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Organization of the Human Superior Olivary Complex

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ABSTRACT The distinctive morphology of the human superior olivary complex reflects its primate origins, but functional evidence suggests that it plays a role in auditory spatial mapping which is similar to olivary function in other mammalian species. It seems likely that the well-developed human medial olivary nucleus is the basis for extraction of interaural time and phase differences. The much smaller human lateral olivary nucleus probably functions in analysis of interaural differences in frequency and intensity, but the absence of a human nucleus of the trapezoid body implies some difference in the mechanisms of this function. A window on human olivary function is provided by the evoked auditory brainstem response (ABR), including its binaural interaction component (BIC). Anatomical, electrophysiological, and histopathological studies suggest that ABR waves IV and V are generated by axonal pathways at the level of the superior olivary complex. Periolivary cell groups are prominent in the human olivary complex. The cell groups located medial, lateral, and dorsal are similar to periolivary nuclei of other mammals, but the periolivary nucleus at the rostral pole of the human olivary complex is very large by mammalian standards. Within the periolivary system, immunostaining for neurotransmitter-related substances allows us to identify populations of medial and lateral olivocochlear neurons. The human olivocochlear system is unique among mammals in the relatively small size of its lateral efferent component. Some consideration is given to the idea that the integration provided by periolivary cell groups, particularly modulation of the periphery by the olivocochlear system, is an extension of the spatial mapping function of the main olivary nuclei. *Microsc. Res. Tech. 51: 403–412, 2000.*

AUDITORY SPATIAL MAPPING IN MAN

Bruce Masterton has written eloquently about the difference between the ear's function in encoding the attributes of sounds, such as frequency, intensity, and temporal patterns, and the contrasting role of the central auditory system in analyzing the attributes of sound sources, such as their location, distance, and movement (Masterton, 1974, 1992). Additionally, he has pointed out the biological relevance, i.e., the survival value, of being able to accurately localize the source of a sound. Can we assume that this process of localization occurs in the human central auditory system? One basis for doing so is electrophysiological investigation of spatial mapping in the human brainstem (Polyakov and Pratt, 1996; Pratt and Polyakov, 1996). In these studies, clicks with varying lateralizations were presented binaurally to human subjects. The activity recorded, the binaural interaction component of the auditory brainstem response, was localized to the pons. Further, the orientation of the dipole sources of the activity within the pons varied with changing lateralization of the sound stimuli. These studies provide strong presumptive evidence that human auditory spatial mapping occurs at a brainstem level.

Early lesion studies in animals (Casseday and Neff, 1975; Jenkins and Masterton, 1982; Thompson and Masterton, 1978) provided experimental evidence of a reorganization of auditory input at the level of the superior olivary complex (SOC). In these studies, the ability of cats to accurately locate a sound source was tested before and after specific brainstem lesions. Lesions located above the level of the superior olivary complex, for example, in the lateral lemniscus, inferior colliculus, medial geniculate body, or auditory cortex, left the experimental animals unable to locate a sound source in the hemifield of space contralateral to the lesion. Damage to the auditory system below the level of the olivary complex created more diffuse deficits. From these results, the investigators concluded that the auditory spatial field is recreated in the brainstem by the transformations occurring in the superior olivary complex.

Strikingly parallel deficits have been seen in human subjects with localized pontine lesions. Vascular or demyelinating lesions of the ventral pons, which interrupted the trapezoid body, caused subjects to localize dichotic clicks with differing interaural time differences to the center of the head (Furst et al., 1995; Pratt et al., 1998). More rostrally located lesions, interrupting one lateral lemniscus, resulted in a side-biased localization. The isolated nature of the localization deficit was apparent in a case of an extensive midline pontine lesion reported by Griffiths et al. (1997). Such a midline lesion would eliminate crossed input to both superior olivary complexes, leaving them with input only from the ipsilateral ear. Testing revealed that the patient had no difficulty in detecting frequency and

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amplitude modulation and no general deficit in detection of auditory temporal information. However, the patient was unable to determine, by sound alone, the direction of travel of a train passing her on the platform, or to determine which of three well separated telephones in her office was ringing. These cases support the notion that analysis of the spatial attributes of sound stimuli occurs centrally, and specifically at the level of the superior olivary complex, in man as in other mammalian species.

MORPHOLOGICAL TRENDS IN THE PRIMATE SUPERIOR OLIVARY COMPLEX

The mammalian superior olivary complex has deep phylogenetic roots, extending back at least to the reptilian nucleus laminaris. Across mammals, the SOC has retained its basic functional role in spatial mapping but has evolved in a variety of anatomical forms, reflecting the auditory specializations of the taxon. Because of their use in experimental studies, the most familiar patterns of SOC morphology are those of carnivores and rodents, but these are not perfect models for the human olivary complex (Moore, 1987; Moore and Moore, 1971). In Figure 1A and B, myelin-stained sections through the level of the SOC in a feline and a human brainstem illustrate some of the differences in their anatomical patterns. The medial superior olivary nucleus (MSO) of the cat is broader dorsally than ventrally, while the human MSO is a uniformly slender column. The lateral superior olivary nucleus (LSO) of the cat has the well-known S-shape, while the human LSO is much smaller and roughly oval. In the cat, clusters of cells of the nucleus of the trapezoid body (NTB) are apparent in the trapezoid body medial to the complex, while no such cell groups are visible in the human SOC. Patches of periolivary cells are visible ventral to the main olivary nuclei of the cat. Similar cell groups are present in the human SOC, but are somewhat less distinct.

