THE WELLCOME PRIZE LECTURE

A MAP OF AUDITORY SPACE IN THE MAMMALIAN BRAIN: NEURAL COMPUTATION AND DEVELOPMENT

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INTRODUCTION

As long ago as the 17th century, Descartes proposed that the brain contains a topographic representation of the visual world. By making a window at the back of the eye of an ox, he directly observed how an inverted image of an object in visual space is formed on the retina. He went on to suggest that a copy of this image is faithfully transmitted by the fibres of the optic nerve to the surface of the ventricles in the brain. Descartes also proposed that the signals from the two eyes are combined to form a fused, binocular image in the pineal gland at the back of the ventricles (Fig. 1). His understanding of the anatomical pathways concerned and of the means by which sensory signals are transmitted along these pathways was, of course, quite wrong. Nevertheless, the basic idea is correct. A monococular image of the visual world observed through each eye is reconstructed in the lateral geniculate nucleus in the thalamus, before conversion into a single binocular representation in the visual cortex.

The presence, within the brain, of topographic projections from the receptor surface is a general feature of sensory systems. For example, afferent nerve fibres entering the spinal cord form an ordered array according to their point of innervation on the body surface. This order is maintained at subsequent levels of the somatic sensory pathway, giving rise
Fig. 1. Descartes observed how an image (1, 3, 5) of the visual world is produced on the retina, and suggested that a corresponding picture (2, 4, 6) is formed on the wall of the ventricles. He also proposed that the image from both eyes is combined at the pineal gland. From his *Traité de l'Homme* (1664).

to neural maps of the opposite half of the body. Similarly, the auditory nerve output from the cochlea is topographically ordered. However, an important difference exists between the functional organization of the receptor cells in the cochlea and those of the retina or the body surface. The cochlea performs a spectral analysis of incoming sounds, with each audible frequency transduced at a different point along its length. Thus, instead of stimulus location, as in the visual and somatic sensory systems, the audible frequency range is mapped across the receptor surface. The pattern of innervation of the receptor cells in the cochlea therefore provides an anatomical basis for the orderly representation or tonotopic mapping of sound frequency within the nuclei of the central auditory pathway (Fig. 2).

In addition to isomorphic maps that are topographically related to the stimulus dimension encoded by the receptor cells in the sense organs, the brain can construct more complex, higher-level forms of sensory map, which bear no direct relationship to the spatial arrangement of axons leaving the receptor surface. Indeed, something of a revolution is currently taking place in central auditory research, with a shift in emphasis away from the properties of sound (such as frequency or intensity) to the properties of sound sources, i.e. the nature or identity of the source, its location, its speed and direction of motion, and so forth (Yost, 1991; Masterton, 1992; Olsen, 1992). This approach has proved to be highly successful in the study of echolocation in the moustached bat, *Pteronotus parnellii*. By employing a neuroethological approach, in which species-specific biosonar signals are used as stimuli, Suga and his colleagues have demonstrated that neurones in the auditory thalamus and cortex of this rather specialized mammal respond selectively to combinations of particular features of these ultrasonic echolocation pulses and their returning echoes (for reviews, see Suga, 1990; Olsen, 1992). Moreover, the tuning properties of these combination-sensitive neurones vary systematically within different areas of the cortex to form maps of target velocity and target range that are separate from the primary tonotopic representation. Topographic representations of stimulus parameters that are extracted within the brain are referred to as computational (Knudsen, du Lac & Esterly, 1987) or centrally synthesized maps (Konishi, 1986). Another example of a computational representation in the auditory system, namely a neural map of auditory space, forms the subject of this article.
Since stimulus frequency, rather than location, is encoded by the receptor cells of the cochlea, our ability to localize sound sources in external space has to be based on more subtle and indirect cues. The most important and well studied of these cues derive from the fact that we have two ears, positioned on either side of the head. If the sound source is located off the midline, the difference in path length gives rise to a difference in the time of arrival of the sound at each ear. In addition, an interaural difference in pressure level results from the fact that the ear further from the sound source is acoustically shadowed by the head. The value of these interaural disparity cues will depend on the frequency content of the sound source and its angle with respect to the midline (Irvine, 1986). Consequently, spatial information can be derived by a neural comparison of the inputs from the two ears if small differences in the timing or pressure level of the sound at each one are associated with particular positions in space.

Most studies of auditory localization have employed direct, closed-field stimulation of the ears to examine the processing of interaural time and pressure level differences by binaural neurones at different levels of the auditory pathway (Irvine, 1986, 1992; Yin & Chan, 1988; Clarey, Barone & Imig, 1992). However, while these studies have contributed to our understanding of the neural coding of auditory localization cues, they do not directly address the question of how the location of a sound source is represented in the brain, which requires that stimuli are presented in the free field rather than in the ear canals. Although a few early mammalian studies employed free-field stimulation, the first demonstration of a neural representation of auditory spatial location was provided by Knudsen and Konishi in their work on the midbrain of the barn owl. Neurones in both the mesencephalicus lateralis pars dorsalis (Knudsen & Konishi, 1978) and in the optic tectum
Corresponding which was recording electrode region & King, Alan Palmer and mammalian room neurones recording receptive usually been included in the central auditory pathway. Therefore, there is considerable interest in the way in which different modalities are represented and integrated in this structure, which has sometimes been referred to as microcosm of the brain as a whole.

