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Research paper

Time course and frequency specificity of sub-cortical plasticity in adults following acute unilateral deprivation

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ABSTRACT

Auditory deprivation and stimulation can change the threshold of the acoustic reflex, but the mechanisms underlying these changes remain largely unknown. In order to elucidate the mechanism, we sought to characterize the time-course as well as the frequency specificity of changes in acoustic reflex thresholds (ARTs). In addition, we compared ipsilateral and contralateral measurements because the pattern of findings may shed light on the anatomical location of the change in neural gain. Twenty-four normal-hearing adults wore an earplug continuously in one ear for six days. We measured ipsilateral and contralateral ARTs in both ears on six occasions (baseline, after 2, 4 and 6 days of earplug use, and 4 and 24 h after earplug removal), using pure tones at 0.5, 1, 2 and 4 kHz and a broadband noise stimulus, and an experimenter-blinded design. We found that ipsi- as well as contralateral ARTs were obtained at a lower sound pressure level after earplug use, but only when the reflex was elicited by stimulating the treatment ear. Changes in contralateral ARTs were not the same as changes in ipsilateral ARTs when the stimulus was presented to the control ear. Changes in ARTs were present after 2 days of earplug use, and reached statistical significance after 4 days, when the ipsilateral and contralateral ARTs were measured in the treatment ear. The greatest changes in ARTs occurred at 2 and 4 kHz, the frequencies most attenuated by the earplug. After removal of the earplug, ARTs started to return to baseline relatively quickly, and were not significantly different from baseline by 4–24 h. There was a trend for the recovery to occur quicker than the onset. The changes in ARTs are consistent with a frequency-specific gain control mechanism operating around the level of the ventral cochlear nucleus in the treatment ear, on a time scale of hours to days. These findings, specifically the time course of change, could be applicable to other sensory systems, which have also shown evidence of a neural gain control mechanism.

1. Introduction

Short-term auditory deprivation can modify auditory physiology. In humans, this has been evident through changes in the acoustic reflex threshold (ART, the threshold sound level for a brainstem reflex that involves the bilateral contraction of the middle ear muscles) after auditory deprivation. When one ear was deprived from input by using an earplug to induce a mild to moderate hearing loss for several days, the ART was decreased in the treatment ear (Maslin et al., 2013; Munro and Blount, 2009; Munro et al., 2014). Moreover, additional stimulation through low-gain hearing aids has been shown to increase the ART (Munro and Merrett, 2013), suggesting that neural response gain in the auditory brainstem might be increased or decreased, respectively, in an activity-dependent fashion (Schaette and Kempter, 2006, 2009).

Enhanced neural gain is hypothesized to be a potential

Abbreviations: ABR, Auditory brainstem response; ART, Acoustic reflex threshold; BBN, Broadband noise; DCN, Dorsal cochlear nucleus; IHC, inner hair cells; SOC, superior olivary complex; VCN, ventral cochlear nucleus

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mechanism in the development of tinnitus and hyperacusis (Auerbach et al., 2014; Brotherton et al., 2015; Eggermont and Roberts, 2014; Schaette and Kempter, 2006), two debilitating auditory conditions that affect a large proportion of the population (Andersson et al., 2002; Dawes et al., 2014). Since plugging one ear for several days can also induce the perception of phantom sounds (Schaette et al., 2012) and increase the perceived loudness of sounds (Formby et al., 2003; Munro et al., 2014), the changes caused by auditory deprivation might also be involved in the generation of tinnitus and hyperacusis. A detailed characterization of the gain mechanism underlying changes in ART could therefore provide insights into how tinnitus and hyperacusis are generated.

Changes in ARTs after deprivation or stimulation have been measured in humans in a series of studies (see Table 1). A detailed characterization of time course and frequency-specificity of the effects are desirable, as the information available from previous studies is incomplete in these respects. Also, the location within the auditory pathway where changes in gain might be generated has still to be identified.

