Title: fMRI of Emotion Regulation During RCT of CBT vs. MBSR for Social Anxiety Disorder

Approval Period: **Draft**

Protocol Director

Name		Degree (program/year if student)		Title
James J. Gross				Assoc Professor
Dept	**Mail Code**	**Phone**	**Fax**	**E-mail**
Psychology	2130	[redacted]		
CITI Training current (within last 2 years for Stanford; within last year for VA)?				Y

Admin Contact

Name		Degree (program/year if student)		Title
Philippe Raymond Goldin				Soc Sci Res Assoc
Dept	**Mail Code**	**Phone**	**Fax**	**E-mail**
Psychology	2130	[redacted]		
CITI Training current (within last 2 years for Stanford; within last year for VA)?				Y

Co-Protocol Director

Name		Degree (program/year if student)		Title
Kelly Werner				Post-doctoral
Dept	**Mail Code**	**Phone**	**Fax**	**E-mail**
Psychology	2130	[redacted]		
CITI Training current (within last 2 years for Stanford; within last year for VA)?				Y

Other Contact

Name		Degree (program/year if student)		Title
Jens Blechert				
Dept	**Mail Code**	**Phone**	**Fax**	**E-mail**
Psychology	2130	[redacted]		
CITI Training current (within last 2 years for Stanford; within last year for VA)?				Y

Faculty Sponsor

Name		Degree (program/year if student)		Title
Dept	**Mail Code**	**Phone**	**Fax**	**E-mail**
CITI Training current (within last 2 years for Stanford; within last year for VA)?				

Other Personnel

Participant Population(s) Checklist	Yes/No
• Children (under 18)	N
• Pregnant Women and Fetuses	N

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• Neonates (0 - 28 days)	N
• Abortuses	N
• Mentally Disabled	N
• Decisionally Challenged	N
• Cancer Subjects	N
• Laboratory Personnel	N
• Healthy Volunteers	Y
• Students	N
• Employees	N
• Prisoners	N
• Other (i.e., any population that is not specified above)	N

Study Location(s) Checklist	**Yes/No**
• Stanford University	Y
• General Clinical Research Center (GCRC)	
• Stanford Hospital and Clinics	
• Lucile Packard Children's Hospital (LPCH)	
• VAPAHCS (Specify PI at VA)	
• Other (Click ADD to specify details)	

General Checklist

Multi-site	**Yes/No**
• Is this a multi-site study? A multi-site study is generally a study that involves one or more medical or research institutions in which one site takes a lead role.(e.g., multi-site clinical trial)	N

Collaborating Institution(s)	**Yes/No**
• Are there any collaborating institution(s)? A collaborating institution is generally an institution that collaborates equally on a research endeavor with one or more institutions.	N

Cancer Center	**Yes/No**
• Cancer Subjects (e.g., clinical trials, behavior/prevention) or Cancer Tissues (e.g., blood, cells, body fluids).	N

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Drug /Device	**Yes/No**
• Protocol involves studying potentially addicting drugs?	N
• Investigational drugs, reagents, or chemicals?	N
• Commercially available drugs, reagents, or other chemicals administered to subjects (even if they are not being studied)?	N
• Investigational Device / Commercial Device used off-label?	Y
• IDE Exempt Device (Commercial Device used according to label)	N

Tissues and Specimens	**Yes/No**
• Human blood, cells, tissues, or body fluids (tissues)?	N
• Tissues to be stored for future research projects?	N
• Tissues to be sent out of this institution as part of a research agreement? For guidelines, please see http://otl.stanford.edu	N

Biosafety (APB)	**Yes/No**
• Are you submitting a Human Gene Transfer investigation using biological agent or recombinant DNA vector? If yes, please complete and attach the Gene Transfer Protocol Application Supplemental Questions to section 16 of the eProtocol application.	N
• Are you submitting a Human study using biohazardous/infectious agents? If yes, refer to the Administrative Panel on BioSafety website prior to performing studies.	N
• Are you submitting a Human study using samples from subjects that contain biohazardous/infectious agents? If yes, refer to the Administrative Panel on BioSafety website prior to performing studies.	N

Human Embryos or Stem Cells	**Yes/No**
• Human Embryos or gametes?	N
• Human Stem Cells (including hESC, iPSC, cancer stem cells, progenitor cells).	N

Veterans Affairs (VA)	**Yes/No**
• The research recruits participants at the Veterans Affairs Palo Alto Health Care System(VAPAHCS).	N
• The research involves the use of VAPAHCS non-public information to identify or contact	N

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human research participants or prospective subjects or to use such data for research purposes.	
• The research is sponsored (i.e., funded) by VAPAHCS.	N
• The research is conducted by or under the direction of any employee or agent of VAPAHCS (full- time, part-time, intermittent, consultant, without compensation (WOC), on-station fee-basis, on- station contract, or on-station sharing agreement basis) in connection with her/his VAPAHCS responsibilities.	N
• The research is conducted using any property or facility of VAPAHCS.	N

Equipment	**Yes/No**
• Use of Patient related equipment? If Yes, equipment must meet the standards established by Hospital Instrumentation and Electrical Safety Committee (650-725-5000)	N
• Medical equipment used for human patients/subjects also used on animals?	N
• Radioisotopes/radiation-producing machines, even if standard of care?	N

Payment	**Yes/No**
• Subjects will be paid for participation? See payment considerations.	Y

Funding	**Yes/No**
• Training Grant?	N
• Program Project Grant?	N
• Federally Sponsored Project?	Y
• Industry Sponsored Clinical Trial?	N

Funding

NONE

Funding - Grants/Contracts

Funding - Fellowships

Gift Funding

Dept. Funding

Other Funding

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Expedited Form

A protocol must be no more than minimal risk (i.e., "not greater than those ordinarily encountered in daily life") AND must only involve human subjects in one or more of the following paragraphs.

