Reasoning Training in Individuals with Bipolar Disorder
Stud Protocol

Statistical Anal sis

NCT02843282
IRB# 14-16

Principal Investigator:
Sandra Chapman

April 3, 2017

Statement of Compliance

The study will be carried out in accordance with Good Clinical Practice (GCP) as required by the following:

- Completion of Human Subjects Protection Training

SIGNATURE PAGE

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements.

Signed: Kandra Chapman Date: 12-8-23

Name
Title

** The protocol should be signed by the local investigator who is responsible for the study implementation at his/her specific site; ie, if Investigational New Drug study, the individual who signs the Form FDA 1572.*

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Title: Reasoning Training in Bipolar Disorder – Pilot Study

Population: Adults with a diagnosis of Bipolar Disorder I or II between ages of 71 and 70, under care of psychiatrist and in euthymic stage (managed mood symptoms)

Number of Sites: 1

Study Duration: 9 months

Subject Duration: 2 months

Objectives:

Primary:

- Change in complex abstraction from pre-to-post training
- Transfer effects to measures of executive function and memory

Secondary:

- Change in resting state brain blood flow
- Correlation between behavioral and brain changes

1 KEY ROLES

For questions regarding this protocol, contact Erin Venza at erin.venza@utdallas.edu.

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2 BACKGROUND INFORMATION AND SCIENTIFIC RATIONALE

2.1 Background Information

Bipolar disorder is a disorder that causes unusual shifts in mood and can cause cognitive dysfunction, poor function in daily living and an inability to carry out day-to-day tasks. Bipolar disorder currently affects approximately 5.7 million American adults. Although a substantial amount of literature has examined both manic and depressive states in bipolar disorder, there is relatively little information about the cognitive and neurophysiological functioning of bipolar patients when they are in a euthymic or stable state. This proposed research study will examine the cognitive and neurophysiological functioning of euthymic patients with bipolar disorder. Additionally, this study will examine the effects of cognitive training on cognitive and neurophysiological abnormalities in euthymic adults with bipolar disorder. It is imperative to not only develop a neurocognitive profile of stable bipolar patients but also to understand ways in which training can improve both cognitive and neurophysiological outcomes for these patients.

Cognitive deficits such as executive function, attention, memory and processing speed have been shown in bipolar patients in euthymic, manic, and depressive states (Gruzelier et al., 1988; Murphy et al., 1999; Sweeney et al., 2000; Bearden et al., 2001; Clark et al., 2002; Quraishi and Frangou 2002; Seidman et al., 2002; Martínez-Arán et al., 2004; Savitz et al., 2005; Pavuluri et al., 2006; Schretlen et al., 2007; Sanchez-Morla et al., 2009). Additionally, studies solely conducted with euthymic bipolar patients have shown impairments in information processing strategies, synthesizing information, abstraction abilities and visuospatial abilities (Clark et al., 1985; Sapin et al., 1987; Tham et al., 1997). Although the aforementioned studies have shown clear cognitive deficits associated with bipolar disorder, there has yet to be a consensus of a cognitive profile of bipolar disorder, specifically in the euthymic state. Characterizing cognitive dysfunction in euthymic bipolar patients would inform cognitive training programs on what abilities should be targeted for intervention.

Patients with bipolar disorder have also been shown to have structural and functional deficits in specific brain regions such as increased left ventricular size, increased amygdala size, disruptions in white matter, and decreased activity in the prefrontal cortex (Drevets et al., 1997; Altshuler et al., 1998; Strakowski et al., 1999; McDonald et al., 2005; Mahon et al., 2009). Structural abnormalities in bipolar patients could be the cause of cognitive and functional deficits in memory and executive function but have yet to be linked. Also, large-scale neural networks, such as the default mode network (DMN), have shown differential activation in bipolar patients versus normal controls (Calhoun et al., 2009; Whitefield-Gabrieli & Ford, 2012). Understanding the structural and functional abnormalities associated with bipolar disorder could lead to a theoretical model of a brain basis for mood disorders.

