

Development of the Superior Colliculus/Optic Tectum

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3.1 NOMENCLATURE

Anatomically, the *tectum* is that portion of the mesencephalon, or midbrain, sitting between the hindbrain and the forebrain. The name is the Latin word for *roof* and reflects the view of early anatomists that the tectum formed a roof over the fluid-filled cerebral aqueduct and the tegmentum. In mammals, it sometimes is referred to as the *tectal plate* (or *quadrigeminal plate*) and is composed of two pairs of bumps or colliculi (*collis* means hill in Latin), one on each side of the midbrain. The more rostral pair is referred to as the *superior colliculi*, and the more caudal pair is known as the *inferior colliculi*.

However, the reader should be aware that there is some confusion in the nomenclature. The term *optic tectum* (OT) properly refers to the nonmammalian homolog of the superior colliculus (SC), and its name reflects its preeminent visual role in these animals. Thus, discussions of the OT are generally specific to the major central nervous system visual nucleus in birds, reptiles, amphibians, and fish, animals from which much has been learned about the function of the OT. But while the mammalian homolog of the OT is called the *superior colliculus*, projections to and from it are called *tectopetal* (e.g., *retinotectal*, *corticotectal*) and *tectofugal* (e.g., *tectoreticular*, *tectospinal*), respectively. The confusing nature of this

nomenclature is compounded by the tendency of some to refer to the SC as the OT and of others to use *colliculo(ar)* for *tecto(al)*.

The primary subject of the following discussion is the SC; however, the OT and SC have fundamental functional similarities, and research on the OT will be referred to when it is instructive for understanding SC organization, function, or both.

3.2 FUNCTIONAL ROLE

Although the SC, like its nonmammalian counterpart, is clearly visually dominant, it is not strictly visual, and neither is the OT. Furthermore, the role of the SC is not restricted to visuomotor behavior (nor is the OT). Rather, it is a multisensory structure that contains visual, auditory, and somatosensory representations, all of which contribute to its role in initiating orientation and localization behaviors that involve multiple sensory organs. Thus, although the visuomotor role in gaze shifts (i.e., movement of the eyes with or without corresponding movement of the head) is well known (Sparks, 1986), it also is involved in orientation of the ears (Stein and Clamann, 1981) and limbs (Stein and Gaither, 1981; Stuphorn et al., 2000). It is best to think of the SC as involved in the transformation of sensory signals (visual, auditory, and somatosensory) into motor commands.

Its ability to represent salient stimuli and engage in sensorimotor transduction so that the organism can initiate rapid orientation to the initiating event is critical to survival. The rapid maturation of the SC compared with that of the cortex reflects its importance in minimizing early ecological vulnerabilities as neonates develop greater independence. This is especially evident in altricial species, whose birth at an early stage of maturation makes observation of neural development far easier than

in their precocial counterparts. However, in the adult stage of both altricial and precocial species, the communication between the cortex and SC reaches its apex, and their complementary and interdependent functions become linked through their reciprocal connections.

Before discussing the developmental features that render the SC capable of performing its adult role or how its inherent plasticity is reflected in changes resulting from sensory experience, trauma, or both, it first is necessary to describe its overall structure and function in the mature brain. A discussion of the major features of this remarkable structure follows.

3.3 GENERAL ANATOMICAL ORGANIZATION OF THE SUPERIOR COLICULUS

The SC is a laminated structure, composed of seven alternating fibrous and cellular layers (Kanaseki and Sprague, 1974), as shown in the illustration of a cat in Figure 3.1. Operationally, however, it is divided into two broad regions: superficial (I–III) and deep (IV–VII) layers (Edwards, 1980; Harting et al., 1973; Stein, 1984). The former is strictly visual. It receives a substantial direct projection from the retina, as well as many visual projections indirectly from a host of other subcortical and cortical structures (Edwards et al., 1979). Its outputs ascend the neuraxis via the sensory thalamus and are relayed from there to the extrastriate cortex. Its descending projections pass through the deeper layers to target another visual site, the parabigeminal nucleus.

In contrast, the deep layers of the SC contain a much more heterogeneous group of neurons, which includes recipients not only of visual inputs (few come directly from the retina, but many are relayed from other brain regions, especially the cortex) but also of inputs from

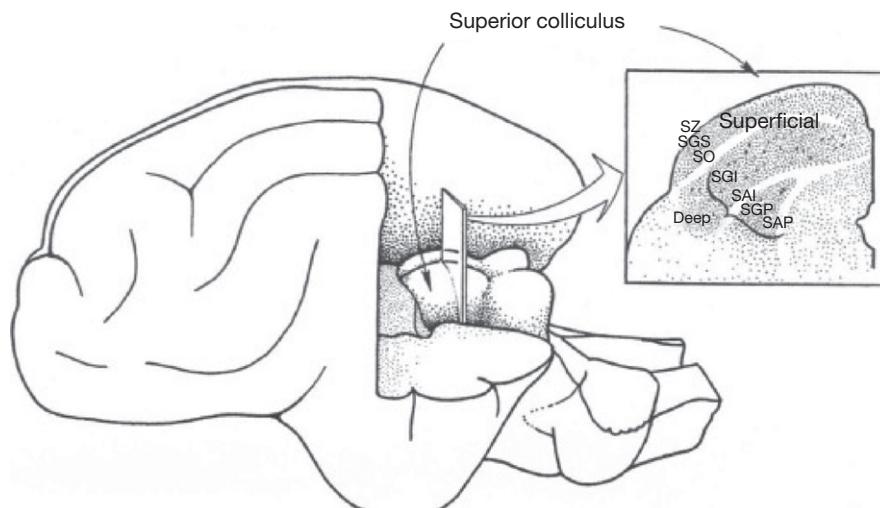


FIGURE 3.1 Lateral view of the cat brain and superior colliculus (SC). A portion of cortex has been removed to reveal the SC and IC (unlabeled). A coronal section of the SC to the right shows its layers: SZ, stratum zonale; SGS, stratum griseum superficiale; SO, stratum opticum; SGI, stratum griseum intermediale; SAI, stratum album intermediale; SGP, stratum griseum profundum; SAP, stratum album profundum. Reproduced from Stein BE, Meredith MA (1993) *The Merging of the Senses*. Cambridge, MA: MIT Press.

the auditory, somatosensory, and motor systems (Stein and Meredith, 1993). In keeping with their role in sensorimotor transformation, the deeper layers send heavy descending projections to the regions of the brainstem and spinal cord that control movements of the eyes, ears, head, and limbs, as well as outputs to nonspecific sensory and motor areas of the thalamus (Edwards, 1980; Edwards and Henkel, 1978; Edwards et al., 1979; Harting, 1977; Harting et al., 1973, 1980; Moschovakis and Karabelas, 1985; Redgrave et al., 1985, 1986a,b; Rhoades et al., 1987; Sommer and Wurtz, 1998, 2004a,b; Stein and Edwards, 1979; Weber et al., 1979). It is the deep layers that are most closely associated with the sensorimotor roles for which the SC is best known; because they contain neurons responsive to multiple sensory modalities, they are referred to as the multisensory layers.

3.4 SPATIAL TOPOGRAPHIES, MULTISENSORY INTEGRATION, AND MOTOR OUTPUT

3.4.1 Visuotopy

Physically, the SC is aligned with the general axis of the brain, so its rostral pole points forward and its caudal pole points backward. Neurons in its superficial visual layers are arranged in a visuotopic (i.e., retinotopic) map of contralateral visual space and the map in the cat SC (e.g., see Feldon et al., 1970) is generally representative of those in animals having forward-facing eyes (see Cynader and Berman, 1972 for a description in monkeys). SC neurons having receptive fields in central visual space are located rostrally in the structure and are the smallest. Thus, this portion of the map has the greatest spatial resolution. Neurons having receptive fields progressively more peripheral (i.e., temporal) in space are located progressively more caudal in the structure and are the largest. This portion of the map has the lowest spatial fidelity. In short, the horizontal meridian from central to peripheral visual space runs roughly rostrocaudal. The vertical meridian is roughly orthogonal to the horizontal meridian, with superior visual space represented medial and inferior space represented lateral. The central visual point (i.e., the fovea in primates and area centralis in carnivores) is the point at which the horizontal and vertical meridians cross.

The central representation of visual space is expanded in the SC. Thus, for example, the central 10° of space occupies more than a third of the tissue devoted to the map in the cat SC and more than half the tissue in monkey SC. In some species, such as the cat, neurons located rostral to the vertical meridian extend the map to represent up to 10° of the ipsilateral hemifield. This nasal representation is essentially nonexistent in monkeys (Cynader and

Berman, 1972), but is much larger in animals such as rats, which have eyes on the sides of their head (e.g., see Siminoff et al., 1966).