The cat and man are end products of two divergent lines of mammalian evolution, but the gap between the morphological patterns of the feline and human SOCs can be bridged by examining a series of primates. Figure 1C through F illustrates the SOC in four primate species. In Figure 1C, we see the SOC of a lorisoid prosimian, the galago, a nocturnal insectivore from southeast Asia and an extant example of the lowest level of primate organization. The SOC of the galago is basically very similar to that of the cat, with a distinct MSO and darkly stained cells of the nucleus of the trapezoid body (NTB) visible in the trapezoid body. The chief difference between the cat and prosimian is in the LSO, which is smaller and not S-shaped in the prosimian. Instead, the LSO in the galago is ovoid, with indistinct convolutions. Periolivary cells in the galago form nuclei that are similar to those of the cat, located dorsomedial, ventromedial, and ventrolateral to the main olivary nuclei. In Figure 1D, we see the SOC of the marmoset, a small member of the group of more primitive ceboid or South American primates. As in the cat and galago, the MSO is a clearly visible column of cells with a greater cell density in the dorsal half of the nucleus. The LSO is an irregularly oval nucleus with some indication of convolutions. The NTB consists of darkly staining cells in the trapezoid body, though these cells are somewhat more scattered than in the galago. Periolivary cells are present dorsally and ventrally, but do not form clearcut nuclei. Figure 1E illustrates the SOC of the macaque, a more advanced cercopithecoid or Asian-African monkey. The MSO is a straight column of cells with only a hint of broadening in the dorsal half. The LSO is less distinct than in the lower primates, and the NTB consists of a restricted number of dark cells scattered in the trapezoid body. In this monkey, periolivary cells form an almost continuous ring around the margin of the complex. In Figure 1F, we see the SOC of one of the anthropoid apes, the southeast Asian gibbon. In the ape, there is a long slender MSO and a small and relatively indistinct LSO. The NTB is difficult to identify as a nucleus, though there are some scattered darkly stained cells in its usual position. With this reduction in size of the LSO and NTB, the olivary complex of the gibbon is very similar to the human cytoarchitectural pattern.

MAIN OLIVARY NUCLEI

Electrophysiological studies provide evidence for two separate systems of auditory localization in the human brainstem (Pratt et al., 1997). In this work, the investigators recorded responses to monaural clicks and binaural clicks with a variety of interaural time and intensity differences, and measured the latency of the binaural interaction component of the auditory brainstem response (ABR). The binaural interaction component (BIC) is obtained by subtracting the response to binaural stimuli from the algebraic sum of the right and left ear monaural responses to the same stimulus. The reduction in total activity in the BIC is presumed to reflect the fact that the binaural response involves convergence of activity from the right and left ears upon some subset of brainstem auditory neurons. In this study, the dipole localizations of the BIC differed for interaural time and intensity differences, indicating that interaural time and intensity cues are processed by spatially separate systems in the brainstem. This human study meshes with a large body of evidence obtained in animals demonstrating a double mechanism of spatial analysis in the SOC. That evidence is discussed in other articles in this issue, and will be considered here only from the standpoint of its implications for human auditory spatial localization.

Medial Olivary Nucleus

The system for analysis of interaural time differences, including phase differences, has been linked to the medial superior olivary nucleus. (These generalizations may not apply to the superior olivary nuclei of bat species, which are described elsewhere in this issue). Early single unit studies in carnivores demonstrated that the discharge rate of MSO neurons is influenced by interaural time differences (Caird and Klinke, 1983; Galambos et al., 1959; Goldberg and Brown, 1968; Inbody and Feng, 1981). Recent studies have confirmed that MSO neurons exhibit sensitivity to variation in interaural time and phase differences, and show phase-locking to both monaural and binaural stimuli (Spitzer and Semple, 1995; Yin and Chan, 1990). These response properties of MSO neurons create a map of interaural time differences along the rostrocaudal axis of the nucleus (Yin and Chan, 1990). The results of

