

INFORMATION SHEET FOR PATIENTS IN THE CLINICAL STUDY:

Title of the study: "Administration of 3,4-methylenedioxyamphetamine (MDMA) to women with chronic Posttraumatic stress syndrome (PTSD) as a result of sexual assault. Dose-finding pilot study.

Hospital Psiquiátrico de Madrid y Departamento de Psicología Biológica y de la Salud, Facultad de Psicología, U.A.M.

Main researchers: Dr. Pedro Sopena Rodríguez and Jose Carlos Bouso Saiz.

Collaborators: Valentín Corcés Pando, M^g Angeles Corral y Alonso, José María García del Valle, M^g Jesús Vico Barranco, Ludgerio Espinosa Gil.

Objectives and pharmacological agents.

The characterization of the psychotherapeutic properties of MDMA (commonly known as Ecstasy) in women suffering from chronic PTSD due to sexual assault is the primary goal of this study. The dosages that will be used are those that were normally given to patients in MDMA-assisted psychotherapy sessions before the medication was made illegal in 1985. MDMA was used in psychotherapy primarily in the USA until 1985, and in Switzerland until 1995 (currently MDMA is prohibited for therapeutic use). In this study, you will receive a single dose of MDMA or a placebo. The MDMA will be administered in the presence of a psychotherapist-physician within a psychotherapeutic context and under strict medical supervision.

MDMA is classified as a stimulant of the central nervous system. When taken abusively or recreationally, without appropriate medical supervision, stimulants can cause insomnia, nervousness, muscular tension, increased heart rate and blood pressure, heart palpitations, dizziness, fever, dryness in the mouth, visual difficulties, chest pains, sweating, nausea, vomiting and anxiety. Psychotic effects in which hallucinations (changes in perception of things) and

paranoia have been reported. Some serious adverse reactions have also been reported, especially when consumed at high or toxic dosage levels. In these cases, high fever, muscular pain, loss of consciousness, convulsions, serious changes in heart rhythm (arrhythmia), chest pain and heart attack may occur. Several people have died from these complications. As mentioned above, these complications may appear when the medication is taken without medical supervision, at very high dosages, or with existing medical conditions. However, when administered to physically healthy subjects in a clinical setting, the normal effects of MDMA are paradoxically different from those observed in stimulants. That is: elimination of anxiety, positive state of mind, better capacity for communicating with others, easier access to personal memories and feelings, and the elimination of the fear of speaking of traumatic facts and experiences from the past — without producing most of the symptoms described as effects of stimulants. In fact, MDMA was used, previous to its prohibition, to help patients analyze their problems in a state of serenity and lucidity in which they could more easily gain access to their traumatic memories without losing control over their emotions and behavior and without the fear and anxiety such memories typically produce. At the dosage that you may receive, MDMA may produce secondary effects such as muscular trembling, changes in heart rate and blood pressure, and fatigue or insomnia after the session. The effects attributed to stimulants are rarely caused by MDMA.

The placebo is a capsule containing an inactive substance. Contrary to what you may think, the placebo may produce beneficial or adverse effects. Some of the symptoms mentioned above have been observed in patients taking placebo.

In this investigation we hope to establish a context of trust with you, where you can express, freely and without fear, anguish or anxiety as well as the feelings and thoughts that come from the psychological pain you are experiencing. We also hope that you will be able to generalize the benefits gained with the help of this medication to the rest of your daily life and thereby find that your symptoms have lessened or disappeared entirely. Past experience with patients suffering from the same disorder as you confirm this possibility. We also hope that the

information obtained in the course of this research may serve to help others who have problems similar to yours and help in developing future treatments.

Selection.

Before the study begins, you must come to the center to undergo a series of examinations (without having eaten previously that day). These will include a physical check-up, psychiatric interview, ECG as well as blood and urine testing to screen for hepatitis and illegal drugs.

In order to participate in this study, the medical tests must show that you are in good general health and that the possible risks the medication may present to you are minimal.

Progress of the study.

