Novel Executive Function Training for Obesity
NCT: 03724396
Study Protocol: Last updated: 12/7/2021

UCSD Human Research Protections Program
New Biomedical Application
RESEARCH PLAN

Instructions for completing the Research Plan are available on the HRPP website.
The headings on this set of instructions correspond to the headings of the Research Plan.
General Instructions: Enter a response for all topic headings.
Enter "Not Applicable" rather than leaving an item blank if the item does not apply to this project.

Version date: 9/30/2013

1. PROJECT TITLE

Novel Executive Function Training for Obesity (NEXT)

2. PRINCIPAL INVESTIGATOR

Dawn Eichen, PhD

3. FACILITIES

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4. ESTIMATED DURATION OF THE STUDY

5 years

5. LAY LANGUAGE SUMMARY OR SYNOPSIS (no more than one paragraph)

Currently, the best behavioral treatments for obesity only work for 50% of adults, and of those who initially succeed, most do not maintain their weight loss. One reason for this failure may be due to neurocognitive deficits found among individuals with obesity, particularly related to executive function, which make it difficult for these adults to adhere to treatment recommendations. Executive function are mental processes that enable us to plan, focus attention, remember instructions, and juggle multiple tasks successfully. The proposed study aims to develop a Novel Executive Function Treatment (NEXT), which when administered prior to the behavioral treatment, could help improve outcomes by addressing the neurocognitive deficits in adults with overweight or obesity.

6. SPECIFIC AIMS

Aim 1: Develop an initial treatment manual for NEXT.

Aim 2: Iteratively pilot NEXT on two cohorts of participants, and collect qualitative feedback which will be integrated into the NEXT program. (Study 1)

Aim 3: Determine feasibility and acceptability of NEXT (Study 1 & 2)

Exploratory Aim: Evaluate Mediators and Moderators of NEXT (e.g, depression, eating behaviors, self-efficacy)

Aim 4: Establish preliminary effects of NEXT on weight loss, executive function, and self-monitoring through a randomized-control trial comparing NEXT + behavioral weight loss (BWL) to BWL alone (Study 2)

7. BACKGROUND AND SIGNIFICANCE

Nearly two thirds of adults in the United States are overweight or obese.[1] The most successful obesity treatment to date is Behavioral Weight Loss (BWL); however, up to half of adults do not respond to BWL initially, and most responders do not maintain a clinically significant weight loss.[2-4] The recommendations and

strategies provided by BWL to change behaviors require high levels of executive function (EF), including planning, decision making, and problem solving.[5] Thus, it is possible that obesity treatment failure is due to impaired neurocognitive mechanisms that negatively impact an individual's ability carry out the recommended behavioral strategies, resulting in non-adherence to treatment or failure to maintain behavioral changes.

Research has shown that individuals with obesity demonstrate difficulties with EF across numerous domains.[5-9] Specifically, impairments have been shown on measures of decision making,[10-12] set-shifting,[8,13] planning,[9] inhibition,[5] working memory,[14] and fluency[5]. Better initial performance predicts weight loss and improvement on some of these tasks was seen after weight loss due to bariatric surgery.[15,16] A recent NIH Working Group Report[17] concluded that a need exists for a "deeper understanding of cognitive function" including: 1) the impact on physical activity and eating behaviors, and 2) if it can be used to develop more impactful strategies for weight loss and maintenance. Training EF is consistent with these recommendations and could be a promising mechanism which can be targeted to improve BWL outcomes.

Cognitive training, which targets aspects of EF, has improved cognitive performance and functional outcomes in healthy individuals and various populations with cognitive impairments.[18-21] Cognitive training has improved delay discounting among individuals with substance use disorders,[22] and inhibition and attention training paradigms in the context of high calorie foods have been associated with reduced palatable food consumption, reduced binge eating, and increased weight loss.[23,24] Cognitive Symptom Management and Rehabilitation Therapy (CogSMART) is a manualized compensatory cognitive training intervention targeting EF which is efficacious among individuals with traumatic brain injury.[25,26] A similar intervention is efficacious with individuals with psychosis.[27] Modifying and applying CogSMART to address EF deficits found in people with overweight or obesity could improve weight loss and maintenance outcomes.

Computer training programs targeting implicit neurocognitive processes (i.e., attention, inhibition) show preliminary effects to change eating behavior and weight. [23,24] A number of experimental studies have demonstrated training inhibition can impact eating behavior and weight loss.[24] Thus, it is promising that changing elements of EF can improve treatment outcomes.

8. PROGRESS REPORT

Study 1 treatment materials were developed and recruitment of participants began in May 2019. The first group of 10 participants began baseline assessments in June 2019 and started in a 12-week pilot group in July 2019. The group program ended in October 2019 and 8 of 10 participants completed their post-treatment assessments thereafter. Some revisions were made to treatment materials based on feedback received from participants. Recruitment for the second pilot group began in September 2019 and participants completed baseline assessment visits thereafter. The second pilot group began group sessions in November 2019 and finished in February 2020 and 8 of 11 participants completed their post-treatment assessments.