2.2 Scientific Rationale

Training programs that have attempted to mitigate cognitive and functional deficits in patients with bipolar disorder have largely been limited to cognitive behavioral therapy (CBT) techniques and have focused more on improving daily living than improving cognitive or brain function (Scott, Garland & Moorehead, 2001; Scott et al., 2006). Although these studies have found that CBT has a significant effect in improving daily living and mood episodes, it is still unclear if training can mitigate the cognitive deficits seen in bipolar patients. Preliminary evidence highlights the potential of reasoning training as well as physical training to modify and strengthen brain and cognitive function in healthy adults as well as patient populations. Evidence from our lab indicates that frontally mediated, gist-based reasoning (defined as the ability to combine detail information to construct abstract meanings) offers a promising cognitive domain to train in many different populations including seniors, veterans, and traumatic brain injury patients. Furthermore, previous studies from our lab have shown that our gist-reasoning training improves cognitive functions in both trained and untrained areas as well as increases brain-blood flow, white matter diffusivity and functional connectivity. As our gist-reasoning training targets cognitive functions such as integrated reasoning and strategic attention, which are known to be impaired in bipolar patients, it is possible that this training would greatly enhance the cognitive and neural functioning of adults with bipolar disorder.

2.3 Potential Risks and Benefits

2.3.1 Potential Risks

There are no known risks associated with the behavioral and psychological testing other than fatigue and frustration. If the participant's responses to questionnaires or the information they provide to study personnel indicate suicidal thoughts or actions, the researchers are obligated to notify authorities. They will refer the participant to a psychiatrist. There is also a risk that bipolar patients may have manic or depressive episodes while undergoing cognitive training. If this is reported to us from the participant, they will be referred to a physician and taken out of the study. There are no known risks or adverse effects resulting directly from exposure to magnetic fields and radio frequency energy used in this study other than a feeling of claustrophobia. As long as the patient has been cleared by the imaging center technicians as safe to go into the magnet, e.g. no pacemaker or incompatible metal in the patient.

Also, the MR scanner produces tapping sounds during operation, which may reach very loud levels. To minimize any discomfort from this noise, the patient will be provided with disposable earplugs or headphones that suppress external noise levels but do not eliminate voice communication with the scanner operator. If the participant is unable to tolerate being in the scanner, we will stop the scan immediately at any time. Other risks of MRI, but that rarely occur: 1) Neurostimulation. In some cases it is possible that the subject might experience neurostimulation effects, such as muscle twitches and tingling sensations, due to the rapid

switching of magnetic field gradients used in these examinations. There are no known risks associated with these effects; 2) Quench Hazard. The MR scanner uses liquid nitrogen and liquid helium. It is remotely possible that the liquid nitrogen and helium will boil off rapidly and fill the magnet room with extremely cold dense gaseous nitrogen and helium, which can be dangerous if breathed for more than a few moments. The scanner operator will obviously detect this and immediately provide assistance to anyone inside the magnet room.

Although there is no evidence of any risk to pregnant women, we will exclude women who are pregnant or suspect they may be pregnant.

The risks associated with specific study procedures will be thoroughly explained to participants. Clinicians will confirm the appropriateness of each participant prior to intervention by phone, and the clinician will check emotional status during weekly sessions of participants. The risks of the cognitive assessment will be mitigated by using highly trained personnel who provide encouragement; schedule breaks, and provide a supportive environment for the study participant. The project staff will explain all procedures, including the time required. Care will be taken to minimize any feelings of anxiety and discomfort that may be aroused. The patients will not be pushed to perform beyond their capacities. They will be encouraged to take breaks if they become tired or frustrated. The participant will have the option to terminate participation at any time during the study. Participants will be checked multiple times for metal or other devices that could pose a danger in the MR environment. Also, participants will be given hearing protection during scanning. During the fMRI, subjects will be able to communicate through the intercom built into the scanner. The procedure will be stopped if the subject is unable to complete the study or shows any signs of intolerance such as frequent movements. Reassurance will be provided as needed and they will be reminded that their continued participation in the study is completely voluntary. In the event of severe adverse effects (e.g. headache, nausea, ear problem due to noise), participants will be removed from the study and appropriate follow-up instituted. Potential to heat tissue is present in all magnetic resonance imaging. The amount of power is monitored with appropriate built-in instrumentation to assure the power and heat absorption is under FDA standards. In any event of system failure or problems scanning will stop.

