DISCUSSION/SIGNIFICANCE OF IMPACT: Our contributions here are expected to be the elucidation of European ancestry as a risk factor for AF. These contributions will be significant because it can provide a robust scientific basis for larger GWAS studies in the Puerto Rican community and further narrow down the mechanism specific to this population. Research in this subject could lead to early identification of patients with high risk of developing atrial fibrillation and further decrease incidence and disease burden in the PRH population. Puerto Rican Hispanics have an exclusive genetic admixture that makes for an appealing research subject that could deliver unique results.

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Expression profile of the ribbon synapse protein Ribeye in the zebrafish

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OBJECTIVES/SPECIFIC AIMS: Although two Ribeye protein isoforms have been identified in zebrafish, information about the identities of their variants is incomplete. This study aims to identify and characterize both of the Ribeye isoforms and their splice variants. METHODS/STUDY POPULATION: Immunohistochemistry was performed on the retina and neuromasts of zebrafish larva and adults.Ribeye expression was analyzed by western blot. Ribeye proteins will be separated, isolated and identified by mass spectrophotometry. RESULTS/ANTICIPATED RESULTS: Immunohistochemistry performed on larval and adult zebrafish retinas revealed the expression of Ribeye A in the inner and outer plexiform layers. Ribeye B was likewise expressed in both plexiform layers in larval zebrafish, but more pronounced expression in the outer plexiform layer in the adult zebrafish retina. Immunohistochemical experiments also demonstrated the co-expression of both Ribeye isoforms in the hair cells of both larval and adult neuromasts. Analysis of Ribeye expression by western blot showed the presence of more than the three previously identified variants. Current experiments are being conducted to characterize the additional Ribeye variants. We expect to identify the residual Ribeye protein as a result of this analysis. DISCUSSION/ SIGNIFICANCE OF IMPACT: This study is necessary in order to gain a clear understanding of Ribeye expression in zebrafish tissues. Doing so will enable us to target this protein for gene editing to address outstanding questions about the mechanisms that govern ribbon synapse function. Synapse and synapse-associated proteins are involved in a wide-array of diseases that arise as a result of their dysfunction (e.g. blindness, deafness, bradycardia, autism spectrum disorders, and schizophrenia). Thus, it is important for us to identify the shared and distinct mechanisms that give rise to diseases associated with synaptic dysregulation. Such information could provide the basis for novel therapeutic interventions for synaptic disorders.

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Functional brain mechanisms of sensorimotor deficits in individuals with autism spectrum disorder

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OBJECTIVES/SPECIFIC AIMS: Abnormalities in sensorimotor behavior are present in the majority of individuals with ASD and associated with core symptoms. Cortico-cerebellar networks that

control sensorimotor behavior have been implicated in ASD, but little is known about their function during sensorimotor actions. The purpose of this functional magnetic resonance imaging (fMRI) study was to examine cortical-cerebellar function during feedback-guided motor behavior in ASD. METHODS/STUDY POPULATION: Individuals with ASD (11-30 years; N = 18) and age-matched controls (N = 15) completed a visuomotor task of feedback-guided precision gripping during fMRI. Participants pressed with their right thumb and forefinger on a force transducer while viewing a green FORCE bar on a screen that moved upwards with increased force toward a fixed white TARGET bar. Individuals were instructed to maintain the FORCE bar at the level of the TARGET bar for 24 seconds. Target force levels were set at 20% and 60% of each participant's maximum voluntary contraction (MVC). Force variability was characterized as the coefficient of variation (i.e., standard deviation of the force time series / mean force output; CoV). RESULTS/ANTICIPATED RESULTS: Mean force did not differ between groups indicating participants were able to follow task demands. Participants with ASD showed increased force variability (F(1,30) = 5.214, p = 0.03) at both 20% (d = .45) and 60% (d = .77)MVC compared to controls. Compared to controls, individuals with ASD showed decreased activation in left angular gyrus during the visuomotor task compared to rest (AG; maximum t = 4.31). Individuals with ASD also showed greater visuomotor activation compared to controls in ipsilateral ventral M1, extending anteriorly into posterior ventral pre-motor cortex (PMv; maximum t = -4.06, cluster size = 38 voxels). This difference reflected the finding that control participants showed a selective deactivation of ipsilateral M1/PMv during visuomotor behavior, whereas individuals with ASD did not show this pattern. A significant group x force interaction was observed for contralateral Crus I activation (maximum t = -2.42) that was driven by an increase in activity during 60% compared to 20% MVC in control participants, while individuals with ASD showed no change in Crus I activation between force levels. DISCUSSION/SIGNIFICANCE OF IMPACT: Increased force variability in individuals with ASD suggests impaired processing of sensory feedback to guide precision motor behaviors. Individuals with ASD did not show deactivation of right motor cortex during visuomotor behavior relative to rest, suggesting reduced ability to selectively modulate motor cortical output. Reduced activation in left AG may reflect an inability to integrate visual, haptic, and proprioceptive inputs to reactively adjust ongoing motor output. Failure to show force-dependent scaling of Crus I in ASD suggests lateral cerebellar circuits do not adapt sensory prediction and error processes to maintain precision motor output during more demanding conditions. Together, our results demonstrate multiple cortical-cerebellar mechanisms associated with sensorimotor imprecision in ASD.

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Genomic Analysis of Primary Plasma Cell Leukemia reveals Complex Cytogenetic Alterations and High Risk Mutational Patterns

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OBJECTIVES/SPECIFIC AIMS: 1) Determine the mutational landscape, including translocation, mutations and mutational signatures as well as copy number variations of pPCL and identify significant