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TITLE: Regulating Together: Randomized Controlled Trial Examining Predictors, Facilitators, and Barriers to Treatment Success in Emotion Dysregulation and ASD

PRINCIPAL INVESTIGATOR: Dr. Rebecca Shaffer, PsyD

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Dr Rebecca Shaffer, PsyD

E-Mail:

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12. DISTRIBUTION / AVAILABILITY STATEMENT

Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT: Intervention research in autism spectrum disorder (ASD) has almost exclusively focused on addressing core deficits, despite individuals with ASD presenting with significant behavioral and emotional symptoms including irritability, reactivity, and aggression. These clinical issues are hypothesized to arise from difficulties in emotion dysregulation (ED) or the inability to control the experience, expression, and intensity of emotions in an adaptable manner. ED has also been linked to higher rates of psychiatric hospitalizations, suicidal ideation, school disciplinary action, rejection by peers, failed transitions to college and employment, comorbid psychiatric diagnoses, and use of psychotropic medications in individuals with ASD compared to their peers with ASD without ED. Yet, ED is very rarely specifically targeted in ASD, particularly for school aged children, those with cognitive impairments, and/or for diverse youth. In an effort to address the critical need for efficient, effective, scalable, and disseminatable intervention strategies for youth with ASD+ED, our group developed Regulating Together (RT) - an intensive outpatient group treatment targeting ED. This program is innovative in its comprehensive approach to improve ED, involving both caregivers and children and exploring issues related to access and delivery for diverse youth. To date we have completed a retrospective chart review (n=20) and a within-subjects trial (8-12 yrs, n=25). Results demonstrate feasibility, acceptability, and initial efficacy reducing reactivity, irritability, and related constructs of ED. At a 10-week follow-up, additional improvement was observed, suggesting continued practice and use of the strategies learned. We consider this Generalization Phase to be a key component of RT. Additionally, diverse participants were satisfied with intervention and identified ways to improve future access. Our preliminary work has set the stage for a larger randomized controlled trial (RCT) with targeted diverse recruitment. Our long-term goal is to validate RT and improve psychosocial outcomes for youth with ASD+ED. wer psychiatric hospitalizations comparing rates of the 6 months prior to study.

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRDC
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TABLE OF CONTENTS

Page

1. **INTRODUCTION:** *Narrative that briefly (one paragraph) describes the subject, purpose and scope of the research.*

144 children with ASD will be enrolled in the study and randomized to an emotion regulation intervention or executive functioning intervention. Participants will complete assessments at five time points: Screen (T1); Week 0: Baseline (T2); Week 7: Post Active Treatment (T3); Week 16: Post Generalization (T4); Week 29: Final outcome visit (T5).
One aim of this study is to evaluate short-term and long-term efficacy of Regulating Together compared to an active control comparison (ACC) on emotion dysregulation. Another aim is to evaluate efficacy of Regulating Together compared to ACC on long-term functional outcomes (emotional outbursts and psychiatric hospitalizations) related to emotion dysregulation.

2. **KEYWORDS:** *Provide a brief list of keywords (limit to 20 words).*

ASD – Autism spectrum disorder. ED – Emotion dysregulation. RT – Regulating Together. AIMS - Achieving Independence and Mastery in School.

3. **ACCOMPLISHMENTS:** *The PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction.*

What were the major goals of the project?
List the major goals of the project as stated in the approved SOW. If the application listed milestones/target dates for important activities or phases of the project, identify these dates and show actual completion dates or the percentage of completion.

Aim 1: Evaluate short-term and long-term efficacy of RT on ED.
Aim 2: Evaluate efficacy of RT on long-term functional outcomes related to ED.
Exploratory Aim 3: Examine facilitators/barriers to treatment response and implementation to guide future implementation research of RT.