A retinotopic organization is also characteristic of the OT, although in some nonmammalian species, the vertical and horizontal meridians are not always as well aligned with the brain's rostrocaudal axis as they are in mammals (e.g., see Gaither and Stein, 1979). The ubiquity of a retinotopy likely represents the ease of using a map to determine the location of a visual event and of transforming the visual cues it provides into motor coordinates for orientation responses. However, this sensorimotor transduction is primarily a function of the deep (i.e., multisensory) layers of the SC, which also contain a map of the visual space.

The retinotopy in the deep layers is similar to that of the overlying superficial layer map; however, the source of visual afferents differs somewhat. Receptive fields are considerably larger than those in the overlying layers, and as a result, there is lower spatial resolution in this visual map (McIlwain, 1975, 1991; Meredith and Stein, 1990). Yet, it has a better representation of the far periphery and also extends a bit further into the ipsilateral hemifield than does the superficial layer map (Meredith and Stein, 1990). Shifts in receptive field size follow the same trend as those in superficial layers, with central visual fields being the smallest and far peripheral receptive fields being the largest. But the visual map in the multisensory layers is only one of three overlapping spatiotopic sensory representations in this region of the structure.

3.4.2 Somatotopy

The somatosensory representation in the multisensory SC is largely of the cutaneous surface and its maplike representation is called 'somatotopic.' Its relationship to the visuotopic representation has also been studied most extensively in cats (see Meredith et al., 1991; Stein et al., 1975; but see also Benedetti and Ferro, 1995; Dräger and Hubel, 1975; McHaffie et al., 1989). Like the visual representation, it is formed from comparatively large receptive fields that are organized into a map of the body, with a geometric expansion of the representation of the face and head. The face representation is made up of the smallest receptive fields, is located rostrally, and roughly overlaps the representation of central visual space. The body and rump are represented more caudal and the limbs extend laterally, so that the upper body space is represented medially to coincide with the representation of upper visual space and the lower body space is represented laterally to coincide with the representation of lower visual space. Given that the SC also receives inputs from pathways

carrying information about potentially harmful stimuli, it is not surprising to find that it also has neurons responsive to noxious stimuli (Stein and Dixon, 1978, 1979). These neurons have many of the same properties found in structures better known for dealing with nociceptive information (Larson et al., 1987; Rhoades et al., 1983). Although this representation has been studied only in rodents and is largely restricted to the face and forelimb (McHaffie et al., 1989; see also Auroy et al., 1991), it incorporates the same general topographic features employed by the other sensory maps (Stein and Meredith, 1993).

3.4.3 Audiotopy

Unlike the visual and somatotopic maps, which are formed directly via afferents from different regions of the retina or skin (albeit with some geometrical distortions), the spatiotopic nature of the auditory representation must be derived via neural computation based on comparisons of the timing, intensity, and frequency of the sound signals at the two ears. Although the term ‘audiotopic’ is not commonly used and hence seems a bit awkward, it is as appropriate as ‘retinotopic’ and ‘somatotopic’ in this context. Its properties have also been examined closely in cats and follow the same general organizational features of the maps that have been outlined earlier. Forward auditory space is represented in the rostral aspect of the structure, temporal auditory space in its caudal aspect, and superior–inferior space is laid out along its mediolateral axis (Middlebrooks and Knudsen, 1984; see also Palmer and King, 1982; King and Palmer, 1983).

3.4.4 Multisensory Integration

The alignment of SC sensory maps is evident in the overlap among modality-specific receptive fields of multisensory SC and OT neurons. Indeed, the individual maps are largely a reflection of the receptive field properties of multisensory neurons that, in cats at least, comprise the majority of sensory responsive neurons in the deep layers. Each multisensory neuron has at least two receptive fields, one for each of the sensory modalities to which it responds (e.g., see Stein and Meredith, 1993 for a review). For example, a visual–auditory neuron with a visual receptive field in central visual space will have an auditory receptive field in an overlapping region of central visual space, so that only visual and auditory cues from roughly the same locations will affect that neuron.

A key element of SC function is derived from the ability of multisensory neurons to integrate the influences of the different sensory modalities and the nature of such integration hinges strongly on map alignment. While

much of the information about multisensory integration comes from studies of single neurons in cat SC, similar observations have also been made in the SC and OT of other species (see, e.g., Bell et al., 2001, 2005; Gaither and Stein, 1979; Hartline et al., 1978; King and Palmer, 1978; Stein and Gaither, 1981; Van Wanrooij et al., 2009; Wallace et al., 1996; Zahar et al., 2009). Operationally defined, ‘multisensory integration’ is the process by which stimuli from different senses combine (i.e., *cross-modal*) to produce a response that differs from those produced by the component stimuli individually. At the level of the single neuron, integration corresponds to a statistically significant difference between the number of impulses evoked by a cross-modal combination of stimuli and the number evoked by the most effective of these stimuli individually (see Stein and Stanford, 2008 for discussion). This difference can be manifested as either a response increase or decrease, depending on how the stimuli are configured in space. Cross-modal stimuli that signal a common event (they are in the same place at the same time) impinge on overlapping modality-specific receptive fields, and the integration of their influences yields response enhancement. Conversely, modality-specific cues emanating from disparate locations affect nonoverlapping regions of their respective sensory maps; disparate cues thus fail to produce enhancement and, in some instances, produce response depression (Kadunce et al., 1997). Examples of multisensory integration that yield response enhancement and response depression are shown in Figure 3.2.

Remarkably, convergence of inputs from different senses alone is not sufficient for multisensory integration in the SC. A matching set of converging unisensory inputs from association cortex is required (primarily from the anterior ectosylvian sulcus (AES); Alvarado et al., 2009; Fuentes-Santamaria et al., 2008a, 2009; Stein et al., 1983 but also inputs from the rostral–lateral suprasylvian sulcus (rLS) play a role – see Jiang et al., 2001). Without these cortical inputs, SC neurons respond to individual cues from different senses but do not integrate them to yield (Alvarado et al., 2007, 2008, 2009; Jiang et al., 2001; Wallace and Stein, 1994). Rather, the neural response to cross-modal stimulation is no greater than that to the best of the stimulus components alone, a finding that is mirrored by an absence of the multisensory advantages that are typical of SC-mediated behaviors (Jiang et al., 2002, 2006, 2007; Wilkinson et al., 1996). The requirement for cortical input has implications for the development of SC multisensory integration and the behaviors it supports, as will be discussed later in this chapter.

Insofar as the magnitude of activity within SC sensory maps corresponds to the physiological salience of an external stimulus, and thus the likelihood that it will generate a motor response, the implications of multisensory integration for behavior are quite clear. Enhanced

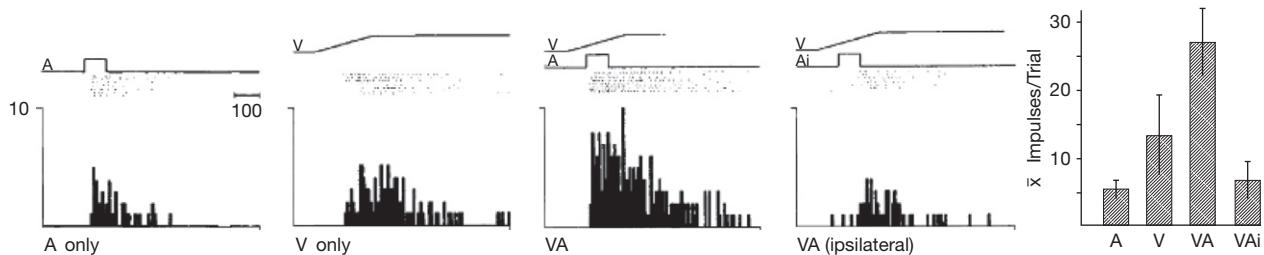


FIGURE 3.2 Multisensory enhancement. Left: A square-wave broadband auditory stimulus (A, 1st panel) and a moving visual stimulus (ramp labeled V, 2nd panel) evoked unisensory responses from this neuron (illustrated below the stimulus by rasters and peristimulus time histograms). Each dot in the raster represents a single impulse; each row, a single trial. Trials are ordered from bottom to top. The 3rd panel shows the response to auditory and visual stimulus presentation at the same time and location, which is much more robust than either unisensory response. Yet, when the auditory stimulus was moved into ipsilateral auditory space (Ai) and out of the receptive field, its combination with the visual stimulus elicited fewer impulses than did the visual stimulus individually. This ‘response depression’ is illustrated within the 4th panel. Right: The mean number of impulses/trial elicited by each of the four stimulus configurations. Note the difference between multisensory enhancement (VA) and multisensory depression (VAi). Reproduced from Stein and Rowland, 2011, Progress in Brain Research.

activity for spatially concordant cues corresponds to an increased likelihood of stimulus detection and an associated motor response to orient to that stimulus. In contrast, the multisensory depression that results from stimuli at competing locations would have an opposing effect (Calvert et al., 2004; Gillmeister and Eimer, 2007; Spence et al., 2004; Stein and Stanford, 2008). In either case, sensory-related activation must be transformed into motor commands, which, like their sensory counterparts, assume the form of a topographically organized map.

