SUBJECT INFORMATION AND CONSENT FORM

Study Title	A TEST OF MDMA-ASSISTED PSYCHOTHERAPY IN SUBJECTS WITH CHRONIC POSTTRAUMATIC STRESS DISORDER (PTSD)
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Daytime telephone number:

24 hour contact number:

PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

This consent form describes a research study and your role as a participant. Please read this form carefully. Do not hesitate to ask anything about the information provided; it should stimulate your questions. The investigator will describe the study and answer your questions. After reading the consent form, the investigators will give you a short quiz to spot any parts of the study that need to be explained even further or in a better way than in the consent form. You will not be excluded from being in the study on the basis of your answers to this quiz.

This consent form may contain words that you do not understand. Please ask the researchers 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.

PURPOSE AND BACKGROUND

This small, early study is designed to gather preliminary information about whether MDMA-assisted psychotherapy is safe and helpful for subjects with posttraumatic stress disorder (PTSD). The researchers plan to use the results of this study to design further studies.

MDMA is experimental, which means it has not been approved by the US Food and Drug Administration (FDA) for medical use, except within research studies. MDMA is also a controlled drug (illegal to use outside of research) and is sometimes known as "Ecstasy" (which is supposed to contain MDMA but often contains other drugs instead of or in

addition to MDMA). MDMA has already been used legally in research and illegally in uncontrolled environments, such as nightclubs. While much is known about MDMA and its risks, there remains much that is unknown.

This study will compare use of MDMA (125 milligrams) with a placebo (an inactive substance or a "sugar pill").

You are being asked to participate in this research study because you have been diagnosed with posttraumatic stress disorder (PTSD) as a result of being the victim of a crime, and because your symptoms have failed to go away after receiving treatment for PTSD.

Length
Participation in this study will take approximately 3 to 4 months and will involve 17 visits. Most visits will last for no more than 90 minutes (an hour and a half). The first two visits might last two to four hours, and the two MDMA or placebo-assisted psychotherapy visits could last for six to eight hours or more. You will also be required to spend the night in the clinic after each experimental session, returning home after the 90 minute non-drug psychotherapy session the next morning.

Conduct
If you and Dr. Mithoefer agree that you should be in the study, you will be asked to agree to the following:

1. To come to all medication, psychotherapy and evaluation sessions.
2. To avoid taking any psychiatric medications from the beginning of the study until the last follow-up session. You will be off any psychiatric drug for up to 17 weeks.
3. If you are currently on any psychiatric medications, you should discuss this with Dr. Mithoefer. You will be required to give Dr. Mithoefer permission to talk to your doctor about your withdrawing from (not taking) medication during the study. We encourage you to talk to your doctor as well if you wish.
4. If you are currently seeing a psychotherapist you may continue to do so. You may not begin any new psychotherapy, or increase the frequency or length of visits with your psychotherapist until after the final evaluation session.
5. You must be able to spend the night after each experimental (MDMA or placebo) session at the office where the session will be held and remain until after the non-drug psychotherapy session the next morning. A private bedroom will be available for you. If you request and if Dr. Mithoefer agrees, you may have one other person stay with you, such as your spouse or partner, or a friend.
6. You must be willing to have an attendant, who will be the same sex as you, stay in the clinic from the time after you are done with the experimental (MDMA or placebo) sessions until the non-drug session on the next day. The attendant will be a registered nurse (RN) and will be trained to be part of this study. The attendant will offer dinner and breakfast, assist you with any physical needs if requested, and contact Dr. Mithoefer to speak with him or to return to the clinic at your request or if the attendant considers it necessary. You will meet the attendant at one of the non-drug psychotherapy sessions prior to the experimental sessions.

7. You must find someone who will take you home from the non-drug session scheduled for the morning after the experimental session because we cannot predict with certainty how MDMA might affect your driving. You might feel tired or feel less alert than usual.
8. You must be willing to speak with one of the researchers over the telephone every day from the day following each experimental (MDMA or placebo) session up until seven days later. One of the researchers will contact you every day to determine if you are experiencing any physical or emotional distress that would require Dr. Mithoefer's attention.
9. If you are a female and are able to get pregnant, you must use an effective method of birth control.

