

Comparative Studies of Diurnal and Nocturnal Rodents: Differences in Lifestyle Result in Alterations in Cortical Field Size and Number

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ABSTRACT

In this study we examine and describe the neuroanatomical organization of sensory cortex in four rodents: laboratory Norway rats (Long Evans; *Rattus norvegicus*), wild-caught Norway rats (*Rattus norvegicus*), wild-caught California ground squirrels (*Spermophilus beecheyi*), and wild-caught Eastern gray squirrels (*Sciurus carolinensis*). Specifically, we examined the myeloarchitecture and cytochrome oxidase reactivity for several well-identified areas in visual cortex (areas 17, 18, and 19), somatosensory cortex (areas S1, S2 and PV), and auditory cortex [areas A1 + AAF (R) and TA] and compared the percentage of dorsolateral cortex devoted to each of these areas. Our results demonstrate that squirrels have a larger mean percentage of dorsolateral cortex devoted to visual areas than rats. The difference is due to the greater percentage of cortex devoted to known

areas such as area 17 and area 18 and not simply to a difference in the number of visual areas, which ultimately makes this distinction even more pronounced. Furthermore, both rat groups have a larger percentage of the dorsolateral cortex devoted to somatosensory and auditory cortical areas. Differences within groups were also observed. The arboreal squirrel had a larger mean percentage of dorsolateral cortex devoted to areas 17 and 18 compared with the terrestrial squirrel. The laboratory Norway rat had a larger percentage of dorsolateral cortex devoted to both somatosensory and auditory areas than the wild-caught Norway rat. Our results indicate that differences in sensory apparatus, use of sensory systems, and niche are reflected in the organization and size of cortical areas. *J. Comp. Neurol.* 518:4491–4512, 2010.

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Although mammalian lifestyles vary along a number of parameters, one ubiquitous feature of lifestyle is the portion of the day in which animals actively perform behaviors directly associated with survival (diel pattern). Slight variations in patterns of activity have been described, but mammals generally fall into one of three major categories, diurnal, nocturnal, or crepuscular, and adaptations associated with each of these lifestyles have been observed throughout the nervous system. For example, the differences between a nocturnal and a diurnal visual system start at the level of the retina and continue through all levels of nervous system organization. The diurnal squirrel retina has been shown to be made up of between 60% and 90% cones; in contrast, the rat retina is composed of over 80% rods (Kryger et al., 1998; Szel and Rohlich, 1988; Van Hooser and Nelson, 2006). Furthermore, the squirrel retina contains cones sensitive to green and blue wavelengths of light, whereas the rat retina

contains cones sensitive to green and ultraviolet (UV) wavelengths of light (Jacobs et al., 2001; Kryger et al., 1998; Szel and Rohlich, 1992). At higher levels of organization, the squirrel has a well-laminated five-layered lateral geniculate nucleus (LGN) compared with the three-layered LGN in the rat (Kaas et al., 1972; Montero et al., 1968). The primary visual area in the squirrel also has a distinct laminar organization, and the response properties of neurons in V1 are similar to those of all other mammals with a well-developed visual system (Heimel et al., 2005;

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TABLE 1.
Lifestyle Information by Rodent Group

	Laboratory Norway Rat (<i>Rattus norvegicus</i>)	Wild-caught Norway rat (<i>Rattus norvegicus</i>)	California ground squirrel (<i>Spermophilus beecheyi</i>)	Eastern gray squirrel (<i>Sciurus carolinensis</i>)
Habitat		Terrestrial/Semifossorial	Terrestrial/Semifossorial	Arboreal
Diel Pattern	Nocturnal	Nocturnal	Diurnal	Diurnal
Mating Pattern	Promiscuous	Promiscuous	Promiscuous	Promiscuous
Gestation	21–23 days	22–24 days	30 days	44 days
Weaning	3 weeks	3–4 weeks	6–8 weeks	7–10 weeks
Sexual Maturity	1.5–2 months	3–4 months	12 months	15 months
Lifespan	1.5–3.5 years	2 years	6 years (10 years)	12 years (20 years)
Diet	Omnivore	Omnivore/prefers meat	Herbivore/Omnivore	Herbivore/Omnivore

Van Hooser and Nelson, 2006). For example, layer specificity for properties such as direction selectivity, simple vs. complex cells, spatial frequency tuning, and temporal frequency tuning of V1 cells have been described (Heimel et al., 2005). On the other hand, in rats, V1 lacks this laminar specificity in direction selectivity and spatial frequency bandwidth tuning (Heimel et al., 2005). Finally, squirrels appear to have more cortical areas devoted to visual processing based on electrophysiological recording studies and inputs from the visual thalamus (Hall et al., 1971; Kaas et al., 1972, 1989; Robson and Hall, 1977). Thus, the retinogeniculocortical system of the squirrel is well developed compared with that of the laboratory rat. Although it is likely that most of these differences reflect true differences associated with a nocturnal vs. a diurnal lifestyle, it is possible that some of these differences reflect the radically different rearing conditions of a wild-caught vs. a laboratory-reared animal. For example, ultraviolet light, which is the only type of light to which certain

photoreceptors in the nocturnal rodent retina respond, is absent under laboratory conditions (Szel et al., 2000; Szel and Rohlich, 1992).

Although previous studies have examined some aspects of cortical organization in a single species of rodent, there are no studies that directly compare the visual, somatosensory, and auditory areas in several species using identical methodologies or that compare the same species reared under laboratory vs. natural conditions. The goal of these experiments is to increase our understanding of the basic mammalian plan of sensory cortical organization, particularly that of the visual system, and the way in which this plan is modified to generate visually mediated behaviors associated with the demands of a nocturnal vs. a diurnal lifestyle in a particular niche. Here we present data on a number of well-defined cortical fields in four rodents: nocturnal Norway rat (laboratory, Long Evans strain), nocturnal Norway rat (wild-caught), diurnal wild-caught California ground squirrel, and diurnal wild-caught Eastern gray squirrel (see Table 1 for more lifestyle information on each rodent and Figure 1 for photographs of whole brains from each group).

The Long Evans strain of laboratory rat was originally derived from the wild-caught Norway rat, so both are the same species, although there were likely small genetic modifications made to different strains. The California ground squirrel and Eastern gray squirrel are both members of the suborder Sciuromorpha and the family Sciuridae, whose lineages diverged from the common ancestor about 40 million years ago (Huchon et al., 2007; Roll et al., 2006; Steppan et al., 2004; Fig. 2). The wild-caught species that we have chosen have overlapping ranges, diets, and day/night and seasonal cycles and are exposed to the same weather conditions and human interactions. We considered these environmental similarities as critical for comparing differences in diurnal vs. nocturnal lifestyles and terrestrial vs. arboreal lifestyles. On the other hand, the environment of the laboratory rat is more controlled and environmentally restrictive, and human interactions are relatively high. Because the rat is

Abbreviations

3a	somatosensory area in anterior parietal cortex
3b	primary somatosensory area
17	primary visual area
18	secondary visual area
19	third visual area
A1	primary auditory area
AAF	anterior auditory area
AC	auditory cortex
EQ	encephalization quotient
IGL	intergeniculate leaflet
LGN	lateral geniculate nucleus
LGNv	lateral geniculate nucleus, ventral division
M1	primary motor area
MM	multimodal cortex
OB	olfactory bulb
OTc	occipital temporal area, caudal division
OTr	occipital temporal area, rostral division
PM	parietal medial area
PV	parietal ventral area
Pyr	pyriform cortex
R	rostral auditory field
S1	primary somatosensory area
S2	second somatosensory area
SWS1	short-wave sensitive
TA	temporal anterior area
TP	temporal posterior architectonic area
V1	primary visual area (Brodmann's area 17)
V2	second visual area (Brodmann's area 18)

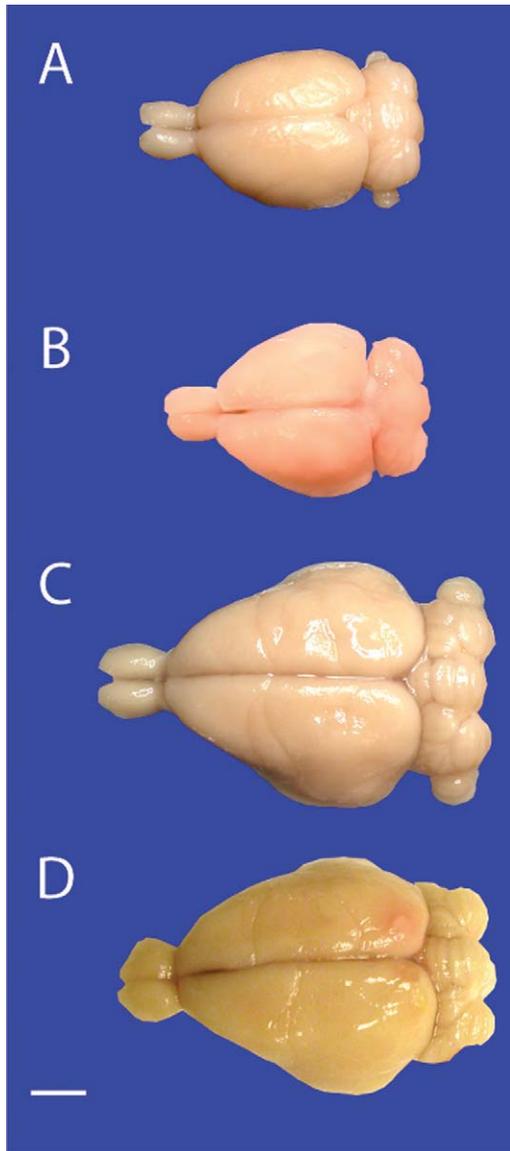


Figure 1. Representative photographs of an extracted brain from each rodent group studied. **A:** Laboratory Norway rat. **B:** Wild-caught Norway rat. **C:** California ground squirrel. **D:** Eastern gray squirrel. These give a dorsal view of the extracted brains showing olfactory bulbs to the left (anterior) and cerebellum to the right (posterior). Scale bar = 5 mm. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

a pervasive animal model for all biological studies, comparisons between it and its wild counterpart are extremely important.

In this study, we have used cortical myeloarchitecture to examine the location, appearance, and boundaries of a number of well-described functional areas in visual, somatosensory, and auditory cortex. Previous studies have demonstrated that lifestyle and associated sensory effectors and morphological specializations affect the size and organization of sensory cortical areas as well as the total area of cortex devoted to a specific type of sen-

sory input (for review see Catania and Henry, 2006; Krubitzer, 2009). We therefore hypothesize that our selected diurnal and nocturnal rodents will have different proportions of sensory cortex devoted to processing different modalities.

MATERIALS AND METHODS

Histological comparisons were made with 12 hemispheres from six (three male) Norway rats (laboratory, *Rattus norvegicus*), 12 hemispheres from six (three male) Norway rats (wild-caught, *Rattus norvegicus*), nine hemispheres from five (two male) wild-caught California ground squirrels (*Spermophilus beecheyi*), and eight hemispheres from four (one male) wild-caught Eastern gray squirrels (*Sciurus carolinensis*). For a complete listing of range and means for body and brain weights for each group see Table 2. Wild-caught animals were visually inspected to ensure that there were no injuries or deformities, particularly of the eyes, ears, paws, and whiskers. Although we could not determine the age of the wild-caught animals, their weights and sizes indicated that they were adults. Norway rats (laboratory) ranged from 3 to 4 months in age. All procedures were approved by the Internal Animal Care and Use Committee (IACUC) and conformed to NIH guidelines.

Histological processing

Animals were killed with a lethal dose of sodium pentobarbital (250 mg/kg) and perfused transcardially with 0.9% saline, followed by 4% paraformaldehyde in 0.1 M phosphate buffer (PB; pH 7.4), and 4% paraformaldehyde in 10% sucrose in PB. After fixation, the brain was extracted from the skull, blocked behind the cerebellum, and weighed. Care was taken to block brains of all animals at the same location, immediately caudal to the cerebellum at the foramen magnum. The hemispheres were separated from the thalamus, weighed, and then flattened between two glass slides. The cortices were immersed in 30% sucrose overnight and sectioned tangential to the cortical surface at 40- μ m thickness on a freezing microtome. This preparation allows the overall organization and positions of fields relative to each other to be determined.