A number of free-field studies, using hand-held stimuli, suggested that, as with visual and tactile stimuli, the location of auditory targets is represented topographically within the deeper layers of the SC (e.g. Gordon, 1973; Updyke, 1974; Dräger & Hubel, 1975; Tiao & Blakemore, 1976; Chalupa & Rhoades, 1977; Harris, Blakemore & Donaghy, 1980). Alan Palmer and I carried out a free-field investigation of the responses of auditory neurones in the guinea-pig SC using precisely controlled stimuli, presented in an anechoic room from a horizontal array of loudspeakers that surrounded the animal. We found that most of the single units we recorded responded best to bursts of white noise from a restricted location, and that the distribution of these cells was such as to produce a map of the azimuthal dimension of auditory space along the rostrocaudal axis of the SC (Palmer & King, 1982; King & Palmer, 1983). Data from one animal are shown in Fig. 4. The recording electrode was lowered vertically through the overlying cortex into the SC. Units could therefore be recorded sequentially in each layer of the nucleus. Within any given electrode track, all the auditory units recorded were tuned to approximately the same region of space (e.g. units P–S in Fig. 4). On the other hand, as the position of the electrode was changed from the rostral to the caudal end of the SC, the directional responses shifted systematically from in front of the animal round into the hemifield contralateral to the recording site.

Similar mapping experiments subsequently carried out in other species have produced corresponding results (Middlebrooks & Knudsen, 1984; Wong, 1984; King & Hutchings, 1987). In addition to the representation of sound azimuth, we now know from studies in which the acoustic stimulus was presented from a single loudspeaker mounted on a movable hoop system (e.g. Annetts, Howse, Hutchings & King, 1987) centred on the animal’s head, that these neurones are also tuned for the vertical location of the sound source and that the elevation axis is mapped across the mediolateral extent of the SC (Middlebrooks & Knudsen, 1984; King & Hutchings, 1987). In the ferret, Mary Hutchings
Fig. 3. Photomicrograph of a transverse section of the guinea-pig superior colliculus with an outline drawing of the other side on which is marked the seven laminae of this nucleus. The arrows indicate the positions of electrolytic lesions made after recording from auditory units. CS, superior colliculus; GM, medial geniculate; IP, interpeduncular nucleus; LM, medial lemniscus; PC, cerebral peduncle; PVG, periventricular grey; RF, reticular formation; SN, substantia nigra. From King & Palmer (1983), with permission.

Fig. 4. Surface view of the right superior colliculus of a guinea-pig, showing the location of six electrode penetrations. The polar diagrams show the responses of all the units recorded in these tracks to 100 ms bursts of white noise as a function of the azimuthal angle of the sound source. The values plotted on the radial axis of these plots represent the mean number of spikes elicited by thirty-two stimulus repetitions. The calibration bar below each plot represents 0.5 spikes per presentation. In each case, the response obtained at a single sound level, usually near threshold, is shown. From King & Palmer (1983) with permission.
Fig. 5. Surface views of the right superior colliculus showing the distribution of auditory units for which a best position (loudspeaker position evoking maximum response) in either azimuth (A) or elevation (C) was obtained. These data are pooled from 13 normal, adult ferrets. The different symbols represent the locations of units that responded best to the positions indicated in the boxes. Negative positions are contralateral to the recording site and positive are ipsilateral. The dashed lines run approximately orthogonal to the isoazimuth and isoelevation contours respectively. The distance from either the rostrolateral (A) or rostromedial (C) margins of the SC to each cell was measured in a direction parallel to the dashed lines and plotted, respectively, in B against the auditory best position in azimuth and in D against the best position in elevation. Adapted, with permission, from King & Hutchings (1987).

and I found that the SC units were responsive to sounds over a large region of space, but usually responded maximally at a particular loudspeaker position (King & Hutchings, 1987). The two-dimensional map of auditory space can therefore be revealed by plotting the value of this auditory best position against the location of the units within the deeper layers of the SC. Figure 5 shows that anterior space is represented rostrally and posterior space in caudal SC, while superior locations are represented medially and inferior locations on the lateral side of the nucleus.
Fig. 6. Azimuthal response profiles of two cells recorded in the guinea-pig superior colliculus before (A and D), during (B and E) and after (C and F) occlusion of the ear ipsilateral to the recording site. Repeated measurements in B and C are shown by dashed lines. The data shown in A, B and C were obtained from one cell using a sound level of more than 20 dB above threshold. D, E and F show the response of a second neurone to near-threshold noise bursts. The star indicates the position of the centre of the visual receptive field of cells recorded in the superficial layers of the same electrode penetration. Adapted, with permission, from Palmer & King (1985).

ACOUSTICAL BASIS OF THE AUDITORY SPACE MAP

Monaural and binaural representations of auditory space

Dichotic studies in the cat have demonstrated that the majority of auditory neurones in the SC receive inputs from both ears (Wise & Irvine, 1983, 1985; Hirsch, Chan & Yin, 1986). The contribution of different localization cues to the synthesis of the map of auditory space can also be inferred from free-field studies, by appropriate manipulation of the acoustical information available. For example, occlusion of one ear alters the interaural level differences associated with a particular spatial location. If the ear ipsilateral to the recording site is temporarily plugged in guinea-pigs (Palmer & King, 1985) or cats (Middlebrooks, 1987), the majority of the spatially tuned responses to white-noise stimuli more than 20 dB above threshold are converted into omnidirectional responses, in which the SC units responded almost equally well to all loudspeaker positions tested. Restoration of a normal binaural input by removal of the ear plug re-established the preocclusion spatial response profiles (Fig. 6A–C). A similar loss of spatial selectivity was found at corresponding sound levels following acute ablation of the ipsilateral cochlea (Palmer & King, 1985).

However, the sensitivity of SC units to the location of the sound source at or near threshold sound levels was unchanged by these procedures (Fig. 6D–F), and, at least in the guinea-pig (Palmer & King, 1985), the near-threshold directional responses are
arranged into a map of auditory space. Figure 7 shows data obtained from an adult guinea-pig in which the ipsilateral input had been removed by ablating the right cochlea just before recording. No binaural cues were therefore available to the animal. The azimuthal response profiles shown by the polar diagrams shifted topographically as the electrode was moved along the rostrocaudal axis of the SC. This monaural representation of sound azimuth is generated as a result of cues provided by the outer ear. Thus, surgical removal of the pinna and concha of the functioning ear in a monaural guinea-pig caused the near-threshold spatial selectivity of units in the contralateral SC to become compressed into a narrow region of space opposite the external auditory meatus (Fig. 8).

