ISU IRB: 23-026-00
Approved Date: 07/25/2023
Expiration Date: 02/20/2024

INFORMED CONSENT DOCUMENT
Iowa State University
Department of Kinesiology

Title of Study: Calm/active Before Therapy Study (CBT+ Study)

Investigators: Dr. Jacob D. Meyer, PhD (Principal Investigator)

This form describes a research project. It has information to help you decide whether or not you wish to participate. Research studies include only people who choose to take part—your participation is completely voluntary. Please discuss any questions you have about the study or about this form with the project staff before deciding to participate.

Funding: This study is funded by the National Institute of Mental Health

KEY INFORMATION

This research examines how pre-therapy behaviors influence the effectiveness of cognitive behavioral therapy as a treatment for depression. You are being invited to voluntarily participate in this research.

If you decide to participate, you will be screened for eligibility during an intake visit. If eligible, you will complete 8 weeks of cognitive behavioral therapy (CBT). Prior to each therapy session you will either rest calmly or exercise for 30 minutes, depending on the group you are randomly assigned to. Blood samples will be taken during some visits. You will also complete additional visits 1 week, 12 weeks, and 12 months after the last CBT session. Total participation lasts for about 15 months, although most study activities occur during the first three months.

Risks include physical discomfort, psychological stress, social stigma, and breach of confidentiality. You may benefit from cognitive behavioral therapy. You do not have to participate in this study to receive those benefits however—you can receive cognitive behavioral therapy by visiting a mental health provider.

Detailed information about study procedures, risks, benefits, and how we protect your confidentiality contained in this document. Please review it carefully and ask the study team any questions that arise.

INTRODUCTION

The purpose of this study is to understand how pre-therapy preparatory activities influence the effectiveness of cognitive behavioral therapy (CBT). This study will provide the necessary first step for future research aimed at improving behavioral treatments for depression. You are being invited to participate in this study because you:

- Are aged 18-65
- Currently meet the diagnosis for a depressive disorder
- **EITHER** not currently taking anti-depressants **OR** are on a stable anti-depressant regimen for the past 8 weeks and are willing to maintain the regimen for the duration of the study
- Have never used structured cognitive behavioral therapy

- Are willing and can safely perform exercise
- Are not abusing alcohol or other substances
- Are not currently using illegal drugs
- Are not currently using tobacco products
- Are not currently taking cardiovascular medications

Due to the potential impact of certain conditions on study outcomes, you will be excluded from participation if you:

- Are currently pregnant, nursing, or planning to become pregnant
- Suffer from comorbid psychiatric conditions (except for Generalized Anxiety Disorder)
- Have a body mass index ≥40

Research staff will make inclusion/exclusion decisions regarding your participation based on your responses to questions during this initial visit. You will be excluded from participation if you are deemed ineligible to participate based on your responses.

*If you have any questions **about the inclusion and exclusion criteria for this study**, please ask the study staff now.*

DESCRIPTION OF PROCEDURES

If you agree to participate, you will be asked to complete an initial Intake Visit (today's visit), 8 sessions of weekly Calm or Active CBT, and a Final Visit within the week after the last CBT session and 2 Follow Up Visits (12 weeks and 12 months after the Final Visit), with further descriptions of each visit listed below.

Intake Visit (~2.5-3 hours)
During the Intake Visit, you will read, ask questions, and sign the informed consent document, verbally verify you continue to meet the inclusion/exclusion criteria, and complete a structured clinical interview for depression with a trained therapist. If eligible to participate, you will complete several other questionnaires about your health, wellbeing, and activity level. Your height, weight, blood pressure, and heart rate will be measured. You will also be given an activity monitor to wear for one week and return it during your first CBT session. At the end of this visit, you will be randomized into CalmCBT (quiet rest prior to therapy) or ActiveCBT (exercise prior to therapy).

Prior to each therapy session, you will be asked to refrain from caffeine containing drinks and using tobacco/nicotine products 2 hours prior to sessions, refrain from consuming alcohol and from fatiguing exercise 24 hours prior to sessions, and refrain from changing regular medications or treatments during the course of the study. These lifestyle considerations are important to limit the variability in the way that people respond to the Calm and Active sessions and how that may then influence the therapy sessions.

