Synaptic Interactions Between Thalamic and Cortical Inputs Onto Cortical Neurons In Vivo

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INTRODUCTION

Each neocortical neuron receives inputs from multiple presynaptic sources, integrates them, and generates an output that is transmitted to other neuronal populations. The major inputs of neocortical neurons arise from other neocortical neurons and thalamic nuclei. Synchronous presynaptic inputs evoke excitatory and/or inhibitory postsynaptic potentials (EPSPs and IPSPs, respectively), whose amplitudes depend in multiple factors. 1) Intrinsic neuronal properties may modify the synaptic efficacy, as shown by amplification or reduction of EPSPs and IPSPs exerted by some ionic currents (Crill 1996; Llina ´s 1996; Marder 1998; Stuart and Sakmann 1995). 2) Rhythmic synaptic volleys of neocortical origin produce frequency-dependent facilitation or depression (Buhl et al. 1997; Gupta et al. 2000; Markram et al. 1998; Reyes and Sakmann 1999; Thomson and Bannister 2003), whereas thalamic afferents generally depress (Gil et al. 1997, 1999). 3) Among the multiple extracellular factors that may affect responsiveness of postsynaptic neurons, the extracellular Ca²⁺ concentration is not stable (Massimini and Amzica 2001) and its modifications influence synaptic efficacy. 4) The state of the thalamocortical network also contributes to the modulation of PSPs. Generally, states associated with membrane depolarization in anesthetized preparations are accompanied by low input resistance (Rm), which decreases PSPs due to the shunting effects associated with network activities (Borg-Graham et al. 1998; Contreras et al. 1996;                        Hirsch et al. 1998; Paré et al. 1998); however, in chronically implanted animals, the Rm is stable and increased during quiet waking (Steriade et al. 2001), probably due to the enhanced release of some neuromodulators, among them acetylcholine that blocks K⁺ conductances (Knjivić et al. 1971; McCormick 1992).

The effects of paired-pulse stimulation (PPS) on responsiveness of cortical neurons have been intensively studied in vitro. Most studies have been performed in slices from CA1–CA3 hippocampal fields (Bi and Poo 1999; Kamiya et al. 2002; Magee 2000). Fewer in vitro studies have been devoted to neocortex, using PPS in pathways from infragranular to supra-granular layers, from layer IV to layer III in slices from the somatosensory cortex (Castro-Alamancos and Connors 1997), or recording layer III responses to white matter stimulation in visual cortex slices (Kirkwood et al. 1999). While in vitro studies on homosynaptic hippocampal pathways generally reported strong facilitation, data resulting from PPS in homosynaptic neocortical pathways reported depression (Volgushev et al. 1995) that was ascribed to a high probability of release in the majority of neocortical synapses (Castro-Alamancos and Connors 1997).

In the present study, we used intracellular recordings of neocortical neurons in vivo and investigated the effects of PPS in heterosynaptic pathways to determine the effects of convergence between single thalamic and cortical inputs onto target cortical and thalamic neurons. We also compared these effects to those exerted by interactions in homosynaptic (corticocortical and thalamocortical) pathways. The results show that in contrast to the strong facilitation obtained with stimulation of homosynaptic thalamocortical pathways, shunting is the major effect by interacting thalamic with cortical stimuli, being associated with both decreased input resistance and disfacilitatory mechanisms.

METHODS

Experiments were conducted on 35 adult cats, under anesthesia with pentobarbital (35 mg/kg ip).

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Preparation

The animals were paralyzed with gallamine triethiodide after the electroencephalogram (EEG) showed typical signs of deep anesthesia, consisting of rhythmic sequences of spindle waves (7–14 Hz). Supplementary doses of anesthetics were administered at the slightest changes toward activated EEG patterns. The cats were ventilated artificially with the control of end-tidal CO₂ at 3.5–3.7%. The body temperature was maintained at 37–38°C, and the heart rate was ~90–100 beats/min. Stability of intracellular recordings was ensured by the drainage of cisterna magna, hip suspension, bilateral pneumothorax, and filling the hole made for recordings with a solution of 4% agar.

