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"The expression of autism gene FOXG1 in the zebra finch brain during vocal development"

Background: Rett syndrome (RTT) is an X-linked neurodevelopmental disorder classified as an autism spectrum disorder. It typically affects young females and causes progressive impairment and loss of motor skills and language. Mutations in the X chromosomes encoding the methyl-CpG-binding protein 2 (MeCP2) gene have been found to cause Rett syndrome. The zebra finch bird is an optimal research design since its song learning process mimics language development in children. The song learning circuitry of the zebra finch includes Area X, a basal ganglia nucleus within the anterior forebrain pathway (AFP), which provides insight into human neurodevelopmental disorders. Although there is little known about the relationship between the forkhead box protein G1 (FOXG1) gene and RTT, the FOXG1 gene is thought to be involved in the song learning circuitry. FOXG1 gene mutations are said to cause FOXG1 syndrome, which overlaps with Rett syndrome symptoms. Children with FOXG1 syndrome have severe physical and cognitive disabilities such as intractable seizures, movement disorders, cortical vision impairment, and language difficulties. To study interactions between the FOXG1 and MECP2 genes, we will first investigate the expression of FOXG1 and MeCP2 genes in the zebra finch brain.

Methods: The location and expression of the FOXG1 and MeCP2 genes within male zebra finch brains will be determined using Immunohistochemistry. Specifically, we will use MeCP2 and FOXG1 antibodies for staining. Once relevant brain regions are identified, the period during which the genes are expressed will be found experimentally. We will locate key times during juvenile and adult brain development such as 45, 60, and 100 days. Relationships will be looked for between MECP2 and FOXG1 as they may affect and/or regulate each other. The FOXP2 gene can act as a control in staining.

Results: We anticipate that the FOXG1 gene will be expressed in the song circuitry, specifically in Area X and is likely to be developmentally regulated. Previous data shows that the FOXP2 gene regulates speech and language development in the zebra finch songbird. It is likely that the FOXG1 gene will behave in a similar manner. The time markers will be crucial to providing information about gene expression as 45 days is early in development, 60 days is when the crystallizing of song development typically occurs, and the birds reach adulthood around 100 days. Studies with the FOXG1 gene are ongoing and we are awaiting results.

Conclusion: We are expecting that the data could indicate that the FOXG1 gene is involved in the zebra finch song circuitry. As such, it is likely that mutations to the FOXG1 gene will lead to language impairment, particularly during a critical song learning period, which requires further analysis.