DETAILED PROTOCOL

9/14/16

NCT# 02772432

Development of a Resiliency Training Program for Parents of Children With Specific Learning Disabilities

PARTNERS HUMAN RESEARCH COMMITTEE DETAILED PROTOCOL

Date: 9/14/16

I. BACKGROUND AND SIGNIFICANCE

According to the 2011/12 National Survey of Children's Health, 14.6 million children in the U.S. have special health care needs (e.g., learning disability, ADD/ADHD, developmental delays, chronic mental or physical health conditions); CSHCN comprise between 14.4%-25.6% of the child population in the United States.[1] Having a child with special health care needs (CSHCN) is associated with an increased risk of problems with emotional and physical health and social well-being. Parents of CSHCN are also at an increased risk for not being employed, [2,3,4,5] financial stress, [6,7,8] and poor health-related quality of life (HRQoL).[7]

There is growing literature on the increased levels of parental stress associated with caring for CSHCN. One study found that chronic stress, as measured by the duration of having a CSHCN, was associated with an increase in clinical aging, determined by telomeres (caps at the end of each strand of DNA that protect chromosomes during aging) sequences.[9] A review article provides a comprehensive overview of the links between high levels of parental stress among parents of children with intellectual and developmental disabilities and child health and well-being.[10] Furthermore, a recent study documented that parents of CSHCN feel socially isolated.[1] Therefore, having a child with special health care needs (CSHCN) is associated with an increased risk of problems with emotional and physical health and social well-being. Resiliency is a multidimensional construct that refers to the ability to maintain adaptation and effective functioning when faced with stressors.

Resiliency provides a framework for understanding the adjustment to stress as a dynamic process. Allostasis refers to the capacity to maintain stability of physiological systems in the face of adversity.[11] When exposed to chronic stressors, such as care for a CSHCN, individuals expend a great deal of energy attempting to maintain allostasis; this can lead to the metabolic wear and tear described as allostatic load. Evidence is accumulating that this wear and tear is mediated by changes in basal stress system activity and by effects of these changes on dependent systems.[12] Allostatic load and resilience can therefore be assessed by measuring basal stress system activity (HPA axis and salivary alpha-amylase).

Thus, research to reduce these parents' exposure to stress and, moreover, improve parental responses to stress, may improve the wellbeing of both parents and their children. Yet, a treatment focused on the psychosocial needs of parents of children CSHCN, particularly for parents of children with learning disabilities has not been developed. Given the less disruptive nature of a learning disability diagnosis, there are fewer resources and support systems in place. Based on qualitative interviews with experts and parents of children with learning disabilities (conducted in phase I of this study #2016P000423), there is a need for skills-based support for parents that can be easily accessible, via virtual delivery.

Research is warranted to examine and intervene upon parental stress. This study aims to design and develop a resiliency intervention to provide support to parents of children with learning disabilities, an under-represented and less severe population of childhood disabilities.

This intervention will be a modified version of Dr. Park's evidence-based 8-week multimodal treatment which is designed to promote adaptation to stress and promotion of

resiliency. This study will refine an 8-session group virtual-delivered resiliency treatment program consisting of 8 virtual group 1 hour sessions. The goal of this study would be to advance our ultimate objective to implement a national parental resiliency program.

II. SPECIFIC AIMS

The proposed research has the following objectives:

Specific Aim 1 (Phase II): Informed by Phase I findings, (approved in a previous IRB protocol #2016P000423), we aim to develop and determine the feasibility (by assessing the number of sessions attended and adherence to Relaxation Response practice) and acceptability (assessed using the Participant Feedback Survey) of an 8-session Relaxation Response Resiliency (SMART-3RP) program for parents of children with learning disabilities.

> **Hypothesis:** The SMART-3RP virtual delivery will be feasible to implement and acceptable to parents of children with learning disabilities.

