continuous recordings of the input signal (periodic electrical stimuli applied to the MG nerve at 2.5 Hz) for the 3 conditions indicated (low, intermediate, and high levels of noise). *B*: continuous recordings of the mechanical input noise (random stretches applied to the LGS muscle) for the same conditions indicated above. *C*: continuous recordings of the output afferent volleys and of the output MSRs for the same conditions of noise indicated above. *D*: same scheme illustrated in Fig. 1*A* indicating how the afferent volleys were recorded. *E*: typical graph of afferent volley (□) and dorsal root potential (●) amplitude versus input noise intensity for 1 animal. *F–H*: MSR amplitude vs. input noise intensity for 6 cats, respectively, when input signal was weak. - - -, control. Error bars indicate the SD obtained from the averaging of 64 MSRs for each level of noise. *, points for which the difference between the effect and the control was statistically significant and the MSR amplitude was increased ($P < 0.05$, Student's *t*-test). *I*: same as *F–H* but for MSRs elicited by suprathreshold stimulus in 1 animal.

two electrodes, one placed distally on the central end of a sectioned L_6 or L_7 dorsal rootlet, and the other close to, but not touching, the spinal cord. Monosynaptic reflexes were recorded from the L_7 ventral root (Figs. 1*A* and 2*D*). In our experiments, we observed that the application of mechanical noise on the LGS muscle did not produce a significant change in the mean amplitude of the dorsal root reflexes (●) or the afferent volleys (□) elicited by electrical stimuli applied to the MG nerve (see Fig. 2*E*).

In other series of experiments, intracellular recordings were obtained from motoneurons receiving synaptic inputs from LGS and MG afferents (Fig. 3*B*). These recordings were made by means of 3 M potassium acetate-filled micropipettes (tip diameter: 1–2 μm) connected to high-impedance DC amplifier. Motoneurons were identified by their antidromic response to ventral root stimulation. Data acquisition was performed with a sampling rate of 10 kHz.

Data analysis

Data acquisition of the input noise and of the spinal potentials was performed with a sampling rate of 10 kHz. Frequency filters were set to 0.3 Hz and 30 kHz. We estimated effects of mechanical noise (applied to the LGS muscle) on monosynaptic reflexes directly from the averaged amplitude of monosynaptic reflexes elicited by stimulation to the MG nerve. The mechanical noise alone applied to the LGS muscle did not produce MSRs. We averaged 64 monosynaptic reflexes for each level of noise or absence of noise. The monosynaptic reflex amplitudes were expressed as a percentage of control (100%) ± SD (error bars in Figs. 2, *F–H*). Control was considered as the monosynaptic reflex response in absence of noise. A Student's *t*-test ($P < 0.05$) was used to test for significant changes of the maximal amplitude value for an intermediate level of noise respect to the mean control amplitude.

Mathematical formulas and model parameters used in computer simulations

To model our experimental results we considered a pool of independent but slightly different motoneurons. The pool received convergent afferent synaptic inputs from sources generating signal and noise (see Fig. 4*F*). The amplitude of the selected signal was weak enough not to produce a spike in the absence of noise.

Because there is experimental evidence that ~6 MG Ia-afferents project to each of the 300 alpha-motoneurons (Mendel and Henneman 1968) in our model we only considered a pool of 300 motoneurons. Furthermore, because the proportion of possible direct excitatory connections between motoneurons is low (Gogan et al. 1977) and there is controversy that there are electrical connections between neighboring motoneurons in adult cats (Hinckley and Ziskind-Conhaim 2006), we have not considered couplings between them. Moreover, we do not expect that our model yield qualitatively different results after including either electrical or excitatory connection between motoneurons.

