Interhemispheric Modulation of Somatosensory Receptive Fields: Evidence for Plasticity in Primary Somatosensory Cortex

Extracellular recordings were made from single and multiple neurons in primary somatosensory cortex (area 3b) of macaque monkeys and flying foxes. When a small region of area 3b (or adjacent area 1) in the opposite hemisphere was cooled, thereby blocking activity that is normally transferred via the corpus callosum, larger receptive fields (RFs) were immediately unmasked for most neurons. RF expansion presumably reflects the expression of afferent inputs that are normally inhibited, suggesting that callosal inputs provide a source of tonic inhibition that contributes to the shaping of neuronal RFs. Quantitative analyses of single neuron responses revealed other effects that were consistent with a release from inhibition, such as increases in response magnitude to stimulation of points within the original RF and decreases in response latency. An unexpected finding was the reversal of these unmasking effects with extended periods of cooling: RFs returned to their original dimensions and within-field response magnitude decreased. In contrast to the initial effects, this reversal of disinhibition cannot be readily explained by an unmasking of previously unexpressed inputs. Any explanation for the reversal requires an increase in the efficacy of intraneuron-mediated inhibition, and presumably occurs in response to ongoing, altered patterns of activity.

The capacity of neocortical topographic representations to reorganize following peripheral damage has been demonstrated in the primary sensory (Rasmussen, 1982; Merzenich et al., 1983, 1984; Wall and Cusick, 1984; Calford and Tweedale, 1988, 1990a; Robertson and Irvine, 1989; Kaas et al., 1990) and motor areas (Donoghue et al., 1990; Sanes et al., 1990) of a variety of adult mammals. The first stage of reorganization of the primary somatotopic representation (area 3b) following limited peripheral denervation is the immediate expansion of receptive fields (RFs) representing the affected body part onto adjacent body surface areas (Merzenich et al., 1983; Calford and Tweedale, 1988, 1991a; Byrne and Calford, 1991). For example, when digit 1 was amputated in a flying fox, neurons in area 3b representing that digit became immediately responsive to stimulation of the adjacent wrist, wing, or arm. Over a period of weeks, these enlarged RFs contracted to normal dimensions and the area of cortex deprived of its principal input was topographically reorganized (Calford and Tweedale, 1988, 1991a). The short-term, dynamic changes are thought to reflect an unmasking of viable, but normally unexpressed inputs. The long-term changes presumably occur in response to ongoing, altered patterns of activity.

The present experiments were designed to investigate further the role of interhemispheric connections in the maintenance of neuronal RFs in cortex. This was achieved by cooling the representation of a small body part in area 3b (or the caudal cutaneous field, area 1) in one hemisphere while recording from neurons with RFs representing the mirror-symmetric body part in area 3b of the other hemisphere. Cortical cooling reversibly deactivated a small region of cortex and its efferents, and allowed observation of RF changes that were presumably a product of cortical mechanisms only. These experiments confirmed the contribution of callosal inputs to RF dimensions and, in addition, revealed a consistent reversal of initial disinhibitory effects.

Materials and Methods

Subjects and Surgery
Observations were based on the responses of multiple (multi-) or single units located in area 3b of adult little red flying foxes (Pteropus scapulatus, n = 19) or adult macaque monkeys (Macaca fascicularis, n = 3). An additional three flying foxes were used for calibrations of the cooling procedure and experiments in which visual cortex was cooled as a control procedure. Animals were initially anesthetized with a ketamine/xylazine mixture (i.m. 50 mg/kg and 5 mg/kg, respectively). In both species, supplemental doses of ketamine and/or sodium pentobarbitone (15 mg/kg, i.m. or i.v.) were given throughout the experiment to maintain areflexia (i.e., absence of pinch-withdrawal and blink reflex). In monkeys, a tracheal cannula was inserted to ensure unobstructed breathing and a venous cannula for administration of supplemental doses of anesthetic. Animals were mounted in a stereotaxic frame and placed on a heating pad. A midline incision of the scalp was made, the temporal muscles were retracted, and the skull and dura mater overlying somatosensory cortex in both hemispheres were removed. In the flying foxes used in control experiments, a more caudal exposure was made in one hemisphere; these animals also received eye drops of 1% atropine sulphate prior to the recording session. The exposed cortical surface was protected with silicone oil and a photograph taken so that electrode placements could be recorded with reference to the surface vasculature.