Primary Aim 2 (Phase III): To test the effectiveness of a pilot waitlist controlled trial on improving resiliency, as measured using the General Self-Efficacy Questionnaire, Current Experiences Scale, and the Visual Analogue 0-10 scales (including stress, distress, coping, and physical discomfort), and on improving stress reactivity (as measured by the Measure of Current Status-A), growth enhancement (as measured by the Cognitive and Affective Mindfulness Scale-Revised), and parental stress (as measured by the Parental Stress Scale). This will be assessed by comparing Baseline-3 mo. scores on primary and secondary outcome measures between the Immediate and Waitlist control groups.

> **Primary Hypothesis:** Patients randomized to the Immediate group will report significantly greater scores on the primary outcomes (measures of resilience) and on the secondary outcomes (measures of stress reactivity, growth enhancement, and parental stress) at 3 mo. post enrollment.

Secondary Aims: Among participants randomized to both conditions, to investigate the extent of pre-post changes in primary and secondary outcomes (Immediate: assessments from baseline-3 mo.; Waitlist: from 3-6 mo.).

> **Secondary Hypothesis:** Scores on primary and secondary outcome measures will improve from pre-post intervention.

Secondary Aim 2: Among immediate condition group only**,** to assess whether end-of-treatment (3 mo. post enrollment) improvements will be sustained at 6-mo. post enrollment.

> **Hypothesis:** These end-of-treatment effects will show sustained improvement on primary and secondary outcome measures from 3 to 6-mo. Post enrollment.

Secondary Aim 3: To pilot test the end-of-treatment effects of the SMART-3RP on parents' stress levels using hair cortisol. A mixed effects models approach will be used to examine group

differences in hair cortisol concentrations (HCC) at baseline and 3 mo. post enrollment. Pearson correlation or Spearman's rank correlation will be used to examine the association of HCC with each of our psychological outcomes.

> **Hypothesis:** Parents randomized to the Immediate group will show improvements in biomarkers of stress system function, in particular the hypothalamus pituitary adrenal (HPA) axis and sympathetic nervous system (SNS) relative to baseline. It is expected that stress-related alterations will be found in parents before the intervention and will improve in those individuals that respond favorably to the treatment. Biomarkers will thus allow an additional level of testing for chronic stress, and efficiency of the intervention; measuring basal HPA axis and SNS activity further allows us to draw conclusions about the adverse long-term health effects of chronic stress and to evaluate the efficiency of the intervention in ameliorating such biological changes.

III. SUBJECT SELECTION

We will recruit through our contacts in the community including other MGH clinicians, as well as through local and national support groups and list serves using IRB approved recruitment materials. MGH child psychologists may also refer potentially eligible participants. Interested participants may call or email the study staff to learn more about the study.

The current study will employ a pretest-posttest, pilot waitlist controlled design to test the 3RP for parents of children with learning disabilities. Participants will be recruited from local, national, and international organizations, school systems, and hospital clinics.

Inclusion/Exclusion Criteria

Inclusion criteria are:

1) Being the parent of at least one child with a learning disability
2) Age 18 or older
3) Can read and speak English

One or more of the following exclusion criteria will render an individual ineligible:

1) Being the parent of a child with a severe mental or physical disability up to the discretion of the principal investigator
2) Regular use of corticosteroids at the discretion of the Principal Investigator
3) Unable or unwilling to sign the informed consent documents
4) Unable or unwilling to participate in an intervention delivered via videoconferencing.

Recruitment

A total of approximately 70 participants will be recruited for this study. Both males and females from diverse racial and ethnic backgrounds will be recruited using IRB approved procedures. Potential participants will be recruited from our contacts in the community including other MGH

clinicians, as well as through local and national support groups and list serves using IRB approved recruitment materials. MGH child psychologists may also refer potentially eligible participants. In each case, interested participants will be directed to our pre-screen REDCap survey and will be given the option to contact the study staff to learn more about the study.

IV. SUBJECT ENROLLMENT

Methods of enrollment

Participants will contact the PI or study staff by telephone, email, or by completing our IRB approved pre-screen REDCap survey in response to advertisements. Subject will be contacted by phone, informed about the study and given a pre-screen REDCap to determine whether they meet inclusion/exclusion criteria (see the attached pre-screening questionnaire). Subjects may also be referred to the study. Subjects must respond "yes" to all inclusion criteria and "no" to all exclusion criteria to be eligible for the study. Eligible participants will be consented and will complete the baseline survey online into REDCap, a secure, web-based application designed to support data capture for research studies.

