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45 **Welcome from the Director**

46
47 The National Institute on Deafness and Other Communication Disorders (NIDCD) is pleased to
48 share our new five-year Strategic Plan for 2017-2021. The Plan helps the NIDCD prioritize its
49 research investments by identifying areas of outstanding promise and areas in need of greater
50 funding due to gaps in our knowledge. By prioritizing research investment in these areas,
51 NIDCD strives to improve the quality of life for people with communication disorders.

52
53 Looking forward, the NIDCD anticipates unprecedented scientific opportunities. We are already
54 using recent advances in science and technology to discover how changes to the molecular,
55 cellular, and systemic pathways can cause communication disorders. The NIDCD hopes to build
56 on these advances by supporting research that will lead to better ways to identify those who are
57 at risk for developing certain communication disorders, with a goal of preventing a disorder from
58 occurring or at least lessening its effects. The NIDCD also continues to support research to
59 develop better treatments for people with communication disorders.

60
61 These unprecedented research opportunities are coupled with the challenge of using our best
62 scientific judgment to make difficult choices about which areas of research to pursue. The
63 objectives in this Strategic Plan have been identified through discussions among outside experts
64 in each of the Institute's mission areas, along with input from NIDCD staff members, the
65 National Deafness and Other Communication Disorders (NDCD) Advisory Council,
66 representatives of the research and advocacy communities, and members of the public.

67
68 Thank you for your interest in the NIDCD's scientific research. For more information, please
69 visit the NIDCD website at <http://www.nidcd.nih.gov/>.

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Sincerely,
James F. Battey, Jr., M.D., Ph.D.
Director
National Institute on Deafness and Other Communication Disorders

79 *Science Capsule: Advances in Hearing Aid Research*

80
81 Approximately 15 percent of American adults (37.5 million) age 18 and over report some trouble hearing, making
82 this one of the most prevalent disabling conditions in the U.S. Hearing loss can be hereditary, or it can result from
83 disease, trauma, medications, or long-term exposure to damaging noise. The condition can vary from a mild but
84 important loss of sensitivity to a total loss of hearing.

85
86 Sensorineural hearing loss is caused by a problem in the cochlea or the auditory nerve, the parts of the ear that help
87 sound impulses reach the brain. It affects people of all ages, in all segments of the population, and across all
88 socioeconomic levels. It can interfere with an individual’s physical, cognitive, behavioral, and social functions and
89 hearing aids are the main form of treatment; however, among adults age 70 and older with hearing loss that could
90 benefit from hearing aids, fewer than 30 percent has ever used them. Even fewer adults age 20 to 69 (approximately
91 16 percent) who could benefit from wearing hearing aids have ever used them.

92
93 A hearing aid works by amplifying sound to allow people to hear sounds that would not be audible. It can also be
94 used to access “hearing loop” wireless signals that are beamed directly to the aid to bypass background noises in
95 specially equipped movie theaters, auditoriums, lecture halls, places of worship, and other areas. A vast array of
96 hearing aid technology is available to provide additional features, such as the telecoil needed to pick up the hearing
97 loop wireless signal.

98
99 Although the development of microelectronic components has enabled development of new digital hearing aid
100 technology to replace earlier devices based on analog circuits, the underlying damage to the inner ear remains a
101 limitation when the user is confronted by multiple speakers or background noise. Hearing aid users often complain
102 of straining to focus on a single speech sound among competing sources at meetings, banquets, and sporting events.
103 One solution to this problem is to move the hearing aid user closer to the person speaking and further from the noise
104 sources. Directional microphones offer another approach to do the same thing simply by pointing a device.

105
106 NIDCD-supported scientists have studied the tiny fly, *Ormia ochracea*, which has such remarkable directional
107 hearing that its design has inspired development of a novel directional microphone. The physics and biology behind
108 this fly’s abilities to localize sound was reverse engineered and provided engineers with strategies to improved
109 directional microphones that are small enough to use in hearing aids and help focus the aid on one sound source at a
110 time. These new principles were highlighted as an opportunity to improve hearing aids.

111
112 Capitalizing on the knowledge learned from studying *Ormia*, another group of NIDCD-supported scientists
113 successfully completed design and testing of a novel microphone based on these design elements. The scientists
114 used silicon microfabrication technology to reliably build the critical sensing elements needed for a functional
115 microphone based on this novel design, characterize its function, and prove it had the capability to provide
116 performance gains over existing designs.

117
118 Other NIDCD-supported scientists have continued research and development efforts based on this proof of concept
119 prototype by adapting the microphone design into a form that could be more readily incorporated in a hearing aid.
120 The scientists are the first to use piezoelectric materials which turn mechanical pressure into electrical signals, or
121 voltage, and allow the microphone to operate with very little power. Because hearing aids rely on batteries,
122 minimizing power consumption is a crucial design requirement.

123
124 The NIDCD recognizes the needs of the majority of adults with hearing loss are not being met, and the cost and
125 accessibility of hearing aids are considered to be part of the barriers to care. In response, the NIDCD is working to
126 fill this need by supporting research or infrastructure that will lead to more accessible and affordable hearing health
127 care for adults. The NIDCD cosponsored a consensus development study with the National Academies of Sciences,
128 Engineering, and Medicine to consider hearing health care from the health care and population health perspectives,
129 including the regulatory environment, access, and affordability. By identifying the research gaps related to effective
130 and affordable hearing health care, devices, and compliance, and by developing novel strategies to overcome these
131 gaps, NIDCD clinical and translational research will endeavor to improve the quality of life for millions of
132 Americans with hearing loss.

134 **Introduction**

135
136 **NIDCD Overview**

137
138 Approximately 46 million Americans experience some form of communication disorder.
139 Communication disorders make the basic components of communication (sensing, interpreting,
140 and responding to people and things in our environment) challenging. In addition,
141 communication disorders not only compromise physical health, but also affect the emotional,
142 social, recreational, educational, and vocational aspects of life. The effects often ripple outward
143 to affect families and social networks, including those at work and school. The total economic
144 impact of these disorders in regards to quality of life and unfulfilled potential is substantial.
145 Furthermore, the prevalence of communication disorders is expected to increase as the
146 population ages, and as survival rates improve for medically fragile infants and people affected
147 by traumatic injuries and diseases.

148
149 In October 1988, Congress established the National Institute on Deafness and Other
150 Communication Disorders (NIDCD) as one of the institutes that compose the National Institutes
151 of Health (NIH), part of the U.S. Department of Health and Human Services. The NIH is the
152 Federal government’s focal point for the support of biomedical research and is among the
153 leading biomedical research funding institutions in the world. NIH’s mission is to seek
154 fundamental knowledge about the nature and behavior of living systems and to apply that
155 knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability.
156 NIDCD’s focus within this broad mission is to bring national attention to the disorders and
157 dysfunctions of human communication and to contribute to advances in biomedical and
158 behavioral research that will improve the lives of the millions of people with a communication
159 disorder.

160
161 The NIDCD mission is to conduct and support biomedical research, behavioral research, and
162 research training in the normal and disordered processes of hearing, balance, taste, smell, voice,
163 speech, and language. The Institute conducts and supports research and research training related
164 to disease prevention and health promotion; addresses special biomedical and behavioral
165 problems associated with people who have communication impairments or disorders; supports
166 research evaluating approaches to the identification and treatment of communication disorders
167 and patient outcomes; and supports efforts to create devices that substitute for lost and impaired
168 sensory and communication function. To accomplish these goals, the NIDCD manages a broad
169 portfolio of both basic and clinical research. The portfolio is organized into three program areas:
170 hearing and balance; taste and smell; and voice, speech, and language. The three program areas
171 seek to answer fundamental scientific questions about normal function and disorders and to
172 identify patient-oriented scientific discoveries for preventing, screening, diagnosing, and treating
173 disorders of human communication. (Please see [Appendix A](#) for more information on the
174 NIDCD’s funding history).

175
176 The NIDCD accomplishes its research mission through three divisions: the Division of
177 Intramural Research (DIR), the Division of Scientific Programs (DSP), and the Division of
178 Extramural Activities (DEA). The DIR conducts research and related support activities in
179 laboratories and clinics housed at the NIH. The DSP and DEA manage complementary aspects

180 of the NIDCD's Extramural Research Program, a program of research grants, career
181 development awards, individual and institutional research training awards, center grants, and
182 contracts to public and private research institutions and organizations throughout the U.S. and
183 abroad. As a whole, the Institute supported approximately 1,300 research grants, training awards,
184 and R&D contracts in Fiscal Year (FY) 2016. Through research and education, the NIDCD
185 strives to reduce both the direct and indirect economic burden of communication disorders on
186 individuals, families, and society, thereby improving the quality of life for people living with a
187 communication disorder.

188

189 **NIDCD Strategic Plan and Priority Setting**

190

191 The NIDCD uses the NIH system of peer review to evaluate research grant applications. The
192 system depends on scientists to submit their best research ideas to drive the spectrum of
193 supported research. NIH then utilizes a structured peer review process where grant applications
194 for funding are scrutinized by a panel of scientific experts from outside of the NIH (who work in
195 the same or a related academic field.) The panel evaluates applications on the basis of
196 significance, investigator(s), innovation, approach, and the quality of the academic environment,
197 in order to identify those with the highest overall impact. This system helps NIH select the most
198 promising ideas to receive federal funding. The NIH will continue and strengthen its
199 commitment to this transparent, evidence-based process of peer review. To learn more about the
200 NIH peer review process, see: <http://grants.nih.gov/grants/peer/peer.htm>. To learn how NIH
201 continuously reviews and updates its peer review process, see:
202 http://grants.nih.gov/grants/peer/continuous_review.htm.

203

204 The NIDCD values investigator-initiated applications submitted to NIH that help achieve the
205 NIDCD Mission. In particular, NIDCD encourages investigators to submit applications for
206 research projects that directly address priorities within the NIDCD Research Strategic Plan
207 (Plan). NIDCD also uses the Plan to develop targeted Funding Opportunity Announcements
208 (FOAs), to stimulate research applications that address a particular and much-needed area of
209 science.

210

211 The NIDCD Strategic Plan helps the Institute (including NIDCD staff and the NDCD Advisory
212 Council) prioritize research investment. The Plan helps identify investigator-initiated research
213 proposals for High Program Priority (HPP) funding, meaning that these projects, if funded, will
214 address a significant research need in the NIDCD portfolio. The NIDCD uses its HPP process to
215 fill scientific gaps in the research portfolio, foster the entry of new investigators, foster
216 innovative research, and increase the diversity of the scientists who lead a research team, known
217 as Principal Investigators, or PIs.

218

219 NIDCD staff distribute the Plan to the research community at workshops and scientific
220 conferences to increase awareness of Institute priorities. Additionally, the Plan informs the
221 public about the state of the science and advances in diagnosis and treatment of communication
222 disorders, while creating a vision for the future. To develop the 2017-2021 Plan, the NIDCD
223 convened a series of working group meetings and solicited input from scientific experts, the
224 NDCD Advisory Council, NIDCD staff, and the public. (Please see [Appendix B](#) for more details

225 on the Plan process.)

226

227 **Enhance Scientific Stewardship at NIDCD**

228

229 **Research Training and Career Development at the NIDCD**

230

231 The number of Americans with communication disorders is expected to rise as the nation’s older
232 population increases and as survival rates improve for a wide range of medical conditions
233 associated with communication disorders. As such, the NIDCD recognizes the importance of
234 research training and career development opportunities to ensure a productive, creative, and
235 innovative cadre of qualified scientists in basic, clinical, and translational research. The NIDCD
236 is continuously adapting its research training and career development efforts to help new
237 scientists establish careers in our mission areas, encourage clinicians to pursue opportunities in
238 translational research, and build shared research resources.

239

240 The field of human communication sciences needs interdisciplinary research teams of clinicians
241 and basic scientists to bridge the gap between laboratory research and patient care. Clinicians
242 need a deeper understanding of the latest research discoveries to bring new diagnostic and
243 treatment approaches into the clinic. Basic researchers need a thorough understanding of the
244 needs, challenges, and opportunities faced by clinicians. The NIDCD believes that cross training
245 these scientists could spark new ways to better prevent, detect, and treat communication and
246 chemosensory disorders. Interdisciplinary teams of basic scientists and clinicians—including
247 physicians, surgeons, and audiologists—will then be able to initiate and support new directions
248 for scientific discovery, conduct hypothesis-driven clinical trials, assess new diagnostic tools and
249 interventions, and improve public health and well-being.

250

251 **Workforce Diversity at the NIDCD**

252

253 Since human communication disorders cross all social and ethnic groups, the NIDCD recognizes
254 that we need a diverse interdisciplinary workforce to tackle the world’s diverse public health
255 needs. In addition, the NIDCD recognizes the underrepresentation of minority scientists in its
256 research and research training activities and diligently works to increase participation for these
257 minority individuals and groups. To this end, the NIDCD has made it a priority to increase the
258 number of minorities, individuals with communication disorders, and individuals and groups
259 from diverse backgrounds in the research enterprise. The NIDCD strives to attract and encourage
260 individuals to consider research careers in the communication sciences at NIDCD or at NIDCD-
261 supported institutions to enable the research community to be in a position to advance the
262 NIDCD mission and to meet the future health needs of individuals with communication
263 disorders.

264

265 **Health Disparities Research at NIDCD**

266

267 Human communication disorders cross all social and ethnic groups. The NIDCD conducts
268 research to understand the basis of health disparities within its mission areas by determining how
269 communication disorders may contribute to, or be worsened by, differences in health among
270 populations. The NIDCD also recognizes minorities and individuals with communication

271 disorders are underrepresented in NIDCD-sponsored research and research training activities and
272 is working to increase participation of individuals and groups from diverse backgrounds.
273 Participation of minority or underserved populations in NIDCD-sponsored research advances the
274 NIDCD mission and ensures that everyone benefits from human communication research.

275

276 **Shared Databases, Registries, and Metrics on Communication Disorders**

277

278 Biomedical research is rapidly becoming data-intensive as scientists generate and use
279 increasingly large, complex, multidimensional, and diverse datasets. The NIDCD ensures
280 scientific rigor and reproducibility by establishing databases with common measures that
281 encompass the human lifespan for hearing and balance; taste and smell; and voice, speech, and
282 language. The NIDCD will continue to support data sharing through the development and use of
283 clinical registries, clinical data networks, and other forms of electronic health data in order to
284 help healthcare providers make evidence-based decisions on best practice and thereby improve
285 outcomes for individuals with communication disorders. The NIDCD is especially committed to
286 developing and implementing infrastructure to identify: 1) investigators with expertise in
287 epidemiology, data registry, clinical trials, and other clinical research and 2) academic- and
288 community- based clinical practice settings with geographical, racial, and ethnic diversity in
289 order to facilitate rigorous, cost-effective, clinical research and maximize human subjects'
290 protection.

291

292 By establishing standard metrics in anatomical, acoustical, and physiological measures,
293 researchers can better define functional communication abilities under real-world conditions.
294 The NIDCD will support new and enhance existing centralized tissue- and cell-banks to aid
295 access to biological source materials. Standard metrics and centralized tissue banks also help
296 researchers to differentiate clinical subtypes and to identify early preclinical pathology.
297 Improving communication among scientists and clinicians across different specialties is
298 important. To do this, the NIDCD supports development of better measures of: 1) performance,
299 2) communication abilities, 3) and disease-specific quality of life instruments, 4) assessment of
300 communication impairments, and 4) outcomes of individuals with communication disorders.