Select one or more of the following paragraphs:

1. Y **Clinical studies of drugs and medical devices only when condition (a) or (b) is met.**
   a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
   b) Research on medical devices for which
      i) an investigational device exemption application (21 CFR Part 812) is not required; or
      ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. N **Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:**
   a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. N **Prospective collection of biological specimens for research purposes by non invasive means.**

4. N **Collection of data through non invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)**
   Examples:
   a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy;
   b) weighing or testing sensory acuity;
   c) magnetic resonance imaging;
   d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography;
   e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. N **Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this paragraph may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4).**

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This listing refers only to research that is not exempt.)

6. Y **Collection of data from voice, video, digital, or image recordings made for research purposes.**

7. Y **Research on individual or group characteristics or behavior(including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)**

Resources:

a) Qualified staff.

Please state and justify the number and qualifications of your study staff.

We have a large staff:
4 PhD trained clinical psychologists delivering CBT for social anxiety,
1 PhD clinical psychologist clinical supervisor
3 trained mindfulness meditation teachers
3 postdocs
4 graduate students
5 undergraduates
8 research assistants

b) Training.

Describe the training you will provide to ensure that all persons assisting with the research are informed about the protocol and their research-related duties and functions.

everyone in our group:

must complete the human subject online tutorial,

attend regular lab meetings in which we go over confidentiality and ethics related to conducting randomized clinical trials

train in clinical diagnostic issues and psychopathology

we provide both an overview of the big picture and the details of the protocol to all people in our lab as part of their training in clinical science

c) Facilities.

Please describe and justify.

we have a single office primary office in the psychology department and use additional space in the

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psychology department as needed.

we use the 3T GE scanner at the Lucas center in the medical school for brain imaging

two therapists see clients at the psychiatry and behavoral sciences building for CBT for social anxiety study. one therapist has an office in san francisco. the MBSR groups will be held in group rooms around the Bay area

d) Sufficient time.

Explain whether you will have sufficient time to conduct and complete the research. Include how much time is required.

if we get this new grant we will have sufficient time of 5 years to complete these studies.

e) Access to target population.

Explain and justify whether you will have access to a population that will allow recruitment of the required number of participants.

social anxiety disorder is the third most common psychiatric condition listed in the DSM-IV (after substance abuse/dependence and major depression). it is very common (up to 13% prevalence in the US). More and more people know about the free treatment we are offering as part of our clinical research. We have not had any difficulties with recruitment thus far. For our previous studies we successfully recruited 135 people with SAD and are confident we can do it again

f) Access to resources if needed as a consequence of the research.

State whether you have medical or psychological resources available that participants might require as a consequence of the research when applicable. Please describe these resources.

we are offering the best non-drug clinical interventions for social anxiety disorder. our treatments have very low risk of complications compared to pharmacological interventions (i.e., SSRIs) for social anxiety disorder. we regularly provide a list of referrals to people with anxiety disorders who do not meet our study inclusion criteria.

g) Lead Investigator or Coordinating Institution in Multi-site Study.

Please explain (i) your role in coordinating the studies, (ii) procedures for routine communication with other sites, (iii) documentation of routine communications with other sites, (iv) planned management of communication of adverse outcomes, unexpected problems involving risk to participants or others, protocol modifications or interim findings.

1. Purpose

a) In layperson's language state the purpose of the study in 3-5 sentences.

The goal is to understand the brain and behavioral mechanisms of cognitive behavioral therapy, mindfulness based stress reduction and acceptance and commitment therapy trainings for adults diagnosed with generalized social anxiety disorder.

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b) State what the Investigator(s) hope to learn from the study. Include an assessment of the importance of this new knowledge.

We hope to identify specific neural patterns that help identify who will benefit from what type of treatment modality and also help clarify biomarkers of social anxiety disorders.

c) Explain why human subjects must be used for this project. (i.e. purpose of study is to test efficacy of investigational device in individuals with specific condition; purpose of study is to examine specific behavioral traits in humans in classroom or other environment)

We are studying adults diagnosed with social anxiety disorder

2. Study Procedures

a) Describe all the procedures, from screening through closeout, which the human subject must undergo in the research project, including study visits, drug treatments, randomization and the procedures that are part of standard of care.

Callers will be screened with an initial 15 minute phone screen. Eligible callers will then be invited in for an diagnostic interview at Stanford. Eligible SAD participants will be assessed at baseline, weekly during treatment/WL, post-treatment/WL, and at 6 months follow-up. The pre and post assessments include online questionairres, a behavioral session and an fMRI session. After the baseline assessment (5 hours), SAD will be randomly assigned to CBT, MBSR, or WL with equal probability. SAD will receive CBT or MBSR at no charge. WL is being used to evaluate habituation to any of the assessment tools. Following completion of the WL, SAD participants will be randomly assigned to CBT or MBSR. HC will be administered the full assessment at Time 1 and only questionnaires at Time 2. All participants will be paid $25 per hour for questionnaire and fMRI assessments (3.5 hours). Participants will not be paid for the clinical interviews as this is part of the initial screening, nor the weekly questionnaires as it is a part of the treatment. The weekly questionnaire will measure changes in emotion regulation, clinical symptoms, and well-being during treatment/WL. Changes from baseline to post assessments (self-report and neural) will be used to examine CBT, MBSR, and WL effects. 6-months follow-up data will be used to examine longer-term CBT versus MBSR effects.