Importance of Honesty
Many of the procedures and tests are designed to reduce the chance of your being hurt by being in this study. It is important that you do your best to fully describe your general medical and psychiatric history as well as your recent and past drug use. If you accidentally break one of the study rules (such as taking a drug that was not approved by the researchers), it is important that you tell the researchers.

Please, if in doubt, discuss this with the researchers.

PROCEDURES/WHAT WILL HAPPEN TO YOU

SCREENING (EVALUATION):
Before you can be in the research study, the researchers must first make sure that you qualify for the study and that you are generally physically healthy. This evaluation will be done during several office visits.

The tests will include the following:
- Questions about your medical history, including questions about your emotional and psychiatric history. This may include any previous medical or psychiatric problems or treatment and may include questions about difficult experiences you may have had during childhood or at other times of your life.
- A questionnaire about your posttraumatic stress symptoms and how you deal with them in your everyday life. Your score on this questionnaire will be used to decide if you can be in the study.
- A physical examination that will include measures of your blood pressure, pulse, temperature, and body weight.
- A study doctor (someone other than the researchers) will listen to your heart and lungs and examine your body for any signs of disease.

- An ECG (electrocardiogram) will also be taken, which is a recording of the electrical activity of your heart.
- You will be asked to provide a blood sample (about 2 tablespoons) and a urine sample for routine laboratory testing.
- Your urine will also be tested for drugs of abuse.
- If you are a woman and are able to get pregnant, a pregnancy test will be done on the urine sample. Your urine drug screen and pregnancy test must both be negative for you to take part in the study. The screening process will take about 3 to 4 hours.
- You will also be tested for HIV. State law requires that the results of positive tests for HIV be reported to a local health agency. This is the legal obligation of the medical personnel.

BEGINNING OF STUDY

If you have decided that you want to be in the study and if the doctors find that you are eligible to be in the study, you will then take some more psychological tests. Within approximately two weeks after the preliminary testing, you will have a two to four hour visit. During this visit, you will be given three different types of evaluation. Each will be given again at the end of the study to compare your results before and after. They include:

1. Three questionnaires about symptoms of posttraumatic stress disorder and how you deal with them in your life.
2. A personality test that measures the way you tend to think and feel about the world, and how you tend to interact with other people.
3. A series of tests of attention, memory and different types of problem solving. These are not tests of intelligence. They are measures of skills and processes we use in thinking and problem-solving.

You will not be taken out of the study as a result of how you do on any of these three groups of questionnaires or tests.

SCHEDULE OF EVENTS

Time is counted from the first study visit after you are selected to be in the study. Screening will be done approximately two weeks before you start the study.

Time: **d=days w=week m=month**	1 to 3 visits within two weeks before				+2 w	+2w , 1d	+2w , 4d	+ 3 w	+4 w	+5 w	+6 w	+6 w, 1d	+ 6 w , 4 d	+ 7 w	+8w	+9 w	+ 3. 5 m
Visit	Screen/Start					Therapy and Evaluation						Therapy and Evaluation					
Screening	X																
Personality Tests		X															
Psycho Therapy only			X	X		X		X	X	X		X		X	X	X	X
MDMA and therapy					X						X						
PTSD Symptom Measures	X						X						X				X
Medical Exam	X												X				
Memory, Problem Solving Tests	X																X

Most visits will last for no more than 90 minutes (an hour and a half). The first two visits might last two to four hours, and the two experimental sessions (MDMA or placebo-assisted psychotherapy visits) could last six to eight hours or more. You will also be required to spend the night in the clinic after each experimental session, returning home after the 90 minute non-drug psychotherapy session the next morning.

INTRODUCTORY PSYCHOTHERAPY SESSIONS:

You will meet with the researchers on two occasions before the experimental session. These visits will last about 90 minutes. During each of the two introductory sessions, you will discuss the traumatic incidents that led to your PTSD, the ways PTSD symptoms are affecting your life and what you would like to achieve during these sessions. You will also learn more about what to expect during the MDMA or placebo sessions, and you will meet the attendant who will work at the clinic on the evening after each experimental session until the non-drug psychotherapy session the next morning.

SELECTION OF DRUG – MDMA OR PLACEBO?

Each subject will be randomly assigned (by chance, as if by flipping a coin) to get either MDMA or placebo (a capsule containing the type of sugar found in milk but no active drug). There will be twenty subjects. Eight will receive placebos (a 40% chance) and

twelve will receive MDMA (a 60% chance). Whatever you are assigned, MDMA or placebo, you will take on two occasions, as there are two separate experimental sessions scheduled three to five weeks apart.