Data Collection
Prior to cooling, somatosensory cortex was partially mapped to determine a site that contained neurons responsive to stimulation of glabrous skin (usually a digit) and the region to be cooled. On average, this involved the determination of the RFs of neurons at 57 cortical sites in monkeys and 12 sites in flying foxes. These partial somatotopic maps of area 3b and the adjacent, caudal cutaneous field (area 1 in monkeys and area 1/2 in flying foxes; e.g., Kaas et al., 1979; Krubitzer and Calford, 1992) were generated using standard electrophysiological procedures. Extracellular multiunit activity was recorded from glass-insulated tungsten microelectrodes oriented approximately orthogonal to the cortical surface. The amplified and filtered signal from the electrode was displayed on an oscilloscope and an audiomonitor. The border between area 3b and the caudal field (area 1 or area 1/2) was identified by a reversal in somatotopy. In flying
on 26 December 2017

The end of the experiment, the flying foxes were overdosed with

to deep layer in and layer IV; a few neurons were located slightly

each animal, except in one flying fox in which both a multi- and a

set, that were stored on computer.

These -were generated from the event times, relative to stimulus on-

and the number of spikes in specific time windows (response mag-

peated up to four times as a check on recording stability and to

that is, each location was retested after intervening measures at other

locations. However, this was considered only a rough indication of the temperature gradient, which may have been influenced by the tissue damage and slight bleeding associated with insertion of the thermocouple. Neverthe-

less, this approximation (57 mm) is consistent with other reports

(e.g., Jasper et al., 1970), including those that have used very fine, specially designed thermocouples (Girard and Bullier, 1989; gradient range of 2.3–5.5°/mm).

Multiunit activity 1 mm beneath the cooling probe was monitored
during calibration and in six of the data collection experiments. A noticeable reduction in the amplitude of the response to cutaneous stimulation of a given body part occurred at a surface temperature of 20–23°. Abolition of activity was observed when surface temperat-

ures reached 15–16°. Given the above estimate of the temperature gradient, this latter observation is consistent with previous reports showing that synaptic function is blocked at temperatures around 20° (see Brooks, 1983, for review), although others have reported lower blocking temperatures (Girard and Bullier, 1989). Additional calibrations determined that the surface temperature at the homo-

topic location in the hemisphere opposite that being cooled did not

vary by more than 2.5° over a period of 1.5 hr, and that surface cortical temperatures approximately 0.5 mm from the cooling probe were 5–7° greater than temperatures determined immediately adja-

tent to the cooling probe.

In a control for nonspecific effects that could account for our results, the effect of cooling visual cortex on responses in area 3b in the opposite hemisphere was examined in three single units and two multiunits (each consisting of two waveforms) from two flying foxes. The cooling probe was placed in the vicinity of visual area 2 (Rosa et al., 1994), located by a series of caudal electrode penetrations that revealed the presence of neurons responsive to moving white bars or spots. In these experiments the position of the computer-con-

trolled brush remained constant at a point within the neuron's RF. Data were collected at 2 min intervals throughout the cooling cycle, and compared to the response of the neuron(s) before and after cooling (4–11 separate runs). There was no evidence for any change in the response magnitude of area 3b neurons or the extent of their RFs. In two cases, there was a small progressive increase in response magnitude through the course of the 1.5 hr cooling cycle. In the remaining cases, there was either a slight, progressive decrease throughout the course of the cycle (n = 2) or no change (n = 1). None of these changes were associated with periods of cooling or rewarming.

Results

Initial Effects of Cooling Area 3b or Area 1: Unmasking

Large RFs

The effect of cooling the representation of a body part in area 3b of one hemisphere on neuronal RFs in area 3b of the

zized and were immediately used in a nonrecovery study of the or-

ganization of somatosensory cortex (Krubitzer et al., 1995).

Cooling Procedures

The cooling apparatus consisted of a short tin-plated copper cylin-

drical probe (1.5 mm diameter) attached to an insulated, hollow copper

pipe connected through which a temperature-controlled antifreeze

circulated. The temperature of the antifreeze was controlled by a Bio-

Rad refrigerated recirculator (model 4850) which led to the passive

cooling of the block and probe. A T-type thermocouple (Anrithcur)

was mounted within the copper block and provided a record of tempera-

ture throughout a given experiment. These temperatures were con-

verted to estimates of cortical temperature under the cool-

ing block using the following formula (Girard and Bullier, 1989;)

3. For three flying foxes. For these determinations the tip of an N-type ther-

couple (0.5 mm diameter) was pressed into the cortical surface (but not piercing the pia) immediately adjacent to the cooling probe.

