

# Proposal for a Study with MDMA and Post Traumatic Stress Disorder

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**Posttraumatic Stress Disorder (PTSD)** is one of the most common psychological disorders today. It is estimated that approximately 25% of the victims of any crime, accident, act of violence or catastrophe can develop this syndrome.<sup>1</sup> The current prevalence rate of PTSD is between 1.3% and 9% for normal populations (a higher rate than that of schizophrenia) and 13% for psychiatric populations.<sup>2</sup> According to the DSM-IV, there are three main symptoms of PTSD: 1) Persistent re-experiencing of the traumatic incident; 2) Persistent avoidance of stimuli associated with the trauma; 3) persistent symptoms of hyperarousal.<sup>3</sup> These symptoms are accompanied, in approximately 80% of the cases, by high levels of associated conditions such as depression, drug abuse, anxiety, manias, personality disorders, anger, low self-esteem, etc.<sup>4</sup> Many people who decide to look to a specialist for help do so because of the associated symptoms rather than for the disorder itself, due to fear and the inability to recall and to face the traumatic incident.<sup>5</sup> This sometimes hinders the intervention of the specialist, particularly if he/she does not discover that the reported symptoms hide a deeper disorder. Symptoms tend to lead the PTSD sufferer to psychological discomfort and significant negative effects on social, occupational or other important areas of life.

FURTHERMORE, the most immediate consequences of these symptoms tend to destabilize the cognitive and emotional aspects of people suffering from PTSD.<sup>6</sup> Subjects experience an emotional numbness or affective dullness, demonstrated by an incapacity to express or experience affection, intimacy and feelings of tenderness.<sup>1</sup> This also causes subjects to lose interest in the activities in which they participated before the appearance of the trauma, leaving their social, professional and interpersonal relations substantially limited.

Although PTSD has always been a disorder associated with war (the first descriptions of the syndrome appeared during the Napoleonic Wars) it is no longer considered solely characteristic of war veterans. There are other groups assumed to suffer from it, such as victims of natural catastrophes, traffic accidents, incurable illnesses, physical abuse, victims of other violent crime and, above all, victims of sexual assault.<sup>7</sup> This last group, as well as survivors of war, have been the most studied.

In this research proposal we intend to administer MDMA to women suffering from chronic PTSD as a consequence of sexual assault. We believe that MDMA can help people who suffer PTSD as it allows them to re-experience the trauma in a secure context, with reduced fear and anxiety, and therefore provides them an opportunity to restructure the consequences that the trauma had in their personal lives. Some research shows that the re-experience of the traumatic incident in a secure context, where victims can recall the trauma without the usual distressing feelings, neutralizes the fear structures and allows a better adaptation in the long term.<sup>8,9</sup> Anecdotal cases of patients treated with MDMA before its prohibition show that the re-experience of the traumatic incident under the effects of MDMA can take place.<sup>10</sup> Furthermore, the fact that MDMA acts selectively on the emotions and feelings could help people afflicted with PTSD to get rid of the affective dullness that they suffer, allowing them gradually to recover their emotional balance. Those were basically the two reasons that led us to propose this study to explore the efficacy of MDMA in PTSD.

There were two reasons for choosing female victims of sexual assaults as a study population. On the one hand, important experimental research with this population has been conducted in Spain.<sup>11, 12, 13</sup> and therefore there are

reliable and valid psychological assessment instruments to measure therapeutic outcome. On the other hand, unfortunately, it is estimated that between 15% and 25% of women have suffered a sexual assault, and that between 50% and 60% of those women develop PTSD.<sup>1</sup> This high rate should facilitate access to an appropriate study sample. The fact that symptoms become stable once they become chronic (there are no significant differences in the symptoms, for example, between the third month and the fourth year) will allow us to correlate the results of the study to the

treatment, more than to the simple progress of PTSD due to the passage of time.<sup>14</sup> We have decided to focus on chronic cases of victims of sexual assault, which will enable us to obtain as homogeneous a sample as possible, although it is obvious that there are always variables that researchers can not control.

This research proposal was approved by the Doctorate Commission of the Department of Biological Psychology and Health Psychology (Departamento de Psicología Biológica y de la Salud) of the Psychology Department (Facultad de Psicología) of the Universidad Autónoma de

Madrid in November 1998. This permission is needed to present the study as my doctoral thesis. In May 1999 the clinical trial's protocol was approved by the Teaching, Research and Training Committee (Comité de Docencia, Investigación y Formación Continuada) of the Psychiatric Hospital of Madrid, and it allows us to carry out the research in said Hospital. Finally, in July 1999 the protocol was approved by the Ethics Committee for Clinical Research (Comité Etico de Investigación Clínica) of the Hospital Universitario "La Paz" (to which the Psychiatric Hospital of Madrid belongs), an essential requirement to be able to present the protocol to the Ministry of Health, which has the last word and whose decision is expected in November 1999. MAPS has pledged \$22,000 in support of this research.

#### **Objectives of the proposed study**

1. Test the therapeutic effectiveness of MDMA in a psychotherapeutic context, in women who are victims of sexual assault and who have developed chronic PTSD.
2. Test the therapeutic effectiveness of MDMA in reducing the secondary symptoms generated as a consequence of chronic PTSD in said women.
3. We will evaluate on which specific PTSD symptoms

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the MDMA treatment acts.

4. Determine the most effective therapeutic dose (dose finding pilot study).

We propose to carry out two pilot studies. The first one would be a dose finding study and the second one a therapeutic effectiveness study. We outline in the first pilot study a range of several different doses to determine the most effective one. The most effective dose will be administered in the therapeutic effectiveness study. All participants are volunteers and will pass rigorous medical examination to be sure that none of them has previous illnesses which could lead to potential risk situations. The psychiatric inclusion criterion is to suffer from PTSD as a consequence of a sexual assault, according to the DSM-IV criteria.