To describe the motoneuron activity, we used the Morris-Lecar model (Morris and Lecar 1981)

$$\frac{dV_i}{dt} = \frac{1}{C_m}(I^{app} - I_i^{ion} - I_i^{syn}) + \sqrt{\sigma n}\,\xi_{OU} \tag{1}$$

$$\frac{dW_i}{dt} = \phi\,\Lambda(V_i)[W_\infty(V_i) - W_i] \tag{2}$$

where $i = 1, \ldots, N$ index the neurons, and V_i and W_i represent the membrane potential and the fraction of open potassium channels, respectively. C_m is the membrane capacitance per unit area. I^{app} is an external bias current. The last term of *Eq. 1* represents the external noise (see *Numerical simulations* section). The ionic current is given by

$$I_i^{ion} = g_{Ca}\,M_\infty(V_i)(V_i - V_{Ca}^0) + g_K\,W_i(V_i - V_K^0) + g_L\,(V_i - V_L^0) \tag{3}$$

where g_a and V_a^0 (a = Ca, K, L) are the conductance and the resting

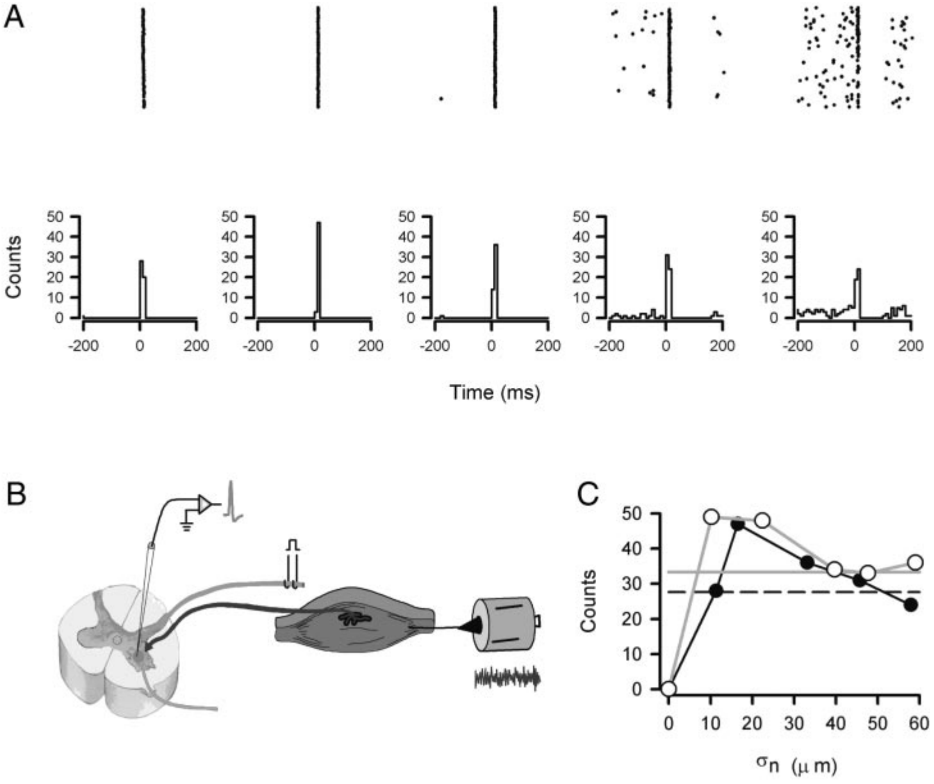

FIG. 3. A particular level of mechanical noise to the LGS muscle increases the probability of response of motoneurons to a weak electrical stimulus applied to the MG nerve. *A*: raster displays and peristimulus time histograms of action potentials evoked in 1 motoneuron for different levels of noise applied to the LGS muscle, 11.3, 16.5, 33.1, 45.7, and 57.9 μm, respectively. *C*: white squares, maximal amplitude of the histograms in Fig. 3*A* (counts). Black circles, corresponding graph obtained from a 2nd motoneuron. A 95% confidence interval is indicated in gray line for the graph in white circles, and in dashed line for the graph in black circles. *B*: scheme of the experimental arrangement for the intracellular recording of spinal motoneurons.

