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Distortion product otoacoustic emissions in geriatric dogs

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ABSTRACT

Recordings of distortion product otoacoustic emissions (DPOAE) were taken from 28 geriatric dogs aged 12.2 ± 2.2 years and 15 control dogs aged 5.9 ± 3.0 years (mean ± standard deviation) to demonstrate frequency-specific changes in cochlear responses. Recordings were performed for primary frequencies of 2–12 kHz in 2 kHz increments. Brainstem auditory evoked response (BAER) recordings were also made from geriatric dogs for comparison with DPOAE responses. Significant decreases in DPOAE response amplitudes were observed at frequencies of 6–12 kHz in geriatric dogs compared to control dogs, reflecting loss of cochlear outer hair cells along the length of the cochlea. Significant decreases in response amplitudes were not seen at frequencies of 2 or 4 kHz. Decreases in BAER response amplitudes subjectively paralleled the depressed DPOAE amplitudes. No significant linear regression relationships were found for DPOAE response amplitude vs. age despite the progressive nature of age-related hearing loss. The reductions in response at all frequencies starting at the age where dogs are considered geriatric indicate that age-related hearing loss begins earlier in the life span. DPOAE recordings provide a means to assess cochlear function across different portions of the auditory spectrum for assessing hearing loss associated with aging, and potentially for losses from other causes of decreased auditory function.

Introduction

Presbycusis, also known as age-related hearing loss (ARHL), refers to reduced auditory perception with age (Willott, 1991; Jennings and Jones, 2001; Seidman et al., 2002; Chisolm et al., 2003; Gates and Mills, 2005; Yamasoba et al., 2013; Ouda et al., 2015; Roth, 2015; Wong and Ryan, 2015). The mechanisms for presbycusis are primarily sensorineural, although conductive middle ear effects may contribute (Willott, 1991). The mechanisms are also primarily peripheral (Zachary and Fuchs, 2015), although central changes may also contribute (Ouda et al., 2015). Little research has been reported on presbycusis in animals (Knowles et al., 1988, 1989; Shimada et al., 1998; Ter Haar et al., 2008, 2009; Wilson et al., 2011). One long term study of dogs using tone evoked brainstem auditory evoked responses (BAER) demonstrated a progressive loss of hearing in aging dogs, with middle and high frequencies affected first (Ter Haar et al., 2008). Similar age-related changes in the BAER have been reported in nonhuman primates (Ng et al., 2015). On the basis of subjective owner assessment, there was loss of hearing in 29% of 45 geriatric dogs (Davies, 2012). It has been estimated that there are more than 30 million geriatric dogs in the USA and 15 million in Europe, based on the criterion of being over the age of 7 years, when β amyloid peptide begins to accumulate in dog brains (Bosch et al., 2012; Schütt et al., 2015). This criterion may not accurately identify the number of dogs in this population, but it is clear that the number of geriatric dogs is large. Accordingly, the prevalence of diseases associated with aging, such as presbycusis, is certainly high. This will have a negative impact on the dog–owner relationship and on the dog's ability to function within its normal environment.

The most common form of clinical auditory testing in animals is the brainstem auditory evoked response (BAER). In its most common implementation, scalp electrodes pick up electrical activity evoked by click stimuli and the average of responses to multiple stimuli shows a patterned response of multiple peaks occurring within about 5 ms of stimulus onset; the peaks represent activation of multiple sites in the ascending auditory pathway (Wilson and Mills, 2005; Strain, 2011). The test is usually completed in 5–10 min. However, the click stimulus simultaneously activates most of the basilar membrane of the cochlea because the click contains most audible frequencies, and it does not permit differentiation of responses to different frequencies of sound. In some applications BAERs are recorded instead in response to tone stimuli to assess different parts of the auditory spectrum (Ter Haar et al., 2002), but doing so usually requires anesthesia and an extended period of testing that may not be clinically practical. Another method of assessing frequency-specific auditory function is the auditory steady state evoked potential (ASSEP) (Markessis et al., 2006), but this method has not been widely adopted.

