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Research report

Electrophysiologic study of globus pallidus projections to the thalamic reticular nucleus

Jorge H. Pazo*, Ana C. Barceló, Emanuel Bellantonio, Valeria C. Pazo, Noel Almarares

Laboratorio de Neurofisiología, Departamento de Fisiología y Biofísica, Unidad académica II, Facultad de Medicina, Universidad de Buenos Aires, Buenos Aires, Argentina

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ABSTRACT

This study was designed to explore the electrophysiological relationships between the globus pallidus (GP), the substantia nigra pars reticulata (SNr) and the thalamic reticular nucleus (TRN) in urethane-anesthetized rats. The neuronal activity of the rostral part of the TRN was recorded by microelectrodes. Single pulse electrical stimulation of the GP and SNr produced inhibition of the spontaneous activity of the majority of TRN neurons. Stimulation of the GP by microinjections of bicuculline (25 ng/300 nl) produced also inhibition of the spontaneous activity of the reticular neurons. This could lead to facilitation of the cerebral cortex, as the reticular nucleus is reciprocally connected to, and inhibits, the thalamic motor nuclei, that in turn excite the motor cortex.

1. Introduction

The thalamic reticular nucleus (TRN) is a thin neuronal layer abutting the anterior and lateral aspect of the thalamus, partially extending to its dorsal and ventral parts (Huguenard and McCormick, 2007; Pinault, 2004). In addition to electrical coupling, the TRN neurons release the inhibitory neurotransmitter, GABA (Crabtree, 1999; Landisman et al., 2002; Steriade, 2005). Corticothalamic and thalamocortical fibers pass through the TRN giving off collaterals that innervate the reticular cells (Guillery et al., 1998; Pinault and Deschênes, 1998; Yu et al., 2009) and in turn, these reticular neurons project inhibitory axons to the thalamic nuclei (Huguenard and McCormick, 2007; Kolmac and Mitrofanis, 1997). Contrasting these reciprocal connections, there is no evidence of direct projections of the TRN to the cerebral cortex (Gandia et al., 1993; Jones, 1975; Haber et al., 1985).

Thalamocortical, corticothalamic and reticulothalamic projections are organized topographically (Cornwall et al., 1990; Crabtree and Killackey, 1989; Guillery et al., 1998; Lam and Sherman, 2011; Raos and Savaki, 1995; Shosaku et al., 1984; Shosaku and Sumitomo, 1983) resulting in auditory, visual, somatosensory and motor sectors identifiable within the TRN. In addition to thalamic and cortical afferents, the reticular cells receive afferents from the forebrain and various brainstem centers (Asanuma and Porter, 1990; Cornwall et al., 1990; Jones, 1975; Kolmac and Mitrofanis, 1998; McCormick, 1992; McAlonan et al., 2006; Sherman and Guillery, 1996).

By virtue of these connections and powerful inhibitory action on most of the thalamic nuclei, the TRN is currently viewed as a key structure that influence many aspects of the forebrain functions, including cognitive processes, sleep mechanisms, genesis of cortical spindle waves and motor functions (Crabtree, 1999; McAlonan et al., 2006; Paré et al., 1990; Raeva and Lukashev, 1993; Strafella et al., 1997)

Projections from the GP (homologue to the external segment of the GP of primates) to the TRN was demonstrated in the rat, cat and monkey by neuroanatomical studies, using anterograde and retrograde tracers and autoradiographic techniques (Cornwall et al., 1990; Gandia et al., 1993; Hazrati and Parent, 1991; Kayahara and Katsuma, 1998). This pallidal innervation of TRN derives from collaterals of the major pallidofugal systems (Hazrati and Parent, 1991).

Anatomical tracing studies and electrophysiological method have shown connections of the SNr with TRN. This projection is preferentially distributed to rostral aspect of the TRN (Cornwall et al., 1990; Gulcevi et al., 2012; Paré et al., 1990).

The presence of dopamine in the TRN was observe in rats and confirmed in primates. The origin of these innervation was

* Corresponding author at: Laboratorio de Neurofisiología, Departamento de Fisiología y Biofísica, Unidad Académica II, Facultad de Medicina, Universidad de Buenos Aires, Paraguay 2155, Buenos Aires 1121, Argentina. Tel.: +54 11 5950 9700.
E-mail address: jpazo@fmed.uba.ar (J.H. Pazo).

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postulated to be from the substantia nigra compacta (Freeman et al., 2001; Gurevich and Joyce, 1999; Sanchez-Gonzalez et al., 2005).

These relationship of the basal ganglia open the possibility that may control the thalamic motor nucleus not only directly through the entopeduncular (EP-motor thalamus) and substantia nigra reticulata (SNr-motor thalamus) but indirectly through the TRN (GP and SNr-TRN projections).

This study was designed to evaluate, from an electrophysiologic point of view, the effect of the GP stimulation on the spontaneous TRN neurons activity in the rat. In addition, we explored the action of the substantia nigra reticulata (SNr) stimulation on the responses of the TRN, assessing for similarities or differences to the GP stimulation and testing whether the same reticular neurons responded to both nuclei.

2. Materials and methods

2.1. Surgery

Experiments were performed in male Sprague-Dawley rats weighing 300–450 g., in accordance with the National Institute of Health, Guide for Care and Use of Laboratory Animals. These were approved by the Animal Care and Use Committee of the Faculty of Medicine, University of Buenos Aires. The minimum numbers of animals consistent with obtaining statistically reliable data were used and every effort was made to minimize animal suffering.