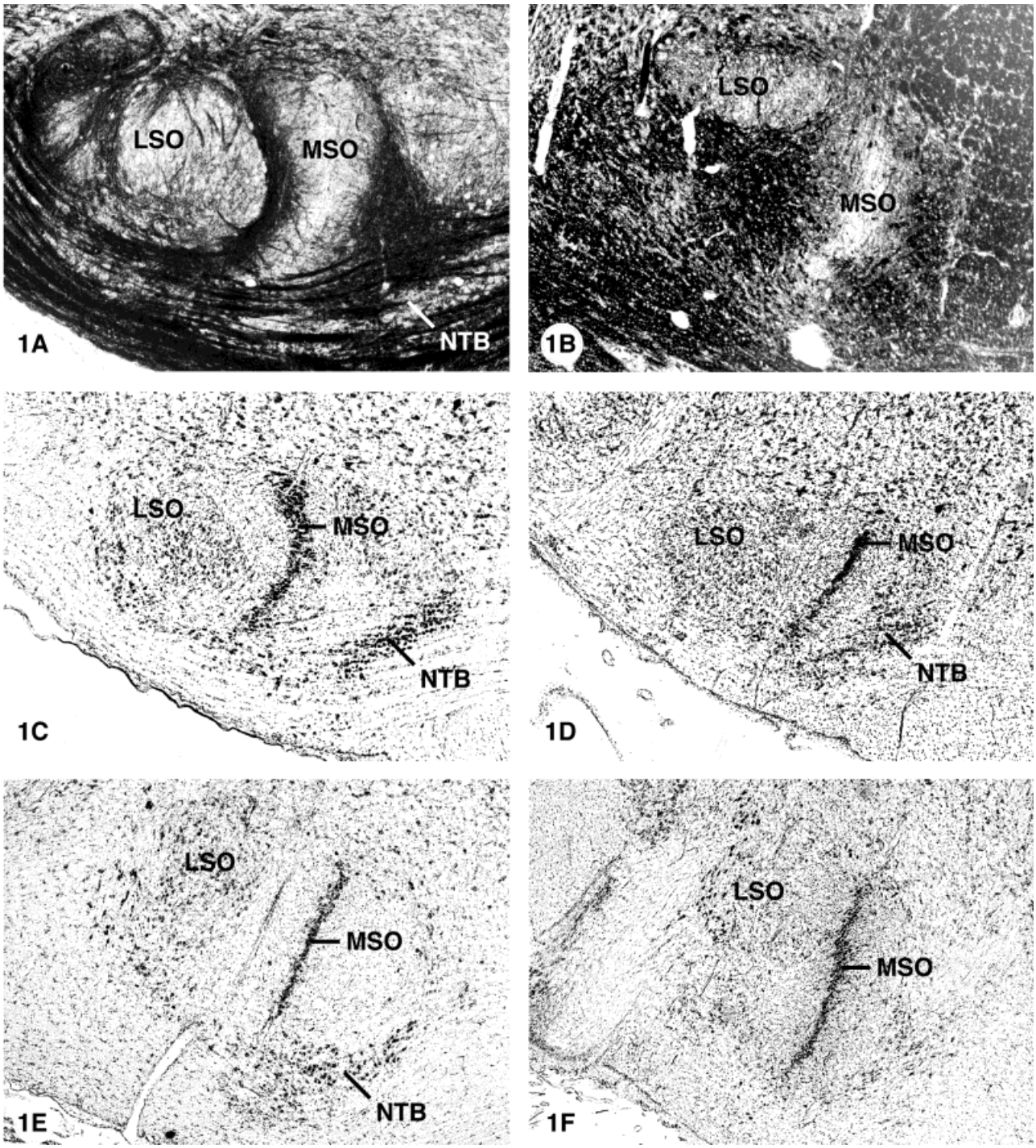


Fig. 1. Brainstem cross-sections through the superior olivary complex in (**A**) cat; (**B**) man; (**C**) galago; (**D**) marmoset; (**E**) macaque; (**F**) gibbon. LSO, lateral superior olivary nucleus; MSO, medial superior olivary nucleus; NTB, nucleus of the trapezoid body. All photos shown at identical magnification.

these studies have been interpreted in terms of an MSO mechanism of binaural interaction based on detection of coincident excitatory inputs from the two ears (Han and Colburn, 1993; Spitzer and Semple, 1995; Yin and Chan, 1990). The dual excitatory input necessary for this process is provided by axonal projections from the ipsilateral and contralateral cochlear nuclei to the medial and lateral dendrites of MSO neurons (Cant and Casseday, 1986; Shneiderman and Henkel, 1985; Smith et al., 1993; Warr, 1982). Though

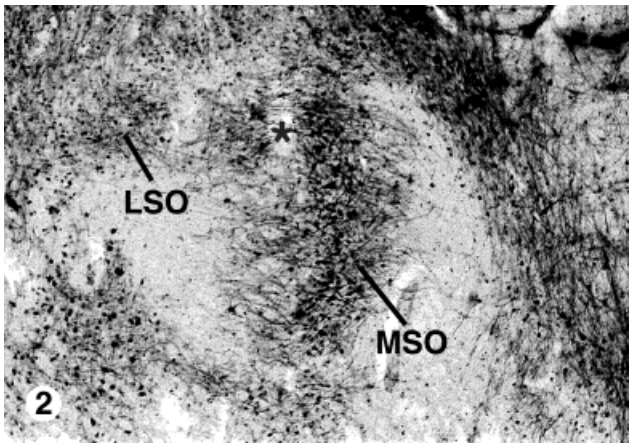


Fig. 2. Human superior olivary complex from a 46-year-old subject, immunostained for MAP2 to illustrate neuronal somata and dendrites. Asterisk marks a blood vessel. LSO, lateral superior olivary nucleus; MSO, medial superior olivary nucleus.

tract tracing studies cannot be carried out in humans, the same pattern of input characterizes one of the great apes, the chimpanzee (Strominger et al., 1977). The medial and lateral dendritic fields of the human MSO, as seen in a brainstem section immunostained for the microtubule-associated protein, MAP2 (Fig. 2), suggests that the input pattern is the same in man.

