Mechanisms of Within- and Cross-Modality Suppression in the Superior Colliculus

DANIEL C. KADUNCE, 1 J. WILLIAM VAUGHAN, 1 MARK T. WALLACE, 1 GYORGY BENEDEK, 2 AND BARRY E. STEIN 1

1 Department of Neurobiology and Anatomy, Bowman Gray School of Medicine, Wake Forest University, Winston-Salem, North Carolina; and 2 Department of Physiology, Albert Szent-Györgyi Medical University, H6720 Szeged, Hungary

Kadunce, Daniel C., J. William Vaughan, Mark T. Wallace, Gyorgy Benedek, and Barry E. Stein. Mechanisms of within- and cross-modality suppression in the superior colliculus. J. Neurophysiol. 78: 2834–2847, 1997. The present studies were initiated to explore the basis for the response suppression that occurs in cat superior colliculus (SC) neurons when two spatially disparate stimuli are presented simultaneously or in close temporal proximity to one another. Of specific interest was examining the possibility that suppressive regions border the receptive fields (RFs) of unimodal and multisensory SC neurons and, when activated, degrade the neuron’s responses to excitatory stimuli. Both within- and cross-modality effects were examined. An example of the former is when a response to a visual stimulus within its RF is suppressed by a second visual stimulus outside the RF. An example of the latter is when the response to a visual stimulus within the visual RF is suppressed when a stimulus from a different modality (e.g., auditory) is presented outside its (i.e., auditory) RF. Suppressive regions were found bordering visual, auditory, and somatosensory RFs. Despite significant modality-specific differences in the incidence and effectiveness of these regions, they were generally quite potent regardless of the modality. In the vast majority (85%) of cases, responses to the excitatory stimulus were degraded by ≥50% by simultaneously stimulating the suppressive region. Contrary to expectations and previous speculations, the effects of activating these suppressive regions were quite specific. Thus powerful within-modality suppression could be demonstrated in many multisensory neurons in which cross-modality suppression could not be generated. However, the reverse was not true. If an extra-RF stimulus inhibited center responses to stimuli of a different modality, it also would suppress center responses to stimuli of its own modality. Thus when cross-modality suppression was demonstrated, it was always accompanied by within-modality suppression. These observations suggest that separate mechanisms underlie within- and cross-modality suppression in the SC. Because some modality-specific tectopetal structures contain neurons with suppressive regions bordering their RFs, the within-modality suppression observed in the SC may reflect interactions taking place at the level of one input channel. However, the presence of modality-specific suppression at the level of one input channel would have no effect on the excitation initiated via another input channel. Given the modality-specificity of tectopetal inputs, it appears that cross-modality interactions require the convergence of two or more modality-specific inputs onto the same SC neuron and that the expression of these interactions depends on the internal circuitry of the SC. This allows a cross-modality suppressive signal to be nonspecific and to degrade any and all of the neuron’s excitatory inputs.

INTRODUCTION

The role of the superior colliculus (SC) in attentive and orientation behaviors is known to be facilitated markedly by its ability to synthesize information from different sensory channels. Visual, auditory, and somatosensory afferents converge in its deeper layers, where a majority of neurons are classified as “multisensory” because they can respond to inputs from more than one sensory modality (Stein and Meredith 1993). However, these multisensory neurons do far more than pool information from multiple modalities; they transform this information into an integrated product that no longer resembles the individual unimodal inputs or their sum. Thus stimulus combinations often result in substantial enhancements in the activity of multisensory SC neurons (King and Palmer 1985; Meredith and Stein 1986a; Wallace et al. 1996) and the behaviors to which they contribute (Frens et al. 1995; Stein et al. 1989; Wilkinson et al. 1996).

For example, a weak visual or auditory cue, when presented alone, may have very little influence on the activity of SC neurons and a low probability of effecting SC-mediated overt behavior. However, the combination of two weak unimodal cues at the same or similar locations in space often results in a vigorous neuronal response as well as a high probability of evoking a coordinated orientation response (e.g., gaze shift). Furthermore, reaction times in response to stimulus combinations are generally far shorter than they are to either individual cue (Frens et al. 1995; Hughes et al. 1994; Lee et al. 1991; Perrott et al. 1990; Stein et al. 1989; Zahn et al. 1978).

