Chapter Twenty-Two

Brain Mechanisms for Synthesizing Information From Different Sensory Modalities[1]

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Perceptual and Behavioral Evidence for Interactions Among the Senses

Sensory Systems Function in Parallel

Decoding and interpreting incoming sensory information are among the brain's most important tasks. These are ongoing processes that make it possible for us not only to know the world in which we live, but to plan and initiate behaviors that are appropriate for a particular circumstance. Because survival depends on the speed and accuracy of such processes, it is not surprising to find that encoding, decoding, and evaluating sensory information have been powerful driving forces in evolution. Consequently, extant organisms have an impressive array of specialized sensory systems.

Having multiple sensory systems provides significant benefits; it allows an organism to monitor simultaneously a host of environmental cues, and also provides a means of substituting one sensory system for another when necessary (e.g., hearing and/or touch can substitute for vision in the dark). The ability to monitor and process multiple sensory cues in "parallel" not only increases the likelihood that a given stimulus will be detected, but, because the information carried along each sensory channel reflects a different feature of that stimulus, it increases the chances that the stimulus will be properly identified. Stimuli that may be difficult to distinguish by means of a single sensory modality (e.g., how they look) can become quite distinct via information from another modality (how they sound or feel). Indeed, we deal so successfully with sensory cues that we have come to have great faith in the ability of our sensory systems to distinguish among important stimuli and provide us with impressions that are accurate reflections of the physical world. So, it is sometimes amusing and occasionally distressing to discover that these perceptual judgments are relative rather than absolute, and that they can be radically different in different contexts. For example, manipulating context by altering perspective and contrast in painting, photography, and cinematography can give apparent depth to a flat surface, make small objects appear large, or large objects appear small, or make objects appear far away when they are really very near, or the reverse. Yet, despite our extensive experience and sophistication with these effects, visual illusions continue to delight us. Apparently, understanding the concept of an illusion does not mitigate the surprise induced by experiencing it.

The relative nature of a sensory judgment is also evident when dealing with combinations

of cues from different modalities. There is, in fact, a rather rich literature filled with examples in which the presence of a cue from one modality can substantially alter perceptual judgments of cues in other modalities. For example, the presence of a visual cue can substantially change a subject's perception of proprioceptive and auditory cues, and proprioceptive cues can alter the subject's perception of where an auditory cue is located (Held, 1955; Pick, Warren, & Hay, 1969; Shelton & Searle, 1980; Thurlow & Rosenthal, 1976; Warren, Welch, & McCarthy, 1981; Welch & Warren, 1980). These cross-modality perceptual effects can be quite potent. Thus, when watching some of the new films on Imax or in a planetarium (e.g., illustrating flight through mountainous terrain or through a starry night) the viewer is apt to experience many of the same vestibular and gastrointestinal sensations that make clear air turbulence and amusement park rides so delightful.

Still, our readiness to acknowledge that judgments of one sensory cue can be altered by another sensory cue comes most easily when the effects are restricted to the same modality, as when the appearance of a visual cue is altered by the visual background against which it is judged, or when the pitch or intensity of a sound seems different when linked to other sounds. The possibility that seemingly "irrelevant" cues, such as those derived from modalities other than the one being evaluated, can substantially alter its perception is less obvious. Although cross-modality influences on perception and behavior are as common as their within-modality counterparts, the fact that a brief sound can strongly alter one's judgment of light intensity (Stein, London, Wilkinson, & Price, 1996) is generally met with greater surprise than the observation that one looks slimmer wearing vertical rather than horizontal stripes.

Sensory Systems Also Function in an Interdependent Fashion

The commonly held impression that sensory systems are unlikely to have an ongoing dialogue with one another may be due, in part, to the fact that the senses have evolved unique subjective impressions, or qualia, for which there are no cross-modality equivalents. Tickle and itch are specific to the somatosensory system, hue to the visual system, and pitch to the auditory system. Therefore, it seems logical that to maintain the modality-specificity of these qualia, the brain must avoid cross-talk between the senses – an issue that harkens back to Johannes Muller's concept that each modality has "specific nerve energies" associated with it, and that these energies provide the basis for their subjective impressions. A modern parallel might be found in the concept of "labeled lines" of information in the central nervous system. However, the different senses not only affect one another quite regularly, but frequently do so with unexpected consequences.

The influences of different sensory modalities on one another are quite obvious in a host of cross-modality illusions, and the reader is referred to Welch and Warren (1986) and Stein and Meredith (1993) for more in-depth discussions. However, consideration of a few cross-modality illusions here is helpful to underscore their potency. The so-called "McGurk Effect" (McGurk & MacDonald, 1976) is an excellent example, and one that is very popular among speech professionals because it shows how strongly a discordant visual signal (i.e., lip movements) can influence the perception of speech. If one hears the word "bows," but sees the mouth form the word "goes," the perception is "doze" or "those,"

percepts that match neither of the two inputs, but rather reflect their synthesis (see Figure 16.5c, p. 510). Similarly, "ga" and "ba" are usually combined to form the percept "da."

While cross-modality influences like the McGurk Effect change (or abolish) the perceived meaning of the signal, others can cause a misperception of its location. For example, a dynamic (e.g., moving) visual cue can cause an observer to believe that an accompanying auditory cue originating from a different location actually comes from the same location as the visual stimulus. For obvious reasons illusions of this type are categorized as examples of the "ventriloquism effect" (Howard & Templeton, 1966). They are also far more common than one might first imagine, and explain why, when watching a movie, speech seems to be emanating from the actors, even as they are moving from one end of the screen to the other, rather than from speakers that are far away and fixed in space. In similar fashion, tactile and/or vestibular cues can lead us to mislocalize visual and auditory cues (Biguer, Donaldson, Hein, & Jeannerod, 1988; Clark & Graybiel, 1966; Graybiel & Niven, 1951; Lackner, 1974a,1974b; Roll, Velay, & Roll, 1991; Wade & Day, 1968).

Cross-modality illusions are simply an extension of the "normal" perceptions produced by combining sensory cues from different modalities that occur close together in space and time. They depend on a critical degree of distortion in the spatial and/or temporal relationships among sensory cues that normally originate from a common event. A larger distortion would lead to an unambiguous perception that these cues originate from separate events, and a smaller distortion would be lost within the "noise" of normal cross-modality coherence. A key factor in the discussions of multisensory integration is that these distortions are not generally provided by cues derived from the same event.

The normal close temporal and spatial linkage between sensory stimuli from different modalities originating from the same event generally produce signals that the brain uses synergistically. This is why being able to see a speaker's face makes it far easier to understand his words, particularly in a noisy room (Sumby & Pollack, 1954). The adaptive significance of multisensory integration is also obvious in enhancing the detection of a stimulus and the speed with which a reaction to it can be organized. Thus, a number of studies have shown that our ability to detect a stimulus is better and our reaction times are shorter when the cues are spatially and temporally concordant multisensory stimuli as opposed to their individual sensory components (e.g., see Andreassi & Greco, 1975; Bernstein, Clark, & Edelstein, 1969; Gielen, Schmidt, & van den Heuvel, 1983; Goldring et al., 1996; Hershenson, 1962; Hughes, Reuter-Lorenz, Nozawa, & Fendrich, 1994; Morrell, 1968a, 1968b, 1972; Posner, Nissen, & Klein, 1976).

The synergistic interaction of concordant cross-modality cues also has been demonstrated in experiments examining the attentive and orientation responses of cats (Stein, Meredith, Huneycutt, & McDade, 1989). The animals show a striking enhancement in their detection of, and orientation to, a dim visual stimulus when it is paired with a neutral auditory stimulus (the animals are either naive with respect to the auditory stimulus or have learned not to respond to it). Similarly, in humans and nonhuman primates, where eye movements often are used as an index of attentive and orientation reactions, the latency of ballistic (i.e., saccadic) eye movements to a visual or auditory cue is significantly reduced when these cues are combined in a concordant manner (Frens, Van Opstal, & Van der Willigen, 1995; Hughes et al., 1994; Lee, Chung, Kim, & Park, 1991; Perrott, Saberi, Brown, & Strybel, 1990; Zahn, Abel, & Dell'Osso, 1978). On the other hand,

when visual and auditory cues are significantly discordant, their combination can have the opposite effect and depress responses (Stein et al., 1989).

Oddly enough, there are individuals called "synesthetes" who are sometimes unable to separate sensory impressions from one another. For them, a stimulus in one modality can elicit an entire complex of subjective impressions in another modality. A humorous example of such a synesthetic experience, described by Ackerman (1990), is that of a woman who tasted baked beans whenever she heard the word "Francis."

The literal meaning of "synesthesia" is "joining of the senses", and it has been said to reflect " . . . an involuntary joining in which the real information of one sense is accompanied by a perception in another sense" (Cytowic, 1989, also see Marks, 1975, 1978). Although at present there is no adequate neural explanation for this "syndrome," modern functional imaging studies have shown that it is associated with a complex of changes in cortical activity that is quite different than that observed in nonsynesthetic individuals (Paulesu et al., 1995).

On the basis of some published observations, one might suppose that the synesthetic experience is less an oddity than a reflection of arrested sensory development. Some researchers have indicated that even among normal neonates, the various sensory impressions are not well differentiated and form what has been called a "primitive unity" (see Bower, 1977; Gibson, 1966; Marks, 1978; Ryan, 1940; Turkewitz & Mellon, 1989; von Hornbostel, 1938). In this scenario, a single, modality-specific stimulus can produce ". . . sensations (that) spill from one sensory system into another" (Maurer & Maurer, 1988, p. 164). This is by no means a generally held view. Some investigators believe quite the opposite, and hold that the senses are well differentiated from one another at birth and that the ability to associate among them is learned during postnatal development (e.g., Piaget, 1952; von Helmholtz, 1884/1968).

As is often true when dealing with conflicting theories seeking to explain complex phenomena without the benefit of a comprehensive database, it is difficult to conclude that one is correct and the other is incorrect. Thus, while the idea of a gradual acquisition of associations during postnatal life seems the more conservative of the two views (and indeed, fits with some of the more recent data from experiments with single neurons, see below), there are a number of observations that conflict with the idea that all intersensory capabilities are acquired gradually via learned associations during early life. One of the most interesting of these comes from studies conducted by Meltzoff and colleagues (e.g., Meltzoff & Moore, 1977, 1983a, 1983b). These investigators reported that newborn human babies could mimic facial expressions very soon after birth; too soon, in fact, to have had the opportunity to develop associations between what they were seeing and what they were doing. For some researchers, these observations are consistent with the idea that human infants are synesthetic, because they appear able to match a visual image with tactile and/or proprioceptive sensations (e.g., Maurer & Maurer, 1988), a process referred to by Meltzoff as "active intermodal mapping."

There are also observations from animal studies that are consistent with the idea that the brain is sensitive to at least some intersensory influences at or before birth. For example, when patterned visual input is provided before it normally occurs (by surgically separating the eyelids in mammals before they normally open, or making it possible for bird embryos to see outside their shells (see Gottlieb, Tomlinson, & Radell, 1989; Lickliter, 1990;

Turkewitz & Mellon, 1989)), there is a striking impact on the animals' ability to use cues from other sensory modalities. Such a result is not surprising in light of anatomical evidence, which suggests that in many species inputs from different sensory modalities are extensively intermingled early in development. Some rodents and at least one species of carnivore are now known to have "exuberant" sensory inputs from "inappropriate" (e.g., visual) modalities converging onto the same target structures as the "appropriate" inputs (e.g., auditory or somatosensory). The former are at a competitive disadvantage with the latter and are retracted during early development unless extraordinary surgical means are taken to eliminate the more competitive, and thus the normally surviving, inputs (Asanuma, Ohkawa, Stanfield, & Cowan, 1988; Frost, 1984; Innocenti & Clarke, 1984; Sur, Garraghty, & Roe, 1988).