3.4.5 Mototopic Representation

Many of the neurons in the deep/multisensory layers are output neurons that project to one or more brainstem and spinal cord regions responsible for moving the eyes, ears, whiskers, head, and limbs (Coulter et al., 1979; Edwards and Henkel, 1978; Grantyn and Grantyn, 1982; Harting, 1977; Holcombe and Hall, 1981a,b; Huerta and Harting, 1982a,b; Moschovakis et al., 1998; Weber et al., 1979; see Gandhi and Katnani, 2011; Hall and Moschovakis, 2004; Sparks, 1986; Sparks and Mays, 1990 for reviews). The term ‘mototopic,’ like ‘audiotopic,’ is not in common usage but, once again, seems equally appropriate in this context, given the more commonly used terms ‘visuotopic’ and ‘somatotopic.’ By far, the most is known about the motor topography for producing gaze shifts and for movements of eyes (or the eyes and head) to place stimuli of interest into the line of sight. Accordingly, the motor map for gaze shifts is in register with the visual, auditory, and somatosensory topographies; therefore, the sensory evoked activity represents the distance and direction of a stimulus from the current line of sight, and the motor activity at that site represents a command for shifting gaze to the corresponding distance and in the corresponding direction.

The SC motor map is two-dimensional, with gaze amplitude (from small to large) represented along its rostrocaudal axis and gaze direction (from upward to downward) represented along its mediolateral axis (du Lac and Knudsen, 1990; Goldberg and Wurtz, 1972; Pare et al., 1994; Robinson, 1972; Schiller and Stryker, 1972; Wurtz and Goldberg, 1972). In a manner analogous to sensory receptive fields, constituent neurons of the SC motor map have *movement fields*, such that they respond most vigorously in association with gaze shifts within a particular range of amplitude and direction, and gaze shifts are produced consequent to the activity of their premotor activity. Figure 3.3 illustrates a typical SC movement field for a neuron recorded from the right SC of a monkey. This neuron discharges most vigorously (peak of the 3D plot) for saccades having a direction of approximately 190° (leftward and slightly downward) and having an amplitude of approximately 7° of visual angle (i.e., deviation of eye from the straight ahead position). Considered in the context of the motor map of the right SC, this neuron would be located toward the rostral pole (small movements) and slightly lateral (downward). Thus, like the SC sensory maps, which constitute ‘place codes’ for stimulus location in sensory space, the SC motor map is a ‘place code’ for movement vector, such that the locus of activation determines the amplitude and direction of an impending movement.

3.4.6 Maintaining Sensory and Motor Map Alignment

The overlap among the sensory and motor maps is unlikely to be serendipitous, as it appears to be the most straightforward way to coordinate the cross-modal sensory cues and movements of the various sensory organs toward a salient event. Nevertheless, given the ability to move the different sensory organs independently, retaining the registry of their midbrain maps presents

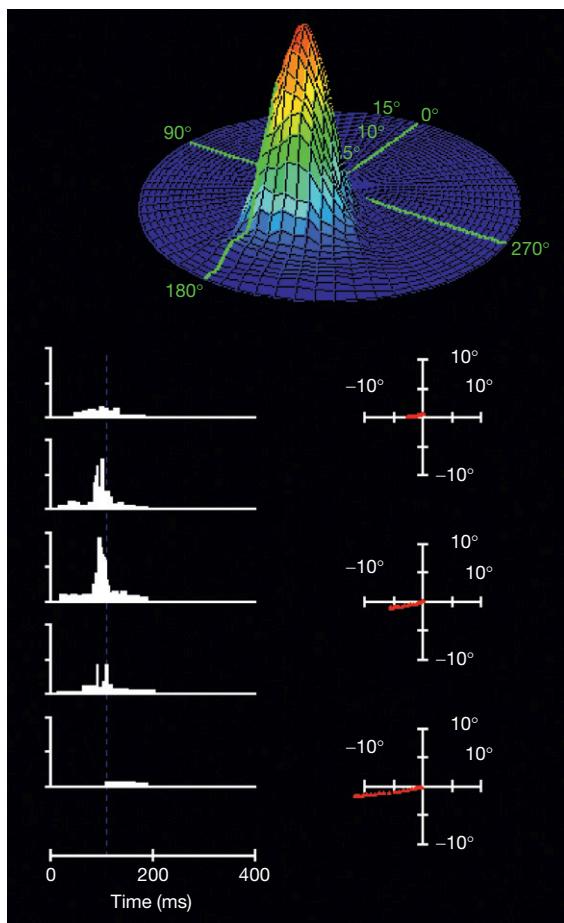


FIGURE 3.3 Superior colliculus movement field. Neurons in the SC have movement fields and discharge most for movements within particular ranges of amplitude and direction. The 3D polar plot (above) illustrates the movement field of an SC neuron that discharges for relatively small and slightly downward saccadic eye movements. Below left, the premotor activity profiles are shown aligned on the onsets of saccades (blue dotted line) of five different amplitudes (top to bottom) and representing a ‘slice’ through the peak of the movement field along the line of best direction. Representative saccade trajectories are shown to the right of the activity profiles. Note that maximum activity corresponds to a slightly downward saccade having amplitude corresponding to roughly 7° of visual angle. *Reproduced from Stanford and Sparks, unpublished observations.*

a nontrivial problem. The problem is partially solved by the nonstatic nature of these maps. Studies in various species show that shifting the eyes voluntarily or inducing long-term shifts in the optical axis via surgical or prismatic means produces a corresponding shift in the SC auditory map (Brainard and Knudsen, 1998; Hartline et al., 1995; Jay and Sparks, 1984; King et al., 1988; Peck et al., 1995). A similar shift may also be initiated in the somatosensory map (Groh and Sparks, 1996). These observations suggest that the different senses are linked to an oculocentric coordinate system, though compensatory shifts in the nonvisual maps do not completely compensate for large ocular misalignments

(Metzger et al., 2004). Maintaining intermap registry ensures that any visual, auditory, or somatosensory cue (and any combination of them) derived from the same location in space activates neurons in approximately the same SC location. This, in turn, accesses the same point in the motor map to produce coordinated orientation of all the sensory organs toward the location of the initiating event. This not only helps determine the nature of that event but also puts the animal in an appropriate position to evaluate it.

3.5 THE MATURATION OF THE SUPERIOR COLICULUS

3.5.1 The Neonate

In altricial species, such as cats, the ability of the SC to use sensory information to initiate overt behaviors is poorly developed at birth. Unlike primates, ungulates, and other precocial species, the newborn carnivore (rodent, lagomorph, marsupial, etc.) is poorly equipped to deal with its sensory environment. Its eyes are closed, there is a vascular network around the lens that impedes the transmission of light (Bonds and Freeman, 1978; Thorn et al., 1976), and it is functionally blind. Similarly, its ear canals are still sealed, and it is deaf. The only sensory inputs that activate SC neurons at this time are tactile. These inputs are already functional prenatally but are only weakly effective and stay that way for some time after birth (Stein et al., 1973a,b). The newborn carnivore’s motor capabilities are also poorly developed, and it depends heavily on its mother for things like warmth and protection, and even the initiation of feeding (Larson and Stein, 1984; Rosenblatt, 1971). The immaturity of the newborn cat’s SC makes it a good model for exploring how sensory responses develop, how the different sensory representations become established, and how multisensory integration develops so that SC neurons can use the available sensory information synergistically to optimize SC-mediated behavior.

3.5.2 Sensory Chronology

As noted, somatosensory responsiveness in some cat SC neurons precedes birth and provides the structure with its first source of information about the world. Auditory responses begin to appear in some SC neurons at 5 days postnatally, and neurons develop visual responsiveness last (Stein et al., 1973a,b). Interestingly, visual responses develop in two sequential phases, first appearing from top to bottom in the most superficial (i.e., visual) layers of the structure and then in a similar manner in neurons in its multisensory (deeper) layers. These phases are widely separated in time, with neurons in the

most superficial strata of the superficial layers beginning to respond to visual stimuli at about 6 postnatal days, and those in the multisensory layers not showing responsiveness to visual stimuli for several weeks (Kao et al., 1994).

