Preliminary Efficacy of Occupational Therapy Integrating Horses on Self-regulation in Youth with Autism Spectrum Disorder

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Original Study Protocol (September 2022)

Design. We will conduct a pilot randomized controlled trial, randomizing 64 youth to OTEE HORS or OT Clinic.

Participants. Based on our previous studies, we will recruit 64 youth with ASD ages 6-11 who meet the following criteria: meet clinical cut-offs for ASD on the Autism Diagnostic Observation Schedule, Second Edition(ADOS-2)[57] and Social Communication Questionnaire (≥ 11),[58] nonverbal IQ≥65 on Leiter International Performance Scale Third Edition (Leiter-3),[59] verbally fluent defined by meeting standard administration criteria for ADOS-2 module 3 (verbally fluent), able to tolerate a helmet and ride a horse for 10 minutes while following safety rules, and able to provide a saliva sample. We will exclude participants who weigh more than 200 pounds (i.e. TGEC Denver safety policy), smoke or regularly use steroids because they affect cortisol levels,[60] receive outpatient occupational therapy, or have 10+ hours horseback riding experience in the previous 6 months (based on Gabriels study[61] demonstrating effects of riding on self-regulation persist at 6-month follow-up). We will also enroll a designated caregiver to complete all study outcome measures for reporting consistency. We will recruit through ASD listservs in the Denver Metro area (JFK Partners Listserv; Autism Society of Colorado Listserv). In our previous study[25] we recruited through the JFK listserv, and currently have a contact list of 95 participants on a study wait list.

Screening. The graduate research assistant (GRA) will screen interested participants by phone. Individuals who meet initial inclusion criteria will attend a screening visit at TGEC Denver to ensure they can ride a horse for 10 minutes, can provide a saliva sample, and meet study criteria on the Leiter-3 and ADOS-2.

Randomization. Similar to the Gabriels study,[11] our statistician will generate random group assignment numbers stratified according to Leiter-3[62] nonverbal IQ standard score (>85 NVIQ and ≤ 85 NVIQ) to assign to a treatment condition: OTEE HORS(experimental) or OT Clinic (active comparison). We will employ block randomization such that the first 16 participants (Cohort 1) will be randomized 1:1 to OTEE HORS or OT Clinic, stratified by IQ. We will repeat this scheme for all four cohorts, each with 16 participants (N=64). In order to prevent attrition, OT Clinic participants will be offered a free adaptive horseback riding lesson after the study.

Qualifying Battery:

1. *Autism Diagnostic Observation Schedule, Second Edition:* A play-based assessment of communication, social interaction and behavior, that is considered the gold-standard assessment to support a clinical diagnosis of ASD.[57] The ADOS-2 has strong predictive validity for diagnosis of ASD.[63]
2. *Social Communication Questionnaire:* a parent-report screen for ASD. A score of 11 or above indicates the individual likely has ASD. The SCQ has strong discrimination between youth with and without ASD and is widely used for entry into ASD research studies.[64]
3. *Aberrant Behavior Checklist- Community Irritability Subscale:* A parent report questionnaire that measures the presence and intensity of problem behaviors related to irritability. ABC-C has concurrent validity with other measures of behavior and is frequently used in clinical trials in ASD research.[65,66] Our pilot demonstrated that youth who score >10 on the irritability scale are more likely to benefit from OTEE HORS.
4. *Leiter International Performance Scale, Third Edition:* a completely nonverbal measure of intelligence and cognitive abilities that is widely used with the ASD population to estimate nonverbal IQ.[59]

