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Neuromodulation and Plasticity for a Rodent Model of Cochlear Implant Use

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Cochlear implants are neuroprosthetic devices that can provide hearing to deaf patients. However, learning rates and peak speech perception performance with cochlear implants are highly variable across patients (Blamey et al. Audiol Neurootol 2013). Adaptation to cochlear implants is believed to require neuroplasticity within the central auditory system (Fallon et al. J Neural Eng 2009). However, mechanisms by which behavioral training enables plasticity and improves outcomes are poorly understood. Here we investigate the hypothesis that neural mechanisms that promote plasticity in the rodent auditory system are key to optimizing cochlear implant usage, and might be especially helpful in cases of poor performance. We focus on noradrenergic modulation of rat auditory cortex by the locus coeruleus, which can enable robust and long-lasting neural and behavioral changes (Manunta and Edeline J Neurophysiol 2004; Martins and Froemke Nat Neurosci 2015; Sara Curr Opin Neurobiol 2015)

We developed a new surgical approach for cochlear implantation in adult rats (King et al. J Neurophysiol 2016). Our approach allows insertion of an 8-channel electrode array covering up to 360 degrees in the cochlea and allows rats to freely behave while using the implant to perform auditory tasks. Rats are trained on a go/no-go task, and self-initiate trials to respond to a target tone. Previously, we showed in normal hearing animals that this task requires auditory cortex, and that this task is sensitive to cortical modulation and plasticity (Froemke, Carcea et al. Nat Neurosci 2013; Carcea et al. Nat Commun 2017).

Here we examined the effect of pairing locus coeruleus stimulation with an auditory stimulus on auditory learning when a new sound becomes the target. This was done both in normal hearing and cochlear-implanted rats. For both groups, initial training was done using acoustic stimuli and without locus coeruleus-auditory pairing. In the case of cochlear-implanted animals the new target was delivered by intracochlear electrical stimulation after implantation whereas in the normal hearing animals the new target was a tone of different frequency. Prior to each daily behavioral training session for the new target, rats underwent a 5-10 min pairing session. Pairing accelerated learning in each case, with respect to animals that did not receive it. We used fiber photometry to monitor neural activity of noradrenergic locus coeruleus neurons, showing strong responses to novel auditory stimuli and noxious stimuli. During auditory learning, normal hearing animals display dynamic locus coeruleus activity, specifically during the acquisition of the new meaning of reward relevant tones. These studies indicate that neuromodulation can play a powerful role in shaping outcomes with cochlear implant use and training. Furthermore, native variability in cochlear implant use outcomes might reflect a difference in level of engagement of neuromodulatory systems across subjects.

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Burden of Ear, Nose and Throat - Voice, Speech and Language Disorders Based on United States Health Surveys, 2011-2016

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Introduction: The Global Burden of Disease 2010 (GBD 2010) produced worldwide estimates for a wide array of health conditions, including an estimate that more than 500 million people have disabling hearing loss. American data were used extensively in GBD 2010. The National Institute on Deafness and Other Communication Disorders (NIDCD) conducts and supports research on disorders of Ear, Nose and Throat – Voice, Speech and Language (ENT–VSL) and has sponsored nationally-representative health surveys to collect epidemiologic, population-based information on prevalence and risk factors for these health conditions.

Objective: To estimate the United States burden of ENT–VSL disorders.

Methods: Two US health surveys were analyzed: (1) National Health Interview Survey (NHIS) and (2) National Health and Nutrition Examination Survey (NHANES),

which are conducted continuously on the civilian, non-institutionalized US population. NIDCD collaborated with the National Center for Health Statistics (NCHS) in developing the 2012 NHIS Voice, Speech, and Language Supplement (voice, swallowing, speech and language questions); 2014 NHIS Hearing Supplement (hearing, tinnitus and hyperacusis questions); and 2016 NHIS Balance Supplement (balance, dizziness and falls questions). NIDCD also sponsored the first national survey of the chemical senses (olfaction/smell and gustation/taste questions) in NHANES, 2011–14. Prevalences were calculated using NCHS-provided weights for the survey years; US population estimates are standardized to the 2015 population (315.8 million).

Results: Reported prevalence of moderate-or-worse hearing difficulty in children and adults was 6.5% (20.6 million); mild-or-worse was 15.7% (49.5 million). Prevalence of moderate-or-worse tinnitus in adults was 3.2% (7.8 million). Combined moderate-or-worse hearing/tinnitus prevalence was 8.0% (25.4 million); prevalence of combined mild-or-worse hearing/tinnitus problem was 20.7% (65.3 million). Prevalence of reported moderate-or-worse balance/dizziness problems (BDP) in children and adults was 3.7% (11.4 million); mild-or-worse BDP prevalence in last 12 months was 13.1% (40.4 million). Prevalence of moderate-or-worse smell/taste problems, adults aged 40+, was 7.8% (11.8 million). The prevalence of moderate-or-worse voice-swallowing-speech-language (VSSL) disorders in children and adults was 3.1% (9.7 million); mild-or-worse VSSL problems lasting one or more weeks in last 12 months was 7.2% (22.0 million). Accounting for multiple conditions in individuals, the combined prevalence of moderate-or-worse ENT–VSL disorders was approximately 17.4% (54.8 million); mild-or-worse ENT–VSL disorders was 42.4% (133.9 million). Speech and language disorders are more common in children but, overall, the combined prevalence of ENT–VSL disorders is highest in older adults.

Conclusion: About one in six Americans have disabling (moderate-or-worse) impairments of hearing and/or other sensory or communication disorders.

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Accelerating Clinical Access and Implementation of Novel Hearing Therapeutics by Early Health Economic Modelling

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Background:

A key challenge facing health systems today is to identify and avoid unnecessary health innovations and accelerate access those that are necessary. This process can be guided by applying health economic modelling at the early stages of development of new therapeutics to direct product development, market access, and pricing.

This is very relevant and timely to the field of age-related sensorineural hearing loss (ARHL), where biotechnology, pharmaceutical and device companies have identified an unmet market need and have dedicated sizeable investments in the development of novel (drugs, genes, cells) hearing therapeutics.

To assess the potential added value of these novel hearing therapeutics, we developed an early health economic model comparing novel regenerative hearing therapeutics with the current standard of care for people with ARHL.

Methods:

A decision analytic model was developed to assess the costs and effects of using novel regenerative hearing therapeutics in patients over the age of 50 with ARHL. This was compared to the current standard of care, including hearing aids and cochlear implants. Input data was derived from systematic literature searches and expert opinion. The study adopted a healthcare perspective of the UK National Health Service (NHS). Four different but related analyses were conducted: 1) headroom analysis to explore the maximum potential value; 2) threshold analysis to search for the minimum effectiveness needed for the innovation to be cost-effective; 3) formal cost-effectiveness to assess the cost per quality adjusted life-year (QALY) gained; and 4) sensitivity analyses, including both deterministic and probabilistic, and scenario analyses to evaluate relevant uncertainty.

Results:

The decision model showed that novel therapeutics for ARHL have potential value both in terms of improved patient outcomes, as well as cost-effectiveness. The base case analysis revealed an ICER of £11,690/QALY (95% CI: £8,810/QALY-£19,058/QALY)for regenerative hearing therapeutics compared with the current standard of care. Results of the threshold analysis revealed that novel hearing therapeutics had to be 75% effective or greater at restoring hearing to the normal range (pure tone average of ≤ 25dB) to remain cost-effective. Finally, the most important uncertainties identified were the estimates of efficacy, uptake, and cost of the novel hearing therapeutics used in the model.

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