The cooling block was reduced to its minimum temperature, then

rewarmed; this allowed a comparison of cortical and block tempera-

tures. At the beginning of each experiment and when cortex was

rewarmed after a period of cooling, the temperature of the block was

maintained around 37°. Calibrations showed that surface tempera-

tures were somewhat cooler than this (around 30°), although tempera-

tures within cortex would presumably have been higher. The minimum temperatures recorded 1 mm below the cooling probe were 5° higher than those recorded near the surface. However, this is

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opposite hemisphere was examined in 14 flying foxes and 1 macaque monkey. The effect of focal cooling of area 1 (area 1/2 in flying foxes) was tested in an additional two monkeys and five flying foxes. In over half the flying foxes (11 out of 19), observations were based on the measurement of multiunit RF areas in response to stimulation with a hand-held brush. The data from all three monkeys and seven flying foxes comprised single unit responses to computer-controlled brush stimulation.

The most common effect of cooling area 3b in one hemisphere was an immediate expansion of the RF of the neuron under study in the opposite hemisphere. This is illustrated by the results obtained from a macaque monkey. Figure 1 shows the poststimulus time histograms (PSTHs) that resulted from controlled brush stimulation of points within and outside the RF of a single unit in area 3b, before, during, and after cooling of the toe 1 (T1) representation in the opposite area 3b. During cooling, the RF expanded (F), and this is indicated by the emergence of a response to stimulation of location 4 (B). There was also a clear increase in response magnitude to stimulation of all points within the original RF (locations 1–3) relative to the initial condition. In addition, a longer latency component appeared in the response to stimulation of the T1 pad (location 1).

Figure 2 illustrates an example of RF expansion following focal cooling of area 3b in flying fox. This area 3b single unit was initially responsive to stimulation of the distal half of digit 1 (D1). The wing of the flying fox incorporates a modified hand, in which only D1 (the thumb) is free of membrane attachments. This cell's RF expanded proximally along the lateral surface of the digit when the opposite D1 representation was cooled. Details of changes in responsiveness are shown in graphs that plot response magnitude and cortical temperature as functions of time for three locations stimulat-
Figure 2. Time course of expansion and subsequent contraction of an area 3b single unit RF during focal cooling of the opposite area 3b in a flying fox (FFZ51). The initial RF (dark stipple), region of expansion (light stipple), and points of controlled brush stimulation (A–Q) are shown in the top illustration of lateral D1. The graphs plot response magnitude (left ordinate, solid lines) and cortical temperature (right ordinate, dotted line) as functions of time (abscissa). Both the evoked (solid circles, solid line) and spontaneous (open circles, dashed line) activity are shown. The latter was calculated from the number of spikes that occurred between 100 and 1000 msec poststimulus. Responsiveness of the unit was determined twice before cooling, and these repeat measures are indicated by separate symbols on the left ordinate.

ed with the controlled brush. The responses that defined the initial RF were determined twice to provide some indication of recording stability. There was a difference in the magnitude of these initial responses (see symbols, left ordinates), but this was minor relative to the changes in responsiveness associated with cortical cooling. Panels A–C illustrate the increase in response magnitude to stimulation of points within (A), on the edge of (B), and outside (C) the initial RF as cortical temperature in the opposite hemisphere decreased.

Focal cooling of area 3b in one hemisphere failed to produce RF expansion of single units in area 3b of the opposite hemisphere in four flying foxes. That is, stimulation of points outside the original RF did not produce an evoked response before (by definition), during, or after cooling. However, in one of these neurons, there was an increase in responsiveness to the controlled brush stimulation within the original RF during two cooling cycles (FF262; see Fig. 5A). This change in responsiveness was qualitatively similar to the within-field changes described above, in cases in which the RF also expanded (Figs. 1, 2). In the remaining three neurons there was evidence that cooling led to a reduction in responsiveness within the original RF. One of the more marked examples of this RF "contraction" is illustrated in Figure 3, in which within-RF responsiveness during cooling was, on average, 32% of the initial level. The lowest magnitude recorded during the cooling period was 16% of the initial response. Spontaneous activity also decreased during the cooling period. When the opposite cortex was rewarmed, responsiveness returned to initial levels.

