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TITLE A Multidisciplinary Intervention for Encopresis in Children with ASD

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CONTRACTING ORGANIZATION: Emory University  
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<b>14. ABSTRACT</b>  Incontinence is a common concern among individuals with autism spectrum disorder. Existing treatments have generally utilized lengthy and invasive procedures and/or lacked methodological rigor. Furthermore, no treatment approach has incorporated medical approaches to address constipation, which is a significant contributor to encopresis in this population. In response to the absence of treatments for this problem, we designed a 2-week multidisciplinary intervention for encopresis (MIE) that combines medical and behavioral approaches. In MIE, gastroenterologist assesses for and treats constipation. Patients also receive outpatient behavioral treatments that include structured sitting on a toilet to promote independent bowel movements. If one does not occur, the behavioral clinician administers a suppository and prompts the child to remain on the toilet. In doing so, continent bowel movements are predictably evoked, allowing for reinforcement. Eventually, the suppositories are gradually faded out to promote independence. The purpose of this study is to demonstrate the efficacy of MIE in a randomized controlled trial with 150 children with ASD.				
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## 1. INTRODUCTION:

Incontinence is a common concern among individuals with autism spectrum disorder. Existing treatments have generally utilized lengthy and invasive procedures and/or lacked methodological rigor. Furthermore, no treatment approach has incorporated medical approaches to address constipation, which is a significant contributor to encopresis in this population. In response to the absence of treatments for this problem, we designed a 2-week multidisciplinary intervention for encopresis (MIE) that combines medical and behavioral approaches. In MIE, gastroenterologist assesses for and treats constipation. Patients also receive outpatient behavioral treatments that include structured sitting on a toilet to promote independent bowel movements. If one does not occur, the behavioral clinician administers a suppository and prompts the child to remain on the toilet. In doing so, continent bowel movements are predictably evoked, allowing for reinforcement. Eventually, the suppositories are gradually faded out to promote independence. The purpose of this study is to demonstrate the efficacy of MIE in a randomized controlled trial with 150 children with ASD.

## 2. KEYWORDS:

Autism Spectrum Disorder, Encopresis, Toileting, Clinical Trial

## 3. OVERALL PROJECT SUMMARY:

### Statement of Work

The following Major Tasks were completed in this year of the grant:

- Randomization of the 56<sup>th</sup> subject (as of 010/9/2019)
- Completed DSMP meeting and report as scheduled (April, 2019)

Table 1. Timeline and Milestones	Timeline
Major Task 2: Active Enrollment	Months
Continue Enrollment	6-45
Milestone: Randomize at least 20 subjects	12
Unblinded statistician & PI evaluate adverse events	12
Continue Enrollment	12-45
Unblinded statistician & PI evaluate adverse events	16
Continue Enrollment	16-45
Data Safety & Monitoring Plan Review	17
Unblinded statistician & PI evaluate adverse events	20
Continue Enrollment	20-45
Milestone: Randomize at least 56 subjects	24
Unblinded statistician & PI evaluate adverse events	24

### Changes

Over the past year, the protocol has undergone the following minor revisions:

Version 3.9 05/30/2019

- Corrected title of protocol

- Changed IRB notification of instances of participant problem behavior from “would” to “may”.
- Removed language about participants being enrolled in IRB #53959.
- Included information on holds/restraining for participants engaging in problem behavior

Version 3.8 01/24/2019

- We changed the definition of “urine continent” under our inclusion criteria. It will now be “Over half of the voids are continent when the child is with the parent and when the child is on a typical toileting routine.
- We removed an inclusion criterion that subjects be enrolled in IRB 53959 (MAC), which was intended to serve as a center-wide repository for recruitment purposes.

## **Personnel**

The only substantive change in personnel during this year of the study was the departure of Chris Page, who had served as the lead research coordinator for the project. He was replaced by Jennifer Shipp, who comes to us with a wealth of experience in conducting clinical trials from Winship Cancer Institute, at Emory University.

## **Problems**

### *Recruitment*

As described in our second quarterly report of this study year, enrollment was below our intended target by the first quarter of the project year. Although monthly enrollment had stabilized at the originally targeted level by the third month, because of delays early in the study we remained behind the target cumulative enrollment. Thus, we spent much of the first quarter focused on recruitment in an effort to boost enrollment to a level that will allow us to catch up. These activities have included:

- A review of potential participants who were screened but did not meet inclusion criteria found that a sizeable proportion failed to meet the requirement that they be fully toilet trained for urination. However, screening these parents led to the finding that many of these children were continent for urination as long as they were taken to the bathroom regularly. Thus, there is no clinical reason why they would be expected to be unable to achieve continence for bowel movements. We submitted an amendment to the IRB that relaxed this inclusion criterion that was subsequently approved. This resulted in a nearly immediate increase in the number of potentially eligible participants.
- We began a host of marketing activities, including a) visiting referring providers in their clinics to describe the study and request additional referrals, b) calling all ABA providers in the metropolitan Atlanta area to request referrals, c) calling the top referring medical or psychotherapy providers who refer patients to our center to request referrals, d) hosting a workshop that included free CEUs for ABA providers on the topic of toilet training that included discussion of this study, e) updating our study flyer to make it more family friendly and obtaining IRB approval, f) having our IRB approved flyer posted on several listservs and social media platforms for groups of parents of children with ASD, g) attended events at several public schools for parents of children with ASD.

These efforts appear to be having the intended effect. The subsequent three quarters have been our most successful for recruiting to date, exceeding the minimum number needed to be enrolled to meet our targets. This rate of enrollment, compared to an average of 2.3 participants per month in the first quarter, is expected to bring the cumulative enrollment back to on track if sustained as anticipated.

