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Reciprocal Interactions Between Intralaminar and Lateral Thalamic Nuclei in Rats

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Summary

Reciprocal interactions between intralaminar thalamic nuclei (ncl. centralis lateralis, CL, and ncl. parafascicularis, Pf), the pretectal area (Pt) and lateral thalamic nuclei (ventrobasal complex, VB, ncl. anterior ventralis, AV, and ncl. ventralis anterior, VA) have been observed in ketamine-anaesthetized rats. Extracellular single unit activity has been recorded after single electrical stimuli. Electrical stimulation of the VB evoked a short latency orthodromic response followed by a pause in spontaneous activity in neurones of medial thalamic nuclei. Lateral thalamic neurones responded to electrical stimulation of the intralaminar nuclei or the pretectal area with the same pattern of response. Striatal, sensorimotor cortical or peripheral electrical stimulation also evoked similar responses. The pauses in spontaneous activity were shown to be the result of inhibition since the responsiveness of the intralaminar nuclei or the lateral thalamic neurones to all inputs was abolished or reduced after a conditioning electrical single-shock stimulation in the VB or in the intralaminar nuclei, respectively. The two components of the response were of a different origin, since most of the short latency responses disappeared after medullary, upper cervical sections or large decortications, while the inhibitions persisted. These inhibitions were shown to be of thalamic origin since their duration was decreased after extensive decortications increased after medullary section. It is concluded that the neuroneal properties studied in this report are probably broadly represented throughout the thalamus and that thalamic neurones are under inhibitory control elicited by afferent volleys. This inhibitory control includes a relay in the nucleus reticularis thalami (nRT). The mechanisms of sensory interaction can be purely thalamic, but they can be modulated by suprathalamic and/or mesencephalic loops.

Key words
Rat – Nucleus reticularis thalami – Intralaminar thalamic nuclei – Ventrobasal complex – Reciprocal interactions – Electrical stimulation.

Introduction

Interactions between thalamic nuclei have been described in the cat by Purpura's group (Purpura and Cohen 1962, Purpura and Shofer 1963, Maekawa and Purpura 1967, Sakata *et al.* 1966). Repetitive electrical stimulation of intralaminar thalamic nuclei (centralis lateralis, CL; centrum medianum, CM; or parafascicularis, Pf) elicits a short latency excitatory response, in lateral thalamic nuclei (ventralis anterior, VA; ventralis lateralis, VL; and ventrobasal complex, VB), followed by a long lasting inhibitory response. In the rat, similar findings were also observed in VB after stimulation of intralaminar thalamic nuclei (Emmers 1976) and in Pf after VB stimulation (Benabid *et al.* 1983). Furthermore, similar responses were obtained in the cat during intranuclear thalamic stimulation of ncl. geniculatum mediale (GM) or VL (Marco *et al.* 1967, Schlag and Villablanca 1968). The anatomical and neurochemical basis of these effects are not yet clear.

Purpura and his collaborators proposed that some of these interactions resulted from either intrathalamic or from complex interneuroneal systems *via* corticofugal projections, or through the mesencephalic reticular system. In contrast, Jibiki (1986) proposed a direct relationship between lateral

and medial thalamic nuclei while Marco *et al.* (1967) almost exclusively devoted their attention towards a search for inhibitory interneurones.

Monosynaptic pathways between lateral and intralaminar thalamic regions have never received any strong anatomical support and thus these interactions may operate indirectly *via* their projections to one or more relays. The same type of inhibition resulted from both central (cortical, striatal or thalamic) stimulation and peripheral skin stimulation (Andersen *et al.* 1964a,b,c, Buser 1966, Horvath and Buser 1976, Dalsass and Krauthamer 1981, Albe-Fessard *et al.* 1983, Sotgiu *et al.* 1983, Shin and Chapin 1990). Since the nRT neurones are mostly GABAergic (Houser *et al.* 1980) and are supposed to be the source of inhibition of the thalamic nuclei, we tested its possible role in these interactions (see Pollin *et al.* 1997).

In the present paper, we have reexamined the reciprocal interactions between intralaminar and lateral thalamic nuclei in ketamine-anaesthetized rats using electrophysiological techniques in order to compare them with the results obtained in nRT lesioned rats. The origin of the activating responses is discussed according to the results obtained in decorticated animals and in animals in which medullary or upper cervical sections were performed. The results obtained in the Pt were added since Pt has recently been implicated in sensorimotor integration (Rees and Roberts 1989a,b). Moreover, efferents from Pt terminate in the nRT (Berkley and Mash 1978, Weber and Harting 1980, Cornwall *et al.* 1990) and Pt neurones exhibited similar patterns of responses to the intralaminar ones.

