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Nov 30, 2017
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Laureate Institute for Brain Research, Inc., Tulsa, OK, United States

RESEARCH SUBJECT INFORMATION AND CONSENT FORM	
TITLE:	Adherence to Antidepressant Treatment in Subjects with Depression

This consent form contains important information to help you decide whether to participate in a research study.

The study staff will explain this study to you. Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this consent form to think about and discuss with family or friends.

- **Being in a study is voluntary – <u>your choice</u>.**
- **If you join this study, you can still <u>stop at any time</u>.**
- **<u>No</u> one can <u>promise</u> that a study will help you.**
- **Do not join this study unless all of your <u>questions</u> are <u>answered</u>.**

After reading and discussing the information in this consent form you should know:

- Why this research study is being done;
- What will happen during the study;
- Any possible benefits to you;
- The possible risks to you;
- Other options you could choose instead of being in this study;
- How your personal health information will be treated during the study and after the study is over;
- Whether being in this study could involve any cost to you; and
- What to do if you have problems or questions about this study.

Please read this consent form carefully.

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RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	Adherence to Antidepressant Treatment in Subjects with Depression
PROTOCOL NO.:	2017-007-00 WIRB® Protocol #20172753
SPONSOR:	Laureate Institute for Brain Research
INVESTIGATOR:	Martin Paulus, MD 6655 S Yale Ave Tulsa, Oklahoma 74136 United States
STUDY-RELATED PHONE NUMBER(S):	Martin Paulus, MD 918-502-5155 918-481-4000 (24 hours)

This consent form describes a research study. Research studies involve only individuals who choose to participate. Please take your time to make your decision about participating in the study.

This consent form may contain words that you do not understand. Please ask the Principal Investigator or the study staff to explain any words or information that you do not clearly understand. You may take home an unsigned copy of this consent form to think about or discuss with family or friends before making your decision.

Why Have You Been Asked To Participate In This Study?

You are being asked to take part in this study because you have symptoms of depression and are seeking treatment.

Why Is This Study Being Done?

This study seeks to determine if adding methylphenidate (MPH) to an antidepressant medication regimen will improve adherence to treatment for depression.

The following definitions may help you understand this study:

- A placebo is a pill that looks like but does not contain any medicine, it is also called a “sugar” pill.
- In this clinical trial, research participants are randomly assigned to a medication treatment, and their outcomes are measured.
- A placebo-controlled study, like this one, means that some participants will receive a placebo, instead of the study drug. A placebo looks like a drug, but it includes no active ingredients.
- Randomization or randomly means you will be placed by chance (like drawing straws) into one of the study groups.
- Standard medical care means the regular care you would receive from your personal medical doctor if you chose not to participate in this research.

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

What Drugs Are Involved In This Study?

Escitalopram
Escitalopram is a selective serotonin reuptake inhibitor (SSRI). It is used to treat Major Depressive Disorder (MDD) and acute treatment of Generalized Anxiety Disorder (GAD). This drug has been approved by the U.S. Food and Drug Administration (FDA). Every participant will receive this drug.

Methylphenidate
Methylphenidate is a mild central nervous system (CNS) stimulant. It is used to treat Attention Deficit Hyperactivity Disorder. This drug has been approved by the FDA. You will receive this drug OR you will receive a placebo.

Since this is a placebo-controlled study, placebos that look just like the actual study drugs will also be used. The placebos will be composed of substances that are not expected to have any beneficial or harmful effect on your body.

After you have been assessed by the clinician you will be randomly assigned to one of the two study plans. Each study plan will include 50 participants, totaling 100 participants for the entire study. You will receive the escitalopram and have a 1 in 2 chance of also receiving the methylphenidate. The clinician will not know whether you are receiving escitalopram with the methylphenidate or with the placebo. A research staff member, not working with you, will keep that information confidential. That information will not be revealed to the clinician until the study is completed. However, the clinician will release the information about all your medications if needed for your safety.

You will receive one of the following combinations:

- Escitalopram & Methylphenidate
- Escitalopram & Placebo

The Escitalopram & Methylphenidate or the Escitalopram & Placebo will be in a capsule and is to be taken by mouth. One capsule will be taken once daily.

What will my responsibilities be during the study?

