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Organization of Sensory Cortex in a Madagascan Insectivore, the Tenrec (*Echinops telfairi*)

LEAH KRUBITZER,[1]* HEINZ KÜNZLE,[2] AND JON KAAS[3]
[1]Department of Psychology and Center for Neuroscience, University of California, Davis, California 95616
[2]Institute of Anatomy, University of Munich, D-80336 Munich, Germany
[3]Department of Psychology, Vanderbilt University, Nashville, Tennessee 37240

ABSTRACT

We identified subdivisions of somatosensory cortex, and the borders and extents of auditory and visual cortex in Madagascan tenrecs (*Echinops telfairi*) by using microelectrode recording techniques and cortical myeloarchitecture. There was evidence for three distinct somatosensory fields. The primary somatosensory area (S1) contained an orderly representation of the contralateral body surface that stained darkly for myelin. Neurons were activated by light touch, and receptive fields were often small, especially for the snout. Immediately rostral to S1, a lightly myelinated rostral field (R) also contained a representation of the contralateral body, although the internal topography was not fully determined. Neurons in R responded to manipulations of body parts and tissue displacements. A small, moderately myelinated area lateral to S1 was termed PV/S2 because it possessed features that were similar to both the parietal ventral area (PV) and the second somatosensory area (S2) in other mammals. Neurons in PV/S2 responded to light tactile stimulation. A densely myelinated oval of cortex caudal to PV/S2, the auditory area (A), contained neurons that responded to clicks, and the densely myelinated caudomedial visual area (V) contained neurons that were activated by stimulation of one or both eyes. Some characteristics of V were similar to the primary visual area (V1) described in other mammals. A visual area located in rostromedial cortex (RV) contained neurons that were highly responsive to visual stimulation. Area RV may be a specialization of tenrecs or an elaboration of a visuomotor field that has been retained in most extant mammals. The results support the view that most of the neocortex of primitive mammals was composed of a few sensory areas. J. Comp. Neurol. 379:399–414, 1997.

Indexing terms: somatosensory cortex; visual cortex; auditory cortex; evolution

The present study on the organization of neocortex in tenrecs is part of a broader comparative effort to determine the early stages of forebrain evolution in mammals. The standard approach for reconstructing the phylogenetic sequences from extant species is to assume that characteristics shared by a great number of taxa are primitive and have been retained from a common ancestor, whereas those features that are restricted to a few closely related taxa emerged later in a particular line of evolution (see Eldredge and Cracraft, 1980; Northcutt, 1984; Butler, 1994; Northcutt and Kaas, 1995). In considering the course of brain evolution in the various lines of mammalian descent, however, we can also benefit from gathering information about the brains of long extinct mammals, obtained from skull endocasts. From such endocasts (Kielan-Jaworowska, 1984; Jerison, 1990), we know that early mammals had small brains relative to their body size, and that the neocortex of these mammals was small relative to the rest of the brain. Thus, in any effort to reconstruct the early stages of forebrain evolution in mammals, there are several reasons to consider not only mammals whose ancestors branched off early in evolution, but especially those that still have small brains and little

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*Correspondence to: Leah Krubitzer, Center for Neuroscience, 1544 Newton Ct., Davis, CA 95616. E-mail: lakrubitzer@ucdavis.edu

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neocortex (Kaas, 1995). First, the small brain surface of such mammals could have been subject to little selective pressure, so that the basic organization of their cortex has been largely retained from that of early mammals and has changed less dramatically than that of other mammals over time. Of course, small brains may reflect recent specializations as well as primitive features. For example, the small brains of echolocating bats have some areas found in all or most mammals, such as S1, but the somatotopy has been modified (Wise et al., 1986). Auditory areas have been elaborated and specialized features acquired (e.g., Suga, 1984), and visual cortex has been greatly reduced (Mann, 1963).

A somewhat different and equally compelling reason for examining mammals with small brains, regardless of phylogenetic position or history of cortical change in a given lineage, is that there may be some minimum number of components necessary for processing sensory inputs and generating appropriate motor outputs. These types of studies could help identify cortical areas that are essential for basic mammalian behaviors.

Among extant mammals, tenrecs have the least neocortex (Stephan et al., 1970, 1991), and their brains approximate those of long extinct mammals which roamed the earth some 75–80 million years ago. Tenrecs constitute a remnant family of insectivores, preserved in Madagascar by isolation, and by the obvious specialization of protective body quills or spines (Eisenberg and Gould, 1970). The tenrec looks much like the European hedgehog (Fig. 1), but is much smaller and has evolved quills independently. Some of the present results have been presented in abstract form previously (Künzle et al., 1995).

MATERIALS AND METHODS

The organization of somatosensory cortex and surrounding regions of auditory and visual cortex were explored in five lesser hedgehog tenrecs (*Echinops telfairi*) by using standard electrophysiological recording techniques, combined with architectonic analysis (see Krubitzer et al., 1995c; Beck et al., 1996). Adult animals, weighing between 100 and 130 g, were initially anesthetized with ketamine hydrochloride (0.5–1.8 mg/kg, im) and xylazine (0.5–0.8 mg/kg, im). Subsequent doses of half of the initial dose were given as needed to maintain surgical levels of anesthesia. Throughout the experiment, the animals were kept hydrated with subcutaneous injections of lactated Ringer's with 4% glucose. A rectal probe was used to record the animal's temperature. This probe was attached to a heating pad, and automatically adjusted the temperature of the heating unit to maintain a constant body temperature. Recording experiments typically lasted from 8–15 hours.

After the animal was anesthetized, the scalp was cut, the temporal muscle retracted, part of the skull was removed so that one entire hemisphere was exposed, and the dura was cut. An acrylic well was built around the opening in the skull and filled with silicone fluid to prevent desiccation and maintain cortical temperature. Tungsten-in-glass electrodes (0.95–1.2 MΩ at 1 kHz) designed to record from small neural clusters were lowered into the cortex with a stepping microdrive, and moved in X/Y coordinates with a micromanipulator. The placement of the electrode was marked, relative to blood vessel patterns, on an enlarged photograph of the exposed cortex. The best neural recordings were obtained from 400 to 600 μm from the pial surface. For cortex on the medial wall, the electrode was lowered tangential to the pial surface, and recordings were typically made every 200 μm along the electrode track. The neural activity was amplified, filtered, and viewed on an oscilloscope and heard through a speaker. For all recording sites, receptive fields for neurons responsive to tactile stimulation were obtained by lightly brushing or touching the skin with a fine probe, gently tapping the skin or body part, or manipulating the joints and muscles. It was possible to lightly deflect one or two spines in isolation which allowed us to delineate receptive field boundaries on the trunk with an error of only 0.5 cm. Clicks, claps, snaps, and whistles were used to determine if neurons were responsive to auditory stimulation. Best frequencies for neurons responsive to auditory stimulation were not obtained. Small moving bars of light or full field flashes of light were used to determine the responsiveness of neurons to visual stimulation. Using these types of stimuli, receptive fields for neurons at a number of closely spaced recording sites were obtained, and two-dimensional maps of the cortex were generated (see below). Lesions were placed at strategic locations (often coincident with judged cortical field boundaries) for later identification in histologically processed tissue.

After electrophysiological recording experiments were complete, a lethal dose of barbiturate was administered, and the animal was transcardially perfused with 0.9% saline followed by 2% paraformaldehyde in 0.1 M phosphate buffer, and then 2% paraformaldehyde in 10% sucrose 0.1 M phosphate buffer. When perfusion was complete, the brain was removed from the cranium, and the cortex was peeled from the brainstem and thalamus, and manually flattened between glass slides (Fig. 2). In one case the brain was left intact and sectioned coronally. In all cases, the cortex and thalamus were soaked overnight in 30% sugar 0.1 M phosphate buffer and 2%

Abbreviations

Cortical areas and structures

A	auditory cortex
cc	corpus callosum
PV	the parietal ventral area
R	rostral deep field
RV	rostral visual area
S1	primary somatosensory area (3b)
S2	second somatosensory area
V	visual cortex (possibly VI)Body parts
Body parts	
cn	chin
fa	face
fl	forelimb
fp	forepaw
he	head
hl	hindlimb
hp	hindpaw
mtr	middle trunk
n	naris
ne	neck
ll	lower lip
ltr	lower trunk
sh	shoulder
sn	snout
t	toes
tr	trunk
utr	upper trunk
vib	vibrassae

Fig. 1. The tenrec (*Echinops telfairi*) is an insectivore weighing 100–200 g. The very sharp quills of the tenrec range in color from almost white to very dark. This small nocturnal creature is found in southern and southwestern Madagascar. Although the tenrec forages on the ground, it nests in tree hollows, and its extensive foraging in trees indicates that it is arboreal.

paraformaldehyde. The flattened cortices were cut on a freezing microtome into 25-μm sections, and alternate sections were stained for myelin (Gallyas, 1979), reacted for cytochrome oxidase (Wong-Riley, 1979), or mounted for fluorescent microscopy (for connectional studies to be reported elsewhere).