Single-unit studies have shown the MSO to be biased toward low frequencies. In several studies, most recorded units had characteristic frequencies of less than 3–4 kHz (Galambos et al., 1959; Yin and Chan, 1990), though units with best frequencies up to 10–20 kHz can be recorded from the ventral tip of the nucleus (Goldberg and Brown, 1968; Guinan et al., 1972). Similarly, recordings from the afferent axons of spherical bushy cells in the ventral cochlear nucleus demonstrated that more than 80% of these axons have best frequencies below 3 kHz (Smith et al., 1993). The electrophysiological data are consistent with anatomical findings that cochlear nucleus axons representing 1.2 to 5 kHz innervate most of the length of the MSO (Warr, 1982), and that output from the MSO is the major source of afferents to the low-frequency region of the central nucleus of the inferior colliculus (Aitkin and Schuck, 1985). This low-frequency bias may account for the fact that the MSO is a major component of the SOC of all primates, including man. With 10,000–11,000 cells (Moore and Moore, 1971; Strominger and Hurwitz, 1976), the human MSO is almost twice as large as that of the cat. The size of the human MSO reflects a steady increase across primates (Moore and Moore, 1971), from prosimians (2,500–2,700 cells) to ceboid and cercopithecoid monkeys (4,500–5,500 cells) to apes (7,000 cells). Because larger head size broadens the range of low frequencies that can be utilized as interaural phase difference cues, increasing head size in primates may contribute to the prominance of the human MSO. In any case, on the basis of size alone, we could imagine that the MSO plays a significant role in human spatial hearing.

Lateral Olivary Nucleus

In the cat, LSO neurons have been shown to have an orderly representation of best frequencies spanning the feline audible range, from 20 Hz to 40 kHz (Guinan et al., 1972; Tsuchitani and Boudreau, 1966). The LSO is extremely large in echolocating species such as bats and porpoises, which have an extended range of high-frequency hearing (Irving and Harrison, 1967; Zook and Casseday, 1982; Zvorykin, 1964), but it is small in small mammals whose usable range is limited to high frequencies and in primates whose hearing is limited to low frequencies (Irving and Harrison, 1967; Moore and Moore, 1971). Thus, in terms of its comparative anatomy, it is probably more correct to say that LSO size correlates with range of usable auditory frequencies, rather than with utilization of high frequencies per se. As seen in Figure 2, the human LSO is a small oval or bilobed nucleus with dendrites confined to the body of the nucleus. Cell counts of the human lateral olivary nucleus show a total of 2,500–4,000 cells (Moore and Moore, 1971; Strominger and Hurwitz, 1976), which is smaller than the LSO in the cat and similar in absolute size to the nucleus in rodents and insectivores.

The lateral olivary nucleus contains many neurons whose firing rate reflects interaural spectral and intensity differences (Tsuchitani, 1977; Tsuchitani and Bodreau, 1969). Though LSO cells also respond to interaural time differences, the rate changes that occur in response to naturally occurring interaural time differences are small in comparison with the changes for interaural level differences (Caird and Klinke, 1983; Joris and Yin, 1995). In the single-unit studies, most binaurally sensitive LSO neurons show an excitatory response to ipsilateral ear stimulation and an inhibitory response to contralateral ear stimulation. Recordings in brain slice preparations demonstrate that the excitatory response occurs to stimulation of axons from the ipsilateral cochlear nucleus, while the inhibitory response occurs to stimulation of the ipsilateral nucleus of the trapezoid body (Sanes, 1990). This combination of excitatory and inhibitory input has been viewed as the basic mechanism of LSO function (Joris and Yin, 1995; Reed and Blum, 1990).

Anatomical studies have verified that ipsilateral excitatory input arrives through axons of cochlear nucleus spherical cells, both in nonprimate mammals (Cant and Casseday, 1986; Shneiderman and Henkel, 1985; Smith et al., 1993; Warr, 1982) and in higher primates (Strominger et al., 1977). The contralateral inhibitory input originates from cochlear nucleus globular cells projecting to the NTB (Smith et al., 1993), and continues as a direct projection from the NTB to the LSO (Friauf and Ostwald, 1988; Glendenning et al., 1985; Smith et al., 1998; Spangler et al., 1985), a projection that is glycinergic and therefore inhibitory (Bledsoe et al., 1990; Glendenning et al., 1985; Spangler et al., 1985). Though this inhibitory limb of LSO circuitry clearly exists in nonprimate mammals, any theory of inhibition as a necessary component of LSO function presents a problem in higher primates. Regression of the NTB can be directly observed in the primate SOC, and this nucleus cannot be identified in any of over 70 human brainstems examined in our laboratory, though a few small clusters of NTB-like

