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Volumes of Cochlear Nucleus Regions in Rodents

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Abstract

The cochlear nucleus receives all the coded information about sound from the cochlea and is the source of auditory information for the rest of the central auditory system. As such, it is a critical auditory nucleus. The sizes of the cochlear nucleus as a whole and its three major subdivisions – anteroventral cochlear nucleus (AVCN), posteroventral cochlear nucleus (PVCN), and dorsal cochlear nucleus (DCN) - have been measured in a large number of mammals, but measurements of its subregions at a more detailed level for a variety of species have not previously been made. Size measurements are reported here for the summed granular regions, DCN layers, AVCN, PVCN, and interstitial nucleus in 15 different rodent species, as well as a lagomorph, carnivore, and small primate. This further refinement of measurements is important because the granular regions and superficial layers of the DCN appear to have some different functions than the other cochlear nucleus regions. Except for DCN layers in the mountain beaver, all regions were clearly identifiable in all the animals studied. Relative regional size differences among most of the rodents, and even the 3 non-rodents, were not large and did not show a consistent relation to their wide range of lifestyles and hearing parameters. However, the mountain beaver, and to a lesser extent the pocket gopher, two rodents that live in tunnel systems, had relative sizes of summed granular regions and DCN molecular layer distinctly larger than those of the other mammals. Among all the mammals studied, there was a high correlation between the size per body weight of summed granular regions and that of the DCN molecular layer, consistent with other evidence for a close relationship between granule cells and superficial DCN neurons.

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Keywords

Auditory system; granular region; anteroventral cochlear nucleus; posteroventral cochlear nucleus; dorsal cochlear nucleus; mountain beaver

1. Introduction

Hearing is critically dependent on the function of the first brain center of the auditory system, the cochlear nucleus. The cochlear nucleus receives all the coded information about sounds from the cochlea and sends information bilaterally to other auditory centers, including especially the superior olivary complex, nuclei of the lateral lemniscus, and inferior colliculus (Warr, 1982). Malfunctions within the cochlear nucleus can lead to distorted hearing and tinnitus (Kaltenbach and Godfrey, 2008; Shore, 2011; Godfrey et al., 2012). The structure of the cochlear nucleus underlies its function. We have carried out a basic study of cochlear nucleus structure, in terms of the sizes of its subregions, in a variety of mammals, particularly rodents, in order to explore similarities and differences among them. Several of the animals included in our study have provided the preponderance of available data on the auditory system of mammals. To the extent that these mammals have patterns of cochlear nucleus structure similar to those of a variety of other mammals, there is support for applying results obtained from them toward understanding human hearing.

The cochlear nucleus is located on the dorsolateral aspect of the rostral medulla, just caudal to the pons, and superficial to the inferior cerebellar peduncle. It is composed of the ventral cochlear nucleus (VCN) and the dorsal cochlear nucleus (DCN). The VCN is further subdivided by the auditory nerve root, or interstitial nucleus (IN), into the anteroventral cochlear nucleus (AVCN) and the posteroventral cochlear nucleus (PVCN). The DCN in most mammals has 3 prominent layers: molecular, fusiform soma, and deep. Also within the cochlear nucleus, mostly near its periphery, there are regions containing dense populations of small granule cells (Osen, 1988; Godfrey et al., 1997). These regions will be collectively referred to here as the granular region.

Volumes of the whole cochlear nucleus and subregions have been previously measured in various mammals, including humans (Hall, 1964, 1966, 1969, 1976; Osen, 1969; Konigsmark and Murphy, 1972; Brawer et al, 1974; Hall et al., 1974; Kiang et al, 1975; Perry and Webster, 1981; Godfrey and Matschinsky, 1981; Gandolfi et al., 1981; Coleman et al., 1982; Lambert and Schwartz, 1982; Trune, 1982; Webster, 1985, 1988; Moore and Kowalchuk, 1988a,b; Anniko et al., 1989; Statler et al., 1990; Doyle and Webster, 1991; Dyson et al., 1991; Fleckeisen et al., 1991; Hultcrantz et al., 1991; Seldon and Clark, 1991; Sutton et al., 1991; Paterson and Hosea, 1993; Willott et al., 1992, 1994, 1998, 2005; Lustig et al., 1994; Saada et al., 1996; Willott and Bross, 1996; Tierney and Moore, 1997; Glendenning and Masterton, 1998; Hardie and Shepherd, 1999; Insausti et al., 1999; Gleich et al., 1998, 2000; Osofsky et al., 2001; Li et al., 2002; Helfert et al., 2003; Fuentes-Santamaria et al., 2005; Stakhovskaya et al., 2008; Zhang et al., 2009; Feng et al., 2012; Malkemper et al., 2012; Rosengauer et al., 2012; Godfrey et al., 2012, 2015; McGuire et al., 2015). Most of these studies have measured the volumes of the entire cochlear nucleus

and/or its major subdivisions: AVCN, PVCN, and DCN. With the exception of a few studies (Kiang et al., 1975; Godfrey and Matschinsky, 1981; Trune, 1982; Statler et al., 1990; Fleckeisen et al., 1991; Hultcrantz et al., 1991; Willott et al., 1992, 1994; Lustig et al., 1994; Osofsky et al., 2001; Li et al., 2002; Godfrey et al., 2012, 2015), the volumes of the granular region and layers of the DCN have not been specifically measured. Historically, regions containing granule cells were considered anatomically part of the AVCN and PVCN (Lorente de Nó, 1981). Studies showing the projections of type II, but not type I, spiral ganglion cells to the granular region (Brown et al., 1988), the projections of many if not all granule cells specifically to the DCN molecular layer (Mugnini et al., 1980; Adams, 1983; Osen, 1988), and convergence of innervation from a variety of auditory and non-auditory structures onto the granular region (Osen, 1988; Godfrey et al., 1997; Shore and Moore, 1998) suggested that the granular region should be considered separately from the parts of the AVCN and PVCN containing neurons with larger somata (Godfrey et al., 1997). The fusiform soma layer of the DCN also contains granule cells (Osen, 1969; Brawer et al., 1974; Mugnaini et al., 1980; Wouterlood and Mugnaini, 1984; Morest et al., 1990; Godfrey et al., 1997) and could therefore be considered as an extension of the granular region (Mugnaini et al., 1980; Osen, 1988). The functions of the granule cells are not entirely clear (Oertel and Young, 2004), but their terminations onto the dendrites of DCN cartwheel and fusiform cells (Berrebi and Mugnaini, 1991; Dunn et al., 1996) imply that they can exert an important influence on the ascending projections from the DCN. These derive predominantly from the fusiform cells, which receive major input from the cartwheel cells (Osen, 1988; Berrebi and Mugnaini, 1991; Dunn et al., 1996; Godfrey et al., 1997). In this study, besides volumes of the AVCN, PVCN, IN, and DCN layers, we compare granular region volumes among mammalian, primarily rodent, species in order to further illuminate the potential role that granule cells play in the central auditory system.