Calm and Active CBT Sessions (~2 hours)
During the 8-week treatment period, we will ask that you to arrive 45 minutes prior to the start of your CBT session. You will begin each session with a few brief questionnaires about how you are feeling, and blood pressure/heart rate will be recorded. You will then begin a Calm or Active condition (depending on randomization). If randomized to CalmCBT, you will begin with a 30-minute quiet rest session, in which you will sit in a quiet room. If randomized to ActiveCBT, you

will begin with a standardized 30-minute moderate or 'somewhat hard' exercise session on a stationary recumbent bicycle. During this time, we will ask that you refrain from using other devices (e.g. cell phone) and sources of entertainment (e.g. music). Both sessions are described in greater detail below. After rest or exercise, you will again complete a few brief questionnaires about how you are feeling. During sessions 1, 4, and 8, we will also take a blood sample before and after you exercise or rest and after your CBT session (3 blood draws total on visits 1, 4, and 8).

Within 10 minutes, you will begin your CBT session with a trained therapist. Each CBT session will last approximately 50 minutes. Audio from these sessions will be recorded to ensure the therapist is applying the CBT techniques in a standardized way across all participants. The therapist and CBT session supervisor (a co-investigator of this study, Nathaniel Wade, PhD, Director of the Counseling Psychology Graduate Program at Iowa State) will be the only study team members who listen to these sessions. Afterwards, we will ask you to complete a few more brief questionnaires and schedule your next appointment. Additionally, after therapy sessions 4 and 8, you will be asked to re-wear the activity monitor for one week.

Final and Follow-Up Visits (~2 hours each)
Your final visit will take place within one week of your final therapy session. During the Final Visit, you will first undergo the structured clinical interview for depression by a clinical interviewer. You will then complete several other questionnaires about your health. Next, height, weight, blood pressure, and heart rate will be taken. Finally, in concluding this visit and your enrollment in the study, you will be provided with printed reports of your personalized physical activity and sitting behaviors from each time that you wore the activity monitor and be able to ask any questions over these documents and the study in general. You will return for Follow-up Visits 12 weeks and 12 months after the end of therapy. This visit will be identical to the Final Visit in procedures.

*If you have any questions **about the study procedures**, please ask the study staff now.*

DESCRIPTIONS OF ASSESSMENTS

Questionnaires. You will be asked to complete several questionnaires about your health, physical activity, how you are feeling and other psychological factors. Most questionnaires will be completed electronically, and all data that will be used from your responses to the questions will only be associated with your study ID number. You will be able to skip any questions that you do not feel comfortable responding to.

Blood Sample. A trained phlebotomist will collect approximately 4 teaspoons of blood before exercise, after exercise, and after CBT sessions during weeks 1, 4, and 8. These samples will be drawn via venipuncture. Blood samples will be collected to examine the response of blood biomarkers before and after the rest or exercise condition.

CalmCBT Quiet Rest Session. Supervised quiet rest sessions will consist of 30 minutes sitting in a quiet room. Continuous monitoring of heart rate and rating of exertion will occur throughout quiet rest. Also, during quiet rest, a standardized animal documentary series ("Nature") will be played.

ActiveCBT Exercise Session. Supervised aerobic exercise sessions will consist of steady-state exercise at a moderate intensity corresponding to a '13' or 'somewhat hard' rating of perceived exertion, using the Borg Rating of Perceived Exertion Scale. The exercise session will

begin with a 3–5-minute warm up and include a built-in cool-down (during the last 3 minutes of the 30-minute exercise session). Continuous monitoring of heart rate, resistance/load, and rating of exertion will occur throughout exercise. Also, during exercise, a standardized animal documentary series ("Nature") will be played.

Cognitive Behavioral Therapy Session. Each CBT session will be conducted by a trained therapist and be under supervision of Nathaniel Wade, PhD, a counseling psychologist at Iowa State University. The sessions will be completed in a private room at the College of Human Science Testing Center. To ensure standardization of the sessions, audio recordings of the sessions will be collected. Information shared in these sessions will solely be used to quality check the sessions and ensure standardization between participant experiences.

*If you have any questions **about the study assessments**, please ask the study staff now.*

RISKS OR DISCOMFORTS

There are some risks and/or discomforts you may experience during participation of this research study. Each risk is detailed below, along with a description of how the research team will attempt to minimize their occurrence.

Exercise. Exercise sessions are generally very safe and tolerable. Most complications are minor and may include shortness of breath and feeling dizzy or fatigued. Very rarely a heart rhythm abnormality or heart attack may occur during exercise, requiring resuscitation and hospitalization. However, this is extremely uncommon even during maximal exertion and you will be closely supervised by trained personnel throughout the moderate exercise session.

