

**eSupplement 1: Extended Protocol for IRB-34059, Dr. Dennis P. Wall  
Randomized Controlled Trial for Superpower Glass**

1. Purpose

**a) In layperson's language state the purpose of the study in 3-5 sentences.**

The purpose of this research is to study the effects of a novel combined software-hardware device built onto commercially available Google Glass technology that provides an automated emotion expression recognition system and face tracker to determine the effects of providing social cues to individuals with a diagnosis of ASD. This novel device will use a camera, microphone, and head motion tracker that will record the behavior of the subject during interactions with other people. The system is designed to give participants non-interruptive social cues in real-time and will record social responses that can later be used to help aid behavioral therapy.

**b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.**

Investigators hope to learn the effects of this novel software-hardware device in terms of providing social cues to individuals with ASD. Refining and evaluating this system has implications to not only help aid behavioral interventions with individuals with ASD, but it also has broader implications on new forms of human-computer and human-human interaction. The system's ability to provide continuous behavioral therapy outside of clinical settings will enable dramatically faster gains in social acuity that may, within a limited and self-directed period of time, encourage the child to engage in more advanced social settings on his/her own.

**c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)**

Human subjects must be used for this project because the purpose of the study is to determine the efficacy of this novel device in social interactions for individuals with ASD. There are no suitable animal models for facial emotion recognition in ASD, nor are there comparable behavioral therapies for animals, and therefore, human subjects must be used.

## 2. Study Procedures

- a) **Please SUMMARIZE the research procedures, screening through closeout, which the human subject will undergo. Refer to sections in the protocol attached in section 16, BUT do not copy the clinical protocol. Be clear on what is to be done for research and what is part of standard of care.**

The study procedure is as follows:

**Participants:** Participants will be at least 6 years old. We anticipate recruiting up to 80 ASD participants. We will also be recruiting family members and friends of participants to consent to participate as "non-participants." The research staff will obtain informed consent before any study procedures begin. Consent and assent will be obtained either electronically or in-person.

**Recruitment and Screening:** We will utilize crowd-sourced recruitment by advertising our study on Facebook, parent groups, and listservs, as well as partner with our collaborators. We will partner with Autism Comprehensive Educational Services (ACES) who offer a variety of behavioral and educational services for individuals impacted with autism or other developmental disabilities in the home, school, community, and at accredited sites throughout the United States. Our main contact will be Heather O'Shea, Ph.D., BCBA-D, Chief Clinical Officer, and she will manage the staff from ACES. ACES will help with participant selection: ACES will help recruit some of our participants. ACES will define and assist in the screening process for eligible participants from said population. They will screen for participants based off of recruitment criteria explained in IRB 34059. Upon selection of participants, ACES will provide contact information to Autism Glass, Wall Lab for which Autism Glass, Wall Lab will officially enroll selected participants.

During recruitment participants will be able to access a RedCap survey from the recruitment website and through other recruitment efforts (i.e. ACES). We will ask interested participants to fill out the Screening Questionnaire. Our goal will be to determine eligibility based on location (needs to be local to Stanford), still interested in participating, has a child that meets our eligibility criteria, and a brief overview of the child. We will also ask these families to provide a short home video of the potential participant. We will ask families to submit a 3-5 minute home video that clearly shows the child's face and hands, as well as includes a "play time" or "conversational" social interaction. We will use this video to get a first pass understanding of the phenotype of the child as well as compare this first video to a 3-5 minute home video of the child at the end of the study to track any behavioral changes in social interactions. The conclusion video will have the same requirements as this first video and will be analyzed in the same way. Families will send home videos to study coordinators via MedSecureSend and video data are stored on Stanford Medicine Box. Study coordinators will send an email to families with the link to use this secure platform. Video data will be reviewed by the Wall Lab. Participants with ASD will then be asked to provide a copy of their diagnosis report when they come in for the in lab assessments. Dr. Feinstein will make judgment on eligibility and other technical questions in diagnosis if needed.

We will end recruitment once we meet our targeted enrollment goal.