3.5.2.1 Retinotectal Inputs and the Development of a Superficial Layer Visuotopy

Because of the visually dominant role of the SC, the development of its visual inputs (especially those coming directly from the retina) has received a great deal of attention. Once again, cats have been one of the primary sources of this information, along with rodents, opossums, and monkeys. Given the functional immaturity of the newborn cat's SC (there is no visual responsiveness yet), it is surprising to note the advanced state of its retinotectal topography during late embryonic development (Graybiel, 1975; Williams and Chalupa, 1982). Although, at this point, the retinotectal projections appear to be restricted to the superficial layers of the SC, segregation of inputs from the contralateral and ipsilateral eyes is already apparent several days before birth (Figure 3.4(b); embryonic day 56), and by embryonic day 61 (Figure 3.4(c)) further refinement leads to an almost adult-like patterning of inputs. This advanced pattern of retinal projections is achieved by sculpting it from a far more widespread projection that is evident at approximately embryonic day 38 (Figure 3.4(a)). At that point, the projections from the two retinas are intermingled and distributed across the entire rostrocaudal and mediolateral extent of the SC. This pattern is

progressively altered so that by embryonic day 61 (4–7 days before parturition) the pattern of ipsilateral and contralateral retinotectal inputs closely resembles the pattern characteristic of the adult. Although the timing is different, similar developmental processes have been noted in monkeys (Rakic, 1977), hamsters (Frost et al., 1979), rats (Land and Lund, 1979), and opossums (Cavalcante and Rocha-Miranda, 1978).

Data from a variety of nonmammalian and mammalian models have suggested that chemoaffinity cues provide the basis for the fundamental topographical order of retinotectal projections and that this coarse representation is subsequently refined by activity-dependent mechanisms (Drescher et al., 1997; Fraser, 1992; Ruthazer and Cline, 2004; Ruthazer et al., 2003; Sperry, 1963; Walter et al., 1987). There is good reason to assume that similar processes are involved in determining the adult-like pattern of sensory afferents to the multisensory layers of the SC, but observations of the development of its retinotectal projections are hampered by weak input, and less attention has been directed toward the maturation of nonvisual inputs. Nevertheless, it has been noted that somatosensory tectopetal afferents are already widespread in the multisensory layers of the SC at birth, and they too appear to have an adult-like configuration (McHaffie et al., 1986, 1988).

The apparent maturity of the representation of tectopetal sensory afferents (inputs) at birth stands in contrast to the significant immaturity in at least one of its tectofugal efferent (output) sensory projections, namely, those to the lateral geniculate nucleus (LGN). This transient

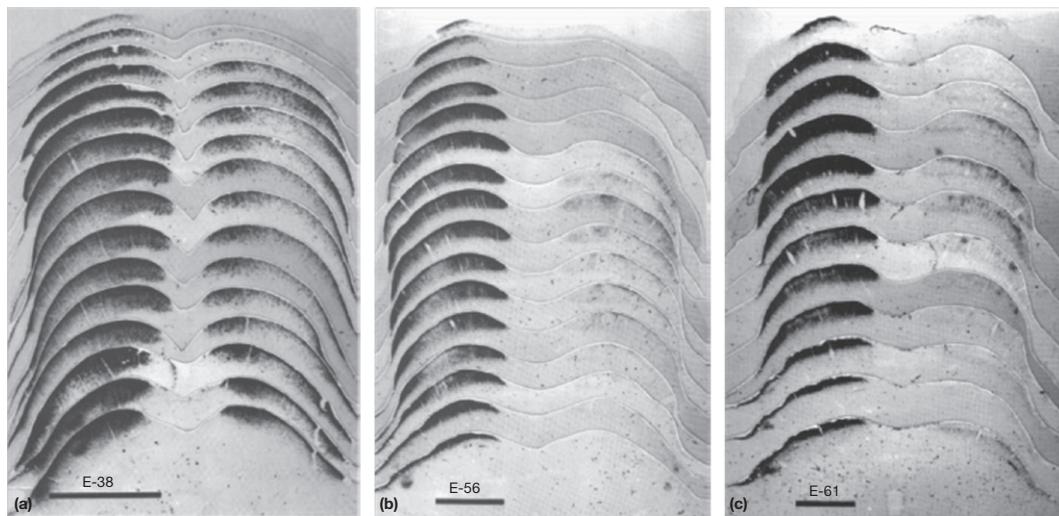


FIGURE 3.4 Retinotectal projection patterns to the superficial superior colliculus are highly developed in cats before birth. Shown are photographic illustrations of the distribution of a tracer (horseradish peroxidase shown as dark regions) from one eye to both colliculi approximately 17 ((a), at E38) and 9 days before birth ((b), at E56). Sections are ordered from rostral (bottom) to caudal (top), with the contralateral SC on the left. The calibration bar is 1 mm. Note that the projection has largely withdrawn from the ipsilateral SC and changed its distribution in the contralateral SC by E56. Several days later, ((c), at E61), an almost adult-like pattern input is apparent. Adapted from Williams RW, Chalupa LM (1982) Prenatal development of retinocollicular projections in the cat: An anterograde tracer transport study. Journal of Neuroscience 2:604–622.

tectogeniculate projection is topographic and is part of the ascending wing of the SC's visual projection that eventually reaches the cortex via polysynaptic pathways. In adults, the tectogeniculate projection is confined to the ventral C layers, but in neonates it extends across all layers of the LGN as well as into the medial interlaminar nucleus. It is retained for approximately 3 postnatal weeks, long after visual function has been initiated, and is eliminated by mechanisms that are not yet fully understood (Stein et al., 1985). Its immaturity contrasts with the more rapidly maturing tectofugal pathways involved in motor functions (Stein et al., 1982, 1984).

Despite the adult-like pattern of retinotectal projections at birth, the visual system is not yet functional. Visual responsiveness begins in superficial layer SC neurons at 6 days of age. At this time, the eyelids are still closed (they open naturally at 7–11 days postnatal) and visually responsive neurons are rare, which are clustered together between ineffective loci (Kao et al., 1994; Stein et al., 1973a). This reflects a random onset of visual activity via random functional coupling of retinotectal afferents and their SC target neurons and/or the random openings in the vascular networks around the lens that begin at about the time of eye opening (Freeman and Lai, 1978). Most active sites are located in the middle portion of the structure and in its most superficial aspect. Nevertheless, the general topographic organization established by the afferent projections is apparent at this time (Kao et al., 1994; Figure 3.5).

Curiously, the initial visual activity is restricted not only across the horizontal aspect of the SC, but also, as noted earlier, in its vertical aspect. Neurons in the most superficial portion of the SC, where inputs from retinal W cells terminate, begin responding earliest. Neurons deeper in the superficial layers, where Y-cell inputs dominate, develop later, and visual responsiveness in the subjacent multisensory layers develops last (Kao et al., 1994; Wallace and Stein, 1997). The bases for this particular pattern of functional development remain obscure, but it occurs at the same time that the number of active loci across the horizontal aspect of the structure increases to yield a continuous retinotopy that underlies its visuotopic organization (Figure 3.6).

These early responsive neurons are functionally immature and have many properties that typify functionally immature neurons elsewhere in the nervous system. Their receptive fields are very large and require either long-duration flashed stationary targets or very slowly moving stimuli for activation. They fatigue readily with repeated stimulation, require very long interstimulus intervals to respond to sequential stimuli, and have very long latencies (Kao et al., 1994; Stein et al., 1973b). They also lack binocularity and direction selectivity, properties that characterize these neurons when