These results suggest that monaural pinna cues are responsible for the directional responses observed in SC neurones at near-threshold sound levels, while the maintenance of spatial tuning at higher sound levels requires the presence of two ears. The broadening of the suprathreshold response profiles following monaural occlusion is consistent with the finding in dichotic studies that the principal type of binaural interaction exhibited by SC neurones involves an excitatory input from the contralateral ear and an inhibitory input from the ipsilateral ear (Wise & Irvine, 1983, 1985; Hirsch et al. 1985).
**Spectral cues provided by the outer ear**

The outer ear can provide directional information because it transforms the spectrum of the incoming sound in a location-specific manner. Acoustical measurements in several species have shown that unique spectral patterns are produced that vary systematically with both the horizontal and vertical location of the sound source (Shaw, 1974; Palmer & King, 1985; Carlile & Pettigrew, 1987a; Middlebrooks, Makous & Green, 1989; Carlile, 1990b; Musicant, Chan & Hind, 1990; Rice, May, Spirou & Young, 1992; Carlile & King, 1993). For example, the maximum gain in transmission of a broadband stimulus through the ferret's outer ear occurs in anterior space from 7–20 kHz, while transmission is reduced at posterior locations for frequencies centred on 14 kHz. A sharp notch is also present that increases in frequency from 24–30 kHz as the location of the sound source is moved from the anterior midline (0°) to the interaural axis (−90°). When the pinna and concha were surgically removed, these monaural spectral cues became symmetrical and therefore spatially ambiguous, about the interaural axis (Fig. 9; Carlile & King, 1993).

The spectral cues generated by the outer ear are thought to underlie the monaural map of auditory space in the SC as well as the capacity of human listeners to localize sounds following deafness in one ear (Middlebrooks & Green, 1991). Although it has yet to be demonstrated that SC neurones are differentially tuned to spectral patterns corresponding...
Fig. 9. The mean monaural spectral cues for ipsilateral sound locations are shown for 5 ferrets before and after bilateral removal of the pinna and concha. A probe microphone implanted across the wall of the auditory canal was used to measure the spectral transfer functions every 10 deg along the audio-visual horizon. The directionally dependent component of the response, the location dependency function, was determined by subtracting from each transfer function the reference transfer function recorded on the interaural axis (−90 deg) in the intact animal (see Carlile, 1990b). The gains in transmission in decibels are indicated by the contour shading. The anterior midline is at 0 deg and the ipsilateral interaural axis at −90 deg azimuth. A number of spectral features can be identified which could be used to discriminate front locations from back in intact animals (see text). All of these features were eliminated by pinnectomy. From Carlile & King (1993).

Fig. 10. Binaural spectral cues in the ferret. The interaural spectrum level differences (ISDs) were calculated by subtracting the monaural response (see Fig. 9) obtained at each position in the contralateral hemisphere from that obtained at the corresponding (mirror image) angle on the ipsilateral side of the midline. The ISDs are shown for the intact (lower) and pinnectomized (upper) animals. As with the monaural spectral cues, pinnectomy clearly results in the elimination of those features of the ISDs that could encode front–back location. From Carlile & King (1993).
to particular regions of space, they generally respond better to broad-band noise than to pure tones, and their frequency tuning curves are often complex and multipeaked (King & Palmer, 1983; Wise & Irvine, 1983; Hirsch et al. 1985; Middlebrooks, 1987). Moreover, in the guinea-pig, frequency sensitivity varies along the rostrocaudal axis of the nucleus in a manner that matches the location-dependent spectral filtering by the outer ear (Carlile & Pettigrew, 1987a, b).

Dichotic studies in the cat have demonstrated a topographic variation in sensitivity to interaural level differences along the rostrocaudal axis of the SC, suggesting that this cue is responsible for coding sound azimuth at suprathreshold stimulus levels (Hirsch et al. 1985; Wise & Irvine, 1985). But binaural cues presented in this way are inherently ambiguous since each cue value is actually associated with a range of spatial locations, commonly referred to as a 'cone of confusion' (see Irvine, 1986). The frequency-dependent directional properties of the outer ear also contribute to the interaural level differences that are generated by sound sources in the free field. Indeed, differences in the spectral filtering of the sound by each outer ear give rise to unambiguous binaural localization cues, at least for locations away from the midline. As with monaural spectral cues, interaural differences in the spectral pattern in intact ferrets vary characteristically along the horizon, with clear differences apparent between anterior and posterior locations (Fig. 10; Carlile, 1990a; Carlile & King, 1993).

Bilateral removal of the outer ear disrupted the interaural spectral differences so that they also became ambiguous for locations on either side of the interaural axis (Fig. 10). An equivalent change was observed in the suprathreshold representation of auditory space in the SC, since many units subsequently exhibited bilobed azimuthal response profiles, indicating that they were tuned to two distinct regions of space (Fig. 11 A; Carlile & King, 1990, 1993). In each case, one lobe of the response profile was tuned appropriately for the recording location in the SC, while the second lobe was tuned to sound locations not normally represented at these recording sites (Fig. 11 B). Together, the best positions of the appropriately tuned lobes formed a map of auditory space. Since interaural time disparities appear to play little, if any, role in the generation of the auditory space map, the topography in this ambiguous representation is presumably based on a gradient in sensitivity to residual interaural level difference cues. The spectral cues generated in the presence of the outer ears appeared to be used by the auditory system to distinguish between locations on either side of the interaural axis, and, in so doing, allow the construction of an unambiguous representation of a specific area of auditory space in the SC.