Cortical maps generated from electrophysiological recordings were related to cortical architecture by matching blood vessel patterns with electrode penetrations, tissue artifacts, and electrolytic lesions. In this way, comprehensive reconstructions of the cortex could be made, and the number and internal organization of fields could be appreciated.

RESULTS

The lesser hedgehog tenrec (Fig. 1) is a member of the Tenrecidae family of insectivores. Their ancestors are thought to have been among the first mammals to arrive in Madagascar, and they constitute one branch of an adaptive radiation that produced 31 species (Eisenberg and Gould, 1970). All have small brains with little neocortex, but they vary in other features, such as type and amount of spines, and in the ecological niche they occupy. Olfaction is important, and they scent mark as a form of communication. As is apparent from Figure 1, much of the dorsal body is covered with protective spines, and thus it is a poor surface for detecting the details of somatic stimuli. The tenrec can form a spiny ball when threatened, much like the independently evolved protection system in hedgehogs. The face has a number of protruding sensory hairs, including mystacial hairs on the muzzle, shorter hairs on the chin, and longer hairs behind the eye. Unlike most mammals, the tail is quite short. The external ears protrude, and the eyes are small.

General features of the brain

Tenrecs have small brains that are characterized by a tiny cap of neocortex over a proportionately large piriform cortex (Fig. 2). In dorsal and lateral views (Fig. 2A), the junction of neocortex with piriform cortex is barely indicated by a slight depression or dimple, rather than a true rhinal fissure. The neocortex fails to cover the inferior and superior colliculi, a further indication of its small size.

The proportions of the brain can be further appreciated in a flattened preparation where the hippocampus is unfolded, the neocortex separated from the underlying fibers, and flattened along with piriform cortex and the olfactory bulb (Fig. 2B). The total surface area of neocortex of one hemisphere, including cingulate cortex, is only about 15 mm^2, and is divided into a number of sensory and probably motor areas. Clearly much of the forebrain is devoted to processing olfactory information, because the surface area of piriform cortex and the olfactory bulb together are well over three times the surface area of neocortex.

The somatosensory areas

Microelectrode recordings provided evidence for three somatotopically organized fields in tenrecs. One of these fields, based on relative position, features of somatotopic

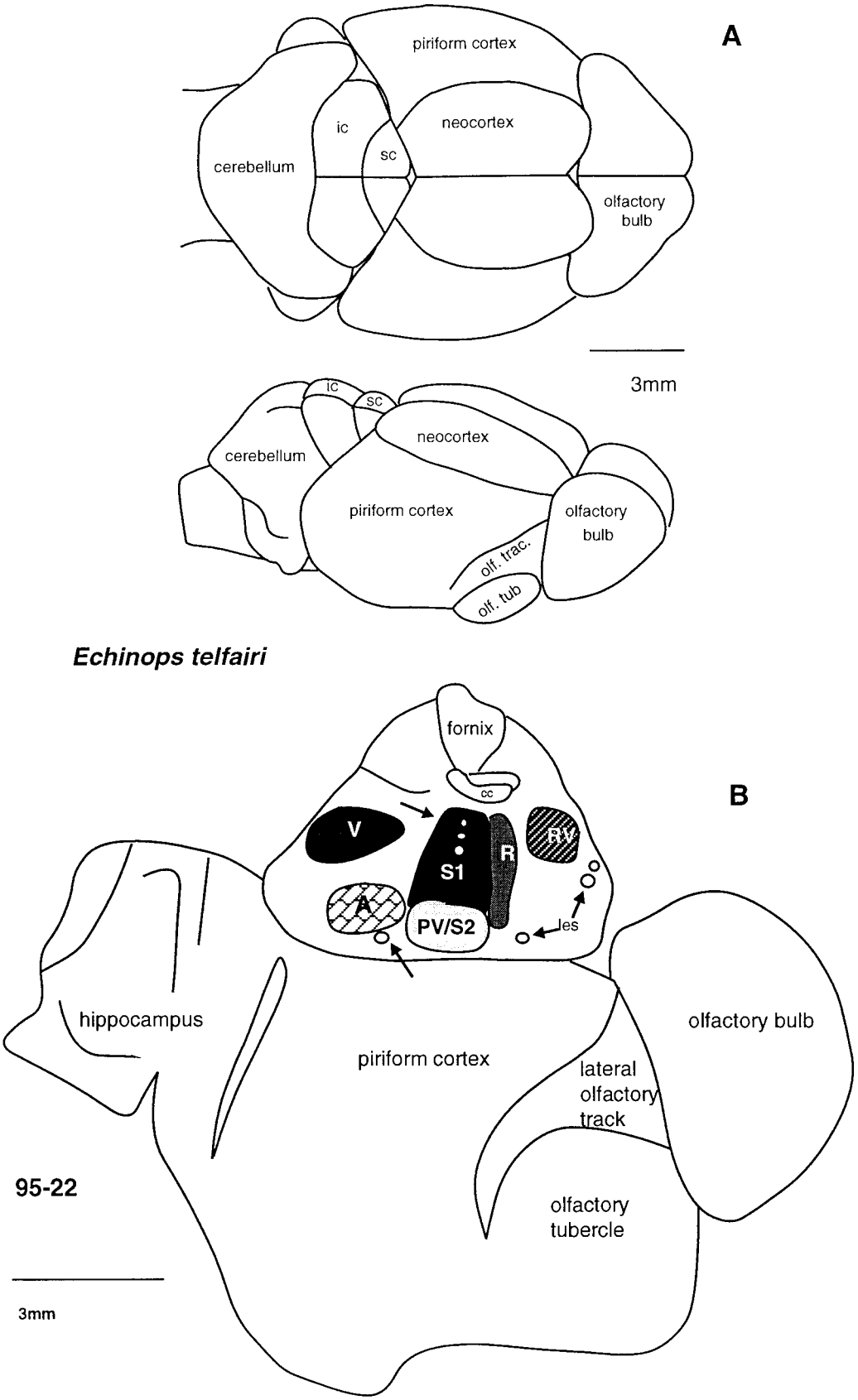

Fig. 2. Dorsal, lateral (**A**) and flattened view (**B**) of the tenrec brain. The overall size of the brain is quite small, and the amount of neocortex relative to other regions of the brain, such as the olfactory bulb and piriform cortex, is small as well. Despite the size of the neocortex, we found evidence for three separate somatosensory areas, a caudal visual area (possibly V1), and a rostral visual area, RV. Neurons in cortex caudal and lateral to somatosensory cortex were responsive to auditory stimulation. In these and the following figures, medial is to the top, and rostral is to the right. cc, corpus callosum; ic, inferior colliculus; les, lesion; olf, olfactory; sc, superior colliculus; tub, tubercle. Other abbreviations in abbreviation list.

organization, and myeloarchitecture, appears to be the primary area (S1) described in other mammals. At least one additional representation of cutaneous receptors was located in cortex immediately lateral to S1, in a position that could be S2 or PV, or a combination of both fields, as defined in other mammals (see Discussion). Because we are uncertain about the identity of this field, we refer to it as PV/S2. In addition, neurons in cortex rostral to S1 and PV/S2 were responsive to stimuli that activated deep body receptors such as muscle spindles. This cortex resembles area 3a of cats and monkeys in relative location and responsiveness, but because this field has not been widely defined in mammals, we refer to this third somatosensory area as the rostral area (R).

The primary somatosensory area (S1). The primary field was defined by responsiveness to light touch on the body surface and a tail-to-face mediolateral somatotopic sequence in cortex. Neurons here responded most often to cutaneous stimulation on portions of the contralateral body, but in some instances the receptive field appeared to extend past the midline onto the ipsilateral body. Recordings at some sites in some cases required more intense stimulation such as light taps. These sites, which varied in location, were not always present, and could reflect suboptimal recording conditions where more intense stimulation of cutaneous receptors or the involvement of deep receptors was required to elicit a neural response. The response of neurons to this type of stimulation would not be noted when cutaneous stimulation proved highly effective in activating neurons in cortex. Another possibility is that this region is distinct from S1 proper, and forms a specialized zone within S1, or is part of a caudal extension of the rostral field. Finally, and quite unexpectedly, some sites responsive to tactile stimulation also appeared to be weakly responsive to visual stimulation, but visually evoked responses were inconsistently obtained. A limitation of the multiunit recording technique is that it is not possible to distinguish whether individual neurons are responding to bimodal stimulation, due to convergent inputs onto a single cell, or if individual cells within the recorded cluster are responding to either visual or somatosensory stimulation.

S1 was approximately 1.2–1.4 mm in rostrocaudal width and a little more than 2 mm in mediolateral length. Thus, only a few recording sites were placed within the field in a given animal. In one of our more informative cases (Fig. 7), receptive fields were obtained for over 30 recording sites within S1, providing a good overview of its internal somatotopy. One site within the field appeared to be responsive to visual rather than cutaneous stimulation.

