MDMA and Basic Research: Issues Within and Beyond Therapeutic Applications

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MDMA (3,4-methylenedioxymethamphetamine, "Ecstasy") is a ring-substituted amphetamine structurally similar to the psychostimulant methamphetamine and the psychedelic/hallucinogen mescaline. While it possesses some stimulant-like and mildly psychedelic properties, it also possesses properties that distinguish it from members of either of the drug classes listed above. MDMA is reported to produce an easily controlled altered state of consciousness with increased sociability, empathy and sensual overtones (Anderson et al. 1978; Greer and Tolbert 1986; Peroutka et al. 1988; Solowij et al. 1992; Vollenweider et al. 1998). Some researchers have classified MDMA and related drugs, such as its congener MDE, as belonging to a novel drug class, the entactogens (Nichols and Oberlender 1986; Oberlender and Nichols 1990), a term meaning "to touch within." A number of studies have examined the physiological and subjective effects of MDMA in humans (Cami et al. 2000; Gamma et al. 2000; Farre et al. 2004; Grob et al. 1996; Forsling et al. 2001; Harris et al. 2002; Hernandez-Lopez et al. 2002; Lamers et al. 2003; Lester et al. 2000; Liechti et al. 2001; Mas et al. 1999; Tancer and Johanson 2001; Tancer and Johanson 2003; Vollenweider et al. 1998). The efficacy of MDMA-assisted psychotherapy in the treatment of posttraumatic stress disorder (PTSD) and other conditions has been described in several anecdotal accounts and an uncontrolled study (Adamson 1985; d'Otalora 2001; Gasser 1994; Greer and Tolbert 1998; 1986; Metzner and Adamson 2001; Widmer 1998). In Spain, six women with PTSD arising from sexual assault were enrolled in a MAPS-funded study of MDMA-assisted psychotherapy that was subsequently halted due to political pressure from the local anti-drug authority (Doblin 2002). A second MAPS-supported study of the safety and efficacy of MDMA-assisted psychotherapy in people with PTSD is underway in South Carolina. Additionally, FDA and the respective institutional review boards (IRBs) at Harvard Medical School's McLean Hospital and the Lahey Clinic have approved or given permission for a proposed study of MDMA-assisted therapy in people with advanced stage cancer and diagnosis-related anxiety.

In addition to its potential value as an adjunct to psychotherapy, MDMA may also prove to be a valuable tool for basic research. Research is basic if it is conducted chiefly to learn more about the area under investigation without specific plans for how to use this information to produce a treatment, program or other immediately useful endeavor. As is the case with psychedelic drugs, studying the effects of MDMA in humans has the potential to provide a better understanding of human cognition, affect (mood and emotion) and behavior. The research problems described below are not intended to be an exhaustive list of possibilities. Rather, they are intended as a sample of possible research programs utilizing MDMA as a tool for exploring social interaction and affect in humans.

The risks involved in administering MDMA to human participants are considerably greater than the risks associated with participation in the typical social psychological or psychophysiological experiment. However, these risks can be minimized by carefully selecting study participants, administering MDMA in a controlled setting, and monitoring physiological signs in each participant throughout and shortly after the procedure. Using MDMA in research in humans may always require collaboration between psychologists interested in basic research and psychiatric researchers. However, I believe that the benefits to be gained by performing human research with MDMA outweigh the risks to participants and the difficulty for researchers.

Some of the studies proposed below may be of immediate importance to those who wish to demonstrate the therapeutic uses of MDMA, and these studies may be performed during or immediately after studies have examined the efficacy of MDMA-assisted therapy. It is encouraging that ethics committees and regulatory agencies have already approved and permitted studies into possible therapeutic uses of MDMA. These studies may pave the way for basic research into the effects of MDMA on emotion, cognition and social interaction. As well, some researchers are already interested in studying MDMA effects on emotion and behavior toward others (see Fiske et al. 2004; Hoshi et al. 2004).