While you are part of this study, the researchers will follow you closely to determine whether there are problems that need medical care. We request that you do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the researchers' and your study doctor's instructions.
- Let the researchers know if your telephone number or address changes.
- Store the study capsules in a secure place at home away from anyone who is unable to read and understand labels, especially children.
- Tell the researchers before you take any new medication, even if it is prescribed by another doctor for a different medical problem or something purchased over the counter.
- Tell other doctors who are treating you about your participation in this study.
- Carry information about the research medication in your purse or wallet.
- Report to the researchers and to your Principal Investigator about any injury or illnesses occurring while you are in the study, even if you do not think it is related to the research medication.

How Many Subjects Will Take Part In The Study?

About 100 individuals will take part in this study at the Laureate Institute for Brain Research (LIBR).

What Is Involved In The Study?

The study involves:

- Questionnaires
- Laboratory tests
- Electrocardiogram (EKG)
- Blood draws
- Physical Measurements
- Urine tests

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Visit Schedule Summary:

Visit 1 – Screening Visit	**Location-** LIBR	**Time**
Consent		1.5 hours
Lab work		
Questionnaires		
Visit 2 – Week 0		1.5 hours
Physician visit		
Questionnaires		
Randomization of Drug & Dispense		
Visit 3 – Week 1	Over the phone	5 min
Questionnaires		
Visit 4 – Week 2	LIBR	30 min
Physician visit		
Questionnaires		
Dispense drugs		
Visit 5 – Week 3	Over the phone	5 min
Questionnaires		
Visit 6 – Week 4	LIBR	30 min
Physician visit		
Questionnaires		
Dispense drugs		
Visit 7 – Week 6	Over the phone	5 min
Questionnaires		
Visit 8 – Week 8	LIBR	60 min
Physician visit		
Questionnaires		
Blood draw		

ALL TIMES ARE APPROXIMATE

Questionnaires

These tests and questionnaires about your health, mood, and personality will measure your mental and physical states.

Laboratory Tests

You will have blood tests. A trained nurse will take a small amount of blood from a vein in your arm. Blood will be collected using sterile techniques by a person experienced in drawing blood.

Physical Measurements

Your weight, height, blood pressure, pulse, Electrocardiogram (EKG), and other like measurements will be obtained for research purposes.

Urine Tests

If you are a female of childbearing years, you will receive an over the counter urine pregnancy test during the screening visit.

How Long Will You Be In The Study?

There are 5 study visits at LIBR and 3 phone call visits. This study will run for about 8 weeks of treatment, plus up to one week prior to treatment for screening eligibility.

There may be circumstances under which your participation in the study may be stopped by the investigator without your consent.

You may stop participating in this study at any time. You may also refuse to be contacted again in the future about participating in the study again.

What Are The Risks Of The Study?

Questionnaires

There is no medical risk associated with the questionnaires. You may experience temporary discomfort, including anxiety and sadness, when recalling particularly negative memories. Members of the research staff are trained to help you if you have an unusually strong reaction to these memories. You can also stop the procedure at any time. Also, if you show a strong reaction, such as extreme sadness, to any part of the study, researchers will stop the procedure and help you relax before leaving the LIBR.

Blood Collection

For the blood collections, you may have some discomfort and bruising at the site of needle entry. There is a very small risk of fainting or infection in the area of the needle insertion.

Study Drugs

The study drug may cause side effects or other problems. The researchers will be checking your medical information during the study to monitor for side effects. However, you should tell the research team about anything that is bothering you or any changes in your health since the last visit. The researchers may be able to take steps to try to reduce side effects. You may have none, some, or all of the side effects listed below. There may be other side effects or risks that are not yet known.

Medication Risks:
Because of your participation in this study, you are at risk for side effects from the study medications.

Methylphenidate

Methylphenidate may cause side effects. The most common are:

- Insomnia
- Nervousness

Less common side effects:

- Heart palpitations
- Loss of appetite, abdominal pain, nausea
- Skin rash
- Fever
- Headache, dizziness or drowsiness
- Changes in blood pressure
- Anemia
- Mood changes, aggression
- Hair loss

Tell your study doctor if any of these symptoms are bothersome or persistent (do not go away):

Escitalopram

Escitalopram may cause side effects. The most common are:

- Insomnia
- Nausea
- Fatigue
- Decreased libido
- Increased sweating
- Drowsiness

Less common side effects:

- Dry mouth
- Dizziness
- Diarrhea
- Constipation
- Abdominal pain
- Decreased appetite
- Sinusitis
- Impotence

Abruptly stopping escitalopram can cause flu-like symptoms. It is best to gradually wean off escitalopram. You may want to continue taking this escitalopram after the study has been completed. We will provide the drug information that you can take to your primary care physician. We will remind you at Visit 4 & 6 to contact your primary care physician. If you choose to continue the escitalopram after visit 8, it will be your responsibility to purchase the drug and to follow-up with your primary care physician.