The mediolateral organization of S1 in tenrecs, as in most mammals, is from the representation of the gluteal region up the body to the forelimb and face. This organization is apparent from the progression of receptive fields for recording sites from medial to lateral in S1 (Fig. 4). Neurons for the most medial recording sites (Fig. 4, receptive field [r.f.] 1) had a receptive field on the caudal end of the dorsal trunk. Neurons at the next recording site had a larger receptive field that extended rostally on the back, and receptive fields for neurons at sites 3 and 4 (Fig. 4) abruptly moved onto the ventral wrist and forepaw. Neurons at sites 5–7 (Fig. 4) had small receptive fields and were activated by moving sensory hairs over the eye, the mystacial vibrissae, and the glabrous nose. More lateral recording sites were in the second representation, PV/S2 (see below).

The internal organization of S1 was similar across all cases (Figs. 3, 5, 7). Thus, the most medial portion of S1 consistently represented portions of the hindpaw, hindlimb, and lower trunk, followed laterally by representations of the upper trunk, forelimb, and forepaw, and most laterally by representations of the chin, vibrissae, and snout. The representations of the chin, snout, vibrissae, and naris occupied approximately half of the entire body representation within S1, whereas the remaining portion of S1 was occupied by representations of the trunk and limbs. Although the density of mapping made it difficult to make detailed dorsoventral distinctions, there was a tendency for the dorsal midline to be represented at the caudal boundary of S1 (Fig. 7).

Receptive fields for neurons in S1 varied in size. Receptive fields on the dorsal body were the largest, and sometimes crossed the midline to include portions of the ipsilateral body surface. Possibly, touching the spines on one side of the body activates somewhat distant receptors, even on the other side of the body, because a muscular system links spines in a system that stretches spiny skin over the ventral body when the tenrec curls. Receptive fields on the trunk were largely or wholly on the spiny skin (e.g., #10, Fig. 4). Smaller receptive fields were observed covering the glabrous pads of the forepaw and included hairs over a small portion of the face (Figs. 4, 8). Receptive fields for the same body part were smaller for neurons in S1 than PV/S2, or R (Fig. 8).

The lateral somatosensory area, PV/S2. A second representation of the body surface was found in a small oval of cortex, roughly 1.5 mm^2, just lateral to S1. The most compelling evidence for this second representation comes from a clear reversal of the progression of receptive fields for neurons in rows of mediolateral recording sites across S1 and PV/S2. Thus, in one such row (Fig. 4), neurons in the most lateral recording site judged to be in S1 corresponded to a small receptive field on the glabrous nose (site 7). The next more lateral site (8) contained neurons that had a larger receptive field including the nose, but also other parts of the upper head and ear, a clear indication of a reversal of the receptive field sequence for sites in S1 (see receptive fields for sites 1–7). The receptive field for neurons at site 9 was more caudal on the body, including the ventral neck and trunk, whereas the receptive field for neurons at site 10 included all of the dorsal body to the tail. Further evidence for a second pattern of representation is included in Figures 3, 5, and 7. In brief, the face and forelimb were represented near the S1 border, whereas the trunk and hindlimb were represented more caudolaterally.

Receptive fields were consistently larger for PV/S2 than S1, although neurons in both areas were activated by light touch on the body surface and the movement of hairs. Some (Fig. 3) to many (Fig. 5) of the sites in PV/S2 also contained neurons that were activated by auditory stimulation, a feature not found in S1.

The rostral field (R). In all cases, neurons immediately rostral to the cutaneous representation in S1 responded to more intense stimulation of the body such as light taps, pressure, and joint manipulation (Figs. 3, 5, 7 and cases not illustrated). This strip of cortex was approximately 500 μm wide, and was less myelinated than S1 (see below). Receptive fields were generally larger for neurons

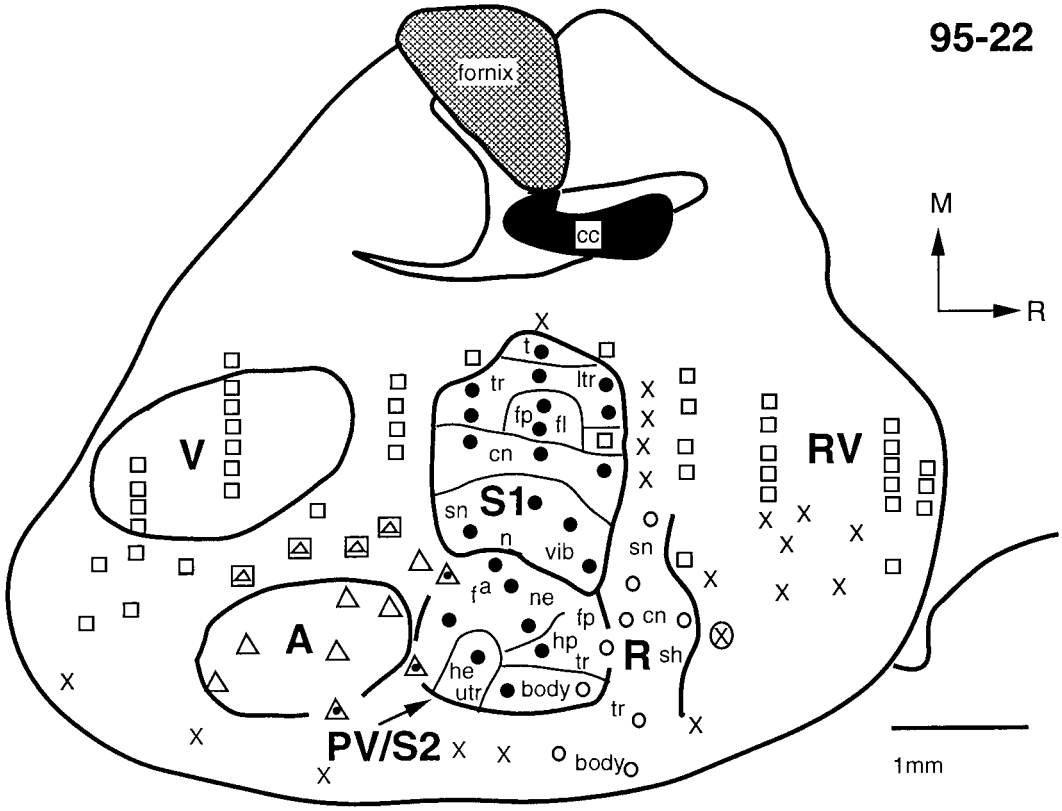

Fig. 3. Cortical field maps generated for tenrec 95-22. Closely spaced recording sites across the neocortex reveal the presence of three separate somatosensory fields, S1, PV/S2, and R. Neurons in S1 and PV/S2 responded predominantly to cutaneous stimulation, but at one site in S1, neurons responded to visual stimulation, and at two recording sites in PV/S2, neurons responded to somatosensory and auditory stimulation. Neurons in R responded to stimulation of deep receptors. Neural responses to visual stimulation could be evoked in two separate locations in the tenrec cortex, from a far caudal location in the region of cortex traditionally considered as visual (possibly V1 and a small region of extrastriate cortex), and from a far rostromedial location. We term this rostral visual area RV. Neurons caudal to PV/S2 responded to pure auditory stimulation. The caudal, darkly myelinated region (see Fig. 8) may be homologous to A1 of other species. Cortex caudal to somatosensory cortex, rostral to visual cortex, and medial to auditory cortex contained neurons responsive to bimodal or multimodal stimulation. Symbols and abbreviations are in the list of abbreviations and Table 1.

in R than for neurons in S1, and neurons in R represented body parts that also activated neurons in S1 (Fig. 6). Thus, a duplication of body part representations was noted at separate locations in the cortex. The internal organization of R was not as refined as that observed for S1, because receptive fields were larger. However, a definite mediolateral organization could be discerned in cases in which the mapping density was high (e.g., Figs. 3, 7). As in S1, neurons in the most medial portions of R had receptive fields on the trunk, whereas neurons in more lateral portions of R had receptive fields on the shoulder, face, and chin. Because the field was relatively narrow, it was not possible to establish the rostrocaudal organization of this field.

Sites judged to be within R by position and myeloarchitecture were not always responsive to stimulation (e.g., Figs. 3, 7). Generally, these sites were medial, where inputs from the trunk and hindlimb would be expected. The lack of responsiveness could indicate that this cortex is not part of R, that we inadequately stimulated parts of the body, that activity was suppressed by the anesthetic, or could be due to unknown reasons.

In one case (Fig. 3), neurons that had receptive fields on the body and trunk were observed far laterally in cortex rostral to PV/S2. These recording sites were judged to be lateral to R because they did not reflect the somatotopic pattern of R, and the neurons were less responsive and required more intense stimulation. Possibly, another somatosensory area exists in this region.