The rats were anesthetized with urethane (1.2 g/kg, i.p.) and additional anesthetic was administrated (0.5 g, i.p.) as necessary to maintain a constant level of anesthesia. The depth of anesthesia was systemically checked by the lack of response to paw pinch and gentle corneal stimulation. The head of the animal was fixed to a stereotaxic frame (David Koft Instruments, USA). The dorsal surface of the skull was reflected and a small craniotomy was performed over the target structures. The exposed cortex was covered with 20% agar in Ringer solution to reduce brain pulsations and prevent dehydration. All incisions and pressure points were infiltrated with a long lasting local anesthetic (bupivacaine) before and after surgery. Body temperature was maintained at 37 ± 0.5 °C with an electric blanket thermostatically controlled by a rectal probe (Frederick Haer & Company, USA).

2.2. Electrophysiological recording

Extracellular single unit recording was performed by means of glass microelectrodes with tip diameters of 2–5 μm (1–10 MΩ) filled with 2% Pontamine Sky Blue in 2 M NaCl. The microelectrodes were placed in the TRN at the following coordinates referred to bregma (Paxinos and Watson, 1997): Bregma: −1.4 mm, Lateral: 1.5 to 2 mm and Height: −5 to −6.6 mm from duramater. The microelectrodes were hydraulically advanced through the TRN until a neuron could be isolated. Identification of TRN neurons was achieved following previously described electrophysiological criteria as means to distinguish between action potentials of neurons from action potentials of fibers. The neurons were characterized by a biphasic or triphasic spike, with a duration of more than 1 ms (Bishop et al., 1962; Fussey et al., 1970; Hakan et al., 1992; Tasaki et al., 1954). In addition, neurons were discriminated with the aid of the software Spike2. In some recordings, more than one unit were recorded. The insolated neurons were monitored for at least 4–5 min to assure the stability of their firing rate, pattern and spike morphology. Then 3–5 min of spontaneous activity was recorded. Only those neurons with a signal to noise ratio >2:1 were analyzed. Neuron activity was recorded with high impedance amplifier, band-pass filters 300–3000 Hz (P511 Grass Instruments), displayed on a digital oscilloscope (Tektronix TDS300) and stored on videotape with a digital data recorder (VR-100B, Instrutech Corporation). Data were analyzed off-line using an analog to digital converter (sampling frequency 10 KHz; DigiData 1200, Axon Instruments Inc.). A personal computer and an analysis software (Spike2, Cambridge Electronic Design Limited).

2.3. Electrical and pharmacological stimulation

Coaxial stimulating bipolar electrodes of 250 μm of outer diameter and inner lead diameter of 100 μm, protruding from the shaft 500 μm (SNEX 100, Rhodes Medical Instrument), were used for stimulation of the GP and/or the SNr. Simultaneously, spontaneous unit activity of the ipsilateral TRN was recorded. The following stereotaxic coordinates (Paxinos and Watson, 1997) relative to the bregma were used for GP: Bregma: −0.92 mm, Lateral: 2.8 to 3 mm and Height: −5.6 to −6.8 mm, from duramater; and SNR: Bregma: −5.8 mm, Lateral: 2.0 to −2.4 mm and Height: −7.6 to −8.4 mm, from duramater. Electrical rectangular pulses were delivery by an electronic stimulator (A300 Pulsemaster and S.I.U.385, Word Precision Instrument) to the electrodes placed in the GP or SNr. The following stimulation parameters were used: pulse width of 300 μs and intensity up to 500 μA, to minimize the spread of current to adjacent structures. Pulses were repeated every 4–5 s. This interval was chosen based on the TRN neurons response to subsequent stimuli, because when the inter-pulse interval was lengthened more than 3 s, a similar amplitude to the first initial response was observed (Yu et al., 2009).

To confirm that the responses observed by electrical stimulation of the GP were due to activation of neurons and not of fibers of passage, we stimulated the GP by microinjecting 25 ng of bicuculline methiodide (Sigma), a $GABA_A$ antagonist, dissolved in 0.3 μl of saline solution. Bicuculline was injected using a stainless steel cannula (300 μm OD) connected via polyethylene tubing to a 5 μl Hamilton microsyringe, which was driven by a microdrive unit (Baltimore Instruments). The above dose of bicuculline has demonstrated to induce neuronal activation of the GP neurons by blocking $GABA_A$ receptors. (Féger et al., 1989; Pazo et al., 2010; Périer et al., 2002; Robledo and Féger, 1990).

2.4. Statistical analysis

For each neuron, the following parameters were calculated: (i) mean discharge frequency integrated over 30 s epochs to obtain mean frequency histograms and poststimulus time histograms; (ii) the frequency distribution of the interspike intervals (ISIs) and their coefficients of variation (CV); and (iii) the autocorrelograms. These values were obtained 1 min before (control) and after the electrical stimulation.

In the pharmacological experiments, the mean control firing rate obtained during 4–5 min preinjection was compared with representative intervals of postinjection firing rate, expressed as percent of control values. The drug or saline microinjection effect was monitored over 40 min after administration. Bursting activity of the recorded units was identified with the aid of the script "burst analysis" of the Spike2 software. Statistical differences between basal and post-stimulation firing rates were determined by one way ANOVA for repeated measures, followed by post hoc testing, Dunnett or Bonferroni *t*-test. In some cases, Student *t*-test was also used. A change of $P < 0.05$ from the basal firing rate was considered a significant alteration.

