B. ACCOMPLISHMENTS

B.1 WHAT ARE THE MAJOR GOALS OF THE PROJECT?

The Specific Aims and corresponding hypotheses outlined for the R33 phase of this project are as follows:
B1. Determine feasibility of the intervention.
Hypotheses: HB1a, ≥ 80% of participants will complete treatment and HB1b, homework.
B2. Determine the acceptability of the intervention.
Hypotheses: HB2a, ≥ 80% of parents and children in FBI will endorse Very Much/Extreme positive ratings on treatment credibility and HB2b, satisfaction.
B3. Assess clinically meaningful change in the intervention group compared to control.
Hypotheses: HB3a, Compared to control, children in FBI will endorse: fewer episodes of abdominal pain (pain thermometer), HB3b, greater reductions in impairment (Children's Global Assessment Scale), and, Exploratory: greater improvements in emotion awareness and regulation via increased abilities to HB3c, discriminate emotion from pain (via daily diaries) and HB3d, regulate emotional experience (laboratory mood induction task).

B.1.a Have the major goals changed since the initial competing award or previous report?

No

B.2 WHAT WAS ACCOMPLISHED UNDER THESE GOALS?

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B.3 COMPETITIVE REVISIONS/ADMINISTRATIVE SUPPLEMENTS

For this reporting period, is there one or more Revision/Supplement associated with this award for which reporting is required?

No

B.4 WHAT OPPORTUNITIES FOR TRAINING AND PROFESSIONAL DEVELOPMENT HAS THE PROJECT PROVIDED?

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B.5 HOW HAVE THE RESULTS BEEN DISSEMINATED TO COMMUNITIES OF INTEREST?

We have presented the results and rationale of our experimental intervention at the International Conference of Eating Disorders in May 2016 and at the National Eating Disorders Association Conference in October 2016. We have been accepted to present our preliminary results at the Anxiety and Depression Conference in April 2017. We have submitted manuscript describing the results of our pilot phase that is currently under review at Behaviour Research and Therapy. On 1/27/17 we were asked to revise and resubmit this manuscript.

B.6 WHAT DO YOU PLAN TO DO DURING THE NEXT REPORTING PERIOD TO ACCOMPLISH THE GOALS?

During the second year of this R33 phase, we will continue the conduct of this clinical trial. During this year we intend to add two additional pediatric practices for recruitment. We anticipate submitting three more manuscripts for publication, one describing the development and results of our laboratory task in which we examine children's capacity to discriminate visceral pain signals from visceral signals of emotional experience. The second manuscript will describe how emotion awareness and regulation changes with the FBI intervention, and whether such changes mediate pain outcomes. The third manuscript will be a qualitative and comprehensive description of the implementation of the intervention. We are planning to submit an administrative supplement to add resting-state neuroimaging as a measure of the mechanistic effects of our intervention.

Treatment Development and Therapist Training

Developing and manualizing a control treatment for pediatric abdominal pain. We reviewed existing practice guidelines and patient handouts from academic medical centers and professional organizations devoted to pediatric gastrointestinal disorders. From these, we derived a 10-session parent education intervention that covers currently recommended components of care for the management of pediatric functional abdominal pain (*Caregivers in Action*, CIA). This protocol was reviewed by our pediatrician consultant at Duke Medical Center, Dr. Gary Maslow. Dr. Maslow is the head of the Division of Child Psychiatry and double-boarded in pediatrics and psychiatry. His specialty is the management of pediatric pain. We are using the opportunity afforded by this clinical trial to further inform the efficacy of seemingly conflicting pain management strategies for children. Historically, the management of pain in children has focused on strategies that utilize distraction techniques – strategies that attempt to divert attention away from pain in order to decrease pain experience. The experimental treatment, Feeling and Body Investigators – FBI (Figure 1), utilizes an acceptance-based strategy whereby children focus on their pain, but from a stance of curiosity and playfulness, essentially directing attention towards pain experience. Thus, in our control intervention (CIA, Figure 1), in addition to psychoeducation about pain management, we instruct children and parents in strategies to distract attention away from pain. In this manner, we obtain preliminary evidence to inform the efficacy of various attention modulation approaches.

Figure 1. Logos from the Feeling and Body Investigator (FBI) and Caregivers in Action (CIA) Interventions

Training therapists in the experimental protocol. We are preparing for the broader dissemination of the FBI intervention that was developed and tested in our R21 phase. During Year 1 of the R33, we have developed materials to train therapists in the adherent administration of FBI. Three therapists are being trained according to this protocol and are currently being randomized cases to treat.