**VISUAL–AUDITORY INTEGRATION IN THE SUPERIOR COLLICULUS**

Besides the presence within this nucleus of a map of auditory space, the sensory organization of the SC is of interest for a number of other important reasons. As previously mentioned, the mammalian SC receives visual and somatosensory, as well as auditory, inputs. All three representations are topographically organized, so that the various sensory maps are in approximate register both with each other and with the motor maps in the deeper layers that are associated with orientating responses (see Stein, 1984; Sparks, 1986, 1988). Indeed, the first indication of a topographic representation of sound direction was based on the observed coincidence of visual and auditory receptive fields recorded from the same position within the SC (Updyke, 1974; Gordon, 1973; Harris et al. 1980).
Fig. 11. A, polar diagram showing the azimuthal response profile of a single neurone recorded from the superior colliculus of a ferret after bilateral removal of the pinna and cochlea. These data were obtained at a sound level of 25–30 dB above threshold. The asterisk indicates the position of the centre of the visual receptive field associated with the superficial layers of the same electrode penetration. About half of the cells recorded exhibited bilobed response profiles like this following pinnectomy. B, the auditory best position of each of the directional lobes of the auditory responses is plotted against the location of the centre of the visual respective field of units recorded in the superficial layers of the same electrode penetrations. Data are shown from 47 auditory single units recorded from 5 bilaterally pinnectomized ferrets. The best positions of the directional lobes nearest to the associated visual response are indicated by the filled circles, while the second lobes of the bilobed responses are shown by the open circles. The continuous line indicates the linear regression for the filled circles. The dashed line indicates the equivalent regression for the intact animals (based on data shown in Fig. 12). The associations indicated by the two lines of best regression are statistically indistinguishable. From Carlile & King (1993).

Fig. 12. Relationship between the visual and auditory space maps in the ferret superior colliculus. For each electrode penetration, the auditory best positions in azimuth (A) and elevation (B) of deep layer neurones are plotted against the corresponding co-ordinates of the centre of the visual receptive fields in the superficial layers.
Fig. 13. Visual–auditory interactions in two neurones of the guinea-pig superior colliculus. Each dot represents an action potential. Fifty successive stimulus presentations are shown in each raster display with the trials ordered from top to bottom. The time courses of the visual (V) and auditory (A) stimuli are shown below each raster display. The visual stimulus was a 50 ms light flash and the auditory stimulus was a 100 ms noise burst. A bar graph showing the mean number of spikes elicited per stimulus presentation for each stimulus is shown on the right of the figure for both cells. The vertical lines through the bars of the graph are standard errors of the mean. Percentage facilitation or depression is defined as:

$$\frac{r_{A+V} - r_A - r_V}{r_A + r_V} \times 100,$$

where $r_{A+V} =$ number of spikes evoked by bimodal stimulation, $r_A =$ number of spikes evoked by auditory stimulation, and $r_V =$ number of spikes evoked by visual stimulation. The cell illustrated in A responded to both visual and auditory unimodal stimulation, whereas that shown in B responded to auditory stimulation only when the two modalities were presented separately. Bimodal stimulation resulted in a much larger response in A, whereas, in B, the auditory response was significantly reduced. Adapted from King & Palmer (1985), with permission.

The alignment between the visual map in the superficial layers and the auditory map in the deeper layers of the ferret SC is shown in Fig. 12. The azimuth and elevation dimensions of both maps cover approximately the same region of space. The spatial extent of the auditory representation varies in different species, and, in each case, corresponds closely to the visual field representation found in both the superficial and deeper layers of the SC, and, therefore, with the position of the eyes (Knudsen, 1982; King & Palmer, 1983; Middlebrooks & Knudsen, 1984; King & Hutchings, 1987). Thus, in the cat (Middlebrooks & Knudsen, 1984), which has frontally placed eyes, the spatial representations of both modalities extend further forward (and cross the anterior midline) than in the guinea-pig (King & Palmer, 1983), whose eyes are located further round on the side of the head. Where both sound azimuth and elevation have been mapped, similarities have also been reported in the orientation and relative magnification of the auditory and visual maps (Knudsen, 1982; Middlebrooks & Knudsen, 1984; King & Hutchings, 1987).
Many neurones in the intermediate and deep layers of the SC receive inputs from more than one sensory modality. Moreover, the responses of SC neurones to multisensory stimulation reveal that the different sensory inputs combine to produce both facilitatory and inhibitory interactions (King & Palmer, 1985; Meredith & Stein, 1986a). Figure 13 shows the responses to combined visual–auditory stimulation of two units recorded in the guinea-pig SC (King & Palmer, 1985). One of these units responded weakly to both the visual and the auditory stimulus, but gave a significantly greater response to bimodal stimulation (Fig. 13A). The second unit also responded to white noise, but did not respond to the visual stimulus. However, presentation of both stimuli together revealed that the visual stimulus, although apparently ineffective by itself, depressed the response of this cell to sound (Fig. 13B).

The relative timing, intensity and spatial positions of the visual and auditory stimuli determine both the magnitude of any response interaction, and whether it is facilitatory or inhibitory in nature (King & Palmer, 1985; Meredith & Stein, 1986a, b; Meredith, Nemitz & Stein, 1987). In particular, the most pronounced bimodal enhancement has been reported when the two stimuli are located at approximately the same spatial co-ordinates, while movement of one of the stimuli away from its excitatory receptive field changes the sign of the interaction to cross-modal depression (King & Palmer, 1985; Meredith & Stein, 1986b). This multisensory centre–surround organization should improve the localization of targets that can be both seen and heard. Indeed, equivalent effects have been observed in behavioural experiments in cats by varying the relative positions of visual and auditory stimuli (Stein, Huneycutt & Meredith, 1988).

