with the mood episodes, we found that patients with bipolar depression showed decreased levels of IL-4 (p = .046) and increase levels of IL-6 (p = .020) in comparison to the manic or euthymic episodes. In the neurocognitive tests, we found that the control participants had better performance in the working memory domain (p = .038) and also in the general performance (p = .036) in comparison to bipolar patients. We found also a positive significant correlation between IL-4 and verbal learning in the control sample (.829, p = .003). DISCUSSION/SIGNIFICANCE: The findings evidence a significant immune activation in bipolar patients, in particular during the depressive episode. Participants with BD have a decrease in the protective levels of IL-4 combined with high levels of IL-6 when compared to healthy controls. Worse neurocognitive functioning was found in bipolar patients.

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Retrospective Evaluation of Whole-Exome Sequencing in Puerto Ricans with Neurogenetic Complex Traits

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OBJECTIVES/GOALS: Assess the diagnostic yield and test utilization of WES in patients having complex traits. We aim to evaluate the use of the first genetic approach for the identification of primary variants that contribute to neurogenetic disease etiology and influence onset and progression in Puerto Ricans. METHODS/STUDY POPULATION: Prospective cohort of 45 Puerto Rican probands (19 months - 36 years old) with complex neurogenetic traits that underwent WES (2019 - 2021). WES was performed, including copy number variant analysis and mitochondrial genome sequencing. We evaluated several factors possibly influencing the rate of WES diagnosis including early age, consanguinity, and family history of neurogenetic diseases. In addition, we only evaluated probands rather than dyads/trios and the clinical phenotypes. Descriptive analysis was performed, including a catalog of all variants reported. Multivariate analysis was performed to estimate the statistical association between variants and phenotypes reported and adjusting for potential confounders (age, sex, family history, income, health insurance and zip code). RESULTS/ANTICIPATED RESULTS: Auspiciously, positive pathogenic findings altered the clinical management in 29% of the probands in this study. A likely genetic diagnosis was achieved in 53% of the probands including pathogenic, likely pathogenic and variants of uncertain significance. Intronic variants, copy number variants detection and mitochondrial genome was included in WES methodology. Despite these facts, a 47% of the reported WES were negative, which deserve re-analysis potentially genotype based. Multivariate analysis is expected to adjust for potential confounders to establish a genotype-phenotype correlations in neurogenetic complex traits in this Puerto Rican admixed population. DISCUSSION/SIGNIFICANCE: Clinical WES offers an alternative approach for identification of variants in patients with complex traits. WES is also applicable in genetically heterogeneous individuals when specific genetic tests are not available or unsuccessful. Variants reported contribute to understand complex neurogenetic disease in underrepresented Puerto Ricans.

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Group Model Building to characterize the experiences of older adults with type 1 diabetes (T1D) with continuous glucose monitoring (CGM) therapy and uncover suboptimal response patterns

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OBJECTIVES/GOALS: As the number of older adults (â‰¥65 years) with T1D grows, there are limited data to guide care. In a six-month trial, CGM reduced hypoglycemia in older adults, yet there are challenges for widespread uptake. Our objective is to characterize older adults experiences with using CGM and define suboptimal responses signaling a need for resources or support. METHODS/STUDY POPULATION: The study will engage key stakeholders (i.e., older adults with T1D, caregivers [recruited as patient-caregiver dyads], and providers [endocrinologists, geriatricians, diabetes educators]) for a Group Model Building (GMB). GMB is a participatory approach to system dynamics in which participants share perceptions and experiences with a problem and collaboratively explore the system structure that shapes those trends. A series of 8 GMB workshops will be held with 3-8 participants. The final study n will be determined by thematic saturation. Workshops comprise 1) a questionnaire, 2) a GMB session, and 3) a focus group discussion. GMB will follow a replicable process to generate a model of the complex web of causal determinants affecting CGM-related experiences, including optimal and suboptimal CGM responses. RESULTS/ANTICIPATED RESULTS: To date, the study has enrolled 33 participants, including 28 older adults living with T1D and 5 caregivers (mean age = 74 years, range 67-83 years). Twenty-four patient participants will be active CGM users and 4 will be CGM non-users. The study will report on patient data capture from the questionnaire and EMR, including demographics, experiences, familiarity, and confidence surrounding CGM use; diabetes duration; insulin pump use; history of severe hypoglycemia. Analysis of aggregated data will generate causal loop diagrams that integrate pertinent theoretical frameworks, lived experiences, and CGM outcomes. Maps will be used to identify a set of suboptimal CGM responses (i.e., key outcome trajectories) that signal a need for action, with a diagram of factors that interact to produce each response. DISCUSSION/SIGNIFICANCE: Delivering CGM to older adults with T1D demands new approaches. This study will yield critical evidence to tailor support and resources for effective CGM use in older adults. Findings may be translated into suite of pragmatic interventions to bolster CGM use and matched to individual patients expected to benefit using a precision medicine framework.

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