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Developmental hearing loss impedes auditory task learning and performance in gerbils

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Abstract

The consequences of developmental hearing loss have been reported to include both sensory and cognitive deficits. To investigate these issues in a non-human model, auditory learning and asymptotic psychometric performance were compared between normal hearing (NH) adult gerbils and those reared with conductive hearing loss (CHL). At postnatal day 10, before ear canal opening, gerbil pups underwent bilateral malleus removal to induce a permanent CHL. Both CHL and control animals were trained to approach a water spout upon presentation of a target (Go stimuli), and withhold for foils (Nogo stimuli). To assess the rate of task acquisition and asymptotic performance, animals were tested on an amplitude modulation (AM) rate discrimination task. Behavioral performance was calculated using a signal detection theory framework. Animals reared with developmental CHL displayed a slower rate of task acquisition for AM discrimination task. Slower acquisition was explained by an impaired ability to generalize to newly introduced stimuli, as compared to controls. Measurement of discrimination thresholds across consecutive testing blocks revealed that CHL animals required a greater number of testing sessions to reach asymptotic threshold values, as compared to controls. However, with sufficient training, CHL animals approached control performance. These results indicate that a sensory impediment can delay auditory learning, and increase the risk of poor performance on a temporal task.

Keywords

development; hearing loss; plasticity; learning; amplitude modulation; attention

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1. Introduction

Developmental hearing loss studies often postulate a causal relationship between impaired sensory encoding and degraded perceptual abilities. There is good reason for this. Both peripheral and central auditory function are vulnerable to auditory trauma or deprivation during development; for the peripheral nervous system: (Bock et al., 1977; Henry, 1973; Kujawa et al., 2006; Lenoir et al., 1980; Saunders et al., 1976; Saunders et al., 1982; Stanek et al., 1977) for the central nervous system (Aizawa et al., 2006; Aizawa et al., 2007; DeBello et al., 2001; Fallon et al., 2008; Knudsen et al., 1984a; Mogdans et al., 1993; Mogdans et al., 1994; Moore et al., 2002; Popescu et al., 2010; Raggio et al., 1999; Razak et al., 2008; Rosen et al., 2012; Salvi et al., 2000; Snyder et al., 2000; Takahashi et al., 2006; Wang et al., 2002; Yu et al., 2005). Even a transient period of monaural hearing loss causes persistent encoding deficits in auditory cortex after normal audibility is restored (Polley et al., 2013). Although a sensory framework likely explains many behavioral deficits that attend hearing loss, there is also compelling clinical evidence suggesting that cognitive skills may also be delayed or impaired (Bennett et al., 1984; Feagans et al., 1987; Manders et al., 1984; Mody et al., 1999; Psarommatis et al., 2001; Reichman et al., 1983; Schlieper et al., 1985; Teele et al., 1990). For example, slight to mild childhood hearing loss is associated with a decline in phonological short-term memory, (Briscoe et al., 2001; Park et al., 2012; Wake et al., 2006) suggesting that non-sensory mechanisms are vulnerable to early deprivation. Therefore, this study was designed to determine whether adult animals reared with conductive hearing loss (CHL) display deficits both in their initial performance on an auditory task, and in their asymptotic performance following a period of practice.

A primary motivation for studying mild to moderate developmental hearing loss is that long-lasting auditory-processing deficits can be induced by the kind of mild, transient hearing loss that is prevalent in childhood. In general, studies on childhood otitis media with effusion that confirm impaired hearing also demonstrate subsequent deficits in perception, speech, and language processing that can persist for months to years, long after normal audibility is restored (Whitton et al., 2011). Moreover, the childhood population with mild to moderate loss is estimated to be relatively large (Niskar et al., 1998) NIDCD Statistical Report 2005, as compared to those with severe or profound loss, and newborn hearing screens typically do not identify infants who have a loss of less than 30–40 dB (Johnson et al., 2005; Morton et al., 2006; Prieve et al., 2013). Since well-controlled clinical studies of childhood hearing loss are challenging, the use of non-human models can provide a valuable assessment of the inherent risk for diminished perceptual development.