Methods

Animals and surgery

Experiments were performed on 106 male Sprague-Dawley rats (260–280 g) anaesthetized with ketamine (90 mg/kg, i.p.). The animals were placed into a stereotaxic frame. All pressure and incision points were infiltrated with local anaesthetic (lidocaine 2%). The heart rate was continuously monitored and the body temperature maintained between 37 °C and 38 °C through a homeothermic blanket system. Additional doses of ketamine (30 mg/kg, i.p.) were given when necessary. A group of six rats were ventilated and immobilized with Flaxedil (gallamine triethiodide).

Stimulation and recording

Two bipolar, concentric stainless steel electrodes were stereotaxically introduced either into the intralaminar thalamic nuclei (CL and Pf, AP: 4.2 and 5.2, L: 1.2, V: 5) or into Pf and the pretectal area (Pf and Pt, AP: 4.5, L: 1.2, V: 5) or into VB (VBp and VBa, AP: 4.5 and 5.5, L: 2.5, V: 4.5) and/or into the striatum (AP: 7.5, and 8.5, L: 3, V: 6.5) according to the atlas of Albe-Fessard *et al.* (1971). Evoked responses were obtained in the VBa electrode after stimulation applied to the contralateral forelimb. VBp responded to face stimulation. Stimulation was delivered through an isolation unit (single shock of 0.05–0.1 ms duration; 0.05–0.1 mA intensity, at a frequency of 0.5 Hz). Antidromic responses were sought by classical tests (3 shocks at a frequency of 300 Hz, and collision). Cortical stimulation was delivered through two silver ball electrodes applied to the pial surface on the sensorimotor cortex area in a zone where evoked potentials were maximal after thalamic stimulation (VB or intralaminar nuclei). When the peripheral receptive field was found, natural stimulation was replaced by electrical stimulation, by inserting two thin sharp needles into the skin. Electrical shocks were well below the threshold for eliciting reflex movements. Bipolar stimulation electrodes were implanted into the dental pulp of a mandibular incisor. Extracellular single unit activities were recorded from the thalamus using glass micropipettes (impedance 8–12 MΩ) filled with a solution of KCl (0.75 M) and pontamine blue (4%). We used the spike shape to distinguish between recordings from the soma or axon (see Tasaki *et al.* 1954, Azérad *et al.* 1977). Only somatodendritic responses are included in the results designated "cells". Thalamic unit activities were recorded and raster displays were constructed.

Histology

The final recording sites were marked by an iontophoretic injection of pontamine blue and the corresponding blue spot was subsequently observed in histological sections of the brain (frozen sections, Nissl stain) and the tracks were then reconstructed using microdrive reference points.

Cortical ablation, medullary or upper cervical sections

Extensive hemidecortication, including the sensorimotor area, was carried out by suction at least two months before the recording sessions in twelve animals. Medullary or upper cervical sections were made under deep anaesthesia and artificial ventilation two hours before the beginning of the recording session in two series of 6 animals.

Data analysis

All results were expressed as mean values ± standard error of the mean (S.E.M.). The mean values were compared using the unpaired t-test. P values less than 0.05 were considered to be significant.

Results

Effect of anaesthesia

Under ketamine anaesthesia the ongoing ("spontaneous") activity of the recorded thalamic neurones was always in the form of tonic ("stationary-