TABLE 1. Stimulus Types

●	Cutaneous
○	Deep
□	Visual
▲	Auditory
◪	Auditory + visual
◬	Somatosensory + auditory
◘	Somatosensory + visual
X	No response
⊗	Lesion

Auditory cortex

Neurons responsive to clicks and other sounds were in a lateral oval of cortex just caudal to PV/S2 (Fig. 3). The oval of cortex was a little over 1 mm in rostrocaudal length and about 1 mm in mediolateral width. We refer to this field as A, for auditory. Field A has at least some of the characteristics of the primary auditory area, A1, as described in other species (see Discussion).

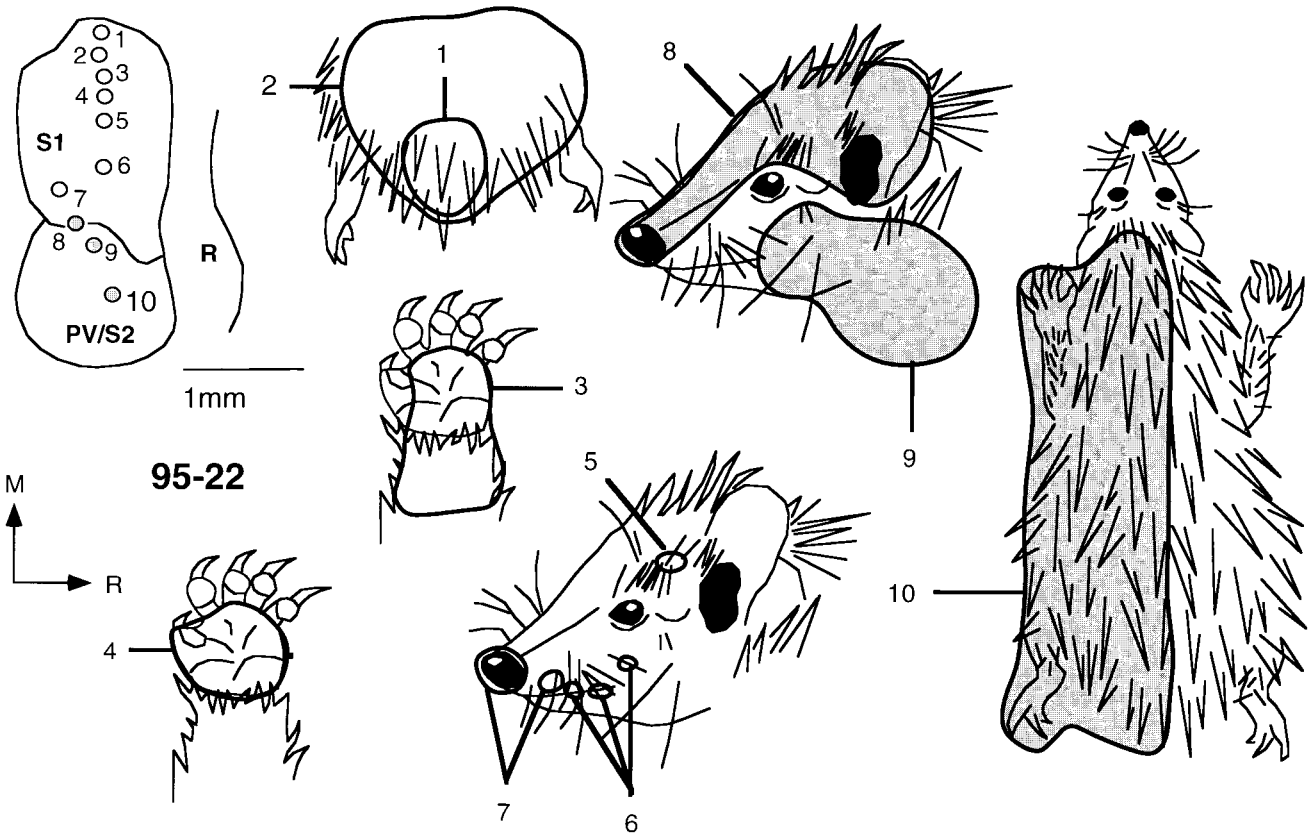

Fig. 4. Receptive field progressions for neurons in S1 and PV/S2 in tenrec 95-22. As recording sites progress from medial to lateral in S1, receptive fields for neurons in those sites progress from the tail, to the lower dorsal trunk, and onto the forelimb and hand (receptive fields 1–4). Recording sites in middle and lateral portions of S1 contained neurons with receptive fields on the dorsal vibrissae, lateral vibrissae, and nose, respectively (r.f. 5–7). At the S1 boundary with the lateral field PV/S2, receptive fields for neurons became dramatically larger, and a reversal in the progression was observed. Thus, as recording sites move from medial to lateral in PV/S2, receptive fields for neurons in those sites move from the nose, snout, and head, onto the face and cheek, and finally on the body, limbs, and paws (r.f. 8–10). Stippled recording sites and receptive fields correspond to PV/S2.

Neurons at some of the sites around A also responded to clicks, although usually less vigorously. Some neurons surrounding A often responded to both somatosensory and visual stimulation. As noted above, sites judged to be within PV/S2 sometimes responded to auditory as well as cutaneous stimulation, and sites medial to A sometimes responded to both visual and auditory stimulation, although usually weakly to both (Figs. 3, 5).

Visual cortex

Neurons responsive to flashes and moving bars of light to one or both eyes were found in several regions of cortex. Most notably, neurons throughout a caudomedial oval of darkly myelinated cortex (see below) were highly responsive to visual stimulation (Fig. 3). This oval, which we term V, for visual, is located in the expected location of the primary visual area (V1) of other mammals.

Other neurons located in sites lateral and rostral to V were also responsive to visual stimulation, although typically they responded less vigorously than neurons in V. Thus, there is evidence for more than one visual area in tenrecs. A third region of visually evoked activity was in cortex rostral to the medial portions of S1 and R (Fig. 3). Part of this region, where visual responses were most consistently found, corresponds to a zone where neurons project to the superior colliculus (Künzle, 1995a). This zone extends from the dorsomedial surface of the brain into the cortex of the medial wall. We refer to this area as RV or the rostral visual area for its rostral location, and clear responsiveness to visual stimulation. The location of RV in the frontal lobe suggests a visuomotor function (see Discussion). We did not attempt to determine the visuotopic organization of any visual area.

The myeloarchitecture of somatosensory, visual, and auditory areas

In most cases, the cortex was flattened and cut parallel to the cortical surface to facilitate two-dimensional map reconstruction. Cortex was stained for Nissl, cytochrome oxidase, and myelin. In this plane of section, the myelin stains were particularly useful for delimiting cortical field boundaries, whereas the Nissl-stained sections and CO-reacted tissue revealed no clear distinctions between the fields. A single section alone did not show all of the boundaries of the fields. For this reason, the entire series of myelin-stained sections was examined so that changes occurring across the cortical layers could be appreciated. In all cases, S1 was coextensive with a darkly myelinated region of cortex (Fig. 8). The boundaries of the myelinated region overlapped with the physiological representation. A