Neither you nor the researchers will know who is getting MDMA or placebo until after the study is completed. However, this information is available if needed in an emergency. You will be told after the study is over whether you received the MDMA or the placebo.

EXPERIMENTAL SESSION:
There will be two MDMA/placebo sessions. The first will occur at about week 2 and the next between week 5 and 7.

First, you and the researchers will discuss your goals, so that all of you will know what you want to achieve during the experimental session. The researchers will also answer any additional questions you may have about this session. Some of the tests done before and during the experimental sessions are meant to make sure you can still be in the study and to spot problems during the experimental session.

- You will be asked not to eat anything or drink any alcohol after midnight on the night before each session.
- You can drink non-alcoholic liquids during this time, such as water or juice.
- Each of the two sessions will last for six to eight hours, though the researchers will remain with you for a longer period of time if necessary. You will also spend the night in the clinic and remain until after the non-drug psychotherapy session the next morning.
- Your temperature, blood pressure and pulse will be measured before you receive the medicine.
- You will also complete a very brief, simple test of how comfortable or distressed you feel. This will involve marking a number on a sheet of paper that coincides with the way you feel at that moment. You will complete the same short test every 60 to 90 minutes throughout each experimental session. This will allow the researchers to know how you are feeling throughout the session and to see whether your feelings of comfort or distress change after receiving MDMA or placebo.
- Before the start of each session, your urine will be tested for drugs of abuse.
- If you are a woman who can become pregnant, a pregnancy test will also be done on your urine.
- If either test is positive, the session may be delayed or cancelled.
- The attendant will arrive during the last hour of the experimental session. If you choose, a significant other such as a close friend or a family member can also come at this point in the session.

The experimental session will be audiotaped, so that the researchers will have accurate records of the session and so that they can gather more information about drug-assisted psychotherapy sessions.
In addition to the doctor and nurse you will work with during the experimental session, a board-certified emergency room doctor and emergency room nurse will be in the adjacent

room to provide medical assistance or opinions if the researchers request it. They will not generally be in the room with you and the researchers. Unless they are in the room, they will not hear anything that takes place during the sessions. If they do overhear anything, they will keep it in confidence.

After the preliminary tests you will receive a capsule that will either contain 125 mg MDMA or a placebo. After taking the capsule, you will sit or lie down in a comfortable position. You can ask for an eye shade if you wish. You will listen to music through headphones during much of each experimental session. Periodically you will be asked to remove the headphones to talk to the researchers. You may also remove them yourself when you want to talk to the researchers or if you choose to request periods of silence. Lying or sitting in a comfortable position and listening to music are meant to bring out emotional thoughts and feelings, including thoughts and feelings about the trauma. Both researchers will remain with you, and they will help you if you need them to help you. They will speak with you and ask you to talk to them at least once an hour, but you can talk to them whenever you wish. There may be periods of time when, after you have been talking, they will suggest that you stop talking for a while in order to pay attention to your inner experience (your inner thoughts and feelings). There will be juices or Gatorade available, and you will be encouraged to drink an adequate amount of fluid. You can drink it whenever you wish to do so, within the limits of the amount that is safe for your body. Later on, food will also be provided that you can eat if you wish to do so.

The researchers will continue to measure blood pressure and pulse at regular intervals. Temperature will also be measured, but slightly less often. You will be monitored for any side effects, which will be treated if they occur. If this should occur, the researchers will explain what they are doing at all times.

The attendant will arrive during the last hour of the experimental session. If you have a significant other who you would like to be with after your session, he/she can also come at this time.

If you are still confused or very upset eight or more hours after the start of the experimental session, the researchers will stay with you until you have recovered more fully. If the researchers think you are at risk for hurting yourself or someone else, they will either remain with you all night or have you stay in East Cooper Medical Center until you are no longer at risk of hurting yourself or someone else. If the researchers determine that the effects of the drug have worn off and you are in an appropriate frame of mind, they will leave the clinic with the attendant in charge. If you or the attendant considers it necessary, the attendant will call Dr. Mithoefer and request that he return to the clinic, which should take him only 10-20 minutes.

