Exp Brain Res (1994) 100:276–286

ORIGINAL PAPER

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Corticothalamic influences on transmission of tactile information in the ventroposterolateral thalamus of the cat: effect of reversible inactivation of somatosensory cortical areas I and II

Received: 21 December 1992 / Accepted: 14 February 1994

Abstract The influence of the corticothalamic projections from somatosensory areas I and II (SI and SII) on the transmission of tactile information through the ventroposterolateral (VPL) thalamus was investigated by examining the effects of cooling-induced, reversible inactivation of SI and/or SII on the responsiveness of 32 VPL neurons to controlled tactile stimulation of the distal forelimb in anaesthetized cats. Both the response levels and spontaneous activity were unaffected in 21 (66%) of the VPL neurons as a result of inactivation of SI or SII singly, or both SI and SII simultaneously. In the remaining 11 neurons, 10 displayed a reduction in response level, an effect observed over the whole of the stimulus-response relations for the neurons studied at different stimulus amplitudes, and one neuron displayed an increase in response level in association with cortical inactivation. When responses in VPL neurons were affected by inactivation of one cortical somatosensory area, they were not necessarily affected by inactivation of the other. Of 14 neurons studied for the effects of the separate inactivation of SI alone and of SII alone, 7 were affected, one from both areas, but the remaining 6 were affected by inactivation of only one of these areas. Phaselocking, and therefore the precision of impulse patterning in the responses of VPL neurons to skin vibration, was unchanged by the cortical inactivation irrespective of whether the response level was affected. The results suggest that SI and SII may exert a facilitatory influence on at least a third of VPL neurons and in this way may modulate the gain of transmission of tactile signalling through the thalamus.

Key words Corticothalamic modulation · Ventroposterolateral thalamus · Primary and secondary somatosensory cortex (SI and SII) · Somatosensory thalamus · Cat

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Introduction

The somatosensory, visual and auditory areas of cortex are each reciprocally connected with the thalamus in a topographically organized manner (for review see Jones 1985). Although it is clear that a major function of the thalamocortical pathway is to distribute sensory information to the cortex, the function of the descending corticothalamic projection is not well understood. In the visual system, it has been suggested that the corticogeniculate pathway modulates the gain of transmission of visual information through the lateral geniculate nucleus (LGN) and may therefore play a role in selective attention to visual stimuli (Singer 1977; Koch 1987). The corticothalamic pathway may have a similar function in the somatosensory system.

Corticothalamic fibres exert excitatory synaptic effects (Andersen et al. 1967; Ahlsen et al. 1982) via terminals on the distal dendrites of thalamocortical relay neurons (Jones and Powell 1969; Ralston 1983; Jones 1985). However, as they also appear to terminate on interneurons of the main thalamic sensory nuclei and on thalamic reticular neurons (Jones and Powell 1969; Jones 1975; Ralston 1983), both of which contain the inhibitory neurotransmitter gamma-aminobutyric acid (Montero and Singer 1985), corticothalamic neurons could potentially exert indirect inhibitory as well as direct excitatory effects on thalamic neurons. Indeed, there have been conflicting findings of the effect exerted by the corticothalamic projection on thalamic sensory

transmission, with some authors arguing for a predominantly excitatory effect (for instance Schmielau and Singer 1977; Yuan et al. 1985, 1986; Villa et al. 1991; Rapisarda et al. 1992), others for a predominantly inhibitory effect (for instance Burchfiel and Duffy 1974; Marrocco et al. 1982; Shin and Chapin 1990), and yet others for mixed excitatory and inhibitory effects (Watanabe et al. 1966, Tsumoto et al. 1975; Geisert et al. 1981).

Although the reasons for the disparate findings are not clear, these studies deal with different sensory systems and embrace a variety of methodological procedures which might contribute to the discrepancies. In the case of somatosensory corticothalamic systems, the possibility of differential effects from the various cortical somatosensory regions, in particular the primary (SI) and secondary (SII) cortical areas, has not been satisfactorily addressed. Furthermore, most studies have investigated the influence of the corticothalamic pathway on responses of thalamic neurons to brief electrical or mechanical stimulation and have not addressed possible cortical modulatory influences on thalamic responses that have been evoked by *sustained* mechanical stimulation of the skin. These longer-lasting tactile stimuli may allow greater opportunity for corticofugal modulatory influences with a longer time course to become apparent. Cortical influences on the responses of individual VPL neurons to controlled, sustained forms of tactile stimuli have therefore been investigated in the present study in association with rapid, reversible inactivation of SI and/or SII by means of localized cortical cooling. Preliminary results have been reported briefly in abstract form (Ghosh et al. 1990a, b).

Materials and methods

Animal preparation

Thirteen adult cats of either sex (weight: 2–3.3 kg) were anaesthetized initially with alfaxalone and alfadolone (Saffan; 18–24 mg/kg, IM) and then anaesthesia was maintained by means of a 4:1 inhalation mixture of N_2O and O_2, supplemented with halothane ($\leq 2\%$). The femoral artery and vein were canulated to monitor blood pressure and to administer fluids. The trachea was canulated, an indifferent electrode (Ag/AgCl) was placed in the neck, and the rectal temperature was maintained, by a thermostatically controlled electric blanket, at $37.5 \pm 0.5°$ C. The animals breathed spontaneously and no muscle relaxants were administered.

The animal was positioned in a stereotaxic frame and a craniotomy performed on the right-hand side to expose SI, SII and the cortex dorsal to the thalamus. The dura was opened and the exposed cortex covered with warm (38° C) paraffin oil. The left forelimb was shaved and fixed in a paraffin wax mould, pads uppermost, to permit accurate positioning of a feedback-controlled mechanical stimulator (Douglas et al. 1978; Bennett et al. 1980).

Inactivation of SI and SII by cooling

Details of our cortical mapping and inactivation procedures have been described previously (Turman et al. 1992a). In brief, they were as follows. The distal forelimb foci of SI and SII were mapped by recording cortical surface potentials evoked in response to a 5-ms mechanical stimulus (400-μm step) delivered to the central pad of the contralateral forepaw. Two cylindrical metal cooling blocks (7 mm diameter) were placed over the defined distal forelimb focus of SI and SII with the cortical face of each block in light contact with the pia. The temperature at the face of the block overlying SI or SII was held at the control temperature of $37.5 \pm 0.5°$ C except during cortical cooling, when it could be changed within 1–2 min to 8–13° C; rewarming had a similar rapid time course. Cooling at each block face to 8–13° C permitted selective inactivation of the underlying distal forelimb area as reflected in the abolition or marked attenuation of evoked potential and single neuron activity recorded from somatosensory cortex underneath the block (see Murray et al. 1992; Turman et al. 1992a). Insertion of a needle thermistor at the end of an experiment verified that the temperature in the thalamus was unaffected by the cortical cooling.