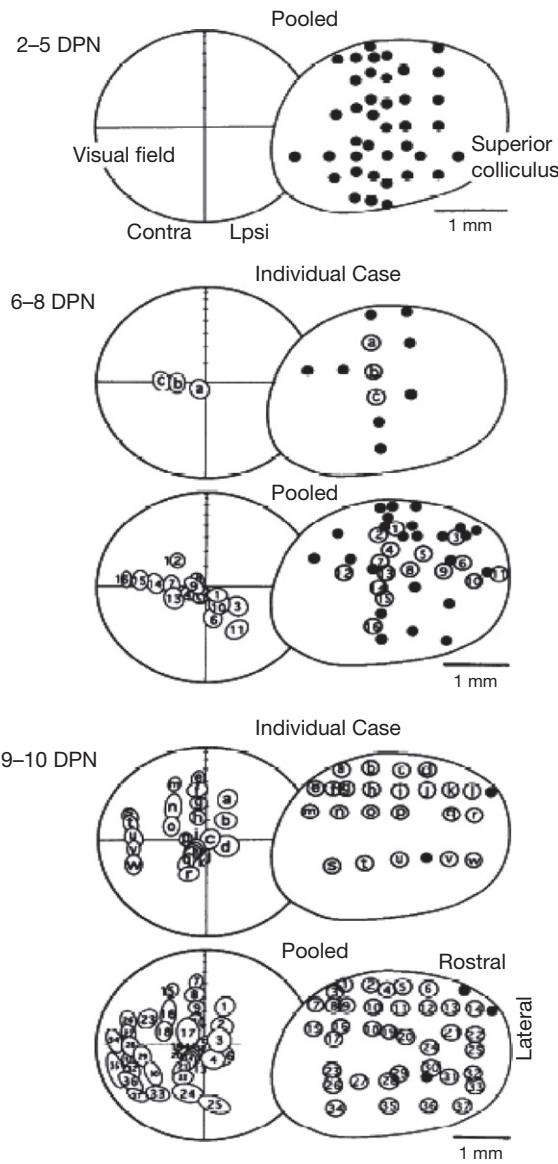


FIGURE 3.5 The maturation of the visuotopic map in the superficial superior colliculus. Data from three age groups are shown. Each contains a diagram of the visual field on the left and a schematic of the dorsal surface of the SC on the right. Circles on the SC represent electrode penetrations (filled, no visual activity, open, visual activity). Correspondence between the electrode penetrations and visual receptive fields are shown by numbers and letters (only the 'best area' of a receptive field was mapped). No visual activity was encountered before 6 days postnatal (dpn) but was already represented in a maplike pattern when first encountered. Adjacent electrode penetrations in the SC yielded visual activity at adjacent sites in visual space. By 9–10 dpn, most SC locations had become responsive to visual stimulation. Reproduced from Kao CQ, Stein BE, Coulter DA (1994) Postnatal development of excitatory synaptic function in deep layers of SC. Abstracts – Society for Neuroscience 20: 1186.

mature and are believed to facilitate orientation to moving targets. These properties develop over a 6- to 8-week period. It is not clear what, if any, visual behaviors these early responding neurons can support, as overt visual

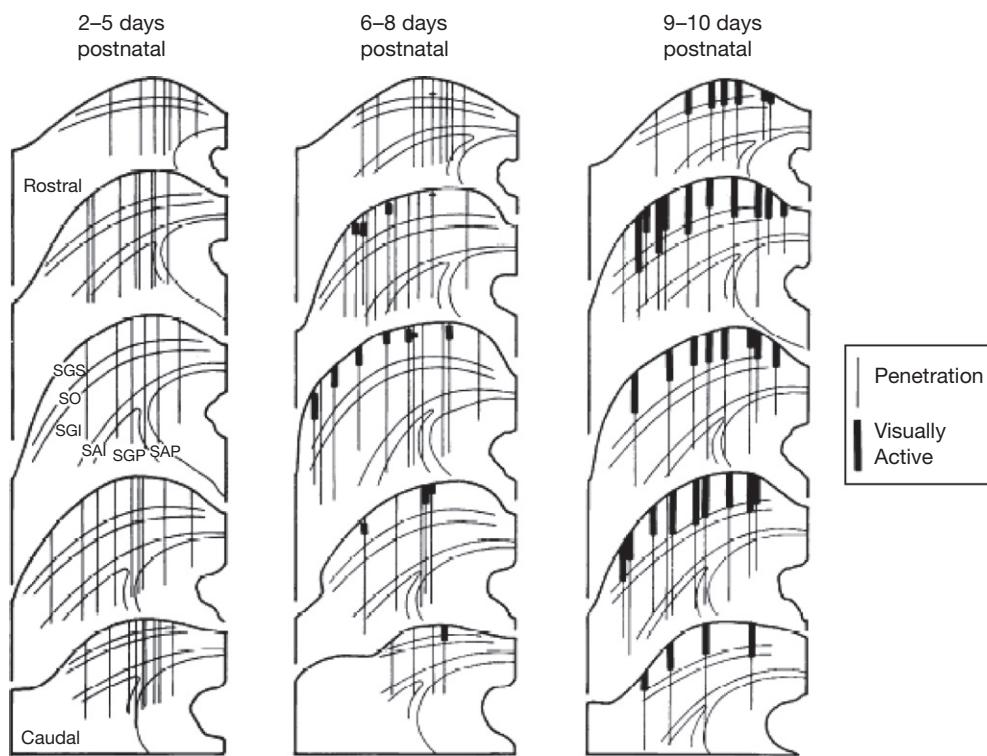


FIGURE 3.6 During maturation, superior colliculus visual activity progresses from the top to the bottom of the superficial layers. Vertical lines illustrate electrode penetrations through coronal sections of the SC in each age group. Sections are arranged rostrocaudally. Each region of visual activity is represented by a thick vertical black line spanning the distance between the first and last location of visually active neurons. Note that the visually active spans increase with age so that by 9–10 dpr, visual activity is evident throughout the depths of the superficial layers. No deep-layer visual activity was present at this time. *Reproduced from Kao CQ, Stein BE, Coulter DA (1994) Postnatal development of excitatory synaptic function in deep layers of SC. Abstracts – Society for Neuroscience 20: 1186.*

function is not observed in cats until 2–3 weeks after birth, by which point they have already matured considerably (Fox et al., 1978; Stein et al., 1973a). Nevertheless, the physiological maturation of the receptive field properties of these superficial layer neurons takes 2 months or more to reach their adult status. This reflects, in part, the physiological maturation of visual tectopetal afferents, especially those from the cortex (e.g., see Stein and Gallagher, 1981).

Although sensory experience is critical for the formation of many neural properties in the central nervous system, the fundamental features of SC visuotopy and the responsiveness of its constituent neurons appear to progress in a manner independent of visual experience. Superficial layer and deep (multisensory) layer neurons in dark-reared cats show robust visual responses and adult-like resistance to fatigue with repeated stimulation, although their receptive fields remain comparatively large and their more sophisticated properties develop more gradually. Similarly, in the newborn monkey, the ocular properties are far more mature than those of the cat, and SC neurons already show a well-ordered and continuous superficial layer visuotopy. Although the receptive fields of its neurons are also larger than

those in the adult and their visual latencies are longer, the neurons respond robustly to visual stimuli and already have many adult-like response properties (Wallace et al., 1997). The maturational differences in the newborn monkey and cat SC likely reflect both the shorter gestational period in the cat and its higher dependence on corticotectal inputs for construction of its neuronal response properties (Stein, 1984).

3.5.2.2 Development of Deep Layer Sensory Topographies

Attention to the maturation of neurons in the deep layers has been focused on their functional properties rather than their topographies. Thus, much of what is known about this feature of their development has to be inferred. The somatosensory and auditory receptive fields of neonatal neurons are, like their visual counterparts, extremely large. Neonatal somatosensory receptive fields cover much of the contralateral body and early auditory receptive fields are ‘omnidirectional,’ having receptive fields that encompass the whole of the contralateral auditory space. They gradually shrink in size over the first few months of life, and in the absence of evidence that neurons have receptive fields that

are ‘mislocated,’ it is assumed that the resolution of their maps gradually increases as individual receptive fields contract. The functional changes that ensue in these layers as a consequence of development are discussed in the section on the maturation of multisensory integration. Examples of receptive field development are also provided.

3.5.3 The Development of Multisensory Neurons

Although a great deal of effort has been expended on understanding the maturation of the superficial layer visuotopy to understand the maturation of SC-mediated orientation behaviors, as noted earlier, it is actually the deep (multisensory) layer visual responsiveness that is most closely linked to this function. Also, these layers are slower to develop. Because the maturation of these neurons has been most closely studied in cats, unless otherwise stated, the descriptions in what follows relate to this species.

Because neurons in the multisensory layers become responsive to visual cues only after 3 postnatal weeks (Kao et al., 1994; Wallace and Stein, 1997), it is obvious that neither the weak direct retinal projection to these layers (Beckstead and Frankfurter, 1983; Berson and McIlwain, 1982) nor the relay of visual input from active neurons in the superficial layers (e.g., Behan and Appell, 1992; Grantyn et al., 1984; Moschovakis and Karabelas, 1985) are capable of activating these neurons before this time. Yet somatosensory- and auditory-evoked neuronal activity is already apparent, though the responsive neurons also have the large receptive fields and tendency toward fatigue that are characteristic of neonatal neurons. This developmental chronology (somatosensory first, auditory second, visual last) parallels the development of sensory-evoked orientation behaviors (Fox et al., 1978; Norton, 1974; Villablanca and Olmstead, 1979).

At this time, there is a gradual increase in the number of SC neurons that can respond to multiple sensory inputs. Thus, each of the different possible convergence patterns of responsiveness to visual, auditory, and/or somatosensory inputs becomes evident. One of the hallmark features of multisensory SC neurons, however, is their ability to use information from the different senses synergistically. This process of integrating cross-modal inputs markedly facilitates SC-mediated behavior and begins at about the fourth postnatal week.