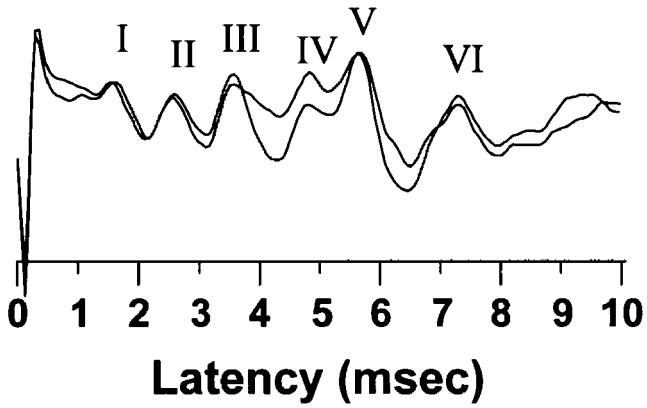


Fig. 3. Two sample tracings of the human brainstem auditory response, illustrating waves I through VI. Taken from a normal-hearing adult subject, and provided by CW Ponton.

cells are sometimes seen in the fetus. As a possible explanation for this discrepancy, it could be that the entire human LSO is homologous to the low-frequency end of the cat LSO, a subdivision of the nucleus that receives only sparse input from the NTB (Glendenning et al., 1985). Whatever the cause, we might suspect that the few NTB-like neurons in the human SOC play a smaller role in LSO function than does the well-developed NTB in other mammalian species.

The extreme reduction of the human NTB may also have implications for function of the MSO, as the NTB provides inhibitory input to MSO neurons (Smith et al., 1998), and binaurally sensitive cells exhibiting excitatory-inhibitory responses to sound comprise a significant fraction of the cells recorded on the MSO (Goldberg and Brown, 1968; Inbody and Feng, 1981). However, it does not appear that these facts have been incorporated into theories of MSO function.

Evoked Potentials From the Human SOC

Since single-unit studies cannot be carried out in humans, a window on human SOC function is provided by evoked potentials, i.e., the auditory brainstem response (ABR). The ABR is assumed to be generated by synchronized activity of neurons in the ascending brainstem pathway. An example of this response in a normal-hearing adult is illustrated in Figure 3. In considering which segment of the ABR might specifically reflect activity at the level of the SOC, it is first necessary to establish what part of this record is generated within the brainstem. In this respect, several studies in human subjects have shown that ABR waves I and II are generated peripherally, by the cochlea and auditory nerve. Dipole localization studies (Scherg and von Cramon, 1985) and direct intrasurgical recordings (Martin et al., 1995; Moller and Janetta, 1982) have indicated that wave I generation is intracochlear, while wave II arises from the cochlear nerve as it passes through the internal auditory meatus and crosses the intradural space. This interpretation is supported by clinical findings in a case of Gaucher's disease with marked brainstem gliosis, in which ABR waves I and II were present but all subsequent waves were absent (Kaga et al., 1998).

Recordings from the surface of the human brainstem (Moller and Janetta, 1982), as well as dipole studies (Scherg and von Cramon, 1985), indicate that wave III arises from the brainstem near the point of entry of the eighth nerve, in or near the cochlear nuclei. This indicates that waves occurring later than wave III are generated higher in the brainstem. In cats, the projection from the cochlear nuclei to the contralateral NTB has been shown to contribute to the early brainstem waves (Melcher and Kiang, 1996; Tsuchitani, 1994), but with the absence of an NTB in man, this should not be a factor in the human ABR. One anlysis of ABR generation (Ponton et al., 1996) theorized that waves IV and V are generated by the two largest components of the human brainstem auditory pathway, wave IV by axons passing uninterruptedly from the CN to the contralateral IC and wave V by axons following the same trajectory but with a synapse in the MSO and LSO (Fig. 4). The idea that there are two main pathways, one asynaptic and one with an interposed synapse, is supported by the work of Waring (1998) in brainstem implant patients. In these subjects, efferents from the cochlear nuclei were directly stimulated by the implant electrodes, thus bypassing earlier synapses in the inner ear and cochlear nucleus. Wave IV remained unaffected at all stimulus rates, but wave V dropped out when the rate of stimulation was increased, presumably due to synaptic fatigue. One study correlated length of the brainstem pathway with latencies of waves III, IV, and V to derive axonal conduction velocity (Moore et al., 1996). The most reasonable conduction velocity, one closely matching that of the known conduction velocity of eighth nerve axons, was obtained by assuming that waves IV and V were generated at the level of the SOC contralateral to the stimulated ear, presumably by the bend in the pathway occurring at that point (Fig. 4).

The notion that waves IV and V of the human ABR are generated at the level of the SOC is supported by the effect of brainstem lesions. On the one hand, extensive lesions of the upper pons leave the IV–V wave complex intact (Gilroy et al., 1977; Starr and Hamilton, 1976). On the other hand, abnormalities in the IV–V complex have been observed following vascular and demyelinating lesions in the lower pons (Cohen et al., 1996; Levine et al., 1993). Similarly, six patients with small vascular lesions in the trapezoid body were shown to have absent or abnormal dipole orientation of the BIC component occurring at the time of waves IV and V, while lesions in the rostral lateral lemniscus caused abnormalities in the dipole occurring at the time of wave VI (Pratt et al., 1998). In an interesting case of a restricted ablation of the right inferior colliculus (Durant et al., 1994), the IV–V complex to right ear stimulation was normal, presumably due to an intact pathway projecting to the left inferior colliculus. With left ear stimulation, peak IV was present but peak V was missing, possibly due to retrograde deneration of the MSO and LSO on the same side as the ablation and resultant loss of the monosynaptic pathway.