Study 2 recruitment began in February 2020.

Dr. Eichen, the PI, has closely monitored the study. Recruitment has progressed according to plan for Study 1. There have been no formal reports given that no adverse events have occurred and all monitoring has been conducted by the PI and other internal team members.

Study 2 recruitment was recently completed.

9. RESEARCH DESIGN AND METHODS

INTERVENTIONS:

NEXT will be an adjunctive program to the gold standard behavioral treatment for obesity, Behavioral weight loss (BWL). NEXT is based on CogSMART[25] and Compensatory Cognitive Training, developed by co-mentor Dr. Twamley, which has been successful at improving EF skills such as planning, problem solving, and cognitive flexibility in individuals with psychiatric disorders or history of traumatic brain injury. I will also use Cognitive Remediation Therapy for AN to inform NEXT.[28] NEXT will focus on teaching compensatory strategies, habit learning, and plan for generalization to real-world behaviors (e.g., self-monitoring of food intake). Each session will include interactive exercises to help train an aspect of EF. Skills taught will be

presented to be practiced with real-world applications. For example, planning skills will be taught and participants will apply the skills learned into developing a weekly meal plan, which is a skill suggested in BWL to help with tracking and staying within the recommended calorie range. The EF domains targeted by NEXT were carefully selected to enhance the EF domains (e.g., planning, organization) which underlie the successful use of skills recommended in BWL. BWL recommends skills, but does not provide in-depth, step-by-step training in these basic functions. As part of NEXT, participants will receive compensatory strategies to overcome deficits in underlying EF that could impede success in BWL. Furthermore, NEXT will teach when it is most advantageous to use these skills with particular attention towards training how the skills can be used in the context of aiding weight loss. For example, BWL encourages participants to plan meals ahead of time. NEXT will provide step-by-step strategies to improve meal planning, such as researching recipes, creating efficient shopping lists, organizing shopping in the store, and using similar ingredients in multiple meals. Implementation of meal planning will also be addressed in NEXT, such as when to purchase ingredients and when to prepare meals to be successful. Additionally, participants in NEXT will practice meal planning in session and will complete practice worksheets to improve chances of success in meal planning outside of group. NEXT will provide an additional benefit in that the cognitive skills taught can be used to improve EF across all domains in life, which could potentially decrease stress and improve quality of life.

BWL includes daily self-monitoring of calorie intake and physical activity. Calorie goals will be shaped down to 1200-1400 calories for females and 1500-1700 for males. Physical activity recommendations will be consistent with guidelines suggesting a minimal of 150 minutes of at least moderate intensity activity each week with the ideal being >250 minutes. Lifestyle activity goals focus on building increased activity into typical, daily activities, such as walking or bicycling. Participants are also instructed to decrease sedentary behaviors, such as TV watching or computer usage outside of work. Participants will be encouraged to work toward achieving 10,000 steps per day. BWL will include elements of behavioral change recommendations including stimulus control, self-monitoring, goal setting, managing high-risk situations, meal planning, slowing eating, problem solving, social support, cognitive restructuring, lapse and relapse prevention skills, and maintaining weight loss.

Study 1: This is a study to aid in treatment development of a Novel Executive Function Treatment for Obesity (NEXT) and thus the design will be open label. After consenting to be a part of the study, participants will attend an in person assessment visit which will take approximately 3 hours. Then when enough people have completed assessments and meet inclusion criteria, they will attend a pilot program group (approximately 10-15 other adults). Group will meet weekly for 12 weeks and be scheduled for 75 minutes. There will be another in-person assessment that will take approximately 3 hours following the 12 weeks of pilot program groups.

Group programs will consist of 12 weekly, 75 minutes groups consisting of NEXT only, NEXT and BWL or BWL curriculum only.

Study 2: Study 2 will consist of a randomized control trial. Study participants will consist of at least 64 adults who will be randomized to one of two conditions, one which will receive NEXT + BWL and one which will receive BWL alone. Each group will consist of 10-20 participants. Study participants will be blind to their condition. All groups will be twenty 75-minute sessions over the course of 6 months. Groups will be held in-person or via password-protected ZOOM meetings. If groups are held via ZOOM, on treatment nights, participants will be sent treatment materials and information on how to access the meetings via email. Assessment measures are specified below but assessments will occur at two additional time points for a total of four assessments per participant: baseline, at mid-program (take place approximately between sessions 10-14), post program, and 6 month follow-up. Assessment visits will be held in-person or in password-protected ZOOM meetings. Links for assessment tasks that can be completed online including computer tasks and surveys will be emailed to the participant before the assessment appointment with instructions on how to access the ZOOM meeting.