For the ACT Study participants are e-mailed an ID#, website, password, instructions and confidentiality and consent information in order to fill out the initial online screener questionnaires. They are then contacted by phone and asked follow-up questions. They are then told over the phone whether they are eligible to participate in the study. If they are not eligible they are emailed referral information. If they are eligible, they are emailed a consent form and instructions to participate in the baseline assessment and treatment group. They then complete the baseline assessment online before the first group session. At the first group session, they sign their consent form and

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hand it in. They also keep a copy for themselves. They then complete nine weekly sessions of ACT. After they complete post assessment online. Additionally they fill out post assessments at three month follow-up.

b) Explain how the above research procedures are the least risky that can be performed consistent with /research/documents/eval_study_designGUI03017.pdf sound research design.

CBT is the gold standard psychosocial intervention for social anxiety disorder. MBSR Stress reduction has also been shown to be effective for adults with social anxiety disorder. ACT is a scientifically proven model that has been shown to be effective with a wide range of issues, such as depression and anxiety. All three of these interventions are associated with very low risk compared to pharmaceutical interventions.

Additionally, we are screening out for current substance/alcohol abuse/dependence, unipolar and bipolar depression, schizophrenia, and medical disorders contraindicated for fMRI scanning.

c) State if deception will be used. If so, provide the rationale and describe debriefing procedures. Since you will not be fully informing the participant in your consent process and form, complete an alteration of consent (in section 13). Submit a debriefing script (in section 16).

no deception.

d) State if audio or video recording will occur. Describe what will become of the recording after use, e.g., shown at scientific meetings, erased. Describe the final disposition of the recordings.

We videotape two 2 minute speeches given during the behavioral session. When training new psychotherapists on the CBT for social anxiety therapy protocol, we will video and audio tape therapy sessions. We will analyze the speech video tapes for changes per/post intervention. Thus, we will keep these. We conduct treatment adherence ratings for the CBT & MBSR for social anxiety protocol, and thus need to keep the therapy session audio tapes. We have asked to keep the recorded information until 2030 for research purposes.

e) Describe alternative procedures or courses of treatment, if any, that might be advantageous to the participant. Describe potential risks and benefits associated with these. Any standard treatment that is being withheld must be disclosed in the consent process and form. (i.e. standard-of-care drug, different interventional procedure, no procedure or treatment, palliative care, other research studies).

The treatments we are providing have very little associated risk. Alternative treatments involve much more risk (i.e., pharmacological agents such as SSRI, etc).

f) Will it be possible to continue the more (most) appropriate therapy for the participant(s) after the conclusion of the study?

Participants can pursue other treatments once they have completed the treatments we are providing in this study.

g) Study Endpoint. What are the guidelines or end points by which you can evaluate the different

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treatments (i.e. study drug, device, procedure) during the study? If one proves to be clearly more effective than another (or others) during the course of a study, will the study be terminated before the projected total participant population has been enrolled? When will the study end if no important differences are detected?

Our goal is to have 44 adults with social anxiety disorder complete CBT,
43 complete MBSR, and 40 complete ACT.
Our aim is to examine the neural/behavioral mechanisms of change for each treatment. Each of the treatments has already been shown to be effective for anxiety in general.

3. Background

a) Describe past experimental and/or clinical findings leading to the formulation of the study.

There are several studies of the neural bases of emotional reactivity in adults with social anxiety disorder, but none directly comparing different types of emotion regulation with different treatments. There are many studies demonstrating the effectiveness of CBT social anxiety study, but none identifying neural mechanisms that change with treatment. There are only one or two fMRI studies of neural mechanisms of change with MBSR for SAD. There is only one pilot study of ACT for SAD.

b) Describe any animal experimentation and findings leading to the formulation of the study.

none

4. Radioisotopes or Radiation Machines

a) List each procedure described in the protocol that uses radiation whether it is performed for research (procedures performed on the participants only due to participation in this study) or is considered standard of care (procedures already being performed on the subjects for diagnostic or treatment purposes). List each potential procedure in the sequence that they would normally occur, whether they are actually performed or not, during the entire study.

Procedures	Type

b) For radioisotope projects, provide the following radiation-related information:

Identify the radionuclide and chemical form.

For each dosage, provide the route of administration and the amount administered (mCi).

Provide dosimetry information and reference the source documents (package insert, MIRD calculation, peer reviewed literature).

c) For radiation machine projects, provide the following diagnostic procedures:

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For well-established radiographic procedures, identify the procedures and the number of times each will be performed on a single research participant.

For each radiographic procedure, provide the setup and technique sufficient to permit dose modeling. The chief technologist can usually provide this information.

For radiographic procedures that are not well-established, provide FDA status of the machine, and information sufficient to permit dose modeling.

d) For radiation machine projects, provide the following therapeutic procedures:

For a well-established therapeutic procedure, identify the area treated, dose per fraction and number of fractions. State whether the therapeutic procedure is being performed as a normal part of clinical management for the research participants's medical condition or whether it is being performed because the research participant is participating in this project.

For a therapeutic procedure that is not well-established, provide FDA status of the machine, basis for dosimetry, area treated, dose per fraction and number of fractions.

5. Devices

a) Please list in the table below all Investigational Devices (and Commercial Devices used off-label) to be used on participants

5.1 Device Name: NA

Describe the device to be used.

Manufacturer:

Risk: **Non-significant**

I confirm the above are true.