HUMAN PERIOLIVARY CELL GROUPS

The periolivary nuclei, as described in rodents (Osen et al., 1984), include a ventromedial nucleus (MVPO), a ventrolateral nucleus (LVPO), and a dorsal nucleus

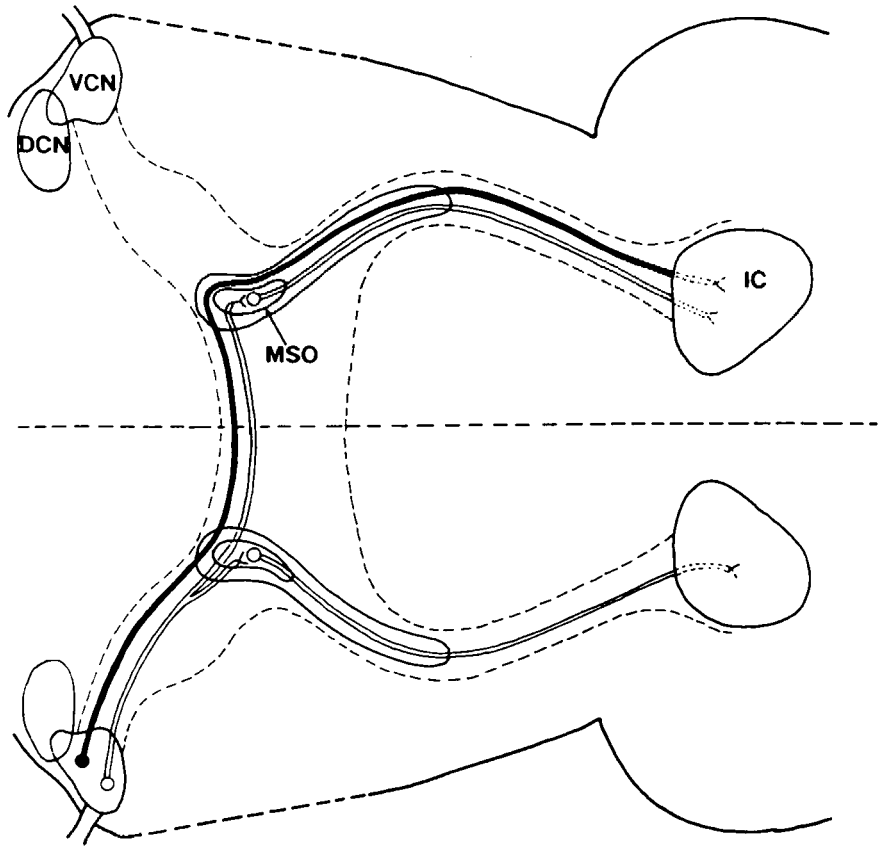


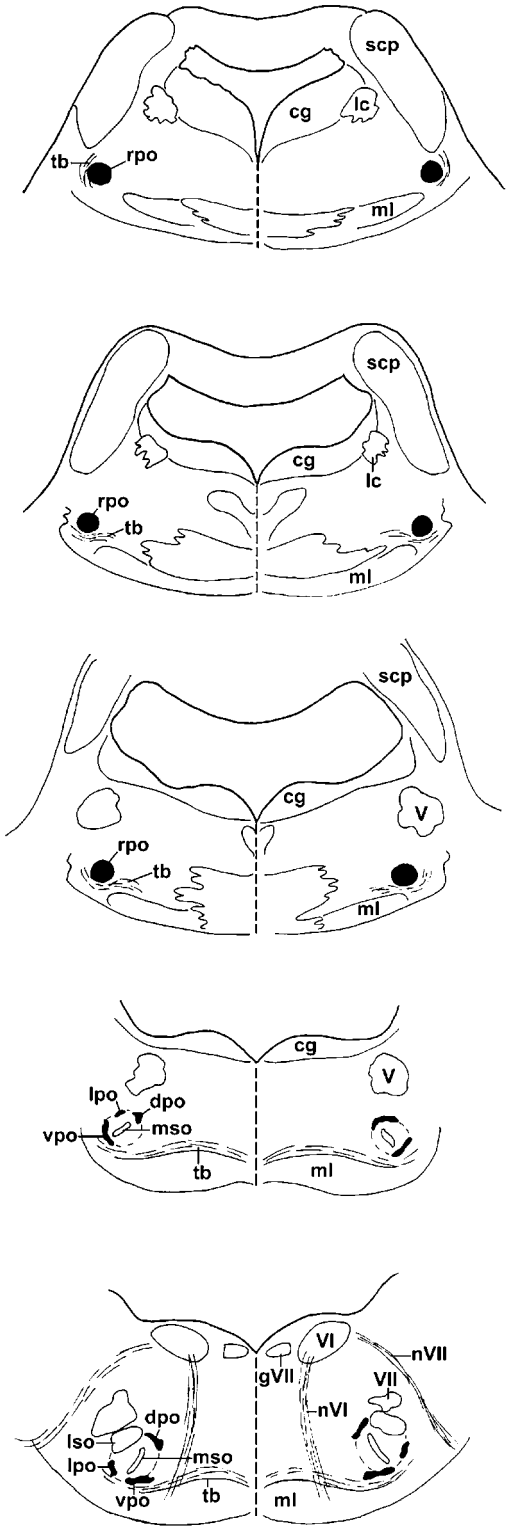
Fig. 4. Reconstruction of human brainstem auditory pathway in horizontal section. The direct pathway from the cochlear nuclei to the contralateral inferior colliciulus is shown in black. The monosynaptic pathway through the superior olivary nuclei is shown in white. DCN, dorsal cochlear nucleus; IC, inferior colliculus; MSO, medial superior olivary nucleus; VCN, ventral cochlear nucleus. (Adapted from Ponton et al., 1996, with permission of the publisher).