**EFFECTS OF EYE AND PINNA POSITION ON AUDITORY SPATIAL TUNING**

The registration of multiple sensory representations in the SC allows different sensory cues, independent of modality, to initiate the motor commands that direct movements of the eyes, pinnae and head towards the location of targets in external space. That different modalities converge onto a common motor pathway is supported by the observation of deep layer neurones that discharge before saccadic eye movements directed toward visual and auditory (Jay & Sparks, 1987a) as well as bimodal targets (Peck, 1987).

However, as we have already seen, neural maps of visual and auditory space are constructed in different ways, with the co-ordinates of visual space centred on the retina, while those of auditory space are centred on the ears and head. The ability of animals to move their eyes or ears independently will alter the spatial relationship between visual and auditory receptive fields, and therefore potentially produce a misalignment of the sensory and motor maps (Pöppel, 1973). Consequently, the accuracy of saccades to auditory targets should depend on the starting position of the eyes. If the registration of sensory maps in the SC is of functional significance, and not an artifact of using anaesthetized animals where the sense organs tend to be aligned (Sparks, 1986), then we might expect that information about the position of different sense organs will be incorporated with the sensory signals into the brain's representation of the outside world.

The question was first addressed by Harris et al. (1980), who observed changes in the position of visual, but not auditory, receptive fields as the eyes of alert cats moved away from the central position. While this suggests that the maps will become misaligned under these conditions, they reported that compensatory head movements ensure that cats actually look straight ahead most of the time, so that the co-ordinates of visual and
auditory space should become realigned before the start of each new saccadic movement. On the other hand, Jay & Sparks (1987b) found that the majority of auditory receptive fields that they obtained from cells in the primate SC shifted in the direction of a change in eye position. This has led to the suggestion that auditory responses are organized in the SC in motor error co-ordinates, incorporating both the position of the sound source and the orbital position of the eyes, which encode the gaze shift that is required to look toward the target (Sparks, 1986, 1988; Jay & Sparks, 1987b).

Although cats have a more restricted oculomotor range than primates (Guitton, 1992), they do fixate targets when their eyes are deviated from the central orbital position. Indeed, the accuracy of auditory localization in head-restrained cats is little affected by the initial position of either the eyes (P. H. Hartline, R. L. P. Vimal, A. J. King, D. D. Kurylo & D. P. M. Northmore, unpublished observations) or the pinnae (Hartline, King & Northmore, 1989b). By monitoring eye and pinna position with electromagnetic search coils, we found cells in the SC of these animals, whose auditory responses changed independently of pinna movement as the direction of gaze changed (Hartline, King, Kurylo, Northmore & Vimal, 1989a). Some cells exhibited a compensatory shift in the location of their spatial response profiles (Fig. 14A). However, as with primates, the magnitude of this shift was less than the magnitude of the change in ocular position, and also less than the degree of behavioural compensation observed in saccadic eye movements. In other units, changes in eye position led to either a decrease or an increase in activity at all loudspeaker positions throughout the spatial response profile, with no overall shift in positional selectivity (Fig. 14B). In other words, the gaze shift had the effect of modulating the responses of the cells.

The large receptive fields of SC neurones lead to the conclusion that stimulus location is encoded by the distribution of activity across much of the nucleus (Middlebrooks & Knudsen, 1984; McIlwain, 1986). Although further work is required to look at the effects of eye position on auditory responses at different sites within the SC, these data are consistent with the possibility that differential modulation of auditory responses within the deeper layers could contribute to a shift in the point image (McIlwain, 1986) of an auditory

Fig. 14. Influence of initial eye position on the auditory spatial tuning of two neurones recorded in the superior colliculus of an alert, head-restrained cat. Eye and pinna position were measured using electromagnetic search coils. A, lateral shift of an auditory spatial response profile in the same direction as a shift in gaze. Continuous lines, eyes 10 deg left; dotted lines, eyes centre; dashed lines, eyes 15 deg right. B, auditory spatial response profile of another unit recorded from the same animal, showing the modulating effect of a change in azimuthal eye position. Continuous lines, eyes 14 deg left, dotted lines, 5 deg left; dashed lines, eyes 10 deg right. These responses were calculated from multiple regression equations in which the pinna and vertical eye positions were held constant.
target, leading to a population response more completely compensated for eye position than appears to be the case for individual receptive fields.

Movements of the outer ears will alter the relationship between the monaural and binaural spectrum level cues and associated spatial locations. In view of the dependence of the map of auditory space on these cues, we would expect that animals with mobile pinnae should encounter additional problems in representing auditory space, and therefore in maintaining the correspondence between different sensory maps. Indeed, passive displacement of the pinnae in anaesthetized cats changes the spatial tuning of SC units in a manner that is predictable from the alteration in interaural level difference values (Middlebrooks & Knudsen, 1987). By appropriate selection of subsets of trials in which the range of eye positions was restricted, or by the application of multiple regression techniques (Vimal, Kurylo, Hartline & King, 1989), we were able to obtain preliminary data showing the effects of volitional changes in pinna position on auditory spatial tuning in the cat SC. When the contralateral pinna was directed backwards, we observed strong responses that were spatially tuned (Fig. 15). The most common effect encountered was a marked reduction in activity as the pinna moved forward. Although a small anterior shift in best position was apparent in some units, this was considerably less than the magnitude of the change in pinna position. Moreover, the change in the auditory spatial response profiles did not match the changes that follow when the contralateral pinna of an anaesthetized animal is displaced passively (Middlebrooks & Knudsen, 1987).

These data suggest that changes in pinna, as well as eye, position may modulate the auditory responses of SC neurones in awake animals. Exactly how such effects influence the overall representation of auditory space or where the signals about eye or ear position originate is unclear. Nevertheless, it seems likely that eye position information is provided by corollary discharge rather than by proprioceptive feedback from the extra-ocular muscles (Guthrie, Porter & Sparks, 1983; Peck, 1984; Nelson, Meredith & Stein, 1989).
The development and plasticity of the visual system has been studied extensively, giving rise to the view that visual experience is required for the maintenance and refinement of connections and response properties in the cortex (reviewed by Movshon & Van Sluyters, 1981; Rauschecker, 1991). One important consequence of experience-dependent modifications during early life is that these effects can compensate for developmental alterations in the relative geometry of different sense organs. For example, plasticity of the input from the two eyes onto binocularly driven neurones in the visual cortex (Pettigrew, 1978; Blakemore, 1979) or optic tectum (Keating, 1974) allows adjustments to be made to changes in inter-ocular relationships during growth.