Any time information is collected; there is a potential risk for loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

2.3.2 Known Potential Benefits

Participants may not benefit from enrolling in this study. However, they may benefit from the intervention sessions by improving their thinking ability, memory and learning skills and by feeling an increase in self-esteem, as a result. They will be not be reimbursed for their time and expenses related to participating in the study. In addition, the information obtained from this pilot study may be of benefit to patients in future, as the investigators may gather more information about the interventional strategies to help bipolar patients.

3 OBJECTIVES

- Examine change in cognitive measures pre-post reasoning training in individuals with Bipolar Disorder
- Examine changes in resting state brain blood flow pre-post reasoning training in individuals with Bipolar Disorder
- Examine correlation between cognitive and brain metrics pre-post reasoning training in individuals with Bipolar Disorder

4 STUDY DESIGN

Participants will only include people who are fluent speakers of English, as not all of the standardized and experimental cognitive tests have been normed for non-English speakers. Participants will be screened for significant medical, neurological, or psychiatric illness other than bipolar disorder. Additionally, two separate cognitive testing and two MRI imaging procedures will be conducted with each participant: one at baseline prior to cognitive training, the second at the end of cognitive training (4 weeks). These testing procedures are explained below.

Each participant will receive an appointment card/schedule of appointments to help them keep track of what is expected of them. During the training program participants will make 1 visit per week for 2 hours each over a 4-week period. Prior to cognitive training, participants' baseline gist and detail processing ability, will be obtained with a battery of cognitive measures. Structural and functional brain measures will also be obtained. All measurements will be taken again at the endpoint of training. Training effects will be measured behaviorally in trained areas (reasoning & physical) and untrained cognitive areas. Additionally, structural and functional brain imaging will measure changes in cerebral blood flow, global and regional brain volume, white matter tracts, efficiency, activation patterns, and blood oxygenation with a particular focus on changes to frontal regions.

5 Study Population

Our study population for this pilot study will include 20-30 adults diagnosed with bipolar disorder I or II; they will be referred by local treating psychiatrists.

5.1 Selection of the Study Population

Participants will be recruited from a Dr. David Tyler at the University of Texas Southwestern Medical Center, as well as through flyers handed out to members of the community who attend lectures related to brain health and express an interest in future and ongoing research studies, and the Center for BrainHealth website. We will also distribute flyers/advertisements to UTD main campus, community mental health organizations, local media sources, support groups, and to physicians who express an interest in the study for their patients. Participants will be asked to complete cognitive testing before their cognitive training, complete four weeks (2 hours/session) of gist-based training, and then undergo post-testing using the same measures tested before training.

5.2 Inclusion/Exclusion Criteria

Inclusion Criteria:

Must have physician or psychiatrist authorization form confirming participant fulfills 4 criteria:

- has diagnosis of Bipolar I or II
- has been stable and consistent with medication for last 3 months
- is in a euthymic, rather than manic or depressive, state
- is appropriate for a group-based intervention

Exclusion criteria:

- Not a native English speaker
- Less than 12 years education
- Additional psychiatric diagnosis

6 STUDY PROCEDURES/EVALUATIONS

6.1 Study Procedures

- Screening Session: A research assistant will conduct screening procedures over the phone including a brief medical questionnaire covering their history, current medications and any pre-existing conditions. Prior diagnosis of bipolar disorder and euthymic state will be confirmed with study psychiatrist. Additionally, given that the participant meets the requirements covered by the phone screen, participants will be asked to come to the Center for BrainHealth to complete further cognitive assessments.