2.5. Histology

At the end of the experiment, the rats were deeply anesthetized. The position of the microelectrode tip was marked by an iontophoretic deposit of Pontamine Sky Blue. The rats were perfused transcardially with saline, followed by 4% buffered formalin. Microinjection cannula and stimulation electrodes were left in place during perfusion to give an accurate estimation of their position. The brain was removed, post fixed in 4% formalin, frozen sectioned in 60 μm slices and stained with safranine O. GP microinjections localization and recording sites were reconstructed from the microdrive readings, cannula position and deposit of dye spots. In addition, the electrical stimulation sites were localized by its electrode tracts. Composite diagrams of these positions were drawn with the aid of a light microscope and the atlas of Paxinos and Watson (1997). Only animals with documented microinjection, stimulation electrode and recordings within the intended target, were analyzed.

3. Results

3.1. RTN neuronal firing under basal conditions

Analysis of the TRN neuronal firing pattern was conducted 3–5 min preceding electrical or pharmacological stimulation. The TRN neurons have an overall mean basal firing rate of 11.64 ± 1.65 Hz (mean ± SEM; $n = 96$). Three types of firing patterns were observed (Fig. 1). The first type showed an irregular activity pattern with occasional bursting episodes. These neurons have flat autocorrelograms, an asymmetric interspike interval (ISI) and high coefficient of variation (Fig. 1A). Forty eight per cent of the TRN neurons belong to this category. A 26% of the recorded neurons have bursting activity, with high frequency bursts of action potential, a flat autocorrelogram with single initial peak, asymmetric frequency distribution (ISI) and high coefficient of variation (Fig. 1B). The rest of the neurons (26%), show a regular discharge pattern characterized by an autocorrelogram with various peaks, symmetrical ISI and low coefficients of variation (Fig. 1C) However, in some cases, neurons from this last group could switch their firing pattern to burst mode.

3.2. Effect of the GP and SNr nuclei electrical stimulation on the TRN neuronal spontaneous activity.

Single pulse electrical stimulation with intensities ranging from 250 to 500 μA were applied to the GP and/or to the SNr with simultaneous recording of the ipsilateral TRN neurons. Recordings were

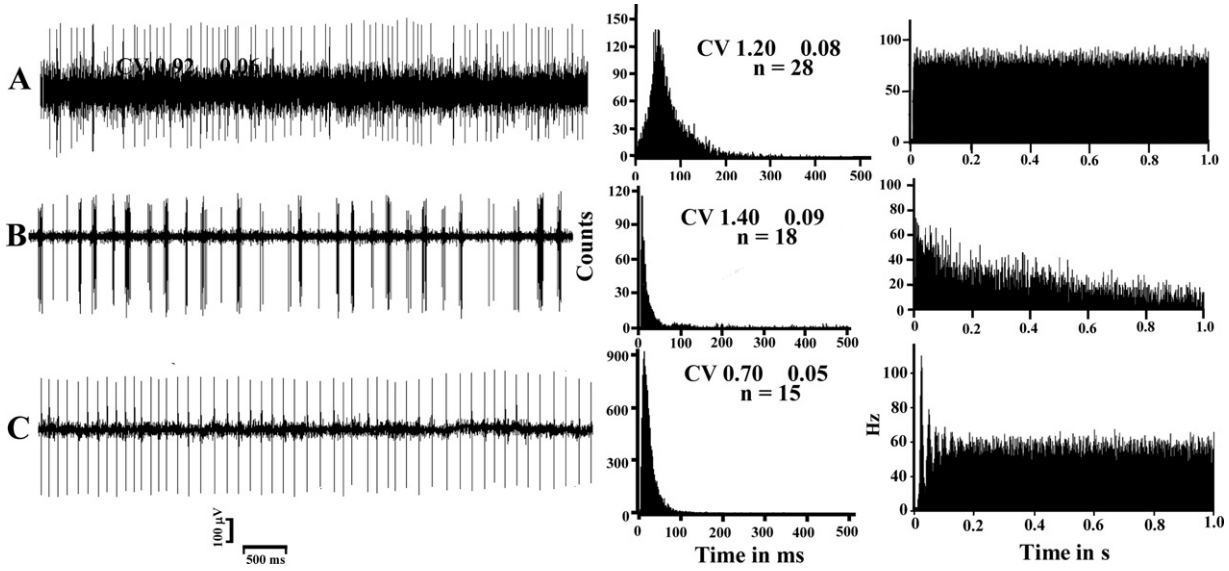

Fig. 1. Examples of different firing pattern observed in the RTN neurons. (A) Irregular firing rate was characterized by tonic discharge activity interrupted by variable length pauses reflected by asymmetric interspike interval histograms with a high coefficient of variation (ISI) and flat autocorrelograms. (B) Bursting neurons were characterized by having grouped discharge activity reflected by a leftward peak in the ISI histograms and autocorrelograms with initial peak. (C) Regular firing neurons were characterized by showing tonic discharge activity and symmetrical sharply peaked ISI histograms and autocorrelograms with various peaks.

taken from the rostral pole of the nucleus (motor sector), where afferents projections from the GP and SNr arrive (Pinault, 2004).

We studied 56 neurons. Twenty nine neurons (52%) responded to the stimulation of both nuclei. Only 14 (26%) responded to one nucleus: eleven responded to the GP stimulation and 3 to the SNr. Thirteen neurons (25%) had no response to stimulation from either nuclei. The responses observed were inhibition of the spontaneous activity of TRN neurons.