301

302 **Trans-NIH Efforts Encourage Innovation through Partnerships**

303

304 While the NIDCD focuses its research efforts on programs that support its mission areas,
305 breakthroughs in related fields (such as neuroscience, genetics, and animal models) improve our
306 understanding of communication disorders and encourage innovation through partnerships. In
307 order to support these discoveries, the NIDCD participates in many Trans-NIH initiatives and
308 programs. (Please see [Appendix C](#) for examples of some of these Trans-NIH activities).

309

310 **Excel as a Federal Science Agency by Managing for Results**

311

312 The NIDCD is a public science agency supported by Federal funds. As part of the NIH, the
313 NIDCD is obligated to base its decisions on science, and to make its decision-making process
314 transparent. The NIDCD upholds its accountability to the American public by managing its
315 scientific endeavors with an eye towards achieving results that improve the health of individuals
316 with communication disorders. The NIDCD approaches this responsibility in several different

317 ways, from its reporting as required by a U.S. Law called the Government Performance and
318 Results Act (GPRA), to developing an administrative strategic plan to complement this NIDCD
319 Research Strategic Plan, and by mitigating the risks involved with administering the NIDCD
320 mission.

321
322 GPRA is a U.S. law enacted in 1993. It is designed to improve government performance
323 management, and it requires agencies to manage their performance by setting goals, measuring
324 results, and reporting their progress. In order to comply with GPRA, the NIH develops an annual
325 plan proposing goals that provide a representative sample of NIH's activities for each year,
326 describes how these goals will be met, and, later in the fiscal year, NIH provides evidence to
327 support any claims for successful achievement of the goals. Each Institute and Center at NIH
328 participates in the GPRA reporting process, including NIDCD.

329
330 The NIDCD's goal represents only one snapshot of NIDCD's entire portfolio, but aligns with our
331 Mission to improve the lives of people with communication disorders. The current NIDCD
332 GPRA goal began in FY 2015 and states: By 2020, increase the number of potential treatment
333 options for communication disorders that are being tested in clinical trials by adding one new
334 treatment option per year. In order to comply with our GPRA obligations for this particular goal
335 under the law, NIDCD proposes a distinct new treatment option that will be tested each fiscal
336 year and then, at the end of that fiscal year, NIDCD submits evidence that we have tested a new
337 treatment option for a communication disorder. The NIH compiles NIDCD's annual submission
338 with those from all of the other NIH Institutes and Centers and presents it to the Office of
339 Management and Budget (OMB). OMB includes the NIH information in an annual report on
340 government agency performance that accompanies the President's annual budget request.

341
342 Another way that NIDCD manages its public funds for results is by developing and using its
343 NIDCD Administrative Strategic Plan. NIDCD staff examine current challenges at the Institute
344 and develop an NIDCD Administrative Strategic Plan to address these challenges. The Plan
345 helps NIDCD manage its services in support of NIDCD's mission, and it helps NIDCD pursue
346 transformative science by:

- 347 • modeling innovative management approaches, encouraging collaboration and the free
348 flow of information, and sharing best practices within and between the NIDCD offices;
- 349 • improving the quality of life and job satisfaction for NIDCD employees by implementing
350 clear, consistent, customer focused service practices;
- 351 • managing services and resources using the principles of efficiency, effectiveness, and
352 quality; and
- 353 • providing better decision making and transparency by setting goals and then looking back
354 to determine if those goals have been met.

355
356 The NIDCD works to ensure that the dollars we invest get results by developing a Risk
357 Management Plan. The plan looks at NIDCD's activities and assesses risks, establishes methods
358 for control of those risks, monitoring adherence to the risk-reduction methods, and mitigating
359 risks involved with administering the NIDCD mission. The NIDCD plan tries to minimize the
360 risk of failure in all of the NIDCD activities, and it is submitted each year as part of the overall
361 NIH Enterprise Risk Management program.

362

363 **Future Directions in NIDCD Program Areas**

364
365 In consultation with communication research scientists and the public, the NIDCD has identified
366 four Priority Areas that have the potential to increase our understanding of the normal and
367 disordered processes of hearing, balance, taste, smell, voice, speech, and language and to further
368 our knowledge in human communication sciences. They are:

369
370 **Priority Area 1: Understanding Normal Function**

371 Deepen our understanding of the mechanisms underlying normal function of the systems of
372 human communication. By defining what is normal in both animal models and humans, we can
373 better understand mechanisms of disease.

374
375 **Priority Area 2: Understanding Diseases and Disorders**

376 Increase our knowledge of the mechanisms of diseases, disorders, and dysfunctions that impair
377 human communication and health. Understanding mechanisms that underlie diseases and
378 disorders is an important step in developing better prevention and treatment strategies.

379
380 **Priority Area 3: Improving Diagnosis, Treatment, and Prevention**

381 Develop, test, and improve diagnosis, treatment, and prevention of diseases, disorders, and
382 dysfunctions of human communication and health. Diagnosis considers normal function and
383 provides targets for prevention and treatment. Improvements in prevention and treatment lead to
384 better outcomes and guide treatment options.

385
386 **Priority Area 4: Improving Outcomes for Human Communication**

387 Accelerate the translation of research discoveries into practice; increase access to health care;
388 and enhance the delivery, quality, and effectiveness of care to improve personal and public
389 health. Scientifically validated prevention and treatment models will lead to better personal and
390 public health only if they are translated effectively into routine practice.

391
392 Although the Priority Areas described in this Plan help the NIDCD identify promising scientific
393 opportunities to advance human communication research over the next five years, the NIDCD
394 will continue to fund as much meritorious research as possible within our program areas of
395 hearing and balance; taste and smell; and voice, speech, and language.

396
397 The Plan is not a comprehensive list of all research areas that NIDCD is currently supporting or
398 plans to support in the future. Basic and clinical research being supported by NIDCD will
399 continue to be given high priority. The NIDCD is committed to supporting new, innovative,
400 hypothesis-driven, meritorious research, which can lead to improving the overall health and
401 quality of life for people with communication disorders.

402

403 **Hearing and Balance Research**

404

405 **Why NIDCD Supports Hearing and Balance Research**

406

407 Loss of hearing or balance imposes a significant social and economic burden upon individuals,
408 their families, and the communities in which they live. Millions of Americans experience a
409 hearing or balance disorder at some point in their life, especially as young children or older
410 adults. Common examples include middle-ear infections (otitis media), noise-induced hearing
411 loss, tinnitus, age-related hearing loss, dizziness, and vertigo. Hearing and balance disorders also
412 decrease quality of life, and cross all ethnic and socioeconomic lines. Approximately 37.5
413 million American adults report some degree of hearing loss and 33.4 million adults report a
414 problem during the past 12 months with dizziness or balance problems^(1, 2). Dizziness and
415 balance problems include vertigo, unsteadiness, blurred vision when moving your head,. Among
416 the younger age group, an additional 5.3% of American children (3.3 million) also experienced
417 balance and dizziness problems in the last 12 months, as reported by their parents or other adult
418 caregivers⁽³⁻⁶⁾. About two to three of every 1,000 children in the United States are born with a
419 detectable level of hearing loss in one or both ears that can affect speech, language, social, and
420 cognitive development^(4, 5). In 2014, one in six U.S. adults ages 18 and older reports trouble
421 hearing without a hearing aid⁽⁶⁾.

422

423 Noise-Induced Hearing Loss

424 Excess noise is a major contributor to hearing loss in the United States. An estimated 15% of
425 Americans between the ages of 20 and 69, or 26 million Americans, may have a permanent
426 hearing loss caused by exposure to excess noise⁽⁷⁾. Recent animal studies suggest that noise
427 exposure causing temporary measurable hearing loss may also cause permanent hearing loss that
428 is not readily detectable using standard audiometric testing. Such damage may underlie the
429 common complaint of having difficulty in understanding speech in noisy situations. The NIDCD
430 encourages research to better understand noise-induced auditory damage to inform potential
431 therapies.

432

433 Otitis Media

434 Otitis media (OM), or middle ear infection, is a condition that affects most young children before
435 three years of age. Repeated episodes of OM can contribute to hearing loss and possibly delay
436 language and cognitive skills development. NIDCD research is improving our understanding of
437 susceptibility and pathogenesis of OM. In the future, this research might identify immune
438 pathways to guide effective OM vaccine development.

439

440 Presbycusis

441 Age-related hearing loss (presbycusis) is the loss of hearing that gradually occurs during aging. It
442 is one of the most common conditions affecting older and elderly adults with approximately one
443 in three people in the U.S. between the ages of 65 and 74 exhibiting a hearing loss, and nearly
444 half of those older than 75 have difficulty hearing⁽⁸⁾. There are many causes of age-related
445 hearing loss. Most commonly, it arises from changes in the inner ear, but it can also result from
446 complex changes along the nerve pathways from the ear to the brain. Understanding the cause of
447 age-related hearing loss and finding ways to prevent it are important research areas supported by
448 NIDCD.

449

450 Tinnitus

451 Tinnitus, or ringing in the ears, is a disorder that affects approximately 25 million Americans,
452 many of whom also have hearing loss. Severity can range from a mild condition, which requires
453 no intervention, to a severe debilitating disease with significant emotional, social, and economic
454 impact. NIDCD research aims to determine the neural basis of tinnitus, and to develop effective
455 interventions for affected people.

456

457 Technology Interventions for Hearing Loss

458 Individuals with mild-to-severe hearing loss can benefit from using a hearing aid, and many with
459 severe to profound hearing loss benefit from having a cochlear implant. Advances in both
460 hearing aid and cochlear implant technology are improving treatment options for many people
461 with various degrees of hearing loss. For example, individuals may be fitted with hearing aids or
462 cochlear implants on both ears instead of only one ear to improve sound localization and
463 discrimination. In recent years, some people with residual hearing for low-frequency sounds
464 have received both a cochlear implant, to aid them in hearing higher-frequency sounds, and a
465 hearing aid to allow them to take advantage of their residual low-frequency hearing. In many
466 cases, this combination ('hybrid') strategy results in a significant improvement when listening to
467 speech in background noise.

468

469 Mouse Models

470 Mouse models of hereditary hearing impairment continue to be instrumental in mapping and
471 cloning many of the gene mutations that contribute to deafness. They help scientists zero in on
472 how gene mutations affect protein function and result in deafness, and are a model in which to
473 test therapeutic approaches to treat or prevent hearing loss. These models help us understand the
474 importance of genes in the development and maintenance of the human ear. In addition, mouse
475 models have enabled scientists to directly examine auditory sensory cells and to characterize the
476 inner ear's response to sound. Recent research has identified some of the cellular processes that
477 contribute to hair cell damage and death, heralding future studies that may determine the inner
478 ear's response to mechanical and chemical trauma.

479

480 Balance Disorders

481 The inner ear contains the vestibular system, which includes sensory parts of the inner ear called
482 the vestibular organs. Tiny canals and pouches on both sides of the head are specialized to detect
483 motion and gravity. Their nerve signals interact with other sensory, motor, autonomic and
484 cognitive circuits in the brain for several functions. The vestibular system regulates balanced
485 posture and locomotion, provides spatial and heading orientation for navigation, and stabilizes
486 visual gaze during movement. Normal balance is maintained by integrating inputs from the
487 vestibular, visual, proprioceptive (position sensation), and musculoskeletal systems. Vestibular
488 disorders can lead to dizziness, vertigo, nausea, migraines, blurred vision, and various forms of
489 postural instability. Dysfunctions of the vestibular system can occur independently or with a
490 hearing loss. The NIDCD supports the development of more efficient vestibular testing for
491 improved clinical diagnoses and safer, better tolerated, and more effective pharmacological
492 treatments for vertigo. NIDCD-supported scientists are also developing vestibular prosthetic
493 devices and minimally invasive surgical techniques to control imbalance and vertigo while

494 preserving hearing and other functions.

495

496 **The Hearing and Balance Program**

497

498 The NIDCD Hearing and Balance Program encompasses over half of NIDCD's research
499 portfolio. To study normal and disordered functions of the auditory and vestibular systems, the
500 NIDCD employs a wide range of research approaches such as molecular genetics, cellular
501 biology, animal models, biomedical imaging, nanotechnology, psychoacoustics, and structural
502 and functional biology. The NIDCD supports research that will lead to improved treatments for,
503 and prevention of, hearing and balance disorders.

504

505 **Recent Advances in Hearing and Balance Research**

506

507 **Hair Cells**

508

- 509 • Scientists have identified TMC1, TMC2, TMHS, and TMIE as proteins important in the
510 mechanotransduction machinery in hair cells that convert sound-evoked mechanical
511 motion in the inner ear into electric signals to the brain. This knowledge has
512 fundamentally advanced our understanding of how hair cells work⁽⁹⁻¹⁵⁾.
- 513 • High throughput RNA-sequencing has provided scientists with new insights into the
514 distinct molecular characteristics that occur during the formation of different cell types in
515 the organ of Corti, including hair cells. This information may aid in development of cell-
516 based therapies for treating hearing loss and balance disorders⁽¹⁶⁻²⁰⁾.
- 517 • Scientists have used proteomics to identify new proteins expressed in hair cell
518 stereociliary bundles. This approach has revealed new insights into hair cell function^(21, 22)
519 and identified new components of the hair bundle necessary for hearing and balance⁽²³⁾.

520

521 **Development and Regeneration**

522

- 523 • *Wnt* signaling and *Lgr5*-expression have been shown to be key for the generation of hair
524 cells in the developing cochlea^(24, 25).
- 525 • Techniques to turn embryonic stem cells into inner ear hair cells and supporting cells, *in*
526 *vitro*, have been developed. This technique is well suited for high-throughput screening
527 of drugs for hair cell regeneration⁽²⁶⁾.
- 528 • Antisense oligonucleotides have been used to rescue hearing and balance function in a
529 mouse model of human deafness⁽²⁷⁾.
- 530 • It is now possible to prevent hearing loss and stimulate repair or regenerate sensory cells
531 of the inner ear by transdifferentiating or directly reprogramming cells, or by using gene
532 therapy⁽²⁸⁻³⁰⁾.