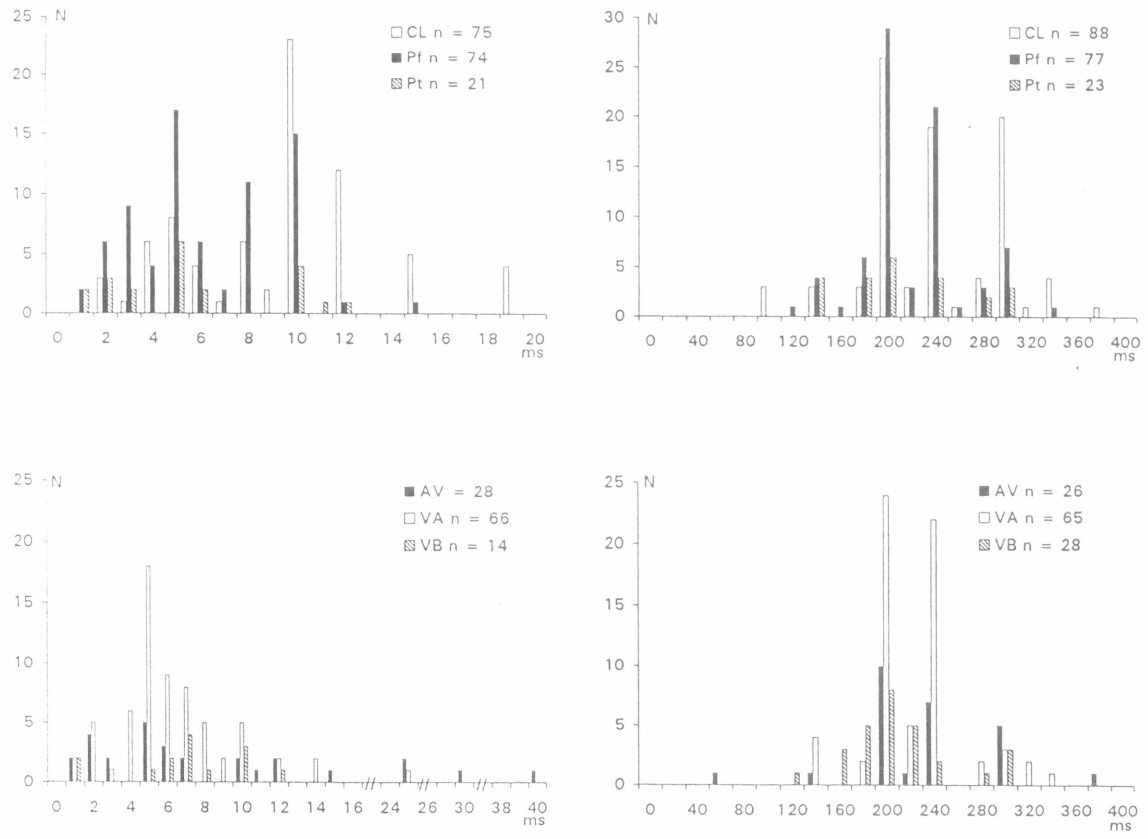

Fig. 1. *Histogram of response latencies in intralaminar nuclei (Pf and CL) and anterior pretectal nucleus (Pt) after either VBa or VBp stimulation (upper left). Histogram of silent period durations in these nuclei after VBa or VBp stimulation (upper right). Lower part: histogram of response latencies in lateral thalamic nuclei (AV, VA, VB and other) after intralaminar (Pf or CL) or Pt stimulation (left). Histogram of silent period duration in the same lateral nuclei after Pf, Pt or CL stimulation (right).*

Short latency excitatory response

Stimulation of VBa or VBp elicited a similar excitatory response in the intralaminar thalamic nuclei or in the Pt. The cells could be classified in two categories in each nucleus according to the bimodal latency of their excitatory responses from 1 to 20 ms (Fig. 1). Cells with a latency from 1 to 4 ms and some with 5 ms latency followed a high frequency train of stimulation up to 300 Hz. Their latency remained stable from one impulse to another but no collision with spontaneous activity could be observed in this "very short latency" group (Fig. 2). The proportion of these very short latency responses was higher in Pt and Pf than in CL (71 % and 52 % vs 24 %). Within the Pf, the highest proportion of very short latency responsive neurones was found after VBa stimulation (66 %). Cells with longer latency (5–20 ms) did not follow a high frequency train of stimulation and the latency was more irregular.

Pause of spontaneous activity

All the activating responses were followed by a pause of spontaneous activity of 232±4 ms (n=188) (Figs 1 and 2), were not influenced by the intensity of stimulation and were quite similar after VBa or VBp stimulation. The duration of the pause was longer in CL than in Pf or in Pt (243±6 ms, n=88; 224±5 ms, n=77 and 216±11, n=23, respectively). A wide dispersion of the duration of this silent period was observed but 94 % of neurones exhibited a very stable pause of spontaneous activity lasting between 150 and 300 ms with two peaks at 200 ms and 240 ms.

Long latency excitatory response

These pauses of activity were usually followed by a long latency excitatory response, a so-called "rebound phase" which contained 2–3 spikes. This rebound phase was often followed by a second silent period before return to the resting condition (Fig. 2). The silent period of initially silenced cells always

terminated by a large burst of firing similar to that observed in other cells. Eleven class I cells only responded with a late burst of firing which had the same characteristics as that of class II cells.

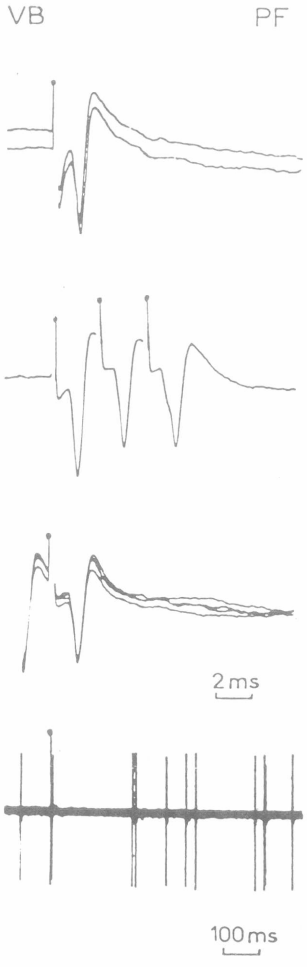

Fig. 2. *Response of a parafascicular class II neurone (Pf) to stimulation of the VB. This orthodromic "very short latency" response follows a high frequency train of stimulation (2nd row) without collision with an orthodromic spike (3rd row), three superimposed traces show the stability of latency (1st and 3rd rows, calibration: 2 ms). The excitatory discharge is followed by a period of complete silence (three superimposed traces, calibration: 100 ms).*