Two psychotherapy sessions will be carried out before and after each session with MDMA or placebo. In the pre-session we intend to prepare the subjects for the MDMA session, and in the post-session we intend to facilitate the integration of the MDMA experience. There will be two psychotherapists, a man and a woman, both psychiatrists. The therapists will stay with the women during the MDMA experience to hear and support them with a phenomenological/existential approach.

The treatment will consist of the re-experience of the trauma under the effect of the drug or the placebo, in a psychotherapeutic context. As we have already mentioned, some research shows that the re-experience of the trauma in a secure context is a good predictor for the therapeutic outcome for the subject in the long term.<sup>8</sup> However, some drugs have turned out to be ineffectual in inducing this re-experience.<sup>16</sup> The hypothesis is that MDMA in a clinical context: 1) allows the re-experience of the trauma without the usual feelings of anxiety, fear and psychological distress; 2) modifies in the subjects the implications of the trauma, and 3) enhances the therapeutic alliance, a factor that has proven to be the best predictor of the therapeutic change.<sup>17</sup>

#### **STUDY DESIGN**

##### **Dose finding pilot study**

We suggest a pilot study with 20 subjects, five groups of four subjects each, and three different MDMA doses. This study will determine the most effective therapeutic dose, as well as the usefulness of the assessment scales. The dose for the subsequent subjects would only be increased when and if it was demonstrated that the previous dose could be

administered safely. The clinical experience of some therapists when MDMA was used in psychotherapy has suggested that it can be effective to give a booster dose of half the initial dose after two hours, when the initial effects start to subside. The effect of the booster is to increase the duration of the psychoactive effects and to facilitate a gradual descent of the effects.<sup>15</sup> This would allow therapists to work with the subjective experiences of the subject during the sessions for a longer period of time than with a single administration and may contribute to the therapeutic effectiveness. The design of the pilot study explores the value of a booster dose.

##### **Dose finding pilot study outline**

Group 1 (4 subjects): 75 mg of MDMA followed by a placebo two hours later (3 subjects); placebo followed by a placebo two hours later (1 subject).  
Group 2 (4 subjects): 75 mg followed by 50 mg of MDMA two hours later (=125 mg) (3 subjects); placebo followed by a placebo two hours later (1 subject).  
Group 3 (4 subjects): 125 mg of MDMA followed by a placebo two hours later (3 subjects); placebo followed by a placebo two hours later (1 subject).

Group 4 (4 subjects): 125 mg followed by 50 mg of MDMA two hours later (=175 mg) (3 subjects); placebo followed by a placebo two hours later (1 subject).

Group 5 (4 subjects): 175 mg of MDMA followed by a placebo two hours later (3 subjects); placebo followed by a placebo two hours later (1 subject).

According to this schedule, subjects will receive a dose of MDMA followed after two hours by either an additional MDMA dose or a placebo dose. A subject from each group will receive a placebo dose followed after two hours by another placebo dose. This way we can compare three different dose levels administered with and without a booster. We will therefore explore which dose and which method of administration is more effective.

##### **Therapeutic effectiveness pilot study**

Twenty four subjects will participate in this study. All subjects will undergo two experimental sessions separated by a two-week interval. They will be divided into two groups. The first group will be administered the dosage of MDMA that was most effective in the dose-finding pilot study, either in a single dose or in two doses (a booster dose two hours after the initial dose). The second group will

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receive a placebo dose under the same conditions as the subjects in group one. The study will be double-blind and assignment to the treatment will be random.

#### **Therapeutic effectiveness pilot study outline**

Group 1 (12 subjects):

2 sessions with the most effective dose of MDMA.

Group 2 (12 subjects):

2 sessions with placebo.

#### **Proposed evaluation measures, validated for the Spanish population**

*Scale of Gravity of the Symptoms of PTSD*

(Echeburúa et al., 1997).

*Semi-Structured Interview About Sexual Aggressions*

(Echeburúa et al., 1995).

*The State-Trait Anxiety Inventory (STAI)*. State version.

(Spielberger et al., 1970).

*The Beck Depression Inventory (BDI)* (Beck et al., 1961).

*The Hamilton Rating Scale (HRS)* (Hamilton, 1960).

*The Modified Fears Scale (MFS-III)* (Veronen and Kilpatrick, 1980).

*Maladjustment Scale* (Echeburúa et al., 1998).

*The Rosenberg Self-Esteem Scale* (Rosenberg, 1965).

*The Penn Helping Alliance Questionnaire (HAQ)*

(Alexander y Luborsky, 1984).

*Hallucinogen Rating Scale (HRS)*. Version 3.06P

(Strassman et al., 1994).

*The UKU Side-Effects Rating Scale* (Lingjaerde et al., 1987).

*The Penn Helping Alliance questionnaire (HAQ)*

(Alexander y Luborsky, 1984).

The experimental research will take place in the Psychiatric Hospital of Madrid, where subjects will have to undergo the treatment. Because of the characteristics of this hospital (an institution reserved for the chronically and acutely "mentally ill"), the subjects in this study will not be formally hospitalized, in order to avoid the possible fearful connotations of admittance to a psychiatric ward. Subjects will leave the hospital once the effects of the drug have worn off, accompanied by a relative or by taxi.

There will be a follow up of the progress of the subjects at one, three, six, nine and twelve months. The outcome measures will be administered by a blind rater, who will be the same person to do the follow up testing.

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preparation of the protocol. He also read the protocol before it was presented to the Ethics Committee and made an essential last-minute improvement in the experimental design.

Of course, I personally made all decisions regarding the protocol, so any existing errors can only be attributed to me.

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