The Measurement of Pupillary Responses in Full Mutation Fragile X Syndrome When Exposed to Social Stimuli

B. McDonald [1,2], M. Hong[1], C. Buck[1,2], L. Mooney[1], J. Guilfoyle[1], L. Wink M.D[1]., E. Pedapati M.D[1,†]., C. Erickson M.D[1, †]

(1) Cincinnati Children's Hospital Medical Center, Cincinnati, OH, (2) Department of Neuroscience, University of Cincinnati, Cincinnati, OH

Abstract

Rationale: Elevated levels of social anxiety have been observed in human subjects with Fragile X Syndrome (FXS). However, why these levels are increased and any cortical correlation still remains an open question in literature.

Methods: We administered a specific geometric/ social Tobii eye tracking paradigm on 5 full mutation Fragile X subjects to measure their pupillary responses. The same social scene paradigm was then administered to 5 age-matched healthy controls.

Results: Here we will present preliminary data as collected by the eye tracking paradigm to measure pupillary responses to social stimuli of FXS subjects. We will then use healthy controls as a baseline to compare the data outcomes and record any significant findings.

Discussion: From this study we hope to better understand any differences in social stimuli processing present in FXS subjects indicated by their pupillary responses. Evidence we find could potentially lead to a future investigation into the cortical anatomy of FXS individuals to what differences preside.

Introduction

- Fragile X Syndrome (FXS) is an x-linked dominant genetic disorder most commonly associated with cognitive delays and mental retardation (1).
- Individuals with FXS have the tendency to be more anxious and anxiety prone to social stimuli. They have a substantially lower anxiety threshold compared to typical individuals (1).
- Neuroimaging studies produce evidence that there is an atypical neural network involved in facial and social cognitive processing in individuals with FXS (2).
- Pharmacological research is currently creating treatments utilizing eye tracking as a way to examine and quantify face-specific pupillary responses. This is then used for treatment-specific outcomes related to hyperarousal and social anxiety of FXS individuals (2).
- The central hypothesis of this project postulates that elevated anxiety levels and increased pupillary responses can be correlated with increased activity in the Autonomic Nervous System. This can be then measured by pupillary changes detected by the Tobii eye tracking program.

Hypothesized FXS Pupillary Response Mechanism

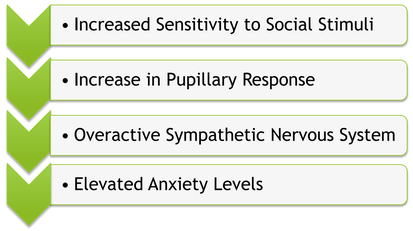

Figure 1: Simplified Schematic of a proposed cortical response in the FXS individuals.

Methods

All methods were reviewed by the Institutional Review Board

Participants

- All FXS individuals were all genetically tested and confirmed to have the full FMR1 mutation.
- Healthy subject controls were matched based on chronological age, having to be within one year or less of the same age.
- Any individual who viewed less than 25% of the video was excluded from the study results.

Tobii Eye-Tracking

- A Tobii Eye Tracker captured the pupillary responses, gaze, and fixation of each individual during the social/ geometric paradigm.
- Each subject viewed the same first 60 seconds of a video where half the screen was spilt into a social scene and the other half a geometric figure. Figure 2 displays two examples of the video paradigms shown to subjects.
- All subjects were recorded on a certified Tobii Program.

Figure 2- Still images of two of the video pairs used in the toddler eye tracking task. Videos were presented in pairs with the social scenes randomly assigned to either left or right side.

Results

Both participants with and without FXS provided ample gaze data for the geometric/ social scene paradigm.

Data Analysis

- All data from the Tobii Program was sorted and exported into Microsoft Excel sheets.
- Each Excel sheet quantified the AOIs (areas of interest) for each video, allowing us to analyze just the first 60 seconds of each paradigm viewed by each subject.
- A script in SPSS was written to analyze all AOIs and filter out any unwanted gaze data.
- The geometric and social scenes were analyzed separately for each individual.
- SPSS statistical software was utilized to run a batch script all of the raw Tobii eye tracking data and make it into a workable spread sheet.
- An independent samples T-Test was then conducted to calculate the means for both the FXS and Healthy Control (HC) subjects. This allowed us to see if there was indeed a difference as stated in our central hypothesis claim.
- An ANOVA was also run to calculate any statistical differences between the FXS and HC subjects.

Measurements

Social Scene Preference Ratio (SSPR)- calculation utilized to determine the amount each subject spent viewing the social scene out of the total viewing time.

Social Pupil Difference (SPD)- calculation that determines the difference in social pupil size compared to geometric pupil size.

- Figure 3 below illustrates the mean values calculated for both SSPR and SPD between the FXS and HC subjects.

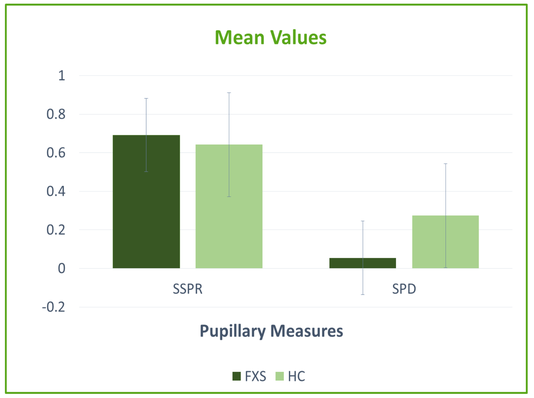

Figure 3- Comparing statistical values for Fragile X Syndrome (FXS) and Healthy Control (HC) subjects.

Discussion

The main goal of this study was conductd to investigate if there was any statistical difference in the SPSS and SPD of FXS subjects as compared to healthy controls. If found, this difference could serve as a physiological tool in the diagnosis of Fragile X Syndrome.

Here we presented preliminary pupillometry data gathered by our test subjects and healthy controls that we then quantified by the Tobii and a SPSS stats program.

- The data from the ANOVA and single t-test comparisons revealed no significant results between the social/ geometric processing of the two test groups.
- There was no significant statistical difference between the SSPR and SPD of the FXS and HC subjects. While some difference was observed, the small sample size could have prevented us from having a statistically significant result.
- For both individuals, they focused on the social figure and geometric around the same time with similar pupillary reponses.
- This data does not support our hypothesized mechanism that elevated pupillary repsonses are why FXS individals have elevated anxiety to social stimuli.

Because our data did not support the hypothesis proposed, this poses the question of why FXS subjects still experience elevated levels of anxiety compared to typical individuals.

We are proposing to expand this research to learn why these elevated levels exist and what is the biological mechasnism behind it. Future studies to investigate this should:

- Increase test group size to 30-40 FXS subjects to allow for more re-test and reliability
- Add behavioral assessment tests (ABC, SRS, Vineland II, etc.) to help narrow down the behavioral differences and hopefully correlate them to specific cortical areas.

Conclusion

The findings of this study will contribute to surfacing more knowledge about Fragile X Syndrome and how pupillary data can be utilized to explain unique social responses in FXS individuals. Understanding the mechanisms of how FXS individuals respond to social stimuli can help provide insight to potential pharmacological and therapeutic treatments for elevated anxiety. Any novel information will be beneficial to the FXS community and help in further understanding this genetic disorder.

References

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2. Farzin, F., Scaggs, F., Hervey, C., et al. Journal of Austim Developmental Disorders (2011) 41:1515.