Risks of the Blood Draws. There is a rare risk of fainting or dizziness. There is also a small risk of bruising or bleeding at the site of the needle (about 1 in 10 cases), and an extremely small risk (about 1 in 1000 cases) of infection. The total quantity of blood collected across all visits will be about 180 mL (~37 teaspoons), much less than that taken during a single donation at the Red Cross Center or a blood drive (500mL or ~101 teaspoons). On rare occasions, the needle may damage a nerve or the vein, causing the vein to become blocked. Additionally, there is a small risk of fainting or dizziness during and after the blood draws. These risks will be minimized by using trained phlebotomists to draw the blood and using sterile equipment in an area designed for the collection of blood samples. Two research staff members will be present in case the participant begins to feel faint or dizzy.

Psychologic stress from mental health questions. There may be limited psychological stress related to discussing mental health questions during the clinical interview. Dr. Meyer and Dr. Wade have supervised the training of the personnel who administer the clinical mental health interviews and CBT sessions. Dr. Wade, a licensed psychologist in the state of Iowa, will provide guidance to the person performing the clinical interviewer and CBT sessions to help them in minimizing any psychological distress that may be experienced while discussing mental health issues. For participant safety, during the Intake Visit or first therapy session, you will collaboratively create a safety plan with the clinical interviewer or therapist (respectively) to provide support if dealing with suicidal thought any time throughout or after the study.

Additionally, the research team will closely monitor suicidality throughout the study. If any severe responses are encountered, the clinical interviewer or therapists will follow up with you to assess suicide severity and facilitate activation of your safety plan if needed. If unable to get ahold of you, emergency services will be contacted to perform a welfare check. If at any time

during the study, it appears you may be an imminent threat to yourself, emergency personnel (either Iowa State University police or city police) will be contacted to help you transport to additional emergency services (e.g., community mental health services). Further, as part of the study safety protocol, participants will discontinue participation in the study if any of the following occur: hospitalization for suicidality, law enforcement transportation to emergency services, suicide attempt, or the therapist or clinical interviewer indicate a high suicide risk on assessments during the study visits or therapy sessions. Please note, these protocols are in place because your health and safety are of the utmost importance to our research team. We will offer help connecting you to other mental health services and treatments if any of the above occur.

Social risk due to stigmatization. There may be some social risk regarding the disclosure of mental health information. The main risks are harm to reputation, embarrassment, or stigmatization if participation in the study becomes known, but given the study procedures, this risk is low. Nonetheless, strategies to reduce this risk include:

- Using a strategic study name that does not disclose the clinical outcome being evaluated in the study
- Having all assessment visits on an individual basis to minimize contact with other participants
- Having assessment visits performed in closed rooms to minimize the chance of being noticed by others
- Having Active and Calm pre-therapy sessions occur in an exercise space that is advertised as hosting numerous studies. Signage and flyers for the multiple studies will be posted outside of the exercise space

Breach of confidentiality. Confidentiality will be a central value of this study. However, there are situations in which confidentiality might need to be breached. Research staff are permissive reporters, meaning they will voluntarily contact local authorities or other health service providers if you reveal (a) that a child or older adult is being abused or severely neglected, or (b) that you are an imminent threat to yourself or someone else. If a report is made, this may be a breach of your confidentiality. We are making you aware of this potential need to breach your confidentiality by informing you here, as well as having this specifically discussed with the clinical interviewer during the Intake Visit.

To further reduce all risks, all research personnel will have had extensive training and supervision prior to assisting with study visits. As noted above, all clinical interviewers and therapists are trained and supervised by Dr. Wade (licensed clinical psychologist in Iowa). Dr. Lansing (Research Scientist with over 5 years of experience conducting physical activity interventions) trains and supervises study personnel on all study visit procedures and assessments. On-going training and supervision of these assessments will occur during the entire study duration.

*If you have any questions **about the study risks or training of the research staff**, please ask the study staff now.*

BENEFITS

By participating in the study, you will receive 8 weeks of cognitive behavioral therapy with a trained therapist for treatment of depression. Cognitive behavioral therapy is currently a frontline

treatment for depression, so enrollment in this study will actively treat depression and may help reduce symptoms and improve quality of life. Additionally, during the Final Visit, you will be provided with personalized activity data.

COSTS AND COMPENSATION

There are no cost and no compensation associated with this study.