Rationale for the device being non-significant risk:

Sponsor of Project

Indicate the project sponsor::

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate, handled according to VAPAHCS memo 151-05-10. If no, please provide an explanation.:

Confirm?

5.2 Device Name: fmri head coil

Describe the device to be used.

fmri head coil for 3t GE magnet

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Manufacturer: **gary glover**

Risk: **Non-significant**

Y I confirm the above are true.

Rationale for the device being non-significant risk:

The fmri head coil transmits and receives radio frequency pulses. This is a standard component of all MRI diagnostic machines used to examine brain tissue and cerbral blood oxygen level dependent signals for both clinical diagnostic and research protocols

Sponsor of Project

Indicate the project sponsor::

Y The sponsor is the device manfacturer.

Ordering, Storage and Control

To prevent the device being used by a person other than the investigator, and in someone other than a research participant: Confirm that the device will be handled according to the SHC/LPCH policy for Investigational New Devices or as appropriate, handled according to VAPAHCS memo 151-05-10. If no, please provide an explanation.:

N Confirm?

the fmri head coil is a piece of equipment that is kept at the 3t GE magnet in the lucas center. Gary glover and anne sawyer are in charge of this piece of equipment.

b) Please list in the table below all Commercial devices to be used on participants

6. Drugs, Reagents, or Chemicals

a) Please list in the table below all investigational drugs, reagents or chemicals to be administered to participants.

b) Please list in the table below all commercial drugs, reagents or chemicals to be administered to participants.

7. Medical Equipment for Human Subjects and Laboratory Animals

If medical equipment used for human patients/participants is also used on animals, describe such equipment and disinfection procedures.

not applicable

8. Participant Population

a) State the following: (i) the number of participants expected to be enrolled at Stanford-affiliated site(s);

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(ii)the total number of participants expected to enroll at all sites; (iii) the type of participants (i.e. students, patients with certain cancer, patients with certain cardiac condition) and the reasons for using such participants.

we will need to screen about 400 in order to enroll 120 social phobics plus 40 healthy adults in the CBT & MBSR.

we will need to screen about 120 in the ACT study to enroll 40 social phobics

b) State the age range, gender, and ethnic background of the participant population being recruited.

we are recruiting 21-55 year old male and female adults diagnosed with social anxiety disorder of all ethnicities.

c) State the number and rationale for involvement of potentially vulnerable subjects in the study (including children, pregnant women, economically and educationally disadvantaged, decisionally impaired, homeless people, employees and students). Specify the measures being taken to minimize the risks and the chance of harm to the potentially vulnerable subjects and the additional safeguards that have been included in the protocol to protect their rights and welfare.

not applicable

d) If women, minorities, or children are not included, a clear compelling rationale must be provided (e.g., disease does not occur in children, drug or device would interfere with normal growth and development, etc.).

we are not recruiting children. the specific types of psychosocial interventions we are using have not yet been shown to be effective for children.

e) State the number, if any, of participants who are laboratory personnel, employees, and/or students. They should render the same written informed consent. If payment is allowed, they should also receive it. Please see Stanford University policy at http://www.stanford.edu/dept/DoR/rph/7-5.html).

not applicable

f) State the number, if any, of participants who are healthy volunteers. Provide rationale for the inclusion of healthy volunteers in this study. Specify any risks to which participants may possibly be exposed. Specify the measures being taken to minimize the risks and the chance of harm to the volunteers and the additional safeguards that have been included in the protocol to protect their rights and welfare.

we will consent 40 healthy volunteers to participate only in the baseline assessments so that we can have a healthy comparison group for the social phobics.

g) Describe how potential participants will be identified for recruitment (e.g., chart review, referral from individual's treating physician, responses to an ad). Describe how participants will be recruited and how they will initially learn about the research (e.g., clinics, advertising). If this is a clinical trial, indicate the recruitment option selected in registering the trial on the Stanford Clinical Trials web site-whether recruitment is limited to "invitation only" (e.g. your own patients), or whether recruitment will be open to the general public. Attach recruitment materials in Section #16 (Attachments). You may not contact potential participants prior to IRB approval. See guidance Advertisements: Appropriate Language for Recruitment Material.

Potential individuals with social anxiety as well as healthy controls are being recruited via electronic bulletin boards (e.g., craig's list), fliers from the general public. We will also do radio announcements.

Advertisement is attached in Section 16.

h) Inclusion and Exclusion Criteria.

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Identify inclusion criteria.

Exclusion Criteria
All participants passed a MRI safety screen. Participants were excluded if they reported current use of any psychotropic medication, psychotherapy, history of neurological or cardiovascular disorders, diabetes, hypo- or hyperthyroidism, or head trauma with loss of consciousness greater than five minutes. Both HC and SAD participants were excluded if they had substance/alcohol abuse in the past year or had a lifetime diagnosis of a psychotic disorder, mania, hypomania, or bipolar disorder. Due to potential effects on blood flow, participants were asked not to consume alcohol, recreational drugs, or pain killers (e.g., ibuprofen or aspirin) during the 24-hour period before their MR scan and not to ingest caffeine at least five hours prior to the scan. Daily cigarette users were excluded from the study. SAD participants were excluded if they met criteria for any current DSM-IV Axis I psychiatric disorders other than social anxiety, generalized anxiety, agoraphobia, or specific phobia disorders.
Clinical Assessment
Clinical diagnostic assessments were conducted by two PhD clinical psychologists and one advanced graduate student using the Anxiety Disorder Inventory Schedule?IV (ADIS-IV36) to diagnose current and lifetime psychiatric disorders based on DSM-IV criteria. Only SAD participants with a primary diagnosis of generalized SAD (greater than moderate anxiety/fear for 5 or more distinct social situations) or HC participants with no history of DSM-IV disorders were invited to participate.