Multisensory depression, which has received considerably less attention than multisensory enhancement, typically is seen when two stimuli are presented in spatial disparity. In these cases, a vigorous response to a unimodal stimulus is lessened substantially or even eliminated by the concurrent presentation of a stimulus from another modality at a different spatial position (Meredith and Stein 1986b, 1996; Wallace et al. 1996). Multisensory depression can be evoked in many of the same neurons that exhibit multisensory enhancement and is paralleled by a similar degradation in overt behaviors (Stein et al. 1989; Wilkinson et al. 1996). The diametrically opposed effects of two (or more) modality-specific stimuli on multisensory SC neurons and overt behavior have been explained on the basis of their spatial relationships to one another and to their respective receptive fields (RFs) (Meredith and Stein 1996; Stein and Meredith 1993).

Each multisensory neuron has multiple RFs, one for each modality to which it responds. The RFs of multisensory SC neurons are in topographic register such that they overlap one another (Meredith and Stein 1996; Stein et al. 1976a).
As a consequence of this organization, two different sensory stimuli that are derived from the same event and thus originate from the same location in space, will fall within the respective RFs of the same multisensory SC neuron. The effect of this combination is almost always an enhancement of the neuron’s response beyond that elicited by either stimulus alone and often beyond the sum of the effects of the two individual stimuli. In contrast, when one of the two stimuli is moved so that it is outside its RF, and thus spatially disparate from the other within-field stimulus (as when two stimuli are unrelated), either no integration occurs or the response to the within-field stimulus is markedly depressed (Meredith and Stein 1986b; Wallace et al. 1993).

Under such circumstances, multisensory enhancement is explained by the synergistic interaction of two excitatory inputs; this interaction increases stimulus salience. It has been assumed that multisensory depression derives from a parallel interaction: an excitatory input from within one RF is antagonized by an inhibitory input derived from stimulation of regions beyond the borders of the RF of the other. The presence of an inhibitory or “suppressive” region is inferred from the results of “within-modality” tests in which two stimuli from the same modality are paired, one within the RF and one outside its excitatory borders. If the pairing results in a significant reduction in the response generated by the within-field stimulus, a suppressive region is assumed to be present (Clemo and Stein 1991; Gordon 1973; Knudsen and Konishi 1978; Pinter and Harris 1981).

The assumption from cross-modality studies has been that suppressive regions are present outside the modality-specific RFs of multisensory SC neurons and are nonselective. On the basis of this assumption, activation of any of the suppressive regions of such a neuron should inhibit excitation from all stimuli regardless of whether they are from the same modality or a different modality (Meredith and Stein 1996; Stein and Meredith 1993). Yet, comparatively little is known about suppressive regions in the multisensory aspects of the SC. The present experiments were conducted to examine and compare these regions in the visual, auditory, and somatosensory RFs of unimodal and multisensory SC neurons. Specifically, the objectives were to determine the comparative incidence and effectiveness of such regions and, most importantly in the present context, to determine whether the inhibitory input from a suppressive region has nonselective effects. An abstract describing some of these data has been published (Kadunce et al. 1994).

**Methods**

All surgery was conducted using aseptic techniques and was in accordance with the Guide for Care and Use of Laboratory Animals (National Institutes of Health Publication 86-23) and an approved Animal Care and Use Committee protocol from Bowman Gray School of Medicine/Wake Forest University. Many of these procedures are similar to those described previously (Meredith and Stein 1986a; Wallace et al. 1993).

**Surgical procedures**

Each cat \( (n = 16) \) was anesthetized with ketamine hydrochloride (30 mg/kg im) and placed into a stereotaxic headholder. The animal was maintained for the duration of surgery with 2% halothane. A recording well, with which the head could be held during later recording procedures, was positioned stereotaxically over a craniotomy centered above the coordinates of the SC. The well was held in place with skull screws and dental acrylic (McHaffie and Stein 1983). After surgery, the animal was allowed to recover from anesthesia, returned to its home cage, and treated with postsurgical analgesics (butorphanol tartrate, 0.25 mg/kg im) as needed. Animals were allowed a 7- to 10-day recovery period before the first recording session.