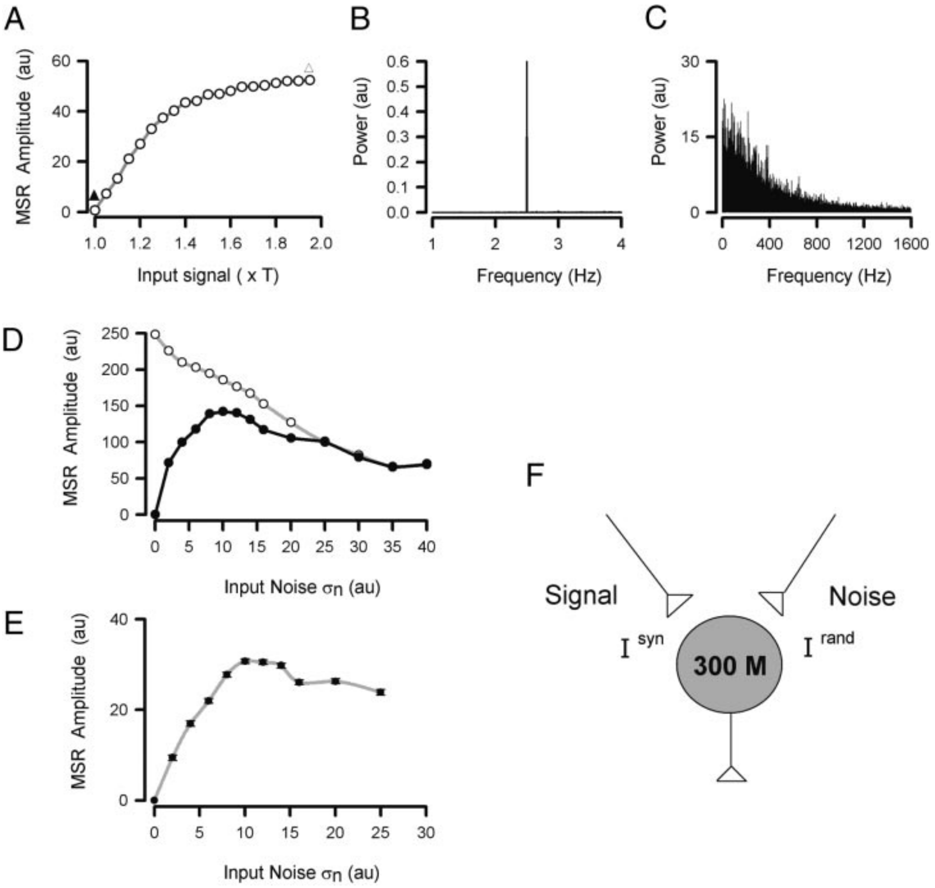

FIG. 4. The model considers diversity in the parameters of the equations that generate postsynaptic potentials in the simulated motoneurons, and diversity in the synaptic conductance. That means that each simulated motoneuron receives synaptic input with a different synaptic weight (w_j, see text for details), which is a random number. Furthermore, each simulated motoneuron receives Gaussian synaptic noise, indicated by I^{rand} (representing the last term in *Eq. 1*). This synaptic-like noise source is modeled (according to Destexhe et. al. 2001) as a colored noise (Orstein-Uhlenbeck process) of correlation time $\tau = 0.5$ ms and amplitude σ_N. *A* and *B*: same format as Fig. 1, *B* and *C*. *C*: power spectrum of the colored noise. *D*: collective summated evoked response of 300 motoneurons (300 M) vs. the input noise intensity, i.e., the simulated MSR amplitude vs. input noise. The graph in ● was obtained when the signal was evoked by a subthreshold stimulus and the graph in ○ when the signal was elicited by a suprathreshold stimulus. *E*: same as *D* (●). The values in the ordinates have been calculated by averaging over 700 periods of the evoked responses. Note the qualitative similitude between these graphs and the experimental results. *F*: scheme of the model

potentials of the calcium, potassium and leaking channels, respectively. ϕ is the decay rate of W_i, and we define the following functions of the membrane potential

$$M_\infty(V) = \frac{1}{2}\left[1 + \tanh\left(\frac{V - V_{M1}}{V_{M2}}\right)\right] \tag{4}$$

$$W_\infty(V) = \frac{1}{2}\left[1 + \tanh\left(\frac{V - V_{W1}}{V_{W2}}\right)\right] \tag{5}$$

$$\Lambda_\infty(V) = \tanh\left(\frac{V - V_{W1}}{2V_{W2}}\right) \tag{6}$$

where V_{M1}, V_{M2}, V_{W1}, and V_{W2} are constant values. The synaptic current is defined as (Destexhe et al. 1994)

$$I_i^{\mathrm{syn}} = \sum_{j \in \mathrm{neigh}(i)} g_i^{\mathrm{syn}}\, r_j(V_i - E_s) \tag{7}$$

where g_i^{syn} is the conductance of the synaptic channel. r_j represents the fraction of bound receptors described as

$$r_j = (1 - e^{-\alpha t}) \quad \text{for } t \leq t_{\mathrm{on}}$$
$$r_j = (1 - e^{-\alpha t_{\mathrm{on}}})e^{-\beta(t - t_{\mathrm{on}})} \quad \text{for } t > t_{\mathrm{on}} \tag{8}$$

where α and β are rise and decay time constants, respectively. Here "t_{on}" represents the time at which the synaptic connection is activated.