Identify exclusion criteria.

see above

i) Describe your screening procedures, including how qualifying laboratory values will be obtained. If you are collecting personal health information prior to enrollment (e.g., telephone screening), please request a limited waiver of authorization (in section 15).

We use the Stanford Department of Radiology Lucas Center fMRI Safety screening form to confirm that potential participants are fMRI eligible before brining people into the lab for a clinical diagnostic interview.

To determine if a person might have social anxiety disorder, we conduct a phone screen that includes a social anxiety screen.

Social Anxiety Screen
Now I?m going to ask you questions about symptoms that may or may not apply to you. The first of these are about social anxiety. For each item, I want you to give me a number to indicate how much you have been bothered by that problem during the PAST WEEK on a scale of 0 to 4. A 0 means not at all bothered. A 4 means extremely bothered. You can use any number between 0 and 4. Here is the first question:

0	1	2	3	4
not at all bothered	a little bit bothered	somewhat bothered	very much bothered	extremely bothered

_____1. I fear being embarrassed or looking stupid.
_____2. My fear of embarrassment causes me to avoid doing things or speaking to people.
_____3. I avoid activities in which I am the center of attention.
_____4. I feel anxious or nervous when making presentations for work or school (or almost always avoid these situations).
_____ 5. I feel anxious or nervous when interacting with others (or almost always avoid these situations)
_____ 6. I feel anxious or nervous eating or drinking in front of others.
_____ 7. I have trouble being assertive with family, friends, or strangers.
_____ 8. I have difficulty interacting with authority figures (eg. boss or teacher)
_____ 9. I have used alcohol or tranquilizers to calm my nerves before interacting with others.

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j) Describe how you will be cognizant of other protocols in which participants might be enrolled. Please explain if participants will be enrolled in more than one study.

On the first page of our consent form, we ask if participants are currently enrolled in other studies.

k) Payment. Explain the amount and schedule of payment, if any, that will be paid for participation in the study. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of participants and that they do not constitute undue pressure on participants to volunteer for the research study. Include provisions for prorating payment. See payment considerations

PAYMENT for Study
All participants will be paid $25 per hour for questionnaire and fMRI assessments (3.5 hours).

l) Costs. Please explain any costs that will be charged to the participant.

Participants do not need to pay for the Stress Reduction nor the CBT study. For the ACT study, participants are asked to pay $40 per session for 9 weeks for a total of $360.00.

m) Estimate the probable duration of the entire study. Also estimate the total time per participant for: (i) screening of participant; (ii) active participation in study; (iii) analysis of participant data.

CBT & MBSR may be funded for 5 years

CBT & MBSR participants are assessed, treated, followed for at least 18 months in the immediate CBT arm, 23 months in the delayed CBT arm.

ACT participants are assessed, treated and followed for approximately 8 months.

After all data collection has been completed, we will continue to analyzed data and submit manuscripts for at least 2-3 years post study completion.

9. Risks

a) For the following categories include a scientific estimate of the frequency, severity, and reversibility of potential risks. Wherever possible, include statistical incidence of complications and the mortality rate of proposed procedures. Where there has been insufficient time to accumulate significant data on risk, a statement to this effect should be included. (In describing these risks in the consent form to the participant it is helpful to use comparisons which are meaningful to persons unfamiliar with medical terminology.)

Investigational devices.

Risks:
Magnetic fields do not cause harmful effects at the levels used in the MRI machine. However, the MR scanner uses a very strong magnet that will attract some metals and affect some electronic devices. If you have a cardiac pacemaker or any other biomedical device in or on your body, it is very important that you tell the operator/investigator immediately. As metallic objects may experience a strong attraction to the magnet, it is also very important that you notify the operator of any metal objects (especially surgical clips), devices, or implants that are in or on your body before entering the magnet room. All such objects must be removed (if possible) before entering the magnet room. In some cases, having those devices means you should not have an MRI scan performed. In addition, watches and credit cards should also be removed as these could be damaged. You will be provided a way to secure these items. If you have any history of head

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or eye injury involving metal fragments, if you have ever worked in a metal shop, or if you could be pregnant, you should notify the operator/investigator.

There is a possibility that you will experience a localized twitching sensation due to the magnetic field changes during the scan. This is expected and should not be painful.

Some of the radio frequency imaging coils, imaging software and devices being used in your scan are not approved by the FDA but are similar to counterparts that have been approved by the FDA. There is a small risk of heating from the cables associated with these devices. Please report any heating sensation immediately.
Dizziness or nausea may occur if you move your head rapidly within the magnet.

IF YOU FEEL DISCOMFORT AND WANT TO STOP THE SCAN, YOU ARE FREE TO TELL THE OPERATOR AND DISCONTINUE THE EXAM AT ANYTIME.

The scans performed in this study are for specific research purposes and are not optimized to find medical abnormalities. The investigators for this project may not be trained to perform medical diagnosis. The investigators and Stanford are not responsible for failure to find existing abnormalities with these MRI scans. However, on occasion the investigator may notice a finding on an MRI scan that seems abnormal. When this occurs, a physician will be consulted as to whether the findings merit further investigation, in which case the investigator will contact you and your primary care physician and inform you of the finding. The decision as to whether to proceed with further examination or treatment lies solely with you and your physician. The investigators, the consulting physician, and Stanford are not responsible for any examination or treatment that you undertake based on these findings. Because the images collected in this study may not comprise a proper clinical MRI scan, these images will not be made available for diagnostic purposes.