Neurophysiological Evidence for Interactions Among the Senses

From the foregoing discussion it should be evident that there is an interesting organizational duality in the brain. Some regions, such as those along the primary projection pathways, are dedicated for modality-specific function. By and large, these regions segregate information on a sense-by-sense basis, so they are likely to be responsible for the qualia that are closely linked to modality-specific experiences (e.g., hue in vision, tickle in somatosensation, etc.). In contrast, other areas are specialized for pooling information regardless of modality. Presumably, these latter areas play a significant role in cross-modality phenomena, with some regions contributing more to overt behavior and others contributing more to perceptual or emotive experiences.

Inputs From Different Senses Converge on Individual Neurons at Many Levels in the Neuraxis

Despite the long history of documenting the potent influences of cross-modality cues on both perception and behavior, and the various suppositions about the brain regions that might be involved, it is only within the past few years that we have begun to identify the neural structures and mechanisms through which these different sensory inputs interact. Although these neuroanatomical/neurophysiological studies have not yet "explained" cross-modal perception, they have been quite successful in furthering our understanding of the impact of cross-modality processing on some overt behaviors, determining the distribution of multisensory neurons in various areas of the brain, and providing intriguing insights into some of the principles by which multisensory neurons integrate cross-modality information.

Many sites in the nervous system have been identified as receiving inputs from different sensory modalities, and many neurons in these sites have been shown to receive converging afferents from multiple modalities (i.e., these neurons are "multisensory"). In some systems (e.g., vestibular), convergence of inputs from different sensory modalities takes place even at the level of first and second order neurons (Highstein & Baker, 1985). However,

the overwhelming majority of this convergence takes place in the brain. A brief list of brain structures in which such multisensory convergence is commonplace includes: reticular formation, superior colliculus, pretectum, posterior thalamus, basal ganglia, and areas of association cortex. Indeed, outside of the primary sensory projection pathways, convergence among sensory modalities is quite common at each level of brain organization (see Stein & Meredith, 1993 for a review).

The Superior Colliculus as a Model to Study Multisensory Processes

One of the best models with which to study sensory convergence and multisensory integration is a midbrain structure, the superior colliculus (SC). The choice of this structure is based on the high incidence of visual-, auditory- and somatosensory-responsive multisensory neurons in its deep layers, and its well-documented involvement in overt attentive and orientation behaviors (Casagrande, Harting, Hall, & Diamond, 1972; Schneider, 1969; Sprague & Meikle, 1965; Stein & Meredith, 1993). Perhaps more than any other brain structure, the SC functions at the interface of sensory and motor processing. It receives inputs from multiple sensory modalities and issues motor commands to produce coordinated movements of the eyes, ears, head, and body toward stimuli in each of these modalities. Consistent with its sensorimotor role, the discharge of an individual SC neuron shows a strong selectivity for the location of a sensory stimulus and/or the metrics (i.e., amplitude and direction) of a movement toward that stimulus. Neurons with sensory-related activity have distinct receptive fields and respond only to stimuli within a restricted region of space. Such neurons may be unimodal, responding only to visual, auditory, or somatosensory stimuli. Alternatively, these neurons can be multisensory, responding to stimuli from two (or even three) sensory modalities. Analogously, neurons with motor-related activity have movement fields, and these neurons discharge in association with orienting movements within a particular range of amplitude and direction.

The Topographic Organization of the Superior Colliculus

In the SC, the representations of sensory space and movement metrics are topographic; that is, SC neurons are arranged in an orderly fashion according to the position of their receptive and/or movement fields to form sensory and motor "maps." In such an organization, sensory stimulus location or movement metrics are represented by the location of activity within the map. Understanding the relationships of the visual, auditory, and somatosensory maps to each other and to the motor maps is important for understanding how multisensory stimuli are translated into motor output. Of particular concern are the relationships among the sensory representations, for they have profound implications for the synthesis of cross-modal sensory cues and the motor behaviors they elicit.

Receptive Field Correspondence in Multisensory Neurons

The notion that inputs from different sensory modalities have access to the same motor maps dictates the need for mechanisms to establish and maintain a correspondence among the receptive fields of the different modalities. Whether a particular location in space is the source of a visual, auditory, or somatosensory stimulus, or some combination thereof, an orienting movement to that location requires activating the same region of a motor map. If sensory activity is a prelude to motor activity in the corresponding region of the SC, then the site of sensory SC activity should be the same regardless of whether the initiating stimulus is visual, auditory, or somatosensory. The register among the receptive fields of different modalities ensures consistent spatial selectivity and, presumably, consistent behavioral outcomes (e.g. movement vectors) across modalities. The presence of this cross-
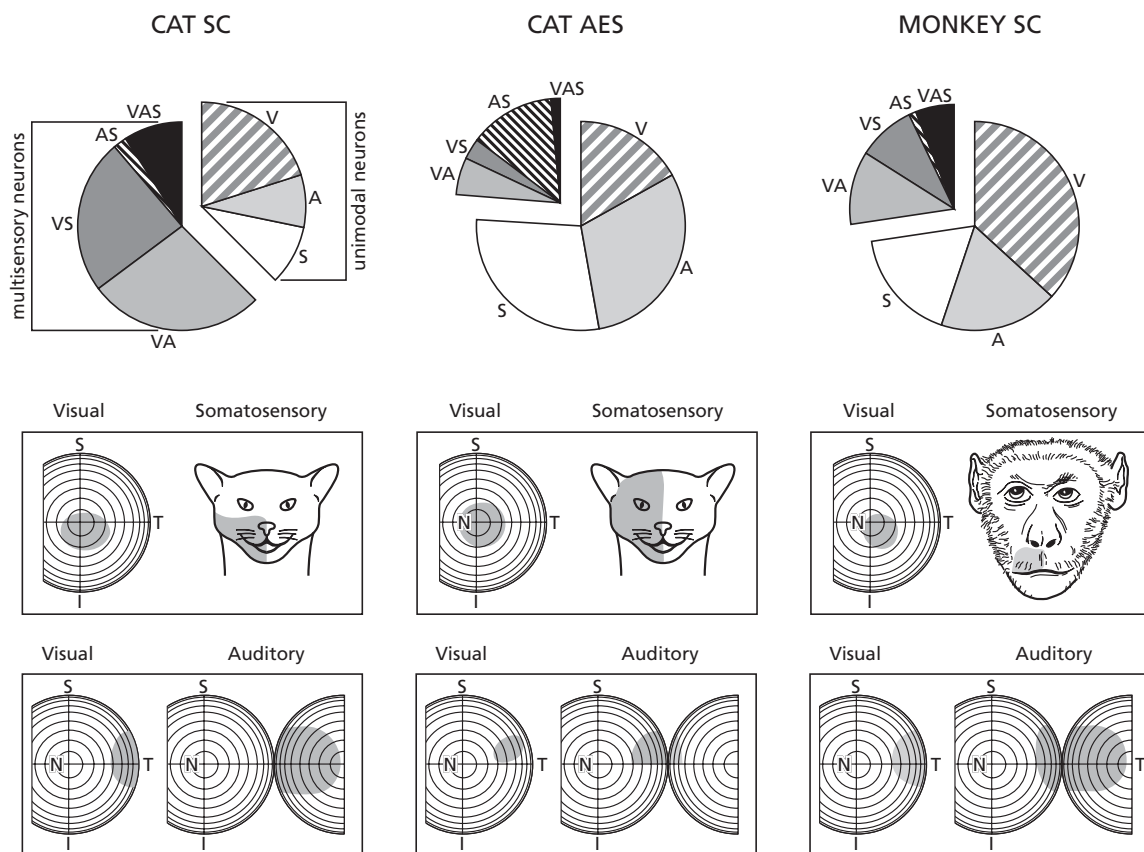

Figure 22.1. Top: Shown are the relative proportions of the various multisensory neurons obtained in cat (SC and AES) (AES = anterior ectosylvian sulcus, see p. 725) and monkey (SC). V – visual, A – auditory, S – somatosensory. Bottom: These multisensory neurons are all characterized by an alignment among their different modality-specific receptive fields (shading), and six characteristic examples are illustrated. In the representation of auditory space (lower left), the caudal half of contralateral space is depicted by a semicircle that is folded forward (the caudal half of ipsilateral space is not shown). S – superior, I – inferior, T – temporal, N – nasal. (Adapted from Wallace et al. (1992) and Wallace & Stein (1996), the latter © 1996 Elsevier Science, with permission.)

modality alignment of receptive fields is particularly evident in multisensory neurons (Figure 22.1), whose role is to integrate cross-modal information, a role which will be described in detail below.

Maintaining Receptive Field Alignment

While it appears simple conceptually, establishing and maintaining receptive field alignment across modalities is not a trivial problem from the standpoint of neural computation. Each sensory system uses distinctly different referents: visual axes are centered on the retina, the acoustic axes are aligned with respect to the head (i.e., the position of the external ears), and the location of a tactile stimulus is referred to the body surface. Given that these reference frames can move independently of one another, there is no unique relationship between a coordinate in one reference frame and that in another. As described below, this places substantial constraints on the neural mechanisms that establish and maintain receptive field alignment in instances in which the eyes, head, ears, and body move with respect to one another.

The receptive field properties of SC multisensory neurons have been examined most often when the eyes, head, and body are aligned so that the axes of visual, auditory, and tactile "space" are in approximate co-registration. With only rare exceptions, these experiments have demonstrated that there is excellent alignment among the modality-specific receptive fields of multisensory neurons. A few examples from different species and brain structures are presented in Figure 22.1. Note that in each case there is an overlap, or spatial register, among the receptive fields. This is easiest to see in the case of a visual-auditory neuron, for which both receptive fields are in extrapersonal space. However, visual-somatosensory and auditory-somatosensory receptive fields show a similar organization. Thus, when the visual or auditory receptive field is in central (i.e., frontal) space, the corresponding somatosensory receptive field is on the face; when the visual or auditory receptive field is more peripheral, the corresponding somatosensory receptive field is further back on the body. Similar observations have now been made in alert animals (e.g., see Frens & van Opstal, 1998; Wallace, Meredith, & Stein, 1998).

But what happens when one set of sensory organs is moved relative to the others? Given that the eyes, ears, head, and body can move independently of one another (to a degree that is species-specific), modality-specific signals cannot be encoded in their original reference frames (e.g., eye-centered, head-centered, body-centered) if receptive field register is to be maintained in the behaving animal. For example, eye movements deviate the eyes in the orbit, and each eye movement changes the relationship between the visual axis and those of the auditory and somatosensory domains. The same result is produced by head, ear, and/or limb movements.

Is receptive field alignment disrupted by relative movement of modality-specific reference frames? Studies in awake animals indicate that compensatory mechanisms attempt to maintain receptive field register. Evidence that many SC auditory and somatosensory RFs are remapped as a function of eye position to maintain alignment with the visual RFs has been obtained in both monkeys and cats (Groh & Sparks, 1996; Hartline, Pandey Vimal, King, Kurylo, & Northmore, 1995; Jay & Sparks, 1987a, 1987b; Peck, Baro, & Warder,

1995). These results suggest that multisensory representations are of a higher order, that is, the product of neural computations that transform signals from different modalities into a common coordinate frame. One possibility, as discussed by Sparks and colleagues (e.g., Sparks & Nelson, 1987), is that SC sensory maps are the end-product of coordinate transformations designed to represent modality-specific information in a common "motor" frame of reference. In such a scheme, the locus of sensory-contingent activity is more closely allied with the movement vector required to orient to the stimulus than to the spatial location of the stimulus itself. The result of this would be a modality-independent code in which stimulus location with respect to the current gaze position is the major determinant of the spatial distribution of activity across the multisensory population.