You will be spending the night in a room in the offices of Dr. Mithoefer. The attendant will be staying in another room nearby. If you request and Dr. Mithoefer approves, you may also have someone of your choosing spend the night. You can use the kitchen or walk around outside if you want. If you find you need to talk with the researchers or you

are having other problems and need to contact the researchers, the attendant will contact them immediately.

On the next day, you will have a non-drug therapy session with the researchers. You will need to arrange ahead of time to have someone take you home from this non-drug session. You will need to have someone drive you home from the non-drug therapy session on the day after the experimental session because we do not know how MDMA will affect your ability to drive, and because some people report feeling tired, less alert or having trouble concentrating a day after having taken MDMA. If you cannot find anyone to take you home, the researchers will find someone to drive you.

After you return home, the researchers will telephone you every day for a week to inquire about how you are feeling and determine whether you should see Dr. Mithoefer before your next scheduled non-drug psychotherapy session. If you need to schedule additional meetings with the researchers besides those that are scheduled as part of the study, then you may do so. There will be no cost to you for any additional meetings with the researchers.

You can contact the researchers at any time. The researchers will give you a card with telephone numbers for reaching Dr. Mithoefer, the organization sponsoring the study, or the Institutional Review Board (IRB) that approved the study. You can keep this card in your wallet to make it easier for you to contact the researchers if you need to do so. Dr. Mithoefer will be on call (reachable by telephone or pager) 24 hours a day throughout the research study, except on occasions when he is out of town. At those times another psychiatrist familiar with the study will be on call and can be reached through Dr. Mithoefer's phone number.

If you have very high blood pressure, get sick, or have a significant lasting negative reaction after the first experimental session, you or the researchers may decide that you should not participate in the second experimental session. You may make this decision to stop being in the study for any reason. If the researchers decide to take you out of the study, they will let you know that they are doing this and they will tell you why they are doing this. If you are taken out of the study at this point, or if you decide you do not want to be in the study, the researchers will ask you to complete some final questionnaires and tests. These include questionnaires about your PTSD symptoms and tests of memory and problem solving. The researchers want to see whether there are any changes in your symptoms or on the memory and problem solving tests. If you wish, you can decide not to complete these questionnaires and tests.

If you decide you do not want to continue in the study during one of the experimental sessions, you will still have to stay in the clinic until the researchers think that you are well enough to go and that all the effects of the drug have worn off. Anything that happens in that session will not count as part of the study.

The second experimental session will occur 3-5 weeks after the first and will be carried out in an identical manner.

Subject's Initials_____

FOLLOW-UP:
There will be three different types of follow-up sessions:

-- Follow-up psychotherapy – to talk about the experience with the study drug.
-- Research (evaluation) follow-up – to assess your responses before and after the experimental session.
-- Regular psychotherapy – to support you.

Two **follow-up psychotherapy sessions** will occur 24 hours after each MDMA/placebo session. These will last for about 90 minutes. During these sessions, you and the researchers will talk about what you experienced during the experimental (MDMA/placebo) sessions and what you thought and felt about it during the MDMA/placebo session and afterwards. You and the researchers will also talk about ways to work with this information and to use what you learned to help treat your posttraumatic stress disorder. You will be asked to guess whether you received the experimental drug (MDMA) or placebo. Asking you to guess which drug you received will allow the researchers to know more about what condition you thought you were in, and whether this belief changed how you felt or thought about the experimental session afterwards. You will not be told if your guess is correct. At the end of the study, the researchers will find out whether you received MDMA or placebo, and they will tell you then whether you received one or the other.

The **first and second research (evaluation) follow-up sessions** will occur four days after the experimental session, and each session will last for about 90 minutes. During these sessions, you will be asked to complete three different questionnaires that measure posttraumatic stress disorder and the symptoms you are experiencing at the time you are completing the measures. There are no right or wrong answers to these tests, and you will not be taken out of the study as a result of these measures. The researchers can compare how you scored on these measures four days after the MDMA or placebo session with your scores at the start of the study, and they can see whether or not your symptoms and problems have changed.

You will also receive a second medical examination and some blood tests. The medical examination will be done in order to make sure that your health has not changed since the start of the study and to measure any possible problems or improvements in your health since the beginning of the study.