**Recording procedures**

The animal was anesthetized with a combination of ketamine hydrochloride (30 mg/kg im) and acepromazine maleate (3–5 mg/kg im). Its head was secured by attaching the recording well to a mount that held the head without obstructing its eyes, ears, or body surface. The trachea was intubated through the mouth, and the saphenous vein was cannulated. Paralysis was induced by the intravenous administration of pancuronium bromide (0.3–0.5 mg/kg, initial dose). For the duration of the recording session, the animal was respired artificially, and its expiratory CO\(_2\) was monitored and maintained between 3.8 and 4.5%. Maintenance doses of anesthetic (ketamine HCl 10–15 mg·kg\(^{-1}\)·h\(^{-1}\) and paralytic (pancuronium bromide 0.6 mg·kg\(^{-1}\)·h\(^{-1}\)) were provided via a constant intravenous infusion, and body temperature was maintained at 37–38°C with a heating pad.

The contralateral pupil was dilated with a 1% solution of ophthalmic atropine, and the image of its optic disk was back-projected onto a translucent 92-cm diam Plexiglas hemisphere positioned 46 cm from the eye. A contact lens was applied to the contralateral eye to prevent corneal drying and to correct for retinoscopically determined refractive errors. An opaque lens was applied to the ipsilateral eye. Thus all visual testing was monocular. A hoop, on which auditory speakers could be moved, was positioned around the animal such that the axis of the rotation of the hoop was aligned with the animal’s interaural axis. The speakers were positioned 15 cm from each ear.

Single-neuron extracellular recordings were carried out with parylene-insulated tungsten microelectrodes (impedance >1 MΩ at 1 kHz). The electrode was advanced through the SC using a hydraulic micromanipulator. At the end of the recording session, the infusion of anesthetics and paralytics was discontinued. When stable respiration was reinstated and the animal was mobile, it was returned to its home cage.

**Receptive field mapping**

Visual RFs of the contralateral eye were mapped directly on the translucent hemisphere using moving and flashing spots and bars of light generated by a hand-held pantoScope. The borders of each RF were determined by moving the optimum visual stimulus from the periphery inward from all directions until an enclosed responsive area was delimited. Auditory RFs were mapped using broadband sound bursts (20–20,000 Hz) delivered from moveable speakers on the auditory hoop. Azimuthal positions first were mapped with the speakers along the horizontal meridian of auditory space. The hoop then was rotated around the interaural axis to map the elevation component of the RFs. Auditory RFs were defined on the basis of a significant difference above background activity (Meredith and Stein 1986a). Somatosensory RFs were mapped with camel’s hair brushes. The amplitude and wave shape of each stimulus were unrelated, either no integration occurs or the response to the within-field stimulus is markedly depressed (Meredith and Stein 1986a,b; Wallace et al. 1994). Quality assessment of neuronal properties
always was established first to determine the nature of the stimuli to be used for quantitative analysis.

All RFs were plotted on standardized representations of visual, auditory, and somatosensory space (Stein and Meredith 1993). The location of each RF was correlated with the position of the neuron within the structure based on histological reconstructions of electrode penetrations (see further text).

**Sensory tests**

Reproducible, computer-controlled sensory stimuli were used for all quantitative tests. The onset, duration, and physical parameters of the visual, auditory, and somatosensory stimuli were controlled independently.

**VISUAL RESPONSES.** Visual responses were studied using moving and stationary flashed slits, bars, and spots of light of various sizes the onset of which were computer controlled. The stimuli were generated from a Prado projector equipped with adjustable diaphragms. The stimuli (53 cd/m² against a background of 2.7 cd/m²) were projected through a rotating prism and reflected from a galvanometer-driven mirror onto the translucent hemisphere. Using this system, stimulus amplitude could be varied from 1 to 90° and stimulus velocity could be varied from 2.7 to 555°/s. Stimuli could be moved in any direction and an electronic shutter aided in the presentation of stationary flashed stimuli in various positions within and outside of the RF. A beam-splitting prism allowed two identical visual stimuli to be presented simultaneously in two separate locations (i.e., 1 inside the RF and 1 in the surrounding region).