PARTICIPANT RIGHTS

Participating in this study is completely voluntary. You may choose not to take part in the study or to stop participating at any time, for any reason, without penalty or negative consequences. You can also skip any questions that you do not wish to answer. Participating or choosing not to participate will not affect your relationship with any of the study personnel or with your health care provider. You can continue receiving care from your primary health care provider regardless of your participation in the research. Your choice of whether or not to participate will have no impact on you as a student/employee of Iowa State University in any way. If you become pregnant during this study or if the medications you routinely take for psychological reasons change, please inform the staff, and you will be removed from the study.

*If you have any questions **about the rights of research subjects or research-related injury**, please contact the IRB Administrator (515) 294-4566), the IRB Director (515) 294-3115), or IRB@iastate.edu*.

RESEARCH INJURY

Please tell the researchers if you believe you have any injuries caused by your participation in the study. The researchers may be able to assist you with locating emergency treatment, if appropriate, but you or your insurance company will be responsible for the cost. Eligible Iowa State University students may obtain treatment from the Thielen Student Health Center. By agreeing to participate in the study, you do not give up your right to seek payment if you are harmed as a result of being in this study. However, claims for payment sought from the University will only be paid to the extent permitted by Iowa law, including the Iowa Tort Claims Act (Iowa Code Chapter 669).

CONFIDENTIALITY

Note: In this section, we will refer to both the National Institutes of Health (NIH) and the National Institute of Mental Health (NIMH). The NIMH is the federal agency funding this research; it is a sub-agency of NIH, which has a set of policies governing data collection, data sharing, and privacy/confidentiality for research to which the agency awards funds.

Records identifying participants will be kept confidential to the extent permitted by applicable laws and regulations and will not be made publicly available. However, federal government regulatory agencies, auditing departments of Iowa State University, The National Institute of Mental Health, and the Institutional Review Board (a committee that reviews and approves human subject research studies) may inspect and/or copy study records for quality assurance and data analysis. These records may contain private information.

To ensure confidentiality to the extent permitted by law, the following measures will be taken:

- Only subject ID codes will be used for randomization, data processing and analyses
- Blood samples, physical activity, self-report and cognitive testing data will be de-identified and marked with subject ID code to minimize any risks of confidentiality
- The single copy of the document linking your name with subject ID codes will be kept in a password protected electronic file, separate from other data and under control of approved researchers.

Additionally, we will use REDCap software which will eliminate the need for hard copies of each questionnaire to be filled out. REDCap is a secure web application specifically developed for building and managing large databases for clinical trials. Most questionnaires in this study will be filled out on a computer or ipad and the data will be automatically stored to a password protected REDCap project, only available to authorized research staff. Any identifying information (e.g., name) will be flagged as an identifier, which will restrict it from being exported from REDCap for data processing and automatically delete the identifier when the project moves to a completed status on REDCap.

Audio recordings from the clinical interviews and therapy sessions will also be kept confidential. The Lyssn platform (Lyssn AI, Seattle Washington) will be used for collection and storage of recordings from clinical interviews and therapy sessions for supervision and quality assurance. Lyssn is an artificial intelligence (AI) software that has been trained to accurately evaluate evidence-based practices, including clinical interview and CBT session fidelity. Lyssn meets the highest industry security standards, as the platform is HIPAA, FERPA, and GDPR compliant. All data rest in the Lyssn cloud, available only to authorized study personnel (e.g., Dr. Nathanial Wade, clinical interviewers, therapists) via password protected account log in.

Further, the individual information that you provide as part of this experiment will not be disseminated in any manner that may identify you. Only de-identified information from this experiment may be disseminated in journal articles, theses, and conference presentations.

CERTIFICATE OF CONFIDENTIALITY

Identifying information gathered about you during this research project is protected by a Certificate of Confidentiality from the National Institutes of Health (NIH). With this Certificate, researchers cannot be forced to share identifying information about you with anyone not connected to the research, even by a court subpoena. The researchers will use the Certificate to resist any court orders or legal demands.

Additionally, identifying information protected by the Certificate will not be shared outside of the research team, <u>except in the following instances</u>:

- If there is a law that requires disclosure (such as to report child abuse or communicable diseases, *but not for legal or other similar proceedings)*;
- If you have consented to the disclosure or sharing of information, including any disclosure or data sharing plans described elsewhere in this consent document; or
- For use in other scientific research, as allowed by federal regulations protecting research subjects; or
- To personnel of the NIH, when information is needed for auditing or program evaluation; or

- To meet the reporting requirements of the Food and Drug Administration, such as for studies of investigational medical devices or drugs; or
- To authorized individuals at Iowa State University if they need to verify that the research is being done correctly.