The inhibition produced by the GP stimulation was 87%, expressed as percent of control values (1 min preceding the

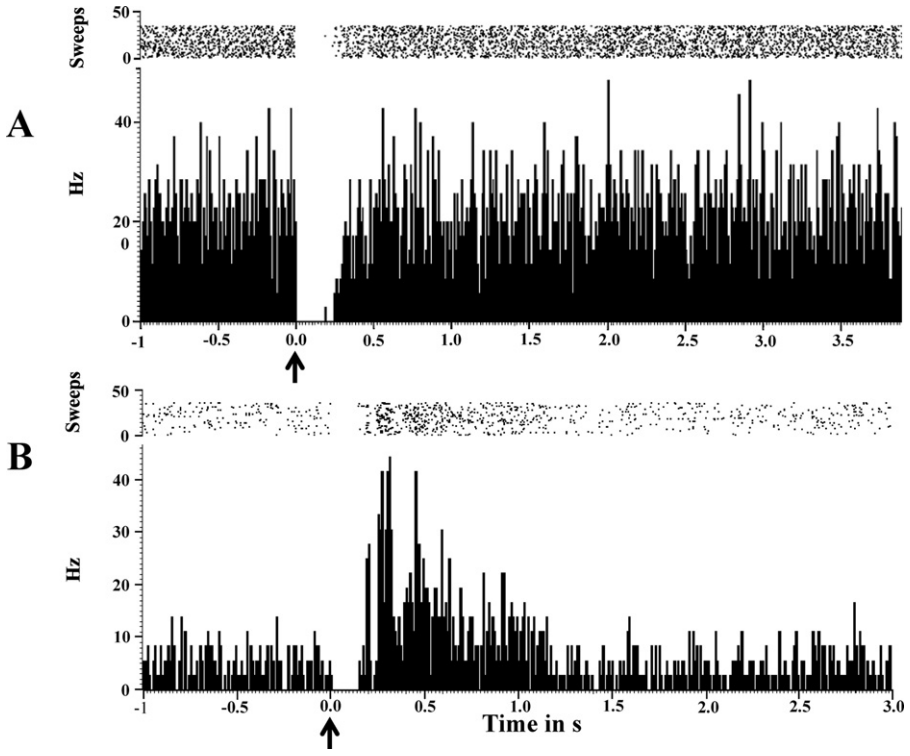

Fig. 2. Representative poststimulus time histograms (PSTHs) of neuronal responses of the reticular thalamic nucleus evoked by electrical stimulation of ipsilateral globus pallidus. (A) Inhibitory response. Mean neuronal discharge before stimulation 11.66 ± 1.03 Hz, after stimulation (arrow) 0.25 ± 0.13 Hz and poststimulation 12.40 ± 1.05 Hz. One way ANOVA for repeated measured, $F_{2,105} = 48.779$, $P < 0.001$, post hoc test Dunnett's test $P < 0.05$. The upper part shows a raster display of the firing pattern of the cell. The PSTH and raster display were constructed from 36 consecutive stimuli repeated each 5 s. Bin size 10 ms. (B) Biphasic response, inhibition followed excitation. Mean firing rate before stimulation 4.94 ± 0.6 Hz, after stimulation (arrow) 0.19 ± 0.12 Hz (inhibition) and 14.10 ± 1.60 Hz (excitation), poststimulation 4.43 ± 0.56 Hz. One way ANOVA for repeated measured, $F_{3,140} = 42.252$, $P < 0.001$, Dunnett's test $P < 0.05$, when compared control values with inhibition and excitation. The raster display and PSTH were constructed from 36 consecutive stimuli repeated each 5 s. Bin size 10 ms.

Table 1
All the values are expressed as percent of the firing rate of 1 min preceding the stimulation.

SNR	GP
Control 100 ± 14.7% (n = 32)	Control 100 ± 16.8% (n = 40)
Inhibition 9.18 ± 2.25% (n = 32)*	Inhibition 12.74 ± 1.91% (n = 40)*
Post-stimulation 99.8 ± 1.43% (n = 32)	Post-stimulation 102.8 ± 16.20% (n = 40)

For SNr, *P < 0.05 Bonferroni t-test after one way ANOVA for repeated measurement $F_{2,98}$ = 36.874, P < 0.001. For GP, *P < 0.05 Bonferroni t-test after one way ANOVA for repeated measurement $F_{2,117}$ = 14.207, P < 0.001.

stimulation), with a latency of 13.5 ± 2.6 ms, n = 40 (Table 1; Fig. 2A). Similar inhibition was observed when the SNr was stimulated. The latency was of 15.70 ± 3.11 ms and the inhibition was 90% of control values (Table 1, Fig 3A). The duration of both inhibitory responses were very similar, GP: 180.73 ± 35.86 ms, n = 40 and SNr: 181.71 ± 46 ms, n = 32. However, nine neurons had a biphasic response characterized by an inhibitory response followed by an excitation one (Figs. 2B and Fig. 3B). This biphasic response was observed after the stimulation of both the GP and the SNr in 5 and 4 neurons respectively. The excitatory response had a delay that depended on the duration of the previous inhibition. The excitatory responses were quantitatively similar and have been combined in the following statistic analysis, control: 100 ± 14.7% vs. 215.52 ± 27.40%, n = 9, P < 0.001 Bonferroni t-test, after one way ANOVA, $F_{3,120}$ = 40.190, P < 0.001, with a duration of 328.11 ± 74.82 ms, n = 9. Trend to biphasic responses were observed when the intensity of the stimulus was high (500 μA). In some neurons, there was a transitory poststimulation change in the firing pattern from bursting to irregular, then returning to the original firing pattern.