In all cases, alternate series of cortical sections were reacted for myelin (Campi et al., 2007; Fang et al., 2005; Gallyas, 1979; Padberg et al., 2005) and processed for both cytochrome oxidase (CO; Carroll and Wong-Riley, 1984) and biotinylated dextran amine (BDA), by using standard avidin-biotin development (Vectastain Elite; Vector Laboratories, Burlingame, CA) for use in another study. These histological procedures have been described previously, so we will only briefly describe them here. Cortical sections were split into

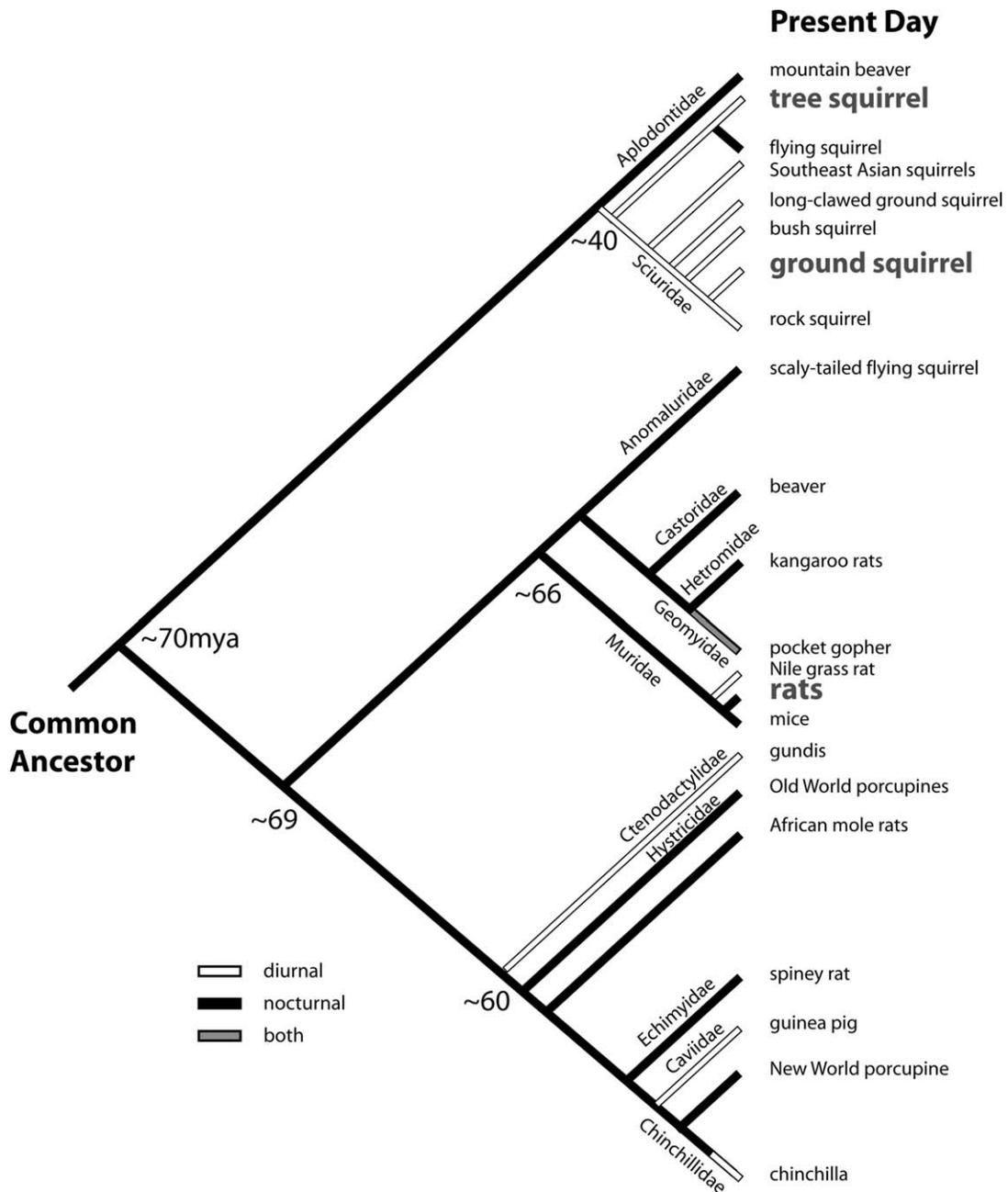


Figure 2. Phylogenetic tree of the order Rodentia with representative individuals of each family listed. The names of the rodent groups examined in this study are set off here by a larger font. Numbers reference time in millions of years ago (mya) to the present for the split of each group are listed. Taken from Huchon et al. (2002, 2007) and Steppan et al. (2004).

three series: myelin, fluorescence, and CO/BDA. The series reacted for myelin were placed in 5% formalin for 1 week and then transferred to distilled water overnight before processing by the Gallyas method. Briefly, sections were transferred into a pyridine/acetic anhydride solution before the flattening procedure in distilled water. Next, sections were immersed in silver nitrate solution for 1 hour before the developing step, which included several solutions (silver nitrate, ammo-

nium nitrate, sodium carbonate, and formalin). The final steps include washes in sodium thiosulfate and distilled water before mounting. The fluorescence series was mounted immediately for microscopy in another study. The CO/BDA series was immediately processed for CO first and then BDA. Briefly, sections were rinsed three times for 5 minutes each in phosphate-buffered saline (PBS) and then transferred into a 3,3'-diaminobenzidine (DAB) solution including cytochrome C, catalase, and

TABLE 2.
Brain and Body Weight Information

	Brain weight (g)		Body weight (g)	
	Average	Range	Average	Range
Laboratory Norway rat (Long Evans; <i>Rattus norvegicus</i>)	1.65	1.4–1.9	337.5	200–500
Wild-caught Norway rat (<i>Rattus norvegicus</i>)	1.57	1.4–1.7	185.32	168–225
California ground squirrel (<i>Spermophilus beecheyi</i>)	4.75	4.1–5.0	680	550–900
Easter gray squirrel (<i>Sciurus carolinensis</i>)	6.46	5.7–7.2	635	550–675

PBS for 1–2 hours. Sections were then incubated in a solution of methanol, hydrogen peroxide, and PBS to deactivate endogenous peroxidases. After five rinses in a solution of PBS and 0.1% Triton X-100, sections were incubated in the 1:100 dilution ABC complex for 1–2 hours. Sections were then rinsed four times in PBS before the final developing step in a solution of DAB, 1% cobalt chloride, 1% NiNH₄SO₄, PBS, and 30% hydrogen peroxide. Sections were then rinsed three times in PBS before mounting.

Allometric brain comparison measures

The brain and body weights were measured in each animal, and the brain weight/body weight ratio was calculated for individual animals. Ratios of cortical hemispheres-to-brain weight (left hemisphere weight + right hemisphere weight/whole brain weight) were also calculated for each individual animal. Group averages were then calculated for each measure. Brain and body weights from each individual animal were used to calculate the encephalization quotient (EQ) as follows: $EQ = w(\text{brain})/Ew(\text{brain})$ where the expected brain weight is $Ew(\text{brain}) = 0.026 w(\text{body})^{3/4}$ (Herculano-Houzel, 2007). Brain-to-body ratio, EQ, and hemispheres-to-brain ratio were then compared across groups by using a one-way ANOVA. Significant F tests were followed up by Tukey's HSD test in order to assess which groups were significantly different.

Reconstruction and data analysis

Architectonic boundaries of the entire series of sections stained for myelin and CO were drawn using a camera lucida (Stemi SV6; Zeiss, Jena, Germany) or a projection microscope (Zeiss). For all cases, the largest section from each hemisphere was selected as the outline for the final composite. Blood vessels and tissue artifacts were used to align individual sections during reconstruction. Boundaries for cortical areas were drawn by successive combination of cortical boundaries from individual sections throughout the entire series of sections into a final summary display (Fig. 3). One section may not encompass the entirety of all cortical sensory areas because of minor differences across brains from the flattening and

cutting process. Borders for the primary motor area (M1), primary somatosensory area (S1), secondary somatosensory area (S2), parietoventral area (PV), primary auditory area (A1), anterior auditory field (AAF in rats) or rostral field (R in squirrels), temporal anterior area (TA), primary visual area (17), second architectonic visual area (18), occipital temporal area (OT/area 19 in squirrels), and temporal posterior area (TP) were drawn. These fields were chosen because they could be reliably and accurately identified in all of our animals (Fig. 4). Other fields are present, but the boundaries of these fields were less distinct, and they are grouped together as nondelineated cortex.

Cortical area size measurements were derived by using areal boundaries drawn in Adobe Illustrator from scanned summary displays (Fig. 5). To normalize the data for comparison, the size of a particular cortical field was expressed as a percentage of the entire dorsolateral surface of the cortex (Table 3). The dorsolateral surface of the cortex did not include the pyriform cortex, olfactory bulbs, or medial wall of the cortex. We did not reflect the medial wall, so some portions of area 17 in squirrels might have been excluded from our measurements. However, this would not have changed our results on the differences between mean percentages of the cortex devoted to area 17 in rats and squirrels, only the magnitude of the difference. Paired *t*-tests were used to look for size differences within a species between the left and right hemispheres. No significant difference between field sizes in left and right hemispheres was found, so the data from both hemispheres were combined in further comparisons. F tests were used to examine differences in cortical field sizes between species. Significant F tests ($\alpha \leq 0.05$) were followed up by Tukey's HSD test in order to assess which groups were significantly different (Table 4). Minimal alterations were made in the brightness and contrast of all photomicrographs prepared in either Adobe Photoshop or Adobe Illustrator.

RESULTS

The goal of these experiments was to compare the anatomical organization of sensory cortex, with a focus on

visual cortex, in four rodents with uniform methods and analysis techniques. Below we describe brain-to-body weight comparisons and the myeloarchitectonic appearance of different sensory fields and then compare the relative size of these fields in the different rodents studied.

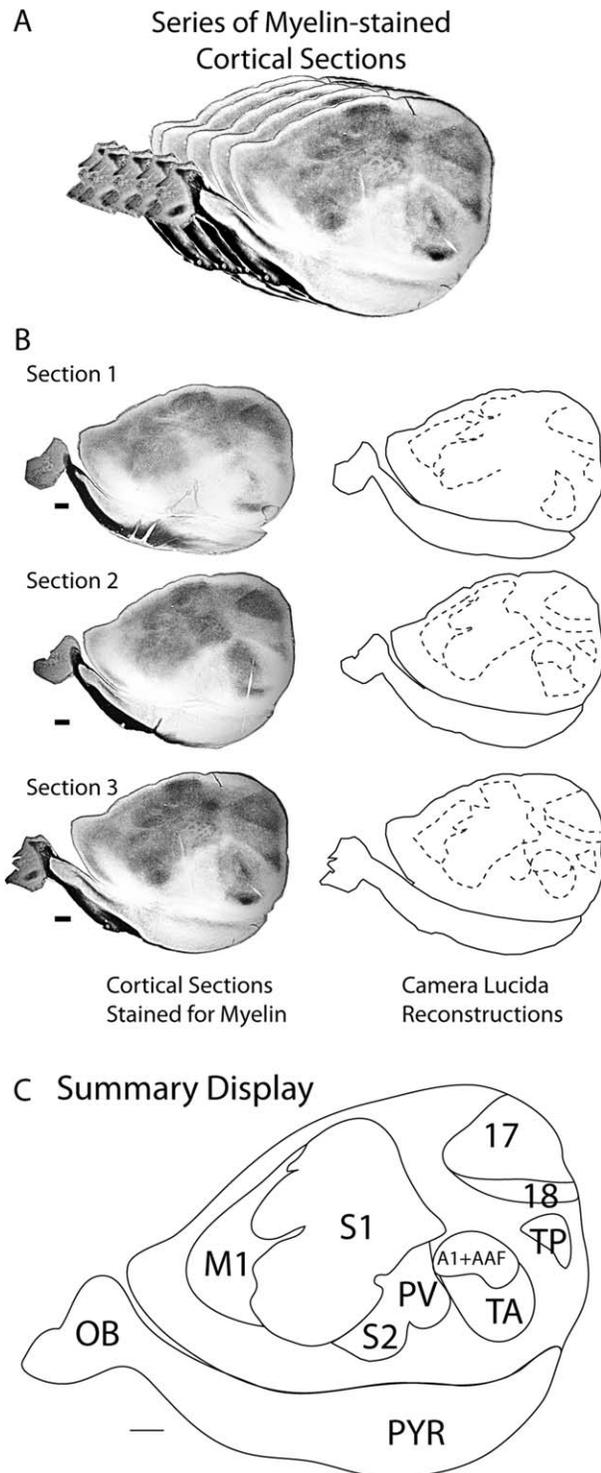


Figure 3

Brain-to-body weight comparisons

The brain-to-body comparisons are depicted in Figure 6, and F values and group differences can be found in Table 4. From post hoc comparisons with the Tukey's HSD test, we found that the wild-caught Norway rat's mean ($0.9\% \pm 0.04\%$; mean \pm SEM) brain-to-body ratio is significantly larger compared with the laboratory Norway rat's mean ($0.6\% \pm 0.1\%$) and significantly smaller compared with the Eastern gray squirrel's mean ($1\% \pm 0.03\%$). Although California ground squirrels had a larger brain-to-body ratio mean ($0.7\% \pm 0.07\%$) compared with the laboratory Norway rat's mean, this difference was not significant. The differences in mean brain-to-body ratios between rat and squirrel groups were not significant.