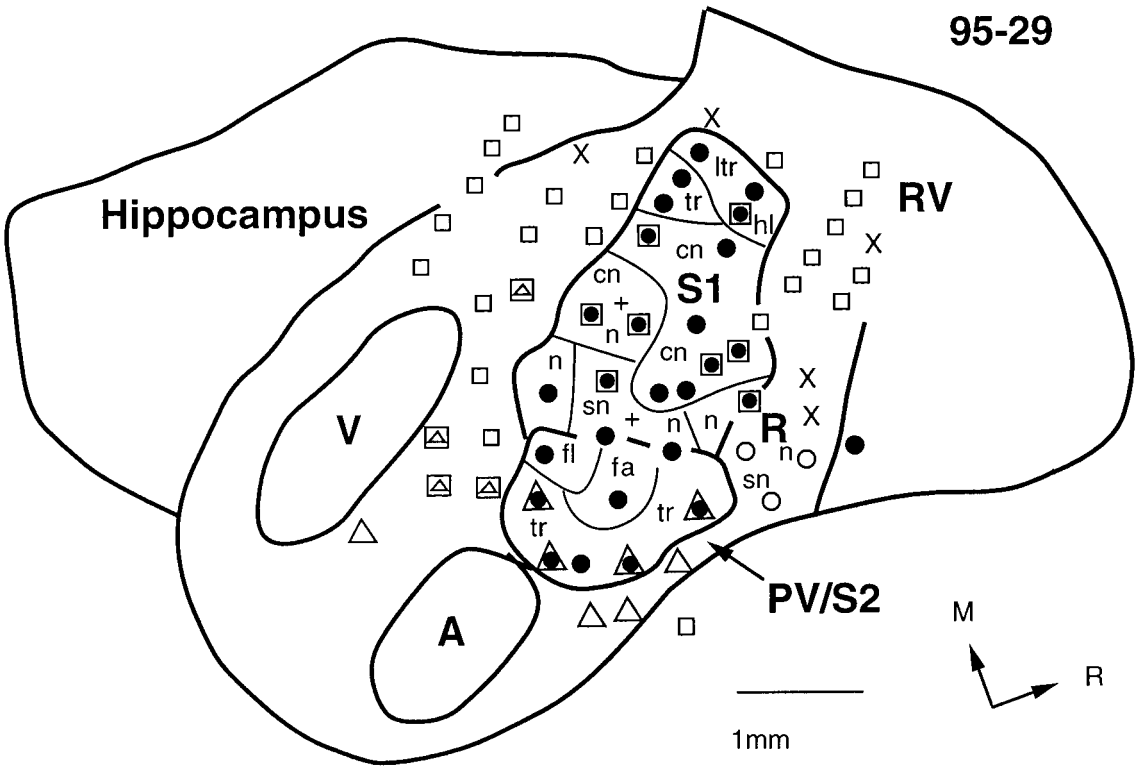

Fig. 5. Schematized cortical maps for tenrec 95-29. A number of closely spaced recording sites within somatosensory and surrounding regions of cortex demonstrate that three separate somatosensory fields are present in tenrecs, S1, PV/S2, and R. Within S1, the tail, lower trunk, and hindlimb are represented most medially, followed by the representations of the chin, nose, and snout more laterally. Because of the small size of the far lateral field, the internal organization is difficult to discern. The location and size of this field is similar to both S2 and PV described in other mammals. However, the overlapping auditory responses make it more like PV described in squirrels. Finally, a field in which neurons responded to more intense stimulation including taps to the body, light pressure, and joint manipulation, was consistently identified rostral to S1. This field is termed the rostral field, R, because of its location and similarities with R described in other mammals. Neurons surrounding somatosensory cortex were responsive to visual, auditory, or combined stimulation. See previous figures and Table 1 for abbreviations.

thin strip of cortex just rostral to S1 was very lightly myelinated and coincided with the rostral field (R) defined electrophysiologically. Both the mediolateral extent and rostrocaudal width of the field were consistent with field R. Cortex just lateral to S1 was moderately myelinated and coextensive with PV/S2. Because PV/S2 was moderately to densely myelinated, the rostral, lateral, and caudal boundaries could be readily distinguished; however, the boundary between this field and S1 was most reliably delimited using physiological criteria.

Several regions in addition to somatosensory cortex could also be distinguished in brain sections stained for myelin. Just rostral to field R, in shoulder cortex extending to the medial wall, a darkly myelinated region of cortex was coextensive with the rostral visual area (RV), defined electrophysiologically. Likewise, a darkly myelinated region of cortex caudal to S1, in which neurons were responsive to visual stimulation, was termed field V. Cortex lateral to V contained neurons that responded to visual and/or visual + auditory stimulation. This cortex was lightly myelinated. Finally cortex lateral to visual cortex and caudal to PV/S2 was densely myelinated and contained neurons that responded to auditory stimulation. We termed this field A.

DISCUSSION

Our basic goal in studying the cortex of tenrecs was to gain a better understanding of the early stages of the evolution and expansion of neocortex in mammals. Mammals in many lines of descent have increased the size of their brains, especially the neocortex, relative to body size (see Jerison, 1973; 1990), whereas the brains of tenrecs appear to have changed very little over time, and most closely resemble endocasts of long-extinct early mammals (see Kielan-Jaworowska, 1984). Indeed they appear to have retained the brain/body proportions, as well as the surface area of the neocortex relative to the entire brain, from the first mammals. The results support the contention that the neocortex of the first mammals had relatively few subdivisions or areas, and that these included the primary somatosensory, auditory, and visual areas, as well as two or more additional somatosensory areas and additional visual areas. These and other conclusions are discussed below. In addition, we consider an apparent specialization of frontal cortex in tenrecs, the rostral visual area (RV), and suggest that RV may have been derived from a rostrally located and primitive visuomotor area that has been identified in a number of extant mammals. We start by evaluating and interpreting the present and previous

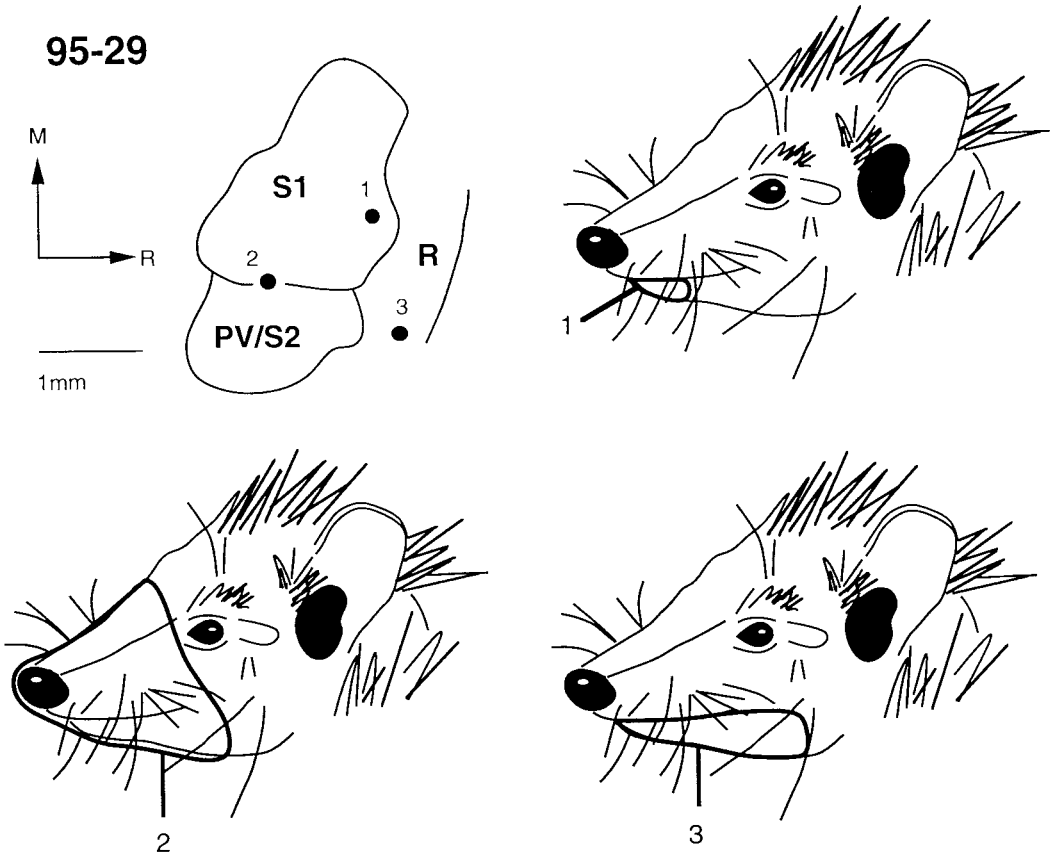

Fig. 6. Receptive fields for neurons in areas S1, PV/S2, and R in tenrec 95-29. Although the recording sites in each field are in distant locations, and over 1 mm away from recording sites shown in the other fields, receptive fields for neurons in all three sites incorporate similar portions of the chin and face. Receptive fields for neurons in S1 are substantially smaller than for neurons in PV/S2 and R. Finally, although neurons in S1 and PV/S2 responded predominantly to cutaneous stimulation, neurons in R were responsive to stimulation of deep receptors. Abbreviations in Table 1.

evidence on the organization of neocortex in tenrecs and other mammals.

The organization of sensory cortex in tenrecs

Although the present results demonstrate that much of the cortex of tenrecs is responsive to sensory inputs, how this cortex should be subdivided is not completely clear. Perhaps the most certain of proposed fields is S1, largely because this field has the location and somatotopic organization of S1 of other mammals (Kaas, 1983; Johnson, 1990). Another defining feature is that S1 in most mammals, as in tenrecs, is more darkly myelinated than adjoining cortex (see Krubitzer and Kaas, 1990; Krubitzer et al., 1993). Additionally, the region of cortex with neurons projecting to the upper cervical spinal cord in tenrecs (Künzle and Rehkämper, 1992) overlaps cortex in the medial portion of S1, where neurons are responsive to stimulation of the forelimb and upper trunk. In other insectivores such as moles and hedgehogs, as well as other mammals, the forelimb portion of S1 provides a major projection to the spinal cord (Nudo and Masterton, 1990; Holst et al., 1991; Catania and Kaas, 1997). Another defining characteristic of S1 in all mammals investigated is the presence of dense inputs from the ventroposterior nucleus of the thalamus. This feature has not yet been established for tenrecs, but it would be difficult to account for the sensitivity and structure of receptive fields of neurons in S1 without such inputs. A ventroposterior nucleus, with inputs from the dorsal column nucleus, has been identified in tenrecs (Künzle, 1994).