### **Intervention Procedures:**

**First session (Onboarding):** Subjects and family members will be asked to come to the Wall Lab at 1265 Welch Rd or 1110 Burnett Ave to obtain written or electronic consent. Individuals will meet the study team, will discuss expectations with study manager, and go over scheduling. Baseline cognitive testing will be conducted in a private assessment by a blinded

## 2. Study Procedures

research coordinator, where participants will complete the ABIQ. Following intake measures, an independent staff member not involved in the data collection process will randomize the participant. Following randomization, if participants were assigned to the experimental group, they will meet the independent staff member to be instructed on Glass usage. The child/family will then take the Glass home for the duration of the study or we will mail the units home.

### **Intervention Delivery:**

Participants randomized to the treatment condition will use the Google Glass system for 6 weeks following onboarding, where they will be asked to use the glasses 3-4x/week for at least 20 minutes each session with either parents or ABA therapist. Participants will have phone calls with study managers to see how usage of the device at home is going throughout the 6 weeks.

Participants randomized to the control condition will not receive any intervention for 6 weeks following onboarding appointment.

### **Follow-Up:**

6 week post-test: Treatment and Control participants will return to Stanford to complete outcome measures 6 weeks following initial onboarding appointment.

After the 6-week post-test appointment, control participants will be able to cross-over to treatment condition and will receive Google Glass device to use for 6 weeks. Treatment participants will return their google glass device. Both groups will schedule their final follow-up appointment for week 12 where they will complete outcome measures.

### **Conclusion:**

At week 12, treatment participants will return to Stanford to complete outcome measures. Cross-over Control participants will return the google glass device and complete outcome measures. At the end of the 12-week period and after completion of the final follow up assessment, a \$50 Amazon gift card is provided as compensation for participation in the study.

### **Measures:**

Parent-rated assessments (Onboarding, Follow-up, Conclusion): Clinical Phenotyping Measures Parents: The Social Responsiveness Scale (SRS-2), The Vineland Adaptive Behavior Scale (VABS-2), Social Communication Questionnaire (SCQ), and Child Behavior Checklist (CBCL).

Child Assessments (conducted by blinded research coordinator at Onboarding, Followup, Conclusion): Participants will also undergo the Abbreviated Battery IQ (ABIQ), which consists of two subsections of the Stanford-Binet, 5th Edition Intelligence Test. We will also collect the NEPSY-II Affect Recognition and Emotion Guessing Game, as well as Overall Social Interaction (Brief Observation of Social Communication Change, BOSCC). At one of the in-person appointments, we will have participants and consented/assented family members read aloud a script (see section 16) into a microphone to collect audio data to later analyze to help with expression recognition software.

### 3. Eligibility Criteria

|                                    |                             |
|------------------------------------|-----------------------------|
| <b>Ages Eligible for Study:</b>    | 6 Years to 12 Years (Child) |
| <b>Sexes Eligible for Study:</b>   | All                         |
| <b>Accepts Healthy Volunteers:</b> | No                          |

#### Criteria

##### Inclusion Criteria:

1. The child has been diagnosed professionally with ASD
2. The child is currently receiving ABA therapy at least twice per week at home.
3. The child's family is willing to drive to Stanford University for up to 4 study appointments.

##### Exclusion Criteria:

1. The child scores less than 15 on the Social Communication Questionnaire
2. The child's family does not speak English

### 4. Outcome Measures & Statistical Methods

#### Primary Outcome Measures :

1. Change in socialization subscale scores of the Vineland Adaptive Behavior Scales, 2nd Edition (VABS-II) from baseline to week 6. [ Time Frame: Baseline (week 0), Week 6 ]

Vineland Adaptive Behavior Scales, 2nd edition (VABS-II) Socialization subscale will be conducted at the university by a trained research team member. Scores from the socialization domain of the VABS-II reflects one's functioning in social situations. The socialization subscale is 32 items, where raw scores are converted to IQ-type standard scores (mean: 100 sd: 15) for each domain and for the composite adaptive behavior score.

2. Change in Parent Rated Social Responsiveness Scale 2 (SRS-2) from baseline to week 6 [ Time Frame: Baseline (week 0), Week 6 ]

The SRS-2 is a 65-item measure where parents rate their child selecting responses on a Likert Scale. This measure will be used to measure and identify social impairment associated with Autism Spectrum Disorder (ASD) and to quantify its severity.

3. Change in NEPSY-II, Affect Recognition subscale scores from baseline to week 6 [ Time Frame: Baseline (week 0), Week 6 ]

The NEPSY-II Affect Recognition subdomain assesses a child's social perception of facial affect recognition. It is designed to assess a child's ability to recognize 6 emotions (happy, sad, angry, fear, disgust, and neutral) from colored photographs of children's faces in four different tasks.