Although the layers of the DCN have been known for many years (Lorente de Nó, 1933), their volumes have not been previously measured for many animal species. The DCN layers are distinguishable by their different histological features. The molecular layer contains relatively few neuronal somata but a dense collection of granule cell axons. Besides granule cell somata, the fusiform soma layer contains the much larger somata of fusiform cells (also called pyramidal cells), for which it is named, as well as cartwheel and some other cell types (Wouterlood and Mugnaini, 1984; Osen, 1988). The deep layer is also called the polymorphic layer because it contains a variety of neuronal types, with somata more sparsely distributed than those of the fusiform soma layer (Lorente de Nó, 1933, 1981). The deep layer has been divided into two or three layers in some mammals (Lorente de Nó, 1933; Osen, 1988), but we will treat it as a single layer because that is all that is easily distinguished in a Nissl stain.

Measurements of cochlear nucleus volumes provide a foundation for speculations about the possible roles of different cochlear nucleus regions and cell types in hearing, partly through comparisons with behavioral information for different animals. For example, the volume ratio of the DCN in relation to the VCN of dolphins represents a minimum among mammals examined so far, and this has been speculated to relate to the restrictions in movability of their heads (Malkemper et al., 2012).

So far, there has been only one comprehensive comparison of cochlear nucleus subregion volumes among mammalian species (Glendenning and Masterton, 1998). That study included all the major subcortical central auditory centers, and the cochlear nucleus was divided only into its major subdivisions, AVCN, PVCN, and DCN. Among other correlations found, one between AVCN and superior olive sizes suggested that functional interconnections are a factor affecting nuclear sizes.

Our study has focused on a more detailed comparison of the volumes of cochlear nucleus subregions in rodents, a large order of mammals that thrive in a wide variety of habitats and environments (Nelson, 1930; Boorer, 1971; Nowak, 1999; Martin et al., 2001; Samuels and Van Valkenburgh, 2008). The variety of habitats among rodents exposes them to different types of auditory environments, which might be reflected in different structural characteristics of their auditory systems. The brain sections available for our study were from a diverse group of rodents having various behavioral adaptations. Besides comparisons among rodents, we explored whether there are any major differences between the structural features of the rodent cochlear nucleus and those of other mammalian orders. Three non-rodent mammals were included in our study: cat, a carnivore whose auditory system has received much study; domestic rabbit, a lagomorph; and greater bushbaby, a primitive primate (Thompson and Thompson, 1995). These non-rodent mammals are nocturnal, as are many rodents, and also share other behavioral characteristics (Table 1).

Preliminary reports of some of the results have been presented (Benjamin et al., 1995; Hamilton et al., 1998), and data for some of the animals have been included in previous publications (Kiang et al., 1975; Godfrey and Matschinsky, 1981; Li et al., 2002; Godfrey et al., 2008, 2012, 2015).

2. Materials and Methods

2.1. Animals included

Data were obtained for available sections of a variety of rodents and, for comparison, of three non-rodents: greater bushbaby, domestic rabbit, and cat (Table 1). Table 1 includes the abbreviation used to represent each animal, the scientific name for each, and the suborder of each rodent. Information about behavioral characteristics of these animals was obtained from several sources (Nelson, 1930; Boorer, 1971; Gulotta, 1971; Hoogland, 1996; Nowak, 1999; Martin et al., 2001; Samuels and Van Valkenburgh, 2008; Connor, 2011) in case there might be some correlation with hearing ability. Characteristics noted include locomotor category (arboreal, terrestrial, fossorial, semifossorial, and saltatorial) and time of major activity (diurnal, nocturnal, crepuscular, and both day and night). Arboreal animals are “capable of and regularly seen climbing for escape, shelter, or foraging” (Samuels and Van Valkenburgh, 2008). A terrestrial animal “rarely swims or climbs, may dig to make a burrow (but not extensively)” (Samuels and Van Valkenburgh, 2008). A fossorial animal “regularly digs to build extensive burrows for shelter or for foraging underground” and “a predominantly subterranean existence” (Samuels and Van Valkenburgh, 2008). A semifossorial animal “regularly digs to build burrows for shelter, but does not forage underground” (Samuels and Van Valkenburgh, 2008). A saltatorial animal tends to travel by jumping (Martin et al., 2001). Diurnal animals are active predominantly during daylight

hours, nocturnal animals at night, and crepuscular at twilight. Some animals have periods of activity during both day and night. The number of animals of each type providing sections varied from 1 to 11. When sections were available for only one or two members of a species, boundaries were traced in both cochlear nuclei whenever possible. The average body weights for the animals shown in Table 1 were derived in three ways. For some, the weights of the animals used were available. For the rest of the animals, the weights of the animals that provided the sections used were not available. For most of these, average weights of animals kept in the laboratory that provided the slides (that of RSH), were used; these fell within the range of weights provided in literature (Nowak, 1999) except for pocket gopher, which was lower, and domestic rabbit, which was higher. For the rest of the animals, an average body weight was estimated as the average of the range of weights found in Nowak (1999), except in the case of mountain beaver, for which average weights for males and females were found (Nowak, 1999) and averaged. The approximate nature of the body weights of many of the animals in our study limited the accuracy of data expressed per body weight, but some results per body weight are presented because of their interest and the likelihood that the trends reported would not be greatly affected by small errors in body weight estimates. Comparison of the average weights obtained from Nowak (1999) with the actual weights of animals in cases where we had those weights suggested that an error of 27 %, $\pm$ 22 % standard deviation, may result from the use of the estimated weights.

2.2. Preparation of sections

The sections for each animal were prepared in one of two ways. Some animals (chinchilla, hamster, guinea pig, house mouse, mountain beaver (or sewellel), pocket gopher, brown and albino rats, and bushbaby) were anesthetized with sodium pentobarbital, or ketamine + xylazine for hamster, decapitated, and the brain removed and frozen, usually within 10 minutes of death, in Freon or a Freon substitute pre-cooled to its freezing point (-130°C) with liquid nitrogen. Frozen brains were stored at -80°C until sectioning in a cryostat (-20°C). Frozen sections were melt-mounted onto slides and stained for Nissl substance or alternately for Nissl substance and acetylcholinesterase activity and/or cytochrome oxidase activity (Godfrey et al., 2015). Other animals (African spiny mouse, chipmunk, deer mouse, fox squirrel, gerbil, grasshopper mouse, additional house mice, naked mole rat, a second pocket gopher, prairie dog, and rabbit) were perfused through the heart with 10 % formalin and the brain post-fixed with formalin. Brains were cryoprotected in 25 % glycerine and sectioned on a sliding microtome. Frozen sections were melt-mounted onto slides and then stained alternately for Nissl substance and with protargol (Heffner and Heffner, 1990). Data for the cat, which was perfused through the heart, were from a previous study of one of the authors (DAG, Kiang et al., 1975). All sections for this study were cut in a coronal plane. Sections from perfused brains available for measurements were at 50–100 μm intervals, whereas those from frozen brains were at 20–25 μm intervals. A previous analysis of numbers of sections needed for accurate volume measurements (Glendenning and Masterton, 1998) suggests that the measurements for the perfused brains should be slightly less accurate than those for the frozen brains, particularly for smaller cochlear nuclei.