S1 of tenrecs is unusual in that this region of cortex does not have a well-defined layer of granule cells (Rehkämper, 1981; Künzle and Rehkämper, 1992). Indeed, in the coronal plane of section, neocortex throughout is poorly differentiated, and no region has a distinct layer IV containing small, tightly packed neurons. Mammals with small brains and little neocortex commonly have poorly differentiated cortical layers (Brodmann, '09; also see Ebner, 1969; Kaas et al., 1970; Walsh and Ebner, 1970; Stephan et al., 1991), but tenrecs are extreme in this regard, suggesting an unusual retention of an early state. However, a number of mammals whose ancestors branched off early in evolution, such as monotremes and marsupials, do have well-differentiated laminae, and a clearly defined granule cell layer (e.g., Ulinski, 1984; Vidyasagar et al., 1992; Weller, 1993). Thus, it is possible that poorly differentiated cortical layers are only a feature of some lineages, such as insectivores, and not a feature of ancestral cortex. Although there is no clearly defined layer IV anywhere in

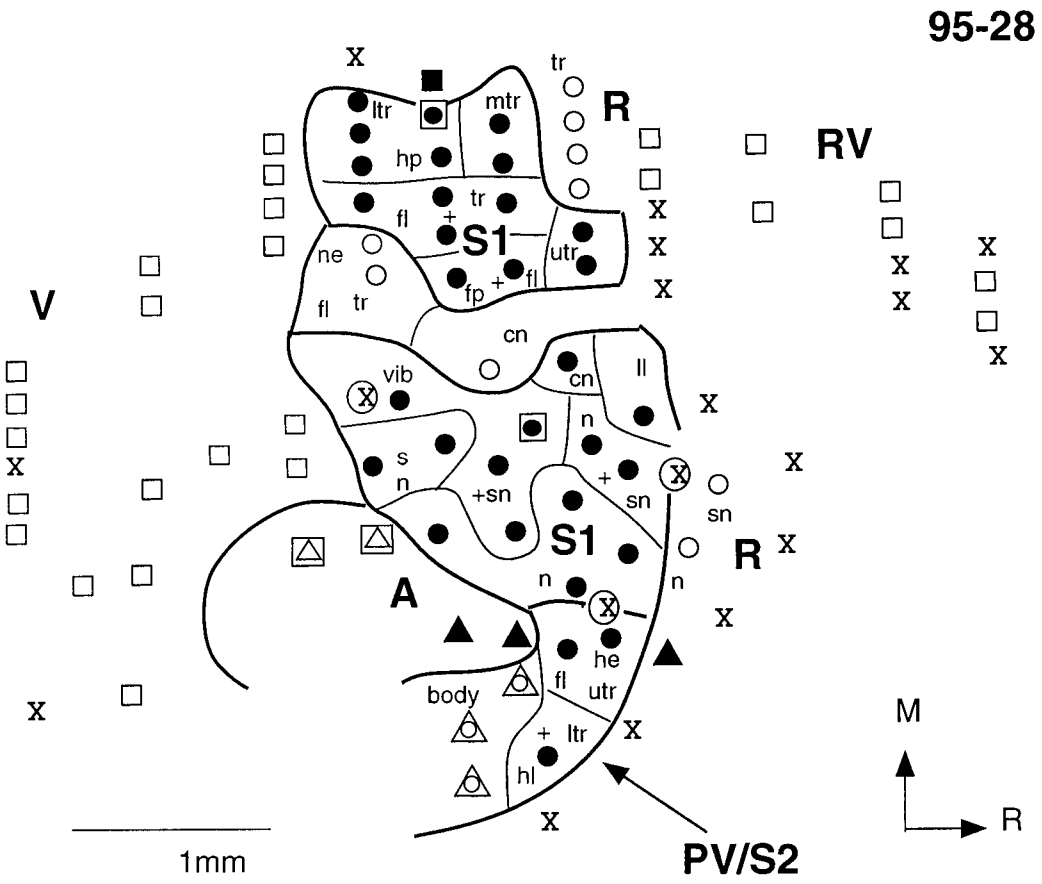

Fig. 7. Cortical field maps of S1, PV/S2, and surrounding cortex generated for case 95-28. As in the other cases, neurons in S1 respond predominantly to cutaneous stimulation of the contralateral body surface. Within the representation, the trunk and limbs are represented most medially, and the large representation of the chin, snout, and lips are represented most laterally in the field. The small lateral field, PV/S2, has neurons responsive to cutaneous stimulation, but neurons here have larger receptive fields that incorporate large portions of the head, upper trunk, and limbs. Neurons responsive to stimulation of deep receptors are found predominantly at the rostral boundary of S1. Abbreviations as in previous figures and in Table 1.

tenrec neocortex and Künzle and Rehkämper (1992) were only able to denote a combined layer III/IV, they were still able to distinguish four main regions of cortex, based on subtle differences in appearance and thickness. S1 corresponds to much of their area 2.

An interesting observation was that in cortex that was sectioned tangentially, and stained for myelin, a number of fields were architectonically distinct and coincided with sharp physiological boundaries. Thus, the notion that early mammals were likely to have poorly differentiated cortex, may only be true for the laminar distribution of cells, but not for areal patterns of organization. The sharp cortical field boundaries observed in the tangential plane suggests that cytoarchitectonic distinctions based on laminar differences across fields need not be present for topographic maps to exist. This also implies that field boundaries may not always be discernible using cytoarchitectonic analysis alone, even in brains with well-developed lamina.

Our area R corresponds to a narrow strip of cortex just rostral to S1 in which neurons were responsive to more intense stimulation of deep as well as cutaneous receptors. Our data for field R are limited, and the topographic organization of this field is difficult to determine from any single case. However, when all cases are considered, a rough topographic organization can be discerned. The somatotopic organization of R appears to parallel that of S1. By location, responsiveness, width, and somatotopic organization, R appears to be a homologue of area 3a of monkeys and carnivores. In area 3a, neurons are activated by muscle spindle receptors (see Jones and Porter, 1980; Kaas, 1983), and in macaque (Tanji and Wise, 1981) and marmoset monkeys (Huffman et al., 1996) cutaneous responses have been observed for neurons in this area. It is also similar to the rostral somatosensory area (SR) defined recently in opossums (Beck et al., 1996), and the rostral deep field (R) identified in monotremes (Krubitzer et al., 1995c). Area 3a, and a similar strip-like field along the rostral border of S1, receives inputs from S1 in all investigated mammals (see Beck et al., 1996), suggesting that this somatosensory field, and its intimate relationship with S1, arose early in the evolution of mammals.

Another possibility is that R is primary motor cortex (M1). However, the narrow width of the field and its responsiveness to somatic stimulation (neurons in M1 typically respond poorly to somatosensory stimulation in anesthetized animals) make R in tenrecs an unlikely candidate for M1, as defined in other mammals. On the

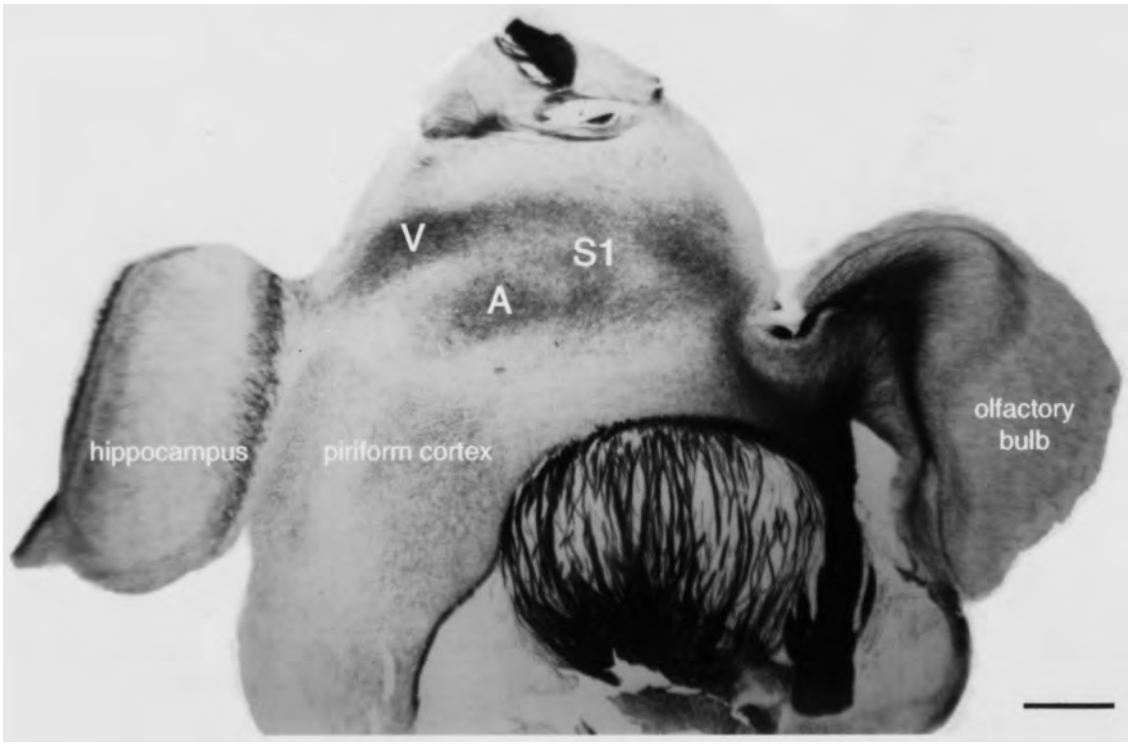

Fig. 8. A digital image taken with a Microlumina slow scan camera. In this image, cortex has been flattened, cut parallel to the cortical surface, and stained for myelin in tenrec 95-22. In this section, S1 stains darkly for myelin relative to surrounding cortex. The visual area (V) and auditory area (A) also stain densely for myelin, as do V1 and A1 in other mammals. In other figures, architectonic boundaries for cortical fields were determined by examining the entire series of sections throughout the neocortex. By matching lesions and tissue artifacts, these boundaries were related to electrophysiological recording results (compare with 2B). The background was made uniformly light using Apple photoshop. Scale bar = 1 mm.

