National Institute of Deafness and Other Communication Disorders

2019 Marmoset Community White Paper

The core mission of the National Institute of Deafness and Other Communication Disorders (NIDCD) to understand normal and disordered processes of hearing, balance, taste, smell, voice, speech and language as well as to improve the treatment of communication impairment and other sensory disorders. The common marmoset (*Callithrix jacchus*) has contributed significantly to research designed to address these key issues for several decades and will remain a cornerstone model to significantly advance the core missions of the NIDCD in the years to come. With their complex and human-like social behavior and brain organization, marmosets are an ideal model for studies of normal and disordered hearing. As a non-human primate with perceptual hearing ranges and auditory brain structures similar to that of humans, marmosets can provide greater insight into basic mechanisms of hearing than studies in more evolutionarily distant rodent models can. Moreover, because they can be easily bred and raised in laboratory conditions, have an average lifespan of 10 years, and exhibit age-related hearing loss, marmosets provide a unique opportunity to longitudinally study the effects of development and aging upon hearing over the entire lifespan. Because they are amenable to genetic manipulation as well as more genetically similar to humans than other species, marmosets may provide better understanding of genetic causes of hearing loss and their rehabilitation. Marmosets are also one of the few non-human mammalian models of vocal communication. Even in the laboratory colony, marmosets are highly social primates in constant interactive vocal contact with each other facilitated by the ability to be kept in natural social and family groups. As a result, marmosets can provide critical insight into normal mechanisms of communication, the evolutionary origins of speech, and disorders in communication that can arise from deafness, neurologic disease, or social isolation. Thus marmosets have substantial potential to understand the critical interplay between hearing and vocal communication and the development of novel strategies to prevent and treat disorders stemming from hearing loss. Notably, work in the marmoset auditory system was the first to leverage the many advantages of this model organism to explore core questions of systems neuroscience research with nonhuman primates, such as sensory coding in neocortex (71) and the cortical basis of vocal communication (32, 72, 73). The potential of the marmoset model also extends beyond hearing, but includes less well investigated facets of the NIDCD mission. As prolific scent markers, marmosets are amenable to studying the neural mechanisms of olfaction in a non-human primate. As a species that naturally moves rapidly in three dimensions and relies more heavily on head than eye movements, marmosets are potentially useful in studying both the peripheral and central aspects of the vestibular system, in particular less-well understood encoding of gravity and tilt.

Breadth of Current Research. Recent work in marmosets has begun to address many fundamental questions central to the mission of the NIDCD. In basic hearing research, neural recordings in the marmoset auditory cortex by Bendor and Wang (35) have localized a pitch-selective brain area, answering a long-standing question in auditory perception and physiology. Marmosets also exhibit human-like pitch perceptual patterns

(27). Marmosets are beginning to be used to understand therapies for hearing loss, having recently become a model species for studying the neural effects of Cochlear Implants, revealing critical similarities and differences from normal sensory processing (28). Marmosets have also shown recent advances in our understanding of hearing loss genetics, with recent studies of the marmoset cochlea showing patterns of hearing-related gene expression that are distinct from that in mice and more similar to humans (74), thus suggesting marmosets may be a better model for genetic hearing loss. Marmosets are also proving themselves to be an excellent model for vocal communication and its disorders (23, 32). Marmosets engage in cooperative, turn-taking vocal conversations with rules similar to that of human communication (75, 76). Some evidence also suggests that infant marmosets babble, similarly to human babies, and their vocal development may be dependent, in part, on interactions with their parents (77-79). Finally, the breadth of current work is not limited to the auditory-vocal domain, with recent anatomic studies of marmoset olfaction showing human-like connections between the olfactory bulb and cortex (80).

The Future. Marmosets are uniquely suited for future advances in our understanding of critical open questions in disordered hearing and communication. For example, what are the long-term effects of hearing loss and hearing restoration on the brain and what are the mechanisms by which this can contribute to cognitive decline? This association has garnered significant recent interest and attention, but the underlying mechanisms remain uncertain. Because of marmosets' lifespan, reproductive patterns, and social behavior, they are an ideal model for studying age-related hearing loss and its consequences on cognitive decline and social isolation that have been revealed as critically important in humans. Furthermore, marmosets would be amenable to more rapid testing of hearing or other rehabilitation to determine its effects on future age-related changes. Second line of critical forthcoming research pertains to genetic and neuroanatomical origins of speech and other vocal communication disorders. Although marmosets do not possess human language, their vocalizations exhibit many similarities and they are the only non-human primate species in which vocal communication can readily be studied in the laboratory, including greater homology with humans than other non-primate research models. When combined with the potential for genetic manipulations and longitudinal studies during development, marmosets are an ideal model for understanding these disorders and potential therapies.

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