The mean of combined cortical hemisphere weights was $28\% (\pm 0.40\%)$ of total brain weight in the laboratory Norway rat, $31\% (\pm 1.03\%)$ of total brain weight in the wild-caught Norway rat, $30\% (\pm 0.38\%)$ of total brain weight in the California ground squirrel, and $28\% (\pm 1.0\%)$ of total brain weight in the Eastern gray squirrel. Post hoc comparisons indicated that the wild Norway rats had a significantly larger mean percentage of cortical hemisphere weight relative to the whole brain weight than laboratory Norway rats and Eastern gray squirrels but not relative to California ground squirrels.

The encephalization quotient (EQ) gives us a measure by which we can compare species with large differences in body weights. From post hoc comparisons by the Tukey's HSD test, we found that the Eastern gray squirrel had a significantly larger mean EQ (1.96 ± 0.06) compared with the means of the three other groups of rodents. The mean of laboratory Norway rat EQ (0.88 ± 0.12) was significantly smaller than that of both squirrel groups. Post hoc examination revealed a trend toward significance, $P = 0.06$, of the mean EQ

Figure 3. Methods of reconstruction from a series of flattened, myelin-stained sections. **A:** Myelin-stained section for successive cortical sections taken from the middle cortical layers. A camera lucida was used to trace the outline of the section, the rhinal sulcus, and the borders of the cortical areas. No single section accurately represents all of the cortical field boundaries, so the entire series of sections was reconstructed from each case, and the boundaries from those sections were compiled to make one comprehensive drawing to represent each hemisphere (middle right illustration). **B:** Photomicrographs of three sections are shown in the first column and camera lucida tracings are shown in the second column. The camera lucida tracings were aligned by using blood vessels. **C:** Summary display made by combining all of the individual drawings and using the largest outline from each tracing as the outer border. Rostral is to the left; medial is upward. See list for abbreviations. Scale bars = 1 mm.

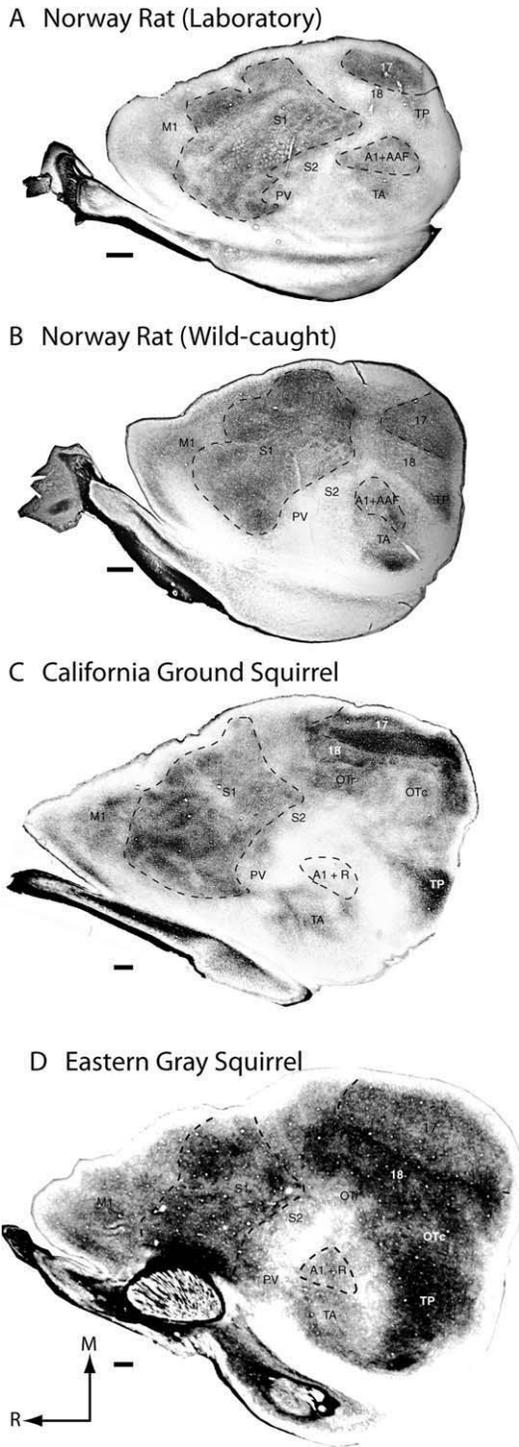


Figure 4. Myeloarchitecture in flattened cortical sections from four species of rodent. Photomicrographs of one section from each species are shown here. The first section (A) is from the laboratory Norway rat. The second section (B) is from the wild-caught Norway rat. The third section (C) is from the California ground squirrel. The fourth section (D) is from the Eastern gray squirrel. Dashed lines denote primary areas. Not all boundaries of cortical fields can be observed in a single section. In all of these sections, S1 and area 17 can be readily identified. However, the auditory core is clearly observed only in rats in these sections. Conventions as in previous figures. See list for abbreviations. Scale bars = 1 mm.

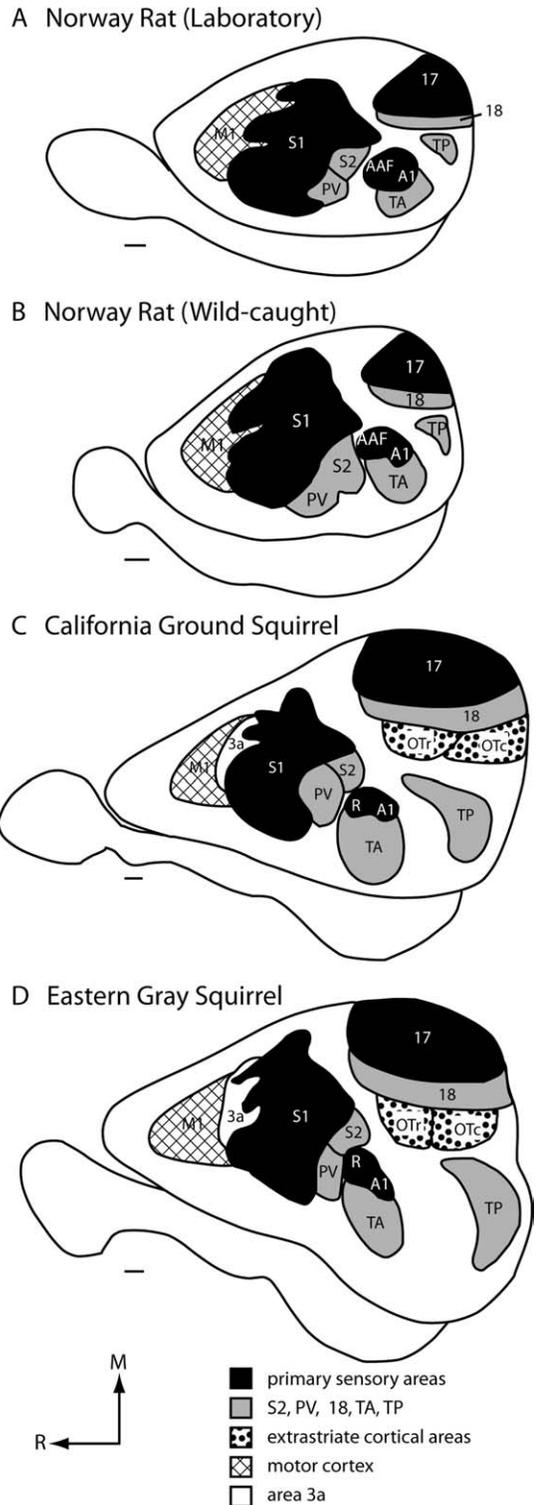


Figure 5. Summary displays from representative cases from laboratory Norway rats (A), wild Norway rats (B), California ground squirrels (C), and Eastern gray squirrels (D). The key to areas is at right. Primary sensory areas are solid black. Second sensory areas are gray. Extrastriate cortical areas are spotted. Motor cortex is hatched. Area 3a is white bounded by a black line. Comprehensive reconstructions such as these were used to make cortical field measurements. Rostral is to the left; medial is upward. See list for abbreviations. Scale bars = 1 mm.