Recruitment

We have continued to successfully employ an “active” recruitment strategy whereby study recruiters remain on-site at a pediatric primary care practice and screen all eligible 5 to 9-year-old children. During this R33 phase, we have added two additional pediatric primary care practices and are in the process of adding a third. For one clinic, the busiest pediatric practice within the Duke Health System, we are implementing an alternative recruitment strategy. We email letters on behalf of our study team and the patient’s primary care physician, to the parents of patients who appear eligible based on a search for eligibility criteria from information within their electronic medical record. We tested out this strategy in our 21 phase, and it was acceptable to both physicians and parents. Given our current goal, recruiting an average of 3-4 participants per month, we have hit our recruitment targets as of December, 2016. Our goal was to have recruited a total of 21 subjects by the end of the month for December, 2016, and we had exactly 21 subjects enrolled and participating in the study by the end of that month.
A new strategy that we are employing this year is the use of social media. Duke Health System has developed a set of policies which allows investigators to use social media to advertise their research studies. Prior study participants can “like” the study and post about their experiences. In this way, we have the potential of extending our reach to friends and communities of prior study participants.

Collaborations to Expand the Breadth and Efficacy of the FBI Treatment

Examining individual difference variables in collaboration with researchers in the United Kingdom. We have been excited by the positive reception of our intervention from other researchers and healthcare providers. We have collaborated with researchers in the United Kingdom (Dr. Kate Stein) to assist in the completion of a Welcome Trust Fellowship application under review that will test a core premise of the

theoretical model that underlies the FBI intervention, namely, that children with functional abdominal pain are viscerally hypersensitive and are preoccupied with gut visceral sensations.

Translating the intervention for telemedicine delivery. In collaboration with leadership in the Division of Child Psychiatry at Duke Health, we submitted an internal application that would translate the delivery of the FBI intervention to a tele-medicine format. This project also proposed to expand the breadth of the intervention to recipients experiencing pain of any form, not only abdominal pain. This proposal was not initially funded by an interdepartmental team of clinicians. However, it was recently taken up by the Chair of Pediatrics who is considering the internal funding of this project via the Duke Department of Pediatrics.

Translating the intervention to a smartphone application. We formed a new collaboration with investigators from the Duke Pratt School of Engineering, Dr. Guillermo Sapiro, and from the Duke Department of Psychology and Neuroscience, Dr. Gary Bennett. These researchers have expertise in the integration of multimodal clinical and behavioral data, particularly when the source of data is in the form of video or qualitative text fields; the use of Apple's ResearchKit®, and Apple's CareKit®, and the translation of interventions to smartphone digital applications. Together, we translated the components of the FBI intervention into playful games – including pain assessment diaries, animations of body sensation characters, interoceptive exposure activities, and decision tree worksheets. We did not receive funding for this application however, received a very enthusiastic review. Our intention is to explore possibilities for funding both within and without the NIH to fund this project. We hypothesize that the availability of this app would greatly augment the efficacy of our intervention and extend the reach of individuals who could benefit from the treatment.

Examining the utility of the FBI intervention with children undergoing organ transplants. The etiological model we propose for the FBI intervention may be relevant for a variety of pediatric medical conditions. Our model is that viscerally hypersensitive children are vulnerable to intensified pain experiences, that they develop a fear of these somatic experiences, and that this fear generalizes to include innocuous somatic sensations. We were approached by clinicians in Department of Pediatric Gastrointestinal Disorders who specialize in liver transplants. These clinicians reported a subset of children who do not fare well after transplant, putatively due to a generalized fear and over-reactivity to somatic symptoms. We are currently working with these clinicians to do a case series of FBI with these challenging clinical cases. If successful, we will explore funding mechanisms for more systematic clinical trial.

We currently have a publication under review, the report of the clinical outcomes for the pilot phase of this project conducted during our R21 phase.

Total Enrollment Report: Number of Subjects Enrolled to Date (Cumulative) By Ethnicity and Race

Ethnic Category	Females	Males	Unknown or not reported	Total
Hispanic or Latino	4	4	0	8
Not Hispanic or Latino	85	58	0	143
Unknown (Individuals not reporting ethnicity)	0	0	0	0
Ethnic Category: Total All Subjects*	89	62	0	151

Racial Categories	Females	Males	Unknown or not reported	Total
American Indian/ Alaska Native	0	0	0	0
Asian	2	0	0	2
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	20	17	0	37
White	61	42	0	103
More than one race	6	3	0	9
Unknown or not reported	0	0	0	0
Racial Categories: Total of All Subjects*	89	62	0	151

***The Ethnic Category total must equal the Racial Categories total.