It has been recently shown that diversity might play an important role in forced excitatory systems, equivalent to the one played by noise in the stochastic resonance phenomena (Tessone et al. 2006). Tessone et al. (2006) demonstrated that the response of a system to an external weak periodic signal can be optimized by an intermediate level of diversity between the elements composing the system even in the absence of any other noise source. Consequently, diversity (represented by a quenched noise) and stochastic noise seem to play qualitatively the same role. Because diversity is intrinsic in nature, we included it in our model assuming that it plays the same role as the internal noise sources.

To account for the natural heterogeneity existing in spinal motoneurons, we introduced diversity in the conductance channel parameters: $g_K = (A{\cdot}w_K + 1)g_K^0$, $g_L = (A{\cdot}w_L + 1)g_L^0$, and $g_{Ca} = (A{\cdot}w_{Ca} + 1)g_{Ca}^0$ also in the synaptic amplitude $g^{\mathrm{syn}} = (A{\cdot}w_{\mathrm{syn}} + 1)g_0^{\mathrm{syn}}$ being w_j (j = K, L, Ca, syn) a Gaussian distributed random number of zero mean and unit variance. $A = 0.1$ is the unitary percent of heterogeneity we considered. In our simulations, we took I_i^{syn} as periodic synaptic pulses every 400 ms (i.e., 2.5 Hz as in the experiments) with time t_{on} equals to 3 ms and amplitude g^{syn}.

RESULTS

Experimental results

All animals that we examined exhibited a SR behavior in the amplitude of MSRs elicited by electrical stimulation to the MG nerve when different levels of continuous random stretches (input noise) on the LGS muscle were applied. We observed the SR-like effect when a weak electrical stimulus was applied to the MG nerve. Figure 1*B* illustrates with an asterisk the weak intensity used to produce MSRs of ~20 μV in one typical experiment. We computed the mean amplitude of successive MSRs in control conditions (elicited by electrical stimuli to the MG nerve) and during the application of different levels of noise applied to the LGS muscle. Figure 1*E* shows in circles the amplitudes of successive MSRs (at 2.5 Hz) for the three levels of noise indicated (low, intermediate, and high).

The MSR amplitude in control conditions is indicated with black circles. Note that the amplitude of the successive MSRs was significantly increased ($P < 0.05$) when an intermediate level of mechanical noise was applied to the LGS muscle (as is illustrated in Fig. 1*A*) and was decreased when a high level of such mechanical noise was added.

Figure 2, *A–C*, shows examples of successive recordings of the input signal (Fig. 2*A*), input noise (Fig. 2*B*), and the corresponding output afferent volleys and output MSRs (Fig. 2*C*) for three different levels of input noise as is indicated (low, intermediate, and high). MSRs were elicited by periodic stimulation to the MG nerve (1.2×T) at a frequency of 2.5 Hz. The input noise consisted of random stretches applied to the LGS muscle (see METHODS and Fig. 1*A*). Figure 2*C* illustrates that the amplitude of the MSRs was facilitated for an intermediate level of noise applied to the LGS muscle. Note that in this example, individual MSRs increased their amplitude for an intermediate level of noise. This observation was confirmed statistically after averaging over 64 MSRs for different levels of noise in six different decerebrated cats (Fig. 2, *F–H*). The maximal point in each graph of Fig. 2, *F–H*, and the corresponding control value were used for the statistical Student's *t*-test. We observed that in these animals the mean MSR amplitude was significantly enhanced ($P < 0.05$, Student's *t*-test) at an intermediate noise level (see asterisks in graphs of Fig. 2, *F–H*). We observed significant maximal changes ($P < 0.05$, Student's *t*-test) in the mean MSR of 108.1, 110.2, 115.2, 141.5, 114.4, and 110.6%, respectively, for the six different experiments. The mean percentage increase in the MSR amplitude respect to control for all the animals was statistically significant 117 ± 12% ($P < 0.05$, Student's *t*-test). We observed that the graphs of MSR amplitude versus input noise exhibited different profiles between animals. Whereas in some cases, a low level of input noise was enough to produce an enhancement of the MSR amplitude, in other cases a high level of input noise was required. This fact reflects not only the intrinsic diversity between the different cats but also that the internal level of noise is different in each animal.