- Cognitive Testing Session: A clinician from the Center for BrainHealth will administer a group of standardized and experimental tests to each participant for each of the cognitive testing sessions. This session may last up to 4 hours, depending on the pace of the participant's response times. The intent of the tasks is to assess higher level thinking skills, working memory, and selective learning. The cognitive test battery will include tests like Delis-Kaplan Executive Function System (DKEFS) Color-Word Interference Test, Delis-Kaplan Executive Function System (DKEFS) Card Sorting Test, Test of Strategic Learning (TOSL), Auditory Selective Learning, Wechsler Memory Scale (WMS-III) Logical Memory Subtest, Verbal Problem Solving, Wechsler Adult Intelligence Scale (WAIS) Similarities Subtest, Rey-Osterrieth Auditory Verbal Learning Test (RAVLT), Trails A, Trails B, the Controlled Order Word Association Test (COWAT), Wechsler Memory Scale (WMS-III) Digits forward and backwards, and Framing task.

- fMRI: Participants who qualify for the imaging portion will lie in the scanner while images of their brain will be recorded. Each session will take up to 90 minutes. During the MRI and during the DTI (diffusion tensor imaging) the patient will be asked just to lie still.

- Cognitive reasoning training: The gist-based reasoning training will be delivered in one, two hour session each week over 4 weeks. The strategy instruction is hierarchical and dynamically interdependent, with each strategy building upon previous strategies to transform the concrete meaning into abstracted gist-based meanings through reasoning and inference. Constructing meaning at a higher level of abstraction promotes learning which is more efficient and long lasting.

- Post Intervention: Following the intervention, patients will repeat the cognitive assessment and fMRI identical to the pre-training assessment. Participants are not paid for any of these tests or training sessions.

7 STATISTICAL CONSIDERATIONS

7.1 Study Outcome Measures

Outcome measures include behavioral measures of cognitive function and resting state brain imaging.

7.2 Sample Size Considerations

We piloted n=27 participants and 12 of those who completed brain imaging. This was a sufficient sample size to conduct a pilot-study analysis of cognitive and brain changes in this patient population pre-post reasoning training.

7.3 Participant Enrollment and Follow-Up

We enrolled 27 participants at baseline and all 27 completed the study. 12 of the 27 also completed brain imaging.

7.4 Analysis Plan

Statistical analysis plan:

General linear models will be used to assess mean changes cognitive outcomes. In resting state fMRI analysis, we will first identify the spatial extent and BOLD signal time course of the default mode network and central executive network for each subject at each time point (pre- and post-training) using advanced statistical methods like ICA. Then, we will compare networks activation across the two time points of the study using repeated measures general linear modeling. Map-wise corrected false positive rates will be controlled at .05 by Bonferroni correction.

8 SUBJECT CONFIDENTIALITY

The study protocol, documentation, data and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

Personally identifiable information (PII) was removed at study closure; de-identified data collected within the online dashboard will remain there. Additionally, participants in this pilot will have the option to consent into the larger BrainHealth Project study and carry forward their pilot data at the end of pilot study.

9 INFORMED CONSENT PROCESS

Informed consent is a process that is initiated prior to the individual's agreeing to participate in the study and continuing throughout the individual's study participation. Extensive discussion of risks and possible benefits of participation in this study will be provided to the subjects. Consent forms describing in detail the study procedures and risks are given to the subject and written documentation of informed consent is required prior to enrolling in the study. Consent forms will be IRB approved and the subject will be asked to read and review the document. Upon reviewing the document, the investigator will explain the research study to the subject and answer any questions that may arise. The subjects will sign the informed consent document prior to being enrolled in the study. The subjects may withdraw consent at any time throughout the course of the study. A copy of the informed consent document will be given to the subjects for their records. The rights and welfare of the subjects will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

10 LITERATURE REFERENCES

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SUPPLEMENTS/APPENDICES

Included Documents:

- *Consent Form*
- *Statistical Analysis*

Reasoning Training in Individuals with Bipolar Disorder Consent Form

NCT02843282
IRB# 14-16

Principal Investigator:
Sandra Chapman

April 3, 2017

The University of Texas Southwestern Medical Center
Parkland Health & Hospital System
Children's Medical Center
Retina Foundation of the Southwest
Texas Scottish Rite Hospital for Children
Texas Health Presbyterian Hospital Dallas