2.3. Volume measurements

Using a Wild dissecting microscope with a drawing tube, boundaries of cochlear nucleus regions in each animal were traced from the Nissl-stained sections at 25 times magnification for larger cochlear nuclei or 50 times magnification for smaller cochlear nuclei (Fig. 1). In cases where regional boundaries were not clearly distinguishable in a Nissl-stained section, the other nearby stained sections were consulted. Sections were traced in order from caudal to rostral, so that determinations of the regional boundaries in each section were made in the context of those in the previous and subsequent sections. All boundaries used in the final volume calculations were traced by the same person (DAG).

Information from published studies (Harrison and Warr, 1962; Harrison and Irving, 1965, 1966; Osen, 1969; Brawer et al., 1974; Morest et al., 1990) aided the determination of boundaries of the cochlear nucleus regions by histological characteristics. The areas considered to be granular regions were characterized by a dense collection of granule cell bodies and few if any large cell bodies. Some lighter appearing zones, corresponding to the plexiform layer of the granular region as defined by Morest et al. (1990), seen in the cochlear nuclei of some of the animals, especially chinchillas, were included in the granular regions. Although granular regions were located in many places throughout the rostral-caudal extent of the cochlear nucleus, they were grouped together for this study and referred to collectively as the granular region.

In the DCN, the small and sparsely dispersed neuronal somata in the molecular layer gave it a light appearance in Nissl stain. A darker fusiform soma layer contained a much higher density of somata of both granule and larger cells, including the fusiform cells, but the density of granule cells was noticeably less than in granular regions. The deep layer was defined as the DCN region deep to the fusiform soma layer, containing scattered larger somata. Its boundary with the underlying PVCN was often marked by intervening fibers of the acoustic striae (dorsal and/or intermediate) or a lamina of granule cells. For one animal, the mountain beaver, there were no clear indications of DCN layers within the Nissl-stained sections or those stained for acetylcholinesterase activity. For the volume measurements, the entire DCN was considered as molecular layer for three reasons: (1) the relatively light Nissl stain appeared similar to that of the molecular layer in the other mammals, (2) the previous study of Merzenich et al. (1973) reported a possible fusiform soma layer (which we were unable to confirm) only in a limited location at the deepest level of the DCN, and (3) unlike in rat and cat, clear superficial-to-deep chemical gradients were not found in the mountain beaver DCN (Godfrey et al., 1996, 1997). An alternative view would be to consider the mountain beaver DCN as combined molecular and fusiform soma layer based on our observation of scattered somata with diameters up to 20 μm in the Nissl-stained sections and the presence of myelinated fiber staining in its deeper portion reported by Merzenich et al. (1973).

The VCN was divided into its PVCN and AVCN components, mainly by their locations caudal and rostral, respectively, to the cochlear nerve root, or IN, and also by their cellular compositions to the extent that they could be recognized in the sections. The IN appeared light in Nissl stain, with few neuronal somata included. Variation of its volume across individual animals can result from variation in the location of cutting the auditory nerve

connection during removal of the brain. The boundary between PVCN and AVCN was difficult to determine with complete confidence but was always assumed to occur within the rostral-caudal extent of the IN. Where AVCN and PVCN were considered to be both present in the same section, the boundary between them was based on histological differences.

The drawings were retraced to import them into a Neurolucida imaging software program (MicroBrightfield, Colchester, VT), which calculated the area of each region in each section. These areas were multiplied by the distance between sections, taken as half the distance between the preceding and succeeding sections in the series, to obtain the regional volumes in a slab of tissue with the measured section at its center. The regional volumes in all the slabs containing each region were added to give the total volume of each region for an individual animal, and the regional volumes were summed to calculate the total cochlear nucleus volume. The volume for each region and for the total cochlear nucleus for a given type of animal was an average of the volumes for all the cochlear nuclei measured for that animal. The relative volume for each region was calculated as a percentage of the total cochlear nucleus volume. The volume of the acoustic striae portion within or adjacent to the cochlear nucleus was measured but was not included as part of the cochlear nucleus volume.

2.4. Statistical analysis

Using SPSS software (IBM SPSS Statistics 23), data for each animal across regions and data for each region across animals were checked for normality using the Kolmogorov-Smirnov test. Correlations between sets of data that fit normal distributions were evaluated by calculating the Pearson correlation coefficient. Correlations between sets of data in cases where at least one set did not fit a normal distribution were evaluated by calculating the Spearman rank correlation coefficient (Zar, 1984). A cluster analysis was performed using R statistical software (The R Foundation for Statistical Computing).

3. Results

3.1. Comparisons of volumes between frozen and perfused brains

Volumes of cochlear nucleus regions in frozen brains are likely very close to in vivo values (Godfrey and Matschinsky, 1981), but perfusion fixation of brains may result in some shrinkage (Glendenning and Masterton, 1998). To determine whether correction factors should be applied to the cochlear nucleus volumes of the perfused animals, we compared the cochlear nucleus volumes of two rodents for which we had sections from both frozen and perfused brains (Table 2). For both house mouse and pocket gopher, the total cochlear nucleus volume was only about 10% less in the perfused brains than in the frozen brains, and the differences were not consistent across regions. Further, these differences were no larger than those among individual members of the same rodent group (Table 3). Therefore, there was no clear basis for applying any correction factor to the volumes in the perfused animals. In these two cases where there were data for both frozen and perfused brains, only the data for the frozen brains are included in subsequent analyses because, being based on measurements in more sections per animal, they were considered more accurate.

3.2. Comparisons between absolute and relative volumes

Glendenning and Masterton (1998) expressed volumes as proportions of the total subcortical auditory system volume. We expressed cochlear nucleus regional volumes both as absolute and relative volumes, with the relative volumes being percentages of the total cochlear nucleus volume. Most of our results are expressed in terms of the relative volumes because of the same reasons expressed by Glendenning and Masterton (1998), such as uncertainty about amounts of shrinkage, but also because we found that, where we had more than one representative for a species of mammal, relative volumes usually varied less among individuals than absolute volumes (Table 3). The amount of variation among individual representatives of a given species provides a measure of the limitation of having sections from only one animal for a species, as for many of the animals in this and previous (Glendenning and Masterton, 1998) studies.

3.3. Comparisons of absolute and relative regional volumes among mammals

Although the appearance of the cochlear nucleus was generally similar across the mammals included in this study (Fig. 2), there were quantitative differences in the volumes of the subregions (Table 4). The volumes expressed per average animal body weight were much larger in some of the smaller rodents, including several of the mice, the gerbil, and the chipmunk, by a relationship that appeared to be logarithmic (Fig. 3). The hamster and naked mole rat had relatively small cochlear nuclei, whereas the pocket gopher had relatively large DCN and granular regions. Among the larger rodents, the mountain beaver had a relatively large cochlear nucleus because of its large DCN and granular regions, whereas the prairie dog had a relatively small cochlear nucleus. The relative volumes, as percentages of total cochlear nucleus volume, were very similar between some pairs of rodents and, surprisingly, between several rodents and bushbaby, as summarized by correlation coefficients (Table 5). Cluster analysis for all the mammals in our study suggested groupings that were similar, although not identical, to those suggested by the correlations (Fig. 4). Most of the rodents and bushbaby clustered into two large and closely related groups: chinchilla, house mouse, brown and albino rats, bushbaby, guinea pig, and hamster formed one group, and chipmunk, fox squirrel, grasshopper mouse, prairie dog, deer mouse, and gerbil formed another. The naked mole rat was outside these groups; the African spiny mouse grouped with cat; the rabbit was only loosely related; and the pocket gopher and mountain beaver were the least similar to any of the other mammals (Fig. 5).