You will also meet with the researchers weekly for **regular psychotherapy sessions** after each experimental session. Regular psychotherapy means talk therapy to help you express, understand and integrate (bring together and connect to your life) any thoughts or feelings you may be having about your symptoms and their causes and about your experiences during your experimental sessions. These sessions will last from about 60 to about 90 minutes. There will be three or four regular psychotherapy sessions after the first experimental session, and three regular psychotherapy sessions after the second experimental session. Regular psychotherapy sessions are provided as part of standard

care for this study. The purpose of these sessions is to help you with any difficulties you may have faced during the experimental sessions and to help you gain maximum benefit and understanding from whatever experiences you had during those sessions. They are not intended to take the place of your regular care if you also are continuing treatment by a therapist other than the researchers.

The **last follow up session** will occur approximately three-and-a-half months after the start of the study (two months after the second experimental session). This follow up should last for 3 to 4 hours. You will take the same tests of posttraumatic stress disorder symptoms that you filled out at the start of the study and during all follow up sessions. The tests that measure symptoms of posttraumatic stress disorder will allow the researchers to see whether your symptoms have changed or stayed the same over time. You will also be completing tests of attention, memory and problem solving that you completed at the start of the study. While all of the tests will involve solving generally similar problems, the specific questions or items may be different when you complete them again. You will also complete a short questionnaire asking you about any good or bad feelings you had about being in the study.

A few days after the last follow up session, you will have a final 60 to 90 minute meeting with the researchers. This will be an opportunity to further discuss your experiences during the study and help you to integrate those experiences into your life in a helpful way.

POSSIBLE RISKS OR DISCOMFORTS

MDMA has not been widely tested in human subjects. Some of the risks observed are listed below.

Side effects during the MDMA experience that are less severe but more frequently reported, are
- lack of appetite,
- teeth grinding or tight jaw muscles,
- dry mouth,
- difficulty balancing or walking, and
- decreased concentration.

These side effects have been reported by 40 to 70% of subjects in previous studies. Less commonly, subjects have reported feeling hot or cold, feeling that their heart is racing, sweating, dizziness, drowsiness, upset stomach, anxiety, tenseness, weakness, shaking, headache, or feeling faint. When any of these side effects occur, they usually last less than four hours, though some subjects report that some of these side effects can last up to twenty-four hours.

Risks from MDMA.

There may be unknown side effects or risks from the use of MDMA.

Changes in vision or hearing: In previous research studies in which MDMA was administered to volunteers, which have included a total of about 200 subjects without emotional disorders and 6 with posttraumatic stress disorder, most subjects reported experiencing minor changes in vision and hearing, such as sounds seeming closer or farther away than usual, or objects seeming brighter than usual, with these changes lasting 2 to 3 hours.

Blood pressure and heart rate. These effects of MDMA usually last 4 to 6 hours. At the dose in this experiment, the increases in blood pressure and heart rate are likely to be moderate.

Blood pressure rose well above normal rates in a few subjects (a little less than 5%) after MDMA was given in previous studies, but these subjects did not report any discomfort and did not require any treatment. Although these higher blood pressures are similar to those that occur after vigorous (heavy) exercise, they could cause serious problems in individuals with pre-existing heart or blood vessel defects. These serious problems could include heart failure or stroke**.** However, we are going to screen all potential subjects for preexisting heart problems before they are allowed to be in this study. This doesn't guarantee that no heart problems will occur, but it does greatly reduce the risk of this happening.

Do not participate if you know you have pre-existing heart or blood vessel problems.

Anxious or jittery feeling: Some subjects reported feeling over-stimulated or anxious at times. It usually lasted less than 30 minutes. Due to your posttraumatic stress disorder, you may experience severe anxiety or panic attacks. Letting yourself accept and feel those emotions deeply can be part of the psychotherapy in the experimental session. If you are not able to deal with these experiences in a way that helps you, the researchers will help you work with these feelings. Having a person stay with you, such as a spouse, friend or relative, may help you feel less anxious after the end of the experimental session. The researchers will also stay with you for as long as necessary after the end of the experimental session if you are still very anxious or upset. It is possible that if such periods of heightened emotion have not been adequately resolved during the session, you could be at increased risk for suicide or other self-harm afterwards. You will be encouraged to ask the attendant to call the researchers immediately if any thoughts about hurting or killing yourself should occur so they can help you resolve them safely. If necessary, they may prescribe anti-anxiety medication or medication for sleep.

If you are in immediate danger of hurting or killing yourself or hurting someone else, then the researchers may require you to stay in East Cooper Medical Center.