You will be closely monitored by your study doctor for side effects to the study drug. If the study staff has concern for your immediate safety because of suicidal thoughts or behaviors, they may contact your designated family member or friend or arrange transport to an emergency room or local hospital. Study clinician and research personnel phone numbers are listed in this consent form. You are encouraged to call should you need additional assistance beyond scheduled appointments. The research personnel will maintain close contact with you and reschedule appointments as needed. Your study clinician may discontinue the study at any time should your symptoms worsen or if you desire to withdraw.

Risk of Placebo
Some participants will receive a placebo, instead of the methylphenidate. A placebo looks like a drug, but it includes no active ingredients. The placebo will not affect the escitalopram that is being used to treat your depression.

Physical Measurements
There are no known risks in taking your physical measurements.

Pregnancy Risks
If you are a woman of child-bearing years, you must not be pregnant while participating in this study. There may be other risks from study participation that currently are unknown.

You Should NOT Participate in the Study if:

- You are pregnant or suspect that you may be pregnant
- You have heart disease, kidney disease or another chronic medical illness
- You are feeling suicidal

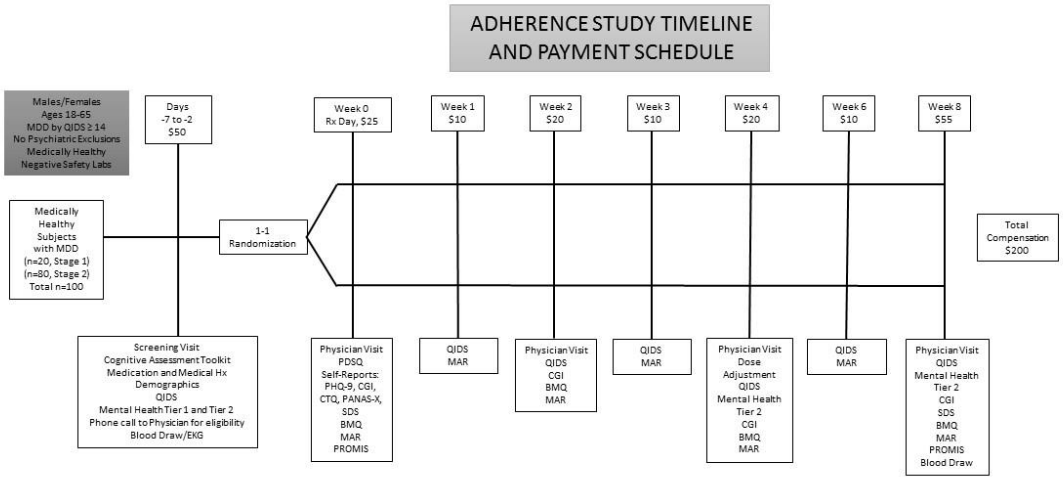
Are There Benefits To Taking Part In The Study?

If you agree to take part in this study, there may not be direct benefits to you. The benefits to participation that are reasonable to expect are that the study drug may improve your symptoms of depression, but it is also possible that you may not benefit. You may find the frequent contact with the study personnel reassuring. The researchers cannot guarantee that you will benefit from participation in this research. Information obtained from this study will benefit the researchers and may benefit patients in the future.

What Are The Costs Of Participating In The Study?

Neither you nor your health insurance will be charged for any of the study tests, procedures, or activities. If you need to be hospitalized, voluntarily or involuntarily, Laureate Institute for Brain Research does not intend to provide payment for this, and you or your insurance provider will be billed for these costs.

Will You Be Paid For Participating In This Study?



Study Visit	Compensation
Visit 1 - Screening	$50
Visit 2 – Week 0	$25
Visit 3 – Week 1	$10
Visit 4 – Week 2	$20
Visit 5 – Week 3	$10
Visit 6 – Week 4	$20
Visit 7 – Week 6	$10
Visit 8 – Week 8	$55
Total	$200

You will be paid after each LIBR visit through a ClinCard (similar to a debit card). It may be used approximately 1 business day after the visit.

What Other Options Are There?

This study is to research the effect of the study agent on compliance only. Other options exist for the treatment of major depressive disorder.

The study doctor will discuss with you the risks and benefits of alternative treatments.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

THE INFORMATION AUTHORIZED FOR RELEASE MAY INCLUDE RECORDS WHICH MAY INDICATE THE PRESENCE OF A COMMUNICABLE OR NONCOMMUNICABLE DISEASE.