3.4. Comparisons among cochlear nucleus regions

Correlations were examined between the relative volumes of pairs of cochlear nucleus regions, and the only significant positive correlations were for granular region vs. superficial DCN (molecular and summed molecular and fusiform soma layers). There were significant negative correlations for the relative volumes of the granular region or superficial DCN vs. AVCN, IN, or AVCN and IN combined (Fig. 6). If instead of comparing relative volumes, a comparison was made of volume per animal body weight, the correlations for granular region vs. superficial DCN were strengthened, whereas those for AVCN or IN vs. granular region or superficial DCN were weakened (Fig. 6).

3.5. Comparisons with auditory functions

Four types of measures of hearing are available from behavioral studies on many of the animals for which we have measured cochlear nucleus regional volumes: threshold of hearing at the best sensitivity, lowest and highest audible frequencies (at 60 dB SPL), and sound localization acuity, expressed as minimum audible angle (Neff and Hind, 1955; Ryan, 1976; Heffner and Masterton, 1980; Heffner and Heffner, 1985, 1990, 1991, 1992, 1993; Heffner et al., 1971, 1994a,b, 2001; Jackson et al., 1997; Koay et al., 1997, 1998, 2002). Little correlation was found between relative volume or volume per body weight of any cochlear nucleus region and any measure of hearing. Examples of the lack of correlation are shown in Fig. 7.

4. Discussion

4.1. Comparisons with previous measurements

For those animals included in both studies, our volumes for AVCN, PVCN, and total DCN can be compared to those reported by Glendenning and Masterton (1998), but only approximately because it is not clear where the granular region and IN volumes were included in their study. Our values for total cochlear nucleus volume for guinea pig, house mouse, and brown Norway rat are similar to theirs, those for African spiny mouse, prairie dog, and albino rat somewhat larger, and those for mountain beaver, pocket gopher, and rabbit several times larger. In terms of relative volumes, a difference between the studies is that their PVCN volume tended to be larger and AVCN volume smaller than ours, presumably reflecting a difference in where the boundary between the two subdivisions was placed. Although they included the chinchilla in their study, their values for regional volumes for all auditory regions are identical to those for guinea pig and do not add up to their total subcortical auditory system volume, so there appears to be an error in the presentation of their chinchilla data.

Our cat cochlear nucleus regional volumes, for which we used values uncorrected for shrinkage (Kiang et al., 1975) to be consistent with our other data for perfused animals, were generally similar to those reported in other studies (Hultcrantz et al., 1991; Lustig et al., 1994; Saada et al., 1996; Glendenning and Masterton, 1998; Hardie and Shepherd, 1999; Osofsky et al., 2001; Stakhovskaya et al., 2008), as were our measurements for gerbil cochlear nucleus (Statler et al., 1990; Tierney and Moore, 1997; Gleich et al., 1998, 2000). Our data for rat are not very different from values for comparable regions reported by Coleman et al. (1982) and Helfert et al. (2003), but volumes reported for albino rat AVCN by Paterson and Hosea (1993) and Glendenning and Masterton (1998) are low compared to our measurements. A variety of volume measurements for various subregions of mouse cochlear nucleus (Webster, 1988; Anniko et al., 1989; Willott et al., 1992, 1994, 1998; Zhang et al., 2009) are consistently lower than those in our and Glendenning and Masterton's (1998) studies. Some differences between studies may result from calibration errors, which we avoided only by extreme care.

Our measured relative volumes of the mountain beaver DCN and granular region are similar to the estimates reported by Merzenich et al. (1973), and our estimate that the VCN volume

is slightly smaller than might have been expected for a mammal of its size (Fig. 3) differs only slightly from their estimate that the VCN volume of the mountain beaver is comparable in size to those of other rodents of similar size.

4.2. Possible correlations with classification and behavioral characteristics

Rodents comprise the largest order among mammals, including over 40 % of all species (Martin et al., 2001), and are found throughout the world. Their habitats range from deserts to Arctic and Antarctic regions and include trees, water, ground and underground (Boorer, 1971; Nowak, 1999). In considering possible bases for similarities among rodent cochlear nucleus structures, classification into the same suborder and similar lifestyles can be considered (Table 1). The rodents in our study represent 3 or 4 suborders, depending on how the pocket gopher is grouped. Another aspect of our study was to determine whether there are any unique structural features of the rodent cochlear nucleus that are not found in other orders. Our results for rodents were therefore compared to those for a carnivore (cat), a lagomorph (rabbit), and a primate (bushbaby).

Although there was some tendency for rodents from the same suborder to have similar relative volumes of cochlear nucleus regions, there were many exceptions. Thus, the house mouse, brown and albino rats, and hamster of the Myomorpha suborder grouped together, but there were also similarities of these species with chinchilla and guinea pig of the Hystricomorpha suborder, and even with the bushbaby, a primate. Three other rodents of the Myomorpha suborder, African spiny mouse, grasshopper mouse, and gerbil, grouped with the prairie dog, chipmunk, and fox squirrel of the Sciuromorpha suborder. African spiny mouse of the Myomorpha suborder grouped with the cat, a carnivore. Although 3 species of the Sciuromorpha suborder grouped together, as mentioned above, two others – pocket gopher and especially mountain beaver, had very different relative volumes of cochlear nucleus regions. There were no clear groupings of cochlear nucleus structure that correlated with behavioral characteristics. One group of mammals with similar relative volumes of cochlear nucleus regions included mostly terrestrial rodents - house mouse, brown and albino rats, and guinea pig, but also a saltatorial rodent, chinchilla, a semifossorial rodent, hamster, and even a primate, bushbaby.

Overall, despite the variations in relative volumes, the basic structural features of the cochlear nucleus were similar among rodents and also the three non-rodents included in our study. The only exception was the lack of discernible DCN layers in the mountain beaver.