	Timeline (Months)	Date Accomplished	Comments
Major Task 1: Project Start up			
Submit and gain acceptance from CCH IRB and DoD HRPO	1-6	IRB: May 2, 2022 HRPO: August 22, 2022	
Clinicaltrials.gov Registration	6	February 2023	
Milestone Achieved: IRB and HRPO Approval	6		
Study staff training on all behavioral/psychological/physiological measures employed	1-2	September 30, 2022	

Study psychologists/social workers trained on Regulating Together and AIMS	2	RT Completed: September 9, 2022 AIMS Completed: January 2023	
One entire 10-session round of RT and AIMS will be observed by the PI to provide supervision and sign off on fidelity of administration.	6-8	Completed February 2023	
Milestone Achieved: Research staff and intervention facilitators trained	8	February 2023	
Modify RT RedCAP database so that all assessments, rating forms are included	1-2	October 12, 2022	
Milestone Achieved: RT RedCAP database updated and ready for data entry	2	October 12, 2022	
Major Task 2: Recruitment and Retention of all human subjects			
Subject screening period (n=144)	6-37	Began September 2022	
Subject randomization: After 12 participants have been recruited and have completed screen assessment, subjects will be randomized to RT or AIMS	6-32	3rd Cohort randomized: 6/2023	4th Cohort will be randomized 8/2023
RT or AIMS groups conducted with 12 cohorts	6-41	1st Cohort: Completed 1/2023 2nd Cohort: Completed 5/2023 3rd Cohort: Completed 8/2023	4th Cohort will be completed 10/2023
RT Study visits completed along with qualitative interviews and long term follow up visits.	6-45	Group 1 of 1st Cohort: Completed 6/2023	Group 2 of 1st Cohort will be completed 8/2023
Milestones Achieved: Screened, randomized, and completed all participants	45		
Major Task 3: Data Preparation			
Enter data into RedCAP within week of data collection, verify with second entry	6-45	Ongoing	
Conduct data checks on a biweekly basis on all collected data	6-45	Ongoing	
Weekly transfer and monthly checks on physiological data	6-45	Ongoing	

At end of each round, transfer of all group videos for fidelity and engagement coding.	6-42	Ongoing	
Resolve any data inconsistencies and/or missingness as needed	6-45	Ongoing	
Milestones Achieved: Data entered, verified, and resolved	45		
Major Task 4: Data Analysis			
Complete preliminary statistical analyses halfway through study (cohort 6)	24-26		
Complete additional preliminary analyses as needed for conference proceedings, invited talks	24-26		
Perform all statistical analyses according to proposal once final cohort is complete	42-48		
Conduct exploratory analyses to examine potential factors that predict treatment response.	42-46		
Perform qualitative thematic analysis from interviews	42-48		
Dissemination of findings through abstracts, publications, DoD	26-48		
Prepare grant application	44-48		
Milestones Achieved: Reported results from data analyses. Submission of secondary manuscript identifying predictive factors of treatment response	48		

What was accomplished under these goals?

For this reporting period describe: 1) major activities; 2) specific objectives; 3) significant results or key outcomes, including major findings, developments, or conclusions (both positive and negative); and/or 4) other achievements. Include a discussion of stated goals not met. Description shall include pertinent data and graphs in sufficient detail to explain any significant results achieved. A succinct description of the methodology used shall be provided. As the project progresses to completion, the emphasis in reporting in this section should shift from reporting activities to reporting accomplishments.

Major Task 2: Participant Recruitment and Retention

We continue to do well with recruitment and have enrolled 43 participants to date (most recent enrolled 7/21/2023).

Cohort 1: Group 1 completed the intervention and all visit timepoints (6/2023), Group 2 completed T1, T2, intervention, T3, and T4 visits (7/2023)

Cohort 2 has completed visits T1, T2, intervention, T3 and the 10 week follow up (T4) visits (7/2023).

Cohort 3: Group 1 completed T3 visits (7/2023), Group 2 will complete the intervention on 8/10/2023.