Furthermore, we observed that when a supra-threshold stimulus was applied to the MG nerve the amplitude of MSRs significantly ($P < 0.05$; *t*-test) decreased as a function of the level of noise applied to the LGS muscle (Fig. 2*I*).

In contrast, it is important to note that in all the experiments the noisy stretching of the LGS muscle did not produce SR-like effects in the MG dorsal root potentials or in the afferent volleys. Figure 2*E* illustrates a graph of the mean amplitude of the afferent volley (white squares) and dorsal root potentials (black circles) for the experiment illustrated in *G* (black lines). Note that no significant changes in the amplitude of the afferent volleys were observed for the different levels of noise. Similar results were obtained in all the experiments. This suggests that in our experimental conditions (and the noise range employed), the SR observed in the monosynaptic reflexes was mediated by postsynaptic actions on the motoneurons. This fact justifies the use of postsynaptic connections in the model that we used to explain our experimental results as described in *Numerical simulations*.

To further investigate in detail the effects of noise on the motor responses, in other series of experiments, intracellular recordings were obtained from motoneurons. However, only in one cat did we obtain successful recordings in two motoneurons (-55 and -65 mV of resting potential) and with stable recordings during all the stimulation protocol (the same used for MSRs recorded from the L_7 ventral root; see METHODS). The only difference was that in this case, we defined one weak (i.e., subthreshold) stimulus as the stimulus that no produces an action potential. With this assumption, we applied a sequence of 64 stimuli to the MG nerve with an intensity to produce a subthreshold monosynaptic response. Figure 3*A* shows the raster displays and the corresponding histograms of the number of action potentials evoked in one motoneuron for five different levels of noise. Figure 3*A* shows the effect produced by increased levels of mechanical noise applied to the LGS muscle. Figure 3*C* shows in black circles the maximum peak of the successive histograms illustrated in Fig. 3*A*. Note that the number of action potentials in the motoneuron was increased for a particular level of mechanical noise applied to the LGS muscle. A similar result was obtained for another motoneuron recorded in the same experiment (see white circles in Fig. 3*C*). Horizontal lines in Fig. 3*C* represent the magnitude of a 95% confidence interval, which provides a scale against which to assess the significance.

Numerical simulations

Recently it was shown that the total conductance resulting from a sum of thousands of synaptic inputs has a power spectrum that approximates a Lorentzian shape, i.e., which decays as $\exp(-t/\tau)$. This was demonstrated in a detailed physiological model of cortical neurons subject to stochastic synaptic inputs (Destexhe et al. 2001). The Gaussian nature of the Orstein-Uhlenbeck process and its Lorentzian spectrum qualitatively match the conductances underlying synaptic noise, thus providing an effective stochastic representation that captures the amplitude of the conductances, their SD and the spectral structure. This motivates the use of the Orstein-Uhlenbeck process as a valid description of synaptic noise (Destexhe et al. 2001) that would match our experimental conditions. Following the Destexhe et al. (2001) idea, for the case of motoneurons, we assumed that external noise $\sqrt{\sigma_N}\xi_{OU}(t)$ that enters the pool of neurons through the synaptic connections is modeled as an Orstein-Uhlenbeck process, i.e., as a colored noise source with a correlation time of $\tau = 0.5$ ms. Integration was made by using a stochastic Runge-Kutta method (known as the Heun method) following ref. (San Miguel and Toral 1999).

As we said before, we initially verified that no neuron fired a pulse under the solely presence of the periodic signal or noise for the subthreshold value of $g_0^{syn} = 1$ mS/cm^2. For the other value of $g_0^{syn} = 1.4$ mS/cm^2, the signal is suprathreshold and induces pulsations even in the absence of noise. In the subthreshold case, we combined the two inputs and fed the 300 neurons with both the signal and noise. To account for the global response, we averaged the membrane potential generated by all of the neurons.