There are three lines of evidence that cooling at the cortical surface to $\leq 13°$ C effectively inactivated the cortex beneath the 40-mm^2 cooling block. First, the initial positive-going component of the evoked potential that was abolished by the cooling can be attributed to the short-latency thalamo-cortical synaptic actions that are concentrated at least as deeply as lamina IV. We have also confirmed that single neurons recorded at different depths *adjacent* to the margin of the cooling block (within 0.5 mm) had their responses abolished or markedly attenuated even though they were located outside the 40-mm^2 cortical area beneath the block face, and were therefore located in tissue that is less effectively cooled than that beneath the block face (Turman et al. 1992a). Finally, temperature changes within the cortex were recorded by insertion of a needle thermistor (Yellow Springs Instruments, model 524) or bead thermistor (RS Components 151-136) to different depths over a distance extending 8–10 mm beyond the margins of the cooling block. From the data, we constructed a set of averaged isotherms around the block when the temperature on the cortical surface was 13° C. These measurements established that the temperature *throughout* the cortex beneath the block was below 20° C, the temperature that has been shown to block synaptic transmission within the cerebral cortex and in other areas of the central nervous system (for review see Brooks 1983).

Recording and stimulation procedures

Once the blocks were positioned over the distal forelimb focus of SI and SII, varnished or glass-insulated tungsten microelectrodes ($R_e = 0.5$–1.5 MΩ at 1 kHz) were inserted stereotaxically to record from VPL neurons responsive to light tactile stimulation of the hairy or glabrous skin of the distal forelimb. Procedures for extracellular single-neuron recording, receptive-field identification, delivery of stimuli from the servo-controlled mechanical stimulator, classification of neurons, and analysis of single neuronal activity were described in our recent papers (Ghosh et al. 1992; Turman et al. 1992a). Precise and reproducible mechanical stimuli were delivered from a servo-controlled stimulator to the point of maximum sensitivity within the neuron's receptive field. VPL neurons were initially classified as rapidly or slowly adapting, then rapidly adapting neurons were tested with 1-s trains of sinusoidal vibration superimposed on a background rectangular displacement. Stimulus repetition rate was not more than 1 per 10 s to allow recovery of skin position. The effect of localized cortical inactivation on individual thalamic neurons was assessed by a statistical comparison of response levels (in impulses per second, for background and response level) obtained to a minimum of 15 repetitions of the 1-s duration mechanical stimulus during SI or SII inactivation, with corresponding activity levels obtained during pre-cooling and post-cooling control periods. These control periods contained usually a minimum of 15 stimulus repetitions. Statistical tests were analysis of variance (ANOVA) and standard post-hoc contrast tests (statistical significance: $P < 0.05$). Analysis periods were (a) prior to inactivation (pre-cooling): the period to the onset of cortical cooling; (b) during inactivation: the period

for which the temperature at the face of the cooling block was at the predetermined inactivation temperature ($\leq 13°$ C, see above); (c) after rewarming (post-cooling): the period from 1–2 min after cooling block temperature had returned to 38° C until cooling was repeated or recording stopped. We waited 1–2 min after the cooling block temperature had returned to 38° C to allow full recovery of somatosensory cortex from the inactivation. Response rates (impulses per second) in association with each stimulus were calculated by counting the number of action potentials during each 1-s period of mechanical stimulation. These rates for each stimulus were then plotted against time and temperature, as shown in Figs. 1, 6 and 7, and the mean and standard deviation values could then be calculated for each period as defined above and plotted in stimulus-response relations such as those of Figs. 3, 4 and 5. Neurons were only classified as being affected when activity levels during inactivation were statistically significantly lower (or greater) than *both* pre-cooling and post-cooling activity levels. Affected neurons exhibited the same relative change in activity levels during each period of inactivation. An index of cooling effect was calculated for affected neurons as the change in response levels during cooling as a percentage of pre-cooling response levels. Effects of cortical inactivation on the tightness of phaselocking in the responses of thalamic neurons to skin vibration were also carried out with procedures described previously (Turman et al. 1992a; Ghosh et al. 1992 and see Figs. 8, 9). Not all neurons in the sample could be tested for the effects of inactivation of both SI and SII because of limitations of recording stability.

Location of recorded thalamic neurons

As we did not make lesions at the site of thalamic recordings, it is difficult to be certain about neuron locations in histological sections in view of the recording depths (usually 15–17 mm) below the cortical surface and some uncertainty over possible shrinkage of the tissue. We believe that our most reliable indices of neuron location were physiological ones (used previously, for example, by Dykes et al. 1981, and in our earlier study, Ghosh et al. 1992) based, in part, on the depth of the neuron *relative* to the depth at which low-threshold responses to cutaneous stimulation first appeared, and then later disappeared. These points have been found to correspond well to the dorsal and ventral borders respectively of the ventroposterior (VP) nucleus (Dykes et al. 1981; Ghosh et al. 1992). These dorsoventral positions were noted in the course of electrode penetrations that were concentrated around stereotaxic A/P plane +8, and ~6 mm lateral to the midline. The depths at which neurons were sampled (see Results) and the brisk, low-threshold nature of responses encountered are consistent with the VPL location. In addition, further evidence that the thalamic neurons were within VPL comes from the observation that, of 15 neurons tested, half (7/15) were antidromically activated from the distal forelimb focus of SI or SII, although electrical stimulation of these sites was limited to the use of the electrode in the face of the cooling blocks. The criteria for the antidromic responses were a fixed, short latency (< 2 ms) of response, a capacity to follow high stimulus repetition rates (200 per second), or collision with the orthodromically generated spike.

Results

Functional classes of VPL neurons studied during inactivation of SI and/or SII

The 32 VPL neurons examined in this study had receptive fields on the hairy or glabrous skin of the distal forelimb and fell into different functional classes (Table 1). Those with input from the hairy skin (20 out of the 32) were all rapidly adapting and were presumed to receive their input from hair follicle afferent (HFA) fibres (Table 1). Those with glabrous skin receptive fields (12 out of the 32) had functional properties, in particular, responses to step indentations and vibrotactile stimuli, which permitted classification (see Ghosh et al. 1992) into those whose input came predominantly or exclusively from Pacinian corpuscle (PC) afferent sources, from rapidly adapting (RA) afferent fibers (and presumed Krause corpuscles), or from slowly adapting (SA) afferent fibers (and presumed Merkel receptors). The sample of neurons was biased towards dynamically sensitive tactile neurons as vibration-sensitive neurons were sought, with the aim of investigating corticofugal influences on impulse patterning as well as response levels in the VPL neurons.

Table 1 Effect of inactivation of SI and/or SII on ventroposterolateral thalamic (VPL) neurones (HFA hair follicle afferent, PC Pacinian corpuscle, RA rapidly adapting fibres, SA slowly adapting afferent fibres)

VPL neurones tested		Peripheral source of input			
		HFA	PC	RA	SA
Total	32	20	9	2	1
Unaffected	21	13	6	1	1
Affected	11	7	3	1	0

Inactivation of SI and/or SII had no effect on the tactile responsiveness or spontaneous activity of 21 of the 32 (66%) VPL neurons examined (Table 1). Ten of the remaining 11 neurons underwent a reduction in spontaneous activity or responsiveness to skin stimulation. Only one neuron displayed evidence of enhanced responsiveness during inactivation of the somatosensory cortical areas. Both affected and unaffected thalamic neurons fell into different functional classes (Table 1). Among the 21 neurons unaffected by somatosensory cortical inactivation were neurons that received HFA input, PC input, RA input, and the one neuron with SA responses to skin stimulation. As different functional classes were also represented among the 11 affected neurons (Table 1), it is clear that corticofugal influences are not confined to particular classes of tactile neurons in the VPL thalamus.