In the SC, different modalities of sensory information may be represented in a coordinate frame that makes for an easy interface with the motor map that produces gaze shifts. Because the visual reference frame is tied to the direction of gaze, it makes sense that the auditory and somatosensory receptive fields shift to maintain alignment with the visual representation. Reinforcing these findings are data from another area involved in movement, the ventral premotor cortex of monkey (Graziano, Yap, & Gross, 1994). Rather than being active in association with shifts in gaze, ventral premotor cortex is active in association with reaching movements. Accordingly, because it is the tactile sensory surface that is bound to the position of the arm, Graziano and colleagues found that the visual receptive fields of visual-tactile neurons are remapped with changes in arm position, so that visual information, like tactile information, is represented in a body-part-centered frame of reference.

Principles of Cross-Modality ("Multisensory") Integration in the Superior Colliculus

The synthesis of multisensory information accomplished by SC neurons is critically dependent upon the relationships between the different sensory stimuli, as well as their individual physical characteristics. Several of the more important factors in dictating an integrated multisensory response are detailed below.

Space

Because cues that are derived from the same event are likely to originate from the same location in space, they also are likely to activate the same multisensory neurons (because of the receptive field overlap described above). These neurons integrate the different sensory inputs, yielding a multisensory response "product" far different from either of the responses to the individual stimuli. Typically, this is manifested as a discharge train with more impulses than that evoked by either of the single-modality stimuli and often exceeding the sum of the unimodal responses (Figure 22.2) (Meredith & Stein, 1986; Wallace, Wilkinson, & Stein, 1996).

If the auditory stimulus is presented outside its receptive field (and is thereby spatially
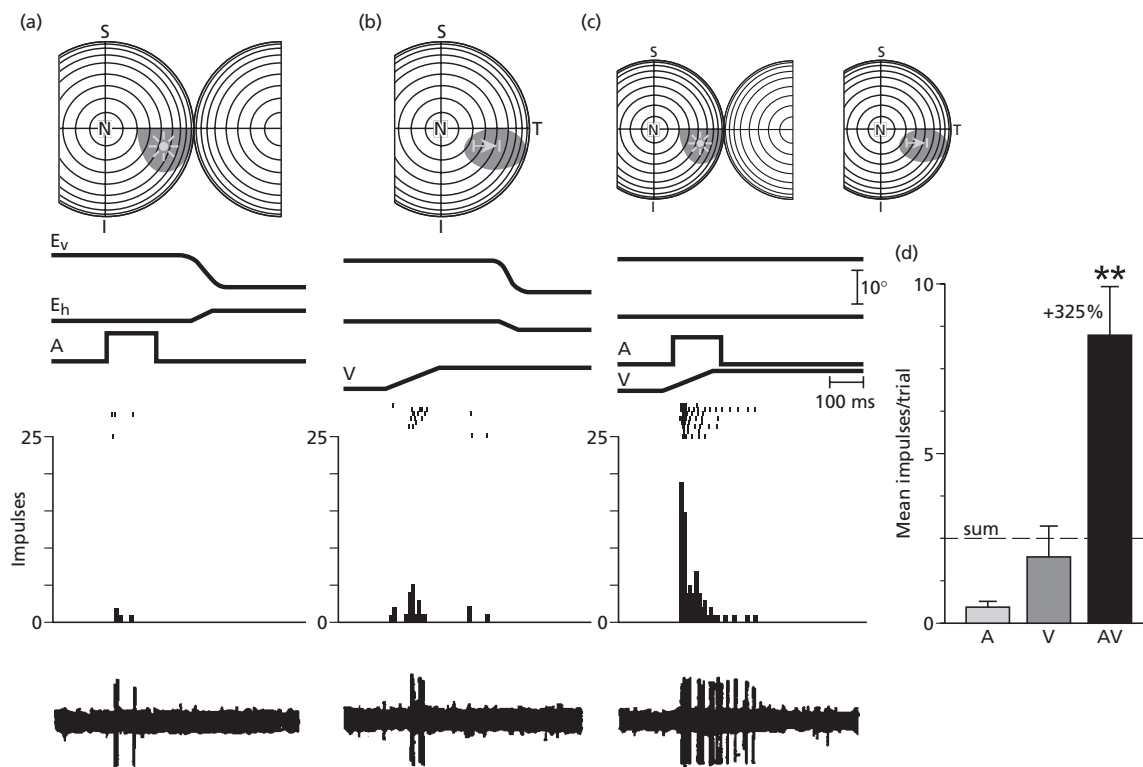
Figure 22.2. Multisensory enhancement in a visual-auditory SC neuron of an awake cat. (a) Shown at the top are the auditory receptive field and the location of the stimulus (icon of speaker). E_v and E_h represent vertical and horizontal components of eye position during a single trial, and the electronic trace labeled "A" illustrates the timing of the auditory stimulus. Raster and peristimulus time histogram show this neuron's response to six presentations of the auditory stimulus alone, and a single response is shown in the oscillograph below. (b) The visual receptive field (shading) and visual stimulus (bar moving as depicted by the arrow) are shown at the top, and the responses to the visual stimulus alone are shown below. (c) Pairing the auditory and visual stimuli produced a marked response enhancement that exceeded the sum of the unimodal responses. The magnitude of the response enhancement is shown in the summary bar graph (d). ** $p < 0.01$. (From Wallace et al. (1998), with permission.)

discordant with the visual stimulus), no such response enhancement is produced. In fact, under such circumstances there is a good probability that the opposite effect – response depression – will occur (Figure 22.3). In this case, even a robust visual response can be abolished by the spatially disparate auditory stimulus (Kadunce, Vaughan, Wallace, Benedek, & Stein, 1997; Meredith & Stein, 1996; Wallace et al., 1996). Multisensory depression can be evoked in many of the same neurons that exhibit multisensory enhancement. There is a parallel phenomenon in behavioral experiments in which spatially coincident visual and auditory stimuli enhance attentive and orientation responses, and spatially disparate visual and auditory stimuli degrade them. This is discussed below in the section entitled SC-Mediated Multisensory Behaviors.

An explanation for the opposing effects that can be evoked with the same stimuli in the
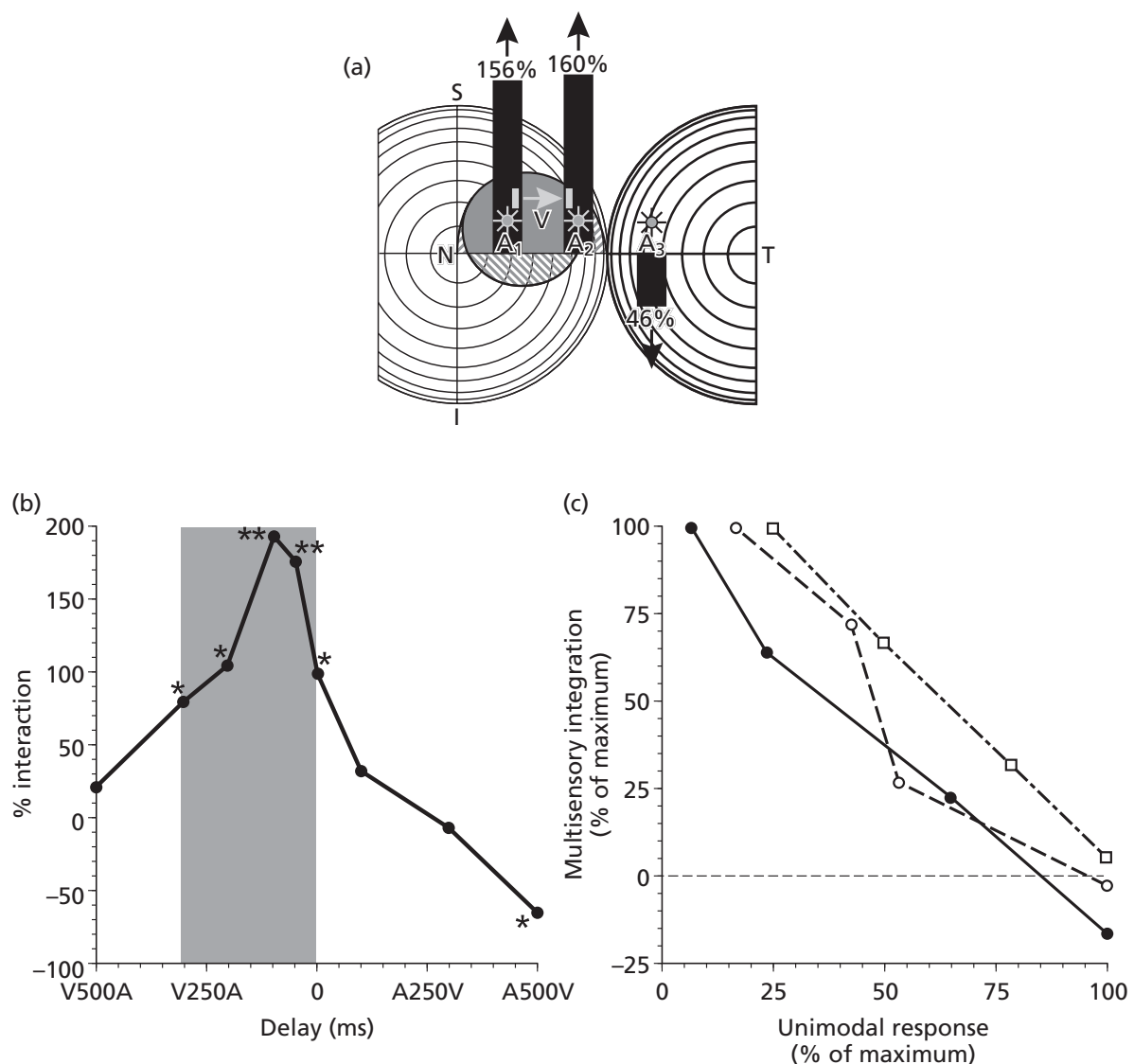
Figure 22.3. Multisensory integration is affected by spatial and temporal factors, as well as by the effectiveness of the modality-specific stimuli. (a) When the two stimuli are presented within their respective receptive fields, their combination results in response enhancement. For this visual-auditory SC neuron in the cat, the auditory receptive field is shown as upward hatch lines, the visual receptive field as downward hatch lines, and the region of overlap as gray shading. The visual stimulus is a bar of light moving as indicated by the arrow (V). The auditory stimulus, depicted by the speaker icon, was presented at three different locations (A_1, A_2 and A_3) in each of three different test series. When the visual and auditory stimuli were within their receptive fields, response enhancement ($A_1 = 156\%$ and $A_2 = 160\%$) resulted, but when the auditory stimulus was outside of its receptive field (A_3), response depression was obtained. (b) In this visual-auditory neuron, multisensory interactions were greatest when the visual stimulus preceded the auditory by 100 ms (V100A) and became progressively smaller as the temporal disparity between the stimuli increased or decreased. Nonetheless, significant interactions were generated within a temporal window of 300 ms (gray shading). * $p < 0.05$; ** $p < 0.01$. (c) In the three multisensory neurons depicted, the largest multisensory interactions were generated when the modality-specific stimuli were at minimal levels of effectiveness. As these stimuli became more effective, the magnitude of the multisensory interactions declined. While other SC neurons also exhibited this effect of "inverse effectiveness," they were far less linear in their response profiles.

same neurons is based on the spatial relationships of the two stimuli to one another and to their respective receptive fields. Response enhancement is the result of the synergistic interaction of two excitatory inputs that occurs when stimuli appear within their respective receptive fields. But, because some receptive fields have an inhibitory, or suppressive, region at their borders, response depression can be explained by the antagonism between the inhibitory input from the stimulus outside the receptive field and the excitatory input produced by the within-field stimulus (Kadunce et al., 1997).