533

534 **Hearing Loss**

535

- 536 • Damage to spiral ganglion neurons or their synapses in the inner ear may contribute to
537 hearing loss. Scientists have discovered that the synapses between cochlear nerve fibers
538 and inner hair cells are the most vulnerable elements in noise-induced and age-related

- 539 hearing loss and nerve fibers with high response, thresholds are the first to degenerate
540 likely contributing to problems of hearing in noise⁽³¹⁻³⁶⁾.
- 541 • Scientists have determined that unmyelinated type II sensory fibers innervating outer hair
542 cells respond to cellular damage resulting from loud sound and thus may serve as the
543 nociceptors of the inner ear^(37, 38).
 - 544 • Dozens of new gene defects responsible for hereditary hearing loss have been identified
545 in recent years, including mutations in the first microRNA (miR-96) involved in hearing
546 loss^(39, 40).
 - 547 • The combination of using whole exome sequencing (a technique for sequencing all the
548 expressed genes in a genome) and hearing testing is ushering in a new area of
549 personalized diagnoses, opportunity for earlier intervention, and ultimately, treatment for
550 individuals with hearing loss⁽⁴¹⁻⁴⁹⁾.
 - 551 • Gene therapy is being used to correct gene defects that cause hereditary hearing loss and
552 restore auditory function in animal models⁽⁵⁰⁻⁵²⁾.
 - 553 • The use of high throughput screening in zebrafish is leading to the discovery of new
554 protective compounds that will help preserve hearing in noise-induced hearing
555 impairment or drug-induced hearing impairment⁽⁵³⁻⁵⁶⁾.
 - 556 • Proof-of-principle studies have shown that small molecules delivered to the cochlea after
557 noise damage can lead to some hair cell regeneration and some functional recovery⁽⁵⁷⁾.
 - 558 • Preliminary studies suggest that, in older adults, hearing impairment is associated with
559 cognitive decline, dementia, and depression. Estimated declines are greatest in
560 participants who do not wear a hearing aid. While data do not currently support a
561 causative relationship, they support future research on causation and potential for reversal
562 with interventions for treatment of hearing loss^(58, 59).
 - 563 • Scientists have identified the genetic bases for accelerated age-related hearing loss in
564 humans⁽⁶⁰⁾.
 - 565 • Research has shown that genetically producing overexpression of proteins called
566 neurotrophins in the inner ear can elicit regeneration of cochlear synapses after noise
567 damage⁽⁶¹⁾.

568 **Otitis Media**

- 569 • Research has advanced understanding of cell signaling and gene expression patterns of
570 the innate immune system in response to OM^(62, 63).
- 571 • The study of microbial genomes has provided a cost-effective and high-throughput tool to
572 determine genome content of a bacteria that causes OM⁽⁶⁴⁾.
- 573 • Advances in vaccine development have enabled scientists to identify and characterize
574 new vaccine candidates for the bacteria that causes OM⁽⁶⁵⁻⁶⁷⁾.
- 575 • Scientists have developed a new drug delivery system for the non-invasive administration
576 of antibiotics and anti-inflammatory agents across the eardrum to treat OM^(68, 69).

577 **Hearing Aids**

- 578 • Advanced digital technology hearing aids provide noise reduction, directional hearing,
579 and feedback suppression. Binaural hearing aids further improve sound source

584 localization and spatial separation⁽⁷⁰⁾.

585

586 Cochlear Implants and Other Implantable Hearing Devices

587

- 588 • Hybrid devices that combine both electric and acoustic stimulation allow individuals with
589 preserved low-frequency hearing and un-aidable high frequency loss to utilize a
590 combination device that includes a cochlear implant for stimulation of high frequencies
591 and a hearing aid to enhance residual low frequency hearing⁽⁷¹⁻⁷³⁾.
- 592 • Scientists are studying further expansion of cochlear implant candidacy in individuals
593 with unilateral deafness who received a cochlear implant. They showed significant
594 improvement in speech perception performance in quiet and in noise after
595 implantation⁽⁷⁴⁾. Another study has shown the benefit of cochlear implants in reducing
596 tinnitus in individuals with unilateral hearing loss⁽⁷⁵⁾.
- 597 • More focused electrical stimulation can improve performance for existing cochlear
598 implant users by limiting the overlap between the number of neurons stimulated by
599 different sound frequencies^(76, 77).
- 600 • For individuals in whom cochlear implantation is not an option, auditory brainstem
601 implants now offer an alternative⁽⁷⁸⁾.

602

603 Balance Disorders

604

- 605 • Similar to the benefit of cochlear implants, vestibular implants provide a means of
606 stimulating the afferent nerves within semicircular canals of the inner ear vestibular
607 system. The vestibular prosthesis can mimic the natural vestibular signals⁽⁷⁹⁾ to the brain
608 without causing surrounding tissue damage⁽⁸⁰⁾. A variety of vestibular disorders can
609 potentially be treated with such a prosthesis⁽⁸¹⁾.

610

611 Tinnitus

612

- 613 • When cochlear hearing loss occurs, the brain becomes more sensitive to sound in order to
614 compensate for the reduced peripheral input. Too much sensitivity can make every day
615 sounds seem too loud (hyperacusis) or can cause tinnitus⁽⁸²⁾.
- 616 • Tinnitus and hyperacusis likely involve distributed neural networks that connect multiple
617 brain regions rather than one discrete region. Increased connection and activity between
618 auditory areas of the brain and those associated with emotion, memory, attention, arousal
619 and spatial location may contribute to some of the maladaptive features of these disorders
620 (e.g., anxiety, fear, etc.)⁽⁸³⁻⁸⁷⁾.
- 621 • Improved understanding of the disordered processes that cause tinnitus is leading to
622 better treatments. Animal model studies have identified tinnitus-associated neural
623 changes that commence at the cochlear nucleus and extend to more central portions of the
624 brain that process sound. Maladaptive changes in nerve cell behavior likely underlies
625 these changes, resulting in increased spontaneous nerve cell firing rates and synchrony
626 (firing together) among nerve cells in parts of the brain that process sound, possibly
627 resulting in a person “hearing” a sound when no sound stimulus is present. Scientists are
628 currently conducting clinical trials to test the effectiveness of drugs that change the way
629 nerve cells fire to treat acute tinnitus in people. Other new approaches including brain

630 stimulation, such as rTMS (repetitive transcranial magnetic stimulation)⁽⁸⁸⁾, hold some
631 promise. Scientists have also had some success with vagal nerve stimulation to eliminate
632 or minimize abnormal nerve cell circuits in individuals with tinnitus. Research has shown
633 that, after cochlear damage, upregulation of somatosensory input to the cochlear nucleus
634 may follow reduction in auditory nerve input, resulting in heightened cochlear nucleus
635 cell responses to somatosensory stimulation. Animals known to have tinnitus have been
636 shown to demonstrate changes in auditory-somatosensory integration, providing a
637 possible mechanism for the treatment of tinnitus in some patients^(89, 90).

638

639 **Auditory and Vestibular Processing**

640

- 641 • Scientists have been able to determine which speech stimuli cause brain activity by
642 making electrophysiological recordings from electrodes placed on the human brain's
643 surface. This advance has high significance for the future development of objective ways
644 to measure ability in the parts of the brain that produce and process speech in individuals
645 with normal hearing and hearing impairment⁽⁹¹⁻⁹³⁾.
- 646 • Several studies have established that the auditory cortex represents only the sounds of
647 interest, and is less effected by the presence of background noise than peripheral auditory
648 neurons in the ears. These findings are crucial for understanding the mechanisms for
649 signal detection in unfavorable listening conditions and the detrimental consequences of
650 even mild hearing loss on those capacities⁽⁹⁴⁻⁹⁶⁾.
- 651 • Scientists have made important discoveries to describe the ion channels responsible for
652 transmitting signals to the brain that help us detect our balance and orientation in space<sup>(97,
653 98)</sup>.
- 654 • Scientists have integrated their study of auditory and vestibular activity with other
655 sensory systems to advance our understanding of how the nervous system combines and
656 jointly encodes input of sound, sight, and position to improve the ability to orient
657 ourselves with objects around us, while maintaining gaze and posture⁽⁹⁹⁻¹⁰⁴⁾.

658

659 *Science Capsule: Balance or Vestibular Disorders in Adults*

660

661 Balance disorders can result from trauma, disease, or aging effects on all the balance-related
662 systems, and the aging American population is steadily increasing. Vestibular dysfunction can
663 lead to dizziness, vertigo, nausea, migraines, blurred vision, and various forms of postural
664 instability. Episodes of vestibular dizziness or nausea may be relatively brief, but when present
665 can be profoundly disturbing, including disorientation, falling, or even complete incapacitation
666 from physical activity. An estimated 14.8% of American adults (33.4 million) had a balance or
667 dizziness problem during the past year⁽²⁾. NIDCD research is supporting the development of
668 more efficient vestibular testing for improved clinical diagnoses and effective pharmacological
669 treatments for vertigo.

670

671 A common balance disorder in adults is Ménière's disease. It can develop at any age, but most
672 often strikes adults between 40 and 60 years old. Characteristic symptoms include a combination
673 of vertigo, hearing loss, nausea, tinnitus (a ringing or buzzing in the ear) and a feeling of fullness
674 in the ear. Ménière's disease usually affects only one ear. At worst, intense vertigo causes a fall,
675 called a "drop attack" with possible injury. Because episodes can be repetitive (recurring several
676 times a day, coming and receding over weeks or months) and intense, it can be a very
677 debilitating disorder for those who have it, which includes more than a half-million Americans.

678

679 Dysfunctions of the vestibular system can occur independently or with a hearing loss, from
680 causes like pharmacotoxicity or head trauma. NIDCD Intramural scientists, at the [NIH Clinical
681 Center](#), evaluate both hearing and vestibular function by testing individuals with and without
682 balance disorders. The goal of the studies is to determine the best way to perform the testing and
683 understand the variations among the test and different individuals. Examples of ongoing research
684 include examining auditory and/or vestibular function in individuals with neurofibromatosis type
685 2 (NF2), Usher syndrome, enlarged vestibular aqueducts (EVA), Niemann-Pick type C (NPC),
686 xeroderma pigmentosum (XP) and Moebius syndrome.

687

688 Balance disorders are associated, as mentioned, with falling, which is the leading cause of injury
689 deaths among older adults. One in three Americans age 65 and older falls each year⁽¹⁰⁵⁻¹⁰⁸⁾, and
690 falls can result in severe trauma and even loss of life. Each year, more than 4 million older U.S.
691 adults go to emergency departments for fall-related injuries at a cost of \$4 billion^(109,110). The
692 NIDCD supports a longitudinal study that measures vestibular function in older adults. The
693 NIDCD is also sponsoring the AVERT (Acute video-oculography for Vertigo in Emergency
694 Rooms for rapid Triage) clinical trial to help diagnose vertigo, dizziness, and other balance
695 problems. The team of researchers is using a diagnostic medical device (video-oculography or
696 VOG) in the triage of patients who go to emergency room with complaints of vertigo and/or
697 dizziness. The device measures abnormal eye movements to differentiate benign causes of the
698 dizziness or imbalance from dangerous causes (like stroke). It is hoped that the study will
699 improve standard of care in the diagnosis and treatment of patients with vertigo or dizziness,
700 leading to better outcomes at lower cost.

701

702 **Priority Areas in Hearing and Balance Research**

703

704 **Priority Area 1: Understanding Normal Function**

705

706 • **Development of the Auditory and Vestibular System:** Identify the molecules, genetic and
707 epigenetic changes involved in development of the peripheral and central auditory and
708 vestibular pathways. Understand how auditory neurons establish tonotopic and other
709 organized sensory representations.

710

711 • **Homeostasis and Microenvironment:** Increase understanding of homeostasis in the inner
712 ear (e.g., ionic composition and maintenance, inflammatory response and toxin elimination,
713 blood-labyrinth barrier, microcirculation, hormonal and other control systems), transport of
714 macromolecules through the round window and in the middle ear (e.g., gas exchange, fluid
715 regulation, innate immunity, and gene expression) and how these homeostatic mechanisms
716 are established developmentally.

717

718 • **Mechanics:** Expand knowledge of three-dimensional mechanics in the cochlea (e.g.,
719 interaction of hair cell membranes and stereocilia with supporting structures); in the middle
720 ear (e.g., resolve important issues of middle ear mechanics, including tympanic
721 membrane/ossicular coupling and modes of stapes motion); and in the vestibular system
722 (e.g., cupular and otolithic maintenance of posture and equilibrium).

723

724 • **Sensory Cell Transduction and Innervation:** Identify all the molecular constituents of the
725 hair cell transduction process: nanomechanical properties, molecular motors in hair cell
726 membranes and stereocilia, ion channels and pumps; and their integration for hair cell tuning
727 and maintenance. Identify the factors that promote and maintain hair cell afferent synapses.

728

729 • **Single Cell Analysis:** Define the gene expression profile at the single cell level for multiple
730 different cell types and regions in the cochlea over multiple different time points.

731

732 • **Functional Connectivity:** Clarify how afferent and efferent neural circuits process auditory
733 and vestibular peripheral input. Understand how coding schemes influence plasticity and
734 enable attention, cognition, and stress. Incorporate advanced techniques of functional and
735 structural neural imaging and connectivity, ranging from molecular to systems scale. Bridge
736 non-invasive lower-resolution assessments (imaging and electrophysiological methods –
737 ECoG) of complex sounds (speech) obtained in humans with combined invasive/non-
738 invasive higher-resolution assessments in animal models.

739

740 • **Perception:**

741

742 ▪ **Auditory System:** Determine how sound detection, discrimination, and recognition
743 interact with learning, memory, and attention as well as with vision, tactile sensation,
744 and balance to better understand auditory perception in real-world listening
745 environments, especially in conditions with unfavorable low signal-to-noise ratios.

746

- 747 ▪ Vestibular System: Determine how vestibular, visual, and proprioceptive (the sensing
748 of motion or position) systems interact to perceive space and motion and to maintain
749 orientation.
750

751 **Priority Area 2: Understanding Diseases and Disorders**

752

- 753 • **Epidemiology:** Investigate natural history; genetic and environmental risk factors; racial,
754 ethnic, and gender differences; and practical objective metrics for subpopulations to inform
755 the development of evidence-based treatment strategies. Explore how complex comorbidities
756 create differences in disease phenotypes and treatment outcomes.
757
- 758 • **Genetic Causes of Hearing Loss:** Leverage new genetic tools and big data to study
759 genotype/phenotype relationships, e.g., genetic risk factors in noise-induced and age-related
760 hearing loss. Test emerging ideas with animal models using cutting-edge gene-editing
761 technologies (CRISPR). Define the spectrum of genetic contributions to inherited, noise-
762 induced and age-related hearing loss and understand the structural and functional
763 consequences of such mutations. Identify the spectrum of mutations in non-coding sequences
764 that contribute to hereditary hearing loss.
765
- 766 • **Single Cell Analysis:** Define the gene expression profile at the single cell level for multiple
767 different cell types and regions in the cochlea over multiple different time points in diseased
768 or disordered tissue.
769
- 770 • **Otitis Media:** Improve understanding of susceptibility and pathogenesis related to genetics,
771 prior upper respiratory infection, eustachian tube dysfunction and reflux, bacterial biofilms
772 and microbiome, polymicrobial infections, dysregulation of innate immunity, inflammation
773 and mucus production, mucosal hyperplasia, and dysregulation of the resolution of
774 inflammation and tissue repair. Define immune pathways for effective middle ear protection
775 by vaccines and for identification of new therapeutic targets. Develop animal models of acute
776 and chronic otitis media. Determine impact of vaccination on disease prevalence and
777 infection by other microbes.
778
- 779 • **Inflammatory and Autoimmune Responses of the Inner Ear:** Identify and characterize
780 first responders to injury in the inner ear. Determine how molecules and cells cross the
781 blood-labyrinth barriers to initiate immune response and autoimmune disease. Identify
782 genetic and epigenetic risk factors. Investigate innate and cognate immunity in resolution of
783 otitis media.
784
- 785 • **Tinnitus and Hyperacusis:** Validate assays for tinnitus and hyperacusis in animal models.
786 Couple behavior and neurophysiology in animals to probe mechanisms. Use human brain
787 imaging to identify networks that are involved in tinnitus and hyperacusis.
788
- 789 • **Other Acquired Disorders:** Improve understanding of the pathogenesis and processes of
790 noise-induced, age-related, traumatic, idiopathic, ototoxic, neurotoxic, metabolic, and both
791 hereditary and non-hereditary auditory and vestibular dysfunction. This includes Ménière's
792 disease, otosclerosis, idiopathic sudden sensorineural hearing impairment, and the slow

793 hearing decline after hearing-preservation cochlear implantation. Relate molecular, cellular,
794 and structural (e.g., temporal bone research) otopathology to the clinical progress of disease
795 and disease treatment.