Cohort 4: 6 enrolled/randomized

Major Task 3: Data Preparation

Data Entry is being completed in a timely manner.

We are doing consistent checks on and transfer of physiological data (i.e., heart rate).

The second DSMB meeting will take place 8/3/2023.

What opportunities for training and professional development has the project provided?
If the project was not intended to provide training and professional development opportunities or there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe opportunities for training and professional development provided to anyone who worked on the project or anyone who was involved in the activities supported by the project. "Training" activities are those in which individuals with advanced professional skills and experience assist others in attaining greater proficiency. Training activities may include, for example, courses or one-on-one work with a mentor. "Professional development" activities result in increased knowledge or skill in one's area of expertise and may include workshops, conferences, seminars, study groups, and individual study. Include participation in conferences, workshops, and seminars not listed under major activities.

Clinicians in the study have received Regulating Together and AIMS training. Coordinators have received training in measures. A fellow completed her fellowship while working on the study completing tasks such as physiological assessment and processing, therapeutic alliance and engagement coding, and intervention study experience.

How were the results disseminated to communities of interest?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the results were disseminated to communities of interest. Include any outreach activities that were undertaken to reach members of communities who are not usually aware of these project activities, for the purpose of enhancing public understanding and increasing interest in learning and careers in science, technology, and the humanities.

Dr. Shaffer completed a training about emotion dysregulation as part of a Diversity, Equity, and Inclusion event through another study and this study was shared in the presentation.

Describe briefly what you plan to do during the next reporting period to accomplish the goals and objectives.

During the next reporting period we plan to accomplish the following goals:

Major Task 2: Recruitment and Retention of Human Subjects

- Recruit and screen for Cohorts 5, 6, & 7.
- Complete study visits for Cohorts 1, 2, and 3.

Major Task 3: Data Preparation

- Collected data will be entered into Redcap
- Fidelity and engagement coding will continue
- DSMB will meet every 6 months

Major Task 4: Data Analysis

- Interim analyses will be completed after the 6th cohort.

4. **IMPACT:** D*escribe distinctive contributions, major accomplishments, innovations, successes, or any change in practice or behavior that has come about as a result of the project relative to:*

What was the impact on the development of the principal discipline(s) of the project?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how findings, results, techniques that were developed or extended, or other products from the project made an impact or are likely to make an impact on the base of knowledge, theory, and research in the principal disciplinary field(s) of the project. Summarize using language that an intelligent lay audience can understand (Scientific American style).

The curriculum for Regulating Together was updated for the current study and these updates have been implemented clinically at sites who provide the program.

What was the impact on other disciplines?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how the findings, results, or techniques that were developed or improved, or other products from the project made an impact or are likely to make an impact on other disciplines.

Nothing to Report

What was the impact on technology transfer?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe ways in which the project made an impact, or is likely to make an impact, on commercial technology or public use, including:

- *transfer of results to entities in government or industry;*
- *instances where the research has led to the initiation of a start-up company; or*
- *adoption of new practices.*

Nothing to Report

What was the impact on society beyond science and technology?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe how results from the project made an impact, or are likely to make an impact, beyond the bounds of science, engineering, and the academic world on areas such as:

- *improving public knowledge, attitudes, skills, and abilities;*
- *changing behavior, practices, decision making, policies (including regulatory policies), or social actions; or*
- *improving social, economic, civic, or environmental conditions.*

Nothing to Report

5. **CHANGES/PROBLEMS:** *The PD/PI is reminded that the recipient organization is required to obtain prior written approval from the awarding agency grants official whenever there are significant changes in the project or its direction. If not previously reported in writing, provide the following additional information or state, "Nothing to Report," if applicable:*

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them
Describe problems or delays encountered during the reporting period and actions or plans to resolve them.