This information is made confidential by law and can be released only with your permission except by order of the court or health department in certain limited cases of persons who have risk of exposure of the diseases. Information from this study may be submitted to governmental agencies in other countries where the study medication may be considered for approval. Because of the need to release information to these parties, absolute confidentiality cannot be guaranteed.

Who may use and give out information about you?
Investigators at the Laureate Institute for Brain Research frequently collaborate with researchers at other nonprofit research institutions or commercial organizations. The data collected as part of this study, including interviews and medical information, research test results, and blood and saliva samples may be shared with these collaborators. Any data shared will not include your name or other personally identifiable information.

Who might get this information?
Laureate Institute for Brain Research, Inc. is the sponsor of this research. “Sponsor” means any persons or companies that are working for or with the sponsor, or owned by the sponsor.

Your information <u>may</u> be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Western Institutional Review Board® (WIRB®)

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
Yes, but this permission will not stop automatically.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

If you have any questions or concerns about your privacy rights, you should contact the LIBR Privacy Officer at 918-502-5155 or via email at privacy@laureateinstitute.org.

You have the right to access the medical information that has been collected about you as a part of this research study. However, you may not have access to this medical information until the entire research study has completely finished.

What If You Are Injured While Participating In This Study?

If you get hurt or sick while participating in this study, emergency medical treatment is available from the Saint Francis Hospital and/or the Laureate Psychiatric Clinic and Hospital. If you get sick after the study is completed, call 911 in an emergency. Be sure to tell the emergency staff and other healthcare providers of your participation in this study. Contact the Principal Investigator of this study, Martin Paulus, MD, as soon as possible at 918-502-5155 or 918-481-4000 (24 hours) if you think you have a research-related injury or illness.

You or your health insurance provider will be billed to cover the cost of the medical or emergency services provided. Some insurance carriers may not provide coverage for injuries received while participating in a research study. You are encouraged to contact your insurance carrier to determine whether coverage is available. Otherwise, you may have unexpected expenses as a result of your participation in this study. No funds have been set aside by the Laureate Institute for Brain Research to compensate you if you are hurt or get sick. However, you still have the right to bring a law suit if you think you were harmed and deserve compensation.

You do not give up any of your legal rights by signing this consent form.

Who Will Provide Funding For The Study?

Funding for this research study will be provided by the Laureate Institute for Brain Research.

What Are Your Rights As A Participant?

Taking part in this study is voluntary. You may choose not to participate. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. If you agree to participate and then decide against it, you can withdraw for any reason and leave the study at any time without penalty or loss of benefits to which you are otherwise entitled.

Can The Researchers Remove Me From This Study?

The investigator may withdraw you from this research activity (without your consent) if certain circumstances arise. For example, you may be withdrawn from this study if the investigator feels that your continued participation places you at unnecessary risk or harm or you become ineligible (because of illness) to continue or because of non-adherence to protocol instructions. You may have to drop out, even if you would like to continue. The investigators will make a decision and let you know if it is possible for you to continue. The decision will be made to protect your health and safety.

What If There Are New Findings?

We will provide you with any significant new findings developed during the research study that may affect your health, welfare, or willingness to continue your participation in this study. You may be asked to sign a new consent form if this occurs.

Whom Should You Call If You Have Questions Or Problems?

Your contact persons for this study are:

Sahib Khalsa, M.D. He can be reached during business hours at 918-502-5743.

Martin Paulus, M.D. He can be reached during business hours at 918-502-5155.

If you have questions about your participation in this study, concerns, or complaints about the study, or have a research-related injury, contact the study doctor, Sahib Khalsa, M.D. at 918-502-5743 or 918-481-4000 (24 hours). For emergencies call 911.

If you have questions about your rights as a research subject or if you have questions, concerns, input, or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who perform independent review of research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in this study, you will be given a copy of this consent form.

Signature

I have read the information in this consent form. I have been given an opportunity to ask questions. All my questions about the study and my participation in it have been answered.

I Agree To Participate In This Study

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

_____
PRINTED NAME OF PARTICIPANT

Consent Signature

_____ _____
PARTICIPANT SIGNATURE (18 years and older) Date

_____ _____
SIGNATURE OF PERSON CONDUCTING INFORMED CONSENT DISCUSSION Date

_____ _____
PRINTED NAME OF PERSON CONDUCTING THE INFORMED CONSENT DISCUSSION Date