From depth measurements for the sampled thalamic neurons, we found first, that there was no difference in the mean depth below the cortical surface of affected and unaffected thalamic neurons. The affected sample had a mean depth of 16.75 ± 0.57 mm and the unaffected sample a mean of 16.1 ± 1.0 mm ($P > 0.05$). Second, there was no aggregation of affected or unaffected neurons within a particular region of the VPL nucleus. Furthermore, within individual experiments, affected neurons could be found above *or* below unaffected neurons.

Effect of cortical inactivation on VPL neurons

The effect of SI or SII inactivation on the responsiveness to controlled tactile stimulation is shown in Fig. 1 for

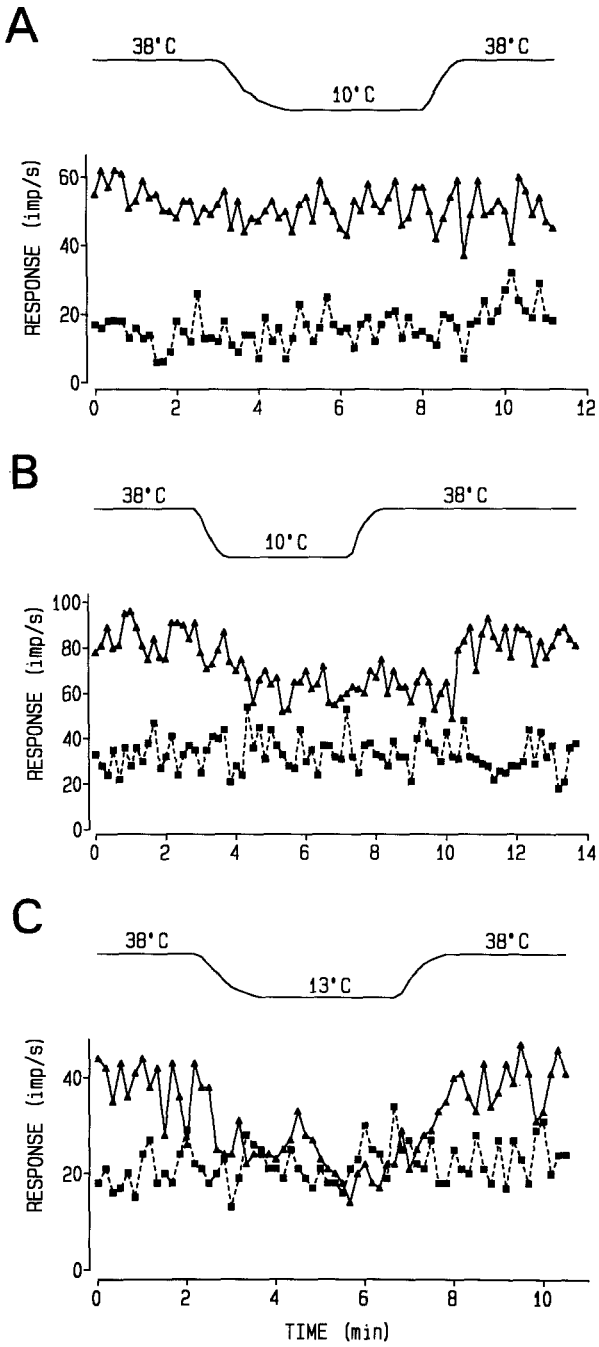


Fig. 1 Effects of inactivation of SI (**A, C**) or SII (**B**) on the responsiveness of three ventroposterolateral thalamic (VPL) neurons. *Uppermost* traces in **A–C** show the temperature at the face of the cooling block over SI (**A** and **C**) or SII (**B**); inactivation occurred at 10° C (**A, B**) and 13° C (**C**). The graphs show, in the *upper* plot (*continuous line, triangles*), the response rate(impulses per second) to successive repetitions of a fixed tactile stimulus and, in the *lower* plot (*broken line, squares*), the background activity (impulses per second) during the 1-s period prior to each skin stimulus. Tactile stimuli: sinusoidal vibration; 300 Hz, 5 μm in **A**, and 30 Hz, 50 μm in **B** and **C**; repetition rate: 1/10 s. Statistical analysis for **A**, ANOVA on evoked activity was not significant ($P=0.4$); for spontaneous, cool was significantly lower than post-cooling ($P<0.05$) but this was not attributed to cortical inactivation because pre-cooling was not significantly different from cool ($P>0.05$). For **B** and **C**, response levels during the cool period were significantly lower than both pre-cooling and post-cooling control periods ($P<0.001$); ANOVA on spontaneous activity was not significant

three thalamic neurons whose input came from PC sources in A, and from HFA input in both B and C. In each panel (A–C), the response level (triangles, upper trace) and associated background activity (squares, lower trace) are plotted for each repetition of the 1-s vibrotactile stimulus (see Fig. 2). The neuron in A responded at rates of 50–60 impulses per second to 300-Hz (5-μm) vibration applied to digit 5. When the temperature at the face of the SI block was lowered from 38° C to 10° C to inactivate the distal forelimb area of SI, the response level was not significantly different from the pre-cooling and post-cooling levels ($P>0.05$). In contrast, the neurons in B and C, with receptive fields on the hairy skin of digit 4 and digit 3 respectively, underwent a reduction in response level in association with the cortical inactivation which involved SII in B and SI in C. The inactivation of SI in C led to a reduction (~43%) in the response (to a 30-Hz, 50-μm vibratory stimulus) from 39/s to 22/s which was little different from the background activity of the neuron. Responsiveness returned to control levels in B and C within 1–2 min of rewarming to 38° C. In neither of these affected neurons was the background activity affected by the cortical inactivation.

Impulse traces obtained in response to 300-Hz (20-μm) vibration for one of the affected VPL neurons (Fig. 2) show that the reduction in response level during SI inactivation (Fig. 2B; 10° C) occurred throughout the 1-s period of the vibration train. The expanded traces of individual spikes on the right side of the figure show that the waveform during the period of SI inactivation (Fig. 2E) was the same as that of pre-cooling and post-cooling controls (SI at 38° C in D and F) and demonstrates that there was no direct spread of cooling from the overlying cortex to the recording site in the thalamus (see Discussion).

Effect of cortical inactivation on stimulus-response relations of VPL neurons

In both Figs. 1 and 2 the effect of SI or SII inactivation is shown for only one stimulus intensity for each of these thalamic neurons. However, when recording stability permitted, the effect of localized cortical inactivation was tested at different stimulus intensities that elicited responses ranging from near threshold up to the plateau response level displayed by the neuron. This more complete form of testing was necessary as the corticofugal modulatory influences on thalamic transmission may be more pronounced at different stimulus intensities within the response range of the VPL neuron. Tests of this hypothesis were carried out by calculating mean response levels (in impulses per second) at a series of stimulus intensities and constructing stimulus-response relations of the type shown in Figs. 3–5.