Effectiveness

In addition to the spatial relationships between the stimuli, the effectiveness, or strength, of the individual stimuli in eliciting a response plays an important role in determining the multisensory product produced by their combination. This relationship makes intuitive sense, because highly effective stimuli typically result in a large neuronal response (and, likely, a consequent behavioral response) and gain little from the additional information provided by the second modality. However, when the stimuli are weakly effective on their own, the benefit of multisensory integration is most obvious. For here, the stimulus combination results in a largely enhanced response, often far exceeding that predicted by summing the two unimodal responses (i.e., superadditive; see Figure 22.3). Not surprisingly, and highlighting the parallels here between the physiology of single neurons and behavior, such a stimulus combination will also have a high probability of evoking an SC-mediated behavior (see below). This principle, known as "inverse effectiveness," is illustrated in Figure 22.3.

Time

Producing an integrated multisensory response, and the magnitude of that response, depends not only on the location and effectiveness of the stimuli, but on their relative timing as well (Figure. 22.3). Not surprisingly, when there is too great an interval between two stimuli, they are treated as independent events, even if they are derived from the same location in space. Yet, the "window" of time during which multisensory interactions can occur is surprisingly long, often exceeding hundreds of milliseconds (Meredith, Nemitz, & Stein, 1987; Wallace & Stein, 1997). This is perhaps most important because it permits stimuli from two sensory modalities to interact despite very different input latencies. For example, the latency range for auditory and somatosensory responses in multisensory SC neurons is approximately 10–25 msec, while the latency range for visual responses spans 40–120 msec. Therefore, if a visual-auditory or a visual-somatosensory neuron depended on an exact latency match in order to integrate cross-modal information, the vast majority of events that take place near the animal (and which produce near-simultaneous sensory cues) would result in signals arriving at the SC at different times and produce very little, if any, cross-modal integration. This is clearly not the case, in large part because each sensory input has a long-lasting effect on a multisensory neuron.

Nonetheless, within the wide temporal window there generally exists an optimum

difference in the time between the onsets of the two stimuli that will result in the largest multisensory interaction. Most SC neurons appear to be "tuned" so that their best multisensory response occurs at one stimulus onset asynchrony (SOA – the difference between the onset of the two stimuli), and progressively smaller interactions are generated at greater or lesser SOAs (Figure 22.3). Some neurons even exhibit response depression at SOAs transitional between those that evoke two unique responses and those that elicit a single integrated response. This finding suggests that such neurons are tuned to events that take place at different distances from the animal and thus respond best to stimuli that have SOAs that are consistent with these distances.

Preservation of Receptive Field Properties

It is interesting to note that the marked changes induced by multisensory enhancement generally do not alter a neuron's fundamental receptive field properties. For example, if a visual-auditory neuron responds best to a certain direction of visual movement, and/or a certain velocity, and/or proves to be binocular when examined with a unimodal visual cue, it will maintain these properties in the presence of an auditory stimulus even when that auditory stimulus enhances the neuron's responses dramatically. Whether this also holds true during response depression is not yet known.

Receptive Field Alignment is Critical for Normal Multisensory Integration

It is apparent from the discussion above that the alignment of the different receptive fields in multisensory neurons is important for the enhancement of responses to stimuli derived from the same event and the depression of responses to stimuli derived from competing events. However, early in life, receptive field alignment in multisensory SC neurons is not readily apparent. Neonatal SC neurons typically have very large receptive fields; many can be activated by stimuli anywhere in sensory space and it is only after a substantial postnatal developmental period that the different receptive fields of multisensory neurons achieve their adult-like precision and cross-modality register (Wallace & Stein, 1997; see also King & Carlile, 1993; Knudsen & Brainard, 1991; Withington-Wray, Binns, & Keating, 1990; Withington-Wray, Binns, Dhanjal, Brickley, & Keating, 1990). Presumably, the same Hebbian mechanisms that operate to strengthen synchronous inputs in any modality-specific system are also likely to strengthen synchronous cross-modality inputs derived from the same event, thereby leading to cross-modality receptive field alignment.

SC-Mediated Multisensory Behaviors

The most direct effects of the SC on overt behavior are mediated via its crossed descending output pathway, the predorsal bundle. It is through this pathway that SC neurons gain access to regions of the brainstem and spinal cord that influence movements of the eyes,

ears, mouth, and head (see Stein & Meredith, 1991). The overwhelming majority of SC neurons projecting into this pathway are responsive to sensory stimuli, with most of these being multisensory (Meredith, Wallace, & Stein, 1992; Wallace, Meredith, & Stein, 1993).

This observation prompted a number of behavioral experiments to test a pair of seemingly straightforward predictions: that the multisensory stimulus configurations that produce enhanced responses in SC neurons will be more salient and will increase SC-mediated attentive and orientation behaviors; and that those multisensory stimulus combinations that reduce SC neuronal responses will be less salient, and will degrade SC-mediated behaviors. These predictions proved to be correct.

Cats were trained using food reward in a perimetry device (see Figure 22.4) to look directly ahead of them and then orient toward, and immediately approach, a briefly illuminated visual target (a light-emitting diode, or LED). Some of the animals were also trained to approach a sound – a very brief, low-intensity broad-band noise burst delivered from a speaker. Still other animals either had no experience with the auditory stimulus, or were trained to ignore it (it was never paired with reinforcement). When the visual and auditory stimuli were presented at the same time and in the same location during testing, the correct responses of animals in the first group were increased far more than was expected based on statistical predictions. Correct responding also was significantly enhanced in all other animals regardless of their training history. But, if the auditory stimulus was presented in a location disparate (e.g., 60° medial) to the visual stimulus, it decreased the probability of correct responses, and did so not only in animals that learned to ignore the auditory stimulus during their training sessions, but also in animals that were never exposed to the auditory stimulus during training (Stein et al., 1989).

The results of these behavioral experiments closely parallel those obtained in physiological studies. As it turns out, the key to the multisensory integration seen both physiologically in the activity of individual SC neurons, and behaviorally in changes in attentive and orientation performance, depends on the development and maintenance of a critical connection between the neocortex and the SC.

Role of Cortex in Mediating Multisensory Integration in the Superior Colliculus

Physiological Studies

Because the SC receives sensory inputs from a large number of ascending and descending (corticotectal) visual, auditory and somatosensory structures (Edwards, Ginsburgh, Henke, & Stein, 1979; Huerta & Harting, 1984; Stein & Meredith, 1991), its neurons could, theoretically, become multisensory by virtue of a host of different afferent convergence patterns. Oddly enough, they appear to receive few, if any, inputs from multisensory neurons in other structures (Wallace et al., 1993; Jiang, McHaffie & Stein, unpublished observations), but become multisensory as a result of the convergence of unimodal inputs. Therefore, it seemed reasonable to expect that any neuron that receives convergent sensory input from two or more modalities will be capable of the kind of multisensory integration
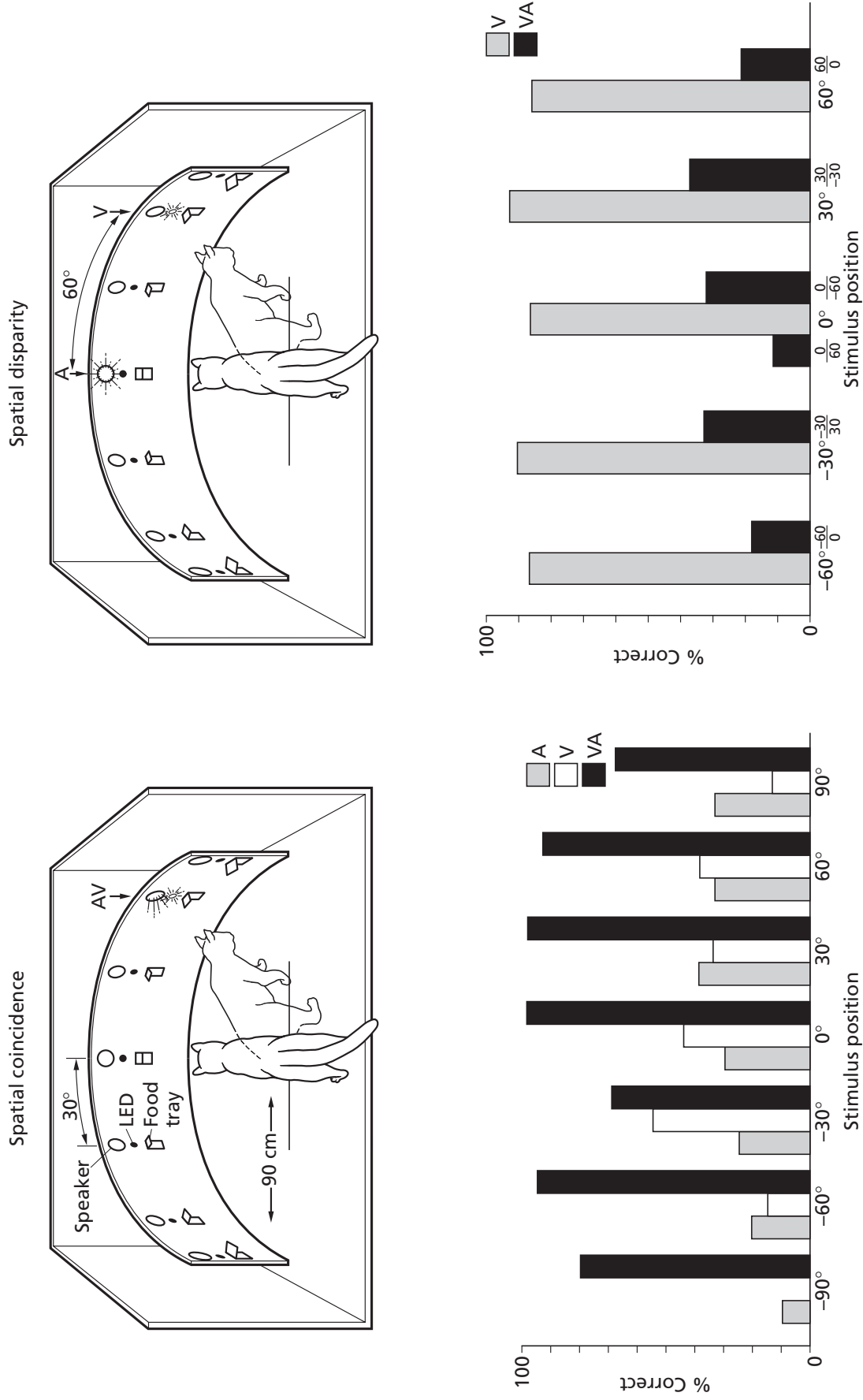
Figure 22.4. Multisensory attentive and orientation behaviors depend on the relative locations of the two stimuli. Left: An animal was trained to approach a visual or an auditory stimulus. When the visual and auditory stimuli were presented simultaneously at the same location (top) the probability of the animal's correct response was enhanced above that to either modality-specific stimulus alone, and generally above their sum. Right: An animal was trained to approach a visual stimulus, but was not trained to approach an auditory stimulus. When an auditory stimulus was presented simultaneously with the visual (but 60% disparate), the probability of a correct response to the visual stimulus was markedly depressed. (Adapted from Stein et al. (1989), with permission from MIT Press.)

discussed above. This proved not to be the case, and as discussed below, not all converging sensory inputs proved to be capable of supporting this process.