3.5.4 Superficial Layer and Deep (Multisensory) Layer Maturational Delay

As noted earlier, visual responsiveness occurs comparatively early in superficial layer neurons, beginning before the end of the first week, and comparatively late

in the multisensory layers, where it begins in the third or fourth postnatal week. This maturational delay relative to superficial layer visual activity underscores the significant maturational difference between the sensory-specific properties of superficial-layer neurons and their multisensory counterparts in the deep layers. Synthesizing information from multiple senses is surely a more complex process than responding to any one of them individually and therefore requires greater maturational time. These superficial–deep-layer differences also extend to the functional roles to which their information processing contributes. Although both neuronal populations probably share functions related to perception and overt behavior, superficial layer visual neurons are believed to contribute more to the former and deep-layer multisensory neurons to the latter.

Developing the ability to integrate cross-modal inputs is a multistep process. Neurons first develop responsiveness to a single sensory input, then to at least two different (i.e., cross-modal) inputs, and can finally develop the ability to integrate the information carried in multiple sensory channels.

The maturation of the various possible multisensory convergence patterns follows closely the chronology of unisensory maturation. Thus, somatosensory–auditory neurons are the first multisensory neurons to appear. They become evident 10–12 days post parturition, and visual–nonvisual neurons become evident at approximately the third postnatal week, as soon as visual responsiveness begins in the multisensory layers. Yet, it still takes many weeks of maturation before the adult-like incidence of the various modality-convergence patterns is reached and the adult-like incidence of neurons capable of multisensory integration is achieved. As might be suspected from their unisensory counterparts, the receptive fields of the initial multisensory neurons are very large. They contract over several months, thereby progressively increasing the spatial resolution of the individual sensory maps to which they contribute and enhancing their spatial register with one another (Figure 3.7). The changes in receptive field size are accompanied by an increase in response vigor and reliability, as well as by a decrease in response latency. These functional changes reflect a combination of developmental factors taking place in afferent systems, as well as within the internal circuitry of the SC.

3.5.5 The Development of Multisensory Integration

The ability to integrate cross-modal inputs is delayed until at least 1 month after birth (Wallace and Stein, 1997), and before it develops, the cross-modal responses of multisensory neurons look like the responses elicited

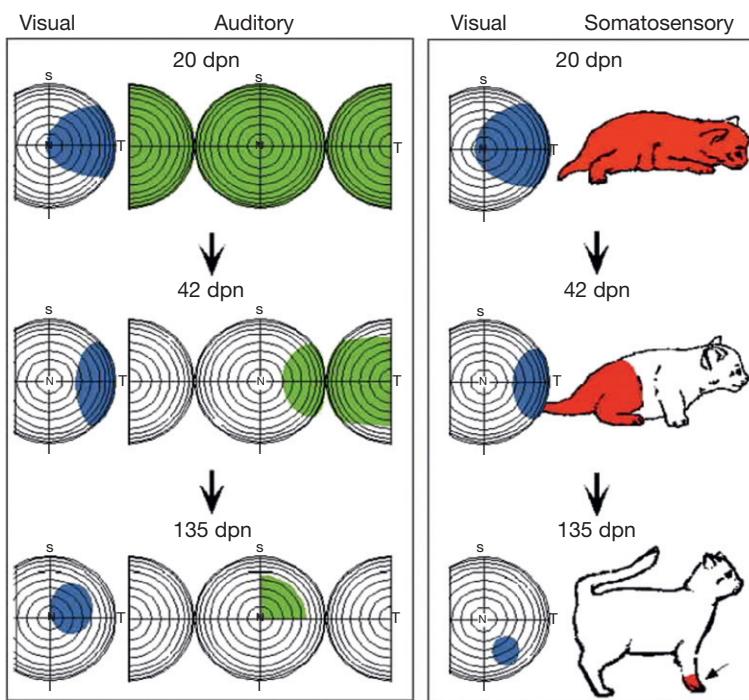


FIGURE 3.7 The maturation of multisensory receptive fields. Shown are exemplar SC receptive fields from visual-auditory (left) and visual-somatosensory (right) neurons that were mapped in animals aged 22–135 dpn. Note that receptive fields become progressively smaller at older ages, increasing their spatial resolution and their register with one another. Adapted from Wallace MT and Stein BE (1997) Development of multisensory neurons and multisensory integration in cat superior colliculus. *Journal of Neuroscience* 17: 2429–2444 (see also Stein and Rowland, 2011).

by one (the more effective) of the component stimuli alone. At this age, however, some neurons respond to cross-modal stimuli with responses that significantly exceed the presumptive unisensory responses, but such neurons are rare at this time. The incidence of these integrative neurons progressively increases with age, but the mature condition is not reached until the animal is several months old and has had a great deal of sensory experience.

The absence of an ability to integrate cross-modal inputs in the neonatal cat's SC is not due to the general immaturity of these neurons. The macaque monkey is born much later in development than the cat. Its eyes and ears are open at birth and it sees and hears quite well, and unlike the cat, it already has multisensory SC neurons in its SC. But they cannot integrate their cross-modal inputs to produce response enhancement (Wallace and Stein, 2001) and, therefore, respond to these stimuli very differently than do their adult counterparts (Wallace et al., 1996). The likely reason is that they have not yet had the necessary sensory experience. Apparently, postnatal sensory experience is not critical for the appearance of multisensory neurons, but these observations strongly suggest that it is necessary for them to integrate their different sensory inputs. Observations from experiments with human subjects are consistent with this hypothesis (e.g., Gori et al., 2008; Neil et al., 2006; Putzar et al., 2007), though critical direct observations showing that the newborn cannot yet use cross-sensory cues synergistically are not yet available. Nevertheless, newborn human infants

are capable of engaging in a host of multisensory tasks, the best known of which is cross-modal matching (see Stein et al., 2010 for further discussion).

3.5.6 The Impact of Sensory Experience on the Maturation of Multisensory Integration

As noted earlier, when discussing multisensory integration, inputs from association cortex (e.g., primarily from the anterior ectosylvian sulcus, or AES, in cats) have been found to be essential for SC multisensory integration. Thus, one might expect that the functional coupling of this input with multisensory SC neurons is a necessary precondition for the development of SC multisensory integration, and this appears to be the case. Anatomically, the corticotectal projections from AES have already grown into the multisensory layers of the SC prior to birth and long before SC neurons are responsive to multiple sensory inputs (McHaffie et al., 1988). However, they are unlikely to be functional at this time. Their critical contribution to multisensory integration becomes obvious as soon as a neuron in the SC exhibits this capability. As noted earlier, this first happens for some rare neurons at about 1 month of age. Deactivating AES at this stage eliminates that capacity as effectively as it does in adulthood. The neurons' responses to the cross-modal stimulus combination are now no longer significantly different from those to the most effective component stimulus (Wallace and Stein, 2000; Figure 3.8).

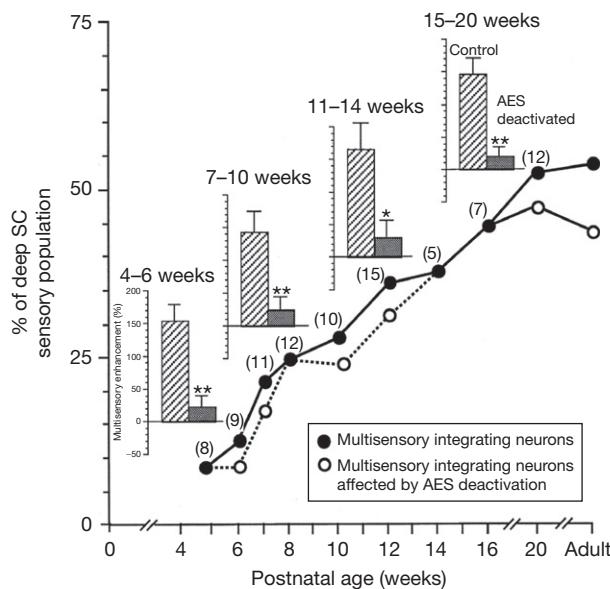


FIGURE 3.8 The maturation of multisensory integration parallels the functional coupling of AES-SC projections. The developmental increase in the incidence of SC neurons capable of multisensory integration is paralleled by the effectiveness of AES deactivation in blocking the expression of this capability. Nearly all SC neurons lost this ability during AES deactivation, regardless of age (the number of neurons tested at every time point is shown in parentheses). The small proportion of SC neurons whose multisensory integration capability was unaffected by AES deactivation likely depended on an adjacent area of association cortex (i.e., the rostral-lateral suprasylvian cortex, see Jiang W, Wallace MT, Jiang H, Vaughan JW, Stein BE (2001) Two cortical areas mediate multisensory integration in superior colliculus neurons. *Journal of Neurophysiology* 85: 506–522). Reproduced from Wallace MT and Stein BE (2000) Onset of cross-modal synthesis in the neonatal superior colliculus is gated by the development of cortical influences. *Journal of Neurophysiology* 83:3578–3582.

Although the association cortex component of the SC circuit appears to be critical for multisensory integration, it is not sufficient. Appropriate sensory experience is also a key factor.