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research: **Brain & Cognitive Changes after Reasoning Training with Individuals with Bipolar Disorder**

Funding Agency/Sponsor: Linda and Joel Robuck Distinguished New Scientist Award

Study Doctor: Sandra Bond Chapman, PhD

Research Personnel: Erin Venza, MS

You may call these study doctors or research personnel during regular office hours at 972-883-3208. After office hours, you can reach the study coordinator, Erin Venza, at 214-587-1604.

Instructions:
Please read this consent form carefully and take your time making a decision about whether to participate. As the researchers discuss this consent form with you, please ask him/her to explain any words or information that you do not clearly understand. The purpose of the study, risks, inconveniences, discomforts, and other important information about the study are listed below. If you decide to participate, you will be given a copy of this form to keep.

Why is this study being done?
This study is being done to obtain long-term follow-up data on participants who previously completed a pilot study. Brain blood flow and cognitive function will be evaluated, 2 booster sessions will be provided, and then cognitive testing will be completed again to measure change from booster session. Booster sessions will be conducted in small groups at the Center for BrainHealth.

Why am I being asked to take part in this research study?
You are being asked to take part in this study because you are an adult between the ages of 21 – 70 with a diagnosis of bipolar disorder who completed the previous pilot

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study.

How many people will take part in this study?
About 30 people will take part in this study at UT Southwestern or The Center for BrainHealth.

What is involved in the study?
If you agree to be in this study, you will be asked to sign this consent form and will have the following tests and procedures.

Procedures and Evaluations during the Research:
Two procedures will be performed on you before you begin the booster sessions:

- Cognitive Communication and Neuropsychological testing
- Magnetic Resonance Imaging (MRI)

Cognitive Communication and Neuropsychological Testing: At your first visit, you will complete this testing session in the privacy of an office at the Center for BrainHealth. Participants will be asked to read information, draw conclusions, remember details, problem solve, name objects, repeat numbers etc. This may take up to three hours. You will be asked to do this again at the of the booster sessions.

Screening for the MRI: The researcher will ask questions to decide whether it is safe for you to have an MRI. For your own safety please tell the researcher if you have a heart pacemaker (a device to treat abnormal heart rate), or if you have metal objects in your body. You will have magnetic resonance imaging (MRI) of your head.

Magnetic Resonance Imaging: This is a type of brain scan, which provides detailed views of the inside of the brain, but without the need for any exposure to x-ray, surgery, or any other type of invasive procedure. You will lie quietly on a comfortable, padded bed that moves mechanically into and out of the machine. A doughnut shaped part of the machine, which is the magnet, arches around the bed to record the images of the scan. Magnetic waves will be used to obtain the pictures of the brain. You will hear a tapping sound produced by the magnet. Scanning will be done while you are resting, viewing images, pushing a button in response to questions, and listening. This session will be no longer than one hour. If you completed imaging in the pilot study and are still appropriate to complete it, you will do so both before the booster sessions. Imaging will not be repeated after the booster sessions.

Claustrophobia: Persons who have a fear of being confined in closed or narrow spaces sometimes cannot stay in the scanner. If you experience an uncomfortable feeling of being closed in, the scan will be stopped right away at your request and the technician will take you out of the scanner immediately. Remember that your participation is voluntary. We want you to be comfortable while taking part in this

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research. The fMRI will be performed at the Advanced Imaging Research Center at the University of Texas Southwestern Medical Center at 2201 Inwood Road Dallas, TX 75235.

It is known that magnets disturb the functions of metal implants in your body. Therefore we request that you inform our technician about any metal implants in your body when she/he asks about it. These include pacemakers, cardiac fibrillators etc.