There have been withdraws in each round of the study. To combat this, we have employed the following courses of action:

1. Scheduling more than the target number of participants for screening visits in case someone drops out before group starts.
2. Confirming with families multiple times before the screening visit that the dates of potential group sessions will work with their schedule.
3. We will be running an additional Round to make up for the lost participants.
4. Confirming with families before the screening visit that they plan to continue with the study regardless of which group they are randomized to.

Changes that had a significant impact on expenditures
Describe changes during the reporting period that may have had a significant impact on expenditures, for example, delays in hiring staff or favorable developments that enable meeting objectives at less cost than anticipated.

Nothing to Report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents
Describe significant deviations, unexpected outcomes, or changes in approved protocols for the use or care of human subjects, vertebrate animals, biohazards, and/or select agents during the reporting period. If required, were these changes approved by the applicable institution committee (or equivalent) and reported to the agency? Also specify the applicable Institutional Review Board/Institutional Animal Care and Use Committee approval dates.

Significant changes in use or care of human subjects

Nothing to Report

Significant changes in use of biohazards and/or select agents

Nothing to Report

6. PRODUCTS: *List any products resulting from the project during the reporting period. If there is nothing to report under a particular item, state "Nothing to Report."*

- **Publications, conference papers, and presentations**
  Report only the major publication(s) resulting from the work under this award.

Nothing to Report

Journal publications. *List peer-reviewed articles or papers appearing in scientific, technical, or professional journals. Identify for each publication: Author(s); title; journal; volume: year; page numbers; status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Books or other non-periodical, one-time publications. *Report any book, monograph, dissertation, abstract, or the like published as or in a separate publication, rather than a periodical or series. Include any significant publication in the proceedings of a one-time conference or in the report of a one-time study, commission, or the like. Identify for each one-time publication: author(s); title; editor; title of collection, if applicable; bibliographic information; year; type of publication (e.g., book, thesis or dissertation); status of publication (published; accepted, awaiting publication; submitted, under review; other); acknowledgement of federal support (yes/no).*

Nothing to Report

Other publications, conference papers and presentations. *Identify any other publications, conference papers and/or presentations not reported above. Specify the status of the publication as noted above. List presentations made during the last year (international, national, local societies, military meetings, etc.). Use an asterisk (*) if presentation produced a manuscript.*

Nothing to Report

- **Website(s) or other Internet site(s)**
  List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Nothing to Report

- **Technologies or techniques**
  Identify technologies or techniques that resulted from the research activities. Describe the technologies or techniques were shared.

Nothing to Report

- **Inventions, patent applications, and/or licenses**
  Identify inventions, patent applications with date, and/or licenses that have resulted from the research. Submission of this information as part of an interim research performance progress report is not a substitute for any other invention reporting required under the terms and conditions of an award.

Nothing to Report

- **Other Products**
  Identify any other reportable outcomes that were developed under this project. Reportable outcomes are defined as a research result that is or relates to a product, scientific advance, or research tool that makes a meaningful contribution toward the understanding, prevention, diagnosis, prognosis, treatment and /or rehabilitation of a disease, injury or condition, or to improve the quality of life. Examples include:
  - *data or databases;*
  - *physical collections;*
  - *audio or video products;*
  - *software;*
  - *models;*
  - *educational aids or curricula;*
  - *instruments or equipment;*
  - *research material (e.g., Germplasm; cell lines, DNA probes, animal models);*
  - *clinical interventions;*
  - *new business creation; and*
  - *other.*

Nothing to Report

7. PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS

What individuals have worked on the project?

Provide the following information for: (1) PDs/PIs; and (2) each person who has worked at least one person month per year on the project during the reporting period, regardless of the source of compensation (a person month equals approximately 160 hours of effort). If information is unchanged from a previous submission, provide the name only and indicate "no change".