(DPO), as well as cells scattered laterally in the periolivary region. In the human olivary complex, three of the cell groups, namely, the medial, lateral, and dorsal periolivary nuclei (MPO, LPO, DPO, Fig. 5) are likely to be homologous to the ventromedial, ventrolateral and dorsal nuclei of nonprimate species (Moore et al., 1999). A unique feature of the human periolivary system is the transformation of the rostral area of periolivary cells into a column of periolivary cells (RPO), which extends up to 8–10 mm through the pons. This hypertrophied rostral cell group is composed of a type of periolivary neuron, which, in the cat, forms a projection to the inferior colliculus (Adams, 1983). It is thus possible that relaying information to the tectum is a particularly important function of the human periolivary system.

Animal studies indicate that the periolivary cell groups show a high degree of convergence and divergence in their afferent and efferent connections. They receive ascending input from the cochlear nuclei (Friauf and Ostwald, 1988; Thompson and Thompson, 1991) and descending input from the inferior colliculus (Caicedo and Herbert, 1993; Schofield and Cant, 1999; Thompson and Thompson, 1993). Projections from periolivary neurons may ascend to the inferior colliculus (Adams, 1983; Aschoff and Ostwald, 1988, Riemann and Reuss, 1998; Schofield and Cant, 1992), form a recurrent projection to the cochlear nuclei (Adams, 1983; Covey et al., 1984; Spangler et al., 1987; Winter et al., 1989), or form an efferent projection to the cochlea (Adams, 1983; Aschoff and Ostwald 1988; Riemann and Reuss, 1998; Vetter and Mugnaini, 1990; Winter et al., 1989). Thus, compared to the main olivary nuclei, the periolivary cell groups seem to form a system more complex in its connections and potentially more integrative in its function.

A subset of the periolivary nuclei that is of particular interest are those cells that form the efferent projection to the organ of Corti, the olivocochlear system. Fortunately, in this particular subdivision of the human SOC, it has proved possible to use neurotransmitter characteristics to map the system. Immunostaining of neurotransmitter-related enzymes and peptides has identified two populations of olivocochlear neurons in the human SOC, which appear to be homologous to the two subsystems in other mammals (Moore et al., 1999). As seen in Figure 6, a population of cells immunoreactive for choline acetyltransferase (ChAT), the synthesizing enzyme for acetylcholine, are present medially, ventrally, and laterally in the periolivary region. These neurons are mostly multipolar cells, about 20 μm in diameter. We believe that these neurons are the hu-

man equivalent of the MSOd, SOCm, and VTB efferent cell groups in the macaque (Thompson and Thompson, 1986), and the human homolog of mammalian medial efferents, the subdivision of the olivocochlear system that projects to outer hair cells in the organ of Corti.



A second population differs in in its distribution and immunostaining. Cells immunostained for both ChAT and calcitonin gene-related peptide (CGRP) form a compact group close to the LSO, with some spread into the olivocochlear bundle (Fig. 6). In addition, a few cells with this immunohistochemical profile are located at the rim of the LSO, though the incidence of these marginal cells shows considerable variation across individual subjects. The ChAT- and CGRP-positive neurons are mostly small oval cells, 10–15 μm in diameter, though a few larger multipolar cells are included in the population. This cell group appears to be homologous to cell groups MSO-LSO and LSOl in the monkey (Thompson and Thompson, 1986), and to the lateral efferent subdivision of the olivocochlear system, which terminates mainly on inner hair cell afferents.

If we are correct in our assumptions about these two subsystems, the biggest difference between the human olivocochlear system and that of other mammalian species is their relative size. In a recent review, Warr (1992) presented data indicating that the lateral efferent component is consistently the largest portion of the mammalian olivocochlear system, making up approximately 75% of the system in the cat and monkey, 85–90% in rodents, and 90–100% in bats. In our human material, the neurons expressing both ChAT and CGRP comprise from 35 to 50% of the total number of efferents. Because most functional studies have used contralateral ear stimulation to activate the medial efferent subsystem, it difficult to speculate on the functional effect of a reduction in the human lateral efferent component. However, this provides another example of specialization in the human brainstem auditory system.