TABLE 3.
Cortical Area Percentages by Hemisphere and Case

Case #	Hemi	17	18/18a	19 (OT)	TP	M1	S1	S2/PV	A1 + AAF	TA
Laboratory Rats (<i>Long Evans</i>)										
07-16	LM	7.11	2.36		1.08	7.32	28.06	5.66	3.80	3.90
07-16	RM	8.83	2.79		2.51	7.65	27.00	4.90	4.52	3.40
07-17	LM	10.16	3.00		1.59	6.71	27.69	5.05	4.21	4.57
07-17	RM	8.56	2.33		1.75	7.29	30.21	6.03	3.89	3.61
08-13	LM	7.91	2.17		1.24	6.91	31.07	4.78	4.68	3.75
08-13	RM	6.85	2.08		2.37	6.36	29.43	6.68	6.42	3.56
08-27	LM	8.51	2.10		1.25	8.87	28.57	5.30	N/A	N/A
08-27	RM	7.66	2.56		1.48	8.99	27.96	6.30	4.69	3.95
08-32	LM	8.85	1.94		1.20	8.40	23.77	N/A	3.88	2.77
08-32	RM	7.34	1.83		1.23	9.70	28.29	3.43	5.05	3.59
08-33	LM	6.53	2.13		1.20	9.44	27.87	4.82	4.02	3.26
08-33	RM	6.55	1.79		1.35	8.81	26.69	4.78	3.42	3.43
Mean %		7.91	2.26		1.52	8.04	28.05	5.25	4.41	3.62
SEM		0.32	0.11		0.14	0.33	0.53	0.27	0.25	0.14
Wild Rats (<i>Rattus norvegicus</i>)										
07-69	LM	7.00	2.14		1.36	7.06	26.23	6.38	3.15	4.23
07-69	RM	9.99	2.01		2.15	11.15	22.20	4.22	2.82	2.35
08-49	LM	7.73	2.40		2.17	8.56	21.54	6.16	3.08	3.84
08-49	RM	7.67	1.57		1.97	9.19	20.94	5.73	2.94	4.00
09-76	LM	8.69	1.36		1.19	6.18	24.94	5.73	2.72	4.26
09-76	RM	8.03	1.32		1.59	11.79	30.01	4.36	5.40	3.16
09-78	LM	6.70	2.06		1.65	8.67	27.12	5.26	4.68	2.91
09-78	RM	6.53	2.00		1.51	7.57	28.31	5.85	3.20	4.76
09-82	LM	6.94	1.43		1.17	8.71	27.26	5.04	3.00	4.49
09-82	RM	9.23	1.89		1.96	9.11	26.83	4.60	2.34	5.43
09-83	LM	7.24	2.02		1.60	9.38	23.13	4.39	2.51	3.64
09-83	RM	8.46	1.86		1.52	12.75	26.74	5.12	3.08	3.54
Mean		7.85	1.84		1.65	9.18	25.44	5.24	3.24	3.88
SEM		0.31	0.10		0.10	0.55	0.83	0.21	0.26	0.24
California Ground Squirrels (<i>Spermophilus beecheyi</i>)										
06-134	LM	9.41	6.12	0.00	5.57	3.45	19.87	3.48	1.52	4.79
07-128	LM	11.76	5.33	6.27	4.80	3.78	14.60	4.31	1.22	5.52
07-128	RM	13.77	7.08	4.95	5.45	4.56	14.16	2.93	1.45	4.24
09-42	LM	8.04	4.07	N/A	5.47	4.28	19.62	3.26	1.56	4.48
09-42	RM	10.49	4.40	4.95	5.95	5.71	19.66	N/A	1.05	4.12
09-69	LM	11.36	4.34	4.28	4.77	4.22	18.45	3.72	1.06	3.41
09-69	RM	11.05	4.42	3.58	5.83	5.91	19.96	3.37	1.13	4.50
09-70	LM	10.48	6.21	N/A	5.44	9.69	22.48	N/A	N/A	N/A
09-70	RM	12.76	5.71	N/A	7.10	6.31	18.98	4.85	1.51	3.30
Mean		11.01	5.30	4.81	5.60	5.32	18.64	3.70	1.31	4.29
SEM		0.57	0.35	0.44	0.23	0.64	0.89	0.25	0.08	0.25
Eastern Gray Squirrel (<i>Sciurus carolinensis</i>)										
09-44	LM	11.54	8.30	7.39	6.60	4.29	16.28	4.00	1.72	4.03
09-44	RM	10.80	4.78	6.78	3.43	5.09	15.59	2.53	1.78	3.03
09-46	LM	12.92	5.70	N/A	4.04	3.78	15.18	2.57	0.95	3.93
09-46	RM	13.74	5.60	N/A	4.00	4.92	15.16	2.70	1.64	3.77
09-152	LM	12.16	4.48	N/A	4.44	5.00	16.01	1.62	2.83	3.67
09-152	RM	13.35	6.53	5.67	3.03	3.82	14.56	1.76	2.71	3.66
09-153	LM	12.81	6.00	N/A	3.94	3.62	14.15	1.80	2.49	3.02
09-153	RM	14.52	7.57	5.67	5.79	4.14	13.93	2.20	2.68	3.07
Mean		12.73	6.12	6.38	4.41	4.33	15.11	2.40	2.10	3.52
SEM		0.42	0.46	0.43	0.42	0.21	0.30	0.27	0.24	0.15

for the wild-caught Norway rat (1.21 ± 0.04) compared with the mean EQ of the laboratory Norway rat. The California ground squirrel mean EQ (1.41 ± 0.10) was significantly larger compared with the laboratory Norway rat mean EQ but significantly smaller than the Eastern gray squirrel mean EQ.

Taken together, these data demonstrate that wild-caught rats have a larger brain-to-body weight ratio and cortical hemisphere-to-total brain percentage than the same species of laboratory-reared rats. They also demonstrate that tree squirrels have a larger EQ than all the other rodent species.

TABLE 4.
Table of F-values and Significance level for one-way ANOVA

	F		significance	Group Differences (Tukey's HSD)		
17	(3,37)	34.618	<.001	Rat < squirrel	Gray squirrel < tree squirrel	
18	(3,37)	70.639	<.001	Rat < squirrel		
OT (19)	(1,7)	6.256	0.04		Gray squirrel < tree squirrel	
TP	(3,37)	87.184	<.001	Rat < squirrel	Gray squirrel > tree squirrel	
Visual cortex (17 and 18)	(3,37)	67.626	<.001	Rat < squirrel	Gray squirrel < tree squirrel	
Visual cortex (17, 18, OT, TP)	(3,29)	151.095	<.001	Rat < squirrel	Trend Gray squirrel < tree squirrel, <i>P</i> = .08	
M1	(3,37)	21.671	<.001	Rat > squirrel		
S1	(3,37)	67.643	<.001	Rat > squirrel	Gray squirrel > tree squirrel	Lab rat > wild rat
S2/PV	(3,34)	28.202	<.001	Rat > squirrel	Gray squirrel > tree squirrel	
Somatosensory cortex	(3,34)	101.449	<.001	Rat > squirrel	Gray squirrel > tree squirrel	Lab rat > wild rat
A1 + AAF	(3,35)	31.874	<.001	Rat > squirrel		Lab rat > wild rat
TA	(3,35)	2.388	0.085			
Auditory Cortex	(3,35)	18.079	<.001	Rat > squirrel		
Brain-to-Body	(3,17)	8.553	0.001		Tree squirrel > lab rat	Lab rat > wild rat
Hemispheres-to-brain	(3,17)	4.242	0.021		Tree squirrel < wild rat	Lab rat < wild rat
EQ	(3,18)	25.137	<.001	Lab rat < tree squirrel	Gray squirrel < tree squirrel	Lab rat < wild rat

Determination of cortical field boundaries and relative size of cortical areas between rodent groups

Cortical fields are defined by a collection of criteria including information on function, architecture, and connectivity. Specifically, primary sensory areas can be defined as containing a complete representation of the sensory receptor array for a specific modality (sense), having a highly myelinated and densely cell-packed layer IV, and having connections with modality (sensory)-specific thalamic nuclei and other cortical areas. In this study, the degree of myelination was used to delineate cortical field boundaries (Figs. 3, 4). The relationship between architectonic boundaries and functionally defined cortical fields has been described previously for visual, somatosensory, and auditory cortex in Eastern gray squirrels (Hall et al., 1971; Kaas et al., 1972, 1989; Krubitzer and Kaas, 1987; Krubitzer et al., 1986; Luethke et al., 1988; Merzenich et al., 1976; Nelson et al., 1979; Sur et al., 1978; Wong and Kaas, 2008); for visual, somatosensory, and motor cortex in California ground squirrels (Cooke et al., 2010; Paolini and Sereno, 1998; Slutsky et al., 2000); and for visual, somatosensory, and auditory cortex in Long-Evans laboratory Norway rats (Adams and Forrester, 1968; Coogan and Burkhalter, 1993; Espinoza and Thomas, 1983; Malach, 1989; Remple et al., 2003; Roger and Arnault, 1989; Rumberger et al., 2001). Complete statistics for relative size of cortical areas can be found in the following tables and figures: for area percentages by case see Table 3, for F values see Table 4, and for area percentages by rodent group see Figure 7.

Visual cortex consists of cortical areas that process predominantly visual inputs (rather than multimodal

inputs), and in rodents this generally consists of two areas; the primary visual area (17) and the second architectonic visual area (18). Other extrastriate cortical areas have been described for both squirrels and rats, and these are detailed below.

Primary visual area 17

Brodman's area 17 is coextensive with the functionally defined primary visual area, V1 and has been delineated in every mammal examined by various methods and techniques (see, e.g., Allman and Kaas, 1971; Caviness, 1975; Coogan and Burkhalter, 1993; Hall et al., 1971; Hubel and Wiesel, 1968; Kahn et al., 2000; Karlen and Krubitzer, 2007; Payne, 1993; Wagor et al., 1980). Area 17, located caudomedially in the occipital pole, is easily delineated with a myelin stain; it is heavily myelinated and thus stains more darkly than surrounding areas (Fig. 4). In both the laboratory and the wild-caught rats, area 17 is a darkly myelinated, wedge-shaped area that is homogeneous in appearance. In contrast, area 17 in both species of squirrel can be readily compartmentalized into a binocular and a monocular zone (Figs. 4C, 8). The medially located monocular zone is more lightly stained compared with the more laterally located binocular zone. Furthermore, the amount of cortex occupied by each zone is different in the different squirrels. The Eastern gray squirrel has a larger binocular zone than the California ground squirrel, as has been documented in previous studies (Paolini and Sereno, 1998; Sereno et al., 1991).

Measurements of area 17 indicate that the mean proportion of dorsolateral cortex occupied by area 17 in the laboratory Norway rat was not statistically significantly different from that of the wild-caught rat (see Tables 3, 4,

Fig. 7A for measurements). The Eastern gray squirrel has a significantly larger mean percentage ($12.73\% \pm 0.42\%$) of the dorsolateral cortex devoted to area 17 compared with the California ground squirrel mean ($11.01\% \pm 0.57\%$; Tukey's HSD, $P < 0.05$), and both species of squirrels have a larger mean percentage of the dorsolateral cortex devoted to area 17 compared with the two rat groups.

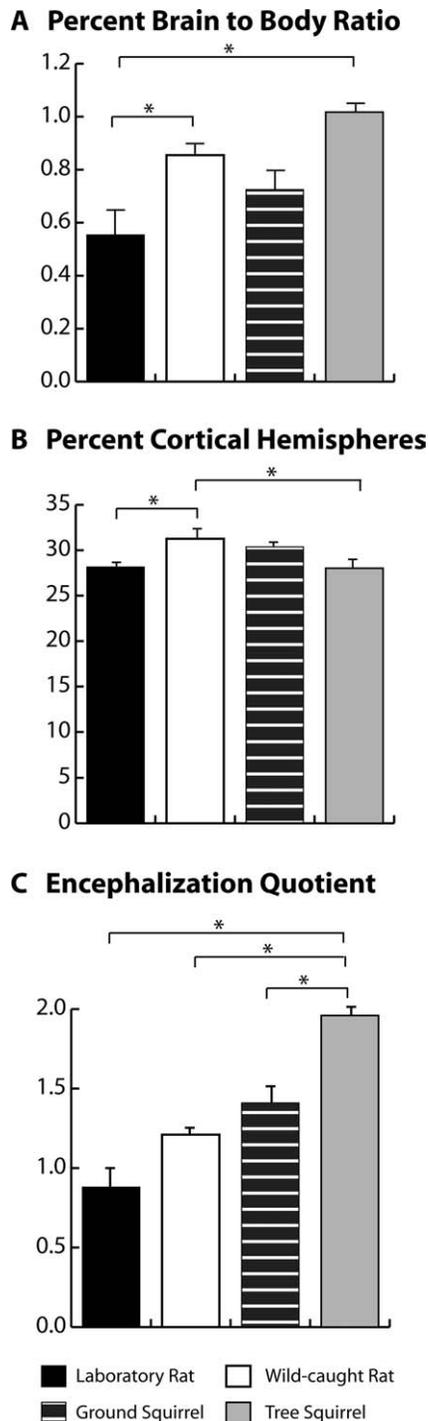


Figure 6

Second visual area 18

Just lateral to area 17/V1 is an architectonically distinct area 18 in all mammals examined (Allman and Kaas, 1974; Hall et al., 1971; Malach, 1989; Rosa et al., 1999; Tiao and Blakemore, 1976; Tusa et al., 1979; Wagor et al., 1980). Area 17 extends to and wraps the medial wall, except in mice and rats, in which two areas surround area 17; area 18a is lateral and area 18b is medial to area 17. For most mammals, area 18b is simply termed *area 18*, and we have done so for this study. In most mammals examined, area 18 is coextensive with a functionally defined area V2 containing a mirror representation of the visual hemifield joined at the vertical meridian with the V1 representation (however, see Espinoza and Thomas, 1983, for alternate interpretation for rats and mice; Wang and Burkhalter, 2007). Area 18 is a rectangular strip of cortex located lateral to area 17. In rats it can be distinguished in cortical sections stained for myelin because it stains less darkly for myelin than area 17 just medial to it but stains more darkly for myelin than surrounding cortex lateral and anterior to it. In squirrels, area 18 is moderately myelinated, and, in favorable preparations in Eastern gray squirrels, alternating dark and light patches can be identified (Fig. 4).