The non-human studies that have explored the effects of CHL on auditory perception primarily focus on the impact of unilateral hearing loss on sound localization, and neural encoding properties that support binaural processing (Clements et al., 1978; Keating et al., 2013a; Keating et al., 2013b; Kelly et al., 1987; Knudsen et al., 1984a; Knudsen et al., 1984b; Moore et al., 1999). However, since otitis media with effusion is more commonly bilateral in humans (Engel et al., 1999), it is important to study the consequences of mild to moderate binaural hearing loss on the perception of spectral or temporal cues that support speech comprehension. In fact, a transient period of mild binaural hearing loss does lead to a perceptual deficit on an amplitude modulation (AM) detection task (Caras et al., 2015b;

Rosen et al., 2012). This perceptual deficit is most severe when transient hearing loss occurs during a well-defined developmental critical period, and closely correlates with a critical period during which auditory cortex synaptic and membrane properties are vulnerable to the same manipulation (Mowery et al., 2015).

To evaluate the behavioral impact of bilateral CHL, animals were subjected to bilateral malleus removal during juvenile development, and reared to adulthood. Using an appetitive reinforcement operant conditioning procedure (Buran et al., 2014a), adult CHL and control animals were trained on an AM rate discrimination task. AM is a favorable acoustic feature to examine because it is an important component of most vocalizations, including speech (Elliott et al., 2009; Rosen, 1992; Singh et al., 2003). The testing procedure allowed us to characterize task acquisition (i.e., learning rate), as well as perceptual sensitivity (i.e., psychometric performance) at the earliest stage of testing and when animals reached asymptotic performance. The results show that CHL animals display a slower rate of task acquisition for AM discrimination, and poorer performance at the outset of testing, although some animals reached control-like performance after sufficient training.

2. Experimental Approaches

2.1. Animals and Groups

Data were obtained from adult Mongolian gerbils (*Meriones unguiculatus*) with normal hearing (NH, $n = 12$, 7 male) and developmental conductive hearing loss (CHL, $n = 8$, 5 male). Animals were assigned to one of two behavioral tasks: amplitude modulation (AM) rate discrimination at 4 Hz ($n = 5$ NH; $n = 5$ CHL) or 32 Hz ($n = 7$ NH; $n = 3$ CHL). All animals were trained and tested on AM discrimination as juvenile-adults ($>P70$) and were weaned from commercial breeding pairs (Charles River). All procedures related to the maintenance and uses of animals were in accordance with the Institutional Animal & Use Committee Handbook and approved by the University Animal Welfare Committee at New York University.

2.2. Hearing Loss Surgery

For the CHL group, bilateral conductive hearing loss was induced at postnatal day 10, just before the ear canals would open naturally, as described previously (Xu et al., 2007). A surgical level of anesthesia was induced (methoxyflurane, Medical Developments International), and the malleus was removed through a perforation in the tympanic membrane. After recovery, animals were reared to adulthood with a permanent bilateral conductive loss of approximately 40 dB (Buran et al., 2014a; Rosen et al., 2012; Tucci et al., 1999). Normal hearing (NH) animals did not undergo a sham surgery. However, previous work from our lab indicates that similar neural effects of CHL are observed whether compared to sham controls or non-sham controls (Kotak et al., 2013; Takesian et al., 2012). As an additional control to assure that poorer task performance was not due to a CHL-related impairment of motor function, we compared behavioral response times between NH and CHL animals. During the discrimination task we found that CHL animal response times for a “Yes” (made contact with the water spout) response (mean $\pm$ SEM; 2.16 ± 0.05 sec) and a “No” (initiated a new trial) response (1.30 ± 0.04 sec) were not significantly slower than

NH “Yes” (2.2 ± 0.04 sec) and “No” (1.36 ± 0.04 sec) responses animals in any of the training phases.