During this early phase of life, the brain is learning about external events and the statistical relationships among stimuli that are derived from the same event. Cross-modal stimuli that are produced by the same event are temporally and spatially coincident, or at least proximate in space and time. These relationships must be learned (e.g., via Hebbian learning rules) and somehow represented in the underlying circuitry responsible for multisensory integration. Given the arbitrary nature of many cross-modal relationships, it is difficult to conceive of an effective scheme for incorporating this information without actual experience. Experience with cross-modal stimuli establishes a principled way of interpreting and interacting with external events so that only a select group of cross-modal stimuli will produce multisensory integration. For example, the brain learns to expect that some visual and auditory cues are linked

to the same event, based on their location and timing. This information is used to establish principles for categorizing cross-modal stimuli derived from the same, or different, events.

To test the hypothesis that sensory experience plays a key role in the development of multisensory integration capabilities, cats were raised in darkness in order to preclude visual–nonvisual experiences. Normally, the physiology of SC multisensory integration is reached at 3–4 months of age (Wallace and Stein, 1997), and these dark-reared animals were not studied until at least 6 months of age. Visual experience was not essential for the appearance of visually responsive neurons, and such neurons were common in these dark-reared animals, as well as in newborn monkeys (Wallace and Stein, 2001). Each of the modality-convergence patterns was also well represented among the neurons encountered (Wallace et al., 2004). However, their receptive fields were still quite large and more typical of the neonate than the mature animal (Figure 3.9). The failure to contract their receptive fields was indicative of their physiological immaturity and this was most apparent in their inability to integrate cross-modal cues. As shown in Figure 3.9, their multisensory response to a cross-modal visual–nonvisual stimulus was approximately equal to their response to the visual component stimulus alone. Multisensory responses that approximate the response to the most effective component stimulus are typical of neonatal neurons that have not yet developed their capacity for multisensory integration and of adult multisensory neurons deprived of the critical input from association cortex.

Human subjects who have had their early vision compromised by congenital cataracts also show persistent visual–nonvisual integration deficits even many years after the cataracts have been removed (Putzar et al., 2007). These observations support the hypothesis that cross-modal experience is a critical factor in the maturation of the capacity to integrate multisensory cues (Figure 3.10), but they do not provide information about whether the nature of that early experience determines the principles that govern this process. To test this possibility, animals were reared from birth to 6 months of age in a dark room in which pairs of visual and auditory stimuli were periodically presented, but these stimuli were always spatially disparate (Wallace and Stein, 2007). The properties of their multisensory SC neurons were then assessed.

Once again, visually responsive neurons were common, as were visual–nonvisual neurons. Yet, the majority of visual–auditory neurons appeared to have been unaffected by the experience with the disparate visual–auditory cues and had properties characteristic of neonates. Their receptive fields were very large and were unable to integrate these cross-modal cues. But there

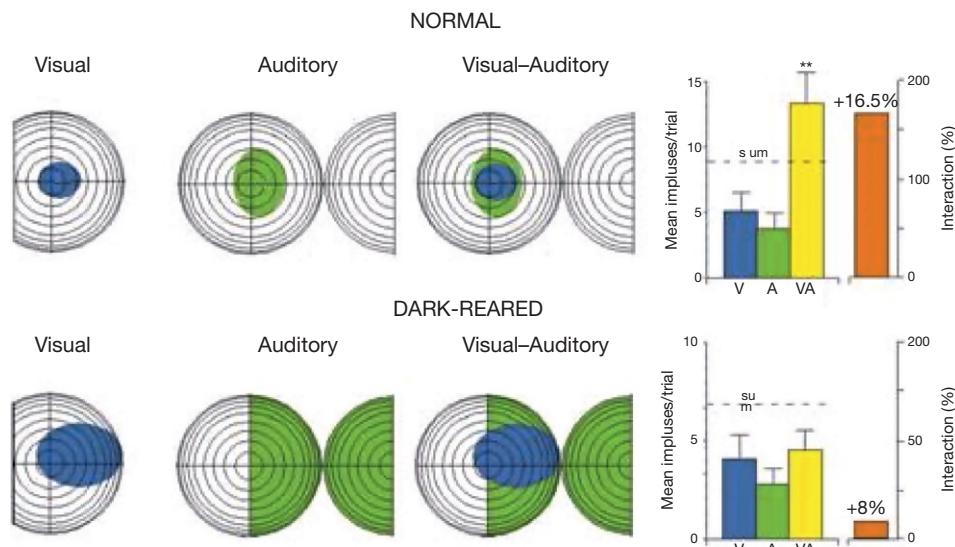


FIGURE 3.9 Multisensory neurons have large receptive fields and lack multisensory integration capabilities after dark rearing. The visual and auditory receptive fields and the multisensory responses of a typical normal SC multisensory neuron are shown at the top. The bar graph to the right shows the characteristic enhanced response to the cross-modal pair of stimuli in spatial and temporal register. In contrast, the neuron below, from the SC of a dark-reared animal, has much larger receptive fields and shows no evidence of multisensory response enhancement to the cross-modal stimulus. V, visual stimulus; A, auditory stimulus; VA, cross-modal stimulus. Adapted from Wallace MT, Perrault TJ, Jr., Hairston WD, Stein BE (2004) Visual experience is necessary for the development of multisensory integration 1. *Journal of Neuroscience* 24: 9580–9584.

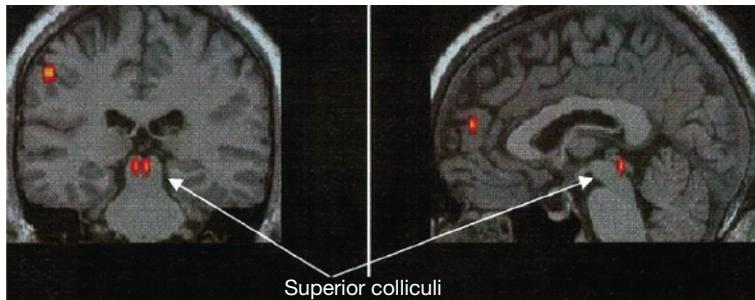


FIGURE 3.10 Multisensory enhancement is evident in the human superior colliculus using fMRI. Coronal (left) and sagittal (right) sections reveal high degrees of enhanced SC multisensory activity (red indicates elevated BOLD responses). Elevated activity is in response to visual-auditory as opposed to the best of these stimuli (i.e., visual) individually. Adapted from Calvert GA, Hansen PC, Iversen SD, Brammer MJ (2001) Detection of audio-visual integration sites in humans by application of electrophysiological criteria to the BOLD effect. *Neuroimage* 14: 427–438.

was a substantial minority of such neurons that did appear to have incorporated the visual-auditory experience. Their receptive fields were somewhat smaller (but still quite large) and were in poor spatial register with one another. Some neurons had visual and auditory receptive fields that were elongated along their horizontal axes and had only small portions overlapping one another. In other cases, there was no receptive field overlap, a configuration that is highly unusual in normal animals, but one that was consistent with the early visual-auditory experience of these animals. Most important in the present context was that they could integrate visual-auditory stimuli. But the cross-modal stimuli had to be spatially disparate in order to fall within their respective receptive fields simultaneously. An example of such a neuron is shown in Figure 3.11.

Collectively, the data reveal that experience is essential for the development of multisensory integration and that the nature of the experience directs the formation of

the underlying neural circuit through which this integration is achieved. Although the specifics of that circuit remain to be fully explored (e.g., see Fuentes-Santamaría et al., 2006, 2008a,b, 2009), the cortex is known to play a critical role (e.g., see Alvarado et al., 2009; Jiang et al., 2001; Stein, 2005; Wallace and Stein, 1994) and its ablation early in life precludes the maturation of SC multisensory integration (Jiang et al., 2006, 2007). It appears that early experience is essential for the brain to learn the statistics of cross-modal events, and there is good reason to suspect that this experience exerts its critical impact on the AES-SC (anterior ectosylvian sulcus-superior colliculus) projection.