other hand, corticospinal projections are expected from M1 as well as S1, and in many mammals, a single focus of corticospinal neurons extends from S1 into M1 (Li et al., 1990; Nudo and Masterton, 1990), including the 3a-like strip. Likewise, the cortico-spinal neurons in dorsomedial cortex of tenrecs extends rostally from S1 to include cortex we now define as R, and beyond (Künzle and Rehkämper, 1992). Thus, there is some evidence for a motor field, M1, rostral to S1 and R. However, cortex rostral to R, corresponding to part of area 1 of Künzle and Rehkämper (1992), does not have exceptionally large layer V pyramidal cells, as does M1 of some mammals (Brodmann, 1909).

Neurons in cortex lateral to S1 also respond to tactile stimulation of the face medially in the field, whereas stimulation of the limbs and trunk activates neurons laterally in this field. This somatotopic pattern is characteristic of both somatosensory fields S2 and PV as described in other mammals (see Krubitzer et al., 1986; Krubitzer and Kaas, 1990; Li et al., 1990; Krubitzer and Calford, 1992; Krubitzer et al., 1995b; Beck et al., 1996). In principle, the two fields could be distinguished by differences in the relative position of forelimb and hindlimb representations, but it would be difficult to come to firm conclusions from the present results in which few electrode penetrations were placed in the small PV/S2 area. Because neurons in part of PV/S2 respond to auditory as well as somatosensory stimulation, a characteristic of PV rather than S2, at least part of PV/S2 could be PV. Although we expect to find both fields in eutherian mammals, as there is evidence for these fields in metatherian mammals such as opossums (Beck et al., 1996), a member of the sister group of eutherians, S2 may be absent in tenrecs, PV/S2 may contain both fields, or PV/S2 may be an amalgam of both fields. Because of these uncertainties, the lateral somatosensory field in tenrecs was termed PV/S2.

The myelinated oval of cortex we term A may be the primary auditory area, A1, of other mammals. Neurons in this region respond vigorously to auditory stimulation, as does A1, and this region in tenrecs is darkly myelinated, as is A1 in other mammals (see Luethke et al., 1988). A field of about the same proportional size and location has been identified by tonotopic organization as A1 in opossums (Gates and Aitkin, 1982) and hedgehogs (Batzri-Izraeli et al., 1990). The field is part of a larger region of caudolateral cortex in tenrecs that projects to the inferior colliculus (Künzle, 1995a), a feature of A1, as well as other auditory areas in other mammals (see Luethke et al., 1989). Yet, the possibility remains that A contains two or more auditory fields. Tonotopically organized A1 and posterior fields have been identified in hedgehogs (Batzri-Izraeli et al., 1990), and additional auditory fields have been described in a number of mammals (see Luethke et al., 1989).

Neurons in cortex rostromedial to A also responded to auditory stimulation, although less consistently. At several sites neurons were also activated by visual stimulation. Sites where neurons respond to bimodal stimulation have been observed in a similar location in monotremes (Krubitzer et al., 1995c), flying foxes (Krubitzer and Calford, 1992), and monkeys (Krubitzer et al., 1995b), but have not been commonly described and studied across

mammals. However, they have been reported and more extensively investigated in some species such as cats (e.g., Wallace et al., 1992), rats (Ramachandran et al., 1993; also see Paperna and Malach, 1991), and monkeys (Bruce et al., 1981). Thus, bimodal neurons or clusters of neurons might be expected in tenrecs, but the comparative evidence seems too sparse to allow speculations on possible homologues of bimodal and multimodal fields across species, other than PV (see above).

Our visual area, V, is in the relative position and has the dark myelination of primary visual cortex, V1, as described in other mammals (e.g., Kaas, 1980). This cortex corresponds to much of the caudal part of field A3 of Rehkämper (1981), where neurons project to the superior colliculus (Künzle, 1995a), and to the dorsal lateral geniculate nucleus (Künzle, 1995b), which are major targets of V1. Neurons in cortex lateral and rostral to V responded to visual stimulation in tenrecs. Part of this cortex is likely to be V2, a narrow visual area on the lateral border of V1 in most or all mammals (see Kaas and Krubitzer, 1991). Most, and perhaps all, mammals have additional visual cortex lateral to V2, but the organization of such extrastriate cortex is poorly understood across species (see Kaas and Krubitzer, 1991). Most visual areas project to the superior colliculus (e.g., Graham et al., 1979; Huerta and Harting, 1984; Harting et al., 1992), and the caudal cortex in which neurons were responsive to visual stimulation in tenrecs closely corresponds to the zone that projects to the superior colliculus (Künzle, 1995a).

A somewhat unexpected finding was that neurons in a rostromedial zone of dorsal cortex extending onto the medial wall were activated by visual stimuli. This same zone of cortex, termed here the rostral visual area or RV, projects to the superior colliculus (Künzle, 1995a; Künzle and Lotter, 1996), as do visuomotor areas of the frontal lobe, especially the eye movement portion of the supplementary eye field (SEF) and the frontal eye field (FEF) of primates (see Huerta et al., 1986; Huerta and Kaas, 1990). In some species, neurons in these visuomotor fields respond to visual stimulation (e.g., Mohler et al., 1973; Schlag and Schlag-Rey, 1987). Two visuomotor areas in frontal cortex have been established in cats, both of which project to the superior colliculus (Segal et al., 1983), and a region of frontal shoulder cortex, proposed to be homologous to the FEF of primates, has been described as projecting to the superior colliculus (e.g., Leichnetz and Gonzalo-Ruiz, 1987). By relative position, the medial of the two projection zones in cats is similar to RV in tenrecs. A medial agranular premotor cortex, possibly including a supplementary eye field, projects to the superior colliculus in rats (Stuesse and Newman, 1990). By position RV is most comparable to the SEF of primates, but further study is needed to determine if RV has a homologue in the cortex of other eutherian mammals. In any case, the considerable responsiveness of neurons in RV to visual stimulation suggests that it is a specialized area, perhaps derived from SEF or FEF.

The presence of a region in which neurons are highly responsive to visual stimulation in the frontal cortex of tenrecs is surprising, as the eye is small, and the structures that receive retinal projections are not well developed (Künzle, 1988). Consistent with their somewhat reduced visual pathways, tenrecs do not appear to possess any behavioral specializations that utilize the visual system. Regardless of their overall dependence on visual processing, it is possible that the visual information that reaches this frontal area is in some way critical for survival. In echolocating bats, which are clearly specialized for processing auditory information, the auditory thalamus projects directly to the frontal cortex (Kobler et al., 1987), suggesting that sensory centers in frontal cortex may have evolved in other small-brained mammals (see also Künzle, 1996).

What tenrecs can tell us about the organization of cortex in early mammals

The forebrain of tenrecs closely resembles that of early mammals in relative size, and in having proportionately little neocortex. The cellular differentiation of neocortex is so slight that it is difficult to clearly distinguish a layer IV of granule cells and define cytoarchitectonic subdivisions of cortex (Rehkämper, 1981; Künzle and Rehkämper, 1992). It is tempting to propose that such poorly differentiated lamina in neocortex has been retained from early mammals. Clearly, the transition from reptiles to mammals was marked by an impressive increase in cortical thickness, neuronal differentiation, and laminar development (Ebner, 1969; Hall and Ebner, 1970; Marín-Padilla, 1992). The cortex of tenrecs could represent an intermediate stage of this transition. However, deducing primitive characters of the mammalian forebrain that have been retained in only a few remnant species is difficult because of the paucity of comparative observations. Usually studies are limited to only a few species in a given lineage. Indeed, our assumptions regarding the lack of laminar differentiation in the cortex of early mammals are derived primarily from observations in only a few species of insectivores.