In writing this essay, I hope to stimulate thought and discussion about what human trials with MDMA might contribute to psychology and neuroscience. I also hope to encourage therapists and psychiatric researchers to design and conduct studies that formally identify and quantify the processes and effects deemed most important to the success of MDMA-assisted therapy. Most importantly, I hope to demonstrate the ways in which human trials with MDMA could bring together researchers in different fields to the benefit of all.

Basic Research on Effects Relevant to Therapeutic Use

While recent investigations have produced a great deal of valuable information concerning the physiological and

subjective effects of MDMA in humans, many questions concerning these effects remain unanswered. Several of the subjective effects of MDMA that first attracted the notice of psychotherapists have yet to be formally verified in controlled settings. For instance, research has not yet determined whether MDMA increases feelings of empathy or compassion and whether MDMA induces people to perform empathetic behaviors, such as helping or forgiving others. Participants in at least one study have spontaneously reported increased feelings of closeness to others as an acute effect of MDMA (Vollenweider et al. 1998), and another controlled study found that people reported feeling friendlier and more talkative after 2 mg/kg MDMA (Tancer and Johanson 2003). Retrospective reports from ecstasy users and reports from an uncontrolled study of MDMA-assisted therapy have consistently reported experiencing increased feelings of empathy, closeness to others or sociality (Davison and Parrott, 1997; Greer and Tolbert, 1986; Liester et al. 1992; Peroutka et al. 1988; Solowij et al. 1992; Siegel et al. 1986). Yet to date, the only study that sought to assess self-reported empathy in people given 1.5 mg/kg MDMA did not detect an increase in empathetic feelings (Harris et al. 2002). This study used only two items from a larger questionnaire, suggesting that research into MDMA effects on empathy may need to rely on more extensive measures. Assessing people's behavior may be an even better measure of empathy or increased closeness to others. Such measures might include increased likelihood of helping or cooperating with others, or sitting closer to another person.

Secondly, therapists have reported in narrative and anecdotal accounts that MDMA stimulated recall for emotionally charged events (e.g. Adamson 1985; d'Otolara 2001; Greer and Tolbert 1986; Greer and Tolbert 1998), yet no one has yet conducted a systematic study of how and to what degree MDMA alters recall for intensely emotional events. Participants in some controlled studies reported facilitated recall after receiving MDMA (Vollenweider et al. 1998), but this effect has not been specifically measured within a controlled clinical study. If it can be shown that MDMA facilitates recall for emotional events, and does a better job at it than other psychotherapeutic techniques, then this would lend support for the use of MDMA in therapeutic contexts.

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Lastly, studies examining the reported reduction in anxiety (anxiolysis) after MDMA should be conducted. MDMA has been reported to reduce anxiety, even while simultaneously stimulating recall of unpleasant or upsetting thoughts or events (Greer and Tolbert 1998; 1986; Liester et al. 1992). Individuals given MDMA in controlled studies reported that anxiety was reduced or did not change after MDMA, although there was reported increased anxiety in association with feelings of loss of control (Liechti et al 2001; Vollenweider et al. 1998). Similarities and differences between the anxiolytic (anxiety-reducing) effects of MDMA and that of another drug, such as diazepam (Valium), or anxiolysis produced by a behavioral method (such as relaxation techniques) have yet to be investigated. Anxiety and facilitated recall occurring during an MDMA-assisted therapy session might also be compared with the effects of other means of relaxation and recall induction.

Relating Brain, Emotion and Behavior: Empathy

Social psychologists seek to understand social interactions and the thoughts, feelings and behaviors associated with social interactions. Social psychologists interested in understanding interpersonal relationships and interactions between dyads (pairs) have investigated the role that feelings of closeness to others, intimacy and empathy play in social interactions (Aron et al. 1997; Ickes 1990; Ickes 1991; Reis and Clark 1988; Stotland 1969). These psychologists are more interested in situationally produced empathy, referred to by Duan and Hill as the empathic experience, rather than trait empathy (Duan and Hill 1996), the tendency of an individual to feel empathetic. Many people studying empathy hope to improve interpersonal and intergroup relations by understanding the bases of empathy and the consequences of feeling empathetic toward another person.