Randomization

After enrollment, participants will be randomized to the Immediate intervention group (IG) or Waitlist control group (WG). Randomization will be conducted using a random plan generator, with 1:1 randomization. The WG will begin their program approximately 3 months after the SMART-3RP group. For both groups, the intervention will last approximately 8 weeks, weekly with groups meeting once per week for approximately 1 hour.

Informed consent process

Eligible and interested participants will be sent a consent form and scheduled for a phone consent. Informed consent and authorization will be obtained and documented through use of a written consent form approved by the Partners Human Research Committee (PHRC) and signed by the participant. The PI or qualified study staff will complete informed consent procedures.

Participants will be asked to read the consent form fully on their own before discussing the consent form with a study staff member (either on the phone or using videoconferencing). The participant will have the opportunity to ask any and all questions about the study. Once all questions have been addressed, they will sign the consent form and send it to the study staff member (either via email, scan, fax, or mail). The study staff member will then sign the participant's signed copy and send a copy back to the participant for their records. As informed consent is a continuous process, participants will be invited to ask questions about their participation at any point over the course of the study.

The consent form will include a description of all study procedures, information about potential risks and benefits of participation, and study contact information (including that of the IRB) in case questions arise at a later time. The consent form will also explicitly state that study participation is voluntary, and that participants may refuse to answer any questions that make them uncomfortable, and may discontinue participation at any time. The consent will also explicitly state that this intervention is psycho-educational and is not clinical care.

In addition, special attention will be given during the consent process to the implications of receiving an intervention online via videoconferencing services. Subjects will be explicitly

informed that videoconferencing services provide secure HIPAA-compliant videoconferencing software. We will explain to participants that although we will do our best to ensure confidentiality on our end, we cannot guarantee 100% that other group members will not share the content of the group. Participants will also be advised to wear headphones and sit in a quiet place to protect their own, and other group members' privacy.

V. STUDY PROCEDURES

Program development
The Phase I (described previously in protocol # 2016P000423) findings will be used to guide the development of a resiliency program targeted to the needs of parents of children with learning disabilities.

Study staff will administer the consent form with participants either on phone or using the videoconferencing system. To facilitate proficiency with the software, participants will test the software with a study staff member either during consent or on a brief test call prior to the start of the intervention.

Assessments
Study assessments include a battery of questionnaires via REDCap and two hair cortisol sample collections. At baseline, participants will be administered baseline questionnaires and asked to provide a hair cortisol sample. At 3 months post enrollment, participants are administered a second set of questionnaires, and asked to complete a second hair cortisol sample. At 6 months post enrollment, participants are administered their final set of questionnaires.
Hair Cortisol
At enrollment (baseline) as well as at 3 months post enrollment, all participants will be asked to provide a hair sample to measure potential changes in cortisol levels, a method used successfully in stress studies. Participants will be asked to cut a small amount of hair (approximately 150 strands, which is about the diameter of a small paperclip) as close to the scalp as possible (about 3 cm), and from the back of their head. They will be asked to band or tie the strands near the scalp end, place on the sample in aluminum foil, and return in an envelope to MGH. Participants will be sent detailed sampling instructions and stamped, addressed envelopes to facilitate mailing. We are going to ask participants whether they regularly take corticosteroids because they may interfere with the accuracy of the hair cortisol sample.

The assessments are itemized below. In addition, participants will be asked to complete practice notes throughout their intervention.