2.3. Auditory Psychophysics

Testing conditions—Gerbils were placed in a plastic cage in a sound-isolation booth (Gretch-Ken Industries) and observed via closed-circuit monitor. A personal computer, connected to a digital input/output interface (TDT RZ6, Tucker-Davis Technologies), controlled acoustic stimuli, reward delivery timing, as well as the acquisition of behavioral data. AM stimuli generated by the Tucker-Davis Technologies system (RZ6) were delivered via calibrated tweeter (DX25TG05-04; Vifa) positioned 1 m above the test cage. Sound levels were measured with a spectrum analyzer (3550, Bruel & Kjaer) via one-quarter inch free-field condenser microphone positioned at the location where animals head aligned with the nose port during a trial. For NH animals, sound level was constant (50 dB equivalent SPL) for all AM stimuli to exclude the use of energy cues. The carrier was broadband noise, with a 25 dB roll-off at 3.5 kHz and a 25 dB roll-off at 20 kHz. All stimuli began with a 200 ms ramp, followed by an unmodulated period of 200 ms, and then transitioned to an amplitude modulation (AM). The delay period prevented animals from making a decision at stimulus onset. For CHL animals, identical stimuli were used however they were presented at 95 dB SPL (i.e., 45 dB louder than that used for NH animals), to compensate for the induced loss. Except for the sound level used for CHL animals, all general training and testing procedures were similar to those described previously for NH animals (Buran et al., 2014b; Sarro et al., 2015).

The difference in sound levels was implemented so as to present stimuli to CHL and NH animals at equivalent sensation levels. The adjustment in sound pressure level for CHL animals was based on physiological measurements (cochlear microphonics and auditory brainstem responses) that show audiometric thresholds for this manipulation produce an attenuation of ≈ 40 – 45 dB (Rosen et al., 2012; Tucci et al., 1999; Xu et al., 2007). In addition, behavioral data indicates that the threshold at which a 100% AM stimulus can be detected is ≈ 10 dB SPL for NH and 50 dB SPL CHL animals (Rosen et al., 2012). Given these measurements, we presented stimuli to NH and CHL at sound levels that were 45 dB above the task-specific threshold for detecting AM. The sound levels should be appropriate, even given small variations in hearing loss as AM detection thresholds are robust to sound level from 20–50 dB above threshold (Viemeister, 1979). Thus, the procedure was designed to address the confounds that might occur should the stimulus range be either very close to threshold or extremely loud. However, we could not determine whether sounds were at a comfortable sound level for individual animals.

Training Phases

Procedural: Animals were placed on controlled water access, and learned to obtain water delivered via a syringe pump (NE-1000; New Era) from a lick spout within the test cage. Initially, the Go stimulus (noise modulated in amplitude at 32 Hz or 4 Hz, depending on animal group) signaled the availability of water at the lick spout. Thus, animals respond to the Go stimulus by approaching the spout. Once animals learned this contingency, a nose port was placed in the testing cage. In one training session, all animals were able to discover

and reliably initiate Go stimulus delivery by placing their nose in the port. On the initial day of nose-port training, only Go trials (noise modulated in amplitude at 4 or 32 Hz, depending on group) were presented.

Discrimination: Once animals learned to cue a Go trial by maintaining a position with their nose in the nose port (one session), the Nogo (Task 1: 4 Hz AM noise; Task 2: 32 Hz AM noise) stimulus was introduced. Thus, animals learned to discriminate between auditory cues, such that the Go AM rate predicted a water reward (50 μ L) and the Nogo AM stimulus was associated with no reward. Trials were scored as a Hit (correctly approaching the water spout on a Go trial), or a False Alarm (FA; incorrectly approaching the water spout on a Nogo trial). A sensitivity metric, d' , was calculated a difference between the z-transform of Hit and False Alarm values: $d' = z(\text{Hit fraction}) - z(\text{FA fraction})$, (Green and Swets 1966). Performance criterion for moving to the next step of training was reached when animals' discrimination sensitivity for Go and Nogo stimuli reached $d' \geq 2.5$ for two consecutive sessions. A single performance criterion was established so that animals would be at equivalent performance levels as they began the next phase of training.