### *Statistical Power and Three Group Design*

As described in a memo submitted to Program Officer Dr. Niu (sent 10/17/19), we recently conducted a Data Safety and Monitoring review of the study (10/14/19). The meeting was attended by Drs. Nathan Call, Lawrence Scahill, Joanna Mevers and Courtney McCracken. We asked the unblinded statistician, Dr. McCracken, to prepare a report on enrollment and attrition. In addition, although we did not request an interim analysis, we asked Dr. McCracken to examine the results on the Improvement item of the Clinical Global Impression (CGI-I) scale. As stated in the protocol, the CGI-I is our secondary categorical outcome. We examined these results while remaining blinded to group assignment. Following the review, we agreed that the original study design warrants reconsideration.

Brief Background. The original design included three groups: a) Two week medical and behavioral intervention for encopresis; b) One-week intervention; c) Parent Education. The three-group design was proposed to extend our previous study findings by comparing the Two-Week intervention to the One-week intervention - allowing each to be compared to control. Based on the large difference between the Two-week intervention and the control group in our pilot study, we proposed an unbalanced randomization: n=60 (Two-week); n=60 (One-week); n=30 (Parent Education). The larger samples in the Two- and One-week groups were designed to achieve sufficient statistical power for this exploratory aim.

Another important difference in the current study compared to our pilot study is the nature of the control condition. In the pilot study, the control condition was waitlist. By contrast, the control condition in the current study, Parent Education, is a more active condition.

Results of Data Safety and Monitoring Review. As noted, the statistician presented the response rates on the CGI-I without breaking the blind. The review of the first 52 participants revealed positive response rates ranging from 33% to 42% across the three groups. Although this is still early in the study and the next wave of participants may show different results, this blinded review indicates that our three-group design is unlikely to detect differences between groups. For example, these results suggest that the positive response rate in the Parent Education control group is greater than the 10% positive response rate in wait list control group in our pilot study.

Proposed Design Revision. The Two-week versus One-week group was included as an exploratory aim. Given the exploratory nature of this comparison, we proposed to Dr. Niu to drop the One-week group and proceed with a two-group study (Two-week versus Parent Education) with balanced randomization going forward. This change will increase the power of the two-group study.

With the time remaining in the study, we proposed to enroll 81 additional participants (n=35 Two-week condition and n=46 to Parent Education). Given our current accrual, the total N would be approximately 56 per group. With this sample size we could detect a 29% difference in response rate on our primary categorical measure with 15% dropout rate and type I error rate of 0.05. We propose that this will be a valid test of the Two-week medical-behavioral intervention, which was, and remains, the primary aim of the study.

Dr. Niu indicated in his response (received 10/18/19) that he is amenable to this proposed change in study design. We have revised the protocol and consent forms and submitted for review to the Emory IRB. We have concurrently revised the scope of work and will submit that to the contract specialist assigned to this study at approximately the same time that this annual report is submitted. Following approval from these two bodies we will seek approval from HRPO.

### **Participants**

Over the previous year, 36 additional parents of have consented to enroll their child into the study, for a cumulative total of 56. Of these, 3 (a total of 4 to date ) failed the in-person screen; As described in the discussion of recruitment (see above), we reviewed and revised our inclusion criteria to decrease the number screened out. This year 31 participants were randomized (56 cumulative).

#### **4. KEY RESEARCH ACCOMPLISHMENTS:**

Nothing to report

#### **5. CONCLUSION:**

We have worked through the recruitment challenges to achieve the necessary pace to meet deadlines. We have identified a solution to the unanticipated higher efficacy of the Parent Training/Control intervention and its impact on statistical power to detect effects in our exploratory aim. Our top priority for the next project period will be to enact that solution, and we have already begun taking steps to do so.

#### **6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:**

- (1) Lay Press: None
- (2) Peer-Reviewed Scientific Journals: None
- (3) Invited Articles: None
- (4) Abstracts: None

- a. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (\*) if presentation produced a manuscript.

“Advancing Behavior Analysis by Extending the Continuum of Research Questions & Methods” Invited lecture delivered at the annual Thompson Center Autism Conference, St. Louis, MO (Sept. 26, 2019) and the Alabama Association for Behavior Analysis, Birmingham, AL (Oct. 10, 2019).

#### **7. INVENTIONS, PATENTS AND LICENSES:**

Nothing to report

#### **8. REPORTABLE OUTCOMES:**

Nothing to report

#### **9. OTHER ACHIEVEMENTS:**

Nothing to report

#### **10. REFERENCES:**

Nothing to report

**11. APPENDICES:**

Nothing to Report

**TRAINING OR FELLOWSHIP AWARDS:**

- Jamila Pitts – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).
- Melanie Parks – Conducted BM protocol, data collection, made recruitment calls, and administrative work (prepping for clients, filing, building folders).
- Jazmin Simms – Assisted in BM protocol, data collection, and administrative work (prepping for clients, filing, building folders).
- Jordyn Saxton - Assisted in BM protocol, data collection, and administrative work (prepping for clients, filing, building folders).
- Mary Elmore Demott - Assisted in BM protocol, data collection, and administrative work (prepping for clients, filing, building folders).
- Mikayla Ries – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).
- Carolyn Maynard – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).
- Sharon Daniel – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).
- Daniel Hoban – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).
- Ashlynn Thompson – Conducted BM protocol, data collection, graphed data, and administrative work (prepping for clients, filing, building folders).

**COLLABORATIVE AWARDS:**

Nothing to Report

**MARKING OF PROPRIETARY INFORMATION:**

Nothing to Report