Table 1. Measurement table and assessment time-points for study 2:

	Instrument	Baseline	During group visits	Mid-program	Post-Program	6-month f-up
Anthropometry	Height/Weight	X	X	X	X	X
Screening Measures	WRAT-4	X				
	MINI	X			X	X
	Medical and medications	X		X	X	X
Binge Eating	EDE	X		X	X	X
	EDEQ	X	X	X	X	X
Executive Function	DKEFS	X		X	X	X
	BRIEF	X			X	X
	PSI	X		X	X	X
	Delay Discounting	X		X	X	X
	Brain Health Index	X		X	X	X
	DFLEX	X	X	X	X	X
	Digit Span	X		X	X	X
	WCST	X		X	X	X
	CVLT- Food	X	X	X	X	X
	Stop Signal Task	X	X	X	X	X
	Tower of London	X	X	X	X	X
	TMT	X	X	X	X	X
	CPT	X		X	X	X
Questionnaires-- psychiatric	PHQ-9	X		X	X	X
	DERS	X		X	X	X
	GAD-7	X		X	X	X
Questionnaires-- stress	PSS	X		X	X	X
Questionnaires-- eating behavior	YFAS 2.0	X		X	X	X
	EAH	X		X	X	X
	Adult Eating Behavior Questionnaire (AEBQ)	X		X	X	X

	Reward Based Eating Drive Scale (RED)	X		X	X	X
Questionnaires-- impulsivity	S-UPPS-P	X	X	X	X	X
Questionnaires-self-efficacy	General Self Efficacy Scale	X	X	X	X	X
Questionnaires-- other health behaviors	GPAQ	X		X	X	X
	Godin leisure time exercise questionnaire	X	X	X	X	X
	Q-LES-Q-SF	X	X	X	X	X
Adherence	ADH	X		X	X	X
	BWL	X		X	X	X
Feasibility/Acceptability	Attendance		X	X	X	X
	Acceptability survey		X	X	X	X
Self-Monitoring	Habit books		X			

Measurements

Screening Measures (baseline only): Participants will complete the Mini-International Neuropsychiatric Interview (MINI)[29] to confirm eligibility (i.e., absence of exclusionary psychiatric condition). The WRAT[30] reading assessment will be administered at baseline to evaluate reading level and ensure valid administration of the assessments.

Anthropometry (all assessment timepoints and each program visit): At CHEAR Height will be measured using a portable Schorr height board (Schorr Inc, Olney, MD) in triplicate. Height will be recorded to the nearest 0.1 cm. Body weight in kilograms will be measured in triplicate on a Tanita Digital Scale (model WB-110A). Body weight will be recorded to the nearest 0.1 kg. The average of the 3 height and weight values will be used for analysis. Height and weight will be converted to body mass index (BMI=[kg/m^2]). If height and/or weight is not collected at CHEAR, participants will be asked to self-report their height and weight using a scale they own or a Bluetooth provided scale.

Binge Eating (all assessment timepoints): The Eating Disorder Examination[31] (EDE) interview will be administered as the EDE is the gold standard for assessing binge eating is a valid and reliable measure.

Executive Function (all assessment timepoints): Standardized, well-validated neurocognitive tests to assess a broad range of EF domains will be conducted. We will include selected subtests from the widely used Delis-Kaplan Executive Function System (D-KEFS)[32] and various other well-validated measures of EF. Lastly, self-report measures of EF are included. Administration of all EF tasks should take about 80 minutes.

BRIEF: To identify individuals with EF difficulties, the Behavior Rating Inventory of Executive Function – Adult[33] (BRIEF-A) will be administered at baseline and again at post-program.

D-KEFS. [32] The D-KEFS is a widely used battery of EF that has strong validity and comparable reliability to other neuropsychological tasks. Three D-KEFS subtests (Color-Word Interference [CWI], Design Fluency, and

Verbal Fluency) will be administered.

Problem Solving Inventory (PSI).[34] Participants rate statements describing their own problem-solving behaviors and attitudes using 32, six-point Likert-type items. Three factors are derived: Problem Solving Confidence (self-assurance while engaged in problem solving), Approach-Avoidance Style (tendency to approach or avoid different types of problem-solving activities), and Personal Control (control over emotions and behavior while problem solving). The PSI has strong validity and reliability.[35]

Delay Discounting[35] – Participants choose between two hypothetical rewards, one sooner and one more in the future to measure decision making.

Brain Health Index [36] – the Brain Health Index includes a measure of nonverbal reasoning and processing speed which provide an index of general cognitive functioning and allow interpretation of other executive function tasks. These tasks are briefly administered on the computer.

Digit Span[37] -- The Wechsler Digit Span Task is a well-established measure of short-term memory. The test administrator reads 1 digit per second. The participant must repeat the digits verbatim. The number of digits increases by one until the participant consecutively fails two trials of the same digit span length.

Wisconsin Card Sort Test (WCST)[38]- The Wisconsin Card Sort Test is a well-validated neuropsychological measure of "set-shifting", or how well a participant can adapt to changing rules. The participant is presented with a number of stimulus cards that can be matched in three ways: the color of its symbols, the shape of its symbols, or or the number of shapes on each card. The participant must classify cards without knowing the classification rule and only receiving feedback on if the classification is correct or not. The classification rule changes every 10 cards.