Intervention (Booster Sessions)

Booster sessions will be 2 hours and will be offered once a month for 2 months. The intervention will be conducted in groups consisting of up to 10 individuals per group at the Center for BrainHealth. These participants will be asked to complete assignments during sessions to practice the strategies previously taught in pilot study. Participants will be evaluated prior to the beginning of the booster sessions and at the end. This "booster" intervention involves similar thinking, reasoning and writing as the initial reasoning training completed, and poses minimal risk to the participant.

The cognitive communication and neuropsychological measures, as well as imaging, in this study are designed for research, not for medical purposes. They are not useful for finding problems or diseases. Even though the researchers are not looking at your cognition and/or brain to find or treat a medical problem, you will be told if they notice something unusual. You and your regular doctor can decide together whether to follow up with more tests or treatment. Because the cognitive communication and neuropsychological measures, as well as imaging, done in this study are not for medical purposes, the research results will not be sent to you or to your regular doctor.

How long can I expect to be in this study?

You can expect to be in the study for up to 6 months. You can choose to stop participating for any reason at any time. However, if you decide to stop participating in the study, we encourage you to tell the researchers. You may be asked if you are willing to complete some study termination tests.

What are the risks of the study?

Risks from the MRI

- The scanner makes a loud, banging or tapping noise while it is taking pictures. You will be given a set of earplugs to help reduce the noise.
- You may experience nervousness from confinement in a tight space (claustrophobia). If you become nervous, you can stop the procedure at any time by pushing the panic button you will have in your hand or by telling us to stop. We will be able to hear you at all times.

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- You may experience some discomfort and fatigue from lying still during imaging. You will be able to move some in between scan sequences that usually last only a few minutes. We can always take you out of the scanner if you are too fatigued and need to bend or stretch, or need a break.
- There are no known effects from exposure to magnetic fields.
- If you have any metal clips or plates in your body, you should tell the investigator.
- MRI may not be appropriate if you are pregnant or are trying to become pregnant. MRI may not be appropriate if you have permanent eyeliner or eyebrows or any pieces of metal in your body, such as the following:
- *heart pacemaker, heart valve replacement, or aortic clips*
- *metal fragments in your eyes, skin, or elsewhere in your body*
- *brain clips or pieces of metal used in aneurysm surgery or intracranial bypass*
- *venous umbrella*
- *pieces of metal in the body resulting from work as a sheet-metal worker or welder*
- *clips placed in an internal organ*
- *prosthetic devices, such as middle ear, eye, joint, or penile implants*
- *joint replacement*
- *hearing aid that cannot be removed*
- *neurostimulator*
- *insulin pump*
- *intrauterine device (IUD)*
  - *shunts or stents*
- *metal mesh or coil implants*
- *metal plate, pin, screws, or wires, or any other metal implants*

Risks to an Embryo, Fetus or Breast-fed Infant

Females: A woman who is pregnant or is breast feeding an infant should not participate in this research. Magnetic waves may harm an embryo/fetus. It is not known whether magnetic resonance imaging may harm an embryo or fetus or an infant who is breast-feeding. If you are a woman who can have children, it is your responsibility to inform research staff about any possibility that you may be pregnant. We may ask you if you would be willing to have a pregnancy test.

If you are pregnant or breast feeding, you will not complete the MRI portion of the study; however, you can complete the cognitive-communication & neuropsychological testing and booster sessions.

Risks with cognitive-communication, neuropsychological testing

You may become tired or anxious during testing or intervention. Other possible risks are boredom or fatigue. If you experience either of these side effects, let the clinician know and we can take a break before resuming the activity. If your test responses and the information you share with the experimenter regarding thoughts of suicide that you are

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feeling or that you have a plan to kill yourself, he or she has a legal obligation to tell the authorities. You will be referred to a psychiatrist.

Study Intervention
Because of your participation in this study, you are at risk of becoming tired, anxious, or fatigued. Booster sessions will be similar to a small classroom environment. Should you want a break, we encourage you to take one. Should you not feel well or desire to leave, you are free to leave at any time.

Psychological Stress
Some of the questions we will ask you as part of this study may make you feel uncomfortable. You may refuse to answer any of the questions, take a break or stop your participation in this study at any time.