Figure 4 contains similar information to that shown in the experiments. As in Fig. 1*B*, the ▲ (△) in Fig. 4*A* indicates the weak (strong) intensity of the periodic stimulus used to evoke the simulated responses of the motoneurons. Figure 4*B* illustrates the power spectrum of the input signal, whereas Fig. 4*C* illustrates the power spectrum of the colored noise. In Fig. 4*D*, we plot the monosynaptic response amplitude, computed as the number of spikes generated in a small time window by the combination of the signal and the noise (where the number of responses generated only by the noise has been subtracted) versus the noise level, normalized to the number of spikes generated under the control noise value, as in Fig. 2, *F–H*, of 25 in this numerical case. Closed symbols stand for a subthreshold signal, whereas open symbols stand for the response of the system to a suprathreshold signal (see DISCUSSION). For the subthreshold signal, a peak at intermediate noise level can be clearly seen. This indicates that the modeled response of the system also exhibits the SR effects for the combination of a subthreshold signal and noise as seen in the experiment. Figure 4*E* shows a graph for the collective evoked amplitude response to a sub-threshold signal of the 300 motoneurons, as a simulation of the monosynaptic reflex response, versus the input noise intensity. The values in the ordinates have been again calculated by averaging over 700 periods of the input signal. A clear maximum at intermediate noise levels that decays for smaller or larger noise strengths can be seen in agreement with the experiments. Error bars indicate a small dispersion of the maximum values over the evoked potentials for the 700 input pulses. Although the comparison is only qualitative, the results agree very well with the experiments, showing that a simple model including pools of motoneurons receiving convergent synaptic inputs from sources generating the periodic signal and the noise is sufficient to explain the experimental observations.

To go further in our numerical predictions we considered a suprathreshold signal for the stimulus ($g_0^{\text{syn}} = 1.4\ \mu\text{S/cm}^2$, see △ in Fig. 4*A*) to check whether SR still holds under this condition. The result is shown in Fig. 4*D* (○). It can be clearly seen that the maximum disappeared; as expected, suprathreshold signals are not amplified and the response degrades for increasing noise level as it was also observed in the experiment.

DISCUSSION

Our results show that the monosynaptic reflex pathway exhibits the stochastic resonance behavior, a phenomenon that can be qualitatively reproduced in a realistic model of synaptic integration on a pool with a relatively small number of motoneurons with diversity.

SR was first proposed in 1981 as a possible explanation for the apparent periodicity of Earth's ice ages (Benzi et al. 1981). A variety of nonlinear systems physical and biological exhibit this phenomenon—in particular, sensory systems. Some examples related with the present study, but in the peripheral nervous system, have been reported: in tactile sensations (Collins et al. 1996), in muscle spindle receptors (Cordo et al. 1996), or in afferents from Golgi tendon organs and primary and secondary endings of the cat muscle spindles (Fallon et al. 2004). However, although the study of Fallon et al. (2004) was performed in cats they did not provide evidence about the existence of the SR phenomenon in the motor system, in particular in the Ia-monosynaptic reflex pathway of the cat spinal cord.

Stochastic resonance in the motor system

We demonstrated experimentally that a particular level of noise applied to the stretching of the LGS muscle can produce an enhancement of the MSRs evoked by a periodic stimulus to the Ia afferent fibers of a synergistic muscle (MG). We obtained a similar result in the intracellular monosynaptic reflex responses of motoneurons, thus providing support to the monosynaptic ventral root responses. These results demonstrate that the SR is not exclusive of the sensory systems and can be exhibited in the output of the motor system, within the CNS. This is consistent with previous reports in sensory systems, visual (Mori and Kai 2002) and somatosensory (Manjarrez et al. 2003) in which the SR has been observed as a result of the synaptic integration of signal and noise within the CNS.

Our study extends observations of Cordo et al. (1996) by showing that the SR occurs in the CNS, specifically in the spinal motoneurons, and not only in the peripheral nervous system at the muscle spindle stage. To our knowledge our study presents the first direct demonstration that the SR can also be exhibited by the motor system.

The idea that noise has an effect on the motor system was first indirectly suggested by Priplata et al. (2002, 2006), who demonstrated that the addition of tactile noise to the feet of quietly standing subjects can lead to an enhanced balance control. However, because tactile noise was applied to the feet they cannot discard that the stochastic resonance phenomenon was also produced by the somatosensory system (Collins et al. 2003; Priplata et al. 2006). In this context, we consider our study in cats as a direct evidence of the stochastic resonance in the motor system because we did not stimulate the skin and instead we exclusively activated the motoneurons by stimulation of group I muscle afferents.