Lateral thalamic unit responses

Intralaminar stimulations (Pf or CL) were performed in 36 rats. In six rats, the stimulating electrodes were located in Pf and Pt. Recordings were taken from 153 lateral thalamic neurones (AV, VA and VB) but only 6 were class I (4 %). Thirty-one cells (20 %) did not respond to any of the tested stimulations. In the 122 remaining cells, intralaminar or Pt stimulation elicited a response in AV (n=30), VA (n=67), VB (n=21) and various other thalamic nuclei (n=4).

Evoked activity

The responses had the same characteristics as those observed in the intralaminar cells described above. Most of the responsive cells exhibited quite a complex response with a short latency excitatory discharge followed by a period of complete silence generally terminated by a burst of firing. Eleven cells (9 %) immediately ceased to fire and this was always terminated by a long latency burst response and 11 responded with a complex response after one of the two stimulations and only by a pause of spontaneous activity after the other site of stimulation. Among AV units, 73 % responded to Pf, 15 % to CL and 12 % responded to both Pf and CL. In VA, the proportions were quite different: 33 % responded to Pf, 22 % to CL and 45 % to both, while in VB 81 % of cells responded to both.

Short latency excitatory responses

Stimulation of Pf, Pt or CL elicited a short latency excitatory response in lateral thalamic nuclei (Fig. 1). The overall latency ranged from 1 to 15 ms in each nucleus, while only a few AV cells had a longer latency. Very short latency cells (with a latency of 1 to 5 ms) followed a high frequency train of stimulation up to 300 Hz. The latency was stable but no collision with spontaneous activity could be observed. Such cells were more numerous in AV and in VA than in VB (47 %, 48 % and 22 %, respectively). Within the AV and the VA, the highest proportion of very short latency responsive neurones was found after Pf stimulation (85 % and 62.5 %, respectively). As in intralaminar cells, the longer latency responses (5–20 ms) did not follow high frequency trains of stimulation and their latency was irregular.

Pause in spontaneous activity

All but 3 excitatory responses were followed by a pause of 225±4.4 ms, n=123 (Fig. 1). The three non-silenced cells were found in AV. The duration of the silent period was quite similar after Pf, Pt or CL stimulation and remained rather constant over a long period (up to 4 hours) in each case. The duration was shorter in VB (210.4±6.5 ms, n=21) than in other lateral thalamic nuclei. As observed in intralaminar cells, 83 % of lateral thalamic neurones presented a very stable pause of spontaneous activity lasting between 150 and 300 ms with two peaks at 200 and 240 ms.

Long latency excitatory responses

As already described above, the pauses of activity were usually followed by a long excitatory response. The silent period of initially silenced cells was always terminated by a similar burst of firing. One

class I cells in VB only responded with a late burst of firing with the same characteristics.

Modulation of sensory responses by thalamic stimulation

Among the neurones responsive to thalamic stimulations, 48 also responded to electrical peripheral stimulation applied either to the vibrissal area, the incisor dental pulp or the forepaw. Peripheral stimulation elicited excitatory responses in these neurones (8.4±5 ms), followed by a pause of the spontaneous activity lasting 192±14 ms. The majority of the responses (75 %) were found in the VB but some were observed in the intralaminar nuclei.

A double shock conditioning-test procedure (C−T) was used to analyze the effects of prior VB or intralaminar conditioning stimulation on the test response to peripheral stimulation and, *vice versa*, of prior peripheral stimulation on the thalamic evoked response. Two kinds of peripheral stimulation were used, namely non-noxious stimulation applied to the head or forelimb and a stimulation of the dental pulp.