In the cat, inputs derived from one region of neocortex, the anterior ectosylvian sulcus (AES), turned out to make a very special contribution to multisensory integration in the SC. Traditionally, the AES has been described as an area of sensory "association cortex." It does not receive its primary inputs from the major thalamic sensory relay nuclei, and it has multiple subregions representing different sensory modalities: a somatosensory area, SIV (Clemo & Stein, 1982); a visual area, AEV (Mucke, Norita, Benedek, & Creutzfeldt, 1982; Olson & Graybiel, 1987); and an auditory area, Field AES (Clarey & Irvine, 1986). It also has many multisensory neurons distributed throughout these subregions (Clemo, Meredith, Wallace, & Stein, 1991; Jiang, Lepore, Ptito, & Guillemot, 1994a, 1994b; Wallace, Meredith, & Stein, 1992). This region of cortex is a rich source of input to the SC, providing one of the largest descending corticotectal projections (Stein, Spencer, & Edwards, 1983; Wallace et al., 1993). Although, as noted above, only unimodal AES neurons send their axons to the SC, they do so in convergence patterns that match the multisensory nature of the SC neuron they contact. For example, AES inputs onto visual-auditory SC neurons will arise from its visual (i.e., AEV) and auditory (i.e., FAES) subdivisions, but not from its somatosensory subdivision (i.e., SIV). However, of primary importance in the present context is the observation that the influences of the AES are essential for normal multisensory integration in SC neurons. For when the AES is temporarily deactivated, most SC neurons continue to respond to the individual sensory cues (because their various other sources of sensory information are unimpaired), but they can no longer integrate these inputs to produce an enhanced response (Figure 22.5). By using its target neurons in the SC in this way, the AES not only controls these cross-modality associative functions, but takes advantage of a circuitry that mediates attentive and orientation behaviors to multiple sensory stimuli. In the few multisensory neurons in which multisensory integration could not be demonstrated, AES inputs were found to be absent (Wallace & Stein, 1994).

Behavioral Studies

Based on these physiological observations, one would predict that the ability to use different sensory cues synergistically to guide SC-mediated behaviors would also depend on the integrity of the AES. Confirmation of this prediction was obtained in behavioral studies with cats that used the same paradigm and perimetry device described above. The animals were trained and then tested for multisensory orientation behaviors with AES intact or temporarily deactivated by infusion with an anesthetic agent, lidocaine. When the AES was deactivated there was no observable effect on orientation to unimodal cues, whereas the behavioral enhancements resulting from spatially-coincident multisensory stimulus combinations were abolished. Furthermore, the ability of spatially-disparate cues to decrease the probability of correct responses was also degraded (Wilkinson, Meredith, & Stein, 1996) (Figure 22.6). These effects were specific to AES deactivation and were not observed during the deactivation of other visual or auditory cortical regions. The behavioral data, in conjunction with data from the electrophysiological studies described above, strongly
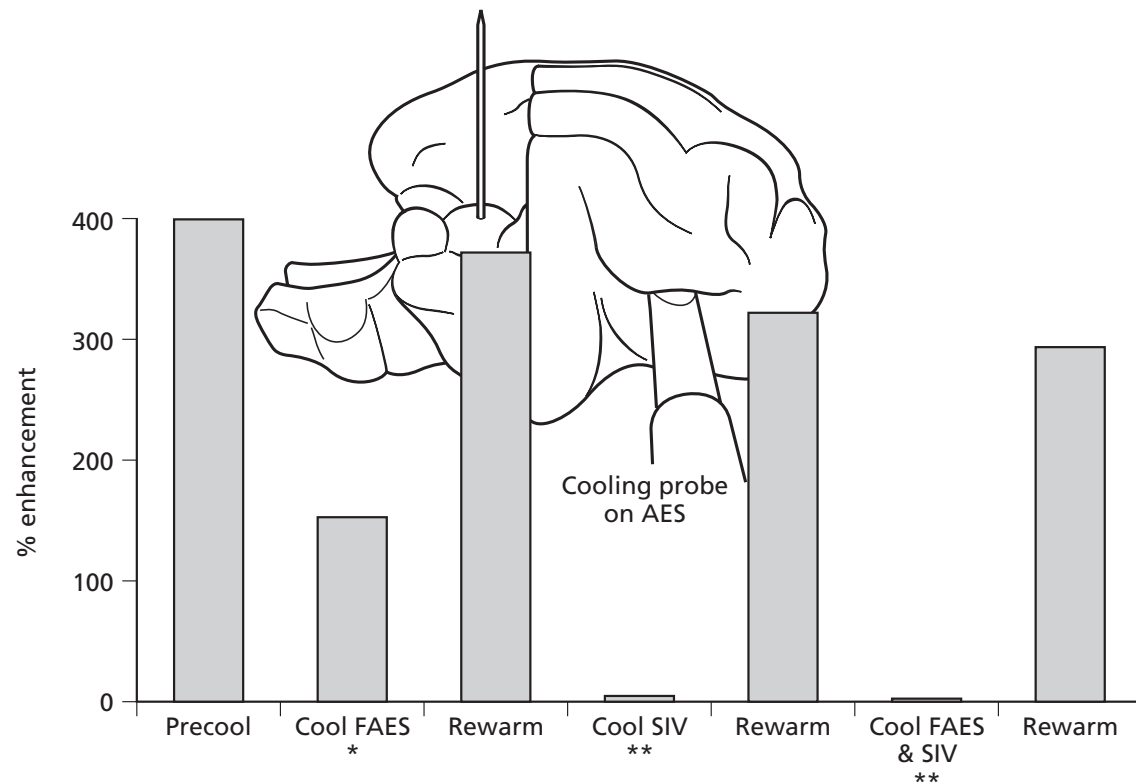
Figure 22.5. Deactivation of AES cortex abolishes multisensory integration in cat SC neurons. In this example a significant multisensory response enhancement was induced in an SC neuron by pairing auditory and somatosensory stimuli. Deactivating (cooling) the auditory (FAES) and somatosensory (SIV) subdivisions of the AES abolished the enhanced response, but did not substantially alter responses to the modality-specific stimuli (not shown). Rewarming the AES reinstituted the SC neuron's response enhancement. * p $<$ 0.05, ** p $<$ 0.01. (Adapted from Wallace & Stein (1994).)

suggest that an intimate relationship must be maintained between the AES and SC in order to support these multisensory attentive and orientation functions.

Development of Multisensory Integration

Animals are not born with the neural processes through which multisensory integration is effected in the SC, and young animals exhibit little of the behavioral facility with multisensory cues that characterizes the adult cat. In fact, during the first few days after birth, the SC functions essentially as a unimodal structure (see Stein, Labos, & Kruger, 1973). During this period the animal's eyelids and ear canals are closed and, not surprisingly, SC neurons do not respond to visual or auditory stimuli. However, some neurons do respond to somatosensory cues and the animal's responsiveness to tactile stimuli is particularly evident in its use of these cues to initiate suckling behaviors (Larson & Stein, 1984). As
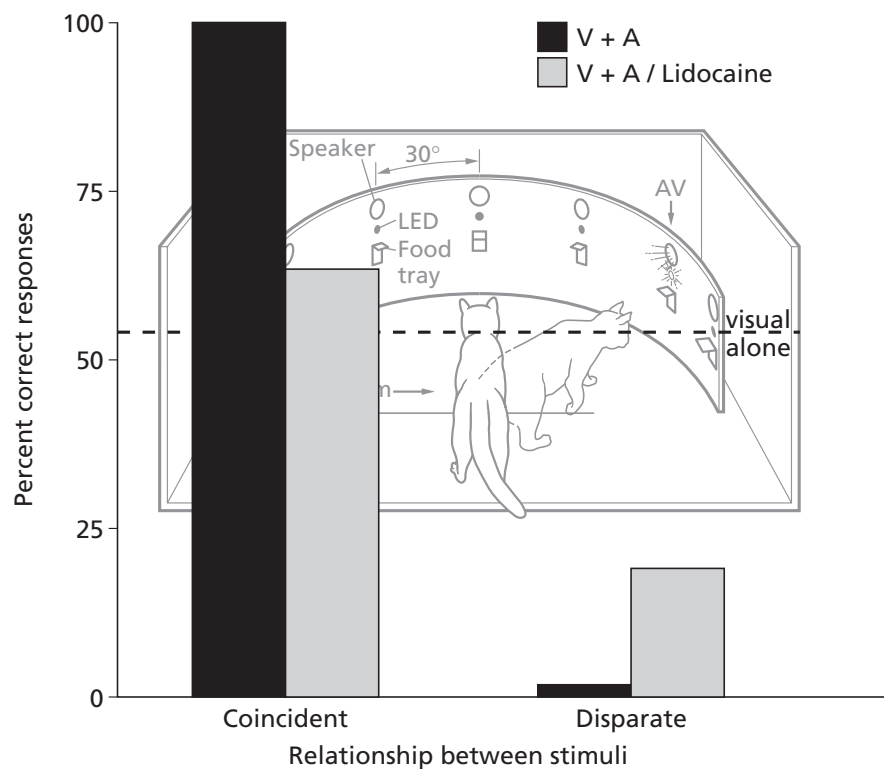
Figure 22.6. Deactivating AES cortex severely disrupts multisensory orientation behavior. Both the enhanced responses to a spatially coincident multisensory combination and the depressed responses to a spatially disparate combination are compromised during transient AES deactivation (lidocaine injections via indwelling cannulae). (Adapted from Wilkinson et al. (1996).)

postnatal development progresses, the incidence of sensory-responsive SC neurons increases. By about the fifth day after birth the first SC neurons become responsive to auditory cues (Stein et al., 1973), and at about 3 postnatal weeks neurons in the multisensory layers begin to respond to visual inputs (Wallace & Stein, 1997). However, these early neurons are very different from their adult counterparts.

The earliest multisensory neurons have very large receptive fields, and they are unable to synthesize their different sensory inputs to increase or decrease their responses (Figure 22.7). This immaturity is not specific to the cat, but is apparent in multisensory SC neurons of the newborn rhesus monkey as well. In many respects, the rhesus monkey is far more mature than the kitten at birth, having already developed a complement of multisensory neurons. Yet, just as in the young cat, these neonatal multisensory neurons have receptive fields that are much larger than they are in adults and they are incapable of synthesizing multisensory cues to significantly enhance or degrade their responses (see Wallace, McHaffie, & Stein, 1995).