Generalization to Go stimuli: Once animals were able to discriminate between the initial exemplar Go and Nogo AM stimuli, animals then learned to generalize across different Go stimuli. In this phase, animals learned that the Go stimulus could be one of many AM rates. The generalization stimuli were introduced on four consecutive sessions (one new rate at the beginning of each session). Stimuli were selected from a power series and were a minimum of 3 times greater than initial discrimination thresholds (Just Noticeable Difference) measured in the final training phase. For Task 1 generalization, we sequentially introduced the AM rates: 24, 16, 12, and 18 Hz. For Task 2 generalization the AM rate stimuli were: 6, 8, 12, and 16 Hz.

Psychometric Performance and Perceptual Improvement: Once animals generalized the Go response to at least five AM rates, perceptual sensitivity was assessed by presenting Go trials at five different AM rates. On the initial day of psychometric testing, five AM rates were chosen from a series of values spaced semi-logarithmically between 4 and 32 Hz. To obtain a measure of AM rate discrimination threshold, two sampled points of the psychometric function (two of the presented stimuli) must span $d'=1$, allowing threshold to be determined from the fit psychometric function. On subsequent days of psychometric testing, if psychometric functions did not produce a threshold estimate, greater-difficulty stimuli chosen from the predetermined distribution. The new stimuli were added and easier stimuli were removed at the start of a session. On each session, five AM rate stimuli were used such that they bracketed the animal's psychometric threshold. Nogo and Go stimuli were randomly interleaved, and presented with equal probability on a given trial. Only sessions during which the FA rate was $\leq 30\%$, and the animal performed a minimum of 200 trials were used to track psychometric performance. The average number of behavioral trials was 224 ± 44 trials per session (approximately 110 Nogo trials, and 110 Go trials with approximately 20 trials at each Go AM rate stimulus).

Psychometric sensitivity was determined by fitting percentage of "Go" responses, plotted as a function of AM rate, using a maximum likelihood procedure from the open-source

package Psignifit for MATLAB. Significant fits for all behavior sessions were obtained using a linear transform of stimulus intensity values (i.e. the “mw0.1” core available in the bootstrap inference algorithm) fitted by a normal cumulative distribution function. The function is parameterized as follows:

$$\Psi(x;m,w,y,\lambda)=\gamma+(1-\gamma-\lambda); F(x;m,w) \\ F(x;m,w)=\Phi\left(\frac{2(\delta)}{w}(x-m)\right); z(\delta)=\Phi^{-1}(1-\delta)-\Phi^{-1}(\delta)$$

Where:

Where Φ is the inverse of the cumulative Gaussian, x represents stimulus difficulty (AM rate), m the midpoint, w the width of the interval over which $F(x;m,w)$ rises from δ to $1-\delta$, λ the lapse rate, and γ the FA rate. Both m and w were unconstrained and δ was fixed at 0.1 (the default value set by Psignifit). Prior distributions for FA rate and lapse rate were identical to those used previously (Buran et al., 2014a; Caras et al., 2015b) and were determined according to guidelines previously described (Frund et al., 2011).