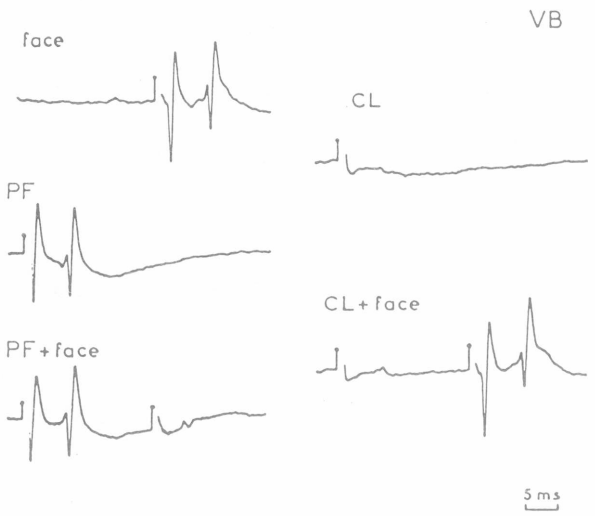

Fig. 3. *Inhibition of a sensory response in a VB class II neurone. Left part, responses to face or Pf stimulation alone (1st and 2nd rows); upper right, CL stimulation only silences this VB neurone without any short latency excitatory response. At a conditioning test stimulus interval of 30 ms, prior Pf stimulation inhibits the excitatory response following face stimulation (lower left row) while CL stimulation (right) does not (calibration: 5 ms).*

When the conditioning thalamic stimulus was delivered (10 to 100 ms) before the peripheral test stimulation (noxious or non-noxious), the excitatory test response was inhibited (Fig. 3). With a wider range of C−T intervals (110 to 180 ms), a response to the test peripheral stimulus could be evoked but it was changed so that the peripheral stimulation produced more intense firing, with a slightly longer latency.

When the conditioning thalamic stimulation only evoked a pause of spontaneous activity, the excitatory response elicited by the peripheral test stimulation was not always abolished, either in intralaminar nuclei or in VB. Likewise, the excitatory discharge elicited in thalamic neurones by intralaminar or VB stimulation was inhibited by prior peripheral stimulation, but the duration of this inhibitory period was shorter (60 ms).

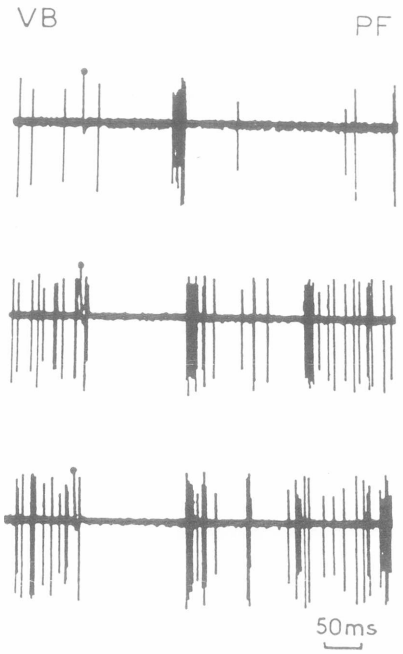

Fig. 4. *Responses of three Pf class II neurones to VB stimulation in a decorticated rat, (three superimposed traces in each row). Short latency excitatory responses are present in these three neurones, but the silent periods are shorter than those observed in intact rats (calibration: 50 ms).*

Effect of decortication or of sections at the bulbar or cervical level

In decorticated rats, the proportion of silent cells (class I) increased (40 % vs 9.3 %) but thalamic stimulations still elicited responses. The responses were somewhat different from those observed in intact rats: 1) the proportion of initially silenced cells was increased (32 % vs 11 %); 2) cells with very short latency (1 to 5 ms) were more numerous (76 %); and 3) the silent period was shorter (134±9 ms, n=56 vs 232±4 ms, n=188, $p<0.0001$) than in intact animals (Figs 4 and 5). The influence of conditioning thalamic stimulation on responses to peripheral stimulation

remained and was effective over an interval of 70 ms (Fig. 5). After a medullary intercollicular section, 30 % of the intralaminar cells failed to give an excitatory response after VB stimulation but the silent phase was still present. When the short latency excitatory response still occurred, it was always longer than 7 ms. The duration of the silent period was longer than in intact rats (293±14 ms, n=35 vs 232±4 ms, n=188, $p<0.0001$).

After upper cervical section, very short (1–5 ms) and short latency (> 5 ms) excitatory responses persisted in 50 % of units and were followed by a pause in spontaneous activity comparable to that of the control group (230±23 ms, ns). But, in 50 % of the intralaminar cells (vs 11 %), VB stimulation only elicited a pause of spontaneous activity, without any excitatory response.