California Verbal Learning Test (CVLT) – Food[39] -- The California Verbal Learning Test-II consists of two lists that are read aloud. Each list is comprised of 16 words drawn from 4 semantic categories (e.g. furniture), with 4 words per category. The first list (list A) is read 5 times followed each time by an immediate free recall test. The second list (list B) is then read, also followed by an immediate recall test. Then short-delay free- and cued-recall of list A is measured followed by a 20-minute non-verbal distractor task (Stop Signal Task- see below). Finally, long-delay free- and cued-recall and recognition of list A are tested. The CVLT-II generates over 30 indices that help to understand an individual's learning strategies. The CVLT-food is identical except for one category of words (4 words) is replaced with high calorie food words that are matched on word frequency with those of the original CVLT-II.

Stop Signal Task- Food Version[40]- The Stop Signal Task measures inhibition to food and non-food cues. On each trial, participants are asked to discriminate between a picture of calorically-dense food or neutral object (e.g, chair). The two primary outcomes, stop signal reaction time for food pictures (SSRT-food) and neutral pictures (SSRT-neutral) will be compared to assess for food-specific impulsivity versus general impulsivity.

Tower of London[41] – The Tower of London test is an extensively used measure of mental planning. Participants move disks between pegs of different lengths one at a time to match a sequence that has been presented to them in the fewest number of moves possible.

Trail Making Test (TMT)[42]- The Trail Making Test is an extensively used neuropsychological test of visual attention and task switching. Participants are instructed to connect a sequence of 25 dots as quickly as possible first connecting numbers, then letters, then switching between numbers and letters.

Continuous Performance Task (CPT)[43] – The Continuous Performance Task is a neuropsychological test that measures a subject's sustained and selective attention. Participants must press a key when a certain stimulus is presented but ignore other stimuli.

Questionnaires (all timepoints): Standardized questionnaires will also be assessed to evaluate psychiatric symptoms, stress, eating behavior, impulsivity and self-efficacy. The following questionnaires will be

administered: Eating Disorder Examination Questionnaire (EDEQ)[44], Detail and Flexibility Questionnaire (DFLEX)[45], Short-form of the UPPS-P Impulsive Behavior Scale (S-UPPS-P)[46], Perceived Stress Scale (PSS)[47], Yale Food Addiction Scale 2.0 (YFAS 2.0)[48], Patient Health Questionnaire – 9 (PHQ9)[49], Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF)[50], General Self Efficacy scale[51], Adult Eating Behaviour Questionnaire[52], Eating in the Absence of Hunger[53], Reward Based Eating Drive Scale[54], global Physical Activity Questionnaire[55], godin leisure time exercise questionnaire[56], GAD 7[57] , Difficulties in Emotion Regulation Scale (DERS)[58]

Adherence: Frequency of behaviors and skills taught in the program (e.g., self-monitoring, use of calendar, problem solving, exercising) will be assessed to evaluate whether treatment impacts behavior.

Feasibility and Acceptability (post-program only). Feasibility will be assessed by attendance of participants in program sessions. Acceptability will be assessed by survey (all time points except baseline), created by the study team based on established surveys used for Dr. Boutelle's current studies (e.g, IRB 151110). Likert-type ratings will be used to respond to questions, such as "How much did you enjoy the program?" and "How helpful did you find the program?" Participants will also be asked to complete a brief interview to describe their experience and respond to certain aspects of program to provide qualitative data to be used in future program development.

Self-Monitoring (at each program visit). At each program session, participants will turn in self-monitoring from the previous week and ratings of adherence will be assigned daily based on completeness of entry.

Audiorecording: All program sessions and assessments will be audiotaped for the purposes of supervision and fidelity. As audiotaping is required, participants will not need to sign a supplemental consent as this will be specified in the standard consent form.

Data collection protocol. The data for this study will include a number of different methods of collecting data. The questionnaires will be available as a secure web-based survey. All surveys and computer tasks administered online will be identified with the unique study ID rather than any identifying information. All interview data and executive function tasks will be collected under the unique ID. Following the first assessment visit, participants will be given the option of completing some surveys via the secure-web-based survey format prior to attending the in-person visit to reduce the amount of time they need to be present at CHEAR. If participants do not complete the surveys in advance, they will complete them as part of the visit. For survey questions completed at home that may warrant immediate follow-up (i.e., questions about suicidal ideation or self-harm), a REDCap alert via email will be set up to notify the study coordinator when those questions are complete. The study coordinator will check these alerts every business day and will send appropriate resources if the participant endorses suicidal ideation or self-harm. All assessors will be trained and certified in the tasks and interviews and supervised by the study PI. De-identified data will be stored in a database. It may be shared with others to aid future research efforts or put in a repository as recommended by the NIH. No identifying information will be kept with the data for future efforts or if entered into a repository. Permission to use this de-identified data has been included in the consent form for future studies on obesity, weight loss or executive function. It specifies that all identifiable data will be removed. The dates that data were collected will not be shared – only the length of time between collections will be provided to aid anonymity. The de-identified data will be kept by Dr. Eichen according to procedures identified with data storage below and she will only share data with those who have received permission to use it (e.g., have an approved exempt protocol).