Outcome Battery

1. *Aberrant Behavior Checklist-Community, Hyperactivity and Irritability Subscales:*[66] A parent-report measure of problem behaviors related to hyperactivity and irritability. Test-retest reliability of parent ABC-C ratings range from r=0.80 to 0.95, suggesting scores are very stable in the absence of targeted interventions.
2. *Emotion Dysregulation Inventory (EDI):*[67,68] The EDI is a 30-item caregiver-report form that includes a 24-item Reactivity item bank, which captures intense, rapidly escalating, sustained, and poorly regulated negative emotional reactions, and a seven-item Dysphoria scale characterized by minimal positive affect and motivation, and the presence of nervousness and sadness. The EDI was developed to assess self-regulation impairment in ASD following guidelines from the *NIH Patient-Reported Outcomes Measurement Information Systems (PROMIS) initiative*, and its final items were based on factor analyses and item response theory (IRT) analyses using data from 1,755 youth with ASD. Validity evidence includes expected group differences (higher scores in an ASD psychiatric inpatient versus community sample), correlations with measures of related constructs, and demonstration of test-retest stability.
3. *Goal-attainment Scale (GAS):* A standardized manner of measuring progress on individual, functional goals. GAS has been identified as a promising outcome measure of individual progress in randomized controlled trials in ASD[69] and is increasingly being used in autism intervention research.[70-73] We will

implement all quality indicators for use of GAS as an outcome measure in rehabilitation research,[74] as next described. During the initial goal-setting visit and guided by the self-regulation skill checklist, occupational therapists will use a standardized semi-structured interview to collaboratively determine goals with parents and participants, using a template to assure goals are systematically scaled across participants. Goals will be scaled onto a 5-point scale, where -2 indicates current level of performance, -1 less than expected level of performance after the 10-week intervention, 0 expected level of performance after intervention, +1 more than expected, and +2 much more than expected. Goals will be peer reviewed using a GAS checklist to ensure each individual scale meets quality criteria. In line with Ruble and colleagues (2012) recommendations, we will also assess equivalence in GAS goals between groups in measurability, equidistance, and difficulty. After intervention, an occupational therapist masked to group assignment will conduct a semi-structured phone interview with parents to determine the child's goal attainment. We will rely on parent report to ensure GAS ratings represent child behavior in home and community contexts, rather than in the equine environment where behavior tends to be improved.

4. *Salivary Cortisol and Alpha-amylase.* Saliva collection methods will mirror those in Gabriels' pilot (co-investigator), which demonstrated saliva was feasibly collected from youth with ASD.[9] Interventions will occur in the afternoons (between 1:00-6:00 PM) to avoid the sharp rise and fall in the AM seen in diurnal cortisol patterns.[75,76] Prior to each OTEE HORS or OT Clinic session, participants will sit at an art table for five minutes. At the end of the five minutes, study personnel will instruct participants to place a foam swab rod under their tongue for one minute while watching a sand timer (sample 1). Each week after the OTEE HORS or OT Clinic interventions, participants will sit at an art table and provide saliva samples at 5 minutes (sample 2) and 20 minutes (sample 3) after post-treatment. Caregivers will receive the following instructions: 1) Participants should avoid eating a substantial meal (other than a snack) and drinking liquids other than water within 30 minutes prior to collection time and 2) cannot brush their teeth for at least 45 minutes prior to collection time. Participants who do eat within the hour before collection will be asked to drink water and then wait 10 minutes before collections.[60] Saliva samples will be stored in a medical grade freezer at Temple Grandin Equine Center until shipped to Salimetrics for analysis. Saliva will be collected all 10 weeks, but only weeks 1, 5, and 10 will be assayed. Samples 1 and 2 will be tested for salivary alpha-amylase using a kinetic enzyme immunoassay (Cat. No. 1-1902). Samples 1 and 3 will be tested for salivary cortisol using a high sensitivity enzyme immunoassay (Cat. No. 1-3002). Different samples will be assayed for cortisol than alpha-amylase due to differing reaction and recovery trajectories.[77] Both immunoassays have average intra-assay and inter-assay coefficients of variation ≤6.00%.
5. *Fidelity Rating Tool* measures structural elements (environment, personnel, session structure) and critical elements of the OTEE HORS and OT Clinic interventions (see Table 2).The tool was used in previous studies[25] and will be used to rate 20% of all intervention sessions (OTEE HORS and OT Clinic).