796

797 • **Pathways and Damage:** Determine how the peripheral and central auditory and vestibular
798 pathways are reorganized following injury. Define the long-term changes resulting from
799 sensory cell or neuronal loss. Identify molecular, genetic, and anatomical underpinnings of
800 plasticity in normal and hearing-impaired models. Use human imaging and
801 electrophysiological methods to assess effects of hearing loss on central speech
802 representations.

803

804 • **Changes in Perception with Disease:**

805

806 ▪ **Auditory System:** Identify sources of variance contributing to large individual
807 differences in response to similar intervention strategies among people with hearing
808 loss. Improve understanding of the time course, sensitive periods, and complications
809 of hearing loss across the lifespan. Clarify the aspects of perceptual impairment that
810 are primarily caused by cochlear synaptopathy rather than by cochlear hair cell loss.

811

812 ▪ **Vestibular System:** Understand how disease affects perception of motion and spatial
813 orientation, including connections with limbic and autonomic systems.

814

815 **Priority Area 3: Improving Diagnosis, Treatment, and Prevention**

816

817 • **Genetic Testing:** Improve comprehensive genetic testing by developing more affordable
818 and faster Targeted Genomic Enrichment and Massively Parallel Sequencing Platforms
819 integrating single nucleotide (SNV) and copy number (CNV) variation detection in coding
820 and non-coding regions. Develop better variant annotating and pathogenicity prediction tools.

821

822 • **Regeneration:** Develop in vitro systems to identify genes and factors that promote
823 regeneration of specific cellular phenotypes (e.g., hair cells, supporting cells, spiral ganglion
824 neurons, cells of the stria vascularis); understand factors that promote or inhibit hair cell
825 regeneration spiral ganglion neurite extension and hair cell synaptogenesis; and determine
826 which genes and extracellular factors control cell-specific differentiation.

827

828 • **Pharmacotherapeutics:** Develop targeted delivery of viral vectors for gene therapy and
829 gene repair/correction and site-specific, controlled, sustained molecular therapy for both
830 developing and dysfunctional pathways. Develop therapies to improve neuronal stimulation,
831 resist cell damage, and enhance cell repair. Determine rules governing the diffusion or
832 transport of small molecules, macromolecules, and viruses across the round window
833 membrane.

834

835 • **Gene Therapy and Gene Delivery:** Develop therapies to prevent progression of hearing loss
836 and/or restore function after hearing loss has occurred; identify and catalog viral and non-
837 viral vectors with cell-specific inner ear tropism.

838

- 839 • **Tinnitus and Hyperacusis:** Apply advanced imaging techniques to provide measures of
840 changed neural activity in people with tinnitus and hyperacusis. Identify pharmacologic
841 agents to prevent tinnitus resulting from traumatic, ototoxic, degenerative, and other acquired
842 disorders. Identify behavioral, pharmacological, surgical, and device-based treatments for
843 improving tinnitus and hyperacusis.
844
- 845 • **Otitis Media:** Develop new vaccines including polyvalent vaccines for middle ear bacterial
846 and viral infections including polymicrobial infections. Develop new therapeutic agents to
847 enhance innate immunity and host defense, suppress uncontrolled inflammation, mucus
848 production, and tissue repair and speed resolution of inflammation for the treatment of otitis
849 media. Develop new drug delivery systems to the middle ear to treat both middle ear and
850 inner ear diseases.
851

852 **Interventions for Hearing Loss:**

- 853
- 854 ■ Expand or combine databases for high-resolution molecular, neurophysiological, and
855 psychophysical diagnostics for evidence-based therapeutic approaches.
856
 - 857 ■ Examine existing and develop better aural rehabilitation strategies across the lifespan.
858 Investigate how aural rehabilitation strategies are affected by treating comorbid
859 conditions that influence success, such as co-occurring issues in children with hearing
860 impairment, dementia, or diabetes.
861
 - 862 ■ Traditional (external) Hearing Aids: Improve device performance in background
863 noise and other real-world settings.
864
 - 865 ■ Auditory Prostheses: Improve efficacy of bilateral implants, short electrode implants,
866 and hybrid cochlear implant/hearing aids in the same or opposite ear in conjunction
867 with auditory/aural rehabilitation, assistive devices, sign language, in home and
868 educational environments. Develop alternative means of stimulating the auditory
869 nerve to provide greater channel resolution of implants. Improve prediction of
870 outcome and maintenance of outcome over time.
871
- 872 • **Interventions for Dizziness and Balance Disorders:** Develop safe and effective
873 pharmacological treatments for vertigo. Develop vestibular prosthetic devices and minimally
874 invasive surgery for better control of imbalance and vertigo while preserving hearing and
875 other functions. Develop improved behavioral approaches for the rehabilitation of chronic
876 vestibulopathies. Develop improved methods of systematic diagnosis and delineation of
877 subtypes of dizziness/vertigo in order to identify subpopulations that might respond best to
878 targeted therapies. Understand post cochlear implantation dizziness and the connection with
879 vestibular migraines.
880
- 881 • **Management of Infants and Children with Hearing Impairment:** Improve early hearing
882 detection and intervention (EHDI) and hearing loss management, including screening,
883 treatment, and rehabilitation. Define the underserved population of older adults for hearing
884 health care. Determine if early access to hearing health care changes health outcomes later in

885 life. Develop and evaluate the effectiveness of screening methods. Test the effectiveness of
886 various types of intervention strategies.

887

- 888 • **Management of Older Adults:** Improve hearing loss management, including screening,
889 treatment, and rehabilitation. Define the underserved population of older adults for hearing
890 health care. Determine if early access to hearing health care changes health outcomes later in
891 life. Develop and evaluate the effectiveness of screening methods. Reduce risk of falls in
892 older adults due to imbalance. Develop assistive balance aids, remote sensing feedback
893 devices, and training programs to improve stability and posture in the elderly.

894

895 **Priority Area 4: Improving Outcomes for Human Communication**

896

- 897 • **Identifying Impact of Hearing Loss and of Hearing Health Care:** Identify factors that
898 influence a person’s motivation and perceived need for hearing health care. Examine the
899 impact of organization, financing, and management of health care services on the delivery,
900 cost, access to, and outcomes of services. Develop innovative delivery systems to increase
901 awareness, access, and affordability. Identify cost-effective approaches for diagnosis and
902 treatment. Determine the impact of hearing loss on quality of life and general physical and
903 mental health and impact of intervention—including hearing aids and other technologies and
904 communication strategies—on the same outcome measures.

905

- 906 • **Comparative Effectiveness Research and Evidence-Based Medicine:** Through clinical
907 trials and epidemiological studies, identify best treatments for a given medical condition for a
908 defined set of individuals. Develop and use clinical registries, clinical data networks, and
909 other forms of electronic health data to inform the conscientious, explicit, and judicious use
910 of current best evidence in making decisions about hearing health care options. Develop
911 generalizable quality of life measures that allow us to compete with other health care
912 priorities.

913

- 914 • **Implementation and Dissemination Research:** Improve implementation of “best practices”
915 among health care providers to translate advances into routine community practice. Increase
916 dissemination of health information to the public to promote healthy behaviors, including the
917 need for intervention in individuals with hearing loss and the dangers of acoustic
918 overexposure to the long-term health of the ear.

919

- 920 • **Community-Based Participation in Research:** Promote community-based research to
921 identify factors that influence outcomes for people with hearing and balance disorders in
922 diverse real-world settings. Engage deaf and hard of hearing individuals in community-based
923 research to aid in developing behavioral interventions to improve their quality of life.
924 Develop methods to address communication disorders in diverse populations, considering
925 variations in care and practice settings.

926

927

928 **Taste and Smell Research**

929
930 **Why NIDCD Supports Taste and Smell Research**

931
932 The chemical senses—more commonly known as taste, smell, and chemesthesis (chemically
933 provoked irritation)—enable us to use chemical signals to communicate with the environment
934 and each other. For people, memories of taste and smell experiences are vivid and long lasting,
935 and play an important role in our enjoyment of life. The chemical senses accomplish three major
936 purposes:

- 937
938
 - Nutrition: Seeking out safe and nourishing food.
 - 939 • Protection: Helping us to avoid spoiled food and toxic chemicals.
 - 940 • Communication: Conveying important information to others.

941
942 Specialized cells in the human oral cavity can detect at least five basic taste qualities: sweet,
943 sour, bitter, salty, and savory (umami). Taste cells may also respond to components of fat, to
944 calcium, and perhaps to other chemical substances found in foods and beverages. Together with
945 the nose and oral cavity, the tongue also plays a role in chemesthesis, a multimodal chemical
946 sensitivity whose burning sensations signal the presence of chemical irritants such as capsaicin in
947 hot peppers and toxic chemicals in the air.

948
949 Olfactory sensory neurons in the nose can detect a wide array of odors and olfaction (smell)
950 plays an important role in the perception of food flavor as well. In 1991, Linda Buck and Richard
951 Axel described a very large family of about 1,000 mouse genes that give rise to an equivalent
952 number of olfactory receptor types⁽¹¹¹⁾. These receptors are located on olfactory sensory neurons
953 that occupy a small area in the upper part of the nasal epithelium. Drs. Buck and Axel received
954 the 2004 Nobel Prize in Physiology or Medicine for this groundbreaking research, which
955 established a foundation for understanding how odorant molecules interact with their odor
956 receptors.

957
958 Each year, more than 200,000 people visit a physician for chemosensory problems such as taste
959 and smell disorders⁽¹¹²⁾. Many more taste and smell disorders go unreported. About 19% of U.S.
960 adults ages 40 and older report having had a problem with their ability to taste, and
961 approximately 23% report having had a problem with their ability to smell. The likelihood that a
962 person will report a diminished sense of taste and/or smell increases with age. In adults ages 80
963 or older, nearly 31% report a problem with their sense of smell, and more than 27% have a
964 problem with their sense of taste⁽¹¹³⁾.

965
966 **Nutrition**

967 The chemical senses are important for regulating food preferences and intake. They evolved to
968 help humans and other animals survive in environments in which required nutrients were scarce
969 and many plants contained poisonous, bitter compounds. Consequently, we seek out sweet, fatty
970 foods and tend to reject the bitterness that characterizes many nutritious vegetables. Although
971 this behavior made sense as humans were evolving, an almost limitless availability of high-
972 calorie foods today can cause the normal function of taste and smell to lead to overconsumption
973 and obesity. More than 2 in 3 adults are considered to be overweight or obese, and more than 1

974 in 3 adults are considered to be obese⁽¹¹⁴⁾. Individuals who are overweight or obese are at risk of
975 numerous serious conditions (e.g., Type 2 diabetes, heart disease, and sleep apnea⁽¹¹⁵⁾).
976

977 People with smell disorders often have problems appreciating the smell of foods and claim that
978 food is less enjoyable. They may change their eating habits, which may have a long-term impact
979 on overall health. Loss of the sense of smell may also cause a person to add too much sugar or
980 salt to make food taste better. This can be a problem for people with certain medical conditions
981 such as diabetes or high blood pressure.
982

983 Humans seek out their preferred flavors in foods. Flavor involves interactions between the
984 sensors that detect taste, smell, and chemesthesis in our foods and the parts of the brain that
985 interpret, remember, or think about them. Flavor plays an important role in determining whether
986 someone accepts a particular food, and how much of it they choose to eat⁽¹¹⁶⁾. Scientists studying
987 the chemical senses are interested in learning more about the molecular and developmental bases
988 for how flavors influence food intake and overall health.
989

990 Scientists are interested in learning more about how the body detects and responds to salt, fats,
991 and other food characteristics that humans seek out. Data gained from these studies can help us
992 determine new strategies to control overconsumption and improve health without reducing our
993 enjoyment of food. Ongoing research is studying the structure and function of discrete taste,
994 smell, and chemesthetic receptors, as well as their targets within the brain.
995

996 Protection

997 The chemical senses evolved to help us avoid environmental dangers. Bitter tastes warn of
998 potential toxins. Odors associated with spoiled food, toxic volatiles, and dangerous organisms
999 protect us against ingesting or contacting dangerous substances. Odors can even be used to label
1000 certain dangerous substances, such as the addition of smelly sulfur compounds to natural gas,
1001 which otherwise has no detectable smell. Chemesthesis primarily serves a defensive function,
1002 triggering a coughing or gagging reaction that allows us to avoid chemical irritants that cause
1003 tissue damage. Loss of chemesthesis results in the inability to detect toxic chemicals in our
1004 environment, possibly leading to increased exposure and greater risk of serious health effects.
1005 This loss of detection ability persists in people involved in the early rescue, recovery, demolition,
1006 or cleanup efforts after the collapse of the World Trade Center towers⁽¹¹⁷⁾. Cancer treatments
1007 such as radiation and chemotherapy may also result in taste and smell loss.
1008

1009 Communication

1010 Many animals, including mammals, detect chemical communication cues (some of which are
1011 called pheromones) given off by animals of the same species. These chemicals convey a variety
1012 of messages, including fertility, social rank, health status, and individual identity. Pheromones
1013 can also inhibit or induce sexual maturation or mark territory via urination or spraying. Since so
1014 many animals use pheromones to communicate information through chemical signals, it seems
1015 reasonable to propose that humans do the same. However, the study of chemical communication
1016 and pheromones in humans is fraught with controversy. Scientists do not yet agree whether and
1017 how humans may use pheromones to communicate. However, other types of odors also affect the
1018 way humans interact. For example, people with smell loss may exhibit poor hygiene because

1019 they cannot detect their own body odor, thus affecting their normal interactions with others.

1020

1021 Regeneration

1022 The cells that detect chemical signals show a remarkable capacity for regeneration. Their
1023 locations (in the nose, on the tongue, in the oral cavity) make them susceptible to damage from
1024 the environment, so regeneration is required if these cells are to continue to function throughout
1025 life. Scientists are interested in learning what enables these tissues to regrow and to re-establish
1026 the appropriate connections with the brain. What they learn could be applicable to other human
1027 systems and could lead to new treatments for not only taste and smell disorders but also for
1028 tissues damaged by stroke or neurodegenerative diseases.

1029

1030 **The Taste and Smell Program**

1031 The NIDCD Taste and Smell Program supports studies of the chemical senses known as taste,
1032 smell, and chemesthesis (chemically provoked irritation) to enhance our understanding of how
1033 individuals communicate with their environment and how human chemosensory disorders can be
1034 diagnosed and treated. NIDCD-supported research on molecular and cellular biology, animal
1035 models, biophysics, and biochemistry of the olfactory and gustatory systems is paving the way
1036 for improved diagnosis, prevention, and treatment of chemosensory disorders.