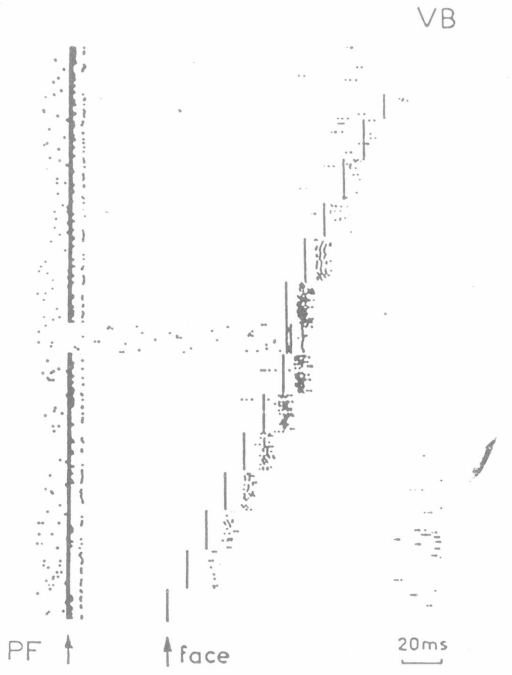

Fig. 5. *Modulation of a response to face stimulation by prior stimulation of the Pf in a VB class II neurone studied in a decorticated rat. Conditioning stimulation of the Pf is followed within a time interval of 50–150 ms by test stimulation applied to the face. The response to Pf stimulation alone can be seen in the upper part; note that the silent period is shorter than in intact rats (135 ms). The response to stimulation applied to the face is presented in the middle part. This response is inhibited when the C–T time interval is shorter than 70 ms and changed when C–T time intervals were in the range of 70 to 135 ms, the latency is longer and the firing is more intense. Note that this response to face stimulation is partially inhibited when C–T time intervals are over 135 ms.*

Striatal and cortical stimulations

Striatal stimulation was performed in 11 rats and 52 responsive cells were recorded. The majority of the responses were observed in the Pf (21), CL (15) and VA (10). Some responsive neurones were also found in the LP, VL and AV. In contrast, no VB cells were influenced by striatal stimulation. The response consisted of a short latency excitatory discharge followed by a long phase of silence and then several rhythmic bursts frequently occurred separated by silent periods (n=41). The other 11 responsive neurones immediately ceased firing which was followed by long latency bursts of responses. Orthodromic (70 %) as well as and antidromic (30 %) excitatory responses were observed. The overall latency ranged from 1 to 20 ms. The average latencies were longer in the intralaminar nuclei than in the VA (7.8±1.4 ms, n=31 and 4.3±1.3 ms, n=6, respectively). The duration of the silent phase was similar to that observed after thalamic stimulation (240±18.6 ms), but the distribution of the duration of the silent period was more widely dispersed (up to 600 ms). Among these 52 neurones, 50 also responded to thalamic stimulation.

Cortical stimulation was carried out in 6 rats. Few responsive cells were recorded. Out of these 17 cells, 11 were in the Pf and 4 in the Pt; they also responded to VB stimulation. The two remaining neurones were in the VA and also responded to Pf stimulation. All but one of the responsive cells showed quite a complex response with a short latency excitatory discharge (5.4±1.5 ms) followed by complete silence (260±25 ms) generally terminated by a burst of firing. One silenced cell presented a long latency burst response. The overall latencies ranged from 2 to 10 ms. As after thalamic stimulation, the duration of the silent period tended to remain constant in each case, but the distribution of the duration of the silent period was wider than that observed after thalamic stimulations. The silent period varied from 140 to 400 ms.

Discussion

The aim of this paper was to analyse the substrate of medial lateral thalamic interactions. We shall thus discuss 1) the very short latency response, 2) the short latency response, 3) the silent period and 4) the relevance to pain pathways.

As previously reported (Pollin *et al.* 1991), we used ketamine anaesthesia since thalamic neurones exhibit spontaneous single-spike tonic discharges without any changes in bursting activity. The "ketamine" behavior of thalamic neurones can be compared to the wakeful state (Mukhametov *et al.* 1970, Steriade *et al.* 1986). Under these conditions, neurones could be recorded for periods lasting up to 4 hours without major changes in the pattern of their responses.

like") discharge, in a range of 1–15 Hz, with a peak at 12 Hz. No bursts of discharges were observed. The characteristics of evoked responses (i.e. latency of the response, duration of the pause of spontaneous activity) remained stable even in recordings of up to four hours indicating that no major changes had occurred in the level of anaesthesia during long-lasting experiments. Results were similar in intact rats under spontaneous or artificial ventilation.

Table 1
Frequency and location of the different types of neurones after central (VBa, VBp, striatal and cortical) stimulations or after peripheral (face or forelimb) stimulations

	CL	Pf	Pt Total		
Class I	10	10	1	21	9%
Class ii	95	85	28	206	91%
Total	77	163	75	227	

Intralaminar thalamic or pretectal unit responses

Altogether 242 neurones were recorded within the intralaminar thalamic nuclei (CL and Pf, 209 cells) and in the anterior pretectal nucleus (Pt, 33 cells) after VBa and/or VBp stimulations in 55 rats. Out of these 242 neurones, 15 units (6.2 %) died before any record could be obtained.