Recording and stimulation

Intracellular recordings from cortical suprasylvian association areas 5/7, cortical pericruciate motor areas 4/6, and thalamic ventrolateral (VL) nucleus, were performed using glass micropipettes filled with a solution of 3 M potassium-acetate. For thalamic recordings in VL nucleus, the middle suprasylvian gyrus was removed. A high-impedance amplifier with active bridge circuitry was used to record the membrane potential (V_m) and inject current into the neurons. Field potentials were recorded in the vicinity of impaled neurons, using coaxial electrodes with the tip (cortical depth) at ~0.8–1 mm. For cortical stimulation, electrodes (similar to those used for field potential recordings) were inserted into the same area from which recordings were performed, while thalamic electrodes were inserted in appropriate nuclei (lateroposterior, LP, for recordings in areas 5/7; and VL for recordings in areas 4/6). In all cases, low-intensity stimuli (50–200 µA) at frequencies of 0.33–1 Hz were used. The paired-pulse protocol was employed at intervals of 5–200 ms, generally in increments of 10 ms. For the paired pulse protocol, the first pulse was considered the conditioning stimulus (CS) and the second one the testing stimulus (TS), which evoked a conditioned response (CR) and a testing response (TR), respectively. Most results are expressed as means ± SD.

At the end of experiments, the cats were given a lethal dose of pentobarbital.

Data analysis

ESTIMATION OF R_m. Synaptic responses evoked by either cortical (Cx) or thalamic (Th) stimulation were recorded under different levels of membrane polarization, obtained by current injection through the pipette (from ~1 to +1 nA steady current). V_m was plotted against different levels of DC injected. Plots were made for multiple time intervals, in increments of 10 ms, after and before stimulation onset. For each plot, a linear function was fitted, whose slope was considered to be the apparent R_m for that particular time interval. This general method is exemplified in Fig. 2C, where the CS was a cortical stimulus. Responses were recorded under three different levels of membrane polarization (0 nA ~81 mV, under +0.5 nA, and under ~0.5 nA). Next, a V_m versus DC plot was made for each of the following time intervals in reference to stimulation onset: ~5, 10, 30, 50, 80, 110, 140, 170, and 200 ms. The slope of the linear fitting in each plot represented the apparent R_m for the corresponding time interval. All values were normalized to the first one (~5 ms), considered as control.

EPSP’s AMPLITUDE. Amplitude was calculated as the difference between the value of V_m taken at 1 ms before the onset of stimulation and the peak of the response. Before starting the paired-pulse protocol, individual responses were characterized in their voltage dependence by steady current injection in the recording pipette as stimulation continued (see Fig. 2, A and B). A plot of amplitude versus V_m was built for each response. In most cases, a linear function was well fitted to the plot, allowing an estimation of the V_security for the recorded responses. Points belonging to the linear fitting were considered to be the “expected amplitude” because they indicate the theoretical amplitude that a response would present at a given V_m value. Later, the paired-pulse protocol was applied and measurements of amplitude were performed for the second TR. In such cases, the amplitude was measured by subtraction of the control CR (Fig. 4). In cases where subtraction was not possible, as in the presence of antidromic responses (Fig. 6), the amplitude was calculated from 1 ms before the onset of stimulation up to the peak of the response as it was done for individual, control responses. Amplitude values obtained in such conditions were considered “measured amplitude.” Finally, amplitude values were compared between those obtained during the paired-pulse protocol (measured) and those estimated from the linear fitting of individual responses (expected). In such way, amplitude values were corrected by V_m and not simply averaged because amplitude was dependent on V_m (Fig. 2B).

DEPOLARIZATION AREA OF THE RESPONSE. Area was considered as the integral of the response, from 1 ms before the onset of stimulation up to the time were V_m recovered the same value as before the onset of stimulation. Area was considered as “expected” and “measured” with the same criteria used for the amplitude. During paired-pulse protocol, area of the TR was obtained by subtraction of the control CR. In cases where subtraction was not possible, as in the presence of antidromic responses (Fig. 6), area was calculated from 1 ms before the onset of stimulation up to the time were V_m recovered the same value as before the onset of stimulation.