Data Analysis and Interpretation: The pilot aspect of this study is to help evaluate the feasibility and acceptability of the program to aid in program development for a future randomized control trial. Data analyses will consist primarily of descriptive data, evaluating weight loss change and changes in executive function by evaluating pre and post assessment changes. Qualitative data will be used to continue to improve the NEXT

program development. Women and minorities will be included in recruitment for this study. Typically previous weight loss studies have had ~75% women participants.

10. HUMAN SUBJECTS

Study 1: It is expected that up to 60 individuals may be consented with a goal to have at least 20 participants enroll in pilot program who meet the following eligibility criteria for study 1,

Inclusion criteria:

1. Age 18-65
2. Ability to read English at a 6th grade level
3. BMI >25 and ≤45
4. Difficulties with executive functioning

Exclusion Criteria:

1) Medical condition that requires physician monitoring to participate in weight control program or prohibits safely participating in recommended physical activity
2) Psychiatric condition that could interfere with program participant (e.g., substance abuse, suicide attempt within previous 6 months, active purging)
3) Currently pregnant, lactating or plan to be in the timespan of program follow-up
4) Current enrollment in an organized weight control program
5) Change in psychotropic medication or other medication that could have impact on weight during the previous 3 months
6) History of bariatric surgery
7) History of learning disorder, neurological condition or injury

Study 2: It is expected that up to 150 participants may be consented with the goal to have at least 64 participants randomized to start group in study 2 with the same eligibility criteria that was used in Study 1 (presented above).

11. RECRUITMENT AND PROCEDURES PREPARATORY TO RESEARCH

Participants will be recruited using online advertisements such as Craigslist, university listservs, flyers to physicians, flyers posting on campus, in the community, and in physician offices, and direct mailings and direct email to participants, radio ads, ResearchMatch, social media, and professional referrals to the lab from local physicians. Participants may be recruited through the use of electronic medical records (EPIC system), a request for partial HIPAA waiver for recruitment purposes is submitted to do so.

We will also recruit potential participants through a "snowball recruitment" effort. Participants who have completed the study and have indicated that they have agreed to be contacted about future research will be sent an email requesting them to refer potentially eligible families to our recruitment team to be screened for the project. Participants who are currently enrolled will also be emailed the same materials. The emails sent to participants will contain information about the programs currently recruiting participants, a link to our lab's website, and a previously approved recruitment flyer.

Participants who respond to recruitment efforts will be asked to complete an initial online screen to determine initial eligibility if individuals do not have online access, they can complete an extended screening call that will include these questions as part of the telephone screen. Participants who meet study inclusion criteria will then complete a phone screen to further assess eligibility. If participants meet initial screening criteria, following the phone screen, they will be scheduled for an orientation at an in-person meeting or in a password-protected ZOOM meeting to learn more about the study, review the informed consent and have all questions answered.

12. INFORMED CONSENT

The online screening will assess for basic inclusion and exclusionary criteria. This process presents no more than minimal risk of harm to subjects, the waiver will not adversely affect the rights and welfare of the subjects and the research could not practicably be carried out without the waiver. For these reasons, we request a waiver of documented consent for the online screening. For individuals who do not have online access, the questions asked on the online screen can be administered over the phone in conjunction with the phone screen.
The phone screening will assess for basic inclusion and exclusionary criteria. Again, this process presents no more than minimal risk of harm to participants, the waiver will not adversely affect the rights and welfare of the subjects and the research could not practicably be carried out without the waiver. For these reasons, we request a waiver of documented consent for the phone screen.

All participants will complete written informed consent prior to enrollment at an orientation session. It is not likely that participants for this population will lack the capacity needed for consent. If there are any concerns, to ensure participants understand the consent form, they will be asked to describe what the study is about. For participants in which capacity for consent is judged to be questionable, they will complete the Mini-mental State Examination (MMSE) and if they receive under a 24, they will not be eligible for enrollment (i.e., surrogate consent will not be acceptable). It is highly unlikely that the MMSE will need to be administered to this patient population but if it is administered, documentation of the test results will be kept in the participant file.

This study will consent participants, either in-person or in a password-protected ZOOM meeting. For those who are consented in a ZOOM meeting, the participant will be emailed a copy of the consent form. During the ZOOM call, the study staff member will provide an opportunity for the potential participant to ask questions. When all of the potential participant's questions have been answered, the study staff member will ask the participant if they are ready to provide consent and then verbal consent will be obtained. Should the potential participant desire more time to make a decision to participate, they will be provided information on how to reschedule their ZOOM verbal consent call. We require a waiver of written consent for participants consented via zoom. Justification for this oral consent procedure is that the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. If the participant consents, they will then be scheduled for the initial assessment to confirm eligibility.