There is no difference in the percentage of cortical sheet devoted to area 18 between laboratory ($2.3\% \pm 0.11\%$) and wild-caught Norway rats ($1.8\% \pm 0.10\%$), nor between California ground squirrel ($5.3\% \pm 0.35\%$) and Eastern gray squirrel ($6.1\% \pm 0.46\%$). However, post hoc comparisons show that the mean percentage of the cortical sheet devoted to area 18 is larger in the squirrel group compared with the rat group.

Temporal posterior area (TP)

A third distinct architectonic visual region was identified in all of the species examined in this study. The field

Figure 6. Histograms of mean percentage for brain-to-body ratios (A), hemispheres-to-whole brain percentages (B), and EQ (C). In all histograms, the x-axis is the rodent group. In A, the y-axis is percentage of brain weight to body weight; in B, the y-axis is percentage of hemisphere weight to whole-brain weight; and, in C, the y-axis is the quotient ratio. The key to bar colors is at right. Laboratory Norway rats are represented by solid black bars. Wild-caught Norway rats are represented by solid white bars. California ground squirrels are represented by black bars with white stripes. Eastern gray squirrels are represented by gray bars. Wild-caught rats have a significantly larger brain to body weight and percentage of cortical hemisphere compared with laboratory rats. Tree squirrels have a significantly larger brain to body weight and percentage of cortical hemisphere to whole brain compared with laboratory rats and wild rats, respectively. Tree squirrels have a significantly larger EQ compared with all of the rodents studied. Error bars represent SEM. Asterisk indicates a significant, $P < 0.05$, difference.

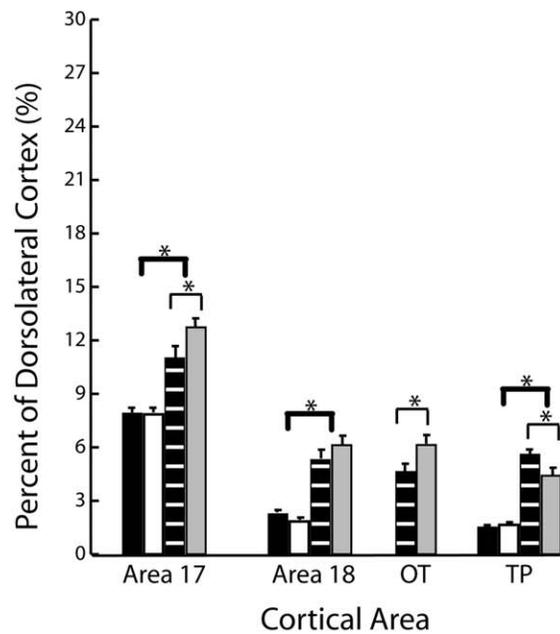
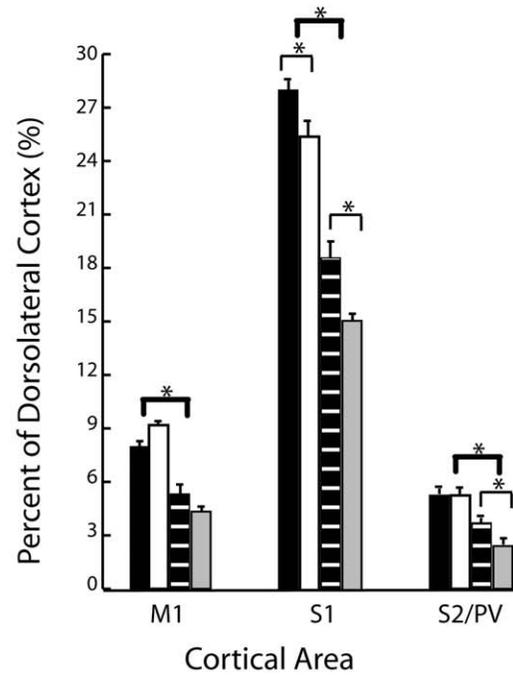
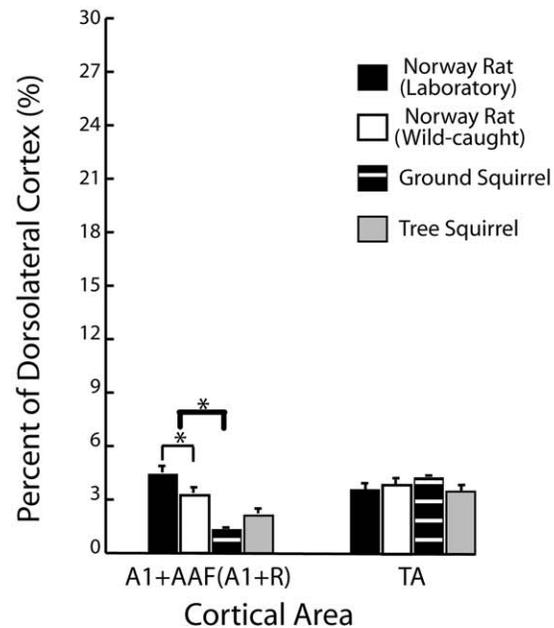
A Dorsolateral Cortex Devoted to Visual Areas**B Dorsolateral Cortex Devoted to Somatosensory/Motor Areas****C Dorsolateral Cortex Devoted to Auditory Areas**

Figure 7. Histograms showing the percentage of dorsolateral cortex devoted to visual (A), somatosensory/motor (B), and auditory sensory (C) areas in each species. The x-axis for all histograms shows the specific area of cortex, and the y-axis shows the percentage of neocortex. The key to bar colors is at right. Laboratory Norway rats are represented by solid black bars. Wild-caught Norway rats are represented by solid white bars. California ground squirrels are represented by black bars with white stripes. Eastern gray squirrels are represented by gray bars. Significant differences are observed both between groups and between animals for visual, somatosensory, and auditory cortices. Error bars represent SEM. Significant differences between squirrel groups and rat groups are depicted with a thick line with an asterisk above, and significant differences between animals are indicated by a thin line with asterisk above. Asterisk indicates a significant, $P < 0.05$, difference. See list for abbreviations.

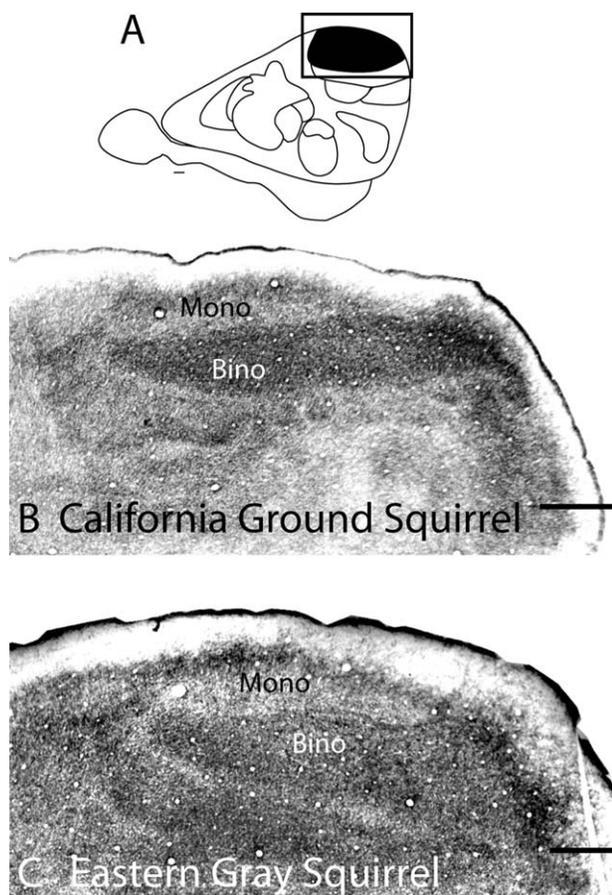


Figure 8. A: Diagram of the dorsolateral cortex in squirrel. The box shows area of magnification for B and C. Photomicrographs of myelin-stained cortical sections showing area 17 in the California ground squirrel (B) and Eastern gray squirrel (C). The monocular (mono) and binocular (bino) segments have been labeled. In both animals, the binocular segment is more darkly myelinated and located laterally. Caudal is to the right; medial is upward. Scale bars = 1 mm.

has been termed the *temporal posterior area* in previous studies, and projections from the visual thalamus and limited electrophysiological recordings in this field indicate that is associated with visual processing (Kaas et al., 1972; Robson and Hall, 1977; Wong and Kaas, 2008). TP is a darkly staining, triangular area located in the temporal pole of cortex caudomedial to auditory cortex in both rat groups and directly caudal to auditory cortex in both squirrel groups (Fig. 9).

The mean percentage of dorsolateral cortex occupied by TP is not different between the laboratory Norway rat ($1.5\% \pm 0.14\%$) and the wild-caught Norway rat ($1.8\% \pm 0.10\%$; Fig. 7A). However, the mean percentage of dorsolateral cortex occupied by TP in the California ground squirrel ($5.6\% \pm 0.23\%$) is significantly larger compared with the mean in the Eastern gray squirrel ($4.4\% \pm 0.42\%$). The difference in means of the percentage of the

cortical sheet devoted to TP between rats and squirrels is also significantly different, with squirrel groups having a larger mean percentage of the cortical sheet devoted to TP than rat groups.

Occipitotemporal area (area 19)

Just lateral to area 18 and rostral to TP is architectonic area 19. This architectonic region has been demonstrated to contain neurons responsive to visual stimulation and to receive direct inputs from V1 in squirrels, and it is coextensive with the functional area termed the *occipitotemporal area* (Kaas et al., 1972, 1989; Wong and Kaas, 2008). This area can be subdivided into rostral and caudal portions based on myeloarchitecture and connection patterns. In the present investigation, the rostral portion of OT is a more darkly staining, elongated oval area lateral to area 18. The caudal portion of OT was slightly less myelinated than OTr rostrally. The rostral and caudal portions of OT could not be delineated from each other in all cases. Therefore, for comparison purposes between the two groups of squirrels, OT was considered as one area.

Statistical analysis indicated that Eastern gray squirrels have a significantly larger mean percentage ($6.4\% \pm 0.43\%$) of dorsolateral cortex occupied by OT compared with the mean ($4.8\% \pm 0.44\%$) of California ground squirrels (Fig. 7A). Area 19 has not been identified, to our knowledge, in small nocturnal rodents such as the prairie vole, mouse, or rat (Campi et al., 2007, 2009; Caviness, 1975; Krieg, 1946).

When areas 17 and 18 are considered together, post hoc analysis indicates that there is no difference in the mean percentage of cortex occupied by visual areas in laboratory Norway rats ($10.2\% \pm 0.45\%$) compared with wild-caught Norway rats ($9.7\% \pm 0.38\%$). However, the mean percentage of dorsolateral cortex occupied by visual areas is smaller in California ground squirrels ($16.3\% \pm 0.88\%$) than in Eastern gray squirrels ($18.9\% \pm 0.99\%$). Further post hoc analysis shows that, as a group, squirrels have a larger amount of dorsolateral cortex devoted to visual areas than do rats.

When the four visual areas, 17, 18, OT, and TP, are considered together, post hoc analysis indicates that there is no difference in the mean percentage of cortex occupied by visual areas in laboratory Norway rats ($11.7\% \pm 0.45\%$) compared with wild-caught Norway rats ($11.3\% \pm 0.38\%$). However, the mean percentage of dorsolateral cortex occupied by visual areas was not significant but did have a trend toward significance, $P = 0.08$, in California ground squirrels ($27.0\% \pm 1.24\%$) compared with Eastern gray squirrels ($30.4\% \pm 1.96\%$). Further post hoc analysis indicates that, as a group, squirrels have a significantly larger amount of dorsolateral cortex devoted to visual areas than do rats.