The first area of interest concerns the time course of changes in the neural gain mechanism following auditory deprivation. Most studies have investigated changes in ART after 7 days of continuous earplug use (Maslin et al., 2013; Munro and Blount, 2009; Munro et al., 2014). Only two studies have investigated a change in ART earlier than 7 days. Decker and Howe (1981) investigated the ART following 10, 20 and 30 h of unilateral earplug use. The authors observed a significant decrease in the mean ART at 2 kHz after 10, 20 and 30 h of unilateral earplug use. There was no difference in the mean change of ART across the different durations of deprivation. Changes in ART after 3–5 days of treatment have also been reported following acoustic stimulation (Munro and Merrett, 2013). Munro and Merrett (2013) investigated the ART following 3 and 5 days of hearing aid use in one ear. The authors reported an increase in the ART relative to baseline in an ear fitted with a hearing aid, and a reduction in the ART in the control ear, 3–5 days after augmented auditory stimulation. However, as the authors did not measure ARTs earlier than 3 days, it is unclear if changes occurred on a shorter time scale. Similarly, little is known about the time course of recovery following earplug removal. Munro and Blount (2009) were able to demonstrate a return of ART values to baseline level 7 days after earplug removal, but earlier time points were not studied. In a further study, Munro et al. (2014) demonstrated that most of the asymmetry between the treatment and control ears had disappeared 1 day after earplug removal. To the authors' knowledge, there are no studies that have investigated a change in neural gain in normal hearing listeners less than 24 h after earplug removal.

Focusing on the second area of interest, much uncertainty exists about the relation between the frequency-range of elevated audiometric thresholds and enhanced neural gain. For example, does the compensatory change in neural gain occur in the frequency region of hearing loss? If so, it would be expected that short-term auditory deprivation would also have most effect on the ART at the frequencies attenuated by the earplug. Munro and Blount (2009) limited ART measurements to 2 and 4 kHz, which received a similar level of attenuation by the earplug, and showed similar changes at both frequencies. Munro and Merrett (2013) investigated 0.5 and 2 kHz and Maslin et al. (2013) investigated 0.5 and 4 kHz, and both studies found a larger change from baseline in ART at the higher frequency (where most earplug attenuation occurred), but the difference was not significant. Only one study in humans has attempted to investigate the change in ART at more than two frequencies. Decker and Howe (1981) measured ARTs for 0.5, 1, and 2 kHz tones. They reported a significant reduction in ART in the treatment ear at 2 kHz in normal hearing listeners after 10, 20 and 30 h of unilateral earplug use. For the lower frequencies (0.5 and 1 kHz), a similar trend was reported, but the changes did not achieve significance. A comparison between the frequencies was not performed. Although inconclusive, due to lack of significance, these findings suggest that the greatest change in neural gain may occur at frequencies most affected by the deprivation treatment. A frequency-specific mechanism would be consistent with tinnitus, which has shown to display a dominant pitch around the frequency range of the hearing loss (König et al., 2006; Sereda et al., 2011), whilst hyperacusis generally shows a change in loudness judgments across a range of frequencies (Anari et al., 1999; Sheldrake et al., 2015).

The pathway of the acoustic reflex arc involves the primary

Table 1
Summary of studies investigating the ART following a period acute deprivation or augmented stimulation in normal hearing adults.

Author	Condition	Measure	Results
Decker and Howe (1981)	Unilateral earplug deprivation	Ipsilateral 0.5, 1 & 2 kHz at baseline, 10, 20 and 30 h	A reduction of around 3 dB in the treatment ear 10 h after earplug use. The change in the control ear was variable across frequencies showing a decrease of 2 dB and an increase of 1 dB 10 h after earplug. A similar change in ART was observed 20 and 30 h after earplug use. The change was statistically significant only at 2 kHz.
Munro and Blount (2009)	Unilateral earplug deprivation	Ipsilateral 2 & 4 kHz at baseline & 7 days	A significant reduction of around 8 dB in the treatment ear, and a significant reduction of around 3 dB in the control ear after 7 days of unilateral earplug use. A similar reduction was observed for 2 and 4 kHz.
Munro and Merrett (2013)	Unilateral hearing aid use	Ipsilateral 0.5, 2 kHz & BBN at baseline, 3 and 5 days	An increase of around 2 dB in the treatment ear and a reduction of around 2 dB in the control ear 3 days after earplug use. The difference in ART between the ears was marginally significant difference between 0.5 and 2 kHz.
Maslin et al. (2013)	Unilateral earplug use	Ipsilateral 0.5 & 4 kHz at baseline and 7 days	A reduction of around 7 dB in the treatment ear and an increase of around 2 dB in the control ear after earplug use. The change in ART was larger at 4 kHz compared to 0.5 kHz. This difference between frequencies was not statistically significant.
Munro et al. (2014)	Unilateral earplug use	Ipsilateral 0.5, 2 kHz & BBN at baseline and 7 days of earplug use, 1 and 7 days after earplug removal	A reduction of around 5 dB in the treatment ear and an increase of around 2 dB in the control ear after earplug use. The change in ART was larger at 2 kHz compared to 0.5 kHz, but this difference between frequencies was not statistically significant. Most of the asymmetry between the ears disappeared within 1 day of earplug removal.