Fig. 4 shows the GP and SNr recording sites in the rostral aspects of the TRN.

3.3. Effect of pharmacological stimulation of the GP on TRN neuronal spontaneous activity

We studied the spontaneous activity of TRN neurons in response to the pharmacological activation of GP, based on the previously described effect after an electrical stimulation. We studied this nucleus because its direct action on thalamic spontaneous discharges has not been explored yet, in contrast to the well known effect of the SNr. The globus pallidus was stimulated with microinjections of 25 ng of bicuculline, in 300 nl of isotonic saline. Subsequently, reticular neurons activity was recorded until a predrug firing activity was observed or after 60 min post-injection, which ever came first. We analyzed 3 neurons for each animal.

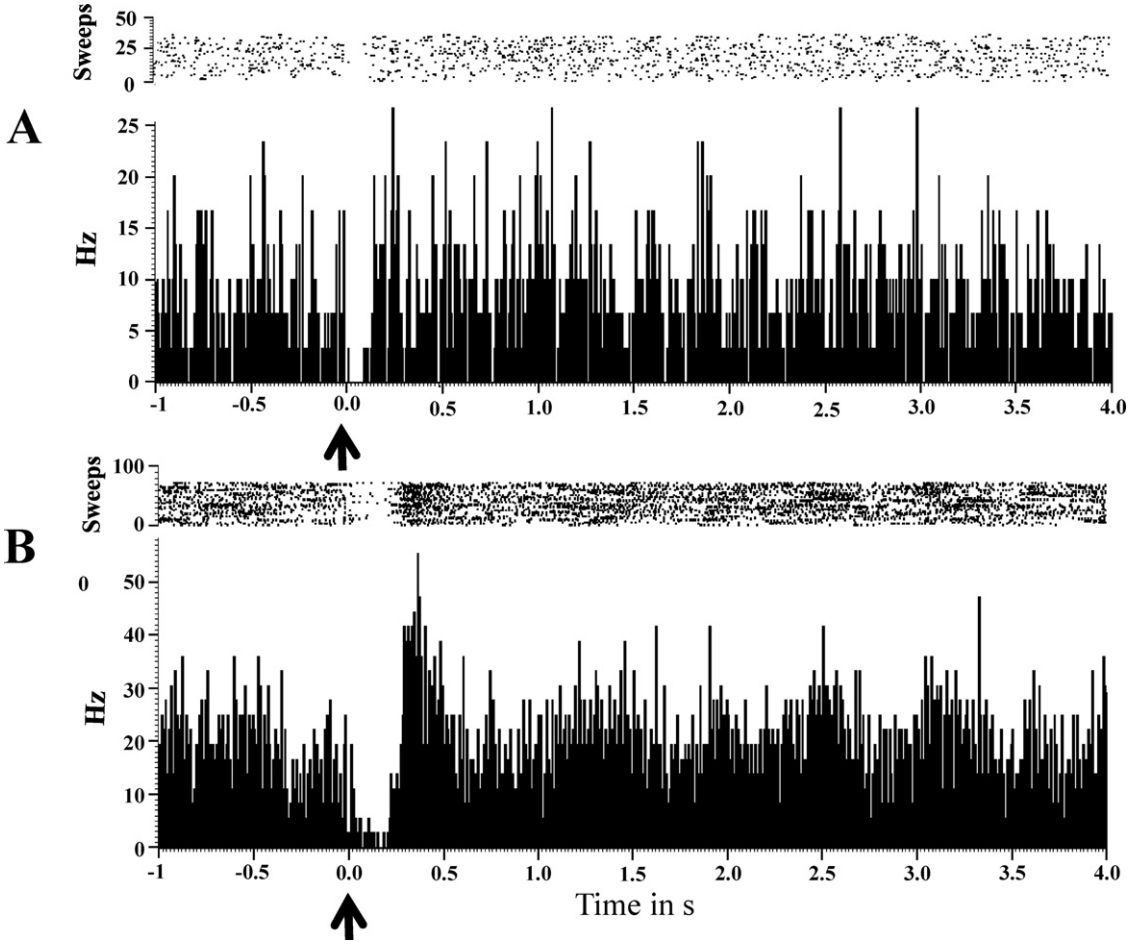

Fig. 3. Representative poststimulus time histograms (PSTHs) of neuronal responses of the reticular thalamic nucleus produced by electrical stimulation of ipsilateral SNr. (A) Poststimulus time histogram (PSTH) of a neuron inhibited by SNr stimulation. Control mean firing rate 7.61 ± 0.90 Hz, after stimulation (arrow) 0.956 ± 0.26 Hz and poststimulation 8.68 ± 089 Hz. One way ANOVA for repeated measured, $F_{2,105}$ = 31.461, P < 0.001, Dunnett's test P < 0.05. The upper part shows raster display of the firing pattern of the cell. The PSTH and raster display were constructed from 36 consecutive stimuli repeated each 5 s. Bin size 10 ms. (B) Poststimulus time histogram of biphasic response (inhibition-excitation) of the reticular neuron to SNR stimulation. Control 19.22 ± 1.40 Hz, after stimulation (arrow) 3.86 ± 0.71 Hz (inhibition) and 27.44 ± 2.11 (excitation), poststimulation 18.92 ± 1.27 Hz. One way ANOVA for repeated measured, $F_{3,140}$ = 46.740, P < 0.001, Dunnett's test P < 0.05 when compared control values with inhibition and excitation. The raster display and PSTH were constructed from 36 consecutive stimuli repeated each 5 s. Bin size10 ms.