Heart Valve: MDMA is similar to fenfluramine (one of the drugs in Fen/Phen; Redux). Fenfluramine might cause heart valve problems in a small percentage of people who have taken fenfluramine daily for a period of several months or more.

One study has found that MDMA causes some of the same biochemical changes in isolated heart valve cells as fenfluramine. These findings suggest that MDMA might cause heart valve problems if taken on a daily basis for several months or more. Given the low frequency of doses of MDMA in this study, the risk of heart valve problems is very low. The only study that did careful heart examinations of a small group of Ecstasy users found their hearts to be normal.

Serious problems and Death: There have been some serious problems, and even deaths, associated with the use of Ecstasy outside of controlled clinical or laboratory settings. Serious problems have included high fever, drinking too much liquid, convulsions, and liver damage. Some recreational users of Ecstasy have become severely anxious, depressed or paranoid (thinking that other people are against them). Since you will be receiving moderate amounts of uncontaminated MDMA in controlled a setting with trained therapists who will be closely monitoring your physical and psychological reactions, these problems are not expected to occur during or after the experimental session. If they do occur, the researchers and/or the emergency room doctor and nurse in the next room are prepared to respond to reduce the chances that you will experience any long-term consequences.

Insomnia & drowsiness: In previous studies, less than 40% of subjects have reported insomnia (difficulty sleeping), and feeling tired, irritable, or drowsy for as long as 3 days after MDMA.

Mood: Some after-effects of MDMA may be noticeable up to 2 or 3 days later. While some subjects feel that their mood is better, others feel it is worse.

Immune response: You will probably have a less active immune system for 2 or 3 days after MDMA. This change in immune system activity is similar to what would occur if you had 4 to 5 drinks of alcohol. This may make you more likely to become sick with a cold or other infection during this time.

Addiction: There is a small chance that you will become dependent on (addicted to) MDMA. One study found that up to 6% of people using Ecstasy for recreational purposes were dependent on it. However, a study of people who had received MDMA for the first time in a legal medical laboratory setting found that they did not want to try MDMA again outside of the laboratory.

You can talk with the researchers about any worries you have about taking a drug with a potential for addiction. People who have recently (in the last 60 days) had problems with drug abuse should not take part in this study.

Possible Brain Damage – Human Laboratory Studies

Only one study has looked at brain scans of people before they have ever taken MDMA and then again after they have received one or two moderate doses of MDMA. No changes in the brain were observed, though it is possible that there were changes that were too small to notice. Therefore, the investigators believe that the amount of MDMA you will receive in this study will not produce any lasting changes in your brain, though they cannot guarantee this.

Studies of people receiving one or two doses of MDMA in a medical laboratory setting have not found any lasting changes in recall or planning. Therefore the investigators believe that the amount of MDMA you will receive will not produce any lasting changes in recall or planning ahead, though they cannot guarantee this. The study investigators will be watching to see if you exhibit any clear signs of confusion or complaints of memory or learning. You will not get a second dose of MDMA if they believe you are showing signs of memory problems.

Some studies comparing those who have used Ecstasy repeatedly with people who do not use Ecstasy found Ecstasy users were more likely to report feeling generally anxious or depressed. Some scientists think that increased reports of feeling depressed or anxious are signs of brain damage from MDMA. However, other scientists believe that these differences in mood are not related to Ecstasy use. For instance, people who repeatedly use Ecstasy may have been depressed or anxious before they began taking the drug, and feeling this way might even have led them to use Ecstasy.

People receiving one or two doses of MDMA in a legal medical laboratory setting did not notice any lasting increase in feeling depressed or anxious after having taken MDMA. The investigators believe that the doses of MDMA used in this study will not make you more depressed or anxious, but we cannot guarantee that this will not happen.

Some scientists think that problems could develop as people who have taken MDMA grow older and their brain chemistry changes. These scientists think that people with brain damage from MDMA may be more likely to develop depression or anxiety disorders when they get old. No studies have examined this possibility.

Possible Brain Damage – Human recreational use

Some studies found that people who had used Ecstasy many times in recreational contexts were not able to recall words, pictures or patterns as well as people who did not use Ecstasy. People who had used Ecstasy many times also performed less well on tests of planning and impulse control. These differences are not great, and most Ecstasy users do not notice having any trouble in everyday life. When found, these differences have lasted for at least a year after people had stopped taking Ecstasy. Not all studies have found Ecstasy users to have difficulty recalling words or pictures, and some studies have not found differences in impulse control. Other scientists believe that these differences are not due to MDMA.

