STUDY PROTOCOL

NCT04606199
IRB ID: 19-27198
Examine the Effects of Meditation on Daily Psychological Stress Responses in Woman With a History of Child Adversity
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Study design: The study uses a small micro-randomized trial design–a design that randomly assigns an intervention at each notification time point. In the proposed study, participants use the study app for 30 days and receive up to 3 notifications/day (morning, afternoon, evening). At each notification time point, participants first complete a brief ecological momentary assessment of their current psychological states (feeling stressed, positive/negative affect, stress appraisals, perseverative cognitions). Then, at each notification, each participant is randomized (50% probability) to either receive a brief mindfulness-based intervention (randomly selected from a pool of interventions) or no intervention. Thus, participants are randomized many times over the study (and each intervention is randomized many times to each person). Psychological states are again measured about 15 minutes after a notification to compare proximal (within 15 min) changes in intervention targets following an intervention vs. no intervention (proximal treatment effect).

Human Subjects Involvement, Characteristics, and Designs
I will recruit a new sample of adults, all of whom are women exposed to early life adversity. The rationale for my focus on this population is informed by the detrimental health effects of early life adversity, and by a lack of empirically-based non-pharmacological interventions to buffer or reverse risk pathways.
The study aims to develop an Ecological Momentary Mindfulness-based Intervention (EMMI) that targets maladaptive daily psychological stress responses. A micro-randomized trial will test target engagement and obtain qualitative acceptability/feasibility data during the development of the EMMI.
Inclusion criteria:
1) female
2) age 30-60
3) ≥2 Adverse Childhood Experiences
4) mild depressive symptoms (Patient Health Questionnaire ≥ 5)
5) having a smartphone

Exclusion criteria:
1) non-English speaker or unable to provide informed consent
2) current regular mindfulness practice (>20 min/week)
3) major psychiatric condition that necessitates priority treatment or interferes with participation, including psychoti disorder, bipolar disorder, Post-Traumatic Stress Disorder (PTSD), substance abuse/dependence, major depression (also indicated by PHQ-9 ≥ 15), self-harm or suicidal ideation (also indicated by PHQ-9, item 9)
4) Medication use and psychotherapy treatment has not been stable over the past 3 months.

Sources of Materials
The data collected in this study will include responses on self-report questionnaires, a short (15-20 minutes) diagnostic interview, app-based ecological momentary assessments and interventions, and audio-recordings of qualitative feedback on acceptability and feasibility. All data will be used for research purposes only. All data will be entered into or collected in electronic form. App-based ecological momentary assessment and intervention data will only use de-identified study ID numbers. Electronic data will be stored on a private, password-protected, encrypted hard drive accessible only to the PI or trained, authorized study staff. Hard copy data will be kept in locked filing cabinets in a locked office. Identifying information will be stored separately from data.

Potential Risks

Psychological distress from self-report questionnaires, diagnostic interviews, ecological momentary assessment of psychological responses, or generally heightened distress: Participants may experience temporary emotional discomfort or stress from responding to questions about their mental and physical health, early life adversities, and current psychological states. Although it is not anticipated that this study will cause significant psychological distress, it is likely that recruitment and assessment procedures will identify participants with elevated levels of distress. Protection against the risk that significant distress, and possibly worsening of depressive symptoms, and, in some cases, self-harm or suicidal ideation is developed during the study is outlined below.

Psychological distress from audio-recorded qualitative interview: Audio-recorded semi-structured interviews will obtain qualitative information on the acceptability and feasibility of the Ecological Momentary Mindfulness-based Intervention (e.g., satisfaction with each intervention component, preferred frequency/duration of assessment and intervention sessions, any challenges that participant encountered in using the app, and general feedback on app usability). Interviews carry a minimal risk for emotional discomfort and stress. Efforts will be taken to maintain the participant's comfort and study procedures will be stopped at the request of the participant.

Psychological distress from participation in the intervention: Participation in the Ecological Momentary Mindfulness-based Intervention (EMMI) includes short ecological momentary assessments (1-2 minutes/notification) and brief audio-guided mindfulness-based interventions. Previous studies of mindfulness interventions, including those recruiting individuals with early life adversity and trauma, demonstrated reduced distress (depression and anxiety), enhanced coping and mood, and improved quality of life. Thus, the EMMI carries minimal risk for emotional discomfort or stress.