Researchers interested in generating empathy in study participants have relied on the use of direct instructions to participants to feel empathetic, or they try to craft staged events or occurrences intended to produce empathy (Duan and Hill, 1996; Stotland, 1969, see, for example, Batson and Moran, 1999; Batson et al. 1999; Batson et al. 1997; Macrae and Milne 1992). Participants are instructed to imagine how another person might feel in a given situation, or they are asked to imagine themselves in the place of another. Instructions and situational manipulation seem to produce empathetic behaviors, such as cooperating on a "prisoner's dilemma" task (Batson and Moran 1999) or allocating resources to another individual, even at the expense of the self (Batson et al. 1999). However, there is a risk that people are behaving in accordance with sociocultural rules on how empathetic people ought to behave in such situations, without actually feeling empathetic. In contrast, MDMA is reported to produce feelings of closeness to others or empathy directly, presumably through its actions on the brain. Setting is probably important, but it appears that ecstasy (material represented as MDMA) and MDMA

consistently produce empathy and feelings of closeness to others in disparate settings. Researchers studying empathy and social interaction might benefit by performing a number of comparative or exploratory studies with MDMA and at least one other form of empathy induction. For instance, a comparison could be made between empathy-related feelings and actions occurring after MDMA, and after people have been directed to imagine another person's feelings.

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Researchers could use functional imaging to compare changes in brain activity seen after MDMA-induced empathy and empathy produced by other means. Such comparisons might identify the types of brain activity associated with feelings of empathy or compassion. Functional brain imaging would be able to detect similarities and differences in brain activity across both empathy-producing conditions. At least one behavioral researcher has proposed using functional imaging to study the effects of MDMA on human bonding and empathy (Fiske et al. 2004).

By varying one or more aspect of the environment, investigators could discover what elements of setting most enhance commonly reported subjective effects of MDMA, such as decreased anxiety or increased feelings of closeness to others. Investigations into aspects of setting that promote MDMA-induced empathy could lead to a model of how MDMA produces this effect. These findings, in turn, might shed light on how other methods create or enhance empathy. For instance, factors such as the proximity of another individual, presence versus absence of direct "face to face" communication versus less direct routes of communication, and the presence or absence of prior commitment to imagining another's feelings may all be compared across conditions, using MDMA-induced empathy and some other means of inducing empathy as treatment conditions.

Researchers specifically interested in social interactions in dyads (pairs) or small groups have studied interactions between strangers, friends and romantic partners by videotaping people interacting, and then asking both the participants and independent observers to watch and code the videotaped interactions (Ickes et al. 1991; Levenson and Ruef 1992). This time-consuming and complex method of behavioral analysis has allowed researchers to generate and test hypotheses concerning cognition and behavior that shape the social interaction. This research has demonstrated that people are sometimes especially good at assessing the actual thoughts and feelings of another, a state referred to as "empathic accuracy." (Ickes 1994). Other researchers studying social interaction via this method have found that interaction between pairs of people go smoothly when the non-verbal behaviors of one partner tends to mirror or move in harmony with the behaviors exhibited by the other partner. Sharing information about the self is with another is reported to enhance intimacy between individuals, with higher rates of sharing information (mutual disclosure) associated with greater feelings of intimacy between individuals (Aron et al. 1997; Clark and Reis 1988). Researchers have found that feelings of closeness toward another can be produced by instructing both members of a pair to disclose increasingly personal information to their partner (Aron et al. 1997), indicating that reciprocal self-disclosure can produce feelings of intimacy.

Behavioral researchers could arrive at a better understanding of empathy and the similarities and differences between naturally existing, behaviorally induced and pharmacologically induced feelings of empathy through examining one or more specific behavior in people given a fully active dose of MDMA versus those given a threshold (or barely active) dose of MDMA. Behaviors worth examining might be imitation or reflection of another's non-verbal behavior, accurate perception of another's thoughts or feelings, or mutual self-disclosure of personal information. These behaviors would then be measured in both situations in order to discover whether MDMA increases empathy by leading people to behave in ways that tend to enhance empathy. For instance, people given a full dose of MDMA might be more likely to share personal information with another person than people given a threshold dose, or they might grow more accurate in assessing another's feelings. A naturalistic study that compared people who reportedly used ecstasy with people who used other substances (mostly alcohol and cannabis) found that ecstasy made people more accurate at recognizing facial expressions of fear, while the same people were less accurate at detecting fear four days later (Hoshi et al. 2004). Perhaps MDMA-induced changes in attention or other-directed behavior (such as talk) might play a role in generating or increasing empathy. Investigators would first have to establish that MDMA induces specific shifts in attention or behavior, and then demonstrate that these changes in attention or behavior are associated with