Setting. The study will occur at the Temple Grandin Equine Center Denver (TGEC Denver) facility, which includes both traditional therapy clinic spaces for OT Clinic, and equine arenas for OTEE HORS (See letter of support). TGEC Denver is a member of the Professional Association of Therapeutic Horsemanship, International (PATH Intl), and accordingly follows all industry standards for safety and equine welfare during the provision of equine-assisted services; this includes standards for equine selection, training, and welfare.

Interventionists. TGEC Denver occupational therapists will provide both the OTEE HORS and OT Clinic interventions. These licensed occupational therapists have experience providing therapy to youth with ASD in both an equine environment and a clinic environment; they have also completed training from the American Hippotherapy Association, "Hippotherapy Treatment Principles" Part 1 and Part 2 (hippotherapy is defined as the use of equine movement as a treatment tool in therapy). Occupational therapists will also complete 10 hours of OTEE HORS or OT Clinic training provided by the PI. In accordance with PATH Intl standards, a PATH Intl certified riding instructor will also supervise all OTEE HORS sessions to ensure all PATH Intl standards are followed, including ensuring equine welfare during the therapy session. If the PATH Intl instructor is ever concerned about equine behavior or welfare, participants will immediately dismount.

Initial Goal-setting Visit. All youth and caregivers will participate in an initial goal-setting visit. The occupational therapist will conduct a semi-structured interview guided by an occupational profile and a study-specific self-regulation skill checklist. Then the occupational therapist, caregiver, and youth will collaboratively set 3 individualized goals related to youth's self-regulation, using a standardized goal-setting template.

OTEE HORS & OT Clinic Similarities. Both OTEE HORS and OT Clinic will be provided in 60-minute weekly sessions for 10 weeks. Both are standardized interventions that can be tailored to individual needs, with a 1:1 ratio between child and therapist. Both OTEE HORS and OT Clinic integrate relevant best practices in occupational therapy for youth with ASD, including collaborative goal-setting, activity-based intervention, use of youths' strength and interests, positive reinforcement, behavioral techniques, and caregiver education.[78-80] Finally, both teach youth the self-regulation skills in Table 1, adapted from the widely-used "Zones of Regulation"[81] program.

Table 1. Self-Regulation Skills in OTEE HORS & OT Clinic

1. Categorizing emotions and alertness states into 4 Zones
2. Recognizing emotions in facial expressions
3. Identifying expected "Zones" for different situations
4. Identifying body cues for different "Zones"
5. Identifying individualized triggers
6. Identifying sensory self-regulation tools
7. Identifying calming self-regulation tools
8. Identifying cognitive self-regulation tools
9. Creating an individualized self-regulation toolbox
10. Using an individualized self-regulation toolbox

OTEE HORS. Each OTEE HORS session follows a general structure: caregiver check-in, mounted therapeutic activities with horses, caregiver education and goodbye. Each session includes the critical elements listed in Table 2. These critical elements are guided by the theoretical rationale that *purposeful integration of horses in occupational therapy can maximize youth's development of new self-regulation skills*.

OT Clinic. Each OT Clinic session follows a general structure: caregiver check-in, therapeutic play activities, caregiver education and goodbye. Each session includes the critical elements in Table 2, designed to control for all non-animal elements of OTEE HORS.