FUNCTIONAL ROLE OF THE SOC

We have discussed the role of the MSO and LSO in constructing a spatial field that is not directly coded at the level of the peripheral receptor. The extraction of interaural differences by the MSO and LSO recreates auditory space, forming the basis for localization of a sound stimulus. This system comes into play when we need to solve the "cocktail party problem," i.e., to make a distinction between two competing stimuli, especially when one is deemed relevant and the other background noise. We are aware of this function in our own ability to selectively listen to one conversation in a crowded and noisy environment. We realize our failure to be able to reproduce this function prosthetically in the large number of hearing aid users who are plagued by unwanted background noise when using their monaural devices. Clinically, we might wonder if the agenesis

Fig. 5. Morphology of the human periolivary nuclei, drawn from Nissl sections separated by 1,500 μm. Periolivary cell groups are shown in black, all other structures in outline. Cg, central grey; dpo, dorsal periolivary nucleus; gVII, genu of facial nerve; lc, locus coeruleus; lpo, lateral periolivary nucleus; lso, lateral superior olivary nucleus; ml, medial lemniscus; mso, medial superior olivary nucleus; nVI, abducens nerve; nVII, facial nerve; rpo, rostral periolivary nucleus; scp, superior cerebellar peduncle; tb, trapezoid body; vpo, ventral periolivary nucleus; V, trigeminal nucleus; VI, abducens nucleus; VII, facial nucleus. (Adapted from Moore et al., 1999, with permission of the publisher).

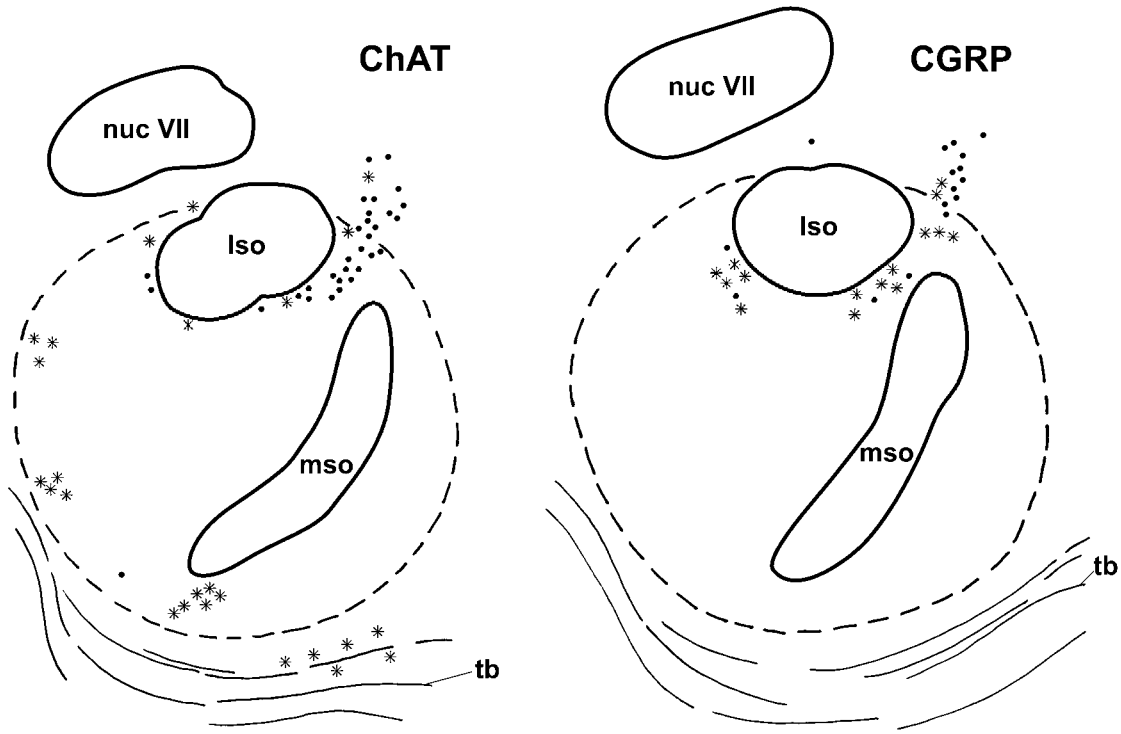


Fig. 6. Distribution of cells immunostained for ChAT and CGRP in the human superior olivary complex in a 12-year-old subject. Cells positive only for ChAT are concentrated ventrally and laterally in the periolivary region, with some extension into the trapezoid body. Cells immunopositive for both ChAT and CGRP are located close to the LSO. (Adapted from Moore et al., 1999, with permission of the publisher).

of the superior olivary complex occurring in autism (Rodier et al., 1996) contributes to the disconnection from the outer world that characterizes that syndrome.

We have discussed the main olivary nuclei separately from the periolivary cell groups, but it may be worth considering if these are actually two separate and unrelated portions of the brainstem auditory system. Is it purely by chance that the periolivary cell groups are anatomically associated with the main nuclei, or do they share some common functional sphere? We could speculate that the olivocochlear system has developed as an extension of the olivary localization system, acting under such difficult conditions as the presence of multiple and competing stimuli. The behavioral effects of olivocochlear activation on auditory function are subtle, but they include enhancement of selective attention (Giard et al., 1994; Puel et al., 1988; Schaf et al., 1997) and improved processing of complex signals in noise (Giraud et al., 1997). As a final thought, we might imagine that it is the function of the entire superior olivary complex, including both the reorganization of ascending impulses occurring in the main nuclei and the complementary integration provided by periolivary cell groups, that enables us to function efficiently in a three-dimensional auditory world.

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