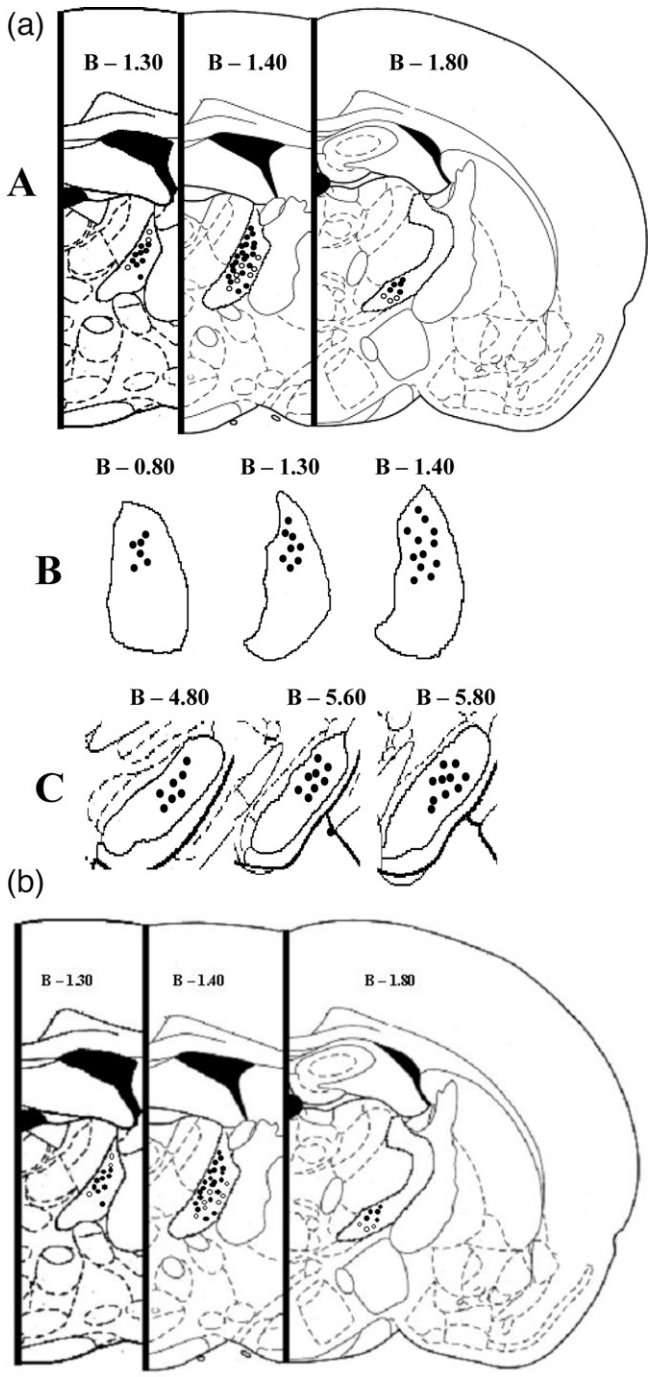

Fig. 4. Histological reconstruction of the recording sites in the RTN in (A), the stimulation sites in the GP in (B) and the SNR in (C). The white circles represent sites which neurons did not respond to stimulation of the GP and/or SNR or both. Outlines and levels were adopted from Paxinos and Watson (1997).

In total, we studied 40 neurons of the rostral aspect of the TRN. Thirty neurons (75%) were inhibited after bicuculline microinjection. Six neurons did not recover to control values after 60 min post bicuculline administration and they were excluded for the inhibition time analysis.

Inhibition had a latency, from the beginning of the microinjection, of 2.8 ± 0.30 min, $n = 30$ and lasted for 23.64 ± 2.36 min, $n = 24$ (Fig. 5). Basal firing rates were significantly inhibited by 60% of the mean frequency of preinjection values ($100 \pm 10.6\%$ vs. $40 \pm 11\%$, $n = 30$, $P < 0.001$), Student t-test for repeated measured. Two neurons of this group had an inhibitory-excitatory biphasic response (Fig. 6), with 10 neurons (25%) showing no response to GP stimulation.

The firing rate of six units was unchanged after the injection of vehicle alone. Fig. 7 shows GP stimulation and TRN recorded sites.

4. Discussion

We observed three distinct patterns of spontaneous neuronal activity in the TRN. These are similar to the ones previously described in urethane-anesthetized rats (Pinault and Deschênes, 1998). Although the existence of projections from the GP and SNR to the TRN has been reported in anatomical studies of rodents and other mammals, including man (Depaulis et al., 1990; Fussey et al., 1970; Gandia et al., 1993; Hazrati and Parent, 1991; Kayahara and Katsuma, 1998), there are no electrophysiologic studies showing the effect of these nuclei on the activity of reticular neurons in the rat. This paper provides evidence confirming the existence of these projections in addition to extending the knowledge to the electrophysiological relationships of these nuclei. We demonstrate that the electrical and/or chemical activation of the GP and SNR nuclei modify the TRN neurons spontaneous activity.

The main effect of electrical stimulation of the SNR and the GP was inhibition of spontaneous activity of the TRN neurons. This effect has a relatively long-lasting suppression time, 180–181 ms. The inhibitory effect of the SNr on the spontaneous activity of TRN neurons is in agreement with the reported by Paré et al. (1990).

We also observed a convergence of projections from the GP and SNr on some reticular neurons. However, not all the neurons that responded to GP responded to the SNr. This could be attributed to the fact that the dorsal aspect of the rostral pole receive limited projections from the SNr (Cornwall et al., 1990; Gandia et al., 1993). Similar convergence on reticular neurons has been demonstrated by afferents from thalamic relay nucleus (denominated double-sensory TR neurons) and projections from different sectors of the same reticular nucleus.