Cooling area 1 in one hemisphere resulted in an expansion of RFs of neurons in area 3b of the opposite hemisphere in both monkeys examined and three (of five) flying foxes. An example of single-unit RF expansion in this paradigm is shown by the results from a monkey in Figure 4. When the D2 representation in area 1 was cooled, the RF of an area 3b neuron in the opposite hemisphere expanded both proximally and distally. This is indicated by the increase in response magnitude to stimulation of locations A and D (Fig. 4A, D), which were outside the original RF. There was also an increase in response magnitude to stimulation of points within the initial RF (B, C) relative to initial levels. Average spontaneous activity was low in this case, but increased threefold within the cooling period (around 30 min, see A).
Changes in neuronal response magnitude associated with focal cooling of the opposite hemisphere are summarized in Figure 5. Data representing response changes in single units in which RF expansion and/or increases in within-field responsiveness was observed are presented in A (left). Although there is interindividual variability in the percentage increase in responsiveness (initial vs cool), these changes in response magnitude were generally quite marked and represent an average increase of 465%. Except for two locations, one within and one outside the RF of the RM9 single unit, all comparisons of response magnitude before and during cooling differed significantly from those expected by chance. A paired t test revealed that within-field response magnitude during cooling differed significantly from that observed before cooling ($t = 6.0, df = 13, p < 0.001$). For the five within-field locations in which RF "contraction" was observed (right detached histogram), response magnitude decreased, on average, to 33% of initial levels. These cells did not differ from those that showed RF expansion in any apparent way, that is, in terms of spontaneous activity, initial response magnitude, or size of initial RF.

Figure 5B illustrates the extent of multi- or single-unit (C) RF expansion observed to hand-held brush stimulation. Expansion was observed in both prowing (left detached histogram) and D1 RFs; however, in two animals in which area 1/2 was cooled there was no detectable change in the RF dimensions of multunit in area 3b of the opposite hemisphere (FF22S and FF227). On average, RF size increased by 360% when the opposite area 3b or area 1 was cooled.

Increases in response strength to stimulation of locations within the original RF were often accompanied by a decrease in response latency (e.g., location 1, Fig. 1A, B). This effect is summarized in Figure 6, which compares the response latencies to within-field stimulation before and during focal cooling of area 3b or area 1. Most data points (12 out of 14) fall to the right of the diagonal line representing unity slope, indicating that response latencies during cooling (when increases in within-field response magnitude were at their maximum) were shorter than those observed initially. In six of these cases (open circles, right of diagonal) differences were statistically significant ($t$ test, $p < 0.05$). In one case, the minimum latency to within-field stimulation during the cooling period was significantly longer than that observed initially. This particular area 3b neuron was the single case, described above, in which within-field responsiveness increased but the RF did not expand when the opposite area 3b was cooled.

**Effects of Extended Cooling of Area 3b or Area 1**

Cooling-induced expansions in neural RFs were observed to reverse when the cooling period was extended beyond 15 min in most flying foxes (9 out of 11) and all three monkeys. The contraction of expanded RFs of area 3b neurons to their original dimensions during cooling of the opposite area 3b is evident in Figures 1 and 2. For example, in Figure 1, the response to stimulation at location 4, which defined the expanded RF, is shown in the top right drawing. Other conventions as in Figure 3.
panded RF early in the cooling period, decreased late in the cooling period, although it did not completely disappear. There was also a reversal of the previous increase in within-field responsiveness, such that response histograms late in the cooling period were similar to those observed initially. Similar effects were evident in flying foxes when the opposite area 3b was cooled (Fig. 2) and in monkeys when the opposite area 1 was cooled (Fig. 4). That is, reversals in both RF expansion and the increased within-field responsiveness are apparent within 40 to 60 min of the commencement of cooling. These examples also illustrate that there was no further change in responsiveness with the subsequent rewarming of the opposite cortex. When cortex was rewarmed, there were some cases that showed slightly reduced responsiveness to within-field stimulation relative to initial (e.g., Figs. 1D, location 3; 4D). However, this was not a consistent finding within a RF or across cells; in the remaining cases, responsiveness was either equivalent (e.g., see other within-field locations in Figs. 1, 4) or slightly greater than initial levels (Fig. 2A).