Investigational drugs. Information about risks can often be found in the Investigator's brochure.

none

Commercially available drugs, reagents or chemicals. Information about risks can often be found in the package insert.

none

Procedures to be performed. Include all investigational, non-investigational and non-invasive procedures (e.g., surgery, blood draws, treadmill tests).

collection of saliva in a plastic container for DNA.

Radioisotopes/radiation-producing machines (e.g., X-rays, CT scans, fluoroscopy) and associated risks.

none

Physical well-being.

Engaging in physical exercise poses a minor risk.

Psychological well-being.

working with emotional material in CBT, MBSR & ACT poses a minor risk

Economic well-being.

not applicable

Social well-being.

no risk

Overall evaluation of Risk.

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Low - innocuous procedures such as phlebotomy, urine or stool collection, no therapeutic agent, or safe therapeutic agent such as the use of an FDA approved drug or device.

b) In case of overseas research, describe qualifications/preparations that enable you to both estimate and minimize risks to participants.

not applicable

c) Describe the planned procedures for protecting against and minimizing all potential risks. Include the means for monitoring to detect hazards to the participant (and/or to a potential fetus if applicable). Include steps to minimize risks to the confidentiality of identifiable information.

All information is kept with an identification number, not the participant's name. We keep a separate form with the participant's name in a locked file cabinet in our office.

d) Explain the point at which the experiment will terminate. If appropriate, include the standards for the termination of the participation of the individual participant Also discuss plans for ensuring necessary medical or professional intervention in the event of adverse effects to the participants.

for CBT & MBSR participation ends after the last follow-up assessment which is at 12 months post-CBT & MBSR. for ACT it ends 3 months after the last session

10. Benefits

a) Describe the potential benefit(s) to be gained by the participants or by the acquisition of important knowledge which may benefit future participants, etc.

Participants will learn many new skills for working with emotions, thoughts, bodily sensations in CBT, MBSR and ACT.

11. Privacy and Confidentiality

Privacy Protections

a) Describe how the conditions under which interactions will occur are adequate to protect the privacy interests of participants (e.g., privacy of physical setting for interviews or data collection, protections for follow-up interactions such as telephone, email and mail communications).

We conduct clinical diagnostic interviews, and behavioral assessments in a private office at the psychology department.

We conduct fMRI brain imaging sessions at the Lucas Center in the medical school. We use an ID for all information.

We conduct group CBT in group rooms in the Psychiatry Department in the medical school, the psychology building and the Bay Area. Therapist and client use real names.

MBSR will be conducted in group rooms in the Bay Area.

Acceptance and Commitment Therapy is conducted around the Bay Area.

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All forms of assessment are identified with a unique ID number, no names. We have regular email contact with participants in order to remind people to complete online questionnaires.

Confidentiality Protections

b) Specify the PHI (protected health information) or other individually identifiable data or specimens you will obtain, use or disclose to others.

We are obtaining saliva from participants but his is coded without any identifying information, only an ID number.

We do collect demographic information, but this is kept separate from other research data.

c) Describe how data will be maintained (e.g., paper or electronic spreadsheet, desktop computer, laptop or other portable device) and how you will maintain the confidentiality and data security, (e.g. password protected computer, encrypted files, locked cabinet and office).

We keep paper material in a locked file cabinet in our office. We keep electronic excel files password protected on our protected space on the psychology department server.

d) Describe how data or specimens will be labeled (e.g. name, medical record number, study number, linked coding system) or de-identified. If you are de-identifying data or specimens, who will be responsible for the de-identification? If x-rays or other digital images are used, explain how and by whom the images will be de-identified.

saliva kits are labeled with a study number, no name. all paper and electronic data files include only ID numbers, no names.

e) Indicate who will have access to the data or specimens (e.g., research team, sponsors, consultants) and describe levels of access control (e.g., restricted access for certain persons or groups, access to linked data or specimens).

only our research team in the psychology department has access to our data.

f) If data or specimens will be coded, describe the method in which they will be coded so that study participants' identities cannot be readily ascertained from the code.

saliva kits inlcude the following id format 79 (research study) - xxxx (4 digit number for unique ID number).

g) If data or specimens will be coded, indicate who will maintain the key to the code and describe how it will be protected against unauthorized access.

we keep a single locked electronic excel file that contains names and ID number.

h) If you will be sharing data with others, describe how data will be transferred (e.g., courier, mail) or transmitted (e.g., file transfer software, file sharing, email). If transmitted via electronic networks, describe how you will secure the data while in transit.See . http://www.stanford.edu/group/security/securecomputing/iso-guidelines.html. Additionally, if you will be using or sharing PHI see http://hipaa.stanford.edu/policy_security.html http://hipaa.stanford.edu/policy_security.html.

We are not sharing data with others.

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i) How will you educate research staff to ensure they take appropriate measures to protect the privacy of participants and the confidentiality of data or specimens collected (e.g. conscious of oral and written communications, conducting insurance billing, and maintaining paper and electronic data)?

Everyone on our research team (from undergrad to graduate student to postdoc to research assistant) must complete the online IRB tutorial. Additionally, because we are conducting clinical trials, we regularly discuss confidentiality in our ongoing lab meetings.