A biphasic response consisting of inhibition followed by excitation response was also observed in some neurons. One interpretation of this type of response could be based on the reciprocal neuronal loop that forms the GABAergic reticular neurons with glutamatergic thalamocortical relay cells. When reticular neurons are inhibited, in turn the relay neurons are excited by desinhibition, with subsequent activation of reticular neurons. However, individual pairs of RTN and relay neurons infrequently form reciprocal connections. This could explain the limited biphasic responses. In the case of the GP, another possibility could be that its stimulation might activate the pallidonigral pathway that in turn inhibits the SNr, resulting in the excitation of reticular neurons.

The pharmacological stimulation of the GP by microinjections of 25 ng/0.3 μl of bicuculline resulted in the inhibition of the spontaneous activity of 75% of the reticular neurons. However, 25% of these neurons did not respond to the activation of the GP.

Within the responding neurons, there were two neurons with biphasic responses, inhibition followed by excitation, similar to some of the responses seen following electrical stimulation. The interpretation of these type of responses could be similar to that given above.

The findings of the present study suggest that projections from the GP and SNR to the TRN could play a role in processing thalamic information. Since the GP and SNR neurons project to the motor region of the reticular nucleus (Cirata et al., 1990; Jones, 1985; Pinault, 2004; Shosaku et al., 1989), they could disinhibit thalamocortical motor neurons including those receiving direct innervation from output nuclei of the basal ganglia, that is the entopeduncular nucleus (GPi of primates) and the SNr. In addition, the GP is known to send inhibitory projections to both the entopeduncular (GPi) and SNr, which in turn both project to the motor thalamic nucleus: the

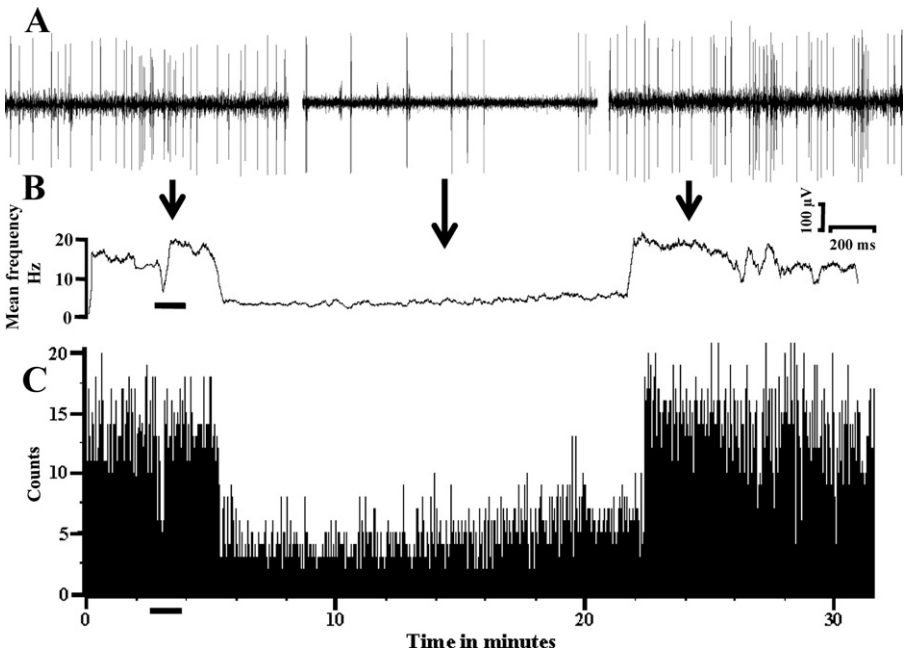

Fig. 5. Representative example of a reticular neuron inhibited by a microinjection of bicuculline (25 ng/0.3 μl) into the ipsilateral GP. (A) Neuronal discharged before, during and after microinjection of bicuculline. (B) Sequential histogram of the same neuron displaying the neuronal spontaneous activity in response to GP microinjection of bicuculline (horizontal line). Bin size 30 s. Before microinjection the mean frequency was 13.40 ± 3.65 Hz, (n = 12 samples of 30 s each), after administration of bicuculline 3.45 ± 0.40 Hz (n = 56 samples of 30 s each) and postinhibition 15.56 ± 2.45 Hz (n = 30 samples of 30 s each). There was a significant difference among the inhibition when compared with control and post inhibition values. One way ANOVA $F_{11,91}$ = 69.117, P < 0.001, Dunnett's test P < 0.05. The latency of the inhibition was 5 min from the start of microinjection and lasted 27 min. (C) Rate histogram of the neuron, bin size 5 ms.

ventrolateral and ventromedial (Faull and Mehler, 1985). Thus, the GP could influence the activity of the thalamic motor nucleus by three routes, the entopeduncular nucleus, the SNr and the reticular thalamic nucleus all of which lead to subsequent activation of the motor cortex.