In six experiments, the cooling-rewarming process was repeated at least two times. In five of these, there was evidence that with repeated cooling cycles the degree of expansion was less marked and/or the period to contraction after induced expansion was reduced. In the most extreme case, the third cooling (after 10 min of normal cortical temperature) failed to produce RF expansion (Fig. 7). The RF of the single unit illustrated in Figure 7 expanded during the first cooling to include all of the medial surface of D1. Over a period of an hour it contracted back to its original dimensions. During the second cooling cycle the RF expanded and contracted over a shorter time period (approximately 15 min). Finally, during the third cooling, which lasted 45 min, the RF did not change its dimensions. An exception to this trend was one case in which the expanded RF failed to contract during two periods of extended cooling (120 and 60 min), but returned to its original dimensions when the opposite cortex was rewarmed.

**Discussion**

In most cases, cooling a small region of area 3b or the caudal, cutaneous somatosensory field (area 1 in monkeys, area 1/2 in flying foxes) resulted in the expansion of neuronal RFs in area 3b of the opposite hemisphere. Within extended cooling periods this effect usually reversed, such that RFs returned to their original dimensions. Both effects may be explicable in terms of a change in the balance between excitatory and inhibitory inputs that determine the dimensions of a neuronal RF. The initial RF expansion can be readily explained in terms of a change in the balance between excitatory and inhibitory inputs that determine the dimensions of a neuronal RF.
of an unmasking (dissinhibition) of previously unexpressed inputs from adjacent parts of the body surface ("off-focus" inputs). In contrast, the reversal of this effect with continued deactivation of callosal inputs would suggest some form of synaptic plasticity, that is, either a change at the synapses providing inhibition of off-focus afferents or at the synapse of an intervening excitatory neuron (see below).

There is evidence from anatomical and physiological studies (e.g., Landry and Deschenes, 1981; Snow et al., 1988; Garraghty et al., 1989), as well as from many peripheral denervation-induced plasticity experiments (e.g., Merzenich et al., 1983; Calford and Tweedale, 1988, 1991a), that a given cortical locus receives viable excitatory inputs from a far wider area of the receptor epithelium than that indicated by the dimensions of a classically defined RF. It is known that interneurons containing GABA (γ-aminobutyric acid), the major inhibitory neurotransmitter in the neocortex, contribute to the architecture of somatosensory cortical RFs. Several studies have shown that local application of a GABA$_A$ receptor antagonist, bicuculline, produces an increase in RF dimensions of neurons in cat primary somatosensory cortex (SI) (Dykes et al., 1984; Alloway et al., 1989; Bateup et al., 1989). The existence of wide-ranging thalamocortical projections (e.g., Snow et al., 1988) and horizontal connections (e.g., Ts'o et al., 1986; Smits et al., 1991) provide a substrate for the expression of larger RFs. Therefore, a simple explanation of the RF expansion observed in the present experiments is that cooling leads to a reduction in ongoing activity in excitatory callosal inputs to inhibitory interneurons that normally suppress off-focus inputs to the recorded cell.

Similar explanations have been invoked to explain the rapid RF expansion of cortical neurons following manipulations to the receptor surface. For example, removal of the "dominant" input to an area 3b cell by amputation or local anes-

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**Figure 6.** Average first-spike response latencies of area 3b single neurons to within-field stimulation before and during cortical cooling (abscissa and ordinate, respectively). Statistical significant differences between the two latencies are indicated by open circles, while nonsignificant differences (p > 0.05) are indicated by dots. Data were from four flying foxes and three macaque monkeys in which cooling of either the opposite area 3b or area 1 led to an increase in single-unit response magnitude to within-field stimulation. Initial minimum latencies were derived from two to four separate runs (20 stimulus presentations in each) and represent the average of these measures. The response latency for the cooling period was calculated from the run that showed the maximum increase in response magnitude.

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**Figure 7.** Expansion and subsequent contraction of an area 3b single-unit RF following repeated focal cooling of the opposite area 3b in FF216. The extent of the original RF and the region of expansion are shown by the dark and light stipple, respectively, in the top drawing. The RF was determined using cutaneous stimulation with a hand-held brush. Changes in RF size (left ordinate, solid line) and cortical temperatures (right ordinate, dotted line) are both expressed as a function of time (abscissa) in the bottom graph.