This possibility was explored by Rowland et al. (2005) and Stein et al. (2008), who deactivated AES and adjacent association cortex ipsilaterally during the period in which SC multisensory integration normally develops. This deprived the cortex of cross-modal experience but did not compromise the responsiveness of SC

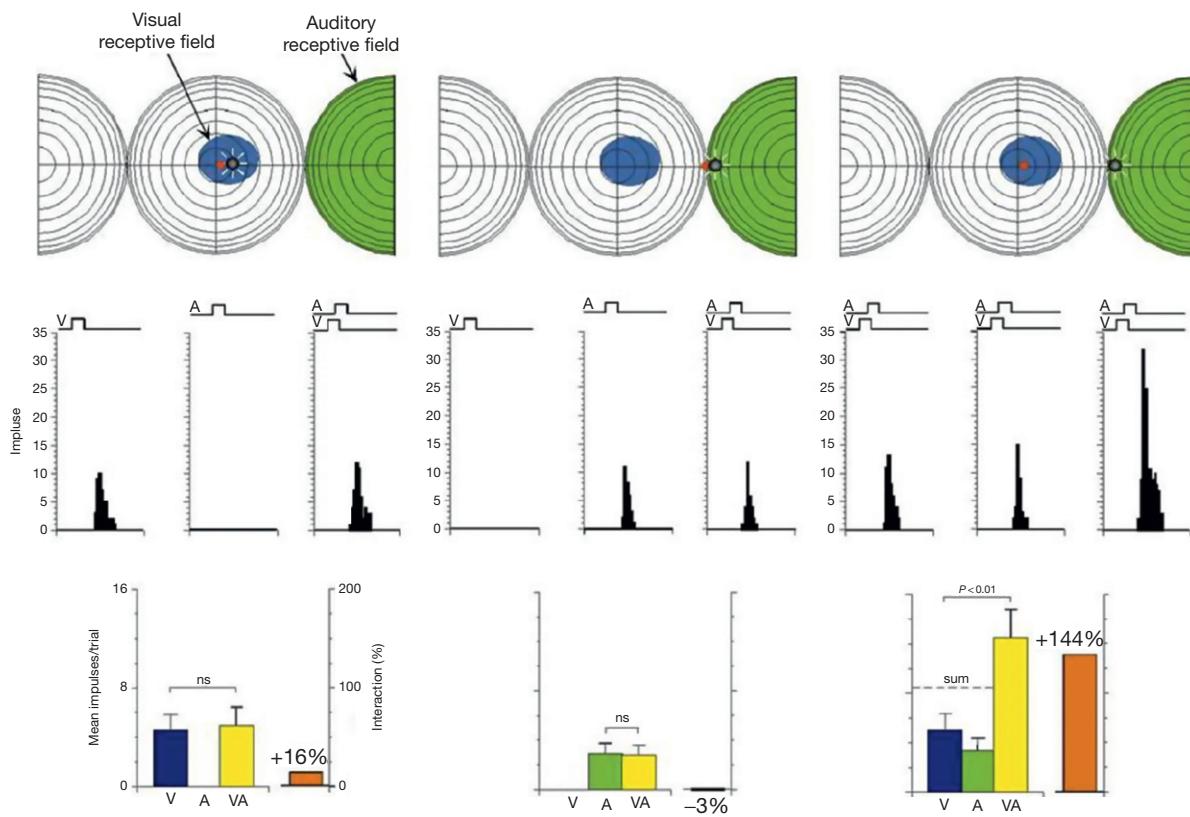


FIGURE 3.11 Early experience with spatially disparate visual-auditory stimuli results in atypical requirements for their integration. Shown is an SC neuron from an animal reared from birth to 6 months of age with simultaneous but spatially disparate visual-auditory cues. The neuron's visual and auditory receptive fields were atypical by being nonoverlapping. When visual-auditory stimuli were spatiotemporally coincident and within the visual (left) or auditory (center) receptive fields, the multisensory response was no greater than that evoked by the most effective component stimulus. But, when the two stimuli were disparate in space and simultaneously presented within their respective receptive fields, they elicited a significantly enhanced multisensory response. Thus, the neuron integrated spatially disparate visual-auditory stimuli as normal animals integrate spatially concordant visual-auditory stimuli, a seeming 'reversal' of the spatial principle. *Adapted from Wallace MT and Stein BE (2007) Early experience determines how the senses will interact. Journal of Neurophysiology 97: 921–926.*

neurons to these stimuli via many other input channels. Chronic deactivation was accomplished by implanting muscimol-infused pledges of Elvax (a polymer) over the association cortex. The GABA_A agonist was slowly released from the polymer, deactivating underlying neurons. When the polymer was depleted or removed, cortical activity returned rapidly and was once again responsive to environmental stimuli. Behavioral and physiological studies were then conducted when the animals had reached 1 year of age. Although experiments are still ongoing, the preliminary data reveal that the animals appeared normal in their ability to respond to visual stimuli in both visual fields. They also benefited from visual-auditory cues in the ipsilateral hemifield as much as normal animals. However, they were severely compromised in their multisensory responses to cross-modal stimuli in their contralateral hemifield. Cross-modal stimuli in this hemifield were no more effective in facilitating SC-mediated behavior than was the visual stimulus alone. Thus, as expected, the inability of association cortex to monitor the statistics of visual-auditory

events compromised the maturation of the circuit necessary for SC multisensory integration. This was also evident in the inability of multisensory neurons in the ipsilateral SC to integrate visual-auditory information.

That these deficits in multisensory integration were apparent long after the cortex was once again active (a period far longer than that required for its normal acquisition in early life) could be interpreted as reflecting a 'critical' or 'sensitive' period for instantiating this process. If the former were the case, this capacity would never develop. This possibility was examined in some of these same animals that were retained for several years. These animals were then tested as before. Their behavior appeared to be normal, indicating that they acquired the ability to integrate visual-auditory cues later in life. That this acquisition likely involved multisensory SC neurons was indicated by the finding that the multisensory responses of ipsilateral SC neurons, while not completely normal, did exhibit multisensory response enhancement to spatiotemporally coincident visual-auditory stimuli.

3.5.6.1 Motor Development

Much less is known about the development of the motor than the sensory properties of SC neurons. Although there is little doubt that the fundamental properties involved in gaze shifts are not species-specific, most of the available information comes from studies in one preparation: the alert monkey trained to make gaze shifts. For obvious reasons, technical limitations make conducting such studies in neonates quite difficult, especially making any direct correlations with the maturation of sensory properties in the primary sensory developmental model, the cat. Nevertheless, for neonatal SC sensory responses to have any direct impact on behavior, their efferents to the brainstem and/or spinal cord must be in place and capable of carrying tectofugal signals.

These pathways can be seen exiting the SC and contacting targets involved in eye movements within hours of birth in the cat. The target areas include the central gray overlying the oculomotor nucleus, an area into which oculomotor dendrites project, as well as segments of the pontine and medullary reticular formation that connect to the abducens nucleus (Stein et al., 1982). Tectofugal projections also reach the cervical spinal cord. This region is involved in controlling head and limb movement, and these projections are detailed in adults by Huerta and Harting (1982a,b).

Using electrical stimulation of the SC, this motor pathway has already been demonstrated to have functional capabilities in 2-day-old cats (Stein et al., 1980), days before natural auditory stimuli can activate multisensory layer neurons and weeks before visual stimuli are effective. Such electrical stimulation elicits eye, ear, neck, whisker, and limb movements, albeit with a higher threshold and lower reliability than in adults. Furthermore, the motor topography in the SC is already evident. Stimulation of homotopic loci in each SC produces mirror-image eye movements. Nevertheless, many SC stimulation sites proved to be ineffective at this stage of maturation. Presumably, this is due to the immaturity of the SC, as direct stimulation of the oculomotor nucleus evoked reliable eye movements. It is not yet known, however, whether tactile stimuli, which can already activate SC neurons in preterm kittens, can initiate SC-mediated movements in neonates. If, on the other hand, the SC is organized in motor coordinates, as has been suggested by some investigators (e.g., see Sparks, 1986; Sparks and Porter, 1983), it could indicate that early motor function could influence later auditory and visual organization. It would also be consistent with the idea (e.g., see Hein et al., 1979) that eye-movement-generated movement of an image across the retina is necessary for interpreting that visual image and that during development, the former precedes the latter (though spontaneous or vestibular cues could produce the necessary eye

movements in neonatal cats; Fish and Windle, 1932; Windle and Fish, 1932).

3.6 SUMMARY

It is important to acknowledge that this chapter has focused on certain anatomical and physiological aspects of SC development for which functional implications are readily apparent. Thus, for example, the formation of topographic representations and the development of multisensory integrative capabilities have obvious implications for producing behavioral output and behavioral correlates in developing animals. In doing so, however, voluminous bodies of literature on, for example, the chronology of synapse formation and the appearance of histochemical markers that parallel SC functional development have been ignored. Likewise, with few exceptions, the focus has been primarily on the SC, but there is also a wealth of comparative data pertaining to the OT from studies of a wide array of nonmammalian species. While the same general principles of development apply, maturational differences dictated by the varied and specialized environmental niches that these animals occupy would require a discussion that is beyond the scope of this chapter. Lastly, it is important to point out what already may be obvious: knowledge of SC development disproportionately favors aspects relevant to its sensory capabilities. This weighting belies the truly integrated sensorimotor function of the SC and highlights a rather substantial gap in the knowledge of how the SC develops to play its adult role. It can only be hoped that future studies will address this imbalance to provide a more complete picture of the SC developmental chronology.

Acknowledgments

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