By the end of the first postnatal month the cat's multisensory capabilities have matured substantially. Some multisensory SC neurons have developed spatially restricted receptive
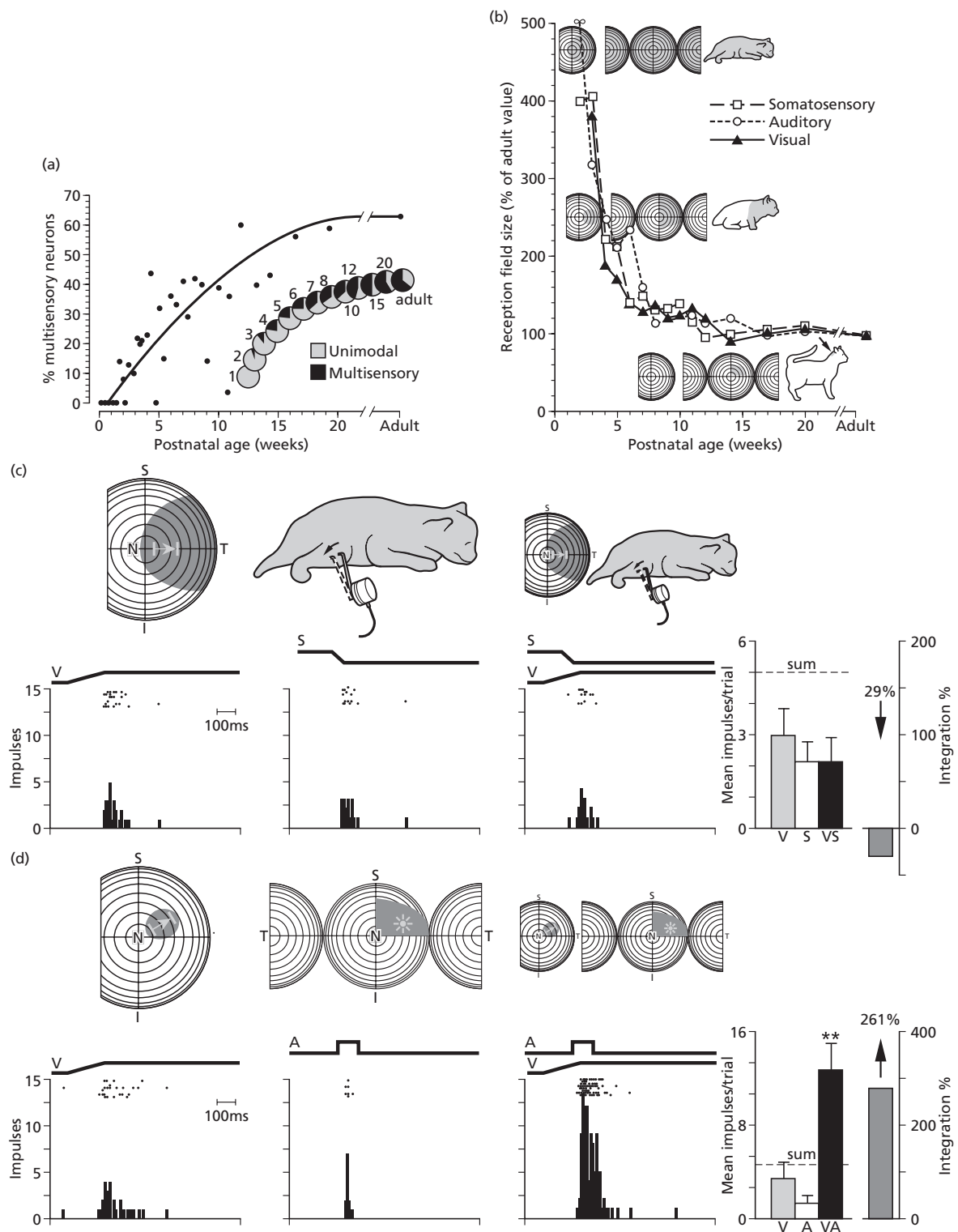
Figure 22.7. The development of cat SC multisensory neurons, multisensory receptive fields, and multisensory integration. (a) Multisensory SC neurons appear gradually over the first several postnatal months. (b) Visual, auditory and somatosensory receptive fields also contract during this period and develop an increasingly obvious spatial register (insets). (c) Early multisensory neurons, which typically have large receptive fields, lack the capacity for multisensory integration (as shown in this example from a 20 dpn animal). (d) shortly thereafter, in neurons in which receptive fields have consolidated (as in this example from a 30 dpn animal), multisensory integration appears. ** p < 0.01. (Adapted from Wallace & Stein (1997), with permission.)

fields and are able to integrate cross-modality cues very much like the adult. Such neurons exhibit significant response enhancement when these cues are spatially coincident, and either no enhancement or response depression when these same cues are spatially disparate (Figure 22.7). During the next two months there is a progressive increase in the incidence of these seemingly mature multisensory neurons.

Unexpectedly, when the first SC neurons exhibit the capacity to engage in multisensory integration, they do so in a manner that appears very much like that observed in the adult. The magnitude of the enhanced (or depressed) product is the same as in the adult, and interactions closely follow the established principles of multisensory integration (e.g., receptive field overlap, spatial coincidence among stimuli yields response enhancement, spatial disparity yields no interaction or a depressed response, inverse effectiveness, etc.). The only characteristic that appears to be different is that early multisensory neurons have a much more limited temporal window during which integration can take place. Generally, these neurons require near simultaneous presentation of the different sensory stimuli in order to exhibit an integrated product. Given the critical nature of AES-SC connections for multisensory integration in adult animals, it seems quite probable that the abrupt onset of multisensory integration in these neurons reflects a rapid transition to the state in which there is an active influence of AES over SC neurons. That a corticotectal influence can develop in a seemingly abrupt fashion is not without precedent, as corticotectal influences from visual cortex show a similar developmental profile (see Stein & Gallagher, 1981).

Fundamental Commonalities in Multisensory Integration

The topographic organization of the sensory representations and the spatial register of the different receptive fields of multisensory neurons are characteristic not only of cat and monkey, but are seen also in hamster (Chalupa & Rhoades, 1977; Finlay, Schneps, Wilson, & Schneider, 1978; Stein & Dixon, 1979; Tiao & Blakemore, 1976), mouse (Benedetti, 1991; Drager & Hubel, 1975), rat (McHaffie, Kao, & Stein, 1989), and guinea pig (King & Palmer, 1985). In addition, these organizational principles have been described in the nonmammalian homologue of the SC, the optic tectum, in a number of species, including birds, reptiles, amphibians, and fish (Bullock, 1984; Hartline, Kass, & Loop, 1978; Knudsen, 1982; Stein & Gaither, 1981; see also Stein & Meredith, 1993). The striking phyletic constancy in the manner in which the different sensory modalities are represented in the midbrain suggests that this multisensory organizational scheme antedates the evolution and radiation of mammals.

The presence of receptive field register in multisensory neurons also characterizes neurons in a variety of neocortical areas (e.g., Bruce, Desimone, & Gross, 1981; Duhamel, Colby, & Goldberg, 1991; Fogassi et al., 1996; Graziano, Hu, & Gross, 1997; Ramachandran, Wallace, Clemo, & Stein, 1993; Rizzolatti, Scandolara, Matelli, & Gentilucci, 1981a, 1981b; Stein, Meredith, & Wallace, 1993; Wallace et al., 1992), where such neurons are likely to be involved in functional roles very different from those in the SC. However, unlike the midbrain, a global topography for each sensory modality is not apparent in all cortical regions, even though individual multisensory neurons exhibit a striking register.

For example, in cat AES, only SIV has been found to have a demonstrable sensory map. The corresponding visual (AEV) and auditory (FAES) regions are far less systematically arranged. Despite this, multisensory AES neurons, regardless of where they are found, have overlapping receptive fields. Furthermore, these multisensory neurons exhibit a number of the integrative properties that are characteristic of SC neurons. These include the spatial principle, inverse effectiveness, and response enhancements that exceed the sum of the unimodal responses (Wallace et al., 1992). These commonalities are consistent with the idea that some of the fundamental principles of multisensory integration are general and supersede structure, function, and species.

This should not be taken to indicate that there are no significant differences in unimodal or multisensory neurons that are associated with different species or structures. There is little doubt that high frequency sounds are more effective in rodent than in primate, that sound is of primary importance in some species (e.g., bats) whereas vision is primary in others (e.g., monkey) and somesthesis in still others (e.g., blind mole). These differences are reflected in the proportion and response characteristics of neurons devoted to processing modality-specific information and are essential adaptations that reflect an animal's ecological specialization. They are also very likely to be reflected in the convergence patterns and responses of multisensory neurons. Specialization is almost certainly the case for different structures as well. For example, multisensory depression appears to be less frequent and less pronounced in cortex than in SC (see Stein & Wallace, 1996). In this context it is interesting to note that the influence of an auditory cue on perceptual judgments of visual intensity (presumably a cortical function) does not require that the auditory and visual cues originate from the same spatial location, an effect very different from that governing SC-mediated attentive and orientation functions (Stein et al., 1996).

Nevertheless, it is likely that specialized characteristics are imposed on a core of common properties, such as those shared by the midbrain and cortex. A common foundation of properties that characterize multisensory integration at different levels of the neuraxis ensures that cues are enhanced (or degraded) simultaneously in areas of the brain involved in different response components of an integrated behavior. The preservation and elaboration of these properties in animals at different phyletic levels attest to the utility of such a scheme in both very primitive and more advanced species.

Note

Suggested Readings

Baron-Cohen, S., & Harrison, J. E. (1997). *Synesthesia*. Cambridge, MA: Blackwell.
Lewkowicz, D. J., & Lickliter, R. (1994). *The development of intersensory perception: Comparative perspectives*. Hillsdale, NJ: Erlbaum.
Sparks, D.L., & Groh, J.M. (1994). The superior colliculus: A window for viewing issues in integra-

tive neuroscience. In M. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 565–584). Cambridge, MA: MIT Press.

Stein, B. E., & Meredith, M. A. (1993). *The merging of the senses*. Cambridge, MA: MIT Press.

Stein, B. E., Meredith, M. A., & Wallace, M. T. (1994). Neural mechanisms mediating attention and orientation to multisensory cues. In M. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 683–702). Cambridge, MA: MIT Press.

Additional Topics

Cross-modal Plasticity

Of substantial interest is whether, and the degree to which, the different sensory modalities can compensate for each other after abnormal experience, disuse, or damage. See Rauschecker (1995) and Neville (1990).

Map Development

Although the formation of topographic maps for the different sensory modalities has been well documented, the issue of how overlapping sensory representations come about in cross-modal structures is of substantial interest. See Knudsen and Brainard (1995) and Schnupp, King, Smith, and Thompson (1995).

Attention

Attentive mechanisms influence much of what we do and the speed with which we do it. Although much of the literature on sensory attention examines intramodal processes, they apply equally well to questions of whether attending to a cue in one modality affects the ability to attend and react to a cue from another modality. See Hillyard, Mangun, Woldorff, and Luck (1995). Sparks and Groh (1994) is a review of the unique role of the superior colliculus in the transformation of sensory information into appropriate motor commands.

References

Ackerman, D. (1990). *A natural history of the senses*. New York: Vintage Books/Random House.

Andreassi, J. L., & Greco, J. R. (1975). Effects of bisensory stimulation on reaction time and the evoked cortical potential. *Physiology and Psychology, 3*,189–194.

Asanuma, C., Ohkawa, R., Stanfield, B. B., & Cowan, W. M. (1988). Observations on the development of certain ascending inputs to the thalamus in rats. I. Postnatal development. *Developments in Brain Research, 41*, 159–170.

Benedetti, F. (1991). The postnatal emergence of a functional somatosensory representation in the superior colliculus of the mouse. *Developments in Brain Research, 60*, 51–57.

Bernstein, I. H., Clark, M. H., & Edelstein, B. A. (1969). Effects of an auditory signal on visual reaction time. *Journal of Experimental Psychology, 80*, 567–569.

Biguer, B., Donaldson, I. M. L., Hein, A., & Jeannerod, M. (1988). Neck muscle vibration modifies the representation of visual motion and direction in man. *Brain, 111*, 1405–1424.