The stimulus-response relations in Fig. 3 were obtained for a VPL neuron that responded to different intensities of a 300-Hz vibratory stimulus applied to digit 3 of the forelimb. In both graphs of Fig. 3, the

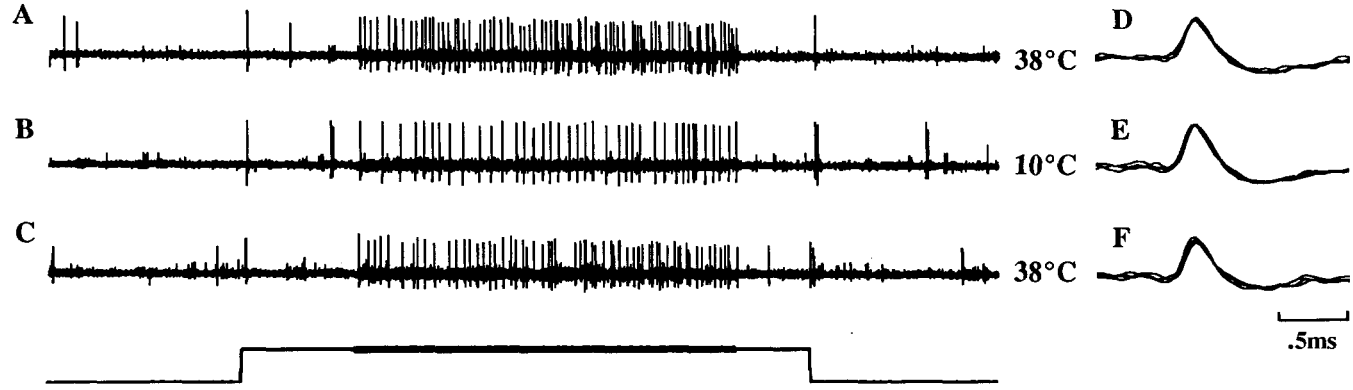


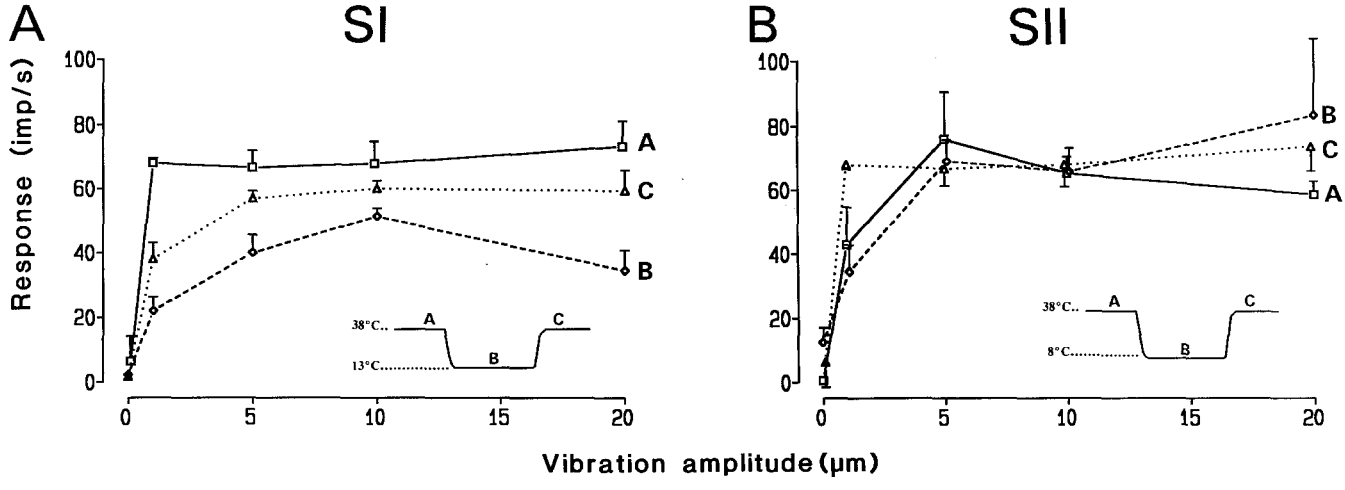
Fig. 2A–F Reduction in responsiveness of a thalamic neuron during SI inactivation (*trace* **B**; SI surface temperature, 10° C) in comparison with pre-cooling (**A**) and post-cooling (**C**) responses. Traces **A–C** show the impulse activity (negativity upwards) in response to a 300-Hz (20-μm) vibrotactile stimulus lasting 1 s, superimposed on a 1.5-s step indentation (400-μm amplitude) delivered to the glabrous skin of digit 3. Expanded traces of individual spike waveforms (**D-F**) show that SI inactivation (**E**) did not alter spike duration. The lowest trace shows the stimulus waveform, with the vibration amplitude exaggerated to indicate clearly the 1-s segment over which vibration was applied. The *time marker* on the lower right applies to **D–F**

Fig. 3A, B Stimulus-response relations constructed from the responses (impulses per second) of a thalamic neuron to 300-Hz vibration delivered at a series of amplitudes, in 1-s trains, to the glabrous skin of digit 3. Relations *A*, *B* and *C* in each of the graphs were obtained *before*, *during* and *after* selective inactivation of SI by cooling to 13° C (*left graph*) or of SII by cooling to 8° C (*right graph*). The *insets* in each graph represent the temperature profiles over each cortical area and indicate the temperature at which relations *A*, *B* and *C* were obtained. *Error bars* in this and subsequent figures represent one standard deviation from the mean. Statistical analysis: in **A**, response levels during SI inactivation (curve *B*) at 1, 5, 10 and 20-μm vibration amplitudes were significantly lower ($P < 0.05$) than corresponding response levels during both pre-cooling (curve *A*) and post-cooling (curve *C*). In **B**, significant differences were identified only between pre-cooling and cool at 20 μm, and cool and post-cooling at 1 μm; all other comparisons were not significant. This neuron was classified as affected by SI inactivation only (see criteria in Materials and methods)

stimulus-response relations A and C represent the pre-cooling and post-cooling controls when the temperature at the surface of SI (Fig. 3A) and SII (Fig. 3B) was held at 38° C. In association with SI inactivation (relation B in Fig. 3A), there was a reduction in response level at all vibration intensities across the stimulus-response range of the thalamic neuron, whereas relation B, obtained in association with SII inactivation (Fig. 3B) shows no apparent difference from the control relations A and C, either in the general form of the relation or in more specific measures that could be derived from the relations. These measures include the threshold amplitude for a response, the initial slope of the relation, the dynamic range for the relation (which is defined as the range of vibration amplitudes over which response increments were seen), or the plateau level of response that was attained.

Differential effects of SI and SII inactivation on the responsiveness of VPL neurons

In our total sample of 32 thalamic neurons, 14 were tested during SI inactivation alone *and*, in a separate cooling trial, during SII inactivation alone. Of the 14, seven were unaffected by both inactivation procedures, five were affected just from SI inactivation (e.g. Fig. 3), one from SII inactivation alone (Fig. 4), and the remaining neuron showed effects from both areas (Fig. 6).