12. Potential Conflict of Interest

a) Does anyone who:

- recruits, selects, consents, or treats participants
- plans to analyze data
- plans to serve as an author on any papers originating from this research
- is an immediate family member(spouse, dependent child as defined by IRS, domestic partner of any of the above)

N i) have consulting arrangements, responsibilities or equity holdings in the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N ii) have a financial relationship with the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s) including the receipt of honoraria, income, or stock/stock options as payment?
N iii) serve as a member of an advisory board with the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N iv) receive any gift funds from the Sponsoring company, vendor(s), provider(s) of goods, or subcontractor(s)?
N v) have an ownership or royalty interest in any intellectual property utilized in this protocol?

b) N To your knowledge, does any one in a supervisory role to you have a conflict of interest related to this study?

If one or more of the above relationships exist, please include a statement in the consent form to disclose this relationship, i.e., a paid consultant, a paid member of the Scientific Advisory Board, has stock or stock options, or receives payment for lectures given on behalf of the sponsor (see sample consent form). The consent form should disclose what institution(s) or companies are involved in the study through funding, cooperative research, or by providing study drugs or equipment (see sample consent form).

If you answer yes to any of the questions above, you must file a Conflict of Interest (CoI) disclosure. See http://www.stanford.edu/dept/DoR/ad_hoc.html for more information.Contact Barbara Flynn at (650) 723-7226, or 'mailto:bflynn@stanford.edu'bflynn@stanford.edu.

c) N To your knowledge, does Stanford University have an ownership or royalty interest in any intellectual property utilized in this protocol?

13. Consent Background

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13.1 Waiver of Documentation ACT waiver

Sponsor's Consent Version Number: (if any):

a) Describe the informed consent process. Include the following.

i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)

ii) When and where will consent be obtained?

iii) How much time will be devoted to consent discussion?

iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?

v) What steps are you taking to minimize the possibility of coercion and undue influence?

vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

Participants are e-mailed the ACT waiver and then they fill out our online screener. Next they have a phone conversation with Clinical Psychologist Dr. Kelly Werner to discuss any questions or concerns. Next they are e-mail the ACT Consent form. They read this at their leisure and are invited to call or e-mail with questions. Next they bring the consent form to the first group workshop. Any and all questions regarding the consent form will will be fielding in the first 10 minutes of the group by a clinical psychologist completely informed about the study. Next they will sign the consent forms and hand them in. They will also keep one signed copy for themselves.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter14.5 for guidance.

All participants understand English and do not have hearing impairment

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent,(iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

Vulnerable populations are ineligible for our study. Participants cannot have cognitive impairment, are not children or elderly, do not have visual or hearing impairment, and do not have major medical conditions

Select one of the following regulatory criteria for a waiver of documentation (signature) and provide a protocol-specific justification:

1) **45 CFR 46.117(c)(1). For research that is not subject to FDA regulation, the only record linking the participants and the research would be the consent document,and the principal risk would be potential harm resulting from a breach of confidentiality; each participant will be asked whether he/she wants documentation linking the participant with the research, and the participant's wishes govern.**

2) Y **45 CFR 46.117(c)(2) and 21 CFR 56.109(c)(1). Research (whether it is or is not subject to FDA regulation) presents no more than minimal risk of harm to participants and involves no procedures for which written consent is normally required outside of the research context.**

Rationale for above selection:

The initial stage to our screening process is conducted online. Therefore it is not practical for participants to sign a consent form in person to engage with our screening process. Therefore we requested a waiver of documentation.

13.2 Consent ACT Consent Form

Sponsor's Consent Version Number: (if any):

a) Describe the informed consent process. Include the following.

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i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)
ii) When and where will consent be obtained?
iii) How much time will be devoted to consent discussion?
iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?
v) What steps are you taking to minimize the possibility of coercion and undue influence?
vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

The research team staff will obtain consent. For the ACT Study participants are e-mailed an ID#, website, password, instructions and confidentiality and consent information in order to fill out the initial online screener questionnaires. They are then contacted by phone and asked follow-up questions. They are then told over the phone whether they are eligible to participate in the study. If they are not eligible they are emailed referral information. If they are eligible, they are emailed a consent form and instructions to participate in treatment group. They then bring the consent form to the first therapy session and sign it with the licensed clinical psychologist. Participants will be asked if they have any questions and as much time as needed will be taken to answer all questions. Participants are told over the phone and in person that they are free to not consent.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter14.5 for guidance.

Participants are not in the study if they have significant cognitive impairment, are children or have significant hearing impairment.

c) What steps are you taking to determine that potential participants are competent to participate in the decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent,(iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

We only enroll people who are able to consent for themselves.

13.3 Consent — CBT & MBSR Consent

Sponsor's Consent Version Number: (if any):

a) Describe the informed consent process. Include the following.
i) Who is obtaining consent? (The person obtaining consent must be knowledgeable about the study.)
ii) When and where will consent be obtained?
iii) How much time will be devoted to consent discussion?
iv) Will these periods provide sufficient opportunity for the participant to consider whether or not to participate and sign the written consent?
v) What steps are you taking to minimize the possibility of coercion and undue influence?
vi) If consent relates to children and if you have a reason for only one parent signing, provide that rationale for IRB consideration.

The research team staff will obtain consent. Eligible phone screened participants are emailed the consent form and they bring it in to their diagnostic interview. The interviewer typically takes the first 10 minutes to review the consent form and ask if the person has any questions. Participants will be asked if they have any questions and as much time as needed will be taken to answer all questions. Participants are told over the phone and in person that they are free to not consent.

b) What is the Procedure to assess understanding of the information contained in the consent? How will the information be provided to participants if they do not understand English or if they have a hearing impairment? See HRPP Chapter14.5 for guidance.