The correspondence between myeloarchitectonic distinctions and two-dimensional maps was likely to have arisen early in evolution, because similar observations in which myeloarchitectonic, or cytochrome oxidase boundaries and somatotopic maps overlap have been made in monotremes (Krubitzer et al., 1995c), marsupials (Elston et al., 1993; Krubitzer et al., 1995a; Beck et al., 1996) and other insectivores (Catania and Kaas, 1995). It is possible that laminar distinctions arose somewhat later in evolution in some lineages. However, as noted previously, not all "primitive" mammals have undifferentiated laminae. An important implication of the present investigation is that "differentiated" cortex need not be associated only with laminar differentiation alone. Indeed, it appears as if different structural solutions have evolved in different lineages, and are associated with similar topographically organized maps across mammals. Thus, cortical maps exhibit a high degree of evolutionary stability whereas cortical architecture does not.

There is evidence for an S1 in every studied mammal, and many mammals appear to have a rostral somatosensory field, R or area 3a, and lateral S2 and PV fields (Krubitzer, 1995). Although we have no direct evidence for a narrow strip-like somatosensory field along the caudal border of S1, such a field is common in other mammals (see Beck et al., 1996). As neurons in nonprimary fields can be rather unresponsive to somatic stimulation in anesthetized animals, our lack of physiological evidence for a caudal somatosensory field in tenrecs is not compelling. Because of this problem, anatomical studies would be very

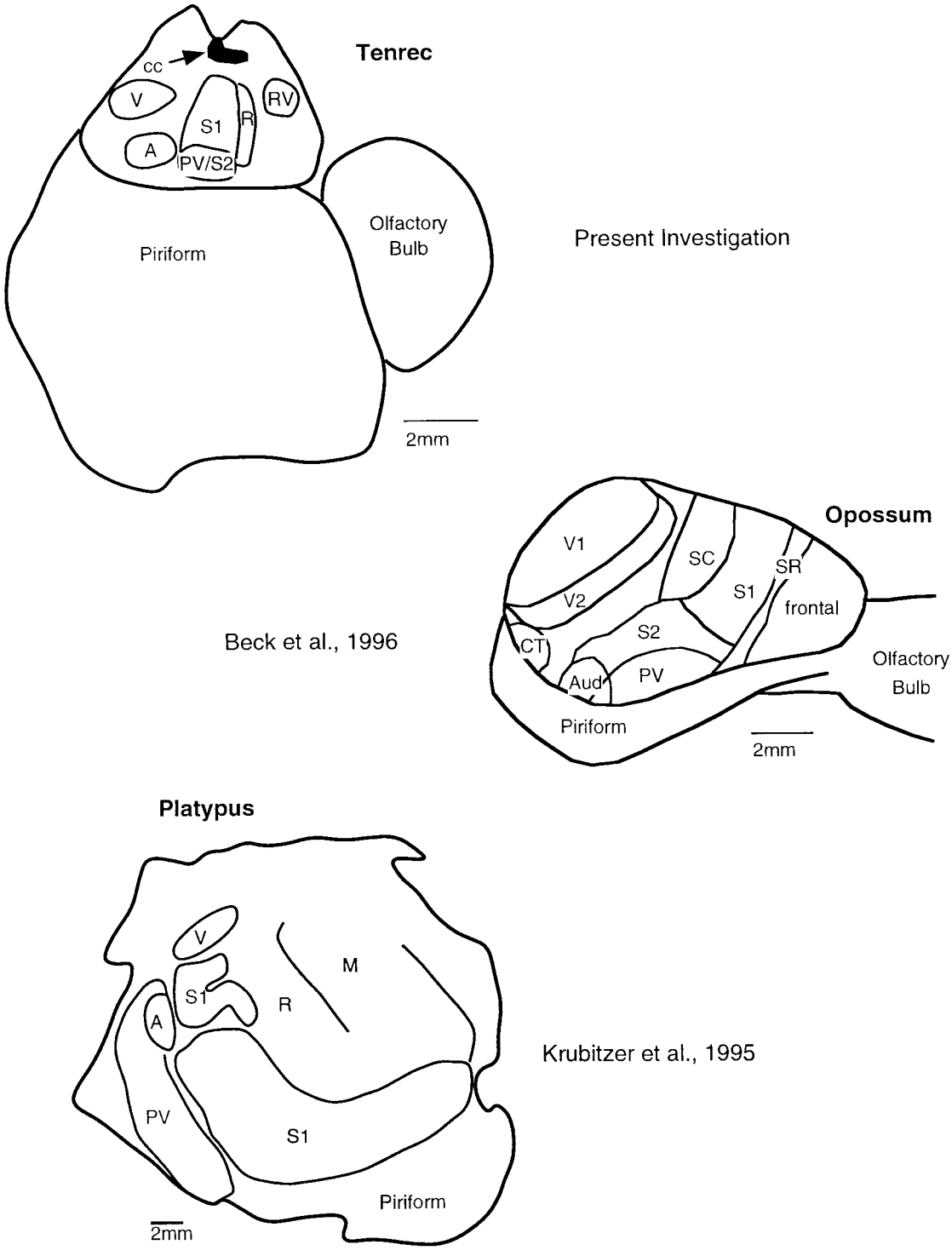

Fig. 9. Comparisons of the neocortex between mammals whose ancestors branched off early in mammalian evolution. These mammals have relatively small brains with only a few cortical fields in each sensory system. Some of these fields such as S1, PV, S2, R, A, and V are found in all mammals. Another similarity is that most of cortex is composed of sensory areas that abut one another, with little room left for nonsensory or association cortex. A notable difference in these brains is the relative location of homologous fields.

informative, and we would expect to find projections of S1 to a caudal zone of cortex, as in other mammals. We propose that early mammals had at least three somatosensory areas, but it is also likely that they had more. Further analysis using both neuroanatomical and electrophysiological techniques may reveal the presence of additional somatosensory fields, not identified using electrophysiological techniques alone.

A related issue is the comparative evidence for early mammals having motor cortex. Presently, there is no clear evidence for a separate motor field, M1, in some marsupials, including opossums (see Beck et al., 1996), although M1 has been demonstrated in placental mammals as well as monotremes (Bohringer and Rowe, 1977). This suggests that M1 was present in the common ancestor of all mammals. In this regard, cortical neurons projecting to the spinal cord exist in cortex rostral to S1 and even R in tenrecs, providing some evidence for a motor field in frontal cortex of tenrecs (Künzle and Lotter, 1996). More conclusive evidence could come from studies of connections and microstimulation. As already noted, no region of cortex has the obvious cytoarchitectonic features of M1 in tenrecs (see Künzle and Rehkämper, 1992).

Tenrecs have at least one auditory field, as do nearly all investigated mammals, and evidence exists in most mammals for more than a single field (Luethke et al., 1988). However, even the primary auditory area, A1, is difficult to identify with assurance, because several fields can often appear to be primary-like (Morel and Kaas, 1992). Patterns of tonotopic organization have been very useful in identifying primary-like fields, but tonotopic mapping has not been attempted in tenrecs. For now, we can conclude that early mammals had an auditory region composed of at least one field.

The present results are consistent with conclusions based on previous comparative evidence that early mammals had V1, V2, and probably additional visual areas, possibly as many as five or more visual fields (see Beck et al., 1996). Neurons in caudomedial cortex in tenrecs were responsive to visual stimulation, and part of this region had the dense myelination and is in the expected location of V1. The multimodal and frontal visual areas of the tenrec cortex deserve further study, and it is still uncertain if they reflect a specialization of retained fields, new additions, or even, in the case of the bimodal areas at least, retained areas that have not been adequately revealed in comparative studies.

Although the sensory and perhaps motor areas occupy most of the small cap of cortex in tenrecs, Künzle and Rehkämper (1992) and Künzle (1995a) have distinguished small cingulate, retrosplenial, perirhinal, and entorhinal fields. Other subdivisions including those of frontal cortex are expected (see Benjamin and Golden, 1985). Thus, early mammals may have had on the order of seven or more sensory areas, one or two motor fields, one or more bimodal areas, and four or more other areas. Hence, in a surface area of 15 mm^2 there may be 13 or more distinct processing divisions. These processing divisions are very small in tenrecs and were probably so in early mammals as well.

An advantage of small cortical areas is that processing time is reduced because connections are short, and the degree of connectivity can be high, subjecting each neuron to more global influences (Ringo, 1991; Ringo et al., 1994; Kaas, 1995). Bigger brains with proportionately more cortex would require longer connections and more processing time. This negative feature can be minimized in large brains by reducing the relative connectivity to distant targets and increasing local connections between fields. After extensive intrareal processing between closely situated cortical fields, processed information would then reach more distant targets such as frontal cortex, posterior parietal cortex, and areas of temporal and entorhinal cortex. Thus, as considerable evidence indicates, mammals with larger brains and proportionately more neocortex have more cortical areas and modular subdivisions within these areas (see Kaas, 1982, 1989, 1993, 1995).

The present study is one of a series of recent efforts to elucidate forebrain organization in tenrecs. In view of the poor cytoarchitectonic differentiation of neocortex, we are pleased that the electrophysiological results could be related to the few myeloarchitectonic distinctions that were apparent. The results clearly support the conclusion that the common ancestor of all extant mammals had little neocortex and that this cortex was largely occupied by sensory fields (Fig. 9).

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