According to the frequency of their spontaneous discharge, 21 neurones (9.3 %) were ranked into class I (no resting discharge) and 206 neurones (90.7 %) into class II (1–15 Hz) (Table 1).

Evoked activity

Among 227 neurones, 197 (87 %) were responsive to VBa, VBp or both stimulations (20 class I and 177 class II). Out of the 20 class I neurones, 9 exhibited only a short latency response, four a short latency response followed by a long latency burst of firing, and seven only a long latency burst of firing (Table 2).

A total of 158 (89 %) from the 177 class II neurones responded with a short latency response always followed by a pause of activity. Nineteen class II neurones were only silenced: the pause in spontaneous activity immediately followed the stimulation without any spikes or practically no spikes after the stimulation and was always terminated by a burst of firing with the characteristic of a postinhibitory rebound (Table 2).

Among CL units, 46 % and 27 % responded to VBa or VBp, respectively, and 27 % responded to both VBa and VBp. In Pf the proportions were similar: 48 % and 26 % responded to VBa or VBp and 26 % to both.

Table 2
Summary of the characteristics of responses of intralaminar nuclei (CL and Pf) and anterior pretectal nucleus (Pt) after VBa and/or VBp stimulations

	Class I	Class II	Total	%/Total
Short latency response	13	158	171	75 %
Only silenced or rebound	7	19	26	11 %
Response	10	177	197	87 %
No response	1	29	30	13 %
Total	21	206	227	
Pause of activity		177	177	100 %
No pause		0	0	
Rebound	11			

As far as the cells with a very short latency response (1–5 ms) are concerned, it is likely that a monosynaptic pathway exists between intralaminar nuclei and VB. Since no antidromic response was observed either in the VB or the intralaminar nuclei, we can assume that a reciprocal projection between "specific and non-specific" thalamic nuclei *via* thalamocortical collaterals proposed by Jibiki *et al.* (1986) does not exist. Furthermore, no anatomical studies using retrograde tracers have observed any direct relation between these thalamic nuclei (Jones 1985). It therefore seems likely that this direct relationship involves an extrathalamic pathway.

It is well known that spino-thalamic tracts (STT) project to both intralaminar and lateral thalamic nuclei in the cat (Boivie 1971), in primates (Willis Jr. 1987) and in the rat (Kevetter and Willis 1983). If the very short latency responses result from a sort of axon reflex along STT collaterals, this could explain the lack of an antidromic response and the ability to follow high frequency stimulation. Intercollicular section suppresses the very short latency responses, but some of the short latency responses and the following pauses in spontaneous activity remain. We may thus assume that collaterals from STT neurones originate in a region between cervical and intercollicular levels. In the monkey, Giesler *et al.* (1981) found, collaterals from STT axons at the level of the medullary reticular formation. Kevetter and Willis (1983) confirmed these observations and found that in the rat, STT axon collaterals represent 15–20 % of the STT neurones which project on the contralateral thalamic nuclei and which are mainly located in the upper cervical segments. These data could explain the larger percentage of inhibitory phases without any excitatory response observed after cervical or medullary sections. The occurrence of cells with a short latency response (5–20 ms) suggests that polysynaptic pathways may also exist between VB and intralaminar thalamic nuclei. These pathways may involve additional structures: the nRT, the cortex or the medullary reticular formation since all receive afferents from VB and intralaminar thalamic nuclei and project to the thalamus.

An intrathalamic loop could be realized through the nRT. Such an hypothesis suggests that VB and intralaminar thalamic neurones are connected to the same nRT neurone which would exert an excitatory effect in either intralaminar or VB neurones. While experimental evidence indicates that some nRT neurones project both to VB and intralaminar thalamic nuclei (Cesaro *et al.* 1986, Pollin *et al.* 1991), this pathway could not account for the excitatory responses since all nRT neurones exert an inhibitory effect *via* a GABAergic process (Houser *et al.* 1980, Jones 1985, Spreafico *et al.* 1987, 1988).

In the cat, Purpura *et al.* (1965, 1966, Purpura 1972) have suggested a role for a corticofugal projection. Contrary to Jibiki *et al.* (1986) we cannot exclude this hypothesis: the proportion of responsive neurones with very short latency discharges or without early excitatory responses increases following cortical ablation. Furthermore, the larger percentage of silent neurones (class I) observed in decorticated rats suggests a tonic facilitatory effect of the cerebral cortex onto the thalamus.

On the other hand, some STT neurones send collaterals to the reticular formation. As the mesencephalic reticular formation in turn projects to the intralaminar nuclei, this brainstem area could be implicated in the polysynaptic pathways between VB and intralaminar thalamic nuclei. This hypothesis is supported by the fact that intercollicular section abolishes some of the short latency responses whereas the cervical section does not. Other pathways could be involved as a loop between intralaminar nuclei and reticular formation (Steriade 1981). Several alternative pathways may be implicated *via* a cortical or a bulbar relay (Bowsher 1976).