People are are significantly cognitively or hearing impaired are not eligible for the study. Children are not in the study.

c) What steps are you taking to determine that potential participants are competent to participate in the

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decision-making process? If your study may enroll adults who are unable to consent, describe (i) how you will assess the capacity to consent, (ii) what provisions will be taken if the participant regains the capacity to consent,(iii) who will be used as a legally authorized representative, and (iv) what provisions will be made for the assent of the participant.

Only people who can consent for themselves are eligible for this study.

14. Assent Background (less than 18 years of age)

15. HIPAA Background

16. Attachments

Attachment Name	Attached Date	Attached By	Submitted Date
Email for Potential HCs Recruitment 111407	06/27/2008	pgoldin	
HC Flyer	06/27/2008	pgoldin	
CBT_AdultADD	06/27/2008	pgoldin	
CBT_BDI-II	06/27/2008	pgoldin	
CBT_BFNE	06/27/2008	pgoldin	
CBT_CAMS	06/27/2008	pgoldin	
CBT_COPE	06/27/2008	pgoldin	
CBT_CTQ	06/27/2008	pgoldin	
CBT_ECR-R	06/27/2008	pgoldin	
CBT_EDI Handedness	06/27/2008	pgoldin	
CBT_ERQ2	06/27/2008	pgoldin	
CBT_IBES	06/27/2008	pgoldin	
CBT_ISEL	06/27/2008	pgoldin	
CBT_LSAS-SR	06/27/2008	pgoldin	
CBT_NEO	06/27/2008	pgoldin	
CBT_PANAS	06/27/2008	pgoldin	
CBT_PSS	06/27/2008	pgoldin	

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CBT_PSWQ	06/27/2008	pgoldin	
CBT_RSES	06/27/2008	pgoldin	
CBT_RSQ	06/27/2008	pgoldin	
CBT_SASCI	06/27/2008	pgoldin	
CBT_SCQ	06/27/2008	pgoldin	
CBT_SDS	06/27/2008	pgoldin	
CBT_SIAS	06/27/2008	pgoldin	
CBT_SPCORE	06/27/2008	pgoldin	
CBT_SSE	06/27/2008	pgoldin	
CBT_STAI-S	06/27/2008	pgoldin	
CBT_STAI-T	06/27/2008	pgoldin	
CBT_SWLS	06/27/2008	pgoldin	
CBT_ULS	06/27/2008	pgoldin	
CBT_WAI	06/27/2008	pgoldin	
CBT_WEEKLY	06/27/2008	pgoldin	
Meditation Monitoring Sheet	06/27/2008	pgoldin	
Physical Activity Readiness Questionnaire PAR-Q	06/27/2008	pgoldin	
Wellness_WEEKLY	06/27/2008	pgoldin	
Mindfulness_Attention_Assessment_Scale[1]	06/27/2008	pgoldin	
MBSR_WEEKLY	06/27/2008	pgoldin	
KIMS	06/27/2008	pgoldin	
AAQ-R-22item	06/27/2008	pgoldin	
3TScreenForm1215051	06/27/2008	pgoldin	
ACT Screener	04/14/2010	kwerner	
Gross Continuing review checklist	04/16/2010	kcheng1	
CBT & MBSR Flyer	08/18/2010	kwerner	
Grant Submission (not funded yet)	08/18/2010	kwerner	

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Obligations

The Protocol Director agrees to:

- Adhere to principles of http://humansubjects.stanford.edu/research/documents/eval_study_designGUI03017.pdf sound scientific research designed to yield valid results.
- Conduct the study according to the protocol approved by the IRB
- Be appropriately qualified to conduct the research and be trained in Human Research protection ethical principles, regulations, policies and procedures.
- Ensure all research personnel are adequately trained and supervised
- Ensure that the rights and welfare of participants are protected including privacy and confidentiality of data
- Disclose to the appropriate departments any potential conflict of interest
- Report promptly any new information, modification, or http://humansubjects.stanford.edu/research/documents/Events-Info-Report-to-IRB_GUI03P13.pdf unanticipated problems that raise risks to participants or others
- Apply relevant professional standards.

Any change in the research protocol must be submitted to the IRB for review prior to the implementation of such change. Any complications in participants or evidence of increase in the original estimate of risk should be reported at once to the IRB before continuing with the project. Inasmuch as the Institutional Review Board (IRB) include faculty, staff, legal counsel, public members, and students, protocols should be written in language that can be understood by all Panel members. The investigators must inform the participants of any significant new knowledge obtained during the course of the research.

IRB approval of any project is for a maximum period of one year. For continuing projects and activities, it is the responsibility of the investigator(s) to resubmit the project to the IRB for review and re-approval prior to the end of the approval period. A Notice to Renew Protocol is sent to the Protocol Director 7 weeks prior to the expiration date of the protocol.

Department Chair must approve faculty and staff research that is not part of a sponsored project. VA applicants must have Division Chief or Ward Supervisor approval. E-mail the Department Chair approval to IRBCoordinator@lists.stanford.edu.

All data including signed consent form documents must be retained for a minimum of three years past the completion of the research. Additional requirements may be imposed by your funding agency, your department, or other entities. (Policy on Retention of and Access to Research Data, Research Policy Handbook,)

PLEASE NOTE: List all items (verbatim) that you want to be reflected in your approval letter (e.g., Amendment, Investigator's Brochure, consent form(s), advertisement, etc.) in the box below. Include number and date when appropriate.

Y The Protocol Director has read and agrees to abide by the above obligations.