1037

1038 Recent Advances in Taste and Smell Research

1039

1040 **Transduction Mechanisms**

1041

- 1042 • The body uses chemosensory transduction mechanisms—processes that enable the
1043 conversion of detection into an electrical signal—throughout the oral and nasal cavities.
1044 These transduction mechanisms play a major role in the regulation of food intake and the
1045 protection of the airways. Scientists have discovered new families of chemosensory
1046 receptors (trace amine-associated receptors, formyl peptide receptors) that could detect
1047 chemical cues used for communication of odors that signal disease⁽¹¹⁸⁾.
- 1048 • Scientists have discovered new chemosensory receptors and transduction mechanisms in
1049 the gustatory (taste)⁽¹¹⁹⁻¹²⁴⁾ and olfactory systems^(125, 126).
- 1050 • Scientists are using novel single cell techniques to make numerous copies of the DNA
1051 expressed in a single cell as it progresses through early development to explore how
1052 olfactory receptor cells choose which receptor to express⁽¹²⁷⁾.
- 1053 • Bacteria release quorum signaling molecules to coordinate behaviors such as biofilm
1054 formation, virulence, and antibiotic resistance, based on the local density of the bacterial
1055 population. Taste receptors expressed in solitary chemosensory cells and ciliated cells of
1056 the respiratory epithelium detect irritants and quorum signaling molecules of pathogenic
1057 bacteria, evoking protective airway reflexes and inflammatory responses to rid the
1058 airways of infection^(128, 129).
- 1059 • The use of novel methods⁽¹³⁰⁾ is rapidly expanding our identification of the ions or
1060 molecules (ligands) that bind to a receptor for the diverse set of identified chemosensory
1061 receptors⁽¹³¹⁻¹³⁴⁾.

1062

1063 **How Genes and Environment Affect Food Preference**

1064

1065 • Experience, internal state, and genetic variation in taste and smell receptor genes affect
1066 chemosensory likes and dislikes⁽¹³⁵⁻¹⁴¹⁾. Thus, the chemical senses play key roles in the
1067 regulation of food intake that underlies major health issues such as obesity and
1068 diabetes⁽¹⁴²⁻¹⁴⁴⁾.

1069

1070 • The discovery that children and adults experience chemical senses differently has broad
1071 implications for the role of flavor in diet selection and health across the lifespan as well
1072 as for basic research into the organization and maintenance of chemosensory
1073 pathways⁽¹⁴⁵⁾.

1074

1075 **Chemical Senses and Disease**

1076

1077 • Some heritable diseases (e.g., channelopathies and ciliopathies⁽¹⁴⁶⁻¹⁴⁸⁾ as well as
1078 neurodegenerative diseases (e.g., Alzheimer's disease)⁽¹⁴⁹⁻¹⁵¹⁾ have a correlated
1079 chemosensory dysfunction that scientists may use to help diagnose diseases or gauge the
1080 effectiveness of treatment.

1081 • Individuals who inherit genes that code for one particular version of a bitter taste receptor
1082 (a genetic polymorphism) are more susceptible to chronic rhinosinusitis (CRS)⁽¹⁵²⁾. New
1083 genetic models of CRS may lead to new therapeutic interventions for the associated
1084 olfactory deficits⁽¹⁵³⁾.

1085 • Radiation, chemotherapy and traumatic head injuries severely disrupt chemosensory
1086 function. Basic research into transcription factors that regulate development and turnover
1087 of chemosensory cells provides a potential basis for restoring chemosensory function<sup>(154-
1088 159)</sup>.

1089 • Understanding invertebrate chemoreceptor mechanisms and sensitivities⁽¹⁶⁰⁻¹⁶²⁾ has
1090 opened avenues for control and prevention of critical insect-borne diseases such as
1091 malaria, dengue fever, encephalitis, and Zika.

1092

1093 **Neural Circuitry**

1094

1095 • By understanding how taste and smell signaling is set up during normal development, we
1096 have a better chance of figuring out how to repair this signaling process if it is damaged.
1097 Information about how taste and smell are interpreted in the brain and influence behavior
1098 may also be useful for helping us understand why certain tastes and smells make us
1099 behave in certain ways, and could help us develop ways to improve mood and modify
1100 behavior by modifying this response. Scientists have learned a lot about the cortical
1101 circuits that process taste and smell, including:

1102

1103 • Scientists better understand the divisions of function in cortical structures that
1104 interpret chemical senses information⁽¹⁶³⁻¹⁶⁹⁾ and how these circuits fail in
1105 pathology^(133, 170).

1106 • They are learning how cortical circuits create and read odor patterns and the basic
1107 circuitry and physiology of these circuits⁽¹⁷¹⁻¹⁷⁴⁾.

- 1108
- 1109
- 1110
- 1111
- 1112
- 1113
- 1114
- 1115
- They are using artificial neural networks and optical imaging to define and dissect the circuitry and coding in the chemical senses⁽¹⁷⁵⁻¹⁷⁹⁾.
 - They have figured out how adult-born neurons can be functionally and synaptically integrated into neural circuits⁽¹⁸⁰⁾.
 - They have better insight into how activity within these neural circuits translates to chemosensory perception and stimulus identification^(169, 181-186) and guide such behaviors as emotional response⁽¹⁸⁷⁾ and parenting behavior⁽¹⁸⁸⁾.

Science Capsule: How Mosquitos Target their Human Hosts

The [NIH](#) and the U.S. Centers for Disease Control and Prevention (CDC) are working to combat a virus that has achieved pandemic status in South American and the Caribbean– Zika.

According to the CDC, people become [infected with the Zika virus](#) primarily through the bite of infected *Aedes aegypti* or *Aedes albopictus* mosquitos. Zika is spread by the same mosquitos that spread dengue and chikungunya viruses. The NIDCD supports research projects that focus on mosquitos, because the insects use olfactory cues to target their hosts, including humans.

If we understood how the olfactory cues activate mosquito olfactory receptors, we may be able to develop compounds or other methods to block or interfere with this activation and prevent the mosquitos from detecting humans. An NIDCD-supported scientist determined that the domestic form of the *A. aegypti* mosquito preferentially seeks out human blood over animal blood due to a genetic tweak that makes it more sensitive to human odor⁽¹⁸⁹⁾. Another NIDCD-supported scientist reports that *A. aegypti* detect plumes of human CO₂ upstream and then use visual cues to zero in on human targets⁽¹⁹⁰⁾. Still another group is working to determine the molecular mechanisms by which mosquitos and other insects seek out moist environments likely to contain human hosts. Scientists now hope to exploit these details to interfere with the insects’ ability to locate human targets.

Another approach to preventing mosquitos from seeking human hosts is to activate a pathway that prevents mosquitos from seeking a blood meal. One project in this area is studying the molecules and receptors that are responsible for keeping female mosquitos from seeking a blood meal for 3 days after a previous meal. If we could simulate these molecule/receptor interactions, we could trick the mosquitos’ systems into thinking they’d already had a meal. NIDCD is also supporting this scientist on another critical project – she is leading a group of scientists in an emergency effort to assemble the genomic sequence of the *A. aegypti* mosquito in a matter of months. The goal is to use the genomic information to develop new ways to stop the insects from spreading disease.

Finally, NIDCD-supported scientists are trying to understand the specific mechanisms by which insect repellants prevent mosquitos from biting humans. An NIDCD-supported scientist determined that the mosquito’s legs, rather than the proboscis, detect diethyltoluamide (DEET) on skin, and is now searching for the specific genes that are responsible for mediating the “repellency” of DEET. Another NIDCD-supported team identified the gene and receptor in the fruit fly that detect repellant molecules in DEET, and is now working to identify additional molecules that also stimulate the same receptor. Scientists hope to use such data to develop longer-lasting, less expensive, and more effective insect repellents.

Priority Areas in Taste and Smell Research

In developing research Priority Area goals, the NIDCD took into consideration areas of research that are within the mission of other NIH Institutes, Centers, and Offices (ICO) and are not primarily supported by the NIDCD but that have relevance to the study of chemical senses. In particular:

1162 Dietary Intake: The NIDCD supports basic research on chemosensory factors controlling flavor
1163 perception, food selection, and related neural pathways. However, research studies that focus
1164 exclusively on the consequences of overconsumption or poor diet, including type 2 diabetes,
1165 metabolic disorders, stroke, cancer, cardiovascular disease, hypertension, and obesity, are
1166 supported in the mission areas of other NIH ICOs, such as the National Institute of Diabetes and
1167 Digestive and Kidney Diseases (NIDDK), the National Institute of Neurological Disorders and
1168 Stroke (NINDS), the National Cancer Institute (NCI), or the National Heart, Lung, and Blood
1169 Institute (NHLBI).

1170
1171 Infectious Diseases: The NIDCD supports studies of basic neural mechanisms of insect olfaction,
1172 including olfaction of insects that serve as disease vectors for encephalitis, dengue fever, and
1173 malaria. However, the funding of studies focusing exclusively on the infectious nature of these
1174 diseases falls within the mission of the National Institute of Allergy and Infectious Diseases
1175 (NIAID).

1176
1177 **Priority Area 1: Understanding Normal Function**

- 1178
- 1179 • **Fundamental Biology of Chemosensory Function:** Continue to develop and apply new
1180 tools and approaches to delineate the organization of molecules, cells, and neural circuits
1181 underlying the function of the chemesthetic (trigeminal), gustatory and olfactory systems,
1182 including development, cell turnover, regeneration, and plasticity.
 - 1183
 - 1184 • **Peripheral and Central Bases of Flavor:** Understand the complex interactions between
1185 peripheral and central aspects of flavor perception, including retronasal or orthonasal
1186 olfaction, oral chemesthesis (chemical irritation), taste, oral somesthesia (temperature,
1187 texture), memory, and motivational state (e.g., hunger).
 - 1188
 - 1189 • **Sentinel/Sensory Functions:** Describe how chemical senses help us avoid dangers such as
1190 spoiled or contaminated foods, how they detect potentially toxic chemicals in the
1191 environment and in our bodies, and how these protective functions can be damaged and
1192 regenerated.
 - 1193
 - 1194 • **Genetic Aspects of Chemosensory Sensitivity:**
 - 1195
 - 1196 ▪ **Genomics:** Identify genes involved in the development and normal function of the
1197 taste and smell systems, including the use of single-cell profiling approaches.
 - 1198
 - 1199 ▪ **Variation:** Describe the normal variation in taste and smell sensitivity. Identify the
1200 genes involved in order to understand what is outside the range of normal function.
1201 Describe how such variation may relate to susceptibility for human communication
1202 disorders.
 - 1203
 - 1204 ▪ **Experience:** Identify genes involved with storing memories of taste and smell.
1205 Determine how experience influences future diet.
 - 1206

- 1207 ▪ **Epigenetics:** Describe how external factors (e.g., sensory experience, diet, stress)
1208 activate and deactivate genes.
1209
- 1210 • **Central Control of Taste and Smell:** Characterize top-down control within the central
1211 nervous system that modulates sensory input, sensory processing and perception, and
1212 determine how such activity may change depending on internal state, motivational or
1213 cognitive factors.
1214
- 1215 • **Developing Tools to Measure Taste and Smell Function:** Provide practicing physicians
1216 with standardized tools to test taste and smell during physical exams or routine office visits.
1217 Develop criteria and metrics for the range of “normal” taste and smell by analogy to hearing,
1218 and vision.
1219
- 1220 • **Develop Novel Approaches to Alter Taste Function:** Alter the levels of salt, sugar, and fat
1221 intake using innovative methods such as using artificial substitutes or changing learned flavor
1222 preferences.
1223

1224 **Priority Area 2: Understanding Diseases and Disorders**
1225

- 1226 • **Genetic Disorders:** Clarify and classify taste and smell disorders caused mainly by
1227 significant genetic alterations (e.g., ciliopathies and channelopathies). Determine the normal
1228 range of variation of function in the chemical senses as related to genetic polymorphisms.
1229
- 1230 • **Environmental Insults on Taste and Smell:** Identify the mechanisms that contribute to
1231 taste and smell loss and/or dysfunction resulting from radiation, chemotherapy, head
1232 trauma, and toxins.
1233
- 1234 • **Sinusitis/Rhinitis:** Identify the molecular and cellular bases for loss of olfaction following
1235 nasal cavity or sinus infection, the most common cause of temporary and permanent
1236 olfactory loss.
1237
- 1238 • **Understanding How the Activity of the Chemical Senses Can Lead to Excessive**
1239 **Consumption or Malnutrition:** Determine whether calorie intake is affected by normal
1240 variation or altered function of taste and smell activity.
1241
- 1242 • **Epidemiology:** Describe the incidence and prevalence of taste and smell loss and
1243 dysfunction. For example, as the population ages, determine how many more people report
1244 taste and smell problems that affect quality of life.
1245

1246 **Priority Area 3: Improving Diagnosis, Treatment, and Prevention**
1247

- 1248 • **Improved Diagnostic Tools and Pharmacological Treatments:** Develop and validate tests
1249 to evaluate taste and smell function that are practical and affordable for use in the office
1250 setting. Develop drugs to treat taste and smell dysfunction, especially drugs which slow
1251 apoptosis (cell death) and promote regeneration.
1252

1253 • **Regenerative Medicine/Tissue Engineering:** Increase understanding of the properties that
1254 enable stem cells in the peripheral taste and smell pathways to proliferate and differentiate,
1255 providing insights not only for the treatment of taste and smell loss but also for the treatment
1256 of other neurological diseases.

1257
1258 • **Enhancing the Clinical Enterprise:** Promote clinical training in the chemical senses to
1259 encourage development of animal models of relevant disorders and promote clinical and
1260 translational research, involving interdisciplinary teams of clinicians and basic scientists.

1261
1262 **Priority Area 4: Improving Outcomes for Human Communication**

1263
1264 • **Translational Research:** Translational Research is in its infancy in the chemical senses, due
1265 in part to the modest amount of clinical research that has been conducted. Currently, there are
1266 no evidence-based preventive measures, interventions, or treatments applied to taste and
1267 smell dysfunction. Comparative effectiveness research is premature because of the lack of
1268 intervention and treatment strategies and decisions. This is a critical gap area in the chemical
1269 senses, especially since taste and smell loss become increasingly common in a population
1270 with an increasing number of older adults.

1271
1272

1273 **Voice, Speech, and Language Research**

1274

1275 **Why NIDCD Supports Voice, Speech, and Language Research**

1276

1277 Communication allows us to participate in society and is a defining characteristic of what it is to
1278 be human. Other organisms clearly communicate; however, in no other species does it appear
1279 that communication—specifically the use of language in communication—is as highly developed
1280 as in humans, nor as central to an organism’s function and identity. Communication impairments
1281 that involve voice, speech, or language often limit a person’s ability to participate in society,
1282 whether the activity is educational, occupational, or social. In addition, because effective
1283 communication is needed to get aid in life-threatening situations, loss of communication can put
1284 people at risk for compromised physical safety and survival.