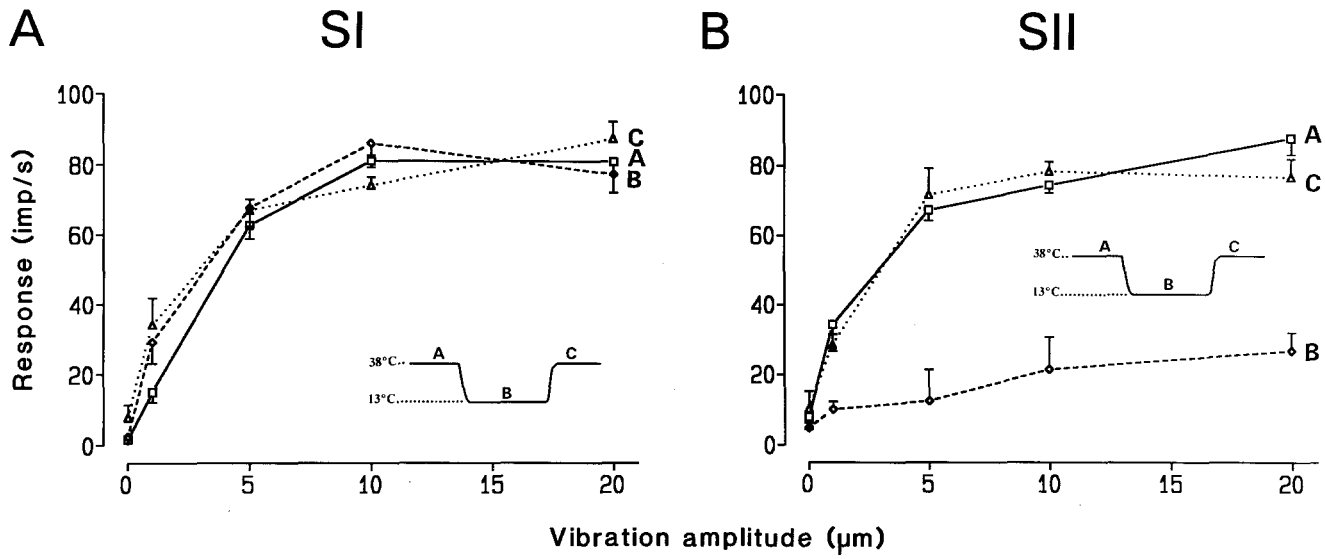
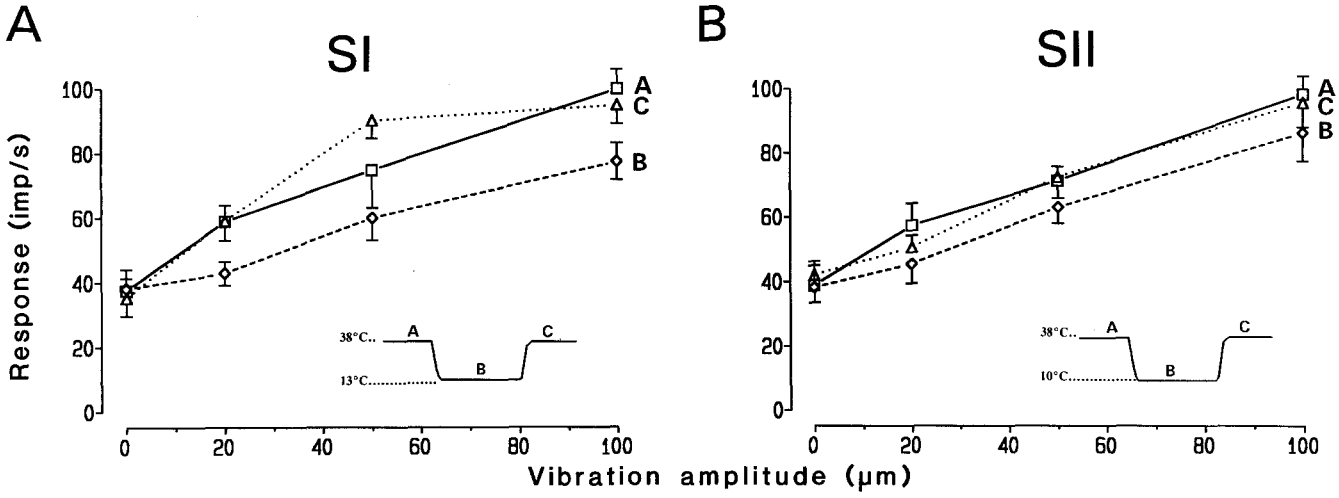


Fig. 4A, B Stimulus-response relations constructed from the responses (impulses per second) of a VPL neuron to 300-Hz vibration delivered to digit 5. Relations *A*, *B* and *C* in each graph were obtained *before*, *during* and *after* selective inactivation of SI by cooling to 13° C (*left graph*) or of SII by cooling to 13° C (*right graph*). Statistical analysis: in **A**, no values were significantly different except cool and post-cooling at 10 μm and 20 μm, and pre-cooling and cool at 1 μm; in **B**, response levels during SII inactivation (curve *B*) at vibration amplitudes of 1, 5, 10 and 20 μm were significantly lower ($P<0.001$) than the corresponding response levels during both pre-cooling (curve *A*) and post-cooling (curve *C*). This neuron was classified as affected by SII inactivation only

Fig. 5A, B Stimulus-response relations constructed from the responses of a thalamic neuron to 30-Hz vibration delivered to the hairy skin between digits 4 and 5. Relations *A*, *B* and *C* in each graph were obtained *before*, *during* and *after* selective inactivation of SI by cooling to 13° C (*left graph*) or of SII by cooling to 10° C (*right graph*). Statistical analysis: in **A**, response levels during SI inactivation (curve *B*) at vibration amplitudes of 20, 50 and 100 μm were significantly lower ($P<0.01$) than the corresponding response levels during both pre-cooling (curve *A*) and post-cooling (curve *C*). In **B**, although curve *B* is lower than both curves *A* and *C* at vibration amplitudes of 20, 50 and 100 μm, significant differences were only identified between pre-cooling and cool at 20 and 100 μm; this neuron was classified as affected only by SI inactivation

In the case of the neuron affected selectively by SII inactivation (Fig. 4), the reduction in response was the most profound observed, and furthermore, was consistent at all vibration amplitudes across the stimulus-response relation (Fig. 4B; relation B compared with A and C showed a reduction that ranged from 70 to 82%). The absence of effect on this neuron of SI inactivation was also a consistent finding across the whole stimulus-response relation (Fig. 4A). The neuron of Fig. 5 was classified as affected by SI inactivation only (see legend). The small but consistent reduction in response level of 23–27% over the whole of its stimulus-response relation in association with SI inactivation (Fig. 5A) was the smallest significant reduction in the sample of affected neurons. For all affected neurons exhibiting a reduction in response levels, the mean ($\pm$SD) reduction in impulse count brought about by the inactivation was 46 ± 20% from a mean ($\pm$SD) control level of 64.1 ± 19.2 impulses/per second. However, it should be emphasized that these values of percentage reduction should be interpreted with caution, as different neurons were studied with a range of different cutaneous stimuli depending upon their response properties, and more than one in-