Furthermore, we consider that our experimental method allowed a selective stimulation of the primary endings of muscle spindles by applying small noisy changes of length (noisy stretching) to a muscle. In fact, the effective range of noisy stretching that enhanced the MSR amplitude in our experiments was similar to the amplitude range (<60 μm) of sinusoidal stimulation (i.e., vibration) that produces selective activation of primary muscle spindles without activating secondary endings and Golgi tendon afferents (Brown et al. 1967). This finding provides additional support to the hypothesis that the interactions between the input signal and the input noise associated to the enhancement of the MSRs were at the postsynaptic level on the motoneurons (see also Fig. 2*E* to support the fact that no presynaptic effects were detected).

Model and its justification

Our model qualitatively agree very well with the experiments, showing that a simple simulation including pools of motoneurons receiving convergent synaptic inputs from sources generating the noise and the periodic signal is sufficient to explain the experimental observations. Other models of neural networks, as Hodgkin-Huxley (Liu et al. 2006), leaky integrator models (Kohn 1998), or Izhikevich (Izhikevich 2003; Izhikevich et al. 2004) could be implemented; however, the Morris-Lecar method (Morris and Lecar 1981) offers a simple system of equations to simulate neuronal networks from the spinal cord (Skinner and Mulloney 1998). Furthermore the natural diversity we introduced in the synaptic and conductance channel parameters makes the model more realistic, still retaining the most relevant features of the SR phenomenon. This point is original because to our knowledge there are not models in the literature that consider diversity in the parameters of the equations modeling the monosynaptic reflex pathway, in the context of the stochastic resonance. Our model is supported by recent theoretical studies in the context that diversity might play an important role in SR phenomena (Tessone et al. 2006).

Furthermore, the modeling of monosynaptic reflexes and their modulation by noise could have some relevance in, e.g., robots development. In this context, the present study could have important implications in robotics and neural motor prosthetics (Ando 2006; Friehs et al. 2004).

To account for the natural heterogeneity existing in spinal motoneurons, we introduced diversity in the synaptic input and in the conductance channel parameters. We consider that the modeling of a group of heterogeneous neurons is interesting because the main difference between homogenous and inhomogenous arrays is that the response of a homogeneous array without interaction is equivalent to the response of a single neuron. In this context, the modeling of a homogeneous network without interactions does not represent the behavior of natural neurons. On the contrary, an inhomogeneous array (diversity) is intrinsic in neuronal systems, and the purpose of including it was to show that the stochastic resonance phenomenon is very robust. Moreover, it has been recently shown that diversity plays a similar role as the internal noise (as shown by Tessone et al. 2006) in which the stochastic resonance behavior can be even favored by the presence of the otherwise natural diversity.

Regarding our simulations, because we considered a large number of motoneurons with diversity we assume that an additional source of internal noise should not change the results qualitatively. Therefore in our computer simulations we have not included internal noise sources. The addition of internal noise may produce an effect that could be quantitatively but not qualitatively different.

Noise sources and functional implications

Because in our experiments the levels of noisy stretching of the LGS muscle did not produce significant effects in the amplitude of MG dorsal root potentials or in the amplitude of afferent volleys (Fig. 2*E*), we suggest that the SR observed in the monosynaptic reflexes was mediated by noisy postsynaptic actions on the motoneurons. However, we cannot exclude the possibility that for higher levels of noise in the stretching of the LGS muscle, relative to the range ($\sigma_n = 0{-}160\ \mu$m) explored in the present study, some presynaptic effects could also contribute to the SR of the monosynaptic reflexes. Although in this circumstance, we should also consider the opposed fact that electrical stimulation to extensor group Ia muscle afferents produces a relative very small primary afferent depolarization in extensor group Ia muscle afferents (Eccles et al. 1962). Therefore further experiments will be necessary to explore in detail this issue. In this context, a discussion of the possible noisy sources participating in the enhancements of the amplitude of the monosynaptic reflexes merits a discussion.