1285

1286 Human communication requires the brain to integrate complex sensory signals collected by the
1287 peripheral organs and to produce neural signals to co-ordinate the muscles involved in speaking
1288 and singing. Human communication systems also rely on the sensory functions of the peripheral
1289 organs responsible for hearing, balance, taste, and smell, located in the middle and inner ear,
1290 nose, mouth, and throat. They also involve vision (used for sign language and visible speech) and
1291 the development of abstract linguistic representations and memory mechanisms, located centrally
1292 in the brain. Additionally, communication systems rely on the motor functions of the hands and
1293 arms (for sign language and co-speech gesture) and on the peripheral organs of speech
1294 production, which include the diaphragm, airway, vocal folds, tongue, lips, and other oral
1295 structures.

1296

1297 The interplay between central and peripheral signals, genetics, and environment makes language
1298 acquisition a vulnerable process. We don’t understand the causes of many voice, speech, and
1299 language disorders, and the path to treatment is often uncertain. Our ability to develop effective
1300 treatment is hindered by gaps in evidence for age-appropriate clinical goals, targets of
1301 intervention, and expected change trajectories. Researchers are only beginning to understand the
1302 developmental course of voice, speech and language markers during childhood that serve as a
1303 guide for clinical interventions suited to particular levels of development. In addition, we also
1304 need more research on communication problems associated with diseases and disorders most
1305 commonly occurring in adults.

1306

1307 While spoken language is the primary way people communicate, it is not the only way. The
1308 symbolic nature of language allows us to attribute meaning through not only the voice, speech,
1309 language and hearing, but also using visual-manual modes of communication, most notably the
1310 use of sign languages and augmentative communication systems. The NIDCD supports research
1311 to understand these communication systems, their acquisition and development, and their use
1312 when spoken language systems are damaged by trauma or degenerative diseases, or when speech
1313 is difficult to acquire due to early hearing loss or injury to the nervous system. This research is
1314 also applicable to other human functions because enhanced understanding of visual-manual
1315 language systems opens a window into general human cognition.

1316

1317 **Developmental Communication Disorders**

1318 Nearly 8% of children aged 3-17 years have had a communication disorder during the past 12
1319 months, according to data from the National Health Interview Survey, 2012⁽¹⁹¹⁾. In children,
1320 delayed speech and language acquisition or impairment are very often significant predictors of
1321 future academic, social, vocational, and adaptive outcomes⁽¹⁹²⁻¹⁹⁴⁾. These impairments also tend
1322 to run in families⁽¹⁹⁵⁾, with converging evidence of genetic effects⁽¹⁹⁶⁾. Many communication
1323 disorders, such as specific language impairment (SLI) and stuttering, first become apparent when
1324 a child normally begins to acquire speech and language. Other developmental disorders may
1325 also include communication problems, such as autism spectrum disorder (ASD), Fragile X, or
1326 cerebral palsy. One of the hallmarks of ASD is the diminished ability to communicate
1327 effectively—particularly in the expression and reception of language. The NIDCD is committed
1328 to supporting research efforts to improve the identification speech and language disorders in
1329 children and to improve treatments for those disorders.

1330

1331 **Language and Literacy**

1332 Hearing loss in infancy and childhood may give rise to difficulties in acquiring spoken and
1333 written language skills. Children who are deaf are at greater risk for delays in learning to read.
1334 Low proficiency in reading and writing limits job opportunities and economic success. Reading,
1335 writing, and communication skills are improving as we add more research on effective ways to
1336 teach and address literacy issues in users of American Sign Language (ASL)^(197, 198), in addition
1337 to use of cochlear implants⁽¹⁹⁹⁾ and hearing aids⁽²⁰⁰⁾.

1338

1339 **Voice and Voice Disorders**

1340 Approximately 7.5 million people in the U.S. have trouble using their voice. Vocal fold tissue is
1341 a complex biological structure that is needed for normal voice production. However, daily insults
1342 such as environmental pollutants or acid reflux may compromise vocal fold integrity over
1343 time^(201, 202). Laryngeal disorders can cause a significant societal burden due to work-related
1344 disability, lost productivity, and direct health care cost (estimated at \$11 billion)^(203, 204). NIDCD
1345 supports basic, clinical and translational research on laryngeal muscle structure and function with
1346 respect to normal and disordered voice use, including new prevention and treatment strategies.

1347

1348 Teachers are occupational voice users who represent one of the country's largest group of
1349 employees. Teachers are particularly vulnerable to voice disorders. It is estimated that 11-38% of
1350 teachers have a voice problem on any given day⁽²⁰⁵⁻²⁰⁷⁾, and cumulative estimates indicate nearly
1351 60% of teachers have been affected over their working lives⁽²⁰⁵⁾. Considering the impact of voice
1352 disorders for teachers—their diagnosis, treatment, and substitute teacher costs—the burden to the
1353 American economy is substantial, estimated to approach \$3 billion annually in 1998⁽²⁰⁸⁾.

1354

1355 **Communication Disorders and Neurodegenerative Disorders**

1356 Stroke is a leading cause of adult disability in the United States⁽²⁰⁹⁾. A significant proportion of
1357 stroke survivors have communication disorders (i.e., post-stroke aphasia or dysarthria) related to
1358 brain injury. Additionally, neurodegenerative disorders, such as Parkinson's disease or
1359 amyotrophic lateral sclerosis (ALS), and injury can lead to impairments in planning and
1360 executing motor speech production such as in apraxia or dysarthria. These types of
1361 communication problems are a strong predictor of poor quality of life and decreased community
1362 participation⁽²¹⁰⁾. The NIDCD supports research to understand the neurological bases of voice,

1363 speech and language impairments, the correlation of brain imaging data with prognosis, and the
1364 development of novel intervention strategies to improve outcomes.

1365

1366 **The Voice, Speech, and Language Program**

1367 The NIDCD Voice, Speech, and Language program utilizes a wide range of research approaches
1368 to develop effective diagnostic and intervention strategies for people with communication
1369 impairments. Research in the Voice and Speech area includes studies to determine the nature,
1370 causes, treatment, and prevention of disorders of motor speech production throughout the
1371 lifespan. The Language area includes the exploration of the genetic bases of child speech and
1372 language disorders, as well as characterizing the linguistic and cognitive deficits in children and
1373 adults with language disorders.

1374

1375 **Recent Advances in Voice, Speech, and Language Research**

1376

1377 **Transformative Genetic Studies**

1378

- 1379 • Scientists continue to discover new genetic and genomic alterations (including the role of
1380 copy number variants) associated with speech and language disorders using new methods
1381 such as next-generation whole-exome sequencing⁽²¹¹⁻²¹⁵⁾. For example, a new gene,
1382 GRIN2A, was identified for focal epilepsies with speech and language disorders,
1383 reinforcing an important role for this gene in motor speech function^(216, 217). These
1384 discoveries are likely to improve the classification, diagnosis, and treatment of speech
1385 and language disorders.
- 1386 • Researchers are learning how reflux from the stomach to the throat and vocal fold tissue
1387 affects the larynx and have demonstrated that reflux significantly alters the expression of
1388 27 genes that are associated with cancer of the larynx^(218, 219). Understanding how changes
1389 in gene expression lead to laryngeal injury provides a comprehensive model for
1390 identifying novel diagnostic and therapeutic targets to treat reflux-related injury.
- 1391 • Researchers generated a transcriptome dataset to capture the complexity of genes
1392 responsible for wound healing of the vocal folds. This dataset serves as a resource in
1393 developing new studies that would accelerate the identification of novel therapeutic
1394 targets to treat reflux-related injury⁽²²⁰⁾.

1395

1396 **Behavioral Phenotyping**

1397

- 1400 • Studies demonstrated that children with developmental speech and language problems are
1401 at a considerable risk for learning disabilities and other psychosocial problems that
1402 emerge during adolescence or adulthood⁽²²¹⁻²²³⁾.
- 1403 • Some families with high incidence of stuttering may also have high incidence of other
1404 fluency disorders and other speech production difficulties. This finding can lead to new
1405 genetic studies across multiple families to define the characteristics of stuttering⁽²²⁴⁾.

1406

1407

- 1408 • Scientists are using new imaging technology to study structural and mechanical
1409 characteristics of laryngeal scarring⁽²²⁵⁾. This could provide the foundation for developing
1410 improved treatments for one of the most common causes of voice disorders.
1411
- 1412 • Researchers have identified distinct and viable characteristics of language disorders,
1413 extending the research to new populations (e.g., children who are deaf, minimally verbal
1414 children with autism) and to language disorders shared across different populations that
1415 may be used in future genetic and treatment studies⁽²²⁶⁻²²⁸⁾. The development of these
1416 classification systems will guide future investigations into the genetic, neurologic, and
1417 other causal factors that contribute to voice, speech, and language impairments.
1418

1419 **Interventions**

- 1420
- 1421 • Researchers suggest that self-administered computer therapy with single word production
1422 improved chronic apraxia of speech. This method shows promise for delivering high-
1423 intensity speech and language rehabilitation for individuals recovering from stroke⁽²²⁹⁾.
1424
- 1425 • Scientists have developed a wearable monitoring device to accurately measure voice
1426 disorders during daily activities and provide real-time feedback^(230, 231). When combined
1427 with knowledge of gene expression changes related to vocal fold vibration exposure⁽²³²⁾,
1428 ambulatory monitoring has shown the potential to revolutionize treatment that could
1429 facilitate healthier vocal function and enhance diagnosis and treatment options.
1430
- 1431 • Studies have demonstrated the clinical benefit of speech and language therapy for school-
1432 age children who have pragmatic and social communication problems⁽²³³⁾ and for
1433 minimally verbal children with autism⁽²³⁴⁾.
1434
- 1435 • Scientists have extended behavioral treatment research to explore the use of a virtual
1436 speech clinician for individuals with aphasia⁽²³⁵⁾. Other studies have shown that spelling
1437 therapy combined with supplemental treatments such as transcranial magnetic and direct
1438 electrical stimulation of the brain enhances treatment outcomes in individuals with
1439 aphasia^(236, 237).
1440
- 1441 • Pairing vagus nerve stimulation with a speech sound can improve how the brain
1442 processes spoken language⁽²³⁸⁾. These discoveries leverage existing knowledge, inform
1443 the development of new treatment paradigms, and improve outcomes for individuals with
1444 speech and language disorders.
1445

1446 **Bioengineering Advances**

- 1447
- 1448 • Researchers have expanded the range of augmentative and alternative communication
1449 through widely available technologies (e.g., tablets)^(239, 240) for individuals with ASD and
1450 related communication disorders.
1451
- 1452 • Researchers have developed a model, which can detect and correct speech production
1453 errors prior to articulation. This model showed a potential for the development of a brain

1454 computer interface (BCI) that use auditory feedback to allow profoundly paralyzed users
1455 to learn to produce speech using a speech synthesizer⁽²⁴¹⁾.

1456

- 1457 • Scientists have made significant advances in replacing, engineering, and regenerating
1458 vocal fold tissue through the use of stem cells⁽²⁴²⁾. In one study, researchers
1459 bioengineered vocal fold tissue using human cells that could produce sound when
1460 transplanted into animals⁽²⁴³⁾. Also, investigators have built computational simulations of
1461 vocal fold vibrations⁽²⁴⁴⁻²⁴⁸⁾ that could provide essential information for designing
1462 biomaterials that will help restore injured vocal folds. These studies help advance the
1463 understanding of normal and disordered vocal function in order to restore vocal fold
1464 structure and function and develop improved treatment options.

1465

1466 **Imaging Correlations**

1467

- 1468 • Brain imaging technology has identified differences in the white matter of the brain in
1469 disorders, such as autism spectrum disorder (ASD) and specific language impairment^{(249,}
1470 ²⁵⁰⁾, and have demonstrated that common neuropathology tied to shared specific
1471 characteristics (e.g., non-word repetition) may be found across different developmental
1472 language disorders⁽²⁵¹⁾.
- 1473
- 1474 • Advanced imaging technology has improved our understanding of the complex actions
1475 that take place in the part of the brain controlling human speech⁽⁹³⁾, and has allowed for
1476 mapping of the functional connections of the brain (connectome) that are responsible for
1477 speech control⁽²⁵²⁾ and mapping the neural interactions involved in critical elements of the
1478 speech motor system⁽²⁵³⁻²⁵⁶⁾. Similarly, other imaging studies have shown that the brain is
1479 organized in specific patterns to perceive speech^(91, 257-264), including processing vocal
1480 tone occurring in the left and right sides of the brain⁽²⁶⁵⁾, and to simultaneously perceive
1481 spoken and signed language⁽²⁶⁶⁾.
- 1482
- 1483 • Significant advances were made in understanding the anatomical differences of the brain
1484 in neurological disorders impairing speech production, such as stuttering⁽²⁶⁷⁻²⁷⁰⁾ and
1485 spasmodic dysphonia^(224, 271-273) and in understanding the neural organization of language
1486 in a range of acquired language disorders^(274, 275) and how language networks change as a
1487 result of treatment in individuals who have had a stroke⁽²⁷⁶⁾.
- 1488
- 1489 • Imaging of the larynx and vocal folds have been refined by ultrasound⁽²⁷⁷⁾ to characterize
1490 the relative concentration of collagen and elastic fibers, which are key factors influencing
1491 the biomechanical properties of the vocal folds, and by nonlinear laser scanning
1492 microscopy and atomic force microscopy-based indentation⁽²²⁵⁾ to characterize scarred
1493 vocal folds. These imaging techniques are likely to enhance diagnostic capabilities and
1494 help evaluate bioengineering techniques used to simulate vocal fold tissue.

1495

1496 **Developmental Timing**

1497

- 1498 • Longitudinal studies have documented the predictors and risk factors that are associated
1499 with behavior and brain development underlying speech and language in children with or

- 1500 without speech and language disorders^(278, 279). This research is now being used to identify
1501 early behavioral and neural risk factors that predict later language disorders⁽²⁸⁰⁻²⁸²⁾.
1502
- 1503 • Studies identified that the quality of caregiver-child interaction is one of the factors that
1504 influences how quickly infants process speech⁽²⁸³⁾. Variations in early language
1505 experience (early vs. late bilingualism) shape patterns of functional connectivity in the
1506 human brain⁽²⁸⁴⁾. Further, researchers found the auditory brainstem of adolescents are
1507 still immature and speech development can still be altered⁽²⁸⁵⁾. Another study helped
1508 scientists understand the differences in how the brain perceives vowels and consonants,
1509 which may explain some aspects of developmental and acquired speech processing
1510 disorders⁽²⁸⁶⁾.
1511
 - 1512 • The first systematic determination of the cellular and molecular progression of vocal fold
1513 epithelium development documented five developmental events of the progression from
1514 vocal fold initiation in the embryonic anterior foregut tube to fully differentiated and
1515 functional adult tissue. The study serves as the necessary foundation for future functional
1516 investigations of vocal fold formation⁽²⁸⁷⁾.
1517
 - 1518 • For the first time, a series of high-speed digital imaging studies have compared vocal fold
1519 vibration between children and adults. Researchers have demonstrated vocal fold
1520 vibration in children is complex and not easily predicted from an adult^(288, 289). Further,
1521 precise characterization of age-related changes in the larynx paves the way for scientists
1522 to design biomaterials with the potential to restore voice to elderly individuals with vocal
1523 fold atrophy⁽²⁹⁰⁻²⁹⁴⁾.
1524

1525 *Science Capsule: Spasmodic Dysphonia*

1526
1527 Voice production and its quality influence the communicative exchange throughout the lifespan.
1528 Some voices are perceived as pleasing and facilitate the message, while others are perceived as
1529 unpleasant and do not facilitate the message. Voice disorders are not trivial though they are
1530 overwhelmingly under recognized. Occupational voice disorders are estimated to affect 28
1531 million Americans and have a significant impact on the livelihood of teachers/professors, TV and
1532 radio journalists, lawyers, and singers. The NIDCD supports basic and clinical research studies
1533 that focus on normal voice production and the prevention and treatment of voice disorders.