FIG. 1. Electrophysiological identification of cortical neuron and its responses to thalamic and cortical inputs. Barbiturate anesthesia in this and all subsequent figures. A and B: 2 traces represent depth-electroencephalographic (EEG) and intracellular recording from area 7 during the spindle oscillation (7–14 Hz). Seven stimuli to closely located site in cortical area 7 (A) or thalamic lateroposterior (LP) nucleus (B) were applied during active (spindles) and silent (interspindle-lulls) phases of the spindle oscillation. In A, 5 superimposed traces illustrate Cs-evoked intracellular responses, consisting of short-latency, monosynaptic EPSPs. In B, EPSPs elicited in cortical neurons by stimulating LP thalamic nucleus (5 superimposed traces). Notice excitatory postsynaptic potentials (EPSPs) to be also short latency and monosynaptic. In this and following figures, → V_m, ▲ and O, thalamic (Th) and cortical (Cx) stimuli artifacts, respectively.
RESULTS

Database and neuronal identification

Of 120 neurons recorded intracellularly, we retained for analysis 43 neurons that could be investigated during long-term recordings (40–150 min), which allowed repeated applications of conditioning stimuli (CS) and testing stimuli (TS) to neocortex and thalamus at different time intervals. Of those 43 neurons, 31 were located in cortical areas 5/7, 6 in cortical areas 4/6, and 6 in the thalamic VL nucleus. Cortical and thalamic neurons were identified by antidromic and synaptic activation. In all cases, recorded neurons were driven by thalamic and cortical inputs; this allowed the study of interactions between such inputs. Stimulation intensity was adjusted to avoid composite responses; thus mostly monosynaptic EPSPs were investigated. Figure 1 depicts responses of a cortical area 7 neuron, driven by both thalamic and cortical inputs. Local (area 7) cortical stimulation evoked a short-latency, monosynaptic EPSP (Fig. 1A). Stimulation of thalamic LP nucleus elicited a short-latency, monosynaptic EPSP with similar characteristics (amplitude and duration) as the cortically evoked one (Fig. 1B). All recordings presented here were performed on electrophysiologically identified regular-spiking (RS) or intrinsically bursting (IB) neurons. Some cortical neurons (7 of 37) were identified as corticothalamic by antidromic invasion from thalamic nuclei (see Fig. 6).

Thalamically evoked EPSPs and cortically evoked IPSPs could be detected in the same neuron (Fig. 2A). For each recorded neuron, we estimated the voltage-current relations for EPSPs and IPSPs, from which we anticipated the reversal potential and the expected amplitude at each given level of the $V_m$ (Fig. 2B). These values were used to compare the expected value of the evoked response with that obtained when TS was preceded by CS. Local cortical stimulation evoked an IPSP in some cortical neurons that was always associated with a drop in $R_{in}$ lasting from 100 to 200 ms. Thalamic stimuli occasionally elicited a compound, slow depolarization that followed the early EPSP with a latency of ~20 ms (not shown). Such late components could result from feedback activation of recurrent axons, and those cases were not considered for analysis to avoid additional variables in the analysis of interacting inputs.

Homosynaptic interactions of cortical or thalamic synaptic inputs onto cortical neurons

Cortically evoked EPSPs displayed a variety of results when stimuli were paired. In some cases (22%, 2 of 9 neurons), CS or TS paired at time intervals of 10–20 ms (i.e., 100 and 50 Hz) produced EPSP facilitation ranging from 15 to 25% (Fig. 3A). In other cases (33%, 3 of 9), the paired-pulse protocol induced a moderate depression (~30%) in EPSP's amplitude, while the

FIG. 2. Identification of thalamically and cortically evoked EPSPs and inhibitory postsynaptic potentials (IPSPs) in cortical neurons. A: the same cortical neuron recorded from area 5 responded with EPSP to Th (LP nucleus) stimulation and with IPSP to Cx stimulation in an adjacent site within area 5. B: estimation of EPSPs and IPSPs reversal potential. EPSP reversed at ~76 mV and EPSP reversed closed to 0 mV. C: PSPs at different $V_m$'s, in area 5 neuron by stimulating the same cortical area. The plot shows the decreased $R_{in}$ lasting for ~150 ms (expressed as percentage of the initial value of $R_{in}$, before stimulation), associated with the cortically evoked IPSP.

FIG. 3. Interaction in cortical neurons between homosynaptic, cortical and thalamic volleys delivered at different time intervals. One neuron recorded from area 4 with conditioning and testing stimuli applied in the same pathway. A: effect of paired pulse protocol on Cx-evoked EPSPs. Three panels show averaged responses ($n = 20$) to single and 2 cortical stimuli paired at different intervals. Plot displays results for various pooled neurons ($n = 8$; mean ± SD). B: effect of paired pulse protocol on Th-evoked EPSPs. Three panels show averaged responses ($n = 20$) to single and 2 thalamic stimuli paired at different intervals. Plot displays results for various pooled neurons ($n = 10$; mean ± SD).
remaining cases (44%, 4 of 9) showed no change at any time-interval (not shown). Interaction between cortical inputs occurred during a narrow time window because after 50 ms, the response had recovered control values (plot in Fig. 3A). Generally, cortico-cortical responses were monosynaptic, as revealed by their short and stable latencies (1.8 ± 0.5 ms, n = 10) as well as time to peak (8.0 ± 3.2 ms, n = 10).