In addition, the researchers may share information if necessary to prevent serious harm to you or someone else; for example, if the researchers learn of ongoing child abuse or neglect, or the imminent threat of harm to you or others, they may share this information with the appropriate authorities.

You should know that a Certificate of Confidentiality does not prevent you from voluntarily sharing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

ADDITIONAL USE OF RESEARCH DATA, INCLUDING BLOOD SAMPLES

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

We are required by our funding agency to provide study data to the National Institute of Mental Health Data Archive. It could also be placed in other data repositories for use by other researchers. We may also need to share the data with a journal or similar entity to meet publication requirements. In these instances, the data will likely be available publicly and may be used by other researchers for various types of research projects. To protect your confidentiality, data will be fully de-identified before it is shared or used in these ways. Additionally, we will never include the audio recordings or transcriptions from your CBT sessions or the actual blood samples in any data we share with other researchers for their research use or for inclusion in the National Institute of Mental Health Data Archive.

In addition, information about your personal characteristics, such as your sex/gender, race, ethnicity, and age, must be reported to the National Institutes of Health (NIH), the parent agency of study's funding agency (the National Institute of Mental Health). The information we report to NIH will not include any information that could identify you.

There are no other known plans for future research using the data, but additional research questions may be explored with collaborators. For example, future research might include the analysis of cerebrovascular assessment to answer new research questions related to depression. In all future analyses, only de-identified data will ever be used.

Your blood samples will have your identity removed and will be securely and confidentially stored for analysis of brain derived neurotrophic factor (BDNF) and other depression-relevant biomarkers. Your stored blood may also be used for analysis of a new marker, such as a protein or hormone when new research indicates it may be relevant (in treatment of depression or physiological response to exercise) after you have finished the study. In some cases, we may ask a collaborator or lab outside of the Iowa State research team to analyze the blood samples for us. We will not perform any genome sequencing of your samples. You will not receive results

from any analysis of blood samples. Please be aware that we will not obtain additional permission from you for the uses of your de-identified data or blood samples described above.

QUESTIONS

You are encouraged to ask questions at any time during this study. ***For further information about the study****, contact Dr. Meyer at (515) 294-1386 or jdmeyer3@iastate.edu.*

PREGNANCY

This study does not allow the participation of female subjects who are pregnant. Female subjects are therefore asked to sign the following statement before proceeding. Please sign this statement only if you are certain you are not pregnant and do not plan on becoming pregnant during your inclusion in this study. If you are not certain or are trying to become pregnant, please do not sign this statement.

I confirm that I am not pregnant and do not plan on becoming pregnant during my inclusion in this study. If I become aware that I am or was pregnant during my inclusion in this research, I will promptly inform the investigators.

Participant's Signature: _____

Date: _____

MAINTAIN CONTACT INFORMATION

Aside from the present research study, Dr. Meyer's laboratory and others in the Kinesiology department routinely conduct research on physical activity, exercise and wellbeing. If you are interested in being contacted about studies in the future, please indicate so below.

____ **Yes.** Please keep my contact and demographic information and contact me regarding future studies that I may be eligible to participate in

_____ **No.** I would not like to be contacted regarding future research opportunities, please destroy my contact information at the conclusion of the study

FINAL CONSENT AND AUTHORIZATION PROVISIONS

Participant Signature
Your signature indicates that you voluntarily agree to participate in this study. When you sign this document, you are stating that the experiment has been fully explained to you, and that you understand that the data obtained from this study are to be used for research purposes only, not for the evaluation or diagnosis of any disorder, and that such data will remain confidential, except as required by law. You are also stating that you have been given the time to read the document, had the opportunity to ask questions concerning all aspects of the procedures, and that your questions have been satisfactorily answered. Your signature indicates that you are aware that participation is voluntary, and that you may withdraw your consent at any time.

I, the undersigned, hereby consent to be a participant in the project described above conducted in the Department of Kinesiology at Iowa State University.

Participant's Name: _____

Participant's Signature: _____

Date: _____

Investigator Statement
I certify that the participant has been given adequate time to read and learn about the study and all their questions have been answered. In my opinion the participant understands the purpose, risks, benefits, and procedures included in this study and has voluntarily agreed to participate.

Researcher Obtaining Consent Name: _____

Researcher Obtaining Consent Signature: _____

Date: _____