Both remote and in-person orientation and consent processes may take place with a group of potential participants. Participants may ask questions as a group and they will also be informed that they can each have an opportunity to privately ask additional questions. For those who attend a group ZOOM orientation, the consent form will be explained to the group of potential participants and then the consent process will occur individually between one staff member and one potential participant using the breakout room function on ZOOM. The potential participant will be given the opportunity to ask questions privately and provide verbal consent privately. If individuals are unsure as to whether they are willing to participate in the study, they may take the consent form home with them. If they later decide they wish to participate, they may schedule their first assessment and sign the consent form or provide verbal assent prior to participating in the assessment.

CHEAR staff members able to provide information about the study and carry out the consent procedures include:
Natalie Alamo, Daylin Anderson, Kerri Boutelle, Anthony DeBenedetto Dawn Eichen, Barbara English, Heather Halford, , Michael Manzano, Kaylen Moline, Monica Montoya, Saori Obayashi, Ellen Pasquale, Nicole Virzi, Jessica Willis.

Partial waiver of HIPAA authorization is being requested to aid in the recruitment purposes. We are requesting this so participants can provide verbal confirmation to their physician about their interest in participating and the physician can provide us the participant's name, age/date of birth, and contact information. This use of disclosure

involves no more than minimal risk, granting this waiver will not adversely affect privacy rights and welfare of the individuals whose records will be used, this recruitment could not practicably be conducted without the waiver, this could not practicably be conducted with the PHI to know who to contact, identifiers will only be used for the stated purpose and will be kept securely in our facility and electronically protected. Identifiers will be destroyed as soon as possible and at a maximum 3 years after study completion. PHI will not be used for any other purposes. Participants will be provided with all pertinent information as soon as possible upon formal consent.

13. ALTERNATIVES TO STUDY PARTICIPATION

The alternatives to participation in this study are to not participate and to seek a program with another therapist or community program.

14. POTENTIAL RISKS

1). Potential risk of psychological assessments. For some participants, disclosing potential information about mental health symptoms and eating behaviors may be uncomfortable. Questions regarding individual behaviors, emotions or attitudes may be considered sensitive to some participants.

2). Potential risk of program. Weight loss program may result in discussions of sensitive or distressing topics (e.g., challenges, difficulties) which may provoke emotional responses. Further, participants will be encouraged to increase their level of physical activity. Improper or too-vigorous exercise or physical activity, if performed by the participant against the advice of the research staff, could be associated with injury or discomfort. Although increasing physical activity can have great benefits, participants may also experience some general fatigue or sore muscles or joints from being active. It is also possible that participants could fall or be injured in association with being physically active. Although engaging in physical activity improves overall health, it is also associated with some risks, such as injuries and rare sudden events (e.g., heart attack, sudden death related to heart problems).

3). Potential risk of loss of confidentiality: Risk associated with breach of confidentiality of behavioral research data. Since this study includes interviews, recorded data and audio recordings, there is a small potential that this information might not be kept confidential (for instance by theft of study material).

15. RISK MANAGEMENT PROCEDURES AND ADEQUACY OF RESOURCES

Risks of psychological assessments: Participants will receive consistent support from the study staff throughout the study. Participants will be told that they are free to choose not to answer any questions that may cause them distress if they wish.

For any unidentified/unreported psychiatric concerns identified during assessments for this project, we will execute the following protocol:

1. Participant will be notified of concerns identified.
2. Participant will be given a list of referrals in the community.
3. If significant concern is warranted (participant reports suicidal ideation, significant binging and purging), participants will be immediately assessed by the clinical staff or a licensed clinical psychologist present at the meeting regarding severity and an appropriate psychiatric referral will be made. If the assessment visit is held via ZOOM, a clinical staff member or licensed clinical psychologist will join the ZOOM meeting to assess the participant for severity. Participants experiencing significant psychological distress or discomfort will be discontinued from the protocol and referred for counseling with their consent. If suicidal ideation is reported, thorough suicide risk evaluation consisting of the assessment of past suicide attempts, plans,

availability of means, and current stressors to evaluate extent of risk will be conducted. A safety plan will be completed in collaboration with the participant and referrals will be made for therapy or to a crisis center. If the participant appears to be at imminent risk for suicide, the clinician will call 911.

Potential risk of program: Participants will receive consistent report from study staff. If significant distress occurs during program, they will be allowed to take a break from program and talk to one of the study staff. If suicidal ideation is reported the above protocol will be followed.