On the other hand, the facilitation of the second response elicited by paired thalamocortical volleys was maximal at time intervals of 60–100 ms, but this potentiation affected the second component of the biphasic EPSP, whereas the early EPSP was diminished (Fig. 3B). Whereas the early EPSP (arrowhead a in Fig. 3B) was of short latency (3.5 ± 1 ms) and the time to peak was 8.8 ± 1.1 ms, the second EPSP (arrowhead b in Fig. 3B) had longer latency and prolonged time to peak (18.4 ± 0.9 ms). It is known that the second component follows by ~3 ms the low-threshold spike-bursts in thalamocortical neurons during augmenting responses elicited by rhythmic stimuli at 7–15 Hz (Steriade et al. 1998).

Interactions between cortical and thalamic synaptic inputs onto cortical neurons

In 90% of cases, and contrasting with data on homosynaptic facilitation, synaptic responses were decreased by interacting cortical with thalamic stimulis that elicited EPSPs in target cortical cells. Thus 18 of 20 neurons tested with cortical CS preceding thalamic TS at different interstimuli intervals (ISIs) showed decreased EPSPs (the remaining 2 neurons did not display changes in EPSPs’ amplitudes). And, 15 of 17 neurons tested with the reversed interaction, namely, thalamic CS preceding cortical TS, similarly exhibited decreased synaptic excitability (1 neuron showed facilitation and the excitability of the remaining one was unaffected).

Figure 4 illustrates typical examples of such interactions in two cortical neurons from area 4. The two plots in Fig. 5 show pooled responses resulting from cortical-thalamic and thalamic-cortical CS-TS interactions in 10 cortical neurons. Changes in synaptic responses were determined by measuring the amplitudes and area of depolarization of EPSPs (see Fig. 4A). The neuron depicted in Fig. 4A, with CS-TS trials between cortical and thalamic volleys delivered at ISIs between 10 and 120 ms, showed slightly more than 40% decrease in EPSP’s amplitude at 10 ms and progressively lower values of reduced response until recovery took place at 120 ms. The area of depolarization showed a similar curve, while full recovery occurred earlier, at ~80 ms. Testing with reversed stimuli (Fig. 4B), namely, CS-TS trials between thalamic and cortical stimuli, showed that maximal reduction in the cortically evoked EPSP was at an ISI of 20 ms, and recovery took place at ~70 ms, while the
The evolution of changes in the depolarization area was quasi-identical to that shown in the preceding panel (Fig. 4). These changes are supported by changes in EPSPs’ amplitude and depolarization area, resulting from pooled neuronal responses (n/1100510) with the two types of CS-TS trials, cortical and thalamic as well as thalamic and cortical (Fig. 5).

Relations between decreased responses in heterosynaptic interactions and changes in input resistance

In 15 neurons, we examined the relations between changes in synaptic excitability during PPS and the apparent $R_{in}$. All five neurons tested with thalamic-cortical paired stimuli showed a decreased $R_{in}$, the temporal evolution of which matched the depressed amplitudes of EPSPs evoked by the cortical TS. On the other hand, in 5 of 10 neurons tested with cortical-thalamic paired stimuli, decreased $R_{in}$ was observed, whereas the decreased amplitude and depolarization area of thalamically evoked EPSPs were the same as mentioned in the preceding section. These data are exemplified in the following text.

Figure 6 depicts a corticothalamic neuron that displayed, after antidromic invasion by stimulating the thalamus (see expanded identification in inset of A), EPSPs that occasionally triggered action potentials. In the same neuron, cortical stimulation elicited EPSPs. The amplitude of cortical (TS)-evoked EPSP underwent maximal decrease at an interval of 10 ms and fully recovered at 50 ms after the CS delivered to the thalamic LP nucleus. The changes in $R_{in}$ paralleled that of EPSP’s decrease. Virtually identical aspects were seen in the other four neurons investigated with thalamic-cortical paired stimuli.