Our results suggest that the monosynaptic reflex pathway uses a stochastic resonance-type mechanism to increase the monosynaptic reflexes via a noisy synaptic input on the motoneurons. Such noisy synaptic input could be originated from descending pathways (Brouwer and Ashby 1992), from dorsal horn neurons producing spontaneous cord dorsum potentials (Manjarrez et al. 2005), or from propriospinal neurons (Swinnen and Duysens 2004). There is evidence that propriospinal neurons provide a linkage between cervical and lumbar neuronal circuits of the spinal cord that act in the interlimb coordination of leg and arm movements during human locomotor activities (Swinnen and Duysens 2004). Therefore stretch reflexes in the lower limbs of humans can be affected by alterations in arm postures, thus suggesting that there might be interlimb reflex modulation with movement (Delwayde et al. 1977). We suggest that random properties of propriospinal neurons could provide the stochastic input required to produce a stochastic resonance mechanism in the Ia-motoneuron reflex pathway. This means that propriospinal neurons could serve as a beneficial intrinsic noise source for the monosynaptic reflex pathway. Enhancements of the monosynaptic reflexes could be mediated by an intermediate level of input noise on the motoneurons provided by the internal noise of the propriospinal system. There are studies supporting the idea that "internal noise" plays a role in information transmission within the CNS via the "internal stochastic resonance" phenomenon (Manjarrez et al. 2002b). This phenomenon has been examined in detail in diverse nonlinear systems (Balazsi et al. 2001; Gailey et al. 1997; Lee et al. 1998; Li and Li 2003; Li et al. 2004; for review, see Lindner et al. 2004) and could be an interesting issue to explore in the cat spinal cord in the context of the motor output.

The possibility that the application of noise could improve the motor performance of stroke survivors has been considered recently in an empirical study (Rogers et al. 2006). Such study was motivated by the fact that 75% of stroke survivors have sensorimotor deficits such as hemi-paresis and proprioceptive losses with resulting change to both muscle activation patterns and reflex modulation during movement. Rogers et al. (2006) suggested that noise can be used as a potential method for eliciting functional neuroplastic change poststroke via the stochastic resonance phenomenon. While pedaling a motorized cycle ergometer, soleus H-reflexes were recorded alone (in control conditions) or, during noise, presented to either the hamstrings or quadriceps of the ipsilateral paretic limb. Electrical noise, in the form of sub-sensation Gaussian white noise, was delivered to the target muscle via surface electrodes. Rogers et al. (2006) found that for noisy stimulation to either the quadriceps or hamstrings muscles there was a significant change between the mean normalized soleus H-reflex amplitudes relative to the control condition ($P < 0.01$) with an increase in soleus H-reflex with noise. We consider that the present study in cats provides support to these empirical observations in persons with poststroke hemiparesis.

In general, it is tempting to suggest that in physiological conditions adjustments in the level of intra-spinal noise sources could contribute to control the size of monosynaptic reflexes via the stochastic resonance phenomenon. For an intermediate level of noise, a desirable enhancement of MSRs could occur; however, for higher levels of noise, a desirable decrease could be produced depending of the requirements for the motor task. This last point could also be of importance in clinics if we consider that some pathological conditions of the motor system involve spastic states in which the attenuation of MSRs in certain muscles is desirable. In this context, our study provides support to examine in future studies the levels of noise that

TABLE 1. *Parameters used in the numerical simulations*

Parameter	Value
C_m	$5\mu F/cm^2$
I^{app}	$65\ \mu A/cm^2$
g^0_K	$8\mu S/ms/cm^2$
g^0_L	$2\mu S/ms/cm^2$
g^0_{Ca}	$4.4\mu F/ms/cm^2$
V_K	-80 mV
V_L	-60 mV
V_{Ca}	120 mV
V_{M1}	-1.2 mV
V_{M2}	18 mV
V_{W1}	2 mV
V_{W2}	30 mV
φ	$1/25\ ms^{-1}$
α	$0.33\ ms^{-1}\ mM^{-1}$
β	$0.2\ ms^{-1}$
g^{syn}_0	(specified in each case)
τ_{syn}	3 ms
E_s	0 mV

could be beneficial in humans to control the amplitude of MSRs by means of noise applied to the Achilles tendon via the stochastic resonance phenomenon. Therefore our study is important because it suggests that certain levels of mechanical noise could be employed in rehabilitation interventions to improve the performance of motor task requiring an enhancement of monosynaptic reflexes.

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