From the fitted percent Go response functions, a d' function was calculated with d' defined as $z(\text{Hit fraction}) - z(\text{FA fraction})$. For the purposes of this study, we define psychometric threshold as the AM rate at which the fitted d' function = 1. Fits were not considered valid if the measured deviance of the fit to the original data exceeded the 95th percentile of the deviance derived from fits generated from 2000 simulated datasets (Frund et al., 2011). Thresholds were then converted to a just noticeable difference (JND), a measure of AM rate discrimination sensitivity that can be compared at different Nogo AM rate values:

$$JND = \frac{|AM_{Threshold} - AM_{Nogo}|}{AM_{Nogo}}$$

3. Results

3.1. Hearing loss lead to slower acquisition of discrimination task

As illustrated in Figure 1A, Gerbils with NH or a developmental CHL were trained to discriminate between two perceptually distinct amplitude modulated (AM) broadband noise stimuli (Task 1: 32 Hz Go vs 4 Hz Nogo; Task 2: 4 Hz Go vs 32 Hz Nogo). AM stimuli were presented at ≈ 45 dB sensation level for both CHL and NH groups. Each animal's performance was tracked across multiple training sessions to determine if there were differences in the rate of task acquisition. Thus, we monitored the number of trials required to learn to discriminate between AM stimuli associated with a water reward (Go stimulus), and those that were not associated with a reward (Nogo stimulus). Animals were trained on a discrimination task until they reached a performance criterion of $d'=2.5$. We found that Task 1 and Task 2 CHL animals' False Alarm rates declined more slowly than NH animals (Figure 1B), while both groups maintained a Hit rate of nearly 100%. Consistent with this observation, we found a slower increase in AM rate discrimination sensitivity (d') for CHL animals, as compared to NH animals. Thus, CHL animals required a greater number of trials

(CHL 457 ± 18 , NH 362 ± 33 , t-test, $t = 2.34$, $p = 0.03$) to reach criterion (Figure 1C). This difference was also quantified in terms of number of sessions to reach criterion (i.e., two consecutive sessions during which animals reached a d' of 2.5). CHL animals required more sessions (9 ± 1.1 sessions) than NH animals (6 ± 0.4 sessions) to reach performance criterion, t-test, $t = 2.07$, $p = 0.03$ (data not shown). This suggests that developmental CHL can delay auditory discrimination learning.

3.2. Hearing loss delayed the generalization of learned rule to new stimuli

To test whether the learned association (Figure 1) could be generalized to perceptually similar stimuli, Task 1 and Task 2 animals were tested on additional Go stimuli (Figure 2A). After reaching criterion performance in the first phase of training (Figure 2B and C, leftmost points) animals were trained to generalize a Go response to new AM rate stimuli (see Methods). One new AM rate was presented, along with previously learned stimuli, during each successive training session (Figure 2A). CHL animals displayed an impaired ability to generalize to newly introduced AM rate stimuli, as compared to NH animals. On the first day of generalization, CHL animals' Hit rate dropped and remained lower for several sessions. In addition, False Alarm rate increased on the first generalization session (Figure 2B). Consistent with this observation we found that CHL discrimination sensitivity (d') decreased with the introduction of the first new Go stimulus. In fact, discrimination performance (d') was significantly lower in CHL animals on sessions 2–4 when new AM rate stimuli were added (t-test, $p > 0.05$). On the fourth testing session (i.e., introduction of the fourth AM rate), the NH and CHL groups displayed similar Hit and False Alarm rates, and discrimination sensitivity (d'); that is, CHL animals reached normal performance values after a delay. This result suggests that the ability to generalize a previously learned auditory association across perceptually similar stimuli can be delayed by developmental CHL.