Possible Brain Damage - MDMA-Animal Studies.

Animal studies can point the way to look in human studies.

Experiments with rats and monkeys show that some doses of MDMA can change two types of nerve cell in the brain, cells that release a chemical called serotonin, and cells releasing a chemical called dopamine. The changes to these cells include a loss of the part of the cell (called "axons") that connects different brain areas. Although axons can sometimes regrow, one animal study detected damage to serotonin cell axons in monkeys seven years after four days of twice-daily doses of MDMA.

Studies have found that animals given doses of MDMA high enough to cause these changes in their brains are affected several weeks later in three ways. First, they are less sensitive to the effects of MDMA and similar drugs. Second, animals are more likely to become overheated when placed in a warm room. Third, some studies have found that animals have worse performance in difficult tests of memory. Other studies found no changes in animal memory. Aside from these changes, animals previously given large doses of MDMA appear to behave the same as animals that did not get MDMA. But some abnormality could have been missed. It is not known if these changes are permanent or reversible.

Other Risks:
You should be very careful when driving or using machinery immediately after each experimental session (up to 24 hours afterwards) until you know how the study drug will affect you. This is because the study medication may cause drowsiness, lack of co-ordination or slower reaction time.

If you are tested for drugs of abuse within three days of each experimental session, you may test positive. You will receive a wallet card the researchers will give you with telephone numbers for reaching the researchers, your doctor and other people related to the study. The wallet card will include a sentence saying that you might test positive for drugs of abuse. You can show this to the person in charge if you are tested for drugs while you are in the study and they can call Dr. Mithoefer to verify that you are participating in this study.

The interviews you receive during the course of the study involve no specific risks or discomforts beyond those of a standard clinical interview situation. You may feel upset at the review of your emotional experiences, or you may feel boredom or fatigue. The medical evaluations involve some blood tests. The risks of blood drawing include temporary discomfort from the needle stick and bruising. Fainting could also occur.

Your condition may not get better or may become worse while you are in this study.

Reproductive Risks:
Effects of MDMA on the growth and development of an unborn baby are not known. Birth defects could include physical deformities, mental retardation and premature birth; therefore you will not be allowed to enter the study if you are pregnant.

Women who are able to become pregnant must use one of the allowed birth control methods while they are in the study and for at least one month afterward. The researchers will explain these methods to you and will help you decide which might be best for you. The researchers can also suggest where you can get more information and advice.

You will be tested at the start of the study and again before each MDMA or placebo session to see if you are pregnant. If, at any time during the study, you suspect that you may be pregnant or are concerned that you may become pregnant, you must advise Dr. Mithoefer immediately. If you should become pregnant during the study, the researchers will help you get proper advice and help you and your unborn baby get proper care while you are pregnant.

NEW FINDINGS

If any new information becomes available about MDMA while you are participating, the investigators will tell you about it.

POSSIBLE BENEFITS

There is no guarantee that you will benefit from taking part in this research study. The knowledge learned from your participation in this study may be able to help in treating people with PTSD in the future.

COSTS

The sponsor of this study (MAPS) will cover the costs that are directly related to this study. This includes the costs for all psychotherapy sessions, for the psychological and laboratory testing, for medical examinations, for experimental study drug. You will not be charged for any procedures done solely for the purpose of the study.

You or your insurance will remain responsible for on-going treatment unrelated to the study.

If you must pay for travel or parking, the researchers will pay you back the costs of travel or parking. Your health insurance may not be willing to pay for the costs of treating a study-related emergency. The study sponsor (MAPS) will pay for any study-related procedure that your insurance will not cover.

PAYMENT FOR PARTICIPATION

You will not be paid any money for taking part in this study. Travel or parking costs will be paid for by the sponsor as needed.

ALTERNATIVES

Participating in this study might not benefit you or treat your PTSD. One alternative is to decline to participate. You do not have to participate in this study to receive treatment for your condition. You may decide to try other treatments for PTSD. There are other medications and other forms of psychotherapy that you could try. If you are currently receiving psychotherapy and/or medication, you could continue with those for a longer period of time.