**SOMATOSENSORY RESPONSES.** Somatosensory responses were studied using computer-controlled mechanical stimuli delivered via a mechanical probe attached to a moving-coil vibrator (Ling 102A shaker). The tip of the probe was loaded against the hair or skin. Stimulation typically consisted of an initial displacement, a plateau phase, and a return to the “rest” position. The excursion amplitude could vary from 0.05 to 5.0 mm and could be presented at velocities of 15–420 mm/s. Two such probes were oriented so that identical stimuli could be delivered simultaneously within and outside the RF.

**AUDITORY RESPONSES.** Auditory responses were categorized with computer-controlled broadband (20–20,000 Hz) sound bursts delivered “free-field” from a set of hoop-mounted speakers positioned 15 cm from each ear. The duration of the auditory stimuli varied from 50 to 150 ms at intensities of 50–70 dB SPL.

A neuron was classified as multisensory if it responded to more than one sensory modality or if a stimulus in one sensory modality produced a significant ($P < 0.05$, 1-tailed Student’s $t$-test) change in the neuron’s responses to a stimulus in a second modality.

**Data acquisition and analysis**

Neuronal responses to each modality-specific stimulus (e.g., visual alone, auditory alone), each unimodal stimulus pair (e.g., auditory-auditory), and each multisensory stimulus combination (e.g., visual-auditory) were assessed by determining the number of impulses evoked and by calculating the mean numbers of impulses, standard deviations, and standard errors of the mean. The response duration (i.e., number of spikes to be counted for analysis) of each neuron to an excitatory stimulus was calculated from the time of stimulus onset to the period of time at which the level of activity of the response was not significantly different from the prestimulus activity of the cell. This same duration was used when testing for suppression effects. For these tests, each unimodal stimulus and stimulus combination was presented 8–16 times. Trials were interleaved randomly and presented at 12- to 20-s intertrial intervals to avoid response habituation. Generally, when testing for multisensory interactions, stimulus combinations were presented simultaneously or within 20–200 ms of one another. Within-modality suppressive interactions were tested using simultaneous stimuli. Cross-modality suppression was tested by timing the stimuli so that their input latencies were matched. To temporally align an excitatory response with a suppressive input, it was necessary to determine the suppressive (i.e., inhibitory) latency. Although latencies varied markedly among modalities, analyses in each modality indicated that the latency to interrupt the firing of a given neuron was approximated readily by the latency of that neuron’s excitatory response to the same stimulus when it was centered within the RF. Therefore excitatory latencies were later used to temporally align stimuli during testing.

Other than its position in space, the inhibitory stimulus used for any quantitative test of within-modality suppression was identical to the excitatory stimulus. The criterion for an inhibitory effect was a significant decrease ($P < 0.05$, 1-tailed Student’s $t$-test) in the response to the within-field stimulus. This was true for both within- and cross-modality suppression. The magnitude of within- and cross-modality suppression was calculated by the following formula

\[
\left( \frac{CM - SM}{SM} \right) \times 100 = \% \text{ interaction}
\]

where CM is the mean number of impulses evoked by the same stimulus in the presence of a second stimulus of either the same or different modality outside the RF and SM is the mean number of impulses evoked by the most effective single-modality stimulus.

**Histology and euthanasia**

During an electrode penetration, the depth of each neuron was recorded from the microdrive. In the final few experiments, a series of electrolytic lesions (10–12 μA; 12 s) were made at strategic locations, and at the end of the last experiment, the animal was euthanized (pentobarbital sodium, 100 mg/kg iv) and perfused transcardially with saline followed by 10% formalin. The midbrain was blocked stereotaxically, removed, and stored in sucrose overnight. Frozen sections (50-μm thickness) were taken in the coronal plane and were counterstained with cresyl violet to facilitate the distinction of laminar borders. The outline of the tissue, along with laminar boundaries and the positions of electrode tracks and lesions, were traced using a projection microscope.

**RESULTS**

A total of 162 sensory-responsive neurons in the deep (i.e., multisensory) layers of the SC were studied. Unimodal neurons accounted for 42% of the sample and multisensory neurons accounted for 58%. The specific unimodal and multisensory neuronal types that were encountered are presented in Fig. 1.