3.3. Hearing loss impaired perceptual sensitivity on an auditory discrimination task

To determine how developmental CHL influences AM rate discrimination thresholds, we obtained psychometric functions. On consecutive sessions directly following generalization training, discrimination thresholds were acquired, both for Task 1 (Nogo value at 4 Hz, Go values > 4 Hz) and Task 2 (Nogo value at 32 Hz, Go values < 32 Hz) (Figure 1A). Initial thresholds represent the average performance measured during the first three days of testing. For Task 1 and 2 the NH animals displayed excellent initial discrimination thresholds 0.23 ± 0.02 JND (0.91 ± 0.11 Hz different from Nogo), and 0.22 ± 0.01 JND (7.02 ± 0.43 Hz different from Nogo), respectively (Figure 3A and B, blue lines). Interestingly, NH gerbil discrimination thresholds on both Task 1 and 2 were similar to those reported for humans (Formby, 1985; Grant et al., 1998; Hanna, 1992). In contrast, the CHL animals displayed significantly poorer initial sensitivity on Task 1 (0.54 ± 0.09 JND; 2.16 ± 0.37 Hz different from Nogo; t-test, $t = -2.86$, $p = 0.03$) when compared to NH animals. For Task 2, the initial CHL thresholds (0.28 ± 0.02 JND; 9.02 ± 0.70 Hz different from Nogo) were similar to those displayed by the NH group.

Given the improvement observed in earlier training phases (Figures 1 and 2), we asked whether psychometric performance would improve with training. Thus, all animals were trained for a total of 15 sessions, including sessions where initial threshold measurements

were obtained. NH animals displayed an improvement of 0.09 ± 0.02 JND on Task 1 ($t=5.23$, $p=0.006$), and 0.08 ± 0.02 JND on Task 2 ($t=3.43$, $p=0.01$). Although CHL animals improved on Task 1 by 0.27 ± 0.04 JND ($t=3.61$, $p=0.02$), they did not improve significantly on Task 2. Despite the large improvement in Task 1, the final JND remained significantly higher for CHL animals, as compared to the NH group (Figure 3A; $t=-2.34$, $p=0.02$). Taken together these results indicate that a sensory impediment can degrade auditory discrimination thresholds despite significant training, at least for slow modulation rates.

4. Discussion

The degraded perceptual abilities that accompany hearing loss are commonly attributed to sensory deficits originating in the auditory periphery. However, when peripheral hearing loss occurs during developmental critical periods, it often has secondary consequences, including the permanent alteration of central nervous system function reviewed in (Sanes, 2013). These cellular changes raise the possibility that both sensory and cognitive processing mechanisms could be degraded following hearing loss. To address this issue, we quantified delays in the acquisition and performance of an auditory task for animals that were reared with developmental CHL. We found that CHL animals showed a delayed acquisition of an AM rate discrimination task, and delayed generalization of a learned rule. NH animals displayed excellent AM rate discrimination, with thresholds that approached those reported for humans (Formby, 1985; Grant et al., 1998; Hanna, 1992), while CHL animals displayed poorer psychometric performance during initial tests. However, with sufficient practice, CHL animals improved on the task and, in many instances, reached NH-like levels of performance. As discussed below, these results suggest that both sensory and cognitive mechanisms that support auditory perception may be vulnerable to developmental CHL.

Our results demonstrate that CHL animals required more training to form an association between an AM rate and a behavioral response (Figure 1). Similarly, CHL animals required more training to generalize this rule to a new stimulus value (Figure 2). One plausible explanation for these learning delays, suggested by the clinical literature, is that CHL-reared animals display deficits in the cognitive skills that support auditory task performance. In fact, dysfunction of selective attention or working memory (e.g., phonological) contribute to the degraded auditory performance that follows prolonged auditory deprivation in humans (Adesman et al., 1990; Kelly et al., 1993; Lin et al., 2011; Pisoni et al., 2003; Pisoni et al., 2011). Furthermore, individuals with developmental hearing loss display deficits in speech and language acquisition that may be due, in part, to cognitive processing deficits (Briscoe et al., 2001; Burkholder et al., 2003; Conway et al., 2014; Cowan et al., 1997; Davis et al., 1986; Gravel et al., 1996; Mody et al., 1999; Pisoni et al., 2003; Pittman et al., 2005) poorer ability to generalize has also been correlated with hearing loss (Anderson et al., 2013; Karawani et al., 2015; Sweetow et al., 2006).