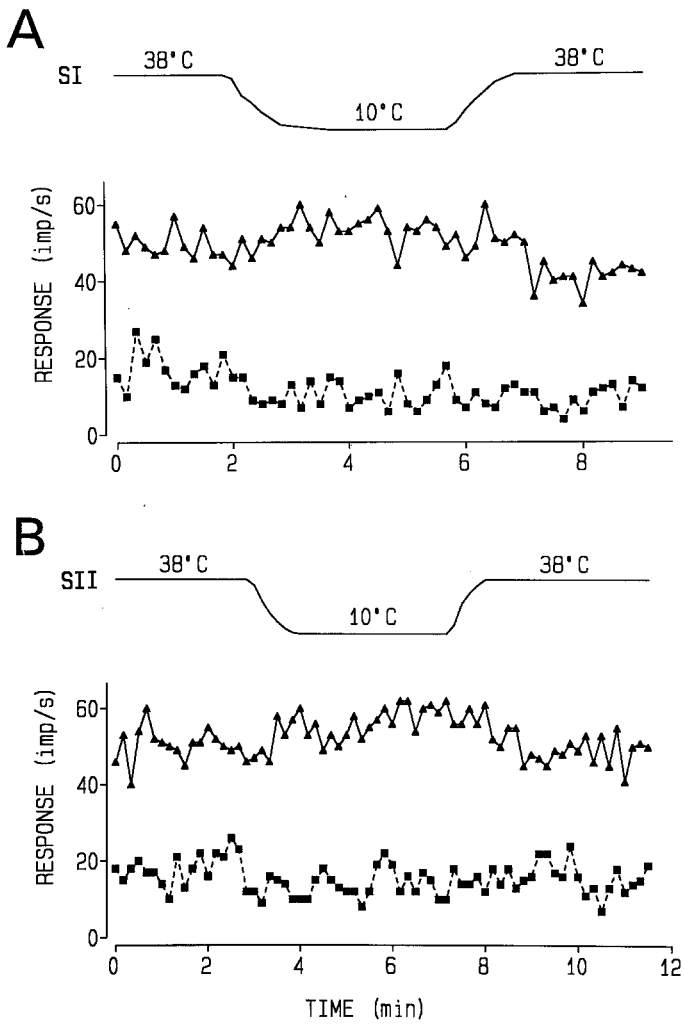


Fig. 6 Enhanced responsiveness of a thalamic neuron during SI inactivation (by cooling at 10° C, **A**) and during SII inactivation (by cooling to 10° C, **B**). Responses in impulses per second (*continuous lines, triangles*) were obtained to a fixed stimulus, in each case a 1-s train of vibration at 30 Hz (20 μm) applied every 10 s to the glabrous skin of digit 3. The lower plots in **A** and **B** (*broken lines, squares*) represent background activity during the 1-s period prior to each delivery of the skin stimulus. Statistical analysis: in **A** and **B**, response levels during cool period were significantly greater than both pre-cooling and post-cooling control periods ($P < 0.01$); ANOVA on spontaneous activity was not significant

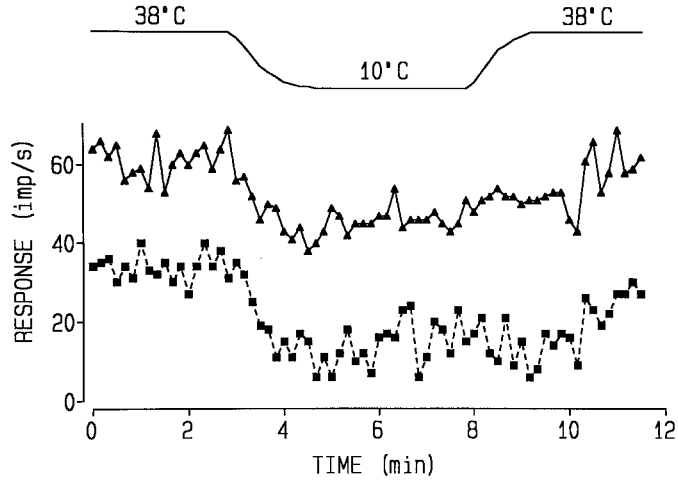


Fig. 7 Reduction in response (*continuous line, triangles*) and background activity (*broken linke, squares*) of a VPL neuron during SI inactivation, achieved by cooling at the surface to 10° C. The response was elicited by a fixed vibrotactile stimulus of 30 Hz (35 μm) lasting 1 s and applied every 10 s to the hairy skin adjacent to digit 3. Both response and background activity levels during the cool period were significantly lower than pre-cooling and post-cooling control periods ($P < 0.001$)

tensity of mechanical stimulus was employed for neurons in which stimulus-response relations were constructed.

The thalamic neuron that was affected by inactivation of SI *and* SII was the one instance in our sample where there appeared to be a small but statistically significant ($P < 0.01$) enhancement of responsiveness during the cortical inactivation (Fig. 6). Although full stimulus-response data were not obtained for this neuron, the plots of response levels evoked by a fixed 30-Hz (20-μm) vibratory stimulus delivered to the forelimb glabrous skin show a small increase ($\sim 10\%$ on control response levels of about 50 impulses per second) during *both* the SI inactivation (Fig. 6A) and during the SII inactivation (Fig. 6B).

Background activity plotted in the lower traces in Fig. 6A and B was unchanged during these inactivation periods. This was the case in 9 of the 11 thalamic neurons whose responsiveness was altered by cortical inactivation. In the remaining two neurons that underwent a reduction in responsiveness, the background activity was also reduced (Fig. 7).

Effect of SI or SII inactivation on phaselocking in the responses of VPL neurons to vibrotactile stimuli

Most of the neurons studied were dynamically sensitive and were examined for their responses to skin vibration. To provide an index of corticothalamic influences on more subtle features of thalamic responsiveness, the phaselocking and temporal patterning of impulse activity evoked by vibrotactile stimuli were examined quantitatively by constructing cycle histograms (Ghosh et al. 1992; Turman et al. 1992a) which display the probability of impulse occurrences during the cycle period of the vibratory stimulus (Fig. 8). The pronounced preferential grouping of impulses within restricted segments of the histograms in Fig. 8 indicates tight phaselocking of the responses to the 300-Hz vibratory stimulus which was at an amplitude of 50 μm in Fig. 8A and 100 μm in Fig. 8B.

The extent of the phaselocking was quantified by determining the maximum percentage of total impulse occurrences that falls within any continuous half-cycle of the vibration cycle period. This measure, the *percentage entrainment*, is indicated on the top right in each his-