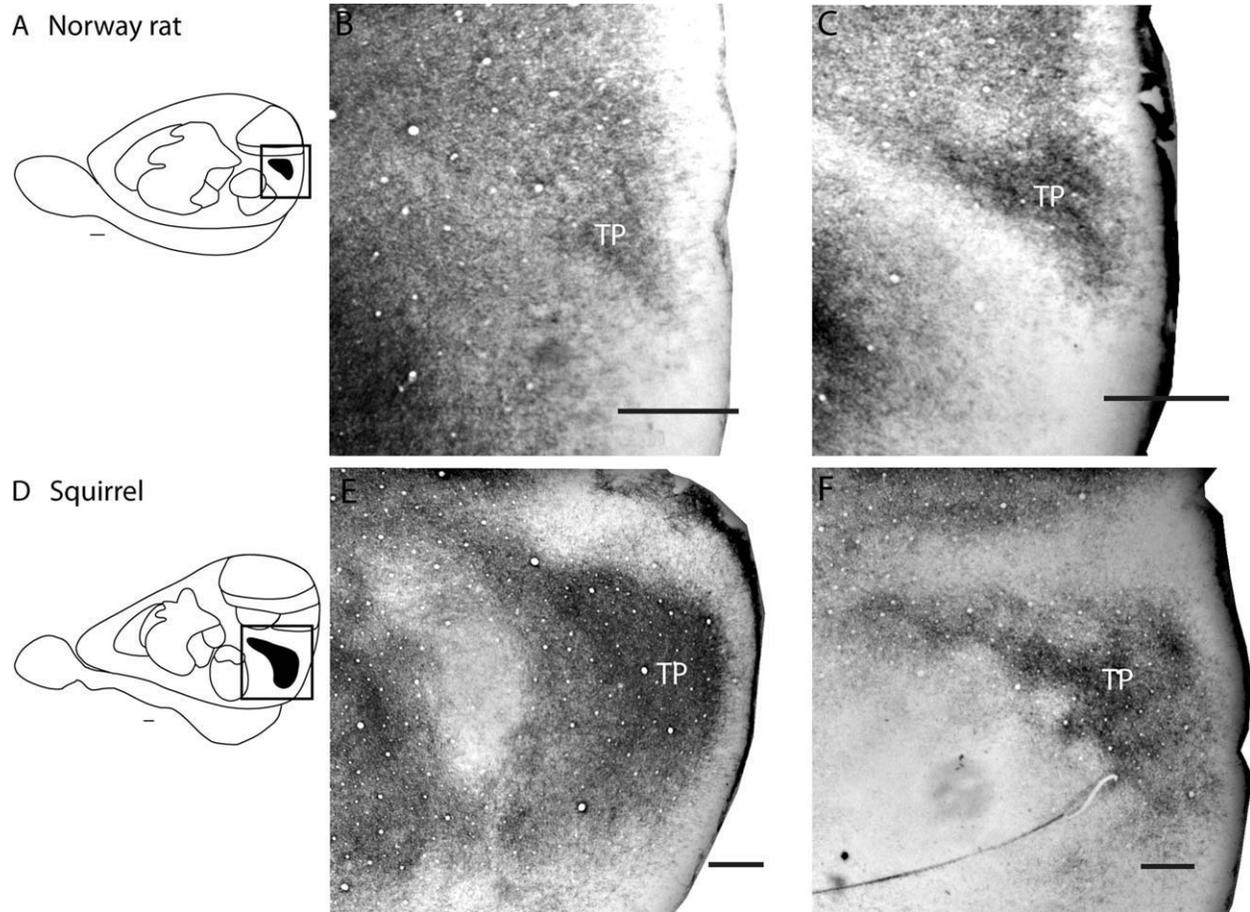


Figure 9. Photomicrographs of myelin-stained cortical sections highlighting area TP in each rodent group. **A:** Diagram of the dorsolateral cortex in Norway rat. The box shows area of magnification for the Laboratory Norway rat (**B**) and the wild-caught Norway rat (**C**). **D:** Diagram of the dorsolateral cortex in squirrels. The box shows area of magnification for the California ground squirrel (**E**) and the Eastern gray squirrel (**F**). In all animals examined, TP is a darkly myelinated, triangular wedge located caudally near the edge of the cortical section. Caudal is to the right; medial is upward. See list for abbreviations. Scale bars = 1 mm.

Somatosensory/motor cortex

Somatosensory cortex in rodents consists of three areas, the primary somatosensory area (S1), the secondary somatosensory area (S2), and the parietoventral area (PV). We delineated primary motor cortex (M1) in all four groups and a region interspersed between S1 and M1, area 3a, in both squirrel groups. The addition or absence of 3a in quantitative analysis did not change the result for either S1 or M1 comparisons. Therefore, 3a was not included in quantitative comparisons.

Primary somatosensory area S1

A primary somatosensory area, S1 or area 3b, has been delineated in every mammal examined by various methods and techniques (Catania et al., 2000; Chapin and Lin, 1984; Felleman et al., 1983; Hunt et al., 2006; Kaas, 1983; Karlen and Krubitzer, 2007; Krubitzer et al., 1986; Nussbaumer and Van der Loos, 1985; Remple et al., 2003; Sur et al., 1978; Welker, 1971; Wong and

Kaas, 2008; Woolsey, 1967). In the present investigation, S1 was similar in appearance in all animals examined, with certain distinct features displayed in some species. S1 is a large, irregularly shaped, darkly myelinated area that is interspersed with lightly myelinated bands (Fig. 10). In some species, such as rats, this area contains the highly recognizable, anatomically specialized “barrel” cortex (Welker, 1971; Woolsey and Van der Loos, 1970; Woolsey et al., 1975; Fig. 11A–D). S1 has a roughly similar shape in all four rodents that we examined and is narrow at its medial pole and widens through the middle and lateral edge (Fig. 10). In both the laboratory and the wild-caught rats, S1 has patches of dark and light myelin staining. Previous studies have demonstrated that these patches coincide with dark and light patches of CO and serotonin reactivity and that these isomorphs represent specific body parts (for review see Catania, 2002). The medial portion of S1 is roughly one-half to one-third of the rostral to caudal width of the lateral portion. Although

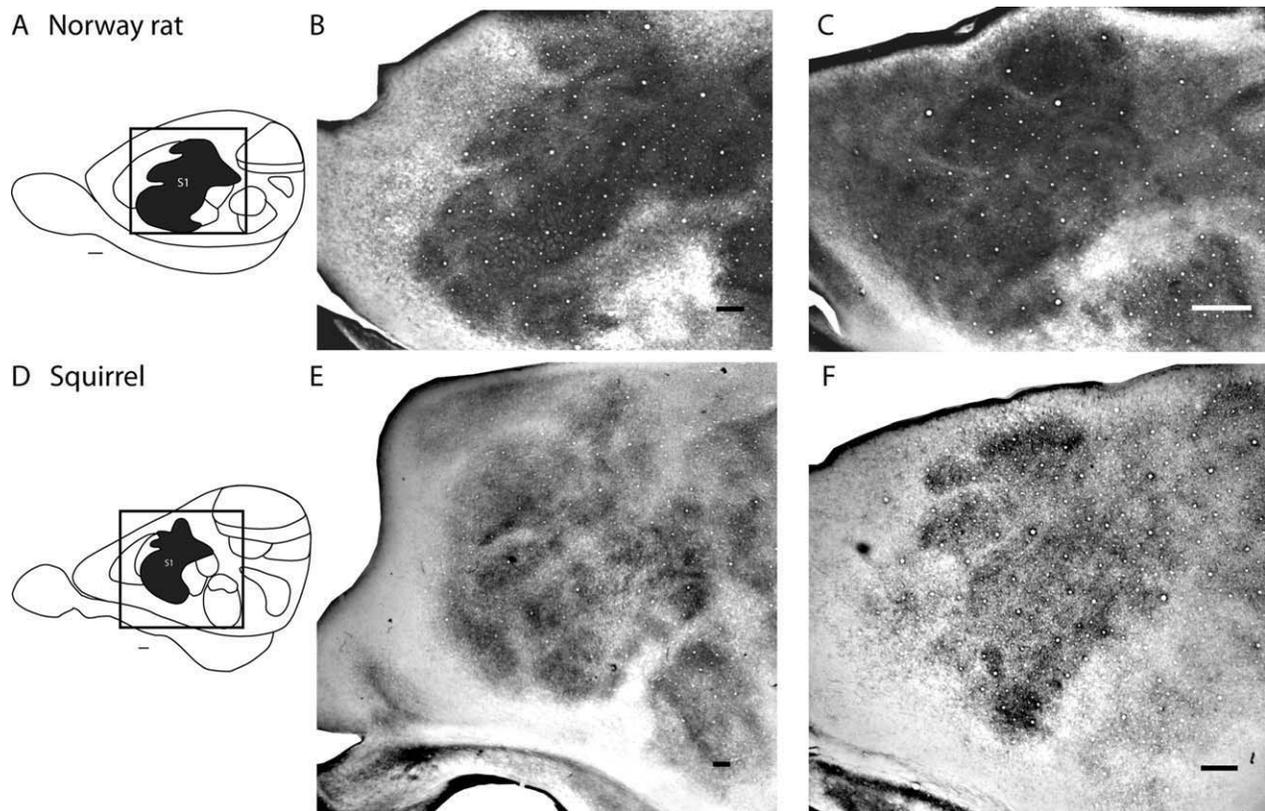


Figure 10. Photomicrographs of myelin-stained cortical sections highlighting area S1 in each rodent group. In all animals, S1 is narrow at its medial pole and widens through the middle and lateral edge with patches of dark and light myelin staining. These patches or isomorphs represent specific body parts. **A:** Diagram of the dorsolateral cortex in Norway rat. The box shows area of magnification for the Laboratory Norway rat (**B**) and the wild-caught Norway rat (**C**). **D:** Diagram of the dorsolateral cortex in squirrels. The box shows area of magnification for the California ground squirrel (**E**) and the Eastern gray squirrel (**F**). Caudal is to the right; medial is upward. See list for abbreviations. Scale bars = 1 mm.

all four rodents examined have a characteristic barrel field located in the middle of S1, it is more distinct in both groups of rats than in squirrels (Fig. 11).

In both wild-caught and laboratory Norway rats, the barrels stain darkly for CO (Fig. 11A,C), and very lightly for myelin (Fig. 11B,D). Thus, the myelin appears as a negative image of the CO stains. Light CO barrels are also visible in California ground squirrels (Fig. 11E) but are very indistinct in myelin stains (Fig. 11F). Finally, although we processed numerous hemispheres in the Eastern gray squirrel, we could not identify any CO barrels, and only a hint of barrels was present in our myelin stains (Fig. 11G,H). This has been noted previously in the Eastern gray squirrel by Wong and Kaas (2008) and Woolsey et al. (1975).

Each species showed a different percentage of dorso-lateral cortex occupied by S1, and these differences all reached statistical significance (Fig. 7B). Laboratory-reared Norway rats had the largest percentage, followed by the wild-caught Norway rat, and the ground squirrel and the tree squirrel had the smallest percentage of cortex devoted to S1.