Since the SNr inhibits directly the thalamic motor nucleus and produces an opposite effect through the RTN, its final effect on the motor cortex could be controversial. Nevertheless, this newly described electrophysiologic pallidoreticular pathway may be viewed as another output route from the basal ganglia with

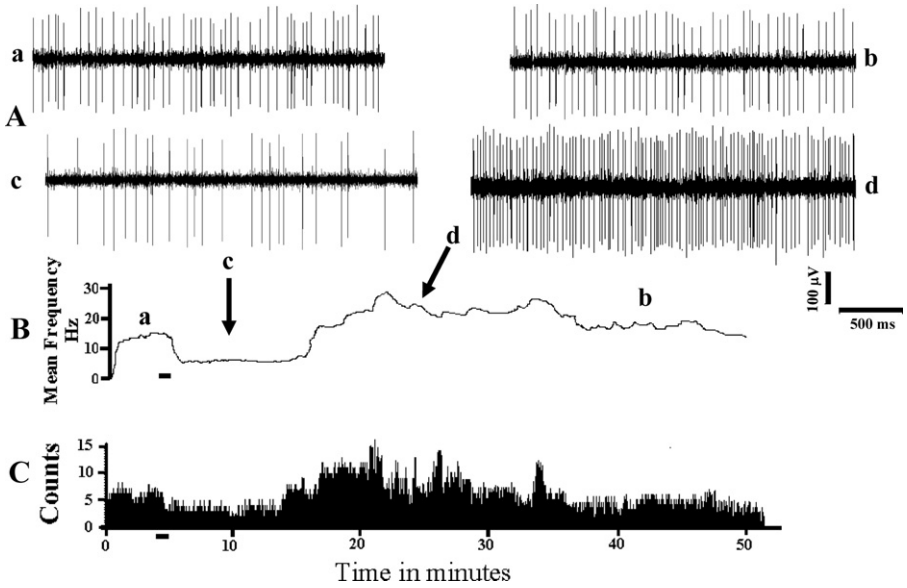

Fig. 6. Representative biphasic response of a reticular neuron (inhibition-excitation) to the microinjection of bicuculline into the ipsilateral GP. (A) Extracellular activity of the neuron: before microinjection (a), after bicuculline administration: inhibition (c), excitation (d) and when firing returned to control values (b). (B) Sequential histogram of the same neuron displaying mean frequency spontaneous activity in response to GP microinjection of bicuculline (horizontal line), bin size 30 s The mean control value was 12.63 ± 3.6 Hz (n = 8 samples of 30 s each), during inhibition 5.78 ± 0.46 Hz (n = 16 samples of 30 s each), during excitation 22.24 ± 6.13 Hz (n = 36 samples of 30 s each) and during recuperation 11.06 ± 6.66 Hz (n = 30 samples of 30 s each). There was a significant difference among control firing rate compared with the inhibition and the excitation responses. One way ANOVA for repeated measured, $F_{4.85}$, P < 0.001, Dunnett's test P < 0.05. The latency of the inhibition was 1 min 20 s from the star of the microinjection of bicuculline and lasted 8 min. The excitation, that followed the inhibition, lasted 18 min. The arrows indicate the firing activity during inhibition and excitation, respectively. (C) Rate histogram of the neuron, bin size 5 ms.

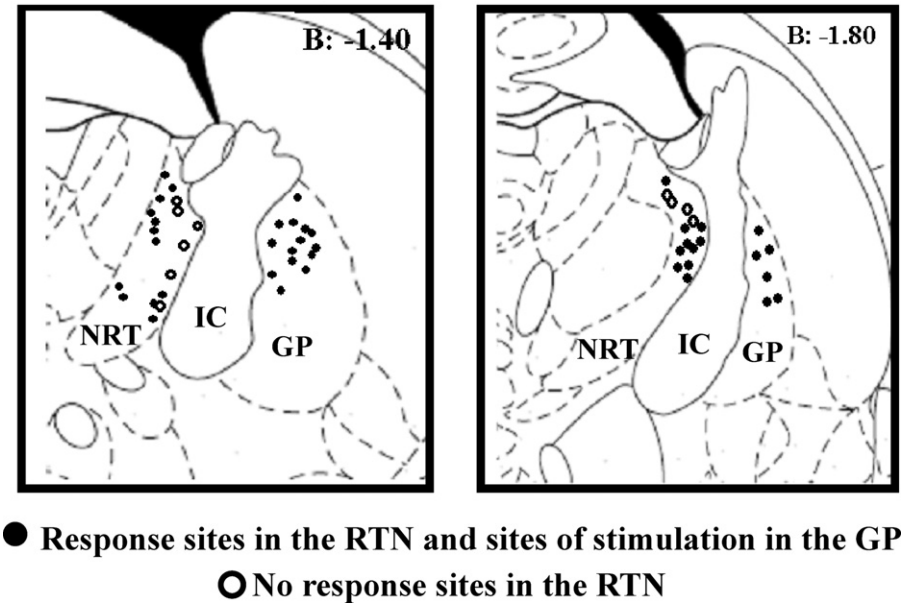

Fig. 7. Histological reconstruction of the sites recorded in the RTN and the stimulation into the GP. Outlines and levels were adopted from Paxinos and Watson (1997).

potential a role in controlling motor function by facilitating the motor cortex.

5. Conclusions

Our experimental evidences obtained in this study suggest that the electrical and chemical activation of the GP and electrical activation of the SNr inhibit the spontaneous activity of the rostral neurons of thalamic reticular nucleus. This area corresponds to an area of the RTN that receives projections from the motor cortex and is connected with thalamic motor nucleus (Cirata et al., 1990; Jones, 1985; Pinault, 2004; Shosaku et al., 1989). Thus, the pallidoreticular pathway could mediate activation of the motor cortex by disinhibition of the thalamic motor nucleus. The role of the nigroreticular pathway could be more complex because the SNr inhibits directly the motor thalamic nucleus, in addition to the action on the TRN.

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