We will aim to enroll individuals in whom the level of activity recommended is highly unlikely to pose a medical problem. To address readiness, questions in the online screen and phone screen will be asked that evaluate whether participants have conditions in need of special monitoring (physical impairments, history of heart condition, doctor ever say can't do physical activity). The staff will be trained in appropriate guidelines, recommendations and advice relating to physical activity for a community-based program of this type, in order to minimize the likelihood of injury or discomfort. For patients who may be at higher risk due to medication or previous history (e.g., taking beta blockers, history of cardiac problems), clearance from their medical doctor may be required before starting program. In these cases, participants will sign a release form and the study team will contact the physician to see whether the physician agrees the participant can participate in the recommended level of activity (at least 150 minutes of moderate intensity exercise). If there is any concern for safety/readiness and physician approval cannot be obtained, participants won't be enrolled. Potential complications associated with moderate intensity exercise training at levels recommended by the CDC/ACSM are rare. However, subjects may find exercising uncomfortable and may experience sprains, other soft tissue injuries, or bone injuries.

Potential risk of loss of confidentiality: The research team will make every effort to keep any information confidential. Any study material will be stored in locked cabinets in UCSD sponsored facilities. Furthermore, a unique identification number will be used for each person in data sets and spreadsheets that do not readily identify a name. The identifying name information containing material will be locked and stored separately from data files. Any electronic files containing identifying information will be password protected and stored on Pediatrics secure servers with only appropriate study staff having access. The online screen will be collected as 2 separate surveys on REDCAP so that the identifying information is collected separately from the other screening responses linked by an ID number. Only study staff, who are trained in confidentiality and HIPAA will have access to the password protected identifying information and ID link. Accordingly, the online screen is submitted as 2 separate parts to delineate this separation. Similarly, the phone screen has been officially split into two documents. An ID number will be assigned and kept password protected with the identifying information only accessible to PI and designated study staff. Part 2 will be identified only with the ID number. Part 1 and Part 2 of the phone screens will be stored in separate locked filing cabinets.

Lastly, participants are informed of the option to complete all of the information on the online screen on the phone where they can provide the information.
To help maintain confidentiality of participants, if emailing more than one participant (e.g., emailing about reminder for program session), all participant's email addresses will be kept confidential by using the BCC function and no participant names will be included. When emailing participants from email templates, staff will copy from our templates instead of forwarding from emails sent to other participants and to always start new e-mail documents to ensure no participant email information is accidentally disclosed to another participant.

Data Safety Monitoring Plan: Because of this low risk status, the data and safety monitoring plan (DSMP) for this trial focuses on close monitoring by the principal investigator (PI) and Drs. Boutelle and Twamley, the primary mentors, and Dr. Robert El-Kareh, the safety officer, along with prompt reporting of excessive adverse

events and any serious adverse events to the NIH and to the IRB at the University of California, San Diego. Although the likelihood is low, there will be established procedures for monitoring and responding to adverse events resulting from moderate intensity physical activity. All participants will be given an instruction sheet at the start of the study that details what to do for common exercise-related injuries. Participants will be asked to reported injuries and health related problems that arise during program to the study PI. In the event of an injury requiring immediate assistance, the participant will be instructed to contact their primary care physician, and if necessary, go to the closest emergency center. All adverse events, UPRs or protocol deviations will be submitted to the IRB and the NIH as appropriate according to current policies. For Study 2, formal reports of adverse events will additionally be send to the safety officer.

Qualifications and responsibilities of the Safety Officer: The safety officer for study 2 will be Robert El-Kareh, MD, MS, MPH. Dr. El-Kareh is an internal medicine physician at UCSD with an MPH in clinical effectiveness. Dr. El-Kareh has an in depth understanding of the types and severity of comorbidities and injuries associated with adult obesity. As Safety Officer, Dr. El-Kareh will review the reports sent by Dr. Eichen or her study coordinator and will evaluate the information below presented to him to determine whether there is any corrective action, trigger of an ad hoc review, or stopping rule violation that should be communicated to the study investigator, the University of California San Diego IRB, and the NIDDK.

16. PRIVACY AND CONFIDENTIALITY CONSIDERATIONS INCLUDING DATA ACCESS AND MANAGEMENT

We will implement the following security plan to promote security of the data and privacy of the participants.

- Data collection will be completed with an emphasis upon maintenance of confidentiality. We plan to extract data from questionnaires and in-study behavioral measures. Only Dr. Eichen /her research staff, each of whom has completed the required trainings will have access to any personal health information collected. We will assign participants a study identification number unrelated to identifying information. The study ID number will be used by participants on their questionnaires and data collection forms. The only materials containing subject identifying information will be the consent and HIPAA forms. We will create a master list linking the de-identified study identification number to the participant's record. The master list will be maintained by Dr. Eichen in her laboratory. There will be only one password protected electronic version of this file. Access to the master list will be limited to the P.I.s and their designees, all of whom will have completed UCSD IRB training requirements. At the earliest opportunity and no later than 36 months following data analysis, the master list (i.e., the only source that links the study identification numbers to the individuals) will be destroyed by Dr. Eichen.