The similarities in cochlear nucleus relative regional volumes between mountain beaver and pocket gopher may relate to their similar underground lifestyles, different from those of the terrestrial, arboreal, and saltatorial rodents, but other fossorial and semifossorial rodents, including the chipmunk, gerbil, hamster, prairie dog, and the completely fossorial naked mole rat, differed in their relative regional volumes. The differences do not appear to relate to a more solitary vs. a more communal lifestyle because, although mountain beaver and pocket gopher are both solitary, so are chipmunk and hamster (Nowak, 1999). The results suggest that structural adaptations of the central auditory system to a primarily or totally underground lifestyle vary among species. For example, all cochlear nucleus regions are small relative to body weight in naked mole rat, hamster, and prairie dog, whereas the pocket

gopher and mountain beaver have relatively large DCN and granular regions, and all cochlear nucleus regions are larger than average in the gerbil and especially the chipmunk. Perhaps consideration of other aspects of lifestyle beyond the categories considered here would reveal some more consistent correlations with cochlear nucleus structure, or perhaps structural differences correlating with lifestyle differences occur in other parts of the central auditory system.

4.3. Regional correlations

The cochlear nucleus of mammals can be roughly divided into two parts based on density of innervation by the auditory nerve. In cat, rat, and guinea pig, the auditory nerve, carrying the ascending information from the cochlea, densely innervates the VCN and the deep layer of the DCN, but more sparsely innervates the molecular and fusiform soma layers of the DCN and granular regions (Powell and Cowan, 1962; Rasmussen, 1967; Osen, 1970; Cohen et al., 1972; Lorente de N6, 1981; Oliver et al., 1983; Merchán et al., 1985). A major constituent of the DCN molecular and fusiform soma layers and granular regions is the granule cell system. The granule cells have their somata in the granular regions and the DCN fusiform soma layer and mostly or entirely project their axons to the DCN molecular layer to terminate on neurons with somata in that layer and in the DCN fusiform soma layer (Mugnaini et al., 1980; Oliver et al., 1983; Osen, 1988; Berrebi and Mugnaini, 1991; Dunn et al., 1996; Godfrey et al., 1997). The high positive correlation between the volume per body weight of the DCN molecular layer and that of the granular region, or granular region and DCN fusiform soma layer combined, is consistent with this anatomical relationship, although the less-than-perfect correlation suggests that these regions also have other relationships.

There is evidence that numerous descending pathways terminate in granular regions (Osen, 1988; Godfrey et al., 1997; Shore and Moore, 1998), including projections from somatosensory nuclei (Itoh et al., 1987; Wright and Ryugo, 1996; Shore, 2011). Also, there are reports that somatosensory inputs affect the physiological activity of DCN neurons that correspond to fusiform cells (Koehler and Shore, 2013; Wu et al., 2015).

Electrophysiological recordings from neurons in the mountain beaver DCN documented responses to somatosensory stimuli, specifically pressure changes understood to be relevant for a tunnel-dwelling animal, as well as low-frequency sounds (Merzenich et al., 1973). Thus, the enlarged granular region and DCN in the mountain beaver, and possibly also the pocket gopher, may be linked to somatosensory inputs that interact with their hearing and facilitate their existence in underground tunnels. The pocket gopher's inability to localize sounds (Heffner and Heffner, 1990) also correlates with its adaptation to tunnel life. In the case of the completely fossorial naked mole rat, although the VCN is of relatively small size in line with its reduced auditory abilities (Heffner and Heffner, 1993), the absence of an enlarged DCN and granular region suggest that it may adapt to its life in tunnels differently than the mountain beaver and pocket gopher. Perhaps the extensive social interaction among naked mole rats makes them less dependent on information provided by the granule cell system, such as effects of somatosensory stimuli on hearing.

4.4. Lack of correlation with auditory functions

The lack of significant correlations between cochlear nucleus regional volumes and hearing abilities suggests that there is still much that we don't know about the functional roles of cochlear nucleus regions. For example, it might have been predicted that sound localizing ability would correlate with the relative size of the AVCN or combined AVCN and IN, because of their projections to superior olivary nuclei concerned with localization of both low and high frequency sounds (Warr, 1982), or that the size of the VCN, which receives the preponderance of auditory nerve projections, would correlate with hearing threshold, but no reliable relationship was found in either case. More sophisticated comparative anatomical, physiological, and behavioral studies, with cellular rather than regional spatial resolution, may be necessary to show correlations with these hearing abilities. On the other hand, the larger volume per body weight of the cochlear nuclei of smaller mammals suggests that a certain minimal amount of cochlear nucleus tissue is needed for effective hearing, or, conversely, as animals become larger, the cochlear nucleus does not need to increase proportionately in size to perform its role in auditory processing.

4.5. Clinical relevance

The overall similarities in cochlear nucleus structure among rodents of widely differing lifestyles and taxonomic relationships, and also non-rodent mammals, suggest that the basic structure and function of the cochlear nucleus may not vary greatly among mammals, including humans, so that experimental results for these mammals might be applicable for understanding human hearing. Results so far from anatomical studies of the human cochlear nucleus are consistent with this possibility for the VCN, where even some of the same neuron types have been reported (Dublin, 1976; Moore and Osen, 1979; Adams, 1986; Wagoner and Kulesza, 2009), but results for the DCN for humans and other primates have been more controversial (Dublin, 1976; Moore and Osen, 1979; Moore, 1980; Heiman-Patterson and Strominger, 1985; Adams, 1986; Rubio et al., 2008; Wagoner and Kulesza, 2009; Baizer et al., 2012, 2014). This might be consistent with our observation that, when we did occasionally find significant differences among rodents in cochlear nucleus structure, as for pocket gopher and especially mountain beaver, these differences tended to be in the DCN and granular region. One difficulty with the histological results for human cochlear nucleus is that the fixation of the tissue cannot be as good as for non-human animals (Baizer et al., 2012), so that preservation of neuronal structure is compromised, and this might affect some neuron types more than others.

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Abbreviations

AVCN	anteroventral cochlear nucleus
CV	coefficient of variation (standard deviation/mean)

DCN	dorsal cochlear nucleus
DCNd	deep layer of dorsal cochlear nucleus
DCNf	fusiform soma layer of dorsal cochlear nucleus
DCNm	molecular layer of dorsal cochlear nucleus
IN	interstitial nucleus (auditory nerve root)
PVCN	posteroventral cochlear nucleus
VCN	ventral cochlear nucleus

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Research highlights

Relative volumes of 7 cochlear nucleus subregions were similar among most rodents

Cochlear nucleus subregion volumes in bushbaby resembled those of most rodents

Sewellel and pocket gopher had large granular regions and dorsal cochlear nuclei

Granular region volume correlated highly with dorsal cochlear nucleus molecular layer

Cochlear nucleus subregion volumes showed little correlation with measures of hearing

Figure 1.

Illustration of the drawing of regional boundaries in coronal sections through a pocket gopher cochlear nucleus. The top row shows photographs of sections through the rostral (s 95) and caudal (s 44) portions of the cochlear nucleus, the rostral section being 1.02 mm rostral to the caudal section. The middle row shows the same photographs with regional boundaries shown as yellow lines. The bottom row shows just the boundaries, with some regions color coded. Abbreviations are: A, anteroventral cochlear nucleus (AVCN); G, granular region; P, posteroventral cochlear nucleus (PVCN); S, acoustic striae; m, f, and d, molecular, fusiform soma, and deep layers of dorsal cochlear nucleus (DCN). Color code: G dark maroon, DCNm yellow, DCNf red. Dorsal is up and lateral to the right for all

photographs and tracings, and 1 mm scale applies to all. The granular region was distinguished from the fusiform soma layer by its distinctly higher density of granule cells, giving it a darker appearance in the Nissl stain. It was especially large in caudal DCN sections, gave way to a more extended fusiform soma layer in central DCN sections, then became more prominent again in rostral DCN.