Bower, T. G. R. (1977). *A primer of infant development*. San Francisco: WH Freeman.

Bruce, C., Desimone, R., & Gross, C. G. (1981). Visual properties of neurons in a polysensory area in superior temporal sulcus of the macaque. *Journal of Neurophysiology, 46*, 369–384.

Bullock, T. H. (1984). Physiology of the tectum mesencephali in elasmobranchs. In H. Vanegas (Ed.), *Comparative neurology of the optic tectum* (pp 47–68). New York: Plenum Press.

Casagrande, V. A., Harting. J. K., Hall, W. C., & Diamond, I. T. (1972). Superior colliculus of the tree shrew: A structural and functional subdivision into superficial and deep layers. *Science*, *177*, 444–447.

Chalupa, L. M., & Rhoades, R. W. (1977). Responses of visual, somatosensory, and auditory neurones in the golden hamster's superior colliculus. *Journal of Physiology (London)*, *207*, 595–626.

Clarey, J. C., & Irvine, D. R. F. (1986). Auditory response properties of neurons in the anterior ectosylvian sulcus of the cat. *Brain Research*, *386*, 12–19.

Clark, B., & Graybiel, A. (1966). Contributing factors in the perception of the oculogravic illusion. *American Journal of Psychology*, *79*, 377–388.

Clemo, H. R., Meredith, M. A., Wallace, M. T., & Stein, B. E. (1991). Is the cortex of cat anterior ectosylvian sulcus a polysensory area? *Society of Neuroscience Abstracts*, *17*, 1585.

Clemo, H. R., & Stein, B. E. (1982). Somatosensory cortex: A "new" somatotopic representation. *Brain Research*, *235*, 162–168.

Cytowic, R. E. (1989). *Synesthesia: A union of the senses*. New York: Springer-Verlag.

Drager, U. C., & Hubel, D. H. (1975). Responses to visual stimulation and relationship between visual, auditory and somatosensory inputs in mouse superior colliculus. *Journal of Neurophysiology*, *38*, 690–713.

Duhamel, J.-R., Colby, C. L., & Goldberg, M. E. (1991). Congruent representations of visual and somatosensory space in single neurons of monkey ventral intraparietal cortex (Area VIP). In J. Paillard (Ed.), *Brain and space* (pp. 223–236). New York: Oxford University Press.

Edwards, S. B., Ginsburgh, C. L., Henkel, C. K., & Stein, B. E. (1979). Sources of subcortical projections to the superior colliculus in the cat. *Journal of Comparative Neurology*, *184*, 309–330.

Finlay, B. L., Schneps, S. E., Wilson, K. G., & Schneider, G. E. (1978). Topography of visual and somatosensory projections to the superior colliculus of the golden hamster. *Brain Research*, *142*, 223–235.

Fogassi, L., Gallese, V., Fadiga, L., Luppino, G., Matelli, M., & Rizzolatti, G. (1996). Coding of peripersonal space in inferior premotor cortex (area F4). *Journal of Neurophysiology*, *76*, 141–157.

Frens, M. A., & Van Opstal, A. J. (1998). Visual-auditory interactions modulate saccade-related activity in monkey superior colliculus. *Brain Research Bulletin*, *46*, 211–224.

Frens, M. A., Van Opstal, A. J., & Van der Willigen, R. F. (1995). Spatial and temporal factors determine audio-visual interactions in human saccadic eye movements. *Perception & Psychophysics*, *57*, 802–816.

Frost, D. O. (1984). Axonal growth and target selection during development: Retinal projections to the ventrobasal complex and other "nonvisual" structures in neonatal Syrian hamsters. *Journal of Comparative Neurology*, *230*, 576–592.

Gibson, J. J. (1966). *The senses considered as perceptual systems*. Boston: Houghton Mifflin.

Gielen, S. C. A. M., Schmidt, R. A., & van den Heuvel, P. J. M. (1983). On the nature of intersensory facilitation of reaction time. *Perception & Psychophysics*, *34*, 161–168.

Goldring, J. E., Dorris, M. C., Corneil, B. D., Ballantyne, P. A., & Munoz, D. P. (1996). Combined eye-head gaze shifts to visual and auditory targets in humans. *Experimental Brain Research*, *111*, 68–78.

Gottlieb, G., Tomlinson, W. R., & Radell, P. L. (1989). Developmental intersensory interference: Premature visual experience suppresses auditory learning in ducklings. *Infant Behavior and Development*, *12*, 1–12.

Graybiel, A., & Niven, J. I. (1951). The effect of a change in direction of resultant force on sound localization: The audiogravic illusion. *Journal of Experimental Psychology*, *42*, 227–230.

Graziano, M. S., Hu, X. T., & Gross, C. G. (1997). Visuospatial properties of ventral premotor cortex. *Journal of Neurophysiology*, *77*, 2268–2292.

Graziano, M. S., Yap, G. S., & Gross, C. G. (1994). Coding of visual space by premotor neurons. *Science*, *266*, 1054–1057.

Groh, J. M., & Sparks, D. L. (1996). Saccades to somatosensory targets. III. Eye-position-dependent somatosensory activity in primate superior colliculus. *Journal of Neurophysiology*, *75*, 439–453.

Hartline, P. H., Kass, L., & Loop, M. S. (1978). Merging of modalities in the optic tectum: Infrared

and visual integration in rattlesnakes. *Science, 199*, 1225–1229.

Hartline, P. H., Pandey Vimal, R. L., King, A. J., Kurylo, D. D., & Northmore, D. P. M. (1995). Effects of eye position on auditory localization and neural representation of space in superior colliculus of cats. *Experimental Brain Research, 104*, 402–408.

Held, R. (1955). Shifts in binaural localization after prolonged exposures to atypical combinations of stimuli. *American Journal of Psychology, 68*, 526–548.

Helmholtz, H. von (1968). The origin of the correct interpretation of our sensory impressions. In R. M. Warren & R. P. Warren (Eds.), *Helmholtz on perception: Its physiology and development* (pp 247–266). New York: Wiley.

Hershenson, M. (1962). Reaction time as a measure of intersensory facilitation. *Journal of Experimental Psychology, 63*, 289–293.

Highstein, S. M., & Baker, R. (1985). Action of the efferent vestibular system on primary afferents in the toadfish, *Opsanus tau*. *Journal of Neurophysiology, 54*, 370–384.

Hillyard, S. A., Mangun, G. R., Woldorff, M. G., & Luck, S. J. (1995). Neural mechanisms mediating selective attention. In M. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 665–681). Cambridge, MA: MIT Press.

Howard, I. P., & Templeton, W. B. (1966). *Human spatial orientation*. London: Wiley.

Huerta, M. F., & Harting, J. K. (1984). The mammalian superior colliculus: Studies of its morphology and connections. In H. Vanegas (Ed.), *Comparative neurology of the optic tectum* (pp. 687–773). New York: Plenum Press.

Hughes, H. C., Reuter-Lorenz, P. A., Nozawa, G., & Fendrich, R. (1994). Visual-auditory interactions in sensorimotor processing: Saccades versus manual responses. *Journal of Experimental Psychology: Human Perception & Performance, 20*, 131–153.

Innocenti, G. M., & Clarke, S. (1984). Bilateral transitory projection to visual areas from auditory cortex in kittens. *Developments in Brain Research, 14*, 143–148.

Jay, M. F., & Sparks, D. L. (1987a). Sensorimotor integration in the primate superior colliculus. I. Motor convergence. *Journal of Neurophysiology, 57*, 22–34.

Jay, M. F., & Sparks, D. L. (1987b). Sensorimotor integration in the primate superior colliculus. II. Coordinates of auditory signals. *Journal of Neurophysiology, 57*, 35–55.

Jiang, H., Lepore, F., Ptito, M. & Guillemot, J. P. (1994a). Sensory modality distribution in the anterior ectosylvian cortex (AEC) of cats. *Experimental Brain Research, 97*, 404–414.

Jiang, H., Lepore, F., Ptito, M. & Guillemot, J. P. (1994b). Sensory interactions in the anterior ectosylvian cortex of cats. *Experimental Brain Research, 101*, 385–396.

Kadunce, D. C., Vaughan, J. W., Wallace, M. T., Benedek, G., & Stein, B. E. (1997). Mechanisms of within-modality and cross-modality suppression in the superior colliculus. *Journal of Neurophysiology, 78*, 2834–2847.

King, A. J., & Carlile, S. (1993). Changes induced in the representation of auditory space in the superior colliculus by rearing ferrets with binocular lid suture. *Experimental Brain Research, 94*, 444–455.

King, A. J., & Palmer, A. R. (1985). Integration of visual and auditory information in bimodal neurones in the guinea-pig superior colliculus. *Experimental Brain Research, 60*, 492–500.

Knudsen, E. I. (1982). Auditory and visual maps of space in the optic tectum of the owl. *Journal of Neuroscience, 2*, 1177–1194.

Knudsen, E. I., & Brainard, M. S. (1991). Visual instruction of the neural map of auditory space in the developing optic tectum. *Science, 253*, 85–87.

Lackner, J. R. (1974a). Changes in auditory localization during body tilt. *Acta Oto-Laryngologica (Stockh), 77*, 19–28.

Lackner, J. R. (1974b). Influence of visual rearrangement and visual motion on sound localization. *Neuropsychologia, 12*, 291–293.

Larson, M., & Stein, B. E. (1984). The use of tactile and olfactory cues in neonatal orientation and localization of the nipple. *Developmental Psychobiology, 17*, 423–436.

Lee, C., Chung, S., Kim, J., & Park, J. (1991). Auditory facilitation of visually guided saccades. *Society of Neuroscience Abstracts, 17*, 862.

Lickliter, R. (1990). Premature visual stimulation accelerates intersensory functioning in bobwhite quail neonates. *Developmental Psychobiology*, *23*, 15–27.

Marks, L. E. (1975). On colored-hearing synesthesia: Cross-modal translations of sensory dimensions. *Psychological Bulletin*, *82*, 303–331.

Marks, L. E. (1978). *The unity of the senses: Interrelations among the modalities*. New York: Academic Press.

Massaro, D. W., & Stork, D. G. (1998). Speech recognition and sensory integration. *American Science*, *86*, 236–244.

Maurer, D., & Maurer, C. (1988). *The world of the newborn*. New York: Basic Books.

McGurk, H., & MacDonald, J. (1976). Hearing lips and seeing voices. *Nature*, *264*, 746–748.

McHaffie, J. G., Kao, C.-Q., & Stein, B. E. (1989). Nociceptive neurons in rat superior colliculus: Response properties, topography and functional implications. *Journal of Neurophysiology*, *62*, 510–525.

Meltzoff, A. N., & Moore, M. K. (1977). Imitation of facial and manual gestures by human neonates. *Science*, *198*, 75–78.

Meltzoff, A. N., & Moore, M. K. (1983a). The origins of imitation in infancy: Paradigm, phenomena, and theories. In L. P. Lipsitt (Ed.), *Advances in infancy research* (Vol. 2, pp. 265–301). Norwood, NJ: Ablex.

Meltzoff, A. N., & Moore, M. K. (1983b). Newborn infants imitate adult facial gestures. *Child Development*, *54*, 702–709.

Meredith, M. A., Nemitz, J. W., & Stein, B. E. (1987). Determinants of multisensory integration in superior colliculus neurons. I. Temporal factors. *Journal of Neuroscience*, *10*, 3215–3229.