Second somatosensory area and the parietal ventral area S2 and PV

Two functional areas, the second somatosensory area (S2) and the parietoventral area (PV), have been identified in rodent somatosensory cortex and are located caudolateral to S1 (Benison et al., 2007; Brett-Green et al., 2004; Fabri and Burton, 1991; Hunt et al., 2006; Krubitzer et al., 1986; Remple et al., 2003). S2 contains a mirror representation of the body surface of S1 and adjoins the snout representation of S1 at its caudolateral boundary. PV contains a mirror representation of the body surface of S2. In the rodents that we examined, these areas were moderately myelinated and oval, as has been previously described. The rostral boundaries of these areas are readily distinguished from darkly myelinated S1, and the caudal boundaries of these fields can also be distinguished because cortex immediately caudal is lightly myelinated. The anatomical boundary separating S2 and PV was delineated and drawn for both squirrel species (Figs. 4, 5). However, in both rat groups, it was sometimes difficult to distinguish the boundary separating S2 from PV. In

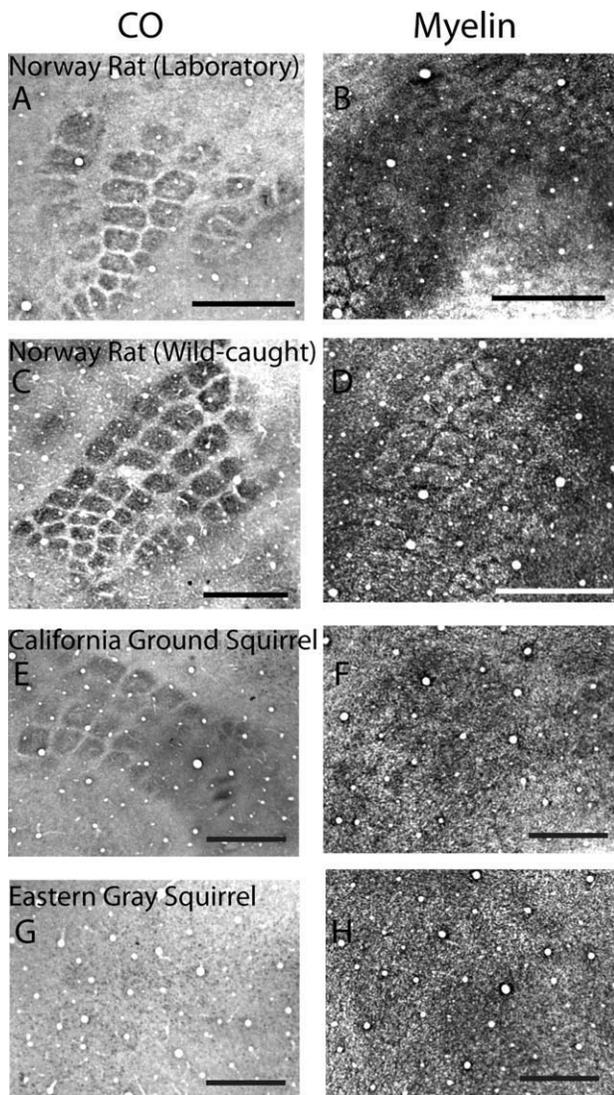


Figure 11. Photomicrographs of barrel cortex for each rodent group as seen in CO-stained (left column) and myelin-stained (right column) tissue. In laboratory Norway rats (A,B) and wild-caught Norway rats (C,D), barrel cortex is distinct in both CO and myelin stains. The myelin-stained barrels are hollow and appear to be a negative of the dense CO barrels. In California ground squirrels (E,F), the barrel cortex can be observed in CO stains (E) but is less distinct in myelin stains compared with CO stains and compared with rats. In the Eastern gray squirrel (G,H), barrel cortex is absent in CO-stained tissue (G) and indistinct in myelin-stained tissue (H). Caudal is to the right; medial is upward. See list for abbreviations. Scale bars = 1 mm.

these cases, we did not draw a boundary, and for statistical analysis these areas were combined for each individual hemisphere.

The mean percentage of dorsolateral cortex occupied by S2/PV was not different between the two types of rats or the two species of squirrels. However, when rats as a group are compared with squirrels as a group using post hoc analysis, it is found that rats have a significantly

larger mean percentage of dorsolateral cortex devoted to S2/PV than squirrels.

When S1, S2, and PV are considered as a group, the mean percentage of dorsolateral cortex occupied by somatosensory areas in the laboratory Norway rats ($33.7\% \pm 0.53\%$) compared with wild-caught Norway rats ($30.7\% \pm 0.83\%$) is not significantly different. The mean percentage of dorsolateral cortex occupied by somatosensory areas in the California ground squirrels ($21.7\% \pm 0.98\%$) is significantly larger, as indicated by post hoc analysis, than in Eastern gray squirrels ($17.5\% \pm 0.50\%$). When rats as a group are compared with squirrels as a group, the mean percentage of cortex devoted to somatosensory areas is significantly larger in rats than in squirrels.

The mean percentage of dorsolateral cortex occupied by M1 in the laboratory Norway rat ($8.0\% \pm 0.33\%$) is not statistically different from the mean percentage in the wild-caught Norway rat ($9.2\% \pm 0.55\%$). The difference in the percentage of dorsolateral cortex occupied by M1 in the California ground squirrel ($5.3\% \pm 0.64\%$) is not significantly different from the mean percentage in the Eastern gray squirrel ($4.3\% \pm 0.21\%$). When rats as a group are compared with squirrels as a group using post hoc analysis, it is found that rats have a significantly larger mean percentage of dorsolateral cortex devoted to M1 than do squirrels.

Auditory cortex

Auditory cortex in mammals generally consists of architectonically distinct core and belt auditory areas. To our knowledge, the parabelt areas in carnivores and primates have not been delineated in rodents.

Core auditory cortex

The core auditory region in rodents generally contains two auditory fields that contain mirror representations of the species-specific auditory frequency range. These areas include the primary auditory area, A1, and the anterior auditory field, AAF, in mice (Caviness, 1975; Stiebler et al., 1997), Mongolian gerbils (Budinger et al., 2006; Thomas et al., 1993), and rats (Kalatsky et al., 2005; Polley et al., 2007; Rutkowski et al., 2003) and in A1 a rostral field termed *R* for squirrels (Luethke et al., 1988; Merzenich et al., 1976). A1 has been defined in all mammals examined and is located caudally in the core. The anterior auditory field (AAF in rats) or rostral field (*R* in squirrels) is located anterior to A1. In the present study, for all species, we could readily identify a darkly myelinated, oval core auditory area caudal to the more lightly myelinated S2/PV and medial to the more lightly myelinated TA (Fig. 12). A1 and AAF are not distinguishable based on myeloarchitecture and are considered here in aggregate.

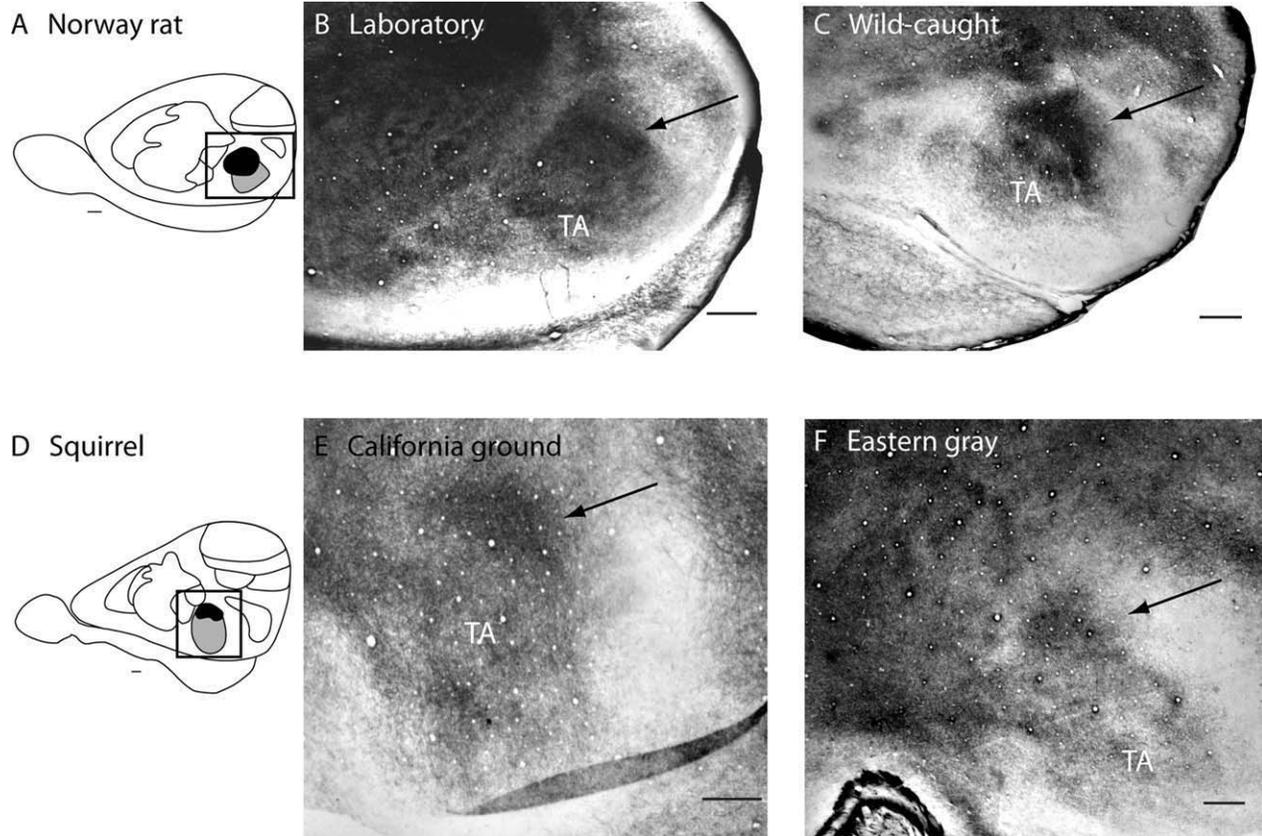


Figure 12. Photomicrographs of myelin-stained cortical sections highlighting auditory cortex (AC) in each rodent group. Only a caudal portion of each section is shown to highlight AC for each rodent group. A1 + AAF (R) is a darkly myelinated, oval core auditory area (arrow) medial to the more lightly myelinated TA. A1 and AAF (R) are not distinguishable from each other based on myeloarchitecture. **A:** Diagram of the dorsolateral cortex in Norway rat. The box shows area of magnification for the laboratory Norway rat (**B**) and the wild-caught Norway rat (**C**). **D:** Diagram of the dorsolateral cortex in squirrels. The box shows area of magnification for the California ground squirrel (**E**) and the Eastern gray squirrel (**F**). Caudal is to the right; medial is upward. See list for abbreviations. Scale bars = 1 mm.

The mean percentage of dorsolateral cortex occupied by A1 + AAF in the laboratory Norway rat ($4.4\% \pm 0.25\%$; see Tables 3, 4, Fig. 7C for complete results) is significantly larger than the mean percentage of A1 + AAF in the wild-caught Norway rat ($3.2\% \pm 0.26\%$). The mean percentage of dorsolateral cortex occupied by A1 + R in the California ground squirrel ($1.3\% \pm 0.08\%$) is similar to that of the Eastern gray squirrel ($2.1\% \pm 0.24\%$). The mean differences in the percentage of the cortical sheet devoted to A1 + AAF in rat groups was significantly larger than squirrel groups, as indicated by post hoc analysis.

Belt auditory cortex

The areas surrounding the core auditory cortex are collectively referred to as *belt auditory cortex*. This area of cortex can be distinguished by lighter myelin staining surrounding the darker myelin staining of the core. For simplicity, we have chosen the nomenclature used in Campi et al (2009) for rodent auditory cortical areas based on myeloarchitecture in prairie vole, laboratory mouse, labo-

ratory rat, California ground squirrel, and Eastern gray squirrel (see, e.g., Merzenich et al., 1976; Wong and Kaas, 2008), and here refer to this area of cortex as the *temporal anterior area* (TA). TA is an elongated oval area located immediately lateral to the more darkly myelinated A1 + AAF and surrounded on three sides by much more lightly myelinated cortex.

In contrast to all other comparisons made in this report, there was no significant difference in the percentage of dorsolateral cortex devoted to TA in any of the four groups. No significant effect of group was found for the TA comparison.

When A1 + AAF (R) and TA are considered together as auditory cortex, the mean percentage of dorsolateral cortex occupied by auditory fields in the laboratory Norway rats ($7.2\% \pm 0.72\%$) and wild-caught Norway rats ($7.1\% \pm 0.26\%$) is significantly larger compared with both the California ground squirrel ($5.6\% \pm 0.27\%$) and the Eastern gray squirrel ($5.6\% \pm 0.22\%$). No significant differences within the rat or squirrel groups were observed.

Sensory/motor cortex vs. nondelineated cortical area comparison

Here we compare the mean percentage of cortex devoted to well-defined sensory and motor areas described above to the percentage of cortex devoted to nondelineated areas. These nondelineated areas are composed of possibly higher order sensory and/or association areas. Thus, sensory/motor cortex aggregates were measured from areas 17, 18, 19, TP, S1, S2/PV, M1, 3a, A1 + AAF (R), and TA. The mean percentage of dorsolateral cortex occupied by sensory/motor cortex is 61.39% ($\pm 1.18\%$) in laboratory Norway rats, 58.32% ($\pm 1.06\%$) in wild-caught Norway rats, 53.99% ($\pm 1.0\%$) in California ground squirrels, and 50.72% ($\pm 2.1\%$) in Eastern gray squirrels. Comparisons of means between groups indicate that squirrels have a significantly smaller mean percentage of defined sensory/motor dorsolateral cortex and a significantly more nondelineated cortex than do rat groups.