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Figure 2.

Tracings of boundaries in a caudal and a rostral Nissl-stained coronal section through the cochlear nucleus of each of 6 rodents. The top, lower-number, section is caudal. Dorsal is up and lateral to the right for all tracings. The sections were sized to occupy similar widths in the figure, with the actual size of each indicated by the 1 mm scale below it. The distances between rostral and caudal sections are 1.33 mm for chipmunk, 1.20 mm for gerbil, 0.68 mm for hamster, 0.84 mm for house mouse, 1.62 mm for mountain beaver, and 0.50 mm for naked mole rat. Abbreviations are as in Figure 1, with additionally I, interstitial nucleus, or auditory nerve root. Granular regions are colored in dark maroon, DCN fusiform soma layer in red, and DCN molecular layer in yellow. Individual layers of the DCN of the mountain beaver were not discernible, and the entire subdivision best resembled molecular layer or combined superficial layers – molecular and fusiform soma. It is colored in light orange.

Figure 3.

Plots of volume per body weight vs. body weight for total cochlear nucleus (CN), ventral cochlear nucleus (VCN), dorsal cochlear nucleus (DCN), and granular region (Granular). Both ordinate and abscissa are on a logarithmic scale so that the data scatter around a straight regression line. Data points are represented by the abbreviations listed in Table 1, which are also listed to the right of the graphs. Colors of data points correspond to classifications as rodent suborders (Histricomorpha blue, Myomorpha red, and Sciuromorpha green) or as non-rodents (black).

Figure 4.
Dendrogram of cluster analysis of the relative volumes of the cochlear nucleus regions,
using R statistical software (courtesy of Dr. Sadik Khuder).

Figure 5.

Bar plots of relative volumes of cochlear nucleus regions. Bars are arranged in the same order as in the cluster analysis of Fig. 4, and colors of bars correspond to classifications as rodent suborders or non-rodents, as in Fig. 3. Horizontal lines are the averages across all rodents excluding mountain beaver and pocket gopher. Regional abbreviations: AVCN, anteroventral cochlear nucleus; DCNm, f, and d, molecular, fusiform soma, and deep layers of dorsal cochlear nucleus; Granular, granular region; IN, interstitial nucleus (auditory nerve root); PVCN, posteroventral cochlear nucleus.

Figure 6.

Scatter plots comparing the relative volumes and volumes per body weight of pairs of cochlear nucleus regions among the various mammals. For the comparisons of relative volumes, the data fit normal distributions when those for mountain beaver are not included, so the Pearson correlation coefficient (r) and regression line are based on all animals except mountain beaver. For the comparisons of volumes per body weight, the data did not fit normal distributions with or without mountain beaver included, so the Spearman correlation coefficients (ρ) are presented. Regional abbreviations are: AVCN, anteroventral cochlear nucleus, and DcNm, dorsal cochlear nucleus molecular layer. Data points for mammals are represented by their abbreviations given in Table 1, as in Fig. 3, with the same color scheme, and are listed to the right of the graphs. Another positive correlation as significant as that shown (with mountain beaver excluded) between relative volumes was for DcNm vs. granular + DcN fusiform soma layer (DcNf) ($r = 0.73$). Other negative correlations were for granular vs. AVCN + interstitial nucleus (IN) ($r = -0.72$), DcNm vs. AVCN ($r = -0.82$) and vs. AVCN + IN ($r = -0.88$), DcNf vs. IN ($r = -0.65$), AVCN vs. DcNm + DcNf ($r = -0.68$) and vs. granular + DcNf ($r = -0.81$), IN vs. DcNm + DcNf ($r = -0.76$) and vs. granular + DcNf ($r = -0.63$), and for AVCN + IN vs. DcNm + DcNf ($r = -0.86$) and vs. granular + DcNf ($r = -0.88$). The only other correlations between volumes per body weight of similar significance as that for granular vs. DcNm were for granular vs. DcNm + DcNf ($\rho = 0.93$) and DcNm vs. granular + DcNf ($\rho = 0.97$).

Figure 7.

Scatter plots comparing sound localization acuity with relative volume and volume per body weight of the anteroventral cochlear nucleus (AVCN), and hearing threshold, in dB re 2 or 20 $\mu\text{N/m}^2$, with relative volume and volume per body weight of total ventral cochlear nucleus (VCN), among the mammals for which the data are available. Data points have the same representations as in Figs. 3 and 6 and are identified in the list to the right of the graphs. Hearing measurement data are from the University of Toledo Department of Psychology Comparative Hearing Lab website: http://psychology.utoledo.edu/showpage.asp?name=mammal_hearing. Better sound localization acuity is quantified as a smaller number of degrees in the angle between two sounds whose direction could be discriminated (minimum audible angle). The pocket gopher (PG) was able to localize sound to left or right only when the duration was increased by about an order of magnitude beyond that used for all other animals (Heffner and Heffner, 1990).

Table 1

Mammals studied

<u>Rodent</u>	<u>Abbrev.</u>	<u>Scientific name</u>	<u>Suborder^d</u>	<u>Behavioral characteristics^c</u>	<u>Number^d</u>	<u>Fixation</u>	<u>Range Body weight (g)</u>	<u>Average Body wt (g)</u>
African spiny mouse	SM	Acomys cahirinus	M	terrestrial, nocturnal	1 (2)	Perfused	11–90 ^e	55 ^f
Chinchilla	Cl	Chinchilla lanigera	H	saltatorial, nocturnal	11	Frozen	496–647	572
Chipmunk (Eastern)	Ck	Tamias striatus	S	semifossorial, diurnal	1 (2)	Perfused	70–142 ^e	90 ^f
Deer mouse	DM	Peromyscus leucopus	M	terrestrial, mostly nocturnal	1 (2)	Perfused	15–110 ^e	62
Fox squirrel	FS	Sciurus niger	S	arboreal, diurnal	1 (2)	Perfused	200–1000 ^e	750 ^f
Gerbil	G	Meriones unguiculatus	M	semifossorial, day&night	1 (2)	Perfused	Ave 50–60 ^e	65 ^f
Grasshopper mouse	GM	Onychomys leucogaster	M	terrestrial, nocturnal	1 (2)	Perfused	30–60 ^e	46 ^f
Guinea pig	GP	Cavia porcellus	H	terrestrial, crepuscular	2	Frozen	800	800
Hamster (golden)	H	Mesocricetus auratus	M	semifossorial, crepuscular	4	Frozen	145–178	162
House mouse	HM	Mus musculus	M	terrestrial, mostly nocturnal	3	Frozen	21–25	22
House mouse	HM	Mus musculus	M	terrestrial, mostly nocturnal	2 (4)	Perfused	12–30 ^e	27 ^f
Mountain beaver (Sewellel)	MB	Aplodontia rufa	S	semifossorial, day&night	3	Frozen	Ave 774–838 ^e	806
Naked mole rat	MR	Heterocephalus glaber	H	completely fossorial	2 (3)	Perfused	30–80 ^e	40 ^f
Pocket gopher (Eastern)	PG	Geomys bursarius	S ^b	fossorial, day&night	1	Frozen	300–450 ^e	175 ^f
Pocket gopher (Eastern)	PG	Geomys bursarius	S ^b	fossorial, day&night	1 (2)	Perfused	300–450 ^e	175 ^f
Prairie dog (black-tailed)	PD	Cynomys ludovicianus	S	semifossorial, diurnal	1	Perfused	700–1400 ^e	1250 ^f
Rat (Fischer, Brown Norway)	Rb	Rattus norvegicus	M	terrestrial, mostly nocturnal	4	Frozen	360–560	459
Rat (Sprague-Dawley, Albino)	Ra	Rattus norvegicus	M	terrestrial, mostly nocturnal	3	Frozen	225–400	313
<u>Non-rodent</u>								
Bushbaby (greater)	B	Oryzomys garnettii		arboreal, nocturnal	4	Frozen	600–2000 ^e	1300
Cat	C	Felis catus		terrestrial, mostly nocturnal	1	Perfused	2900	2900
Rabbit (domestic)	R	Oryctolagus cuniculus		saltatorial, nocturnal	1 (2)	Perfused	1350–2250 ^e	3500 ^f