- All study data will be electronically entered only using the study ID number. These data will be stored on secure UCSD pediatrics servers only accessible to study staff.

Use of the study data will be limited to the proposed study unless future approval of use of the de-identified data is granted. The consent form has been modified to include permission of the participants for their de-identified data to be used. De-identified data will be kept securely by the PI Dawn Eichen. It is common practice to store de-identified data for use in the future.

17. POTENTIAL BENEFITS

Potential benefits include weight loss and improvement in executive function.

18. RISK/BENEFIT RATIO

There is a relatively low risk to participants given the potential benefit of losing weight and improving

executive function and the knowledge gained from this study is significant. Given that the risks are minimal and the potential for benefit is great, the risk/benefit ratio is considered to be small and reasonable for the conduct of this study.

19. EXPENSE TO PARTICIPANT

There is no cost to participants to participate in the study

20. COMPENSATION FOR PARTICIPATION

Each study 1 participant will receive $25 for the baseline assessment, and $50 for the post-group assessment.

Each study 2 participant will receive $50 for the mid-program assessment, $100 for the post-program assessment, and $150 for the 6-month follow-up assessment. Participants who withdraw, but who wish to have their weight measured or self-report their weight to study staff at follow-up time points will receive a $25 gift card at each assessment time point (mid-program, post-program, and 6-month follow-up) that remains after the point which they withdrew. Participants who enroll and complete all assessment visits can earn up to $300.

21. PRIVILEGES/CERTIFICATIONS/LICENSES AND RESEARCH TEAM RESPONSIBILITIES

Dawn Eichen Ph.D. (PSY27823) is a licensed clinical psychologist and PI of the study. She will be responsible for training and supervising study and certifying assessors and will oversee the budgetary and administrative tasks management of the study, including the budget, hiring personnel, personnel issues, equipment management, NIH compliance and implementation of refinements to the protocols. She may also conduct assessment and group and supervise group.

Kerri Boutelle, Ph.D (PI) is a professor in residence in the UCSD department of psychiatry and a licensed clinical psychologist. Her research specializes in the study of obesity and eating disorder behaviors. Dr. Boutelle will help with study design, supervision of treatment and assistance with interpretation of findings.

Elizabeth Twamley, PhD, is a licensed clinical psychologist and mentor on this project. She will aid in development of the treatment, supervision of treatment

Sonia Jain, PhD, is a statistician and may help with study analysis and database set up. She will only have access to de-identified data.

Dr. Eastern Kang, is a postdoctoral fellow. He will oversee data analyses including evaluating all data entry accuracy, merging of data files, creation of scales, and evaluating initial frequencies and means.

Ms. Ana Lopez, is the data manager. She will assist with creating the database, entering and cleaning the data.

Kaylen Moline is the study recruitment coordinator. She will coordinate all the recruitment and maintenance of the cohort for the study.

Allison Tietz is the study coordinator. She will maintain and communicate with the study cohort, run assessments, and aid in recruitment, the preparation of assessment and group materials, scheduling, and the collection of program data.

The following individuals are part of the CHEAR Assessment staff. They include graduate students and recent graduate program graduates and postbacs who conduct clinical assessments and can serve as group leaders or co-leaders. They may also introduce the study and obtain consent. Everyone has CITI training:
Natalie Alamo

Daylin Anderson
Paige Awtrey
Anthony DeBenedetto
Barbara EnglishCarmen Garcia-Sevillano
Heather Halford
Farah Krayem
Michael Manzano
Monica Montoya
Saori Obayashi
Ellen Pasquale
Mieko Pretlow
Alicia Rickels
Alexiss Rivas
Nicole Virzi
Jessica Willis
Rachel Wynveen

The following individuals are Research Assistants at CHEAR. These include undergraduate research assistants and high school volunteers who help oversee the assessments and introduce the studies to the participants and may obtain consent. They also may help assist with group material preparation and obtaining heights/weights. Everyone has verified CITI training prior to beginning.
Research assistants:

Corinne Blucher
Lucia Ferrer
Lauren Hamel
Andre Hirakawa
Alexander Lane
Matthew Moncayo
Sarah Perlman
Nyako-Senait Saadiq
Maya Selvaraj

Connie Zhang
Alison Zhao

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23. FUNDING SUPPORT FOR THIS STUDY

Funding will be provided by NIDDK K23DK114480-01A1

24. BIOLOGICAL MATERIALS TRANSFER AGREEMENT

N/A

25. INVESTIGATIONAL DRUG FACT SHEET AND IND/IDE HOLDER

N/A

26. IMPACT ON STAFF

N/A

27. CONFLICT OF INTEREST

There are no conflicts of interest

28. SUPPLEMENTAL INSTRUCTIONS FOR CANCER-RELATED STUDIES

N/A

29. OTHER APPROVALS/REGULATED MATERIALS

none

30. PROCEDURES FOR SURROGATE CONSENT AND/OR DECISIONAL CAPACITY ASSESSMENT

N/A