Both binaural and monaural localization cue values depend on the size and shape of the head and outer ears. This would suggest that neural sensitivity to these cues should be calibrated to allow for physical variations from one individual to another. Moreover, growth of the head and ears will alter the relationship between the values of these localization cues and positions in space (Moore & Irvine, 1979; Carlile, 1991a, b). Consequently, we might expect to see some degree of developmental plasticity in the neural mechanisms by which neurones achieve their auditory spatial selectivity. Indeed, there is now considerable evidence that sensory experience plays an essential role in the development of the representation of auditory space in the SC (Knudsen, 1988; King & Moore, 1991).

Postnatal maturation of auditory spatial tuning

In our laboratory in Oxford, we have been studying the development and plasticity of the auditory space map in the SC of the ferret. This species is particularly suitable for this type
Fig. 17. The development of the representation of auditory space in the SC. The auditory and visual receptive fields were mapped in ferrets at different postnatal ages. The neonatal responses were grouped by age as indicated at the top of the figure. A, the auditory best positions are plotted against the rostrocaudal location of the recording electrode. B, the registration between the auditory and visual representations is shown by plotting the auditory best positions against the locations of the centre of the visual receptive field recorded in the same electrode penetration. There is a gradual emergence of the topography of the auditory representation and a concomitant improvement in the registration between the visual and auditory representations in the SC, which, by the 8th to 9th postnatal week, is similar to that in the adult.

of work, as it is born in an immature state and does not begin to hear until approximately 1 month after birth (Morey & Carlile, 1990).

In order to understand the nature of any plasticity in the auditory representation, it is first necessary to describe the normal response properties of SC neurones at various stages of development. In contrast to the spatially tuned and topographically organized receptive fields of units recorded in adult animals, we found that the responses recorded in the SC of ferrets a few days after the onset of hearing were very broadly tuned (Fig. 16; King & Carlile, 1991). Multiunit recordings revealed that both the degree of spatial tuning and the topography of the auditory best positions gradually improved over the next few weeks, and that an adult-like representation appeared at approximately 60 days after birth (Fig. 17A). Despite the poor optical quality of the eyes in the youngest ferrets examined, visual responses in the superficial layers were easily mapped, and the representation of the azimuthal dimension of visual space along the rostrocaudal axis of the SC closely resembled that found in adults. Consequently, the registration of the visual and auditory maps gradually improved over the same postnatal period (Fig. 17B). Qualitatively similar findings have been made in the more precocious guinea-pig, where SC cells respond to sound within a day of birth, but are also initially very broadly tuned for sound location.
In this species, no topographic order was observed in the auditory representation until postnatal day 32 (Withington-Wray, Binns & Keating, 1990a).

It is not clear whether the gradual emergence of the auditory space map reflects the postnatal development of monaural and binaural response properties or simply the acoustic cues available at each age, which, at least in the ferret, are changing continuously over the same time period (Carlile, 1991a, b). The maturation of responses in the central auditory system does, in part, reflect the development of the auditory periphery (Rubel, 1984; King & Moore, 1991), and adult-like sensitivity to interaural time and level disparities has been described in the auditory cortex of kittens (Brugge, 1988). A similar situation may be found in the SC, since the emergence of the auditory space map in the ferret (King & Carlile, 1991) coincides with the maturation of monaural spectral cues (Carlile, 1991a, b).

Role of auditory experience in the development of the auditory space map

The variation in localization cue values, both within and between individual animals, suggests a likely role for auditory experience in the development of the space map. In order to investigate whether SC responses are functionally plastic, we have examined the effects on map development of altering monaural and binaural cues during postnatal development.

The extent to which a map of auditory space can be generated by monaural pinna cues alone was examined by restricting the input to one ear throughout postnatal life (King, Hutchings & Moore, 1987; King, Moore & Hutchings, 1993). Recordings were made in adult ferrets that had been deprived of binaural inputs by ablation of the ipsilateral cochlea before the onset of hearing. At sound levels of around 10 dB above threshold, the auditory units were tuned to a specific region of space that was restricted in both azimuth and elevation. This near threshold representation closely resembled that found in normal adult ferrets. Thus, the auditory best positions varied topographically in azimuth along the rostrocaudal axis of the SC (Fig. 18A) and in elevation along the mediolateral axis (Fig. 19A). However, at higher sound levels, SC neurones in the monaural ferrets were either very poorly tuned or they exhibited tuned spatial response profiles with highly inappropriate best positions. Consequently, in contrast to the near-threshold map, no topographic order was apparent in the representation of either azimuth (Fig. 18B), or elevation (Fig. 19B) at sound levels of approximately 30 dB above threshold.

These data indicate that monaural pinna cues provide sufficient directional information for the construction of a two-dimensional map of auditory space, which, like the normal representation, is in register with the visual map in the superficial layers of the SC (King et al., 1993). However, as in adult guinea-pigs that have been monaurally deafened just prior to recording (Fig. 7), this topographic representation is apparent at near-threshold sound levels only.