One of the five neurons in which the reversed interaction (cortical-thalamic) was used, and the decreased EPSP’s amplitude was not associated with diminished $R_{in}$ is shown in Fig. 7. Although the decreased amplitude and depolarization area of the thalamic-evoked EPSP was comparable to that seen in the preceding figure, no concomitant changes in $R_{in}$ were detected in this and the other four neurons belonging to the same category.
Cortical stimulation decreases firing in thalamic relay cells and induces disfacilitation in the feedback thalamocortical pathway

Although corticothalamic projections use glutamate as neurotransmitter that excites both thalamic reticular and thalamocortical neurons, electrical stimuli applied to neocortex or naturally synchronous volleys fired by cortical neurons during slow-wave sleep give rise to powerful excitation in GABAergic reticular neurons that, in turn, produces overwhelming inhibition of target thalamocortical neurons associated with rhythmic IPSP-rebound spindle sequence (see Fig. 1 in Steriade 2000). We investigated the effects of corticothalamic volleys on thalamocortical neurons ($n = 6$) for possible answers to the question of decreased synaptic responses in the cortex in the absence of changes in $R_{in}$ (see Fig. 7).

The intrinsic excitability of a thalamocortical neuron and the effect of corticothalamic volleys on its firing ability are illustrated in Fig. 8. Figure 8A, inset, shows two of the major intrinsic properties of such neurons: hyperpolarizing current steps produced a depolarizing sag leading to a low-threshold spike-burst (reviewed in chapt. 5 of Steriade et al. 1997). The cortical stimulus induced an early excitation, followed by slight but long-lasting (90 ms) hyperpolarization associated with silenced firing, whereas thalamic stimulus produced early synaptic excitation giving rise to action potentials ($B$). Preceding thalamic by cortical volleys at different ISIs led to 50–60% reduction in the firing probability of thalamocortical neuron, which lasted for 40 ms and progressively recovered control values ($C$ and $D$). The time course of the reduction in firing probability of the thalamocortical neurons was similar to the decrease of EPSPs of cortical neurons (see Figs. 4, 5, and 7).
Similar effects, consisting of abolishing or reduction of the firing probability of thalamocortical cells, were observed during cortical-evoked rhythmic IPSPs of spindle sequences \( n = 3 \). However, in such instances the time course of the effect was much longer, lasting for the entire duration of the spindle sequence (Fig. 9). A thalamic neuron displayed antidromic activation (arrow in Fig. 9A) followed by a spindle sequence. In the same neuron, thalamic-evoked EPSPs invariably leading to single action potentials (top right) were transformed into subthreshold EPSPs at ISIs ≤ 0.8 s after the onset of the cortical-evoked spindle (Fig. 9B). The same EPSP was able to elicit a low-threshold rebound spike-burst toward the end of the spindle (ISI: 1.1 s) even when the membrane potential was not significantly different, and recovered the control pattern only after cessation of spindles (ISI: 1.5 s). A summary of this temporal succession is shown in Fig. 9C.

**DISCUSSION**

Our data show that PPS of intracortical pathways produced a variety of results, including facilitation, depression, and no change; PPS of thalamocortical pathways produced compound responses with the early component being depressed and the second one giving rise to incremental responses; at variance with these results using responses in homosynaptic circuits, interactions between heterosynaptic (cortical and thalamic or thalamic and cortical volleys) produced decreased peak amplitudes and depolarization area of TS-evoked EPSP with maximal effect at ~10 ms and lasting from 60 to 100 ms; all neurons tested with thalamic-cortical stimuli showed decreased \( R \) in the time course of which paralleled that of decreased synaptic excitability, whereas only half of neurons tested with cortical-thalamic stimuli displayed changes in \( R \) in; and firing probability of thalamic relay neurons was dramatically reduced

**FIG. 9.** Evolution of Cx-induced decreased excitability of antidromically identified thalamocortical neuron during spindle sequence elicited by Cx stimulus. Recording and stimulation within VL nucleus. Cx stimulus applied to area 4. A: spindle sequence elicited by Cx stimulus. Insets: antidromic invasion of VL neuron from area 4 (left) and Th-induced EPSP leading to action potential in VL neuron (right). B: Th-evoked EPSPs at different ISI after the onset of spindle sequence (0.3, 0.8, 1.1, and 1.5 s), as indicated with arrows in the preceding depicted (minimized) spindles). Note abolition of action potential at 0.3 and 0.8 s (evoked in A), rebound low-threshold spike-burst at 1.1 s (the end of spindle), and recovery of the control response with single action potential at 1.5 s (after cessation of spindle sequence). C: plot showing the probability of single spike (spike) and low-threshold spike (LTS) at different time intervals after a cortical stimulus.
for ~100 ms after cortical stimuli; this may induce disfacilitation in cortical networks and account for those cases in which decreased excitability was not associated with decreased Rm.