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Any explanation of unmasking of previously unexpressed inputs requires a source of tonic input to inhibitory interneurons. In a subsequent report it was shown that peripheral application of capsaicin—a C-fiber neurotoxin—also results in RF expansion, and it was proposed that C-fibers may be this source of tonic, modulatory input to GABAergic interneurons in area 3b (Calford and Tweedale, 1991b). The present study provides evidence for another source of tonic input to the interneurons that shape the responses of cortical neurons, namely, that from another cortical field (conveyed by inter- and intrahemispheric projections). Presumably either tonic input alone is not sufficient to activate GABAergic inhibition optimally since abolishing either of them alone leads to the unmasking of larger RFs.

Callosal axons make excitatory (asymmetrical) synapses in the opposite sensory cortex (Sloper and Powell, 1979), some of which project upon inhibitory interneurons (Somogyi et al., 1983). Intracellular and extracellular recordings of cat SI neurons have shown that stimulation of the rostral corpus callosum or SI in the opposite hemisphere can produce either excitatory or inhibitory effects (Fadiga et al., 1972; Innocenti et al., 1972). In those studies, some SI cells were shown to be responsive to both peripheral stimulation and stimulation of the opposite SI; callosal inhibition was shown to suppress both the response to peripheral stimulation and spontaneous activity. Similar results have been reported in primary auditory (Kitzes and Doherty, 1994) and visual cortex. In the latter, excitatory callosal effects were shown to be direct (monosynaptic) and inhibitory effects indirect (disynaptic) (Peelen and Orem, 1971; Toyama et al., 1974; Innocenti, 1980). Together, these studies suggest the involvement of local interneurons in mediating inhibitory interhemispheric effects.

The above explanation of RF expansion requires that the corpus callosum is a source of tonic input to inhibitory interneurons. Studies of single fibers within the rostral corpus callosum of awake (Spidalieri et al., 1985) or anesthetized cats (Innocenti et al., 1974) have shown that they are tonically active in addition to being responsive to mechanosensory
stimulation. Innocenti et al. (1974) noted that the resting discharge of callosal fibers was not random but had a distinct, regular firing pattern. They also found that a few callosal fibers exhibited inhibitory RFs, that is, their spontaneous activity was suppressed by peripheral cutaneous stimulation. "Suspected" interneurons in SI shown to receive callosal as well as other sources of input also exhibit high levels of tonic activity (Swadlow, 1990).

Whether the inhibitory neuron necessary to explain RF expansion is located in the immediate vicinity of the recorded cell cannot be determined from the present experiments. Traditionally, nonpyramidal inhibitory interneurons were thought to make only local connections, largely confined to a cortical column (for review, see Houser et al., 1984). However, long-range inhibitory connections have been described, that is, GABAergic neurons with axon collaterals that spread horizontally for some distance within and between adjacent fields (Martin et al., 1983; McDonald andBurkhalter, 1993; Matsubara et al., 1987). Thus, inhibitory input could arise from neurons located at a distance within the same cortical field or in an adjacent cortical field. In addition, a small proportion of callosally projecting axons in cat primary visual and auditory cortex have been shown to arise from nonpyramidal neurons (Code andWiner, 1985; Peters et al., 1990). These findings raise the possibility of a direct callosal inhibitory influence.

Initial RF expansion indicates that callosal input to area 3b exerts an inhibitory influence. In a few neurons, cooling produced a reduction in evoked activity of neurons in the opposite hemisphere suggesting that callosal input to these cells normally exerts a facilitatory effect. Deactivation of callosal inputs to rat SI by local application of lignocaine has been shown to produce either a "potentiation" or reduction of responses in some neurons with bilateral RFs (Armstrong-James andGeorge, 1988). Both increases or decreases in evoked and spontaneous activity have also been observed in primary visual cortex following cooling of callosally projecting regions of visual cortex in the opposite hemisphere (Payne et al., 1991).