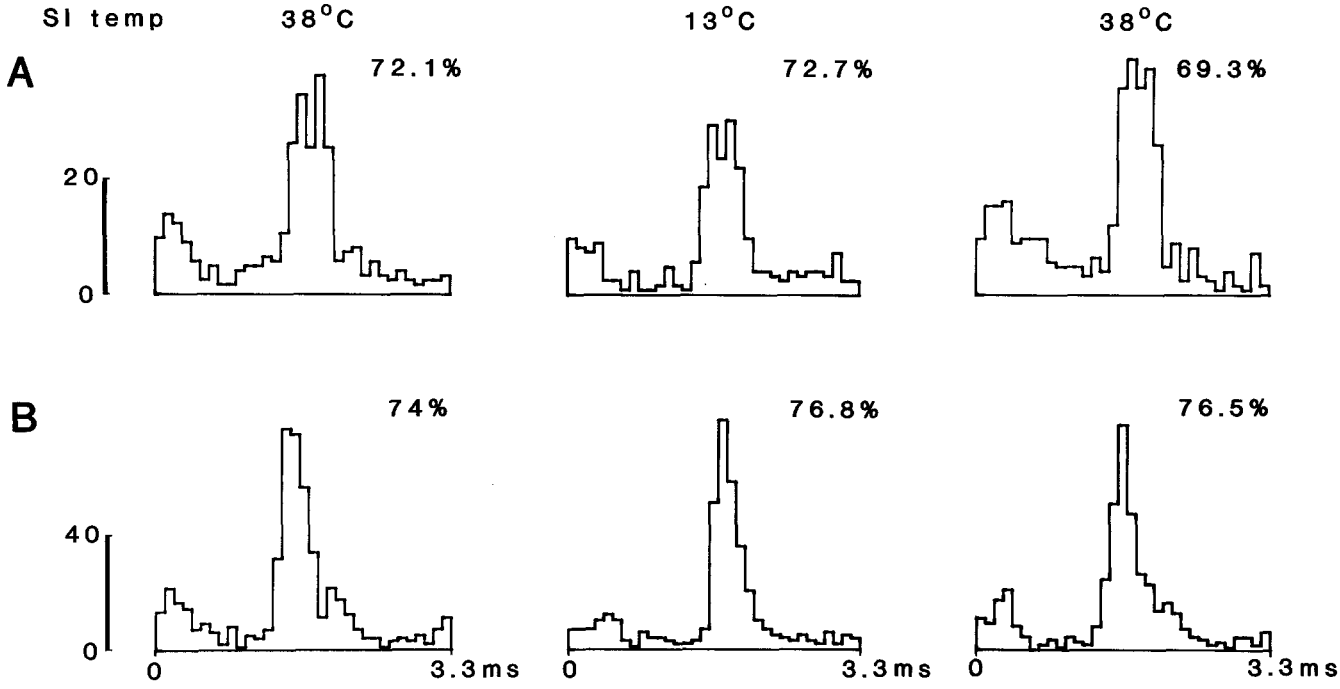
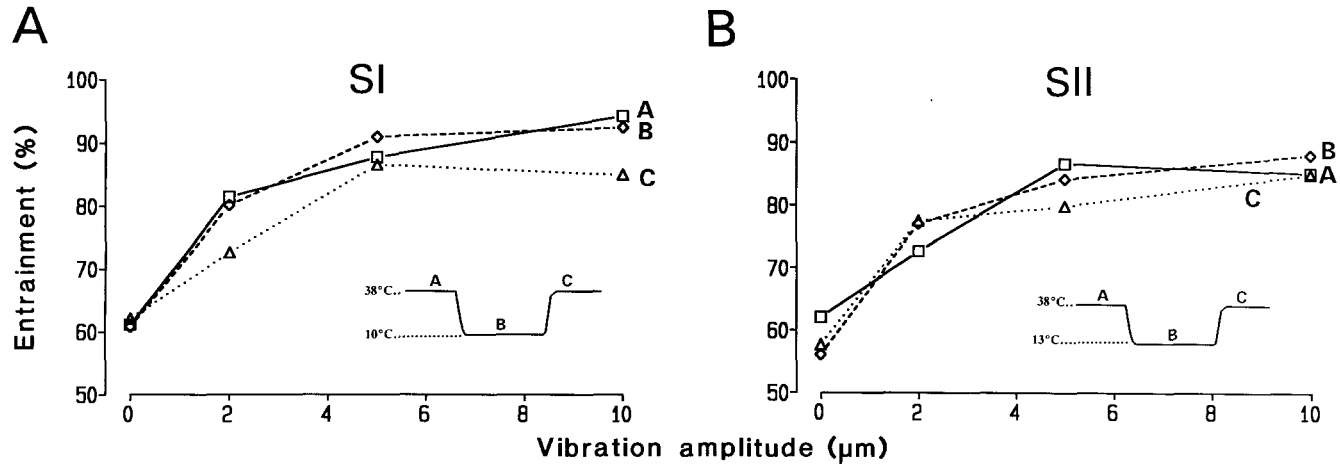


Fig. 8 Absence of effect of SI inactivation on the phaselocking in responses of a thalamic neuron to 300-Hz (50-μm in **A**; 100-μm in **B**) vibrotactile stimulus lasting 1 s and applied to the hairy skin between digits 4 and 5. The cycle histograms in **A** and **B** have an analysis time that corresponds to the vibration cycle period of 3.3 ms for the 300-Hz stimulus. They were constructed from responses to five repetitions of a 1-s train of 300-Hz vibration and show the time of impulse occurrence during successive cycles of the vibration stimulus. Left hand *scale bars* provide a calibration for the number of impulses accumulated in each address of the cycle histograms in **A** and **B**. The *left* and *right histograms* were obtained as pre-cooling and post-cooling controls respectively when SI was at 38° C, whereas the *centre histograms* were obtained when SI was inactivated by cooling to 13° C. Percentages on each histogram provide a measure of the tightness of phaselocking

Fig. 9 Effect of SI (**A**) and SII (**B**) inactivation on the tightness of phaselocking in VPL responses to vibrotactile stimulation at 300 Hz. The graphs plot the percentage entrainment as a function of vibration amplitude for a thalamic neuron whose responsiveness was lowered by SI, but not by SII inactivation (see Fig. 3). Relations *A* and *C* in each graph were obtained as pre-cooling and post-cooling controls, whereas relation *B* in each graph was obtained during the period of SI inactivation by cooling to 10° C (see *inset* in **A**) or SII inactivation by cooling to 13° C (see *inset* in **B**)

togram in Fig. 8. When these measures of phaselocking are compared in Fig. 8 for the cycle histograms constructed prior to (left histograms), during (centre histograms), or after (right histograms) SI inactivation, there was no consistent change. Values of the percentage entrainment were very similar (i.e. ~70–75%) in each of these histograms and were clearly unaffected by SI inactivation. This was also the case for other thalamic neurons tested in this way, as shown in Fig. 9 for the neuron whose stimulus-response relations were plotted in Fig. 3, and whose responsiveness was affected preferentially by SI rather than SII inactivation. However, the plots of percentage entrainment in Fig. 9 as a function of vibration amplitude show no change in phaselocking *either* when SI was inactivated (Fig. 9A) *or* when SII was inactivated (Fig. 9B). Relation B in each of these graphs was obtained during the cortical inactivation, whereas A and C were the pre-cooling and post-cooling controls.



Discussion

The results indicate that SI and SII exert a facilitatory influence on the tactile responses of at least a third of VPL neurons and may therefore have the capacity to modulate the gain of transmission of tactile signals through the thalamus. The demonstration that these corticothalamic influences can modulate responsiveness to sustained tactile stimuli extends previous reports that the corticofugal pathway can exert a facilitatory influence on background activity and on thalamic responses to peripheral electrical stimuli (Andersen et al. 1967; Yuan et al. 1985, 1986; Rapisarda et al. 1992).

The study also establishes that these influences on thalamic tactile transmission may arise from *both* the SI and the SII areas of cortex. However, for *individual* thalamic neurons, there were often differential effects exerted from these two spatially separate forelimb areas of cortex, a similar result to that of Watanabe et al. (1966), who found, in the auditory system, that the primary and secondary auditory cortical fields had differential effects on the auditory responsiveness of some medial geniculate neurons. As cooling blocks were positioned in the present study over the SI and SII forelimb areas, it was not possible routinely to identify, by antidromic activation, the cortical projection target of thalamic neurons studied. More detailed study would therefore be needed to determine whether, for example, those neurons affected just by SI inactivation, all had the same (perhaps SI) cortical projection target.