Loss of Confidentiality
Any time information is collected; there is a potential risk of loss of confidentiality. Every effort will be made to keep your information confidential; however, this cannot be guaranteed.

Other Risks
There may possibly be other side effects that are unknown at this time. If you are concerned about other, unknown side effects, please discuss this with the researchers.

What are the possible benefits of this study?

Benefit to you: If you agree to take part in this study, there may or may not be direct benefits to you. The researchers cannot guarantee that you will benefit from participation in this research. You may benefit by participating in the reasoning program "booster sessions," possibly improving your ability to think. The knowledge and material you gain from this program may benefit you even after your study participation is complete.

Benefit to others: It is possible that the results of this study will provide researchers additional information with regards to the brain function of individuals with bipolar disorder. This could potentially benefit others in the future. The researchers will also learn information about new ways to use magnetic resonance imaging (MRI), cognitive communication and neuropsychological testing, which could improve medical care.

What options are available if I decide not to take part in this research study?
This is not a treatment study. You do not, have to be part of it to get treatment for your condition.

Will I be paid if I take part in this research study?
Yes, you will be paid $50 to participate in this research study via a UT Dallas ClinCard,

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which will be given to you at the post-assessment visit after the booster sessions.

How will I be paid?
The UTD ClinCard is a reloadable MasterCard debit card and will be ready for your use immediately following the post-assessment visit. There are no funds available to pay for transportation to and from the research center, lost time away from work and other activities, lost wages or child care expenses.

Will my insurance provider or I be charged for the costs of any part of this research study?
No. Neither you, nor your insurance provider, will be charged for anything done only for this research study (i.e., the Screening Procedures, Experimental Procedures, or Monitoring/Follow-up Procedures described above).

What will happen if I am harmed as a result of taking part in this study?
It is important that you report any illness or injury to the research team listed at the top of this form immediately. Compensation for an injury resulting from your participation in this research is not available from the University of Texas Southwestern Medical Center at Dallas, UTD Center for BrainHealth, or The University of Texas at Dallas.
You retain your legal rights during your participation in this research.

Can I stop taking part in this research study?
Yes. If you decide to participate and later change your mind, you are free to stop taking part in the research study at any time. If you decide to stop taking part in this research study, it will not affect your relationship with the UT Southwestern staff or doctors. Whether you participate or not will have no effect on your legal rights or the quality of your health care. If you are a medical student, fellow, faculty, or staff at the Medical Center, your status will not be affected in any way.

If your doctor is a research investigator in this study, s/he is interested in both your medical care and the conduct of this research study. At any time, you may discuss your care with another doctor who is not part of this research study. You do not have to take part in any research study offered by your doctor.

Will my information be kept confidential?
Your identifiable records will be kept in a locked room and in a secure cabinet. Only study personnel will have access to these records. Hard copies of deidentified data will be kept in a locked file cabinet within a locked room, and soft copies will be stored on a password protected secured database that only study personnel can access. Identifiable and deidentified data will be stored separately.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you.

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At most, the Web site will include a summary of the results. You can search this Web site at any time.

In addition to this consent form, you will be asked to sign an "Authorization for Use and Disclosure of Protected Health Information." This authorization will give more details about how your information will be used for this research study, and who may see and/or get copies of your information.

Whom do I call if I have questions or problems?
For questions about the study, contact Erin Venza at 972-883-3208 during regular business hours and at 214-587-1604 after hours and on weekends and holidays.

For questions about your rights as a research participant, contact the UT Southwestern Institutional Review Board (IRB) Office at 214-648-3060.

SIGNATURES:

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

Your signature below certifies the following:

- You have read (or been read) the information provided above.
- You have received answers to all of your questions and have been told who to call if you have any more questions.
- You have freely decided to participate in this research.
- You understand that you are not giving up any of your legal rights.

_____
Name of Participant (Printed)

_____ _____ _____ AM / PM
Signature of Participant Date Time

_____
Name of Person Obtaining Consent (Printed)

_____ _____ _____ AM / PM
Signature of Person Obtaining Consent Date Time

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