Example:

Name: *Mary Smith*
Project Role: *Graduate Student*
Researcher Identifier (e.g. ORCID ID): *1234567*
Nearest person month worked: *5*

Contribution to Project: *Ms. Smith has performed work in the area of combined error-control and constrained coding.*
Funding Support: *The Ford Foundation (Complete only if the funding support is provided from other than this award.)*

Name: Rebecca Shaffer, PsyD (CHCMC)
Project Role: PD/PI
Researcher Identifier (e.g. ORCID ID): 0000-0001-6935-4403
Nearest person month worked: 3.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Administrative oversight, training of staff and clinicians, coordinator of relationship with Alabama and Northeastern teams.

Name: Carrie Fassler (CCHMC)
Project Role: Senior Clinical Research Coordinator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 4.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Regulatory coordination and study visit completion

Name: Jennifer Harms (CCHMC)
Project Role: Clinical Researcher Coordinator II
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 11.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Lead coordinator for study, recruitment, data collection, behavior assistant in group sessions

Name: Paul Horn, PhD (CCHMC)
Project Role: Co-Investigator, Statistician
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Created randomization plan and statistical analysis plan

Name: Mya Jones (CCHMC)
Project Role: Clinical Research Coordinator III
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 3.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Assistance with recruitment and study visits

Name: Sungeun Kang, PhD (CCHMC)
Project Role: Research Fellow
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 12.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Study clinician and assistance with heart rate variability analysis

Name: Shivali Sarawgi, PhD (CCHMC)
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Study clinician and qualitative interviewer

Name: Jennifer R Ruberg, LISW (CCHMC)
Project Role: Study Therapist
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 3.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Completed training and was the study clinician. Completed screening visit assessments

Name: Lauren Schmitt, PhD (CCHMC)
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Oversee the probabilistic reversal learning data collection and analysis

Name: Susan White, PhD (UAB)
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Administrative oversight of the Alabama site and training of video coding

Name: Nicole Powell, PhD (UAB)
Project Role: Co-Investigator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Training and planning for video coding

Name: Nicole Friedman (UAB)
Project Role: Graduate Student (Research Assistant)
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Video coding of engagement and fidelity

Name: Shanta Burrell (UAB)
Project Role: Project Coordinator
Researcher Identifier (e.g. ORCID ID): n/a
Nearest person month worked: 1.0 cm (08/01/22 – 07/31/23)
Contribution to Project: Video coding of engagement and fidelity

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

If the active support has changed for the PD/PI(s) or senior/key personnel, then describe what the change has been. Changes may occur, for example, if a previously active grant has closed and/or if a previously pending grant is now active. Annotate this information so it is clear what has changed from the previous submission. Submission of other support information is not necessary for pending changes or for changes in the level of effort for active support reported previously. The awarding agency may require prior written approval if a change in active other support significantly impacts the effort on the project that is the subject of the project report.

Nothing to Report

What other organizations were involved as partners?
If there is nothing significant to report during this reporting period, state "Nothing to Report."

Describe partner organizations – academic institutions, other nonprofits, industrial or commercial firms, state or local governments, schools or school systems, or other organizations (foreign or domestic) – that were involved with the project. Partner organizations may have provided financial or in-kind support, supplied facilities or equipment, collaborated in the research, exchanged personnel, or otherwise contributed.

Provide the following information for each partnership:
Organization Name:
Location of Organization: (if foreign location list country)
Partner's contribution to the project (identify one or more)

- *Financial support;*
- *In-kind support (e.g., partner makes software, computers, equipment, etc., available to project staff);*
- *Facilities (e.g., project staff use the partner's facilities for project activities);*
- *Collaboration (e.g., partner's staff work with project staff on the project);*
- *Personnel exchanges (e.g., project staff and/or partner's staff use each other's facilities, work at each other's site); and*
- *Other.*

University of Alabama
Tuscaloosa, AL
Contribution to the project: Video coding of engagement and fidelity

8. SPECIAL REPORTING REQUIREMENTS

COLLABORATIVE AWARDS: ***N/A***

QUAD CHARTS: *N/A*

9. APPENDICES: *N/A*