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increased feelings of empathy or closeness to others. If it turns out that MDMA does shift the type or degree of attention given to others, or alters specific types of behavior toward others, then investigators could try to produce empathy in people not given MDMA by instructing them to behave in the same way as the people who got MDMA. These findings could help us learn how to enhance or accentuate feelings of empathy or compassion within and outside of a psychotherapy session.

Research comparing feelings of empathy and empathy-related processes in people who have received MDMA and people who have not has the potential to make a strong contribution to an understanding of the links between brain, behavior, thought and emotion or affect. Specifically, such research might locate the common pathways shared by apparently separate routes for inducing feelings of empathy. Conversely, such research might also discover the differences between MDMA-induced changes in feelings toward others and similar emotional changes produced through some other process. It might also prove interesting to compare and contrast pre-existing feelings people have for each other and their feelings for one another after MDMA.

Physiological Effects Versus Psychological Effects: The "Stress Response" and Emotion Research

Paradoxically, MDMA tends to reduce anxiety, yet its physiological effects are similar to those seen when people are under stress. Though effects on the cardiovascular, immune, and neuroendocrine systems are similar to those seen in the human stress response, effects on mood are generally positive (Grob et al. 1996; Lester et al. 2000; Liechti et al. 2001; Mas et al. 1999; Pacifici et al. 1999; Pacifici et al. 2000; Pacifici et al. 2001; Vollenweider et al. 1998). People receiving MDMA usually do not feel any more anxious than they would without pharmacological challenge (Grob et al. 1996; Vollenweider et al. 1998), and in some cases they report feeling less anxious than usual (Greer and Tolbert, 1986). Yet MDMA increases heart rate and blood pressure (Grob et al. 1996; Lester et al. 2000; Mas et al. 1999; Tancer and Johanson 2001; Vollenweider et al. 1998), and MDMA is associated with the release of stress hormones such as ACTH and cortisol in rats and humans (Grob et al. 1996; Harris et al. 2002; Mas et al. 1999; Nash et al. 1988). MDMA also acutely produces a number of immunological changes in humans, including decreased CD4 cell count, increased NK cell count and increase in the ratio of Th1 cytokines to Th2 cytokines (Pacifici et al. 1999; Pacifici et al. 2000; Pacifici et al. 2001). These immunological effects, lasting no more than 48 hours, are similar to the immunological effects of a psychological stressor (Cacioppo, 1994; Cacioppo, 1996; Pacifici et al. 2000). This ability of MDMA to stimulate many of the physiological and immunological aspects of the stress response without producing the subjective effects usually associated with experiencing stress deserves further study. Similar, though not identical, immunological changes are produced by other psychoactives, such as alcohol (Pacifici et al. 2000), raising questions as to whether these immunological changes can be considered an accurate marker of experiencing psychological distress.

Researchers who study the outcomes of stress in humans could test hypotheses concerning the contributions of physiological versus psychological stress to the stress response by comparing the effects of MDMA with the effects of other stressors. Explanations of the effects of stress on health usually trace effects directly to physiological changes produced by experiencing stress, and several psychological stressors, such as making a public speech, do exhibit physiological effects (Cacioppo, 1994). It is difficult to separate the acute psychological effects of a stressor, such as anxiety or feelings of frustration or powerlessness, from physiological effects, such as increased stress hormones, increased sympathetic activity, or immunological changes. Researchers do not yet know whether negative feelings like anxiety or frustration may, in and of themselves, produce direct or indirect effects on outcomes after stress