Rather than ablate the cochlea, which completely removes the input from one ear, we can disrupt binaural localization cues by plugging one ear early in life. Rearing ferrets (King, Hutchings, Moore & Blakemore, 1988) and barn owls (Knudsen, 1985) with one ear chronically occluded leads to a compensatory adjustment in the auditory space map in the SC. Thus, despite the unilateral conductive hearing loss caused by the ear plug, the auditory responses of SC units were spatially tuned at all sound levels tested (Fig. 20A). However, following a similar period of monaural occlusion in adult ferrets, we observed sharply tuned responses near threshold, but omnidirectional receptive fields at higher sound levels (Fig. 20B; King, Hutchings & Moore, 1992). This is the same result as that obtained when the ipsilateral ear is occluded acutely in an adult animal (Fig. 6). It therefore appears that
there is a sensitive developmental period during which the neural mechanisms responsible for spatial selectivity can compensate for the presence of an ear plug.

The azimuthal best positions of SC units recorded from ferrets that had been reared with one ear occluded were topographically organized. The distribution of suprathreshold best positions, obtained with the ear plug still in place, closely resembled that found at corresponding sound levels in normal, adult ferrets (Fig. 21 A and B). The lack of topography in the auditory representation at these sound levels in monaurally deafened
ferrets (Fig. 21C) indicates that binaural localization cues are required to maintain the map as the stimulus level is increased. These data therefore suggest that the auditory system has compensated for the presence of the ear plug during development by adjusting the interaural level differences to which SC cells are most sensitive, so that they respond best to the appropriate region of space. This has recently been confirmed in the barn owl, where chronic monaural occlusion leads to an adaptive change in the tuning of tectal units to binaural localization cues (Mogdans & Knudsen, 1992).

The compensatory change observed in the auditory space map after rearing animals with distorted binaural cues suggests that experience plays an important role in shaping the response properties of SC neurones according to the acoustic cues available to individual animals. This leads to the question of what source of information causes this adaptive change in auditory response properties to occur. Several possibilities have been considered in the barn owl, including residual auditory cues and information provided by other senses (Knudsen & Mogdans, 1992). Since the hearing loss induced either by an ear plug or ablation of the cochlea was restricted to one ear, both groups of ferrets had access to monaural pinna cues provided by the unaffected ear. It is therefore possible that the monaural map generated by these cues at near-threshold sound levels plays an instructional role in the development of binaural interactions.

Simon Carlile and I have examined the contribution of the outer ear to the development of the auditory space map in the ferret SC by removing the pinna and concha bilaterally before the onset of hearing. Once these animals were fully grown, acoustical measurements showed that both monaural and binaural spectral cues were spatially ambiguous, closely resembling those available in adult ferrets following acute bilateral pinnectomy (Figs 9 and 10). Recordings from SC units in these animals revealed spatial response profiles at near-threshold sound levels that were broadly tuned to the contralateral hemifield. A similar lack of topography was also evident at the higher sound levels where spatially tuned responses

![Diagram](image-url)
Fig. 21. The effects of disrupting binaural localization cues on the development of the map of sound azimuth in the superior colliculus. All the data shown were obtained at suprathreshold sound levels (more than 20 dB above threshold) that would normally stimulate both ears at all positions. Auditory best positions are plotted against the location of each unit measured in terms of the distance from the rostrolateral margin of the nucleus (see Fig. 5). A, data from normal, adult ferrets. B, data from adult ferrets that had been reared from before the onset of hearing with the ipsilateral ear occluded with a plug that caused a frequency-dependent attenuation of 5-60 dB. Despite the presence of the ear plug, the auditory responses were spatially tuned and topographically organized. C, data from adult ferrets that had been completely deafened in one ear by ablation of the ipsilateral cochlea in infancy (see Fig. 18B). Based on data from King et al. (1988, 1993).

are normally achieved as a result of binaural interactions. Instead of the bilobed responses that appear in adult ferrets following acute removal of the pinna and concha, the majority of the units recorded in the SC responded almost equally well to all positions tested (Fig. 22). Thus, despite the continuous availability of interaural level difference cues, which, in pinnecotmized adults, provide the basis for the construction of an ambiguous map of sound azimuth (Figs 10 and 11), a topographic auditory representation failed to develop (King & Carlile, 1989). This may reflect an inability of the auditory system to construct a neural map based on binaural cues that are ambiguous about the interaural axis. Alternatively,
Bilateral pinnectomy

Near threshold (monaural response) 30 dB above threshold (binaural response)

Fig. 22. Surface view of the right superior colliculus of an adult ferret, showing the location of three electrode penetrations. The polar diagrams represent the responses of a single unit (at two different sound levels: left column, near threshold; right column, suprathreshold) recorded in each track to 100 ms bursts of white noise as a function of the azimuthal angle of the sound source. The pinna and concha were removed bilaterally before the onset of hearing.

Different localization cues relating to a particular position in space may be correlated through the use of the near-threshold monaural map as a template for the development of sensitivity to appropriate binaural cue values.

Role of visual experience in the development of the auditory space map

The presence of topographically aligned visual and auditory maps in the SC raises the question of how this registration is established and then maintained during development. Cross-modal plasticity has been demonstrated at several levels of the developing brain, including the SC (for review see King, 1990). In particular, anatomical, physiological and behavioural changes in the auditory system can be induced by altered visual experience.

In order to see whether vision influences the development of the auditory space map in
the SC, we have carried out a series of experiments in which the visual cues available to ferrets during postnatal development were either deprived or altered. After rearing ferrets with binocular eyelid suture, a procedure that both attenuates and blurs the visual signals, without eliminating them altogether, spatially tuned auditory responses were recorded in the SC, which were organized into normally orientated maps of both azimuth and elevation (King & Carlile, 1993). However, marked abnormalities were apparent in the topography and precision of these representations and, therefore, in the correspondence with the overlying visual map (Fig. 23). In particular, some azimuthal best positions were more contralateral than expected according to both their recording locations and the associated visual receptive fields (Fig. 23 A and C). Most of the inappropriate responses were exhibited
Fig. 24. Changes in eye position during the postnatal development of the ferret. A reversible ophthalmoscope was used to align the Purkinje–Sanson series of images with the centre of the pupil in awake, hand-held animals, in order to provide a measure of the position of the optic axis. All the values plotted represent the means (±S.D.) of 3–5 measurements of the azimuthal co-ordinate of the back-projected ophthalmoscope beam. The filled circles represent the values obtained from six normal ferrets at various times after birth, as indicated on the abscissa. The other symbols represent estimates of eye position in five different ferrets, identified by the numbers in the key, in which the medial rectus muscle had been sectioned on P27–28.