Confidentiality: Participation in research may involve a loss of privacy, however information will be handled with the upmost confidentiality. One limit to confidentiality is if a participant is at imminent risk of harming herself (see more under Protection Against Risk).

Inconvenience: There may be some burden associated with filling out self-report questionnaires and completing repeated ecological momentary assessments and interventions in the flow of everyday life. However, participants will be provided with compensation for their time and effort.

ADEQUACY OF PROTECTION AGAINST RISKS

Recruitment and Informed Consent

Prior to study commencement, all procedures will be approved by the UCSF Committee on Human Research (CHR, the equivalent to IRB). Potential participants will be recruited using methods my mentors, advisors, and I have found successful in previous research with participants with high exposure to early life adversity. Participants will be recruited via advertisements posted in Bay Area newspapers, listservs, Craigslist, Facebook, community-based self-help groups (e.g., Children of Alcoholics), and ResearchMatch. Research assistants will contact potential participants who respond to the recruitment ads by phone. Participants will undergo a phone screening to determine eligibility for the first assessment visit. If eligible for an initial visit, they will receive more details of the study by phone and a study appointment will be scheduled. At the beginning of the appointment, a trained research assistant will obtain written informed consent adhering to the following procedures: provide the potential participant with an opportunity to read the consent form; review the consent form in detail; answer questions; and, ask the potential participant to explain back in her own language what she understands the procedures to involve. Potential participants will have the opportunity to sign the form, decline participation, or to consider their decision further. The consent forms will provide the following information: background and purpose of the study, scope and length of participation, randomization procedure, study procedures, follow-up assessments, legal and ethical limits to confidentiality (including, for example, imminent risk of harming oneself), audio taping procedures, risks, benefits, alternatives, ability to discontinue participation, privacy and confidentiality, posting of clinical trial information at ClinicalTrials.gov, compensation, and whom to contact with questions. Participants will be assured that their decision to participate or decline participation in the study will have no effect on their current or future receipt of healthcare services at UCSF or affiliated clinics. Participants providing informed consent will complete further in-person screening procedures (e.g., complete PHQ-9) to determine eligibility. Only participants meeting all criteria (see above for inclusion and exclusion criteria) will be enrolled in the study.

Many efforts will be taken to promote retention: A research assistant will demonstrate the use of the app during the initial visit to ensure compliance. While using the study app, participants also have the option to postpone a notification if they are currently unavailable and prefer to complete assessments/interventions at a later time

point. Lastly, a trained research assistant will also make weekly phone contact with participants to address potential difficulties with adherence.

Protection Against Risk

Participants will be told that their participation is voluntary, and they can choose to withdraw from the study at any time without further obligation.

Psychological distress from self-report questionnaires, diagnostic interviews, and ecological momentary assessments: Participants will be told that they do not have to complete any questions, interviews, assessments, or interventions they do not want to complete and can stop at any time. Participants can also contact study staff to discuss any concerns.

Identification of participants with heightened distress: The proposed study aims to develop and pilot test an intervention tailored for individuals who have been exposed to early life adversity. As such, the recruitment and assessment procedures will identify individuals who will have subclinical or higher depressive symptoms. Some of these participants may be experiencing particularly significant distress and require clinical services beyond what the intervention will be able to provide. Thus, major psychiatric conditions (as determined by a diagnostic interview and the 9-item Patient Health Questionnaire, PHQ-9), including current moderately severe depressive symptoms (PHQ-9 ≥ 15) and self-harm or suicidal ideation (e.g., participant endorsed item 9 on PHQ-9: "Thoughts that you would be better off dead or of hurting yourself in some way") are an exclusion criterion. Dr. Mayer's study and mentoring team will immediately intervene and make appropriate referral for community care for participants. The study team will closely monitor depressive symptom severity and suicidal ideation among enrolled participants via weekly administration of the PHQ-9. Participants are instructed to make immediate contact with study personnel with any issues, questions, or concerns regarding worsening symptoms. At the first assessment visit, regardless of their current expressions of distress, participants are provided study contact information as well as local therapeutic and crisis resources. All study staff will be trained to probe for suicidal thoughts, intent, and psychotic behavior. If there is any suspicion of suicide risk or if participant endorses item 9 on the PHQ-9, study staff will immediately contact Dr. Mayer so that appropriate steps can be taken to ensure the safety of the participants. Dr. Mayer is a clinical psychologist who has extensive experience in assessing suicidal ideation and treating depression. She is a licensed Psychologist in the State of California. Dr. Mayer and her study team will follow a written protocol for assessing and responding to suicide risk. This includes the evaluation of risk factors (e.g., plan, intent, access to lethal means) and protective factors (e.g., social support). For imminent risk, study staff will call emergency services and remain with the participant until emergency services arrive. For low to medium risk, study staff will provide mental health resources or psychological referrals, if needed.