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Ears of humans and other species have been demonstrated to generate otoacoustic emissions (OAE), either spontaneously (SOAE) (Ruggero et al., 1984; Sims et al., 1991; Mayhew et al., 1995; Burke, 1996; Hall, 2000; Kemp, 2002) or evoked in response to introduced sound stimuli (Lonsbury-Martin et al., 1993; Hurley and Musiek, 1994; Hall, 2000; Kemp, 2002). These sounds are transmitted backwards from the cochlea through the middle ear, and are thought to reflect a cochlear amplifier system generated by outer hair cells, which contain contractile proteins (Kemp, 2002). Evoked OAE can either be a transient evoked response to a series of wideband clicks or chirps (TEOAE), or a distortion product (distortion product otoacoustic emission, DPOAE), where pairs of input tones (f_1 and f_2, $f_2 > f_1$) result in tones generated in response by the cochlea at a frequency of $2f_1$ f_2 (Hall, 2000; Kemp, 2002). It is thought that the DPOAEs are generated in a cochlear region corresponding to the geometric mean of the test frequencies (Moulin et al., 1994). In both OAE forms, the amplitude of the evoked response above the noise level (in dB) provides a measure of the strength of the response at the test frequencies. Studies of DPOAE and TEOAE have been reported in dogs (Rogers et al., 1995; Sockalingam et al., 1998, 2002; McBrearty and Penderis, 2011; Schemera et al., 2011; Gonçalves et al., 2012; Venn et al., 2014) and horses (McBrearty et al., 2013). Applications have included screening puppies for hereditary deafness (McBrearty and Penderis, 2011; Gonçalves et al., 2012), toxicology studies (Sockalingam et al., 2002), and assessing noise-induced sound trauma (Venn et al., 2014).

A number of studies have examined the use of OAE in assessing presbycusis in humans (Lonsbury-Martin et al., 1991; Karzon et al., 1994; Moulin et al., 1994; Gorga et al., 1997; Avan and Bonfils, 2005), but there do not appear to have been any studies of their use in aged dogs. In the present study, DPOAE were recorded from unanesthetized normal and geriatric dogs using a portable handheld device. The first hypothesis of the study was that DPOAE amplitudes would be reduced in geriatric dogs and that the effects would be most pronounced for the middle and high frequencies of the canine hearing range of 67 Hz–45 kHz (Fay, 1988). A second hypothesis was that rates of hearing loss would differ among groups of dogs segregated on the basis of the different life spans that accompany different dog sizes.

Table 1
Demographics of geriatric dogs included in the study.

Breed	Sex (M/F)	Age (year)	Normalized age[a]	Weight (kg)	Class[b]
German shepherd	M	9	1.01	39.5	L
Akita	F	9	1.01	39.5	L
German shepherd	F	9.5	1.01	29.5	L
Hound mix	M	10	1.12	27.3	L
Golden retriever	F	10	1.12	24.1	L
Mix	M	10	1.12	30	L
Border collie	F	10	1.00	19.1	M
Mix	F	11	1.23	25.0	L
Samoyed	M	11	1.23	31.8	L
Shepherd mix	M	11	1.24	28.2	L
Beagle	F	11	1.00	13.6	M
Bouvier des Flandres	M	12	1.34	30.5	L
Hound mix	F	12	1.10	17.3	M
Mix	M	12	1.10	11.4	M
Shetland sheepdog	M	12	1.10	11.8	M
Shih tzu	F	12	1.00	2.7	S
Schipperke	M	12	1.04	5.5	S
Labrador retriever	F	13	1.46	26.0	L
Mix	F	13	1.19	13.6	M
Beagle	F	13	1.19	17.3	M
Border collie	F	14	1.57	40.0	L
Mix	F	14	1.57	27.3	L
Jack Russell terrier	F	14	1.21	5.5	S
Chihuahua	M	14	1.17	5.5	S
Miniature dachshund	F	14	1.17	5.5	S
Shih tzu	F	14	1.17	2.7	S
Hound mix	F	17	1.55	19.1	M
Mix	F	18	1.65	16.4	M
					$n = 28$
Mean		12.2	1.20	20.2	
Standard deviation		2.2	0.19	11.26	
Median		12	1.17	19.1	

M, male; F, female.
[a] Age normalized to age for onset of geriatric classification based on size classification (Table 1).
[b] Size classification of large, medium, or small.