CONFIDENTIALITY
All information collected will be treated and handled as confidentially as possible.

Absolute confidentiality cannot be guaranteed.

When not in use, information will be stored in a locked office.

Some people need access to the information to monitor the study. Any paperwork copied should have had any information that could be used to identify you removed first. Medical records, including audiotapes, which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes. First any information that could directly identify you will be removed. Medical records may be looked at by

- the sponsor, MAPS;
- the FDA and similar agencies in other countries;
- the Department of Health and Human Services (DHHS) agencies;
- governmental agencies in other countries; and
- the IRB

The results of this research study may be presented in meetings or in publications. Your identity will not be disclosed in those presentations.

All records in South Carolina are subject to subpoena by a court of law.

Audiotapes: Only the researchers will listen to these recordings, and no identifying information will be written or otherwise attached to the tape recordings. You will also receive a copy of your recorded experimental sessions. This is to give you an opportunity to listen to what you and the researchers said during the session, and to think about what happened during the experimental session at a later date. You may listen to the tape if you wish, but you do not have to listen to it.

TREATMENT AND COMPENSATION FOR INJURY
In the event of a study-related injury, the physician who treats you will bill your insurance company. If your insurance company denies coverage or insurance is not available, then MAPS will pay for any costs that arise from treating a study-related injury. Neither the Sponsor nor the study doctor has a program in place to provide other compensation in the event of an injury.

LEGAL RIGHTS
The above section does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this Subject Information and Consent Form.

VOLUNTARY PARTICIPATION
Your decision to take part in this research study is completely voluntary. There will not be any penalty or loss of benefits to you if you decide not to take part.

In addition, you may withdraw from the study at any time. There will be no penalty if you decide to withdraw from the research study. Before withdrawing from this study, notify your study doctor that you wish to withdraw. This notice will allow your study doctor to inform you if there are any potential medical risks of withdrawal. You may be asked to return to the clinic for tests.

WITHDRAWAL

Your doctor, the sponsor company, or the FDA has the right to stop the study at any time, with or without your consent, for any of the following reasons: if you have an adverse effect from the study drugs, if you need a treatment not allowed in this study, if you do not keep appointments, if you do not take the study drug as instructed, if you become pregnant, or if the study is canceled by the FDA or the sponsor company

Subject's Initials_____

QUESTIONS

If you have any questions about this study, its procedures, risks, benefits or your alternatives or rights or if at any time you feel you have experienced a research-related injury, contact

Dr. Michael Mithoefer

If you have other questions about other effects of MDMA, you can contact Rick Doblin, Ph.D., President of MAPS, the organization sponsoring this study.

The address is

Rick Doblin, Ph.D.
3 Francis St.
Belmont, MA 02478
Tel: 617 484-8711

If you have concerns that you don't feel comfortable asking the investigator or sponsor, you may contact the Institutional Review Board (IRB) that approved this study:

The IRB

An Independent Review Board is a group of scientific and non-scientific individuals who perform the initial and ongoing ethical review of the research study with the study subject's safety and welfare in mind.

The researchers will give you a wallet card containing contact information for the researchers, the sponsor and the IRB.

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.

Subject's Initials_____

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedures involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Subject's Initials_____

SUBJECT'S STATEMENT OF CONSENT

"A TEST OF MDMA-ASSISTED PSYCHOTHERAPY IN SUBJECTS WITH CHRONIC POSTTRAUMATIC STRESS DISORDER (PTSD)"

Your participation in this study is voluntary. You may refuse to take part in or you may stop taking part in this study at any time. You should call the researchers if you decide to do this. Your decision will not affect your current or future regular medical care or any benefits to which you are entitled at this site. The researchers and/or the sponsor may stop your participation in this study at any time without your consent if they decide it is in your best interest or if you do not follow the researchers' instructions.

You will need to have someone drive you home on the day after the experimental session. If you cannot find anyone to take you home, the researchers will find someone to drive you.

You have read the information in this consent form and it has been discussed with you. All of your questions so far about the study and my participation in it have been answered. You freely consent to participate in this research study.

By signing this consent form, you have not waived any of the legal rights which you otherwise would have as a subject in a research study. **You have been told that you will be given a copy of the consent form signed by you and the investigator.**

	SUBJECT		INVESTIGATOR
Printed name			
Signature			
Date			

Subject's Initials_____