4. Change in Emotion Guessing Game (EGG) scores from baseline to week 6 [ Time Frame: Baseline (week 0), Week 6 ]

The Emotion Guessing Game is a novel test created for purposes of this study to evaluate the child's ability to correctly label emotions expressed by an examiner in real time. EGG is a pre-set list of 8 emotions, listed 5 times each (Happy, Sad, Angry, Afraid, Surprised, Calm,

#### 4. Outcome Measures & Statistical Methods

Disgust, and "Meh"/contempt). During the quick 40-question evaluation, the research coordinator first lists the various emotion choices to the child before beginning the evaluation. Then, the examiner acts out each emotion listed, in order, and waits for a guess from the child, who labels the emotion. The EGG is scored by summing the number of correct responses from the child.

##### Secondary Outcome Measures:

1. Change in ASD symptoms as measured by Brief Observation of Social Communication Change (BOSCC) from baseline to week 6 [ Time Frame: Baseline (week 0), week 6 ]

The Brief Observation of Social Communication Change (BOSCC) is designed to measure change in core symptoms of children with autism. It aims to capture change in social communication, interaction, and eye contact. The BOSCC is a play based assessment that consists of two boxes filled with specific toys and takes about 12 minutes to complete.

2. Change in adaptive social and personal skills as measured by Vineland Adaptive Behavior Scales, 2nd edition (VABS-II) Full Scale from baseline to week 6. [ Time Frame: Baseline (week 0), week 6 ]

The VABS-II is a robust and comprehensive measure of personal and social skills needed in everyday living. The VABS-II covers a child's conceptual, social, and practical skills and can assess children from birth to 90 years. The parent can complete the entire questionnaire in about 20-30 minutes.

3. Change in child's emotional, behavioral, and social problems from Baseline (week 0) to Week 6 as measured by Child Behavior Checklist (CBCL). [ Time Frame: Baseline (week 0), Week 6 ]

The CBCL is a caregiver-directed report that identifies emotional, behavioral, and social problems in children. It is a 20 item measure completed by parents.

##### Other Outcome Measures:

1. Stanford-Binet Intelligence Scales, Abbreviated Battery, Fifth Edition (ABIQ) score at baseline [ Time Frame: Baseline (week 0) ]

The ABIQ assessment measures a child's IQ based on an abbreviated (10 minute) task that measures Nonverbal Fluid Reasoning and Verbal Knowledge to create a standard score for IQ. It will be completed for each child during Intake.

2. Mobilized Machine Learning Autism Risk Assessment (MARA) score of autism severity at baseline [ Time Frame: Baseline (week 0) ]

The MARA screens for, quantifies, and tracks the severity of core autism symptoms. Parents respond to the survey and it takes less than 5 minutes to complete. The core behavioral domains the MARA focuses on are communication, social reciprocity, and restricted, repetitive, and stereotyped behaviors. Each response to a question is run through a machine learning

#### 4. Outcome Measures & Statistical Methods

model that uses an alternating decision tree algorithm to generate a total score ranging from most severe, -10 to least severe, 7.

3. Social Communication Questionnaire (SCQ) score at baseline [ Time Frame: Baseline (week 0) ]

The social communication questionnaire (SCQ) screens for autism in children over 4:0 years in age. Parents are asked 40 Yes/No questions and the resulting score is out of 39 (the first question is not associated with a numerical value). The SCQ assesses a child's communication skills and social functioning. It takes less than 10 minutes to complete and is administered by clinical research coordinators to parents of children during the phone screen to participants who have already completed the online screening questionnaire. A score of 15 or above is indicative of autism and is required to be eligible in the research study.

#### Statistical Methods

This study will follow an intention-to-treat (ITT) analysis, which will include all participants randomized in the study, regardless of missing data. Our hypothesis is that children randomized to receive the Superpower Glass intervention will show a significant improvement on the primary outcome measures, as compared to controls. We will also perform sensitivity analyses to examine the extent to which outcome measures are correlated to the child's age and autism severity, as well as by usage factors, such as variation in compliance with recommended dosage and missing data from families lost to follow-up. We will use the same approach to assess differences on secondary outcomes between groups under different statistical assumptions (shifting from random to nonrandom effects, for example).