1534
1535 Spasmodic dysphonia (SD) is a voice disorder that belongs to a family of neurological disorders
1536 called focal dystonias. SD can affect anyone. When a person with SD attempts to speak, the
1537 muscles in the larynx spasm involuntarily and cause the voice to break up and sound strained or
1538 breathy. It is a rare disorder, occurring in roughly one to six people per 100,000 people⁽²⁹⁵⁾. The
1539 first signs of this disorder start to appear in individuals between 30-50 years old. More women
1540 than men are affected. There is no cure for SD, and the most common treatment is the injection
1541 of very small amounts of botulinum toxin directly into the affected muscles of the larynx. Repeat
1542 injections are necessary as the effects last only a few months.

1543
1544 The NIDCD currently funds research to determine the causes and pathophysiology of SD in
1545 order to develop new diagnostics and better treatment options. NIDCD-supported scientists are
1546 using multi-modal imaging and next-generation DNA sequencing to identify brain abnormalities
1547 and genetic risk factors for SD. By identifying genes responsible for this voice disorder, the
1548 Institute is directly addressing the need for better, more accurate detection and diagnosis in this
1549 clinical population. NIDCD-supported scientists are now pursuing two new areas for therapies
1550 and surgical interventions: 1) Locating specific brain areas involved in regulating laryngeal
1551 muscles and 2) understanding the neural mechanisms by which they exert their control.

1552
1553 The NIDCD will continue to support voice disorders research, guided by recommendations from
1554 a 2013 NIDCD-sponsored workshop on voice sciences and disorders. Leading experts in the
1555 field agreed that it is essential to strengthen the pipeline of future voice scientists by creating
1556 collaborative teams to address lingering research questions. Accordingly, the NIDCD issued two
1557 Funding Opportunity Announcements (FOA) on Advancing Research in Voice Disorders. The
1558 initiatives seek cutting-edge research proposals such as the development of biomaterials for
1559 engineering vocal fold tissue and development of ambulatory biofeedback approaches for
1560 management of patients with voice disorders. Additionally, the FOAs encourage patient
1561 outcomes research, health services research, and community based research with special
1562 attention to the needs of individuals with low socio-economic status, disparities, rural, second
1563 language populations, and women's health.

1564

1565 **Priority Areas in Voice, Speech, and Language Research**

1566

1567 The NIDCD Voice, Speech, and Language Program contains areas of research that overlap with
1568 mission areas of other NIH ICOs. In particular:

1569

1570 • **Language:** The normal acquisition of language is within the mission area of the Eunice
1571 Kennedy Shriver National Institute of Child Health and Human Development (NICHD).
1572 Additionally, normal language decline as a result of normal aging is within the mission of
1573 the National Institute on Aging (NIA). NIDCD research focuses on language acquisition
1574 in the presence of dysfunctions, diseases, and disorders that alter the traditional
1575 developmental course such as hearing loss, ASD, SLI, and aphasia.

1576

1577 • **Literacy:** As with language, the normal acquisition of literacy skills and individual
1578 outcomes in educational settings are within the mission of NICHD. The NIDCD supports
1579 research into literacy for people who are deaf and hard of hearing, the acquisition of
1580 written language for people with pre-existing language disorders, improving reading and
1581 writing deficits often associated with stroke, and educational interventions to support
1582 improved individual outcomes.

1583

1584 **Priority Area 1: Understanding Normal Function**

1585

1586 • **Modeling:** Improve physical, computational and theoretical modeling of human
1587 communication, including vibratory properties of the larynx, neural and speech motor
1588 control, and speech language processing.

1589

1590 • **Laryngeal System:** Examine effects of laryngeal muscle function and structure (e.g., muscle
1591 fiber and mucosal changes at the cellular and molecular level) on vocal health, in particular
1592 with respect to development, aging, environment and to voice training and vocal dose—the
1593 amount, intensity, and distribution of voice use.

1594

1595 • **Motor Speech Production:** Determine the similarities and differences in development and
1596 functioning of neural and musculoskeletal systems for human voice and speech production
1597 vs. non-speech oral motor control in order to identify the sensorimotor principles underlying
1598 typical speech development and adult speech motor control, and to understand overlapping
1599 sensorimotor mechanisms of the larynx.

1600

1601 • **Developmental and Neural Plasticity:** Identify the developmental course of sensory and
1602 motor plasticity and the underlying neural mechanisms associated with voice and speech
1603 motor learning in children and adults (e.g., sensorimotor adaptation).

1604

1605 • **Sign Language Research:** Investigate the acquisition, processing, and neural underpinnings
1606 of languages within the visual-manual modality.

1607

1608 • **Literacy and Deafness:** Identify central and peripheral factors associated with the successful
1609 comprehension and use of written language for people who use sign language as their
1610 primary way of communication.

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Priority Area 2: Understanding Diseases and Disorders

- **Natural History and Epidemiology:** Identify genetic, neural, sensorimotor, cognitive, linguistic, behavioral, demographic, and environmental factors associated with the progression, developmental course and longer-term outcomes of voice, speech, and language impairments. Determine the relative contribution of those factors to risk for the development and recovery from impairment.
- **Pathophysiology:** Identify the pathophysiologic and cognitive mechanisms underlying both common and rare voice, speech, and language impairments.
- **Genetics:** Identify genetic and epigenetic factors that contribute to voice, speech, and language impairments, including studies that identify prenatal factors that can modify genetic and epigenetic expression in offspring.
- **Developmental and Neural Plasticity:** Examine changes in brain structure and functioning in response to behavioral, pathologic, or environmental insult as a basis for voice, speech, and language impairments with an emphasis on developmental timing.
- **Co-Occurring Conditions:** Examine factors (e.g., social context, inflammatory response, co-morbid conditions) that interact or coexist with primary voice, speech, and language impairments. Examine diagnostic and treatment strategies for voice, speech, and language impairments that may coexist in individuals with deafness, and in individuals with communication disorders. Examine cross-system deficits and their influence on communication health and responsiveness to treatment.

Priority Area 3: Improving Diagnosis, Treatment, and Prevention

- **Detection, Diagnosis and Hypothesis-Driven Interventions:** Develop biomarkers (e.g., genetic, imaging, behavioral) of objective diagnosis, prognosis, treatment monitoring for developmental and acquired voice, speech, and language impairments. Develop models of intervention informed by cognitive, linguistic, biological, or neurophysiological processes, accounting for cultural and linguistic variation and including predictors of response to treatment. Develop and refine techniques, technology and instrumentation for improved diagnosis to aid in treatment and prevention.
- **Efficacy:** Using outcomes-based clinical studies and randomized clinical trials, determine the efficacy of proposed interventions for the prevention and treatment of voice, speech, and language impairments, which can include accounting for cultural and linguistic variation.
- **Prevention:** Develop and expand programs that prevent the onset or limit the severity of developmental and acquired voice, speech, and language impairments for people with genetic, occupational, environmental, or other risks.

- 1656 • **Understudied Populations:** Identify the etiology and pathophysiology for understudied
1657 populations (e.g., school-aged, minimally verbal children with ASD, health disparity groups,
1658 multicultural) or conditions (e.g., stuttering and apraxia of speech in children and adults).
1659 Develop methods of assessing and new effective interventions or approaches tailored for
1660 understudied populations or conditions.
1661
- 1662 • **Rare Disorders:** Develop biomarkers for improved diagnosis, prediction of risk, and
1663 treatment response for patients with rare voice, speech and language disorders (e.g.,
1664 spasmodic dysphonia, paradoxical vocal fold motion).
1665
- 1666 • **Bioengineering, including Assistive Technologies:** Harness recent advances in
1667 bioengineering to inform the development and evaluate efficacy of such things as wearable
1668 monitoring devices, imaging procedures, tissue engineering, bioreactors, novel augmentative
1669 and alternative communication (AAC) approaches and to enhance brain computer interface
1670 (BCI) technologies for communication.
1671
- 1672 • **Improving Literacy:** Develop methods that promote the acquisition of English literacy skills
1673 during childhood and improve the reading and writing abilities of people who are deaf and
1674 native ASL users.
1675

1676 **Priority Area 4: Improving Outcomes for Human Communication**
1677

- 1678 • **Novel Delivery:** Translate and evaluate efficacy of conventional interventions into new
1679 delivery models (e.g., group, family, telehealth, cell-based therapies, emerging technology
1680 platforms).
1681
- 1682 • **Screening:** Develop effective and efficient clinical screening tools for use in health and
1683 community settings such as schools, primary care physician offices, and senior centers.
1684 Develop novel screening tools to document treatment outcomes, to determine communication
1685 status, and to improve clinical outcomes in real-world settings. Determine efficacy of
1686 screening for improving clinical outcomes.
1687
- 1688 • **Comparative Effectiveness Research and Evidence-Based Medicine:** Through clinical
1689 trials and epidemiological comparative effectiveness research, identify best treatments for a
1690 given communication disorder for a defined set of individuals.
1691
- 1692 • **Patient-Oriented Research:** Conduct research to help define the impact of voice, speech,
1693 and language communication problems and the desirable/reasonable expectation for quality
1694 of life outcome from the individual's perspective.
1695
- 1696 • **Community-Based Research:**
1697
- 1698 ▪ Promote community-based research and data collection to identify factors that influence
1699 outcomes for people with voice, speech, or language impairments, and to inform the
1700 development of public policy recommendations.
1701

- 1702 ▪ Examine community-level health promotion strategies to prevent the occurrence of,
1703 reduce the risk of, or improve the adherence with treatment of voice, speech, and
1704 language impairments.
1705
- 1706 ▪ **Bridging the Gap between Research and Practice:** Determine effective dissemination and
1707 implementation strategies that enhance the adoption of voice, speech, and language clinical
1708 discoveries into routine community practice.
1709
- 1710

1711 **Summary**

1712

1713 The mission of the NIDCD is to conduct and support biomedical and behavioral research and
1714 research training in the normal and disordered processes of hearing, balance, taste, smell, voice,
1715 speech, and language. The Institute also conducts and supports research and research training
1716 related to disease prevention and health promotion; addresses special biomedical and behavioral
1717 problems associated with people who have communication impairments or disorders; and
1718 supports efforts to create devices that substitute for lost and impaired sensory and
1719 communication function.

1720

1721 The goals listed in the NIDCD Strategic Plan are an assessment of research areas that present the
1722 greatest scientific opportunities and public health needs over the next five years for the three
1723 program areas: hearing and balance; taste and smell; and voice, speech and language. The goals
1724 in the Strategic Plan’s Priority Areas are a guide for:

1725

- 1726 • Scientists: To better understand the directions that NIDCD research may take in the
1727 future;
- 1728 • The NIDCD: To assist in developing FOAs and to identify projects for HPP nomination;
1729 and
- 1730 • The Public: To understand the state of communication sciences and to discover the
1731 scientific breakthroughs that are possible with sustained investments in biomedical
1732 research.

1733

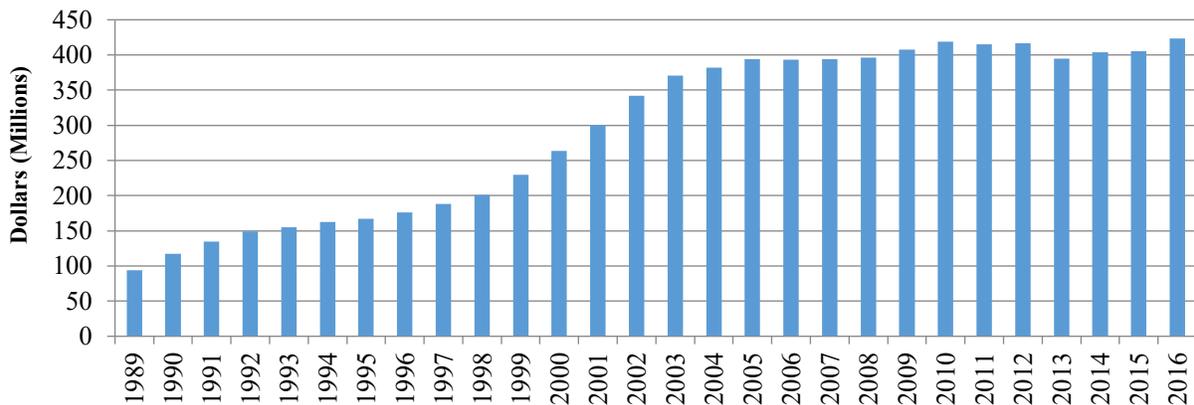
1734 The Plan is not a complete list of all research areas that the NIDCD is currently supporting or
1735 plans to support in the future. The NIDCD is committed to supporting new, innovative,
1736 hypothesis-driven, meritorious research. The Plan will assist us in identifying research areas that
1737 have a great opportunity to help the NIDCD improve the health and quality of life of people with
1738 communication disorders.

1739

1740 **Appendix A: NIDCD Funding History**

1741
 1742 Appropriated funds for the NIDCD increased dramatically in the first 15 years after the
 1743 establishment of the Institute in FY 1989. Funding for NIDCD has remained relatively
 1744 constant since FY 2005. A notable decrease of approximately 5.2% occurred in FY 2013 with
 1745 the government-wide sequestration, while the FY 2016 appropriation saw an increase of 4.4%.
 1746

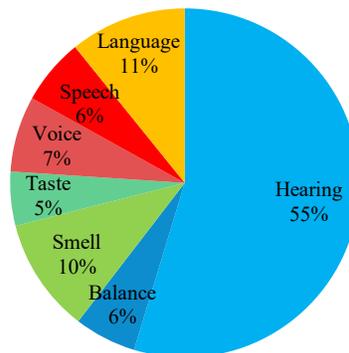
**NIDCD Congressional Appropriations
 FY 1989 - FY 2015
 (non-ARRA**)**



1747
 1748
 1749 Figure 1: Annual Congressional Appropriations for NIDCD. **An additional \$102.9 million
 1750 was appropriated to NIDCD for FY 2009 through the American Recovery and Reinvestment
 1751 Act (ARRA). Data compiled by the NIH Office of Budget
 1752 (http://officeofbudget.od.nih.gov/approp_hist.html).
 1753
 1754

1755 NIDCD funds extramural and
 1756 intramural research in hearing,
 1757 balance, taste, smell, voice,
 1758 speech, and language (Figure
 1759 2).

**Total NIDCD Extramural and Intramural Obligated
 Funds for FY 2015 by Program Area**



1760
 1761
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 1764
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 1766
 1767
 1768 Figure 2: Total NIDCD Extramural and Intramural Obligated Research Funding (excluding
 1769 ARRA funding and research management and support) for FY 2015. (Data compiled by the
 1770 NIDCD Financial Management Branch).