Administered at Baseline:
3RP Battery of questionnaires
Hair Cortisol Sample

Administered 3 months post enrollment:
3RP Battery of questionnaires
Hair Cortisol Sample

Participant Feedback Questionnaire

Administered during Intervention (either starting after baseline or 3 months post enrollment)
Progress Note

Administered 6 months post enrollment
3RP Battery of questionnaires
Participant Feedback Questionnaire

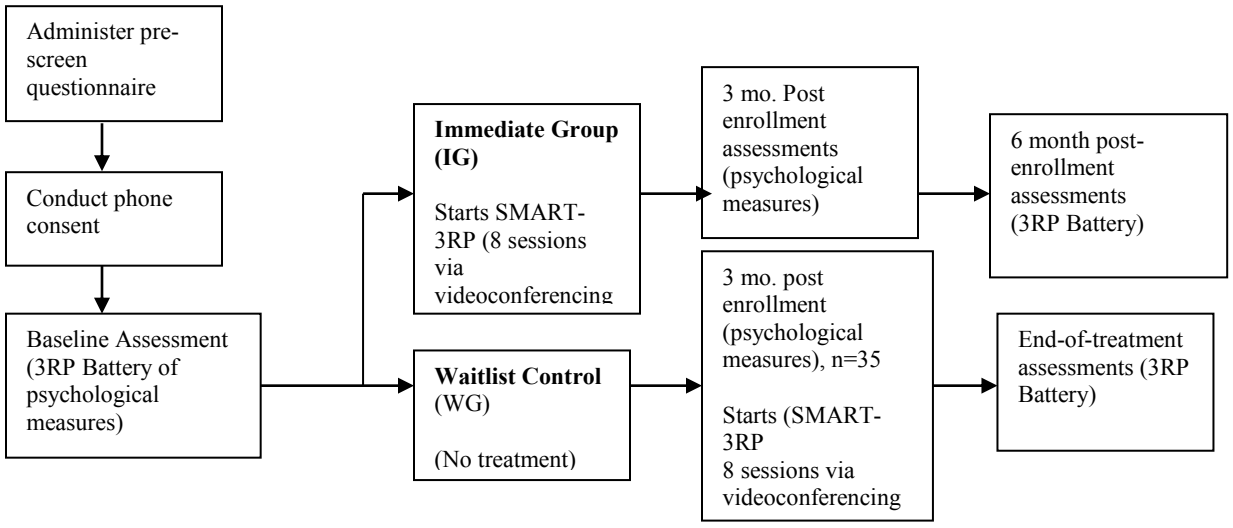
In the SMART-3RP intervention, sessions focus on developing an understanding of stress physiology and the physiology of the relaxation response (RR), on developing a regular practice of eliciting the RR, and on learning cognitive behavioral and positive psychology/resilience skills. In addition to the weekly group sessions, participants will receive audio recorded guided meditations for independent relaxation practice. Participants are expected to practice eliciting the RR for approximately 20 minutes a day throughout the course of the study, using the audio recording provided and/or any other meditative or mind body techniques. Participants will complete a daily log reporting how often and by which methods they are practicing the RR. (Please see attached practice log).

Participants randomized to Immediate or Waitlist will participate in the SMART-3RP program. Participants in the Immediate arm will be encouraged to practice the skills taught in the program during the 3 month follow up period after completion of the 8 session SMART-3RP. Participants in the Waitlist arm will wait for approximately 3 months before beginning the SMART-3RP.

Participants in both groups will be given questionnaires at the same time points (baseline, 3 month post enrollment, and 6 month post enrollment). Study staff will email these questionnaires to the participants via the REDCap system. Participants who have not responded within two weeks of each time point will be contacted by telephone to ensure receipt of study data.

Figure 1 (below) illustrates the administration of questionnaires in both groups.

Figure 1. Study Design.



Baseline	3 mo. Post Enrollment	6 mo. Post Enrollment
T1	T2	T3

Remuneration
Participants will be given a $20 gift certificate for completing 3 mo. survey and another $20 gift certificate for completing the 6 mo. survey assessment.

VI. BIOSTATISTIC ANALYSIS

We plan to conduct a pilot trial of a virtual-based SMART-3RP intervention for parents of children with learning disabilities. Participants in this trial will be randomized to one of two groups: 1) Immediate SMART-3RP intervention, or 2) Waitlist control SMART-3RP group (starting approximately 3 months after enrollment).

The following questions will be assessed:

1) Is the virtual SMART-3RP feasible and acceptable for parents who have children with learning disabilities?