Other changes in neuronal responsiveness sometimes associated with RF expansion are consistent with a disruption in the balance between excitatory and inhibitory inputs. First, a removal or reduction of "in-field" inhibition would be expected to lead to an increase in response magnitude to stimulation of points within the original RF; as has been proposed in experiments in which bicuculline was applied intracortically (e.g., Dykes et al., 1984). Second, certain response characteristics that are dependent on central inhibitory processes, such as directional selectivity in SI neurons responsive to vibrissal stimulation, are associated with longer response latencies compared to nondirectional neurons (Batuev et al., 1989). Removal of inhibition might therefore be expected to lead to a decrease in response latency. Third, the appearance of distinct, secondary responses (> 60 msec) in a few cases may reflect an unmasking of longer latency inputs to the cell that may normally be suppressed by the slower (50-270 msec) GABA<sub>a</sub> receptor-mediated inhibition (Connors et al., 1988).

Reversal of Disinhibitory Effects: Evidence for Synaptic Plasticity?

The above explanation of RF expansion (or initial RF contraction) does not need to invoke any form of synaptic plasticity since it is compatible with knowledge of neocortical neuronal circuits and interactions between excitatory and inhibitory inputs that shape neuronal RFs. The unmasking of larger RFs following deactivation of a given region within the somatosensory pathway and the notion that this represents disinhibition is in itself not a unique result or conclusion (e.g., Burchfiel and Duffy, 1974; Wall, 1977; Casanova et al., 1991). This "physiological" explanation is worth emphasizing since short-term changes in cortical RFs resulting from manipulations to the receptor surface that are thought to be mediated by similar unmasking mechanisms have been described as representing functional plasticity (e.g., Calford and Tweedale, 1991a; Gilbert and Wiesel, 1992). In contrast to initial RF expansion, the subsequent RF contraction and reduction of within-field response magnitude observed during the cooling period cannot be readily understood in terms of unmasking but must involve some form of synaptic plasticity; that is, a regulation of inhibition that is triggered by the continued deactivation of callosal inputs. A homologous temporary change in the dimensions of the RFs of area 3b neurons was also observed in a previous study that used a different technique for the disruption of inputs to the primary field (Calford and Tweedale, 1990b). When a digit was amputated, neurons in area 3b that were previously responsive to that digit immediately became responsive to adjacent body surfaces. This intermediate RF expansion was mirrored in neurons responsive to digit stimulation in the opposite hemisphere (i.e., ipsilateral to the amputated digit). This "indirect" RF expansion lasted for less than 30 min and is comparable to the time course of the RF changes observed in the present study.

If the initial disinhibitory effects are due to the disruption of input to inhibitory (presumably GABAergic) interneurons, then it is reasonable to assume that the subsequent RF changes are mediated by the activity of these same interneurons. Therefore, one explanation of the reversal of the initial effects is that an effective increase in inhibition counteracts the effects of the initial disinhibition. This "recovery" of inhibition could be mediated by the inhibitory interneuron itself or an intervening excitatory neuron (e.g., ipsilateral area 1 to area 3b projection). The difficulty with this explanation is the absence of an obvious trigger for an increase in inhibition, since no further experimental manipulations were taking place and the inactivation of callosal inputs, and presumably any intervening excitatory neurons, was maintained. However, the sensitivity to other sources of tonic input to the GABAergic interneuron may have undergone a change due to the reduction in activity. This change may take the form of (1) an increase in the efficacy of the remaining tonic, excitatory inputs to the interneuron; or (2) an increase in the efficacy of the efferent synapses of the interneuron. The former explanation supposes that the imbalance in the tonic inputs to inhibitory interneurons triggers an increase in the effectiveness of some of the excitatory inputs to it. The latter explanation supposes that inhibitory synapses show plasticity, that is, their effectiveness changes in the face of altered patterns of activity. Pharmacological studies have provided clear evidence of the capacity for the GABA-receptor to vary in efficacy (e.g., Sieghart, 1992, for review), and endogenous mechanisms by which an increase in the binding efficacy of GABA can be induced under certain conditions (e.g., Purdy et al., 1991; Majewska, 1992). Whatever the mechanism, the outcome is an increased functional inhibition to the neuron under study.

To our knowledge, the reversal of disinhibitory effects (RF contraction following expansion) within periods of extended but reversible deactivation has not been noted by other researchers using similar techniques. There are several reasons why such an effect may not have been reported. First, the present study continuously monitored responsiveness within and outside original RFs (PSTHs were collected every 1-2 min). Studies that have tended to report a "snapshot" of activity may have overlooked a temporary effect if observations were made some time after the commencement of focal deactivation; in such cases a null effect would be reported.
ond, we found evidence for a reduction in the extent and duration of RF expansion with repeated episodes of cooling; in the most extreme case, the third cooling cycle failed to produce RF expansion. Many cortical cooling studies have encountered multiple trials within a single animal, and a null effect might be more likely in later trials. For this reason, recordings were made from only one single or multiunit per animal. Third, the temporary nature of RF expansion may reflect some specific function or characteristic of interhemispheric connections. This issue is difficult to address, given that only a few experiments have examined interhemispheric connections with deactivation techniques and the above methodological considerations apply.

