THE HARTWELL FOUNDATION

2018 Individual Biomedical Research Award

C. Daniel Meliza, Ph.D.

Assistant Professor
Department of Psychology

University of Virginia

Early Detection of Auditory Learning Deficits in a Novel Model of Dyslexia and Other Developmental Language Disorders

Nearly 8% of American children ages 3–17 suffer from learning impairments in speech and language. Despite having normal hearing and nonverbal intelligence, children affected with these disorders exhibit delays in development of speech production, oral language comprehension and reading skills. The most common language-based disorder is dyslexia, characterized by poor word reading, word decoding, oral reading fluency and spelling. It is not caused by hearing loss or cognitive deficits but is nonetheless, neurobiological in origin. Dyslexia is especially pernicious because it is usually not diagnosed until children start formal reading instruction. For example, by the time children with dyslexia become adolescents, they are 2–3 times more likely to develop major depression and anxiety or to attempt suicide. It is thought that developmental language disorders begin early in life, when infants are learning to decode speech into phonemes, the fundamental units of words. Failure to correctly identify phonemes in infancy is associated with an increased risk of developing a language-learning impairment, but diagnosis often only occurs several years later, when children begin school. By this age, basic speech and language skills are already firmly established and interventions are much less effective. Early identification of abnormalities in phonetic learning is therefore crucial in the first year of life. To meet this need, I propose to develop a novel animal model of early auditory learning using a songbird, the zebra finch, that will enable examination of the underlying biological causes of dyslexia and other developmental language disorders, including preclinical trials of therapeutic interventions. Although language is unique to humans, zebra finches communicate using complex vocalizations and undergo a similar process of auditory development early in their life. The songs a bird hears early in life shape how its brain processes sound, laying the foundation for it to learn how to produce its own song and how to understand the songs of other individuals. Based on genomic screening studies in humans, I will transfer genetic mutations associated with developmental language disorders into zebra finches by combining electroporation in vivo with CRISPR Cas9 gene editing. The purpose will be to test how the mutations affect the experience-dependent development of the songbird brain and whether a neural signature of auditory development exists in birds that reliably predicts the quality of vocal development or is significantly impacted by mutations associated with dyslexia or other developmental language disorders. If I am successful, I will translate the measurement and analysis methods for the purpose of a clinical trial that targets early intervention with high risk children to correct phonetic processing abnormalities before they can impact later language development.