Feasibility will be assessed using attendance and homework completion (i.e. 6/8 sessions and homework completion).
Acceptability will be assessed using a Participant Feedback questionnaire (See Feedback questionnaire attached).

2) Is the virtual SMART-3RP program effective for parents of children with learning disabilities?

a) Is there a significant difference in primary and secondary outcome measures between participants in the Immediate and Waitlist SMART-3RP groups at 3 mo. post enrollment?

We will use paired samples t-tests to compare within group differences on primary and secondary outcome measures from 3 mo. to baseline for the Immediate and Waitlist Groups. Primary outcome measures are the General Self-Efficacy Questionnaire (GSE), Current Experiences Scale (CES; from the Post Traumatic Growth Inventory), and the Visual Analogue 0-10 scales (VAS; measuring stress, distress, coping, and physical discomfort). Secondary outcome measures are: the Measure of Current Status-A (MOCS-A; to assess stress reactivity), Cognitive and Affective Mindfulness Scale-Revised (CAMS-R; to assess growth enhancement), and the Parental Stress Scale (PSS; to assess parental stress).

We will then use independent samples t-tests to compare the difference between the Immediate group's 3 months post enrollment and baseline assessment results with the

difference between the waitlist group's 3 months and baseline assessment results on primary and secondary outcome measures.

b) Among participants randomized to both conditions, will there be improvements in primary and secondary outcome measures from pre-post SMART-3RP (IG: assessments from baseline-3 mo.; WG: from 3-6 mo.)?

We will use paired samples t-tests to compare all primary and secondary assessments from pre-post SMART-3RP (for the IG, assessments are from baseline-3 mo.; for the WG, assessments are 3 mo. to 6 mo.).

c) Among the Immediate group only, will the changes from baseline to 3 months post enrollment (end of treatment) be sustained at 6 months post enrollment (3 months post treatment)?

We will use paired samples t-test to assess within-group differences in long-term outcomes. We will compare measures at the 6 months assessment to measures at the 3 months assessment for the Immediate group.

3) Will the virtual delivery SMART-3RP be effective in reducing participants' stress levels, measured by hair cortisol?

A mixed effects models approach will be used to examine differences in hair cortisol concentrations (HCC) at enrollment (baseline) and at 3 months post enrollment for each study arm. Pearson correlation or Spearman's rank correlation will be used to examine the association of HCC with each of our psychological outcomes.

VII. RISKS AND DISCOMFORTS

Participants may feel uncomfortable completing various psychosocial questionnaires. As in any research study, there is a small risk that confidentiality may be breached; all efforts to minimize this risk will be taken, as outlined below. In addition, participants may find it time consuming to practice techniques learned in the intervention or tracking behavior such as elicitation the relaxation response.

Hair cortisol collection: some participants may feel uncomfortable sending us a hair sample. If they feel this way, they will not need to. Participants can still remain in the study if they do not wish to send a hair cortisol sample.

VIII. POTENTIAL BENEFITS

Participants in the current study may observe a reduction in symptoms of parental stress. It is hoped that the intervention will result in a statistically significant reduction of symptoms across these domains.

The current study may provide support for parents of children with learning disabilities. This intervention may enhance our understanding of the role of mind-body interventions such as the SMART-3RP in parents of children with learning disabilities. This intervention may have widespread implications for types of resources available that may ultimately improve health and well being of parents and children with learning disabilities.

IX. MONITORING AND QUALITY ASSURANCE

All study staff will complete required Partners human subjects trainings prior to the start of study procedures. All interventionists and assessors will have advanced training in interviewing and assessment. Participants will be informed that they may refuse to answer questions that make them feel uncomfortable. Participants will be advised to wear headphones and sit in a quiet place during each virtual session. Participants will also be asked not to share the contents of the group with anyone else.

Electronic information will be stored in REDCap (Research Electronic Data Capture), a free, secure, and HIPAA-compliant web-based application hosted by the Partners HealthCare Research Computing Enterprise Research Infrastructure & Services (ERIS) group (based at the PHS Needham corporate datacenter).