by units with spatially ambiguous bilobed response profiles, in which one lobe was located within the normal range of the auditory map while the second best position occurred outside this range. Similar changes have been reported in the auditory space map in the optic tectum of barn owls (Knudsen, Esterly & du Lac, 1991) and in the SC of guinea-pigs (Withington, 1992). Thus, while patterned visual cues do not appear to be necessary for the generation of at least a crude topographic representation of auditory space, the more accurate and reliable spatial cues provided by the eyes do appear to play an instructive role in fine tuning the developing auditory map. On the other hand, there may be a requirement for some form of visual experience as no map is found in the SC after rearing guinea-pigs in complete darkness (Withington-Wray, Binns & Keating, 1990b).

We have also carried out two procedures aimed at altering the spatial relationship between the retina and the visual world (King et al. 1988). Firstly, the left medial rectus muscle was removed in young ferrets before eye opening, which had the effect of stabilizing the eye in a new position that was deviated laterally by 15–20 deg compared to age-matched normal ferrets (Fig. 24). Since the visual map is retinotopic, this change in eye position produced a corresponding displacement in the region of visual space that was represented in the superficial layers of the contralateral SC (Fig. 25A). Examination of the auditory responses in the SC of fully grown animals revealed a similar lateral shift in the best positions compared to normal adult ferrets (Fig. 25B). Consequently a comparison of the visual and auditory receptive field positions associated with each electrode track indicated
that the registration of the two maps was just as close in the ferrets reared with one eye deviated laterally as in the normal ferrets (Fig. 25C).

A similar adaptive change in auditory spatial tuning has been obtained by optically displacing the visual field of barn owls that were reared with prisms mounted in front of their eyes (Knudsen & Brainard, 1991). Moreover, this procedure also leads to a corresponding adjustment in the accuracy of head orientation to sound sources, even though both visual and auditory localization are subsequently incorrect (Knudsen & Knudsen, 1989). Taken together, these findings raise the possibility that a mechanism exists
by which neural sensitivity to auditory localization cue values may be correlated with positions in visual space.

To see if the auditory map can adjust to a larger change in eye position, we sectioned all six extra-ocular muscles and rotated the eye about the optic axis by 110–210 deg. Again this was done before eye opening when the ferrets were visually naive. As expected, this procedure resulted in a corresponding rotation of the visual field representation in the contralateral SC. Although the acoustic cues available were unaffected, the auditory
responses recorded in the deep layers of the SC in these animals were abnormal in several ways (King et al. 1988). In particular, examination of the relationship between auditory best position and cell location failed to reveal any clear topographic order in the representation of auditory space (Fig. 26B), compared to that found in normal animals (Fig. 26A). Moreover, the change in auditory spatial tuning was not adaptive since the best positions did not correspond to the rotated array of visual receptive fields. This appears to represent a developmental interaction, since identical eye rotations performed within a few days of eye opening had little discernible effect on the precision and topography of the auditory representation (Fig. 26C; King, Hutchings, Moore & Blakemore, 1985).

Since the auditory responses of SC cells can be modified by voluntary changes in eye position in awake animals (see Fig. 14), the effects of neonatal eye rotation on auditory spatial tuning may result either from abnormal signals about eye position or from the chronic shift in the visual field representation. The considerably reduced susceptibility of the auditory responses to eye rotation just after eye opening seems most likely to be due to the brief period of visual experience received by these animals, which may have been sufficient to stabilize the subsequent development of the auditory map. Further evidence that these effects are mediated primarily by visual signals, rather than the change in eye position, is provided by the finding that the disorganization of the auditory representation in animals receiving an eye rotation before eye opening does not occur if they are visually deprived at the same time (King, 1991).

These experiments indicate that vision plays an instructive role in the development of auditory spatial tuning and therefore in maintaining the registration of the two maps in the SC. However, the process by which auditory neurones adjust their sensitivity to sound location, in order to match changes in the visual representation, appears to operate over a limited range. Thus, a small change in eye position produces a corresponding shift in the auditory map, while a larger disturbance of the visual field exceeds the capacity of the mechanism for maintaining alignment, and results in a highly disordered auditory representation. The auditory responses are poorly tuned and not topographically organized at the age when these procedures were carried out (see Figs 16 and 17). Hence visual cues presumably contribute to the gradual emergence of the auditory space map, possibly via a direct, Hebbian-style interaction in which auditory spatial selectivity is adjusted by spatially coincident visual signals. On the other hand, the organization of auditory responses observed after early eye rotation is compatible with the possibility that this procedure may impair or prevent the further maturation of the auditory representation beyond the developmental stage reached when the aberrant visual receptive fields are introduced.

**SUMMARY**

The experiments described in this review have demonstrated that the SC contains a two-dimensional map of auditory space, which is synthesized within the brain using a combination of monaural and binaural localization cues. There is also an adaptive fusion of auditory and visual space in this midbrain nucleus, providing for a common access to the motor pathways that control orientation behaviour. This necessitates a highly plastic relationship between the visual and auditory systems, both during postnatal development and in adult life. Because of the independent mobility of difference sense organs, gating mechanisms are incorporated into the auditory representation to provide up-to-date information about the spatial orientation of the eyes and ears. The SC therefore provides a valuable model system for studying a number of important issues in brain function,
including the neural coding of sound location, the co-ordination of spatial information between different sensory systems, and the integration of sensory signals with motor outputs.

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REFERENCES


NEURAL REPRESENTATION OF AUDITORY SPACE