You agree to abstain from alcoholic drinks and caffeine for the 24 hours before and after each session in which you will be receiving medication. You must not take any type of medication or drug other than those prescribed by one of the doctors on the research team while you are involved in this study.

You will participate in one session in which you will receive either MDMA or placebo. This session will take place in the Hospital Psiquiátrico in Madrid. You will also participate in five other sessions, which will be normal psychotherapy sessions. These sessions will help to prepare you emotionally for your experience with the medication, and to help us analyze the content of the experience you have when the medication is given. Several types of psychological tests will also be given during these sessions to help evaluate the state and changes in psychological symptoms. The person responsible for evaluating the state and changes in symptoms will be a psychologist on the research team other than the therapist who participates in your treatment.

The treatment scheme in which you will participate will be as follows:

Session 1 Psychiatric interview, medical check-up, evaluation of psychological symptoms using psychological tests and psychotherapy session. This session will last approximately 4 hours.

Session 2 (7 days after session 1): Psychotherapy session. About 1 hour.

Session 3 (7 days after session 2): Psychotherapy session. About 1 hour.

Session 4 (7 days after session 3): Administration of MDMA or placebo and psychotherapy session. About 4-5 hours.

Session 5 (1 day after session 4): Psychotherapy session. About 1 hour.

Session 6 (7 days after session 5): Psychotherapy session and final evaluation of the psychological symptoms. About 3 hours.

The study concludes with session 6. All sessions will be recorded on audio tape. There will also be follow-up monitoring of psychological symptoms at 1, 3, 6, 9 and 12 months after the study period ends. Each of these follow-up sessions will last between an hour and 90 minutes.

The medication (MDMA or placebo) will be given in capsule form in two doses two hours apart, orally, along with 120 ml of non-carbonated water. The medications will be given in such a way that the researchers will not know which substance you have received (MDMA or placebo). If there is a need to know which substance you have taken because of some unexpected incident, this information will be on-hand in sealed envelopes. During the experimental session, vital signs will be monitored every 30 minutes. A physician-psychotherapist will be present at all times to ensure that no medical complications arise.

Participation.

As your participation in this study is voluntary, you can withdraw at any time without any having to offer any explanations. The researchers will not blame you or be angry if you decide to stop your participation. You may also be excluded from the study by the researchers

in the following cases:

- 1) Significant transgression of the protocol.
- 2) Undesirable effects caused by the medication.
- 3) Illnesses or having taken other medications that might increase the risk or invalidate the results of the study.
- 4) Consumption of illegal drugs.

The sponsor of the study has insurance which covers the possible damages that could be caused by the medications being used in this study.

All information collected concerning your participation in this study will be considered confidential and may only be used by the investigators for scientific purposes. If this information is published for the scientific community, your identity will be kept anonymous through the use of a code or your initials.

If you have any doubt about any facet of this study or you would like to comment on some aspect of the information given here, please do not hesitate to contact the members of the research team. You can reach them directly (from 9 to 3) at the Hospital Psiquiátrico of Madrid (Ctra. de Colmenar Viejo, Km. 13,800, 28049 Madrid) or by telephone (91 586 74 81/75 03).

In case of emergency, the researchers can be called at home

(Sopelana: 949 33 48 59; Bouso: 91 522 08 20; Corral: 619 23 22 32).

Consent.

(according to Annex 6, point 2 del Real Decreto 561/1993 of 16-04-1993)

Title of study: "Administration of 3,4-methylendioxitamfetamine (MDMA) to women with chronic posttraumatic stress syndrome (PTSD) as a result of sexual assault. Pilot dose-finding study. "

I,

Have read the information sheet I was given.

Have had the opportunity to ask questions about the study.

Have received enough information about the study.

Have spoken with ..

Understand that my participation is voluntary.

Understand that I can withdraw from the study:

1. At any time I choose.
2. Without having to explain.
3. With no effect on my medical care.

I freely offer my participation in this study.

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(Date)

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(Signature of participant)