Table 2. Critical Elements of OTEE HORS and OT Clinic

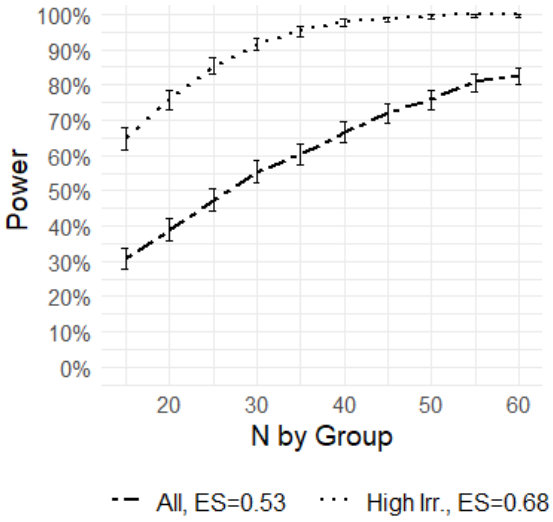
OTEE HORS	OT Clinic
1. Use horses to optimize attention and engagement in therapy session (use equine movement to facilitate optimal physiological arousal; integrate strengths, interests, and motivators, including preferred equine activities)	1. Optimize attention and engagement in therapy session (use play activities to facilitate optimal physiological arousal; Integrate strengths, interests, and motivators)
2. Direct instruction of a self-regulation skill (See Table 1)	2. Direct instruction of a self-regulation skill (See Table 1)
3. Design therapeutic activities with horses to practice the self-regulation skill (minimum 40 minutes mounted; minimum 3 opportunities to practice the skill)	3. Design play activities in the clinic to practice the self-regulation skill (minimum 3 opportunities to practice the skill)
4. Provide positive reinforcement for practicing the self-regulation skill (natural reinforcement if possible; equine activities as reinforcement)	4. Provide positive reinforcement for practicing the self-regulation skill (Natural reinforcement if possible; preferred play as reinforcement)
5. Scaffold skill performance using behavioral techniques (prompting, fading, shaping, chaining, feedback)	5. Scaffold skill performance using behavioral techniques (Prompting, fading, shaping, chaining, feedback)
6. Arrange environment to best support skill performance (horse selection; tack selection; physical, social, sensory characteristics of environment)	6. Arrange environment to best support skill performance (physical, social, sensory characteristics of environment)

Fidelity. The principal investigator (PI) and GRA will obtain at least 80% interrater reliability on the fidelity rating tool by observing and rating three OTEE HORS and three OT Clinic sessions. Following this, the GRA will then rate fidelity of 20% of all intervention sessions (OTEE HORS and OT Clinic) by observing the session and using the fidelity rating tool, developed and used in previous studies.[25]

Implementation Conferences. The PI will host four 1-hour implementation conferences throughout each 10-week intervention (OTEE HORS and OT Clinic). During conferences, the PI will provide feedback on intervention implementation, answer questions, and discuss challenging cases, to optimize treatment delivery.

Sample Size and Power: Proposed analyses for the study are based on a multilevel model (MLM) wherein predictors will include active experimental conditions (i.e., treatment vs control), testing occasion (i.e., pre- vs. post-intervention), and the interaction between experimental condition and testing occasion (i.e., to determine whether pre-post changes are dependent on treatment condition). Random intercepts for each outcome will be modeled to account for pre-post dependencies in individuals' scores. To determine adequate sample sizes for the analyses, we conducted multilevel power simulations using the simr package[82] for R statistical software.[83] Power simulations were based on parameter estimates previously reported from Gabriels adaptive horseback riding randomized controlled trial.[11] Because we observed substantially larger treatment-related effects for high-irritability participants (i.e., individuals with irritability scores>10) in our pilot, we accordingly re-ran the simulations after adjusting estimates for the group-by-occasion interactions proportionally to the differences in effect sizes expected for high-irritability participants. The resulting power curves for hyperactivity are shown in Figure 2. Unadjusted curves indicate that group sample size required for 80% power with α=.05 is N=55. Adjusting for participants with high baseline irritability, expected group sample size for 80% power with α=.05 is N=22.

Figure 2. Power curve for OTEE HORS-related changes in hyperactivity (Aim 1)



Analytic Plan. The aims are independent of one another, and therefore will be analyzed independently. The primary MLM described above will include the 2 active treatment conditions (OTEE HORS vs OT Clinic). We expect a 10% attrition rate based on previous studies, for a total expected group sample of N=29 (~90% power for hyperactivity, see Figure 2). We will test the interaction effect of treatment condition x testing occasion for each outcome to determine if pre-post changes are dependent on treatment condition (Aim 1). To assess changes in physiological measures, we will use MLM to test whether the OTEE HORS group demonstrated significantly greater same day changes and 10-week changes than the OT Clinic group in each physiological measure across the 10-week period (Aim 2). Additionally, we will use structural equation modeling to concurrently estimate associations between individuals' Aim 1 behavioral outcomes and Aim 2 physiological outcomes (Exploratory Aim 2E).