Table 2
Ages and body weights (mean ± standard deviation) for classification of dogs as geriatric (Goldston, 1989).

Size	Weight (kg)	Age (year)
Small	0–9.1	11.48 ± 1.85
Medium	9.2–22.7	10.90 ± 1.56
Large	22.8–40.9	8.85 ± 1.38
Giant	>41.0	7.46 ± 1.94

Materials and methods

Subjects

Control dogs consisted of 15 hounds (two male, 13 female) from a university colony with age 5.9 ± 3.0 years and weight 24.4 ± 5.2 kg (mean ± standard deviation, SD). Geriatric dogs consisted of 28 animals (10 male, 18 female) solicited from personnel of the Louisiana State University (LSU) School of Veterinary Medicine and the local community (Table 1). Dogs were considered to be geriatric when, based on weight and age, they fell into age ranges in which diseases associated with aging begin to occur in small, medium, large and giant sized dogs (Goldston, 1989; Table 2). The mean ± SD age of geriatric dogs was 12.2 ± 2.2 years (median 12 years) and the mean ± SD weight was 20.2 ± 11.3 kg. The study was approved by both the Institutional Animal Care and Use Committee and the Clinical Study Protocol Review Committee of LSU (protocol 15-031; date of approval 14 July 2015). To explore the possibility that aging rates differ among the different size categories, a normalized age was calculated for each geriatric dog to account for different size-based lifespans and geriatric age onset. Normalized age was calculated by dividing the dog's age by the cutoff age for being geriatric for its size group (Table 2): 11.5 for small dogs, 10.9 for medium dogs, and 8.9 for large dogs; mean ± SD normalized age was 1.20 ± 0.19 years with a median of 1.7 years.

Distortion product otoacoustic emissions recordings

Ears were cleaned if detritus was visible in the external canal. DPOAE recordings were recorded from control hounds without sedation at six primary (f_1) frequencies at intervals of 2 kHz spanning 2–12 kHz; the frequency ratio was constrained by $f_2/f_1 = 1.21$. An OtoRead Clinical OAE test instrument (Interacoustics) was used to generate the stimuli and record responses. A disposable ear probe with a 9 or 10 mm tip was inserted into the ear canal (Fig. 1). After a mechanical seal was produced by the device in the canal, the ear probe, which contained two pure tone speaker tubes, simultaneously presented stimuli (f_1 and f_2) at different frequency pairs and intensities. Stimulus intensities were set at 65 (f_1) and 55 (f_2) dB sound pressure level (SPL). A microphone in the probe measured both noise levels and evoked OAE response levels; if the response signal level exceeded the noise level by 4 dB or more, the result was considered 'passing'.

Aged dogs recruited from the university and local community underwent the same protocol. Twenty-eight dogs meeting the age and size inclusion criterion were evaluated. The 'seal/calibration' process was bypassed in order to facilitate recordings without undue stress to the subjects. DPOAE tests were followed by BAER hearing tests for comparison with the DPOAE recordings using standardized methods (Wilson and Mills, 2005; Strain, 2011). BAER recordings were performed with stimuli at a screening intensity of 94 dB and were performed without chemical restraint.

Data collected consisted of the amplitude of the DPOAE signal-to-noise ratio (signal minus noise in dB SPL) at each tested frequency, producing DPOAE audiograms from the recordings. At least two tests were recorded per ear, but more were often required to acquire repeatable responses. Results from only one ear from each control and each geriatric dog were analyzed, since the results from both ears could not be considered to be independent measurements.

Statistical analysis

Analysis of variance (ANOVA) was performed with GraphPad version 6.0. Differences between control and geriatric dog DPOAE signal-to-noise ratio measurements were analyzed by two-way ANOVA using a mixed effects model; fixed effects were group (control or geriatric), frequency, and group*frequency interaction. Post hoc