**Within-modality suppression**

In many cases, the excitatory response initiated by a stimulus centered within its RF was inhibited markedly by the presentation of a second stimulus from the same modality that was positioned beyond the border of the RF (Fig. 2). In the example shown in Fig. 2, a bar of light that moved through the most responsive portion of the RF evoked a train of impulses on almost every trial. However, when a second visual stimulus, presented outside the RF (in this case beyond its medial or nasal border), was paired with the within-field stimulus, the neuron’s response was diminished by 70%. Tests of the suppressive effects of stimuli beyond the
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The presence of a suppressive region beyond the borders of one of the RFs of a multisensory neuron was not a reliable predictor that the neuron’s other RFs also would have suppressive regions. It was, in fact, common to find multisensory neurons in which only the RF in one modality had an adjacent suppressive region, and in only 18% of bimodal (e.g., visual-auditory) neurons and 33% of trimodal (i.e., visual-auditory-somatosensory) neurons was more than one of the RFs bordered by a suppressive region.

For the majority (85%) of unimodal and multisensory neurons tested for within-modality suppression, the presentation of a stimulus within the suppressive region decreased the number of impulses evoked by the same stimulus presented concurrently within the RF by 50% (see Fig. 4). Modality, but not convergence type, was found to be the significant factor in determining the degree of within-modality response suppression. Post hoc analysis revealed that the magnitude of response suppression was lower for somatosensory-responsive neurons than for visual ($P < 0.04$) or auditory-responsive neurons ($P < 0.05$).

Suppressive regions were quite large and always enroached on the ipsilateral side. Like excitatory RFs, these suppressive regions also appeared to be spatially heterogeneous with the magnitude of suppression varying with location but usually being greatest from regions in the ipsilateral hemifield. Moreover, some neurons revealed a graded trend in the degree of suppression, with points near the RF border demonstrating only minimal response suppression and more eccentric regions demonstrating a much higher degree of response suppression. Although the absolute size of these suppressive regions was not determined in this study, in some neurons it was apparent that the suppressive region included all of space outside the RF.

Special concerns regarding within-modality suppression in auditory RFs

Previous psychophysical research has shown that the concurrent presentation of identical auditory stimuli from two locations can induce the perception of a “phantom” sound originating from an intermediate position between the two sources. This effect is known as summing localization (Yin 1994). This presents a problem in the current context. The degradation of a neuron’s response in the presence of a stimulus outside the RF might be the result of an apparent translocation of the effective sound source rather than a true inhibitory effect.

This possibility was examined in five neurons, and an illustrative example is shown in Fig. 5. First, the spatial response profile of the neuron was mapped quantitatively with a single speaker placed at various positions. Two speakers then were placed beyond the opposing RF borders ($-45^\circ$ and $+45^\circ$), and a paired stimulus was presented. The prediction based on summing localization is that a response should be elicited by stimulation of these two normally ineffective sites. Indeed, a response, albeit one much weaker than that predicted, was obtained in this example and in the other neurons examined.

In the example provided in Fig. 6, the greatest decrease
FIG. 2. Within-modality suppression in a unimodal neuron (visual). Stimuli were drifting bars of light the direction and excursion length of which are indicated (+). Receptive field (RF) of this neuron is plotted onto a standard representation of visual space. Horizontal and vertical lines depict the meridians, and each concentric circle represents 10°. A bar graph (bottom) summarizes the responses in the different test conditions and illustrates the magnitude of the within-modality suppression. When the visual stimulus (V) was placed within the RF of this neuron (top right), a vigorous response was evoked (top left). Response is illustrated in the raster display (each dot = 1 impulse, each row = 1 trial) and the peri-stimulus time histogram below it. In each case, the movement of the visual stimulus is depicted as a ramp above the raster and histogram displays. When the same visual stimulus (V') was presented outside the RF (middle), no change in activity was noted, but when the 2 stimuli were presented together (bottom), V' profoundly depressed responses to V. N, nasal; T, temporal; S, superior; I, inferior.

in the excitatory response was produced when the eccentric stimulus was furthest from the RF borders. These results are consistent with a large suppressive region the effectiveness of which increases with increasing distance from the border of the RF and with stimulus translocation toward a less effective portion of the RF. Thus for within-modality auditory tests, it was difficult to differentiate between the possibilities of a true suppressive region outside the RF and the effective translocation of the excitatory stimulus. Yet, as described below, no such ambiguity is seen in cases of cross-modality suppression.