REDCap (Research Electronic Data Capture) is a free, secure, HIPAA compliant web-based application hosted by the Partners HealthCare Research Computing Enterprise Research Infrastructure & Services (ERIS) group. The system offers easy data manipulation with audit trails, reports for monitoring and querying participant records, and an automated export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus).

Data will be stored on password protected computers that will be stored in secure locations at all times. Paper data files (with coded subject identification) will be stored in a locked filing cabinet. Only research staff will have access to these data locations.

A unique anonymous identifier will be assigned to each subject; subsequently, all data collected will be associated exclusively with this identifier. This includes all questionnaires administered over the course of the study, as well as home practice logs.

Data Management and Quality Control Procedures

To maximize accuracy and security, all survey data will be collected and stored on REDCap. Research staff will ensure that proper consent has been obtained before sending the REDCap survey to each participant.

Data and Safety Monitoring Plan

Adverse Event Monitoring: Throughout the study subjects will be monitored for the occurrence of events defined as any undesirable experience or unanticipated risk. Lack of effect of treatment is not considered an event. All adverse events will be reported on an adverse event form.

The principal investigator is ultimately responsible for data and safety monitoring. If study staff becomes aware of any adverse events, the event will be reported immediately to the Principal Investigator. The Principal Investigator has the responsibility of reporting serious adverse events (death, life threatening illness or injury, serious injury, or permanent disability) to PHRC within 72 hours of notification.

Subject Safety

In the case that an issue related to mandatory reporting or duty to warn arises, we will contact the Office of General Council for advice on how to proceed.

X. REFERENCES

[1] Caicedo C. Families with special needs children: family health, functioning, and care burden. *J Am Psychiatr Nurses Assoc*. 2014 Nov-Dec;20(6):398-407. Epub 2014 Nov 26.

[2] Kuhlthau, K., Perrin, J. M. Child health status and parent employment. *Archives of Pediatrics and Adolescent Medicine*. 2001;155, 1346-1350.

[3] Leiter V., Kraus M.W., Anderson B., Wells N. The consequences of caring: effects of mothering a child with special needs. *Journal of Family Issues*. 2004;25, 379-403.

[4] Heck, K. E., Makue, D. M. Parental employment and health insurance coverage among school-aged children with special health care needs. *American Journal of Public Health*. 2000;90,1856-1860.

[5] Kuhlthau K. A., Orlich F., Hall T.A., Sikora D., Kovacs E., Delahaye J., Clemons T. E. Health-related quality of life in children with autism spectrum disorders: results from the Autism Treatment Network. *Journal of Autism and Developmental Disorders,* 2010;40, 721-729.

[6] Strickland B., McPherson M., Weissman G., van Dyck P., Huang Z. J., Newacheck P. Access to the medical home: results of the national survey of children with special health care needs. *Pediatrics*. 2004;113,1485-1492.

[7] Witt W. P., Litzelman K., Mandic C. G., Wisk L.E., Hampton J.M., Creswell P.D., Gottlieb C.A., Gangnon, R.E. Healthcare-related financial burden among families in the U.S.: the role of childhood activity limitations and income. *J Fam Econ Issues.* 2011;32(2),:308-326.

[8] Kuhlthau K. A., Kahn R., Hill K. S., Gnanasekaran S., Ettner S.L. The well-being of parental caregivers of children with activity limitations. *Maternal and Child Health Journal.* 2010;14:155-163.

[9] Epel E.S., Blackburn E.H., Lin J., Dhabhar F.S., Adler N.E., Morrow J.D., Cawthon R.M. Accelerated telomere shortening in response to life stress. Proceedings of the National Academy of Sciences. 2004;101:17312-17315.

[10]Miodrag N., Hodapp R.M. Chronic stress and health among parents of children with intellectual and developmental disabilities. CurrOpin Psychiatry. 2010;23:407-11.

[11] McEwen, BS & Stellar, E. (1993). Stress and the individual. Mechanisms leading to disease. *Arch Intern Med.*153(18):2093-101.

[12] Adam, EK & Kumari, M. (2009). Assessing salivary cortisol in large-scale, epidemiological research. Psychoneuroendocrinology. 34(10): 1423-36.