^aBased on Boorer (1971), Nowak (1999), and Myers et al. (2016); abbreviations: H, Histricomorpha; M, Myomorpha; S, Sciuromorpha

^bBased on Boorer (1971); others have classified as Castorimorpha (Myers et al., 2016) or Myomorpha (Begell et al., 2007)

^cReferences for most behavioral characteristics are Nowak (1999) and Samuels and Van Valkenburgh (2008)

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Number of animals; number in parentheses is number of cochlear nuclei traced when different from number of animals
Values found in Nowak (1999) in cases where the weights of animals actually used were not available
From the Univ. of Toledo Dept. of Psychology Comparative Hearing Lab website: http://psychology.utoledo.edu/showpage.asp?name=mammal_hearing

Mean and relative volumes of cochlear nucleus regions in rodents with sections from both frozen and perfusion-fixed brains

Table 2

		Granular	DCNm ^a	DCNf	DCNd	PVCN	AVCN	IN	Total
House mouse	Mean Volume (mm ³)	0.148	0.086	0.052	0.068	0.088	0.196	0.038	0.676
	perfused	0.102	0.037	0.055	0.070	0.108	0.183	0.047	0.602
	Relative Volume (%)	21.8	12.8	7.6	10.1	13.0	29.0	5.7	100
	frozen	16.9	6.1	9.1	11.6	17.9	30.4	7.8	100
Pocket gopher	Mean Volume (mm ³)	0.945	0.603	0.203	0.244	0.308	0.496	0.248	3.046
	perfused	0.818	0.499	0.224	0.242	0.448	0.377	0.102	2.711
	Relative Volume (%)	31.0	19.8	6.7	8.0	10.1	16.3	8.1	100
	frozen	29.7	19.1	10.8	7.0	10.7	17.1	5.5	100

^a Abbreviations for DCN layers: DCNm, molecular layer; DCNf, fusiform soma layer; DCNd, deep layer

Table 3

Variations in regional cochlear nucleus volumes among individual animals where there were at least 3 individuals^a

Animal	N	mean volume (mm ³)													
		Granular		DCNm ^d		DCNf		DCNd		PVCN		AVCN		IN	
		mean	CV	mean	CV	mean	CV	mean	CV	mean	CV	mean	CV		
Chinchilla	11	1.107	0.219	0.829	0.270	0.482	0.299	0.538	0.283	0.818	0.317	1.362	0.170	0.233	0.483
Hamster	4	0.135	0.061	0.111	0.175	0.086	0.187	0.045	0.386	0.136	0.172	0.289	0.246	0.049	0.308
House mouse	3	0.148	0.127	0.086	0.080	0.052	0.134	0.068	.183	0.088	0.221	0.196	0.095	0.038	0.253
Mountain beaver	3	8.381	0.376	7.449	0.199					0.565	0.254	1.019	0.216	0.288	0.806
Rat (brown)	4	0.453	0.083	0.347	0.056	0.264	0.107	0.213	0.158	0.388	0.135	0.994	0.127	0.196	0.446
Bushbaby	4	0.886	0.276	0.776	0.356	0.483	0.170	0.542	0.154	0.910	0.246	1.762	0.407	0.414	0.470
Animal	N	relative volume (%)													
		Granular		DCNm		DCNf		DCNd		PVCN		AVCN		IN	
		mean	CV	mean	CV	mean	CV	mean	CV	mean	CV	mean	CV		
Chinchilla	11	20.7	0.150	15.2	0.146	8.8	0.197	9.9	0.184	15.0	0.245	25.9	0.212	4.4	0.438
Hamster	4	16.3	0.200	13.0	0.048	10.1	0.153	5.2	0.217	16.0	0.089	33.7	0.096	5.8	0.273
House mouse	3	21.9	0.137	12.8	0.049	7.6	0.059	10.0	0.118	12.9	0.176	29.1	0.126	5.6	0.171
Mountain beaver	3	46.3	0.116	43.0	0.115					3.3	0.261	5.9	0.146	1.5	0.608
Rat (brown)	4	15.9	0.049	12.2	0.048	9.2	0.031	7.4	0.108	13.6	0.104	35.0	0.146	6.8	0.401
Bushbaby	4	15.5	0.197	13.4	0.176	8.5	0.097	9.6	0.117	16.5	0.308	29.6	0.173	6.9	0.386