Cross-modality suppression

Each category of multisensory neuron exhibited cross-modality suppression, and there were examples in which it could be generated with visual, auditory, and somatosensory stimuli presented outside of the RF. Nevertheless, this inhibi-
tion could be quite selective, and multisensory neurons demonstrated within-modality suppression far more frequently (69%) than they showed cross-modality suppression (20%). This is apparent in the visual-auditory example presented in Fig. 7. A stimulus within the visual suppressive region profoundly inhibited the excitatory visual stimulus yet had no significant influence on auditory-induced excitation.

Yet, when cross-modality suppression was present, it was generally quite powerful. In the example shown in Fig. 8A, an auditory stimulus presented outside of the RF border eliminated the neuron’s robust responses to a visual stimulus. In this particular example, only the auditory RF had a suppressive region. Such a unidirectional effect (e.g., an auditory stimulus inhibits visual excitation, but a visual stimulus does not inhibit auditory excitation) characterized 90% of the cases of cross-modality suppression.

It must be noted that when cross-modality suppression (e.g., auditory stimulus suppresses visual response) was demonstrated, the extra-RF stimulus was also capable of suppressing responses to excitatory stimuli from its own modality (e.g., auditory suppresses auditory; within-modality suppression). Thus in the example shown in Fig. 8A, the suppressive effect of the extra-RF auditory stimulus was evident not only on visual responses but on auditory responses as well (Fig. 8B). The generality of this observation held even for the comparatively rare examples of bidirectional cross-modality suppression, and one such example is provided in Fig. 9.

As was the case for within-modality suppression, the incidence of cross-modality suppression among multisensory neurons was significantly higher ($P < 0.03$) for the auditory modality (16/68, 24%) than for the visual (8/68, 12%) and somatosensory (3/23, 13%) modalities (see Fig. 10). Nevertheless, no statistically significant differences in the magnitude of response suppression were observed between within- and cross-modality suppression.

**DISCUSSION**

These experiments demonstrate that a substantial proportion of the auditory-, visual-, and somatosensory-responsive neurons in the deep SC are inhibited by stimuli presented outside their RF borders. A substantial percentage of both unimodal and multisensory neurons were found to have such suppressive regions. The incidence and magnitude of these suppressive regions differed considerably for different modalities, being most common and most powerful among auditory RFs and least common and least powerful among somatosensory RFs. Although the absolute number of RFs with suppressive regions is likely to be an underestimate (variations in the latency of the inhibitory and excitatory inputs for individual neurons might have produced mismatches that obscured inhibitory influences), the relative distributions of suppressive regions among modalities are likely to be reasonably accurate.

It is not yet clear why suppressive regions are so prevalent bordering auditory RFs, but the present observations are consistent with previous observations in the SC of cat (Stein and Meredith 1993) and monkey (Wallace et al. 1996). Perhaps these findings reflect a more prominent role for inhibitory circuits among auditory afferents to the SC. Indeed, inhibitory inputs from the ipsilateral ear are critical for the normal formation of auditory RFs in the SC (King 1993; Middlebrooks and Knudsen 1984; Wise and Irvine 1983, 1985).

The commonalities in RF organization and topography among the visual-, auditory-, and somatosensory-responsive neurons in the SC (Stein and Meredith 1993) lend credence to the idea that response suppression depends on a single, common element of RF construction: a suppressive region adjacent to the RF. The construction of such a suppressive region is quite straightforward for the visual and somatosensory modalities, where RFs represent a spatial reconstruction.
of the peripheral epithelium. Unfortunately, within-modality auditory suppression raises special concerns because of the computational nature of auditory RFs.