Site of corticofugal influences

The influences observed on the thalamic neurons in association with the SI or SII inactivation are presumably mediated directly at the thalamic level by the very substantial corticothalamic pathway (see Jones 1985 for review). Another possibility is that the effect is mediated by corticofugal systems that affect transmission at lower levels of the pathway, in particular within the cuneate division of the dorsal column nuclei (Gordon and Jukes 1964; Weisberg and Rustioni 1979). However, as preliminary observations reveal little effect of SI or SII inactivation on the tactile responsiveness of cuneate neurons (Turman et al. 1991), it appears that the thalamic relay must be the site of the modulatory influences observed in the present study. This conclusion is consistent with very similar observations on the visual system that show that reversible inactivation, by cooling, of areas 17 and 18 affect photically and electrically activated responses of a proportion of lateral geniculate neurons, an effect attributed to the direct cortico-geniculate pathway (Kayama et al. 1984).

Evidence against direct spread of cooling to VPL thalamus

Alteration in VPL neuronal responsiveness could not be due to a direct spread of cooling from somatosensory cortex, since the waveform of the action potential from the thalamic neurons was not prolonged during SI inactivation (see Fig. 2). Cooling-induced waveform changes are known to precede any alteration in responsiveness to direct cooling (Sherk 1978; Turman et al. 1992a). Furthermore, no changes in temperature were recorded in the thalamus during SI or SII inactivation.

Role of the corticofugal pathway in somatosensory transmission

The SI and SII areas are reciprocally interconnected with the VPL thalamus in a topographically organized manner such that each somatotopic region within SI and SII projects to and receives input from the corresponding somatotopic region of VPL (Jones 1985). Within VPL, synaptic profiles of lemniscal origin contact the large proximal dendrites or cell bodies of the thalamic neurons, while synaptic profiles of cortical origin are largely restricted to the distal dendritic trees of the neurons (Ralston 1983). This suggests that lemniscal afferents may exert more powerful excitatory actions on VPL neurons than do the descending corticofugal axons whose connections are more consistent with a modulatory role (see Rall 1962).

Similar thalamocortical interconnections exist in the visual system (see Jones 1985 for review), where it has been proposed that the corticogeniculate pathway may modulate the transmission of visual information through the lateral geniculate nucleus, and, by enhancing certain aspects of the ascending visual signals, may contribute to selective visual attention (Koch 1987). The present evidence for modulatory influences from SI and SII on the transmission of tactile information through VPL suggests a similar role for the somatosensory corticothalamic pathway. Furthermore, as phaselocking in the responses of the VPL neurons to vibrotactile stimuli was unchanged by the cortical inactivation, it appears that the modulatory influence from SI and SII on the responsiveness of the thalamic neurons may be exerted without altering the precision of impulse patterning in the responses (see Figs. 8, 9). Perhaps corticofugal modulatory influences are implicated in the recent findings that the responsiveness of thalamic neurons to somatic inputs may change with shifts in arousal or shifts of attention to somatic rather than visual cues (Morrow and Casey 1990, 1992). Another observation consistent with this hypothesis is the finding of Hyvärinen et al. (1980) that some somatosensory cortical neurons, including neurons in lamina VI that may be corticothalamic neurons, increase their firing rates during selective attention to cutaneous vibratory stimuli.

As somatosensory cortical inactivation had less effect on background activity than on the peripheral evoked responses in many of the thalamic neurons studied (see Fig. 1B, C), it appears that corticothalamic facilitatory influences enhance thalamic evoked responses and improve signal-to-noise ratios. A number of mechanisms have been proposed to explain similar findings. These

include inhibition of thalamic relay neurons (Yuan et al. 1985) and activation of NMDA receptors (Koch 1987).

The present evidence for a predominantly facilitatory influence from SI and SII on VPL thalamic transmission is consistent with the effects observed on the lateral geniculate neurons from areas 17 and 18 by Kayama et al. (1984) and the facilitatory effects of lidocaine-induced inactivation of SI on the responsiveness of thalamic neurons to peripheral electrical stimulation (Yuan et al. 1985, 1986). However, some studies of corticothalamic influences, whether on somatosensory transmission (Burchfiel and Duffy 1974; Tsumoto et al. 1975; Shin and Chapin 1990) or on visual transmission (Geisert et al. 1981; Murphy and Sillito 1987) have argued for predominantly inhibitory or mixed inhibitory and excitatory effects on thalamic transmission. As some corticothalamic fibres terminate on thalamic inhibitory interneurons in the cat (Ralston 1983; Montero and Singer 1985), a corticothalamic inhibitory influence may co-exist with an excitatory influence, and, in the present study, evidence for inhibition was demonstrated for one neuron in the sample. The balance of these excitatory and inhibitory influences may depend on a number of factors such as the type of stimulus and context as suggested by Grieve and Sillito (1991).

Corticothalamic inhibition may play a role in surround or lateral inhibition in the thalamus, as suggested by Sherman and Koch (1986) for the visual system. Indeed, the presence of both excitatory and inhibitory effects may benefit transmission of appropriate tactile signals through the thalamus, the former enhancing transmission from skin regions of interest, and the latter suppressing signals from the surrounding skin. Such selectively directed excitation and inhibition could explain the differences in findings of past studies that have differed in the extent of cortex inactivated, the nature of the stimuli used and the method of recording evoked responses (single unit, multiunit and evoked potentials) and the presence and type of anaesthetic used (see Discussions in Burchfiel and Duffy 1974; Yuan et al. 1985, 1986; Shin and Chapin 1990). However, in relation to the last factor, anaesthetic influences, it should be noted that previous studies on corticofugal effects on VB neurons in the rat (Yuan et al. 1985, 1986) found that the effects were qualitatively and quantitatively similar in anaesthetized and awake rats. If anything, the corticofugal effects were more apparent in the anaesthetized rats, suggesting that the use of anaesthesia in our present experiments has not masked corticofugal influences.

Corticothalamic modulation as an explanation for interactions between SI and SII

In our recent analysis of SI and SII interactions in the cat (Turman et al. 1992a) we found that about 20% of SII neurons exhibited some reduction in tactile responsiveness during SI inactivation, but none exhibited consistent changes in measures of phaselocking. We concluded that this reduction in SII responsiveness may reflect the removal of a facilitatory influence exerted by SI neurons, either directly, via the well-documented and elaborate intracortical connections between SI and SII (Burton 1986; Jones 1986), or indirectly via corticofugal influences on, for example, thalamic transmission. In the present study, four (27%) of 15 VPL thalamic neurons underwent reductions in responsiveness during SI inactivation, and these changes also occurred without any changes in phaselocking in vibration-induced responses. Our present observations indicate that the SI facilitatory influence on SII neurons (Turman et al. 1992a), and similar effects of SII on SI neurons (Turman et al. 1992b), could be mediated via corticothalamic influences on tactile transmission at the thalamic level.

Acknowledgements We acknowledge the technical assistance of C. Riordan and P. Mackie. The study was supported by the National Health and Medical Research Council of Australia and the Australian Research Council.

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