Taken together, our data demonstrate that the mean percentage of cortex devoted to visual areas, including areas 17 and 18, is significantly larger in diurnal squirrels vs. nocturnal rats and that it is larger in the arboreal squirrels compared with terrestrial squirrels (see Fig. 7A). On the other hand, the mean percentage of cortex devoted to somatosensory areas is significantly larger in the nocturnal rodents vs. the diurnal rodents, in the terrestrial squirrels vs. the arboreal squirrels, and in the laboratory vs. the wild-caught rats (see Fig. 7B). Furthermore, the mean percentage of cortex devoted to the primary auditory cortex is significantly larger in the rat groups vs. the squirrel groups and the laboratory vs. the wild-caught rats (see Fig. 7C). Finally, the diurnal squirrels have a larger amount of nondelineated cortex compared with the nocturnal rats.

DISCUSSION

As hypothesized, our results suggest that lifestyle and sensory morphology are reflected in the size and organization of sensory cortical areas as well as in the proportion of cortex devoted to a specific sensory modality. The diurnal rodents have a larger amount of cortex devoted to visual cortical areas compared with nocturnal rodents, and arboreal squirrels have a larger percentage of dorsolateral cortex devoted to visual processing than terrestrial rodents. Although nocturnal rodents have a smaller percentage of cortex devoted to visual cortical areas, they have a larger percentage of cortex devoted to somatosensory and auditory cortex compared with the diurnal rodents. Although a meta-analysis of previous studies of cortical areas in diurnal and nocturnal species came to different conclusions

(see, e.g., Kaskan et al., 2005), this previous study did not control for the type of technique used, number of animals per group, criteria employed, or data analysis techniques utilized for determining cortical field boundaries. We believe that these differences may account for the different results observed in the previous study and in the present investigation. Another interesting observation is that the proportions of cortex devoted to the primary somatosensory and auditory areas are significantly larger in laboratory vs. wild-caught rodents and that the relative brain size as measured by brain-to-body weight ratio and EQ is larger in wild-caught rodents than in the same species of a laboratory-reared animal. A reduction in brain size has previously been shown to correlate with domestication across several species, including rats, pigs, rabbits, ferrets, cats, and dogs (for review see Kruska, 1988). However, the picture is not as clear when considering the percentage of cortical hemisphere weight as a fraction of whole-brain weight. These disparities in the amount of cortex devoted to a specific modality are an excellent example of the flexibility in cortical allocation with increased reliance on a specific sensory modality. First, we discuss our choice of species for comparison. Then, we discuss the delineation of cortical fields and problems specific to defining visual cortical areas in rodents. Finally, we discuss the relationship between lifestyle and cortical field size.

Choice of species for comparison

Our choice of animals for comparing the effects of a diurnal vs. a nocturnal lifestyle was driven by the overlapping habitat, food sources, and climate that all but the laboratory Norway rat shared. Although a comparison of nocturnal squirrels with diurnal squirrels or conversely nocturnal rats with diurnal rats would allow us better to disentangle phylogeny from lifestyle effects on the visual cortex organization in rodents, there are important factors that would make interpretation of these results difficult. Most notably, the nocturnal squirrels (i.e., flying squirrel) and diurnal rats (i.e., the Nile grass rat) have a highly derived and evolutionarily mixed form of the nocturnal and diurnal visual system (see Fig. 2 for phylogenetic relationships between species). Examination of opsin genes has demonstrated that the genes for the shortwave-sensitive (SWS1) class of visual pigments differs between rats and squirrels but not between nocturnal and diurnal species of each group (Carvalho Ldos et al., 2006; Gaillard et al., 2009). Murid rodents have a nocturnal ancestor, and species within this group have the SWS1 opsin sensitive to UV light. Sciurid rodents have a diurnal ancestor, and species within this group have the gene for the SWS1 opsin sensitive to violet light. The difference in the diurnal and nocturnal rat and

squirrel visual systems manifests in the cone-to-rod ratio (Gaillard et al., 2009; Jacobs et al., 1976). The nocturnal squirrels would represent a diurnal system that has lost or regressed partially to a nocturnal system, and diurnal rats would represent a nocturnal system that has partially changed to a diurnal system. Although these systems are interesting and worthy of study, we chose to compare the organization of nocturnal and diurnal visual systems that would exhibit the greatest contrast in visual systems specifically evolved for that particular niche.

Relationships among cortical field size, number, and lifestyle

The relationship between peripheral morphology and use and aspects of cortical organization such as magnification factors within a field, cortical field size, and cortical field number has been well established (for review see Krubitzer, 2007). Probably the most ubiquitous example of this relationship comes from the rodent barrel cortex in S1. Previous studies have demonstrated that the representation of the vibrissae in murine rodents is magnified in S1 and that this magnification is associated with both high innervation density of the whiskers and use (Welker and Van der Loos, 1986a,b). We add here that this magnification likely contributes to the overall increase in the size of S1 in both laboratory and wild-caught rodents. Other examples of specialization of rodent somatosensory cortex indicate that there are similar principles of magnification. For example, about 30% of the S1 representation in the naked mole rat is devoted to the incisor representations (Catania and Remple, 2002). Although increased innervation of the periodontal ligament has not been identified in the mole rat, heavy and specialized use of the incisors has been demonstrated and posited as the reason for the cortical magnification (Henry et al., 2006). Specialized use in combination with dense innervation has also been linked with cortical magnification such as that demonstrated in the star-nosed mole. The star-nosed mole's eleventh star appendages on the left and right sides are the most highly innervated and the most used of the 22 appendages and have the largest representation in S1 (Catania and Remple, 2004; Sachdev and Catania, 2002).

With respect to the current study, rats and squirrels differ both in their visual and somatic sensory morphology and behavior and in their diel pattern (diurnal vs. nocturnal). Rats with a photoreceptor complement of 80% rods are well suited to a nocturnal lifestyle, and they explore their environment through primarily whisking, a repetitive back and forth motion of their mystacial vibrissae or whiskers (for review see Diamond et al., 2008). The relationship between use of mystacial vibrissae and anatomi-

cal distinctness of the barrel cortex has been demonstrated in comparative studies across several mammalian orders (Woolsey et al., 1975). In general, a distinct barrel cortex is observed in rodents known to exhibit whisking behavior, and the barrels are absent or indistinct in rodents that do not exhibit whisking behavior regardless of brain size. Thus behavior appears to be a good predictor for the emergence of barrels. Results from the current study support this hypothesis by demonstrating distinct barrels in the whisking laboratory and wild rats and an absence or lack of distinction of barrels in squirrels.

On the other hand, squirrels rely more on their visual system for navigation and object identification. In fact, it has been proposed that diurnal squirrels are the ideal rodent model for examination of visual cortex (Van Hooser and Nelson, 2006). As noted previously, squirrels have two-cone color vision, a well-laminated LGN, and a distinct laminar organization in V1. Behaviorally, California ground squirrels use visual and odor cues to identify and react to snakes (Hennessy and Owings, 1978; Mitrovich and Cotroneo, 2006). Furthermore, Eastern gray squirrels rely a great deal on vision for jumping between branches and predator identification (Koprowski, 1994). This greater reliance on vision is reflected in the larger proportion of the cortical sheet devoted to areas 17 and 18 in the arboreal squirrel compared with the terrestrial squirrel (present study). We conclude, based on previous research and our own data, that differences in cortical sheet allocation for sensory cortex in diurnal and nocturnal as well as arboreal and terrestrial rodents are due to alterations in both sensory morphology and behaviors associated with this morphology. Both of these are components of the more general term *lifestyle*. What is not clearly understood is how these lifestyle components drive alterations in the cortical phenotype or whether and how these become genetically encoded and evolve. The alternative is that the large alterations in terms of relative size of cortical fields and the amount of cortical space allocated by any one sensory system is largely context dependent and persists only in stable environments (for review see Krubitzer and Kaas, 2005).

One way to address this issue would be to examine genetically identical (or highly similar) animals that have radically different lifestyles. Our comparison between wild-caught and laboratory Norway rats suggests that some aspects of organization are in fact context dependent, because large differences in the relative size of the brain, percentage of neocortex, and cortical fields were significantly different in these genetically similar species. However, these groups do represent genetically different strains of the same species, and differences likely are due to some combination of genetic modifications and experience. A larger percentage of cortex was devoted to

S1 and A1 + AAF in laboratory Norway rats compared with wild-caught Norway rats, and these differences may reflect the fact that these modes of sensation are the least impoverished in laboratory rats. Caged laboratory rats are able to ambulate, dig in bedding, whisk on several different surfaces (metal cage tops, plastic cages, metal sipper tubes, care fresh bedding, and food pellets), and manipulate bedding and food with their paws. These items are also available in the visual and auditory environment. Furthermore, species-specific vocalizations are available. However, an entire set of photoreceptors, the UV cones, is not normally stimulated in a laboratory environment. Recent studies indicate that this is a highly salient source of sensory input, because the rat retina has a specialized distribution of UV cones, and cFos expression can be induced in the suprachiasmatic nucleus, LGNv, IGL, area 17, and extrastriate cortex with exposure to UV light (Amir and Robinson, 1996; Jacobs et al., 2001). Although there is no specificity of UV vs. middle-wavelength responses in V1 neurons (Ekesten and Gouras, 2008), and only a small percentage, 6%, of the cells were responsive to only one type of light stimulus, color discrimination between UV and middle-wavelength lights was demonstrated in rats using a three-alternative, forced-choice discrimination test (Jacobs et al., 2001). Also, these studies were performed with mice and rats that had been reared in the absence of UV light. Although a decrease in the size of area 17 was not observed in laboratory rodents, it is likely that alterations in the functional organization of V1 exist and that additional alterations occur at higher stages of processing, which were not examined in this study. It is interesting that wild-caught rats have a relatively larger brain and cortical hemispheres compared with laboratory rats, but laboratory rats have a larger somatosensory and auditory cortex. Visual and nondelineated dorsal cortex are the same size in both types of rat, suggesting that the differences in cortex are in regions that were not measured, such as cingulate, prefrontal, or pyriform cortex.

We are fairly certain that the differences in cortical field size that we see in laboratory and wild-caught rats are not due to age differences in the two groups for two reasons. First, developmental studies examining plasticity of S1 in rats have demonstrated a critical period for peripheral alterations affecting the S1 representation that ends at about P14 (Dawson and Killackey, 1987; Wallace and Sakmann, 2008). Second, developmental studies in our own laboratory on S1 map formation across rats aged P5 to adulthood (>P60) demonstrate that the relative size of the cortical field compared with the size of the entire cortical sheet (similar to measurements made in this study) is constant from P5 through adulthood (Seelke and Krubitzer, 2009; Seelke et al., 2010).

In conclusion, our results demonstrate that the differences in the size of cortical areas have a consistent relationship with the sensory lifestyle and morphology of the species. This of course does not rule out any genetic changes that might have evolved in different species either as a direct adaptation to lifestyle or as an adaptation for some unrelated function. Specifically, although all rodent groups have the primary sensory areas (V1, S1, A1) that occupy the same geographic locations on the cortical sheet, there are differences in the size of visual, somatosensory, and auditory areas in diurnal vs. nocturnal, wild vs. laboratory, and arboreal vs. terrestrial rodents. Furthermore, there appears to be a complex interaction between the sensory systems and how they are utilized. Thus, highly visual rodents not only have larger, well-defined visual areas, and possibly more visual areas, but consequently have smaller somatosensory and auditory areas, compared with nocturnal rodents. This expansion and contraction of cortical fields associated with specialized lifestyles suggests that the developmental mechanisms that regulate cortical sheet size (generated early in development) operate independently from those that regulate the proportion of dorsal cortex devoted to particular sensory systems.

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