STUDY POPULATION: MEF2C Haploinsufficiency Syndrome (MCHS) occurs when there is one functional allele and one disrupted allele of MEF2C. To study the role of MEF2C in GABAergic populations during mouse development, we bred Vgat (vesicular GABA transporter)-Cre mice, which express cre recombinase broadly in early developing GABAergic neurons, with a floxed Mef2c loss-of-function mouse to create offspring that are GABAergic cell-specific Mef2c heterozygous mutants (Mef2c cHetVgat-cre). We then subjected these mutants and littermate controls to a battery of tests measuring MCHS-relevant phenotypes, including spatial working memory, anxiety-like behavior, social preference, sensory sensitivity, and Pavlovian learning and memory. RESULTS/ANTICIPATED RESULTS: Mef2c cHetVgat-cre mice showed significant deficits in spatial working memory, social preference, and contextual fear memory, all of which are prefrontal cortex (PFC)-dependent behaviors. Interestingly, we noted that conditional Mef2c knockout mice (Mef2c cKOVgat-cre) showed embryonic and early postnatal lethality, probable seizures, and severe motor coordination problems, highlighting the importance of MEF2C function in GABAergic populations. DISCUSSION/SIGNIFICANCE: We hypothesize that MEF2C plays a cell-autonomous role in GABAergic cells to control the balance of excitatory and inhibitory synaptic transmission in the developing and mature brain, which in the Mef2c cHet mice might be critical for PFC-dependent learning and memory and sociability.

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Cortisol cut off point to diagnose adrenal insufficiency (AI) using a monoclonal antibody immunoassay*

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OBJECTIVES/GOALS: AI is diagnosed when peak cortisol level after a cosyntropin stimulation test is <18 mg/dL using polyclonal antibody (pAb) immunoassay. However, the polyclonal assay is being replaced by a specific monoclonal antibody (mAb) immunoassay which yields lower cortisol levels, leading to the over diagnosis of AI and use of unnecessary steroid use. METHODS/STUDY POPULATION: We obtained 36 samples from patients undergoing 1 mcg cosyntropin stimulation tests for diagnosis of AI. Samples were analyzed using pAb immunoassay (Abbott Architect Cortisol), mAb immunoassay (Roche Elecsys Cortisol II), and mass spectrometry (MS). AI was diagnosed if serum cortisol level was <18 using the pAb immunoassay. Measurements by MS and mAb immunoassay were individually used in simple logistic regression models to predict AI. For each model, we calculated a cortisol level corresponding to a 50% probability (median) of AI and used the delta method to determine the standard error and 95% confidence interval of the median. We used receiver operator characteristic (ROC) curve, area under the curve, sensitivity, and specificity to evaluate the potential of the median values as thresholds for each predictor. RESULTS/ANTICIPATED RESULTS: Data showed a mean cortisol level of 17 mcg/dL using the pAb immunoassay, 12 mcg/dL using the mAb immunoassay, and 12.96 mcg/dL using MS. The mean difference in cortisol level between the mAb immunoassay and the pAb immunoassay was 5.12 mcg/dL (p-value <0.01). The ROC curve model indicated an area under the curve of 0.997 with a median value of 11.2 mcg/dL for the mAb immunoassay. This provides a sensitivity of 95%, specificity of 95%, positive predictive value of 95%, and negative predictive value of 94%. This new threshold has a Kappa coefficient of 0.89 when compared to the pAb immunoassay. DISCUSSION/SIGNIFICANCE: New and highly specific mAb immunoassays are being used more widely but yield lower cortisol results. This reflects the need for further studies to determine new cut off points for highly specific cortisol immunoassays. A cut off level of 11.2 mcg/dL would provide a sensitivity of 95% and specificity of 95%.

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Behaviors and Quality of Life in Children with Neurodevelopmental Disorders Undergoing Refractive Surgery*

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OBJECTIVES/GOALS: The goal of this project is to characterize the adaptive and social behaviors of ametropic children with neurodevelopmental disorders (NDD) including Autism Spectrum Disorder (ASD) undergoing refractive surgery due to spectacle intolerance. Eye-related quality of life and visual behaviors will also be measured. METHODS/STUDY POPULATION: This is an ongoing prospective cohort study of children with NDD who are spectacle-intolerant and undergoing refractive surgery at St. Louis Childrens Hospital starting July 2020. The method of refractive surgery (photorefractive keratectomy (PRK), phakic intraocular lens implantation (phIOL), and refractive lens exchange (RLx)) is chosen based on degree and type of refractive error, astigmatism, and characteristics of the cornea and anterior chamber. Behaviors are characterized using the Adaptive Behavioral Assessment System, 3rd edition (ABAS-3) and Social Responsiveness Scale, 2nd edition (SRS-2), completed by parents/caregivers. Eye-related quality of life is measured using the pediatric Eye Questionnaire (PedEyeQ). Visual behaviors are assessed with optokinetic nystagmus tracking. RESULTS/ANTICIPATED RESULTS: In a preliminary sample of 9 patients, 4 have undergone PRK, 3 phIOL, and 2 are awaiting surgery. Pre-surgical SRS-2 scores had a median t-score of 70 (range 57 to 90), indicating a clinically significant deficiency in reciprocal social behaviors as this score is consistent with moderately severe ASD. Pre-surgical ABAS-3 scores had a median General Adaptive Composite (GAC) of 51 (range 48 to 74.5). This corresponds to a percentile of 0.100 (range <0.1 to 19th percentile for age). As rated by the Parental PedEyeQ, the domains most affected were "Parent Worry About Childs Eye Condition" (median 42.0, range 15.0 to 80.0) and "Parent Worry About Functional Vision" (median 18.8, range 3.2 to 68.7), where 0 represents the worst quality of life or functional vision and 100 the best. DISCUSSION/SIGNIFICANCE: Prior research has shown that refractive surgery can improve observed visual awareness, attentiveness, or social interactions in children with NDD. This is the first study to characterize the baseline adaptive/social behaviors and quality of life using validated surveys, with the goal of subsequently identifying patients most likely to benefit.

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