1771 **Appendix B: The NIDCD 2017-2021 Strategic Plan: The Process**

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In the fall of 2015, NIDCD’s Science Policy and Planning Branch (SPPB) began the process of updating the current NIDCD Strategic Plan for research, which was expiring in 2016. SPPB took the following steps to update the previous strategic plan:

1. **Established a Scientific Expert Working Group:** In January 2016, the NIDCD identified and invited 12 outside scientific experts to serve on the Working Group to update the NIDCD Strategic Plan. The experts represented NIDCD’s mission areas (Hearing and Balance; Taste and Smell; Voice, Speech, and Language). A roster of the Working Group is on page 45-46. NIDCD staff also selected a working group chairperson, who is a current NDCD Advisory Council member, and will serve as Council Liaison. SPPB and other NIDCD staff served as resource persons.
2. **Convened Scientific Expert Working Group via Teleconference:** The Working Group held its first conference call in February 2016. SPPB hosted separate working group teleconferences for each of the three main program areas in March 2016. Prior to the teleconferences, working group participants received instructions (including a current NIDCD portfolio analysis, templates with the previous science advances and scientific objectives, and roster/contact information of working group members and NIDCD staff). The Working Group discussed scientific advances that they considered suitable and identified areas of outstanding opportunity and unmet need within their areas of expertise.
3. **Face to Face Working Group Meeting:** The Working Group met in Bethesda, Maryland, at the NIDCD to finalize the draft science advances and research objectives in May 2016.
4. **Presentation to NIDCD Advisory Council:** Dr. Charles Liberman, chair of the Working Group, presented the Working Group’s recommendations for research objectives in all three program areas of the NIDCD Plan at the May 20, 2016, meeting. Council members had the opportunity to comment on the draft objectives. In June 2016, the NIDCD SPPB sent the first draft of the Plan to Council for review and comment. At the September 2016 NDCD Advisory Council meeting, NIDCD staff announced that the draft Plan will be made available for public comment.
5. **Solicited Public Comments:** The draft Plan was made available for a 30-day Public Comment Period on the NIDCD website in the fall of 2016. To announce the public comment period, the NIDCD published the Notice (NOT-DC-16-XXX) in the NIH Guide for Grants and Contracts on XX. The NIDCD also published a Notice in the Federal Register on XX. NIDCD received XX comments.
6. **Finalized and Posted the Plan on the NIDCD Website:** Once appropriate Public Comments were incorporated into the draft approved by NIDCD staff, SPPB finalized the Plan and published it on the NIDCD website in early 2017.

1817 **Working Group Roster**

1818

1819 **Hearing and Balance**

1820

1821 **M. Charles Liberman, Ph.D. (Chair)**

1822 Director

1823 Eaton-Peabody Laboratories

1824 Massachusetts Eye and Ear Infirmary

1825

1826 **Andrew Groves Ph.D.**

1827 Professor and Co-Director, Program in

1828 Developmental Biology

1829 Departments of Neuroscience and Molecular

1830 and Human Genetics

1831 Baylor College of Medicine

1832

1833 **Jian-Dong Li, M.D., Ph.D.**

1834 Professor & Director, Institute for

1835 Biomedical Sciences

1836 Georgia Research Alliance Eminent Scholar

1837 Georgia State University

1838

1839 **Jay T. Rubinstein, M.D., Ph.D.**

1840 Professor

1841 Department of Otolaryngology

1842 Virginia Merrill Bloedel Hearing Research

1843 Center

1844 University of Washington

1845

1846 **Christoph Schreiner, M.D., Ph.D.**

1847 Professor and Vice Chairman of

1848 Otolaryngology – Head and Neck Surgery

1849 UCSF Kavli Neuroscience Center

1850 University of California San Francisco

1851

1852 **Richard J. H. Smith, M.D.**

1853 Professor

1854 Department of Otolaryngology

1855 University of Iowa

1856

1894

1895 **NIDCD Staff Participants**

1896

1897 James F. Battey, Jr., M.D., Ph.D.

1898 Kathy Bainbridge, Ph.D.

1899 Laura K. Cole, Ph.D.

1857 **Debara L. Tucci, M.D.**

1858 Professor of Surgery

1859 Division of Otolaryngology – Head and

1860 Neck Surgery

1861 Duke University Medical Center

1862

1863 **Taste and Smell**

1864

1865 **Sue C. Kinnamon, Ph.D.**

1866 Professor

1867 Department of Otolaryngology

1868 University of Colorado, Denver

1869

1870 **Donald A. Wilson, Ph.D.**

1871 Senior Research Scientist and Deputy

1872 Director, Emotional Brain Institute

1873 New York University School of Medicine

1874

1875 **Voice, Speech, and Language**

1876

1877 **Diane M. Bless, Ph.D.**

1878 Professor Emeritus

1879 Departments of Communicative Disorders

1880 and Surgery

1881 University of Wisconsin – Madison

1882 School of Medicine

1883

1884 **Kristina Simonyan, M.D., Ph.D.**

1885 Associate Professor of Neurology and

1886 Otolaryngology

1887 Icahn School of Medicine at Mount Sinai

1888

1889 **Helen Tager-Flusberg, Ph.D.**

1890 Professor

1891 Department of Psychology

1892 Boston University

1893

1900 Judith A. Cooper, Ph.D.

1901 Janet Cyr, Ph.D.

1902 Susan Dambrauskas, M.A.

- | | | | |
|------|-------------------------------|------|------------------------------|
| 1903 | Amy Donahue, Ph.D. | 1912 | Roger Miller, Ph.D. |
| 1904 | Nancy Freeman, Ph.D. | 1913 | Christopher Platt, Ph.D. |
| 1905 | Andrew Griffith, M.D., Ph.D. | 1914 | Alberto Rivera-Rentas, Ph.D. |
| 1906 | Steven Hirschfeld, M.D. | 1915 | Elka Scordalakes, Ph.D. |
| 1907 | Howard Hoffman, M.A. | 1916 | Lana Shekim, Ph.D. |
| 1908 | Craig Jordan, Ph.D. | 1917 | Susan Sullivan, Ph.D. |
| 1909 | Lisa M. Kennedy, Ph.D. | 1918 | Bracie Watson, Ph.D. |
| 1910 | Chuan-Ming Li, Ph.D. | 1919 | Ginger Webb, M.S. |
| 1911 | Melissa McGowan, M.H.S., CHES | 1920 | Baldwin Wong, B.S. |
| 1921 | | | |

1922 **Appendix C: Trans-NIH and Intra-Agency Activities in which NIDCD**
1923 **Participates**

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1925 For the most up-to-date listing of Trans-NIH Activities in which NIDCD participates, please visit
1926 this website: <https://dpcpsi.nih.gov/collaboration/index>.

1927
1928 **Trans-NIH Activities in Which NIDCD Participates**

1929
1930 **NIH Autism Coordinating Committee (NIH/ACC):** formed by the NIH in 1997, at the request
1931 of Congress. The mission of the NIH/ACC is to enhance the quality, pace and coordination of
1932 autism research efforts at the NIH. The NIH ACC has been instrumental in planning trans-NIH
1933 research initiatives to advance the understanding of autism. In addition to program staff from
1934 seven ICs, the NIMH Office of Autism Research Coordination (OARC) and the NIMH National
1935 Database for Autism Research (NDAR) Office participate in NIH ACC meetings, keeping NIH
1936 program offices apprised of their activities and coordinating projects of mutual interest. The NIH
1937 ACC continually monitors the NIH autism research portfolio and the agency's progress toward
1938 meeting the goals of the Interagency Autism Coordinating Committee (IACC) Strategic Plan for
1939 ASD Research.

1940
1941 **The Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative:**
1942 part of a Presidential goal aimed at revolutionizing our understanding of the human brain. By
1943 accelerating the development and application of innovative technologies, researchers will be able
1944 to produce a revolutionary new dynamic picture of the brain that, for the first time, shows how
1945 individual cells and complex neural circuits interact in both time and space. Long desired by
1946 researchers seeking new ways to treat, cure, and even prevent brain disorders, this picture will
1947 address major gaps in our current knowledge and provide unprecedented opportunities for
1948 exploring exactly how the brain enables the human body to record, process, utilize, store, and
1949 retrieve vast quantities of information, all at the speed of thought.

1950
1951 **National Advisory Board on Medical Rehabilitation Research:** established by the Director of
1952 NIH to advise the directors of NIH ICs, the Eunice Kennedy Shriver National Institute of Child
1953 Health and Human Development (NICHD), and NICHD's National Center for Medical
1954 Rehabilitation Research on matters and policies relating to the Center's programs. The Board is
1955 comprised of 12 members representing health and scientific disciplines related to medical
1956 rehabilitation and six members representing persons with disabilities.

1957
1958 **NIH Medical Rehabilitation Coordinating Committee:** established by the NIH Director to
1959 comply with Public Law 101-613 to make recommendations with respect to the content of the
1960 Research Plan and the activities of the NIH Clinical Center that are carried out in conjunction
1961 with other components of NIH and with other Federal Government agencies.

1962
1963 **The NIH Human Connectome Project:** an ambitious effort to map the neural pathways that
1964 underlie human brain function. The overarching purpose of the Project is to acquire and share
1965 data about the structural and functional connectivity of the human brain. It will greatly advance
1966 the capabilities for imaging and analyzing brain connections, resulting in improved sensitivity,

1967 resolution, and utility, thereby accelerating progress in the emerging field of human
1968 connectomics. <http://www.neuroscienceblueprint.nih.gov/connectome/>

1969
1970 **NIH Neuroprosthesis Group:** is a trans-NIH group of program officers and staff that share an
1971 interest in neural prosthetics and neuroengineering research. The group hosts discussions about
1972 funding opportunities, meetings, and ongoing projects.

1973
1974 **NIH Obesity Research Task Force:** established to accelerate progress in obesity research
1975 across NIH in view of the importance of the obesity epidemic as a public health crisis. The task
1976 force has been instrumental in fostering trans-NIH collaboration on obesity research, including
1977 basic, clinical, and population studies. The task force also sponsors an NIH seminar series on
1978 obesity research topics.

1979
1980 **Prevention Research Coordinating Committee (PRCC):** serves as a venue for exchanging
1981 information on recent scientific advances in disease prevention; examining the impact of new
1982 policies on research; planning new or discussing ongoing initiatives; and highlighting program
1983 accomplishments. As a Trans-NIH, trans-agency committee, the PRCC provides a broad
1984 perspective on the current state-of-the-science and actively disseminates information about
1985 prevention-related activities sponsored by federal and non-federal organizations to the NIH
1986 Institutes and Centers.

1987
1988 **Trans-NIH Rare Diseases Working Group:** charged to develop an integrated NIH-wide plan
1989 for research in rare diseases that addresses basic, translational, and clinical aspects aimed at the
1990 prevention and cure of rare diseases.

1991
1992 **NIHSeniorHealth.gov:** is a senior-friendly NIH Web site is specially formatted for optimal use
1993 by seniors seeking health information. It features health information on a variety of topics
1994 pertinent to older adults and includes videos, interactive quizzes, and FAQs to reinforce learning
1995 on the Web.

1996
1997 **Trans-NIH Zebrafish Coordinating Committee:** established in 1997 in response to the
1998 scientific community's recommendation to promote the use of zebrafish as a model organism for
1999 the study of vertebrate development and disease. The committee developed a website to provide
2000 a central information resource, focusing on major NIH-organized zebrafish meetings; funding
2001 opportunities for zebrafish genomics and genetic resources; major resources generated from
2002 grants funded in response to Trans-NIH zebrafish initiatives; training courses and scientific
2003 meetings related to the zebrafish initiatives; and selected reports and publications.

2004 2005 **Trans-Agency Efforts in which NIDCD Participates**

2006
2007 **Early Hearing Detection and Intervention:** Collaboration with the Centers for Disease Control
2008 and Prevention (CDC) and HRSA focuses on a bringing together Federal agencies that are
2009 interested in issues related to screening infants for hearing loss and providing early intervention.

2010
2011 **It's a Noisy Planet. Protect Their Hearing® Public Education campaign:** NIDCD sponsors
2012 [It's a Noisy Planet. Protect Their Hearing®](#), a national public education campaign to increase

2013 awareness among parents of children ages 8 to 12 about the causes and prevention of noise-
2014 induced hearing loss (NIHL). Our current federal partner includes the National Institute for
2015 Occupational Safety and Health (NIOSH) at the CDC, as well as several private partners.

2016
2017 **Interagency Autism Coordinating Committee (IACC):** was established in accordance with the
2018 Autism Collaboration, Accountability, Research, Education, and Support (CARES) Act of 2014,
2019 the Interagency Autism Coordinating Committee (IACC), a federal advisory committee, is
2020 charged with coordinating all efforts with the Department of HHS and across member federal
2021 agencies concerning autism spectrum disorder (ASD). The committee was established in an
2022 effort to accelerate progress in ASD biomedical research and services efforts by improving
2023 coordination and communication across the Federal Government and by working in partnership
2024 with the autism community.

2025
2026 **NIDCD-Supported Epidemiological Studies with the Centers for Disease Control and
2027 Prevention (CDC):**

- 2028
- 2029 • **NIOSH Audiometric Examinations for three Population-Based Surveys:** provides
2030 funding for scientific and technical support as well as quality assurance of three large
2031 audiometric examination surveys funded by NIDCD. These health surveys are: 1) The
2032 National Health and Nutrition Examination Survey (NHANES), 2) Age,
2033 Gene/Environment Susceptibility Study–Reykjavik Study (AGES–RS), and 3) the Early
2034 Childhood Longitudinal Study.
 - 2035
 - 2036 • **National Center for Health Statistics (NCHS) Balance/Dizziness Problem
2037 Examinations:** provides funding for the inclusion of Balance/Dizziness Examinations for
2038 a representative sample of U.S. adults (age 18+ years) and children (age 3–17 years) in
2039 the 2016 National Health Interview Survey (NHIS).
 - 2040
 - 2041 • **NHIS Hearing Testing:** provides funding for a hearing component to the National
2042 Health Interview Survey (NHIS) by sponsoring inclusion of many additional questions on
2043 hearing loss and tinnitus.

2044
2045 **Department of Education Early Childhood Longitudinal Study:** support hearing screening
2046 examinations in the Early Childhood Longitudinal Study for the Kindergarten cohort.

2047
2048 **Advanced Electrode Microfabrication for Neural Prostheses at the Department of Energy:**
2049 provides funding support for the Lawrence Livermore National Laboratory to develop precise
2050 and rapid construction micromachining techniques and construct arrays of microelectrodes
2051 suitable for recording and stimulating neural tissue. These devices will be specifically optimized
2052 for use in the NIDCD mission areas of voice, speech, hearing, and balance.

2053
2054 **Interagency Committee on Disability Research (ICDR):** a Government-wide group that meets
2055 monthly to discuss the issues related to identifying people with disabilities and to coordinate
2056 research in this area.

2057
2058

2059 **Appendix D Glossary and Acronym List**

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2061 Glossary

2062

2063 Placeholder

2064

2065 Acronym List

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2067 Placeholder

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2069 **Appendix E: Bibliography**

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