Psychological distress from qualitative interviews (feedback on acceptability/feasibility): Participants will be invited to a private and comfortable interview room to provide feedback on the acceptability and feasibility of the study app. A research assistant will conduct the semi-structured interview with the participant. Participants will be asked to provide permission for the audio recording. For participants who do not provide permission, the research assistant will take written notes during the interview.

Discomfort associated with participation in the intervention: Participants will be provided with a thorough description of the Ecological Momentary Mindfulness-based Intervention prior to initiating treatment. They are notified that they can withdraw participation at any time without penalty. We expect that the proposed intervention would be associated with improved outcomes. However, important precautions will be taken to minimize risks, including weekly monitoring of depressive symptoms and suicidal ideation.

Confidentiality: All data will be handled with the maximal attention to participants' confidentiality. Subjects will be assigned unique, coded, confidential identifiers that will be used to label all data forms, data entries, and questionnaires. Identifiable information, such as name, will not appear on these materials or data files. The key linking the subjects' identity to their unique coded identifier will be kept in a confidential manner in a locked file cabinet within a locked office at UCSF or password protected on an encrypted and secure server at UCSF, which will only be able to be accessed by Dr. Mayer, and the study coordinator, when necessary. One limit to confidentiality is when a participant indicates being at imminent risk of harming herself. Participants will be informed of the legal and ethical limits to confidentiality during the consent process. If a participant endorses self-harm or suicidal ideation, we will follow above outlined procedures.

Inconvenience: All efforts will be made to minimize participant burden. Participants may be inconvenienced by the time spent during the daily ecological momentary assessments and interventions. Participants will be compensated for their time and effort.

POTENTIAL BENEFITS OF THE PROPOSED RESEARCH TO THE SUBJECTS AND OTHERS

There is strong conceptual basis to predict the benefit of a mindfulness-based ecological momentary intervention, including for participants with early life adversity. The minimal risks participants may experience in this study are reasonable in relation to anticipated benefits. Participants may experience improved psychological responding to daily stressors, improved mental and physical symptoms, as well as improved physiological markers as a result of daily mindfulness practices that are incorporated into everyday life. In the long-term, there are substantial benefits to be gained by developing and evaluating a mindfulness-based ecological momentary intervention to improve daily psychological stress responses, and ultimately to reduce or reverse psychological risk pathways associated with early life adversity.

IMPORTANCE OF THE KNOWLEDGE TO BE GAINED

Despite evidence that early life adversity can have detrimental consequences for midlife mental and physical health, there is a paucity of mechanism-focused non-pharmacological interventions. As a result of the proposed study, we will learn more about the psychological mechanisms linking early life adversity with midlife health outcomes, which will inform intervention targets, and about the acceptability, feasibility, and adherence of a mindfulness-based ecological intervention. This research will provide the preliminary data needed to evaluate the intervention in an adequately powered study.

STATISTICAL ANALYSIS

Using the centered and weighted least square method, which has been recommended for the analysis of proximal treatment effects in micro-randomized trials, I will test proximal (within 15 min) target engagement (also termed “proximal treatment effect”) by comparing changes (from current states at notification to about 15 min later) in each primary intervention target (positive/negative affect, threat/challenge appraisal, perseverative cognition) after an intervention vs. no intervention.