In the current study we suggest that disrupted task acquisition and the ability to generalize to a learned rule could plausibly be explained by a cognitive deficit in CHL animals. In principle, it is also possible that a degraded sensory representation could have contributed to the delays in task acquisition. However, the final CHL discrimination thresholds (Figure 3) suggest that the stimuli used for the initial procedural learning or generalization were easily

discriminable. All stimuli used were three times greater than the measured Just Noticeable Differences (i.e., well above animals' discrimination threshold). Given how unchallenging it was for animals to discriminate between stimuli presented during task acquisition and generalization testing, it seems unlikely that deficits in sensory coding would have impeded performance. While our behavioral approach cannot separate potential peripheral from central effects, the CHL manipulation does produce profound effects in the CNS (Kotak et al., 2007; Kotak et al., 2008; Kotak et al., 2013; Kotak et al., 2005; Takesian et al., 2010; Takesian et al., 2012; Takesian et al., 2013; Xu et al., 2007). Therefore, it is plausible to argue that dysfunction in areas that subserve non-sensory roles may explain, in part, the phenotype reported here.

The assessment of AM rate discrimination thresholds on a well-trained task demonstrated that CHL animals were initially much less sensitive to differences in AM for modulation rates at 4 Hz. In contrast, CHL and NH animals displayed similar thresholds at 32 Hz. Selective deficits in either sensory encoding or decoding would be reasonable explanations for this finding. In fact, deficits within primary auditory cortex have been reported for both transient and permanent developmental CHL, suggesting that encoding mechanisms are impaired (Mowery et al., 2015; Takesian et al., 2010; Takesian et al., 2013; Xu et al., 2007). Furthermore, the clinical literature suggests that prolonged periods of developmental hearing loss results in persistent deficiencies in auditory processing skills, including the ability to locate sounds, detect weak signals in noise, and discriminate frequency or frequency modulations, for otosclerosis (Hall et al., 1994; Hall et al., 1995) atresia, (Wilmington et al., 1994), and mild to moderate SNHL (Halliday et al., 2005; Halliday et al., 2006; Rance et al., 2004). While it does not change our general finding, it is worth noting that the initial threshold measurements for CHL Task 2 (Figure 3D) were consistent, however, the sample size was relatively small. The impaired discrimination thresholds of CHL animals at a low modulation frequency may reflect deficits in central encoding. Auditory cortex responses to AM stimuli are reduced in CHL animals at lower modulation frequencies, and normal or even enhanced at higher modulation frequencies (Rosen et al., 2012; Zhong et al., 2014). Thus, while it is possible that the initial impairment in Task 1 may reflect cognitive mechanisms, a degraded central encoding mechanism is more likely to explain the permanent deficit (Rosen et al., 2012). This difference in CHL performance across tasks may also reflect limits on the ability of central mechanisms to compensate for the peripheral loss given differences in central encoding. Finally, it is possible that the difference in difficulty reflects a differential peripheral effect for 4Hz vs 32 Hz stimuli.

This study provides evidence that developmental CHL leads to disrupted auditory learning that could be attributable to either sensory encoding or cognitive mechanisms. However, we also found CHL animals displayed significant improvement in performance during task practice. For discrimination and generalization training phases, CHL animals were able to improve to performance levels displayed by NH animals. However, despite significant improvement, CHL animals did not achieve a level of psychometric sensitivity similar to NH animals on Task 1. Improvement in performance following a developmental hearing loss has been reported in the literature in both human and animal studies. Animals reared with bilateral or unilateral earplugs, following removal of earplugs show improved levels of performance over time (Caras et al., 2015a; Knudsen et al., 1982; Knudsen et al., 1984a; Knudsen et al.,