A possible explanation of these results is that they are an artefact of focal cooling that indirectly resulted in a delayed, widespread change in neuronal responsiveness that counteracted the initial RF expansion and increases in within-field response magnitude. Some nonspecific effects of cooling, such as a systemic change in blood flow, were ruled out by Kalil and Chase (1970), although these experiments were carried out in the cat. Control experiments of the present study showed that cooling visual cortex did not produce any change in the response magnitude of area 3b neurons in the opposite hemisphere that could account for the reversal of RF expansion. Since a “nonspecific” explanation applies to all previous cooling studies, one might also expect similar results in similar studies. This is difficult to reconcile with the variety of outcomes of deactivation (disinhibition, disinhibition, no effect) that are consistent with known anatomy, and the fact that deactivation of cortex with lidocaine generally supports the findings derived from cooling experiments (e.g., cf. Sherk 1978; Calford and Tweedale, 1990). However, since some measures of neuronal responsiveness that have been reported when cortical temperature drops from 37° to 30° (see Brooks, 1983, for review) may potentially influence interpretation of the present results. However, it is unlikely that a period of “hyperexcitability” could have influenced the present results, since observations consistent with inhibitory plasticity were made outside this temperature range (i.e., at cortical temperatures below 15°).

**Routes of Interhemispheric Modulation of Area 3b Neurons**

Area 3b receives sparse callosal input, particularly to regions representing distal body parts (macaque monkeys: Jones and Powell, 1969; Jones and Hendry, 1980; Shanks et al., 1985; Cusick and Kaas, 1986; flying foxes: Krubitzer et al., 1992). The likelihood that the effects of cooling observed in the present study were conveyed by the more substantial callosal projections of the caudal cutaneous field (area 1 or area 1/2) (Vogt and Pandya, 1978; Killackey et al., 1983; Pons and Kaas, 1986; Krubitzer et al., 1992, 1993) was supported by the finding that cooling these regions induced changes in the responses of area 3b neurons in the opposite hemisphere. The route of this effect could be either direct, that is, area 1/2 interconnects with the D1 representation in contralateral area 3b (Krubitzer et al., 1992) or indirect, that is, via the intrahemispheric projection from area 1 (1/2) to area 3b (Krubitzer et al., 1993). In the placement of the cooling probe, we have assumed that hetero- and homoaireal interhemispheric somatosensory connections are topographic. However, in the flying fox, callosal connections are both topographic and non-topographic (Krubitzer et al., 1992), as are the intrahemispheric connections (Krubitzer et al., 1993). Anatomical studies in macaque monkeys have generally not been designed to address the issue of whether or not callosal connections are strictly somatotopic and have, for instance, used large tracer injections or made large lesions. Studies that made relatively restricted lesions (Jones and Powell, 1969; Shanks et al., 1985), and showed that distinct cortical foci contain degenerating terminals, are not definitive since they did not physiologically define the lesioned site or the regions that contained degenerating terminals in the opposite hemisphere.

It is possible that other areas, such as the second somatosensory field (SII), are also involved in the interhemispheric transfer of information involving distal body parts (e.g., Manzoni et al., 1984). Finally, we cannot rule out the possibility that the observed interhemispheric effects are not mediated cortically (or only partly so), but involve indirect subcortical routes.

**Notes**

We wish to thank Leah Krubitzer for valuable assistance with surgery and electrophysiological mapping in the macaque monkeys. We are grateful to staff of the Division of Ophthalmology, Department of Surgery, The University of Queensland, and the John Curtin School of Medical Research for providing the monkeys. This work was supported by the National Health and Medical Research Council and a Special Research Centre Grant from the Australian Research Council. Address correspondence to Dr. J. C. Clarey, Vision, Touch and Hearing Research Centre, Department of Physiology and Pharmacology, The University of Queensland, Queensland, Australia 4072.


206 Interhemispheric Modulation of Receptive Fields • Clarey et al.