**Within-modality suppression among auditory neurons**

Unlike in the visual and somatosensory systems, the location of an auditory stimulus must be derived computationally by comparing the timing and intensity of the inputs arriving at the two ears (Boudreau and Tsuchitani 1968; Goldberg and Brown 1969; Rose et al. 1966). Given this, it has been postulated that manipulation of the timing of two free-field sounds originating from symmetric locations and of similar spectral content will bias judgments of the perceived location of the stimulus (Blauert 1983). Indeed, psychophysical experiments have shown that when subjects are presented with two similar sounds in quick succession (2–8 ms) and from different locations, they will perceive a single sound source the location of which is dominated by the location of the leading sound, i.e., the *precedence effect* (Haas 1951; Wallow et al. 1949). At interstimulus delays of <2 ms, a phantorn sound source is perceived the location of which is biased toward the leading speaker, and at simultaneity (as in the present experiments), it is perceived as being at a location between the two speakers. The latter effect is defined as *summing localization* (Blauert 1983), and its neurophysiological correlates now have been demonstrated in the inferior colliculus (Keller and Takahashi 1996; Yin 1994; Yin and Chan 1988).

The suppression seen in the within-modality auditory tests performed here could be the result of the presence of a true suppressive region outside the RF, summing localization, or some intermixing of these effects. Unfortunately, the cause of the suppression seen in these tests could not

**FIG. 5.** Two auditory stimuli, presented on opposite sides and outside of the RF, can interact to evoke excitation. In the center is the neuron’s RF (dark shading) plotted onto a representation of auditory space. Caudal halves of contralateral and ipsilateral auditory space are represented as half circles, which have been folded forward. Stimulus location is depicted by the speaker icons. Peristimulus time histograms show the responses of this neuron to the same auditory stimulus presented at different locations within and outside the RF. When 2 such auditory stimuli were positioned beyond the medial and lateral borders of the RF (where they were ineffective individually), their combined presentation produced a statistically significant (*P < 0.01*) response. This result is consistent with summing localization (see text).

**FIG. 6.** Suppressive region is heterogeneous. In this auditory-responsive neuron, a stimulus within the RF was paired with each of the stimulus locations outside the RF. Percentage decrement of the excitatory response is plotted at each position at which the auditory stimulus was presented in the suppressive region. Note that despite the statistically significant response depression at most points (*P < 0.05*), there is substantial variability in the magnitude of this effect.
be unequivocally determined. In each auditory-responsive neuron that was tested, the presentation of two stimuli on opposite sides and outside of the RF produced a response. Because neither of these stimuli was capable of eliciting a response when presented alone, these results are consistent with summing localization. Yet, the responses generated in this way were invariably weaker than predicted from summing localization alone (Yin 1994). They were substantially less vigorous than those that were evoked by a single stimulus at the midpoint between the two stimuli (i.e., the RF center) and far weaker than responses evoked at any position within the RF except its most peripheral border regions. It is quite possible that these observations reflect an intermixing of the consequences of simultaneously acti-
Cross-modality suppression is always linked to the presence of within-modality suppression. A: visual stimulus (V) in this visual-auditory neuron evoked a train of impulses when presented within its RF (top left), and the auditory stimulus (A') was without effect when presented outside the auditory RF (middle left). However, when the 2 stimuli were paired, the visual response was eliminated (bottom left), thereby indicating the presence of a suppressive region bordering the auditory RF. In this example, these effects were specific to the auditory RF of this bimodal neuron. Note the absence of such effects (right column) when equivalent visual tests were performed. B: presence of within-modality suppression in the auditory modality was confirmed by pairing auditory stimuli within and outside the auditory RF (left). Within-modality suppression was observed in every case in which cross-modality suppression was demonstrated. Note, however, the absence of within-modality suppression in this neuron’s visual responses (right).

Nevertheless, it is the presence of cross-modality inhibitory influences that provides the most direct evidence for the presence of a suppressive region bordering auditory RFs because these observations are not confounded by the possibility of summing localization. Under these circumstances, the inhibitory effects of an eccentric auditory stimulus on non-auditory responses were very much like the cross-modality inhibitory effects produced by eccentric visual and somatosensory stimuli.
Construction of suppressive regions

A consistent observation in each of the modalities examined was that stimulation of the suppressive region could produce within-modality suppression without producing cross-modality suppression. Such a decoupling is not consistent with the previously proposed model to explain the suppressive effects of eccentric stimuli in SC neurons (Meredith and Stein 1996; Stein and Meredith 1993). In such a model, the region adjacent to the RF was believed to produce a nonspecific inhibitory signal that degrades excitatory inputs from all afferent sources. The present observations, however, demonstrate that in the majority of cases, the inhibition evoked from a suppressive region is modality specific.