1984b). Similarly, children who experience a transient hearing loss have difficulty with binaural hearing (Hall et al., 1995; Hall et al., 1998; Hogan et al., 1996; Moore et al., 1991; Pillsbury et al., 1991) and speech processing (Gravel et al., 1992; Gravel et al., 1996; Hall et al., 2003; Jerger et al., 1988) gradually improve once peripheral hearing is restored. Even adult humans with earplug induced or age related hearing loss benefit from training (Ferguson et al., 2014; Irving et al., 2011; Moore et al., 2001). Since training is unlikely to restore cochlear function, the resulting behavioral improvements are likely due to central mechanisms. One possibility is that the central nervous system can utilize or decode a degraded sensory signal with sufficient practice. Alternatively, cognitive skills, such as attention, may be improved with practice. However it is more likely that both mechanisms are involved. Taken together, these findings suggest that training-based remedial strategies for developmental hearing loss may need to consider cognitive limitations that could interact with sensory impairments that impede auditory perception.

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Abbreviations

AM	amplitude modulation
CHL	conductive hearing loss
CNS	central nervous system
NH	normal hearing

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Research highlights

1. Hearing loss leads to slower discrimination task acquisition.
2. Hearing loss delays generalization of learned rule to new stimuli.
3. Hearing loss impairs perceptual sensitivity on an auditory discrimination task.

Figure 1.

Summary of training required for normal hearing (NH) and conductive hearing loss (CHL) animals to reach performance criterion on the Go-Nogo appetitive task. (A) Schematic illustrates the two tasks and behavioral procedure. Animals were trained to initiate a trial during which they would hear a Go stimulus (Task 1: 32 Hz AM; Task 2: 4 Hz AM) or a Nogo stimulus (Task 1: 4 Hz AM; Task 2: 32 Hz AM). After a trial was initiated, the possible behavioral responses are shown for the two trial types: On Go trials, animals could correctly obtain water (Hit) or fail to obtain water (Miss, top row). On Nogo trials, animals could incorrectly seek water at the lick spout (False Alarm) or abstain and repoke to initiate

the next trial (Correct rejection, bottom row). (B) The decrease in False Alarm rate is shown for NH (solid blue line; shading represents SEM) and CHL (solid red line; shading represents SEM) animals. The Hit rate (dashed lines) remained stable across trials. (C) The improvement in discrimination sensitivity (d') is shown for NH (blue line) and CHL (red line) animals across training trials. NH animals reached criterion performance ($d'=2.5$) significantly earlier in training, as compared to CHL animals.

Figure 2. CHL animals display a delay in generalizing across new Go stimulus values. (A) Schematic illustrates that new Go stimulus values (shaded green rectangles) were added during successive training sessions. (B) The Hit rate declined during the initial introduction of a new AM rate for CHL animals (solid red line; shading represents SEM), but remained stable for NH animals (solid blue; shading represents SEM). The False Alarm rate increased for CHL (red dashed line), but not NH (blue dashed line) animals during the introduction of new Go values. (C) Discrimination sensitivity (d') declined for CHL animals (solid red line; shading represents SEM) during the addition of new stimulus values, however remained stable for NH animals (solid blue line; shading represents SEM). (B and C) Grey shaded boxes indicate performance measured immediately following discrimination performance.

Figure 3.

CHL animals initially displayed poorer discrimination thresholds (just noticeable difference) for Task 1, but sensitivity improved to thresholds that matched or approached the performance of NH animals. (A) CHL (red) and NH (blue) discrimination sensitivity to 4 Hz AM rate (Task 1) across testing sessions. Inset shows example psychometric functions from an initial and final testing session for a CHL (red) and NH (blue) animal. (B) A comparison of average (rectangles) and individual (lines) performance for CHL (red) and NH (blue) animals on Task 1 (the 4 Hz AM discrimination task). (C) and (D) show the measurements obtained for separate groups of NH and CHL animals trained and tested on Task 2 (the 32 Hz AM rate discrimination task). Shaded area represents SEM.