Investigating Social Competence in Youth with Autism: A Multisite RCT

Statistical Analysis Plan (SAP)

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3.C.12. ANALYTIC PLAN: Aims and Hypotheses (Hyp)

Handing missing data, Full information maximum likelihood (FIML) estimation methods will be used.

Specific Aim 1: Show Efficacy of SENSE via Target Engagement of Memory for Faces

Hyp 1.1: Youth in the EXP group will demonstrate significantly faster growth in memory for faces (MFD and IMF) than youth in the ACC group. EXP youth will also have higher levels of memory for faces at follow-up.

Hyp 2.1: Youth in the EXP group will demonstrate significantly faster growth in social behavior (SRS and CASS) than youth in the ACC group. EXP youth will also have higher levels of prosocial behavior at follow-up.

Statistical Analysis: To address the above-mentioned hypothesis, we will use a 2-level multilevel growth model with treatment (EXP vs. ACC) predicting random intercepts and random linear slopes. The levels are (1) time of testing in months from study entry and (2) participant. Time will be centered at follow-up to enable interpreting the intercept as an end-point estimate. We will test EXP vs. ACC differences on means of the linear slope of time in order to test for differential change over time. We will also test EXP vs. ACC differences in follow-up-centered intercepts. A linear model is a reasonable model of social growth for such a short period (i.e., three months) with people who have a social impairment. The random intercept and slope accommodate dependency of time (pre, post, follow-up) within participant. Dependency of participants within cohort will be corrected for using design-robust standard errors (following procedures in Sterba [126]. Site effects are not anticipated but will be examined by including 2 dummy covariates for site as predictors of intercepts and slopes; if not significant, these covariates will be removed. This model will be run in Mplus [127] general multilevel and structural equation modeling software capable of fitting both the univariate multilevel models for Specific Aim 1 and the multivariate multilevel models for Specific Aim 2, below.

Specific Aim 2: Linking Degree of Target Engagement and Mechanism-Based Functional Outcomes

Hyp 2.2. Growth in memory for faces (NEPSY, ERP) will mediate the effect of treatment on growth in social behavior (SRS, CASS).

Statistical Analysis: To address Hyp 2.2, we will use a multivariate multilevel growth model (involving a linear growth model for memory and another linear growth model for social behavior). We will specify a mediation pathway at the participant-level from treatment (x) to the slope of memory for faces (m) to the slope of social behavior (y). The indirect effect will be tested using the 95─ confidence interval around the product of the unstandardized coefficients for the (x→m) and (m→y) paths of the multilevel mediation model following procedures of Lachowicz, Sterba, and Preacher[128]. The confidence interval will be estimated using the Monte-Carlo procedure described in Preacher and Selig, [129]. Exclusion of zero will be interpreted as a significant indirect effect.

Power Using Attrition-adjusted Sample Size: Because missing data will be handled using FIML, the only dropouts will be those with no data (they were randomized but did not show up for any assessment). Past SENSE Theatre studies, including the previous RCT, had less than 10% post-Time 1 attrition. Virginia Tech, in unrelated, recent intervention RCTs had <17─ attrition (teens) and 0─ (adults); Stony Brook has had 0─ attrition in recent RCTs of teens and adults. Thus, to plan conservatively, we will plan for a 90% retention rate. Power analyses were conducted using a proposed sample size that is adjusted for a 10% attrition rate, which is quite feasible. The probability of detecting a treatment effect and the effect size of between-group differences are understandably lower for dependent variables derived from far transfer procedures and for distal variables. The primary dependent variable (memory for faces) and the behavioral measure of social behavior (CASS variable) represent such outcomes. While the estimation of effect sizes from small pilot studies may be limited due to sampling variability [130], an established literature of theatre-based interventions does not exist. Using past meta-analyses of such outcomes and professional discussion about such effect sizes, clinically important outcomes for treatment-control differences in slopes are those exceeding Cohen's *d* of .25 [131,132]. The guidelines for effect sizes of indirect effects call indirect effects (i.e., product of the standardized coefficients for the x→m and m→y paths) greater than .10 'medium' effect sizes, and such effects are judged to be clinically important [133]. Regarding Specific Aim 1, we anticipate a Cohen's *d* of at least .5 for the efficacy tests. Regarding Specific Aim 2, based on the past mediation analysis, we expect an indirect effect of at least .23. To demonstrate that our proposed sample size is more than adequate to detect even lower-than-expected effect sizes, we compute the minimally-acceptable effect size for 80% power with 216 participants. For the 2-level multilevel models used in investigating Specific Aim 1, with 216 participants, we will have 82% power for a Cohen's d as low as .2 with an ICC for within-participant dependence of .1. For Aim 2, involving mediation effects, we'll need a product of the x→m and m→y standardized coefficients of at least .056 with 216 participants using the confidence interval around the indirect effect to test significance [133]. There will be plenty of power with the proposed sample size to detect the predicted effect sizes.