One possibility is that neurons exhibiting only within-modality suppression are reflecting a functional property of the modality-specific pathways that project to the SC, whereas cross-modality suppression reflects an inhibitory circuit intrinsic to the SC. Although there are many unimodal cortical and subcortical areas that project to the multisensory
FIG. 9. Bidirectional cross-modality suppression. A: in this auditory-somatosensory neuron, a somatosensory stimulus (S) evoked a reliable response (top left schematic) when presented within its RF. An auditory stimulus (A'), placed outside its RF, evoked no response from the neuron (middle left schematic). When the somatosensory and auditory stimuli were paired (bottom left schematic), a statistically significant (38%) reduction in the neuron's response to the somatosensory stimulus was apparent. Similarly, a somatosensory stimulus (S'), placed outside its RF borders, substantially reduced the neuron's response to an excitatory auditory stimulus (A) (right column). B: presence of within-modality suppression in the auditory (left) and somatosensory (right) modalities was confirmed with within-modality tests.
layers of the SC (Edwards et al. 1979; Huerta and Harting 1984), in only a few cases have these afferent sources been examined for the presence of within-modality suppression. Nonetheless, these few observations are consistent with the above postulate. For example, neurons in the postero-lateral lateral suprasylvian (PLLS) cortex, a major source of visual input to the multisensory layers of the SC (Kawamura et al. 1974), have large RFs with a center/surround organization (von Grunau et al. 1987). Center/surround antagonism is also a feature of neurons in the ascending auditory tectopetal pathways (i.e., inferior colliculus) in the barn owl (Knudsen and Konishi 1978).

Multisensory neurons are constructed within the SC by the convergence of unimodal afferents (Wallace et al. 1993). As a consequence of this, the cross-modality suppressive interactions observed in the present studies are likely to be
depend on mechanisms intrinsic to the SC. Yet, by whatever mechanisms this physiological property is achieved, its presence is likely to have as much of an impact on overt behavior as is the better known case of cross-modality enhancement. In the latter case, spatially coincident combinations of different modality-specific cues (e.g., visual and auditory) do not only enhance the responses of individual multisensory SC neurons, but enhance the overt attentive and orientation responses these neurons are believed to mediate (see Stein et al. 1989; Wallace et al. 1993). Degrading the responses of these neurons with spatially disparate stimuli, produces the opposite effect, an inhibition of SC-mediated attentive and orientation responses.

Although the nature of the intrinsic circuitry that gives rise to cross-modality suppressive interactions remains unclear, recent evidence suggests that afferents from the anterior ectosylvian sulcus (AES) are involved. The AES is a rich source of projections to the multisensory layers of the SC (Stein et al. 1983) and is composed of three distinct sensory representations: a somatosensory area, SIV (Clemo and Stein 1982) a visual area, AEV (Mucke et al. 1982; Olson and Graybiel 1983), and an auditory area, Field AES (Clarey and Irvine 1986). Unimodal inputs from each of these subregions converge on SC neurons in various combinations (Wallace et al. 1993). If their influences are removed by temporarily deactivating the AES, SC neurons no longer exhibit their characteristic response enhancement to multisensory stimuli (Wallace and Stein 1994). Although the effects of AES deactivation on suppressive interactions have not been studied physiologically, the results of behavioral experiments are consistent with the postulate that multisensory enhancement and depression depend on the same afferent convergence patterns. Thus animals trained in SC-mediated orientation tasks have been shown to have both multisensory enhancements and depressions compromised by AES deactivation (Wilkinson et al. 1996). The key to the remarkable ability of AES corticocortical afferents to support multisensory integration in SC neurons remains elusive. However, one recent suggestion is that the answer lies in its unique pattern of dendritic contacts on multisensory SC neurons (Harting et al. 1997).

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Address for reprint requests: B. E. Stein, Dept. of Neurobiology and Anatomy, Bowman Gray School of Medicine, Wake Forest University, Medical Center Blvd., Winston-Salem, NC 27157.

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