Meredith, M. A., & Stein, B. E. (1986). Visual, auditory and somatosensory convergence on cells in superior colliculus results in multisensory integration. *Journal of Neurophysiology*, *56*, 640–662.

Meredith, M. A., & Stein, B. E. (1996). Spatial determinants of multisensory integration in cat superior colliculus. *Journal of Neurophysiology*, *75*, 1843–1857.

Meredith, M. A., Wallace, M. T., & Stein, B. E. (1992). Visual, auditory and somatosensory convergence in output neurons of the cat superior colliculus: Multisensory properties of the tecto-reticulo-spinal projection. *Experimental Brain Research*, *88*, 181–186.

Morrell, L. K. (1968a). Cross-modality effects upon choice reaction time. *Psychonomic Science*, *11*, 129–130.

Morrell, L. K. (1968b). Temporal characteristics of sensory interaction in choice reaction times. *Journal of Experimental Psychology*, *77*, 14–18.

Morrell, L. K. (1972). Visual system's view of acoustic space. *Nature*, *238*, 44–46.

Mucke, L., Norita, M., Benedek, G., & Creutzfeldt, O. (1982). Physiologic and anatomic investigation of a visual cortical area situated in the ventral bank of the anterior ectosylvian sulcus of the cat. *Experimental Brain Research*, *46*, 1–11.

Neville, H. J. (1990). Intermodal competition and compensation in development. Evidence from studies of the visual system in congenitally deaf adults. *Annals of the New York Academy of Science*, *608*, 71–87.

Olson, C. R., & Graybiel, A. M. (1987). Ectosylvian visual area of the cat: Location, retinotopic organization, and connections. *Journal of Comparative Neurology*, *261*, 277–294.

Paulesu, E., Harrison, J., Baron-Cohen, S., Watson, J. D., Goldstein, L., Heather, J., Frackowiak, R. S., & Frith, C. D. (1995). The physiology of coloured hearing. A PET activation study of colour-word synaesthesia. *Brain*, *118*, 661–676.

Peck, C. K., Baro, J. A., & Warder, S. M. (1995). Effects of eye position on saccadic eye movements and on the neural responses to auditory and visual stimuli in cat superior colliculus. *Experimental Brain Research*, *103*, 227–242.

Perrott, D. R., Saberi, K., Brown, K., & Strybel, T. Z (1990). Auditory psychomotor coordination and visual search performance. *Perception & Psychophysics*, *48*, 214–226.

Piaget, J. (1952). *The origins of intelligence in children*. New York: International Universities Press.

Pick, H. L., Jr., Warren, D. H., & Hay, J. C. (1969). Sensory conflict in judgements of spatial direction. *Perception & Psychophysics*, *6*, 203–205.

Posner, M. I., Nissen, M. J., & Klein, R. M. (1976). Visual dominance: An information-processing account of its origins and significance. *Psychological Reviews*, *83*, 157–171.

Ramachandran, R., Wallace, M. T., Clemo, H. R., & Stein, B. E. (1993). Multisensory convergence and integration in rat cortex. *Society of Neuroscience Abstracts*, *19*, 1447.

Rauschecker, J. P. (1995). Compensatory plasticity and sensory substitution in the cerebral cortex. *Trends in Neuroscience*, *18*, 36–43.

Rizzolatti, G., Scandolara, C., Matelli, M., & Gentilucci, M. (1981a). Afferent properties of periarcuate neurons in macaque monkeys. I. Somatosensory responses. *Behavioral Brain Research*, *2*, 125–146.

Rizzolatti, G., Scandolara, C., Matelli, M., & Gentilucci, M. (1981b). Afferent properties of periarcuate neurons in macaque monkeys. II. Visual responses. *Behavioral Brain Research*, *2*, 147–163.

Roll, R., Velay, J. L., Roll, J. P. (1991). Eye and neck proprioceptive messages contribute to the spatial coding of retinal input in visually oriented activities. *Experimental Brain Research*, *85*, 423–431.

Ryan, T. A. (1940). Interrelations of the sensory systems in perception. *Psychological Bulletin*, *37*, 659–698.

Schneider, G. E. (1969). Two visual systems: Brain mechanisms for localization and discrimination are dissociated by tectal and cortical lesions. *Science*, *163*, 895–902.

Schnupp, J. W. H., King, A. J., Smith, A. L., & Thompson, I. D. (1995). NMDA-receptor antagonists disrupt the formation of the auditory space map in the mammalian superior colliculus. *Journal of Neuroscience*, *15*, 1516–1531.

Shelton, B. R., & Searle, C. L. (1980). The influence of vision on the absolute identification of sound-source position. *Perception & Psychophyics*, *28*, 589–596.

Sparks, D. L., & Groh, J. M. (1994). The superior colliculus: A window for viewing issues in integrative neuroscience. In M. Gazzaniga (Ed.), *The cognitive neurosciences* (pp. 565–584). Cambridge, MA: MIT Press..

Sparks, D. L., & Nelson, J. S. (1987). Sensory and motor maps in the mammalian superior colliculus. *Trends in Neuroscience*, *10*, 312–317.

Sprague, J. M., & Meikle, T. H., Jr. (1965). The role of the superior colliculus in visually guided behavior. *Experimental Neurology*, *11*, 115–146.

Stein, B. E., & Dixon, J. P. (1979). Properties of superior colliculus neurons in the golden hamster. *Journal of Comparative Neurology*, *183*, 269–284.

Stein, B. E., & Gaither, N. (1981). Sensory representation in reptilian optic tectum: Some comparisons with mammals. *Journal of Comparative Neurology*, *202*, 69–87.

Stein, B. E., & Gallagher, H. (1981). Maturation of cortical control over superior colliculus cells in cat. *Brain Research*, *223*, 429–435.

Stein, B. E., Labos, E., & Kruger, L. (1973). Sequence of changes in properties of neurons of superior colliculus of the kitten during maturation. *Journal of Neurophysiology*, *36*, 667–679.

Stein, B. E., London, N., Wilkinson, L. K., & Price, D. D. (1996). Enhancement of perceived visual intensity by auditory stimuli: A psychophysical analysis. *Journal of Cognitive Neuroscience*, *8*, 497–506.

Stein, B. E., & Meredith, M. A. (1991). Functional organization of the superior colliculus. In A. G. Leventhal (Ed.), *The neural basis of visual function* (pp. 85–110). Hampshire, UK: Macmillan.

Stein, B. E., & Meredith, M. A. (1993). *The merging of the senses*. Cambridge, MA: MIT Press.

Stein, B. E., Meredith, M. A., Huneycutt, W. S., McDade, L. (1989). Behavioral indices of multisensory integration: Orientation to visual cues is affected by auditory stimuli. *Journal of Cognitive Neuroscience*, *1*, 12–24.

Stein, B. E., Meredith, M. A., & Wallace, M. T. (1993). The visually responsive neuron and beyond: Multisensory integration in cat and monkey. *Progress in Brain Research*, *95*, 79–90.

Stein, B. E., Spencer, R. F., & Edwards, S. B. (1983). Corticotectal and corticothalamic efferent projections of SIV somatosensory cortex in cat. *Journal of Neurophysiology*, *50*, 896–909.

Stein, B. E., & Wallace, M. T. (1996). Comparisons of cross-modality integration in midbrain and

cortex. *Progress in Brain Research*, *112*, 289–299.

Sumby, W. H., & Pollack, I. (1954). Visual contribution to speech intelligibility in noise. *Journal of the Acoustical Society of America*, *26*, 212–215.

Sur, M., Garraghty, P. E., & Roe, A. W. (1988). Experimentally induced visual projections into auditory thalamus and cortex. *Science*, *242*, 1437–1441.

Thurlow, W. R., & Rosenthal, T. M. (1976). Further study of existence regions for the "ventriloquism effect." *Journal of the American Audiological Society*, *1*, 280–286.

Tiao, Y.-C., & Blakemore, C. (1976). Functional organization in the superior colliculus of the golden hamster. *Journal of Comparative Neurology*, *168*, 483–504.

Turkewitz, G., & Mellon, R. C. (1989). Dynamic organization of intersensory function. *Canadian Journal of Psychology*, *43*, 286–307.

von Hornbostel, E. M. (1938). The unity of the senses. In W. D. Ellis (Ed.), *A sourcebook of Gestalt psychology* (pp 211–216). New York: Harcourt Brace.

Wade, N. J., & Day, R. H. (1968). Apparent head position as a basis for a visual aftereffect of prolonged head tilt. *Perception & Psychophysics*, *3*, 324–326.

Wallace, M. T., McHaffie, J. G., & Stein, B. E. (1995). Sensory response properties in the superior colliculus (SC) of the newborn rhesus monkey. *Society of Neuroscience Abstracts*, *21*, 655.

Wallace, M. T., Meredith, M. A., & Stein, B. E. (1992). Integration of multiple sensory modalities in cat cortex. *Experimental Brain Research*, *91*, 484–488.

Wallace, M. T., Meredith, M. A., & Stein, B. E. (1993). Converging influences from visual, auditory and somatosensory cortices onto output neurons of the superior colliculus. *Journal of Neurophysiology*, *69*, 1797–1809.

Wallace, M. T., Meredith, M. A., & Stein, B. E. (1998). Multisensory integration in the superior colliculus of the alert cat. *Journal of Neurophysiology*, *80*, 1006–1010.

Wallace, M. T., & Stein, B. E. (1994). Cross-modal synthesis in the midbrain depends on input from association cortex. *Journal of Neurophysiology*, *71*, 429–432.

Wallace, M. T., & Stein, B. E. (1996). Sensory organization of the superior colliculus in cat and monkey. *Progress in Brain Research*, *112*, 301–311.

Wallace, M. T., & Stein, B. E. (1997). Development of multisensory neurons and multisensory integration in cat superior colliculus. *Journal of Neuroscience*, *17*, 2429–2444.

Wallace, M. T., Wilkinson, L. K., & Stein, B. E. (1996). Representation and integration of multiple sensory inputs in primate superior colliculus. *Journal of Neurophysiology*, *76*, 1246–1266.

Warren, D. H., Welch, R. B., & McCarth, T. J. (1981). The role of visual-auditory "compellingness" in the ventriloquism effect: Implications for transitivity among the spatial senses. *Perception & Psychophyics*, *30*, 557–564.

Welch, R. B., & Warren, D. H. (1980). Immediate perceptual response to intersensory discrepancy. *Psychological Bulletin*, *88*, 638–667.

Welch, R. B., & Warren, D. H. (1986). Intersensory interactions. In K. R. Boff, L. Kaufman, & J. P. Thomas (Eds.), *Handbook of perception and human performance, Volume I: Sensory processes and perception* (pp.1–36). New York: Wiley.

Wilkinson, L. K., Meredith, M. A., & Stein, B. E. (1996). The role of anterior ectosylvian cortex in cross-modality orientation and approach behavior. *Experimental Brain Research*, *112*, 1–10 .

Withington-Wray, D. J., Binns, K. E., & Keating, M. J. (1990). The maturation of the superior collicular map of auditory space in the guinea pig is disrupted by developmental visual deprivation. *European Journal of Neuroscience*, *2*, 682–692.

Withington-Wray, D. J., Binns, K. E., Dhanjal, S. S., Brickley, S. G., & Keating, M. J. (1990). The maturation of the collicular map of auditory space in the guinea pig is disrupted by developmental auditory deprivation. *European Journal of Neuroscience*, *2*, 693–703.

Zahn, J. R., Abel, L. A., & Dell'Osso, L. F. (1978). Audio-ocular response characteristics. *Sensory Process*, *2*, 32–37.