The present in vivo intracellular study was performed on cortical neurons driven by both cortical and thalamic inputs. Synaptic responses were evoked by stimulation of either cortical local areas or related thalamic nuclei. Generally, such responses were short-latency, monosynaptic EPSPs, in view of their short and invariant latency. The EPSPs evoked in cortical neurons by stimulation of cortical pathways in vivo or in vitro are commonly followed by a long-lasting inhibition, resulting from fast and slow inhibitory components that have been attributed to inhibitory GABAergic neurons. In the present experiments, low-intensity stimulation allowed cortical stimuli in most cases not to engage inhibitory networks because no IPSP activation was seen during or after the repolarizing phase of the initial EPSP (Figs. 1, 4, and 6); even though in those cases, resting conditions were quite hyperpolarized (Vm < −73 mV), identification of the response by changing the Vm showed the absence of inhibitory components in such cases. However, in other cases, an EPSP-IPSP sequence was activated, characteristic of cortical networks (Fig. 2C). Thalamic volleys were efficient in triggering a simple or composite EPSP, which was commonly followed by a rebound after 100–150 ms (Fig. 3B) that could occasionally develop into a spindle sequence. However, the time scale of that process (>100 ms) was very different from the short time reported here for interactions between CR and TR.

Facilitation or depression of cortical synaptic responses are thought to be due to calcium-dependent changes in the probability of transmitter release, observed at both excitatory and inhibitory synapses (Fisher et al., 1997). In the present study, PPS of intracortical pathways induced a variety of results, including facilitation, depression, or no change that can be explained in terms of the heterogeneous release probability at involved synapses in the cortex. In fact, it has been proposed that the release probability is the main determining factor for the direction of short-term plasticity, synapses with low release probability displaying predominantly facilitation and high probability synapses exhibiting predominantly depression (Thomson 2000; Thomson et al. 1995). The main result of PPS in thalamocortical pathway was depression of the initial component of EPSP; this may be similar to the heterosynaptic effect produced by conditioning thalamic volleys on cortically evoked responses. On the other hand, a progressive and higher facilitation was seen at time intervals >60 ms that are explained by the mechanism of thalamocortical augmenting responses (Steriade et al. 1998). In fact, the results presented here showed for all cortical neurons stimulated from thalamic pathways maximal amplitude of the second EPSP at ~100 ms (105 ± 15 ms), consistent with stimulation within the frequency (10 Hz) of spindle waves, which is typically used for induced augmenting potentials. Rhythmic volleys produce augmenting responses during the pulse trains but also facilitation outlasting the stimulation period, and the self-sustained activity displays patterns and frequencies similar to those of evoked responses, reminiscent of “memory” processes in thalamocortical neuronal loops (Steriade 1999). Our results partially corroborate those in experiments with homosynaptic PPS visual cortex slices in which however depressed EPSPs were only elicited by stimuli that presumably elicited single-axon EPSPs but not with larger EPSPs that were facilitated by PPS (Volgushev et al. 1995).

While the majority of tested cortical neurons displayed the expected reduction in Rm that was associated with the depressed synaptic excitability, some thalamic neurons did not show such a decrease in Rm. In those cases, their disfacilitation could be invoked as cortical CS produced IPSPs in some cortical neurons that stopped firing and, consequently, no longer excited target thalamic relay neurons, thus creating a period of disfacilitation. This interpretation is congruent with our previous studies (Bazhenov et al. 1998; Timofeev and Steriade 1997; Timofeev et al. 1996) in which low-intensity prethalamic stimuli were unable to induce firing of thalamocortical neurons during periods of disfacilitation.

The present results have functional implications for understanding information processing during sensation of multiple qualities of the same object. In the visual system, the processing of one quality of information significantly diminishes or might even be lost if another quality of sensory information is simultaneously processed (Hills et al. 2002). Our data suggest that the primary source for that loss of information processing is due to active inhibition followed by a period of disfacilitation, and both these processes decrease the network ability to respond to incoming excitatory signals. It is likely that similar mechanisms would provide the neuronal basis for contrast discrimination and other phenomena involving responses of a large neuronal network.

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