

Hearing Restoration Research Program

Strategic Plan

INTRODUCTION

The Congressionally Directed Medical Research Programs (CDMRP) represents a unique partnership among the U.S. Congress, the military, and the public to fund innovative and impactful medical research in targeted program areas. In 2015, an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine was assembled to evaluate the CDMRP’s two-tier review process and its coordination of research priorities with the National Institutes of Health (NIH) and the Department of Veterans Affairs (VA). As part of their final report,¹ the committee recommended that each CDMRP program “... develop a strategic plan that identifies and evaluates research foci, benchmarks for success, and investment opportunities for 3–5 years into the future,” and that these strategic plans “should specify the mission of the program, coordination activities with other organizations, research priorities, how those priorities will be addressed by future award mechanisms, how research outcomes will be tracked, and how outcomes will inform future research initiatives.”

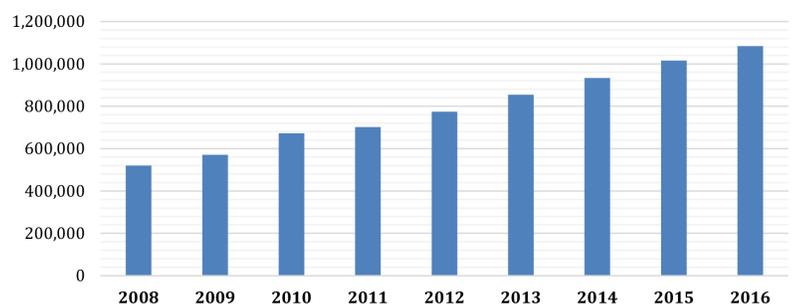
In response to these recommendations, this document presents the current strategy for the CDMRP’s Hearing Restoration Research Program (HRRP). The HRRP Strategic Plan identifies the high-impact research goals most important to its stakeholders while providing a framework that is adaptable to changes in the medical research environment to address those goals. This plan has been formulated to provide greater clarity of the program’s goals over time to the public and other stakeholders. Funding for the HRRP is Congressionally appropriated on an annual basis; therefore, there is no guarantee of future funding. The HRRP Strategic Plan will be reviewed during the program’s annual Vision Setting meeting and updated as necessary.

HRRP BACKGROUND AND OVERVIEW

It is estimated that more than 30 million Americans over the age of 12 years have hearing loss in both ears, and an estimated 48 million have hearing loss in at least one ear.² Hearing loss may be congenital or may be induced by diseases, medication, aging, injury, or exposure to excessive noise.

Hearing loss is highly prevalent in the military population. The most recent data from the VA’s Veterans Benefits Administration indicates that more than 5% of Veterans (approximately 1.1 million) are affected by Service-connected disability due to hearing loss³ (**Figure 1**). In comparison to the general public, military personnel are at higher risks of noise-induced hearing loss and auditory system injury.⁴ Service members are exposed to high levels of noise (e.g., gunshots, helicopters, explosions, etc.) that are unique to combat and the combat training environment. Unlike noise in construction, agriculture and recreation, encountering combat noise is not predictable, and protection against combat noise is further complicated by the need for Warfighters to hear sound and communicate. Exposure to loud noise triggers hearing loss and auditory dysfunction that not only put the affected Service member at increased risk on the battlefield, but may also endanger others in the unit and the mission.

Figure 1. Cumulative Number of Veterans with Disabilities Due to Service-Connected Hearing Loss





The HRRP was initiated in 2017 to support innovative and impactful research that pursues the treatment of auditory system injuries and the restoration of hearing. Funds for the HRRP and for other CDMRP programs are directly responsive to the needs of Service members, beneficiaries, research communities, and the public at large. Research supported by the HRRP is expected to make significant impact on improving the health and well-being of Service members, Veterans, and the American public.

VISION: Improve the operational performance, medical readiness and quality of life of Service members and Veterans with auditory system injuries.

MISSION: Advance the science of hearing restoration by delivering groundbreaking research and solutions that remove barriers to the successful treatment of auditory system injury.

FUNDING HISTORY

The HRRP received a \$10 million (M) Congressional appropriation in fiscal year 2017 (FY17), its inaugural year, and selected seven grant applications for funding. Award data and abstracts of funded research proposals can be viewed on the CDMRP website (<http://cdmrp.army.mil>). The FY18 HRRP appropriation is \$10M.