Synaptic excitation of thalamocortical relay neurones of both specific or non-specific thalamic nuclei is followed by a pause in their spontaneous activity. This silent period probably originates from an inhibitory process, since no evoked responses can be elicited by central or peripheral stimulations during this pause. Furthermore, the silent period remains after cortical, intercollicular or upper cervical lesions, suggesting that it originates from an intrathalamic process. Since nRT coagulation (Pollin *et al.* 1997) or systemic injection of picrotoxin (Pollin *et al.* 1991) suppress this silent phase, we suggest that nRT is involved and that this silent period originates from a GABAergic inhibitory process. Other experimental data support this role of the nRT. In rat brain slices, an inhibitory phase is only recorded in the GL if the nRT is present within the slice (Kelly *et al.* 1979). After destruction of the visual sector of the nRT the inhibitory responses are suppressed in the GL (French *et al.* 1985, Shosaku *et al.* 1989).

An influence of striatal stimulation on intralaminar thalamic neurones has already been described in the rat (Albe-Fessard *et al.* 1983), and in the cat (Buser 1966, Feltz *et al.* 1967, Horvath and Buser 1976, Dalsass and Krauthamer 1981). The nRT could be involved in the inhibitory response since it has been demonstrated that intralaminar cells send collaterals to nRT *en route* to the striatum and the cortex (Cesaro *et al.* 1985).

Furthermore, some authors implicated the nRT in the genesis of IPSP recorded intracellularly (French *et al.* 1985, Thomson 1988). Since decortication reduces the duration of the silent period while intercollicular section enhances it, a partial role of the cortex and/or the reticular formation in the duration of the silent period cannot be ruled out. Others factors may be involved such as the membrane

properties of the thalamic neurones (Spreafico *et al.* 1988, McCormick 1989).

The present study show that VB conditioning stimulation abolishes the excitatory response of intralaminar thalamic neurones to nociceptive and non-nociceptive peripheral test stimulations. The duration of this effect was shorter than the duration of the silent period evoked by VB stimulation. Since it occurs within the evoked silent period, we suggest that it results from hyperpolarization induced by the VB stimulation through the nRT rather than an occlusion phenomenon. Roy *et al.* (1984) have shown that cortical stimulation elicits an excitatory response in VL followed by a hyperpolarization which is GABA-dependent and controlled by nRT. Dalsass and Krauthamer (1981) examined by C-T procedure the interaction of caudate stimulation with peripheral stimulation and found an inhibitory effect which paralleled the duration of the IPSP generated by prior stimulation. Since similar inhibition of the excitatory response to test peripheral stimulation is observed in the VB after intralaminar conditioning stimulation and, *vice versa*, the spike discharge elicited in the VB neurones by intralaminar stimulation is inhibited by prior peripheral stimulation, we propose that these inhibitory phases have a common basis.

Medial and lateral thalamic nuclei are known to be involved in the perception of pain. The nociceptive inputs are mainly provided by the spinothalamic fibres which end both in ventralis posterior nucleus (VPL) and intralaminar nuclei (medial thalamus), or from spinoreticulothalamic tracts (SRT). Benabid *et al.* (1983) have shown that VPL exerts an inhibitory influence on the medial thalamus which could originate from a multisynaptic non-opioid pathway. Stimulation of thalamic somatosensory relay nuclei (VPL, VPM) in man relieves neuropathic pain (Mazars *et al.* 1976). Gerhart *et al.* (1981) suggest that the inhibitory effects exerted on nociceptive responses in the VB involve antidromic activation of nociceptive spinothalamic collaterals. Since STT neurones send collaterals to the periaqueductal gray matter (PAG) and the raphe nuclei, VPL stimulation may antidromically activate the PAG or the raphe magnus through the axonal branches of STT. A transsynaptic activation would also be possible from the VPL to the somatosensory cortex and from the somatosensory cortex to the PAG. The PAG or the raphe magnus would in turn activate a descending pain inhibitory pathway (Sakata *et al.* 1989). The involvement of these pathways in the thalamic inhibitory process is not supported by our results, since we observed that the inhibition is effective in both nociceptive and non-nociceptive responses and that it persists after collicular section or after decortication.

In conclusion, the excitatory and the inhibitory responses recorded in VB and intralaminar thalamic nuclei involve different pathways. The excitatory response originates from peripheral inputs such as STT or SRT and from cortical inputs. The nRT appears to play a central role in inhibitory control mechanisms, and may thus be involved in the control of thalamo-cortical input/output mechanisms including those concerned with pain.

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