^a Abbreviations as in Table 2, plus CV, coefficient of variation

Table 4

Average regional volumes and percentages of total cochlear nucleus

	Volumes in cubic millimeters							Percentages							
	Granular	DCNm ^a	DCNf	DCNd	PVCN	AVCN	IN	Total	Granular	DCNm	DCNf	DCNd	PVCN	AVCN	IN
African spiny mouse	0.129	0.090	0.047	0.071	0.127	0.333	0.179	0.976	13.2	9.2	4.8	7.3	13.0	34.2	18.3
Chinchilla	1.107	0.829	0.482	0.538	0.818	1.362	0.233	5.368	20.6	15.4	9.0	10.0	15.2	25.4	4.3
Chipmunk	0.470	0.424	0.252	0.297	0.273	1.037	0.319	3.071	15.3	13.8	8.2	9.7	8.9	33.8	10.4
Deer mouse	0.134	0.065	0.036	0.055	0.107	0.201	0.059	0.657	20.4	10.0	5.4	8.3	16.4	30.6	9.0
Fox squirrel	0.928	0.526	0.473	0.612	0.519	1.519	0.495	5.072	18.3	10.4	9.3	12.1	10.2	29.9	9.8
Gerbil	0.253	0.158	0.081	0.082	0.260	0.535	0.160	1.530	16.5	10.3	5.3	5.4	17.0	35.0	10.4
Grasshopper mouse	0.227	0.144	0.049	0.063	0.175	0.379	0.186	1.223	18.6	11.8	4.0	5.2	14.3	31.0	15.2
Guinea Pig	0.784	0.893	0.579	0.608	0.851	1.401	0.298	5.414	14.5	16.5	10.7	11.2	15.7	25.9	5.5
Hamster	0.135	0.111	0.086	0.045	0.136	0.289	0.049	0.850	15.9	13.0	10.1	5.3	16.0	34.0	5.8
House mouse	0.148	0.086	0.052	0.068	0.088	0.196	0.038	0.676	21.8	12.8	7.6	10.1	13.0	29.0	5.7
Mountain beaver	8.381	7.449			0.565	1.019	0.288	17.702	47.3	42.1			3.2	5.8	1.6
Naked mole rat	0.063	0.029	0.021	0.003	0.087	0.128	0.051	0.383	16.4	7.7	5.6	0.8	22.7	33.4	13.4
Pocket gopher	0.945	0.603	0.203	0.244	0.308	0.496	0.248	3.046	31.0	19.8	6.7	8.0	10.1	16.3	8.1
Prairie dog	0.610	0.245	0.178	0.221	0.332	0.959	0.415	2.960	20.6	8.3	6.0	7.5	11.2	32.4	14.0
Rat (brown)	0.453	0.347	0.264	0.213	0.388	0.994	0.196	2.855	15.9	12.1	9.3	7.5	13.6	34.8	6.9
Rat (albino)	0.320	0.230	0.340	0.130	0.430	0.800	0.220	2.460	13.0	9.3	13.8	5.3	17.5	32.5	8.9
Cat	1.300	1.300	0.800	3.000	2.800	7.700	3.800	20.700	6.3	6.3	3.9	14.5	13.5	37.2	18.4
Rabbit	1.461	0.896	0.602	1.575	1.249	4.440	0.856	11.080	13.2	8.1	5.4	14.2	11.3	40.1	7.7
Bushbaby	0.886	0.776	0.483	0.542	0.910	1.762	0.414	5.774	15.3	13.4	8.4	9.4	15.8	30.5	7.2

^a Abbreviations as in Table 2

Table 5

Correlations between animals for relative sizes of cochlear nucleus regions, represented as Pearson or Spearman correlation coefficients^{a,b}

	SM	CI	Ck	DM	FS	G	GM	GP	H	HM	MB	MR	PG	PD	Rb	Ra	B	C	R
African spiny mouse (SM)	x	0.58	0.75	0.85	0.50	0.92	0.95	0.64	0.81	0.72	0.52	0.87	0.17	0.93	0.85	0.82	0.83	0.92	0.43
Chinchilla (CI)	0.58	x	0.75	0.90	0.86	0.83	0.75	0.93	0.89	0.97	0.78	0.70	0.68	0.76	0.88	0.74	0.91	0.42	0.71
Chipmunk (Ck)	0.75	0.75	x	0.79	0.82	0.61	0.82	0.57	0.46	0.64	0.76	0.54	0.79	0.82	0.57	0.14	0.50	0.45	0.61
Deer mouse (DM)	0.85	0.90	0.79	x	0.75	0.97	0.94	0.83	0.92	0.95	0.81	0.90	0.51	0.94	0.93	0.85	0.94	0.71	0.64
Fox squirrel (FS)	0.50	0.86	0.82	0.75	x	0.57	0.64	0.68	0.46	0.82	0.58	0.43	0.64	0.64	0.68	0.18	0.71	0.43	0.93
Gerbil (G)	0.92	0.83	0.61	0.97	0.57	x	0.96	0.84	0.96	0.89	0.60	0.95	0.36	0.94	0.96	0.92	0.96	0.80	0.57
Grasshopper mouse (GM)	0.95	0.75	0.82	0.94	0.64	0.96	x	0.71	0.86	0.84	0.67	0.92	0.46	0.96	0.88	0.81	0.87	0.77	0.54
Guinea pig (GP)	0.64	0.93	0.57	0.83	0.68	0.84	0.71	x	0.94	0.88	0.63	0.71	0.40	0.69	0.92	0.83	0.95	0.57	0.61
Hamster (H)	0.81	0.89	0.46	0.92	0.46	0.96	0.86	0.94	x	0.91	0.65	0.88	0.37	0.86	0.99	0.96	0.98	0.68	0.39
House mouse (HM)	0.72	0.97	0.64	0.95	0.82	0.89	0.84	0.88	0.91	x	0.70	0.76	0.64	0.88	0.93	0.78	0.93	0.57	0.75
Mountain beaver (MB)	0.52	0.78	0.76	0.81	0.58	0.60	0.67	0.63	0.65	0.70	x	0.60	0.99	0.67	0.70	0.29	0.60	-0.06	0.31
Naked mole rat (MR)	0.87	0.70	0.54	0.90	0.43	0.95	0.92	0.71	0.88	0.76	0.60	x	0.27	0.86	0.85	0.90	0.86	0.73	0.39
Pocket gopher (PG)	0.17	0.68	0.79	0.51	0.64	0.36	0.46	0.40	0.37	0.64	0.99	0.27	x	0.46	0.36	0.14	0.38	0.13	0.39
Prairie dog (PD)	0.93	0.76	0.82	0.94	0.64	0.94	0.96	0.69	0.86	0.88	0.67	0.86	0.46	x	0.90	0.81	0.86	0.78	0.54
Rat (brown) (Rb)	0.85	0.88	0.57	0.93	0.68	0.96	0.88	0.92	0.99	0.93	0.70	0.85	0.36	0.90	x	0.94	0.99	0.75	0.57
Rat (albino) (Ra)	0.82	0.74	0.14	0.85	0.18	0.92	0.81	0.83	0.96	0.78	0.29	0.90	0.14	0.81	0.94	x	0.91	0.73	0.18
Bushbaby (B)	0.83	0.91	0.50	0.94	0.71	0.96	0.87	0.95	0.98	0.93	0.60	0.86	0.38	0.86	0.99	0.91	x	0.74	0.71
Cat (C)	0.92	0.42	0.45	0.71	0.43	0.80	0.77	0.57	0.68	0.57	-0.06	0.73	0.13	0.78	0.75	0.73	0.74	x	0.58
Rabbit (R)	0.43	0.71	0.61	0.64	0.93	0.57	0.54	0.61	0.39	0.75	0.31	0.39	0.39	0.54	0.57	0.18	0.71	0.58	x

^a Pearson coefficients are shown for all animals except Chipmunk, Fox squirrel, Mountain beaver, and Rabbit, for which Spearman coefficients are shown because their regional volumes did not fit a normal distribution. Animal abbreviations as in Table 1.

^b Correlations statistically significant at $P < 0.01$ are underlined; those significant at $P = 0.001$ are double-underlined. Because of the large number of comparisons, some of the correlations significant at $P < 0.01$ may be false positives.