RESEARCH AND FUNDING ENVIRONMENT

STATE OF THE SCIENCE

Recent years have seen exciting advances in a number of areas of hearing research, such as hair cell development, hair cell function, synaptopathy, hybrid cochlear implants, and others.⁵ However, significant knowledge and technical gaps remain that must be closed in order to effectively restore hearing in human patients. To identify promising opportunities to further the goal of hearing restoration, especially restoration after noise exposure and/or auditory system injuries, the HRRP surveyed the hearing research community for unanswered research questions and hosted panel discussions with scientists, as well as audiologists and otolaryngologists with first-hand experience of serving Warfighters, Veterans with hearing loss, and other program stakeholders. The following categories of questions emerged as of the highest interest to the HRRP:

► **Drugs and Therapeutics to Promote Regeneration and Restoration**

Examples: What drugs and therapeutic interventions can we use to restore hair cells and spiral ganglia neurons? Are there existing drugs that can be used to promote regeneration or restoration?

► **Define and Diagnose Hearing Dysfunction**

Examples: How should we define and diagnose the loss of functional/operational hearing in humans as related to synaptopathy, hidden hearing loss, central auditory processing disorder, etc.? What is the dysfunction and where is the damage?

► **Genetic and Epigenetic Regulation of Hair Cell Production**

Examples: How can genetic programs and gene regulatory networks be exploited to stimulate cell proliferation and appropriate differentiation? How do genetic and epigenetic factors and metabolism impact hearing restoration?

► **Timely Mitigation of Auditory Damage**

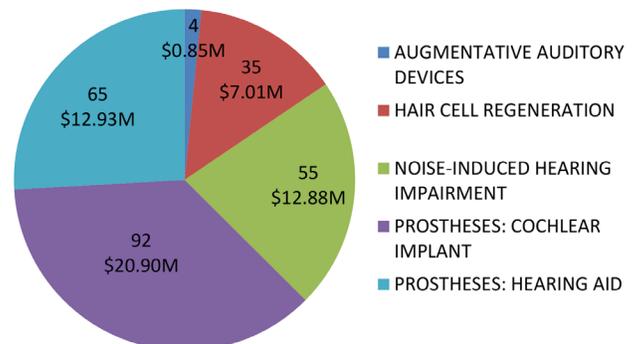
Examples: How can we detect injury sooner so that treatment can be started earlier? What can be done in the few hours after noise exposure to minimize damage?

FUNDING LANDSCAPE

The primary public funder across all areas of hearing research is the National Institute on Deafness and Other Communication Disorders (NIDCD). In FY17, the NIDCD made awards to hearing research projects totaling almost \$247M, supporting a broad portfolio of hearing research topics ranging from the basic mechanisms of normal hearing to epidemiology, etiology, genetic testing, prevention, and intervention of diseases and disorders related to hearing. With regard to hearing restoration, the largest number of extramural projects were awarded to scientists studying cochlear implants and hearing aids (**Figure 2**).

The VA Rehabilitation Research and Development Service (RR&D) sponsors hearing research as part of its Sensory Systems/Communication Disorders portfolio, which encompasses hearing, vestibular, communication disorders, and vision research projects. In

Figure 2. NIDCD FY17 Extramural Grants in Hearing Restoration Categories*



* Individual projects may be included in more than one category.



FY17, the VA RR&D funded 83 Sensory Systems/Communication Disorders research awards totaling ~\$16.4M, including 13 awards related to hearing loss and 5 awards related to tinnitus.

Tinnitus research has also received funding from the CDMRP's Peer Reviewed Medical Research Program (PRMRP) since FY08. Between FY08 and FY17, the PRMRP invested more than \$26M to fund 18 tinnitus research awards ranging from early discovery to clinical trials.

Additional sources of funding for hearing research include the Defense Medical Research and Development Program (DMRDP), the Noise-Induced Hearing Loss Program within the Office of Naval Research (ONR), and non-federal organizations such as the American Otological Society, American Hearing Research Foundation, American Tinnitus Association, and Hearing Health Foundation.

HEARING CENTER OF EXCELLENCE

The Department of Defense (DoD) Hearing Center of Excellence (HCE) plays a unique and critical role in hearing research. The HCE was legislated by Congress in 2008 to foster and promote the prevention, diagnosis, mitigation, treatment, rehabilitation, and research of hearing loss and auditory injury. The HCE has established and maintains a collaborative research network composed of strategically aligned research laboratories, medical treatment facilities, nonprofit organizations, academic partners, industry, international bodies, and other government Centers of Excellence. It leads the Pharmaceutical Interventions for Hearing Loss (PIHL) working group to develop and disseminate current and comprehensive understanding of the state of the science, evidence-based research methodology standards, and capability-based requirements for technology transfer to the DoD. Moreover, the HCE develops tools, databases, and educational materials that facilitate hearing research and promote hearing health, such as the Joint Hearing and Auditory System Injury Registry (JHASIR) and the Comprehensive Hearing Health Program (CHHP).

STRATEGIC DIRECTION

The HRRP developed its near-term (5-year) strategic direction based on recommendations from the HRRP Programmatic Panel, which is composed of clinicians and subject matter experts from the military Services; program officials from the HCE, NIDCD, VA, and other government entities; academic scientists; and consumer representatives. To pursue promising scientific opportunities while coordinating research funding, initiatives, and priorities across organizations, the Programmatic Panel considered the state of the science, including major unanswered questions and emerging technologies, the funding landscape, the NIDCD 2017-2021 Strategic Plan, and hearing research initiatives and outcomes of other entities such as the DMRDP, ONR, and U.S. Army Medical Materiel Development Activity.

STRATEGIC GOALS

The HRRP has identified two program priorities and set the following goals to address them:

► Accelerate drug discovery and therapeutic development for hearing restoration

Currently, there is no Food and Drug Administration (FDA)-approved drug to treat hearing loss. There has been significant progress in the molecular and cellular understanding of hearing loss and regeneration mechanisms in the inner ear. However, the majority of research is preclinical, and the findings need to be verified in more clinically relevant research and translated to clinical applications. Translation of preclinical findings into drugs and therapeutics is an area with great potential for growth and breakthroughs within the next 5 years.

► Accelerate advances in the assessment and treatment of auditory dysfunction

Noise exposure may induce auditory dysfunction such that an individual's hearing sensitivity is within normal limits, but their capacity to listen and understand speech is substantially impaired. This type of auditory dysfunction is often referred to as "hidden hearing loss." The military has a great need to reliably assess and mitigate auditory dysfunction, including hidden hearing loss, in the battlefield/deployed environment.

While these strategic goals are expected to be stable for the next 5 years, they will be reviewed during the HRRP's annual Vision Setting meetings and revised/updated as needed.

INVESTMENT STRATEGY

To achieve the strategic goals identified above, the HRRP will focus its investments on translational and applied research over the next 5 years. The HRRP will solicit and support research that accelerates drug discovery and therapeutic development; for instance, research that translates promising laboratory findings into clinical applications, and research that removes barriers and/or builds paths to drug discovery. Additionally, the HRRP will solicit and support research that accelerates advances in the assessment and



treatment of auditory dysfunction, including technology and methods to assess auditory dysfunction in the battlefield/deployed environment, diagnosis of auditory system injuries, and technology and methods to prevent and/or mitigate auditory system injuries and treat auditory dysfunction.

For each fiscal year, the specifics of the HRRP's investment strategy, including award mechanisms, focus areas, and funding levels, will be determined at the annual Vision Setting meetings, taking into account the most current state of the science and available Congressional appropriations.

In FY18, the HRRP is offering two award mechanisms. The Translational Research Award (TRA) mechanism is intended to support translational research that will accelerate the movement of promising laboratory research relevant to hearing restoration into clinical applications. The Focused Applied Research Award (FARA) mechanism is intended to support applied research that will advance the diagnosis and treatment of auditory dysfunction where hearing sensitivity may be within normal limits but the individual's capacity to listen and understand speech is substantially impaired.

MEASURING PROGRESS

The HRRP will measure its near-term success based on its impact on research activity, as well as scientific output in the aforementioned priority areas. Program evaluation will be conducted on an ongoing basis using a multitude of parameters. Some examples are provided below.

ASSESSING RESEARCH ACTIVITY

- Quantity and quality of grant applications received
- Awards funded in each priority area
- Investigators and institutions that engage in HRRP-sponsored research projects

ASSESSING SCIENTIFIC OUTPUT

- Publications
- Presentations
- Patent applications and patents

The long-term success of the HRRP will be evaluated by the scientific and clinical returns on its investment; for example, drugs and therapeutic targets identified and/or tested, diagnostic tools and methods developed, Investigational New Drug/Investigational Device Exemption applications submitted to and approved by the FDA, clinical trials that resulted from HRRP-funded projects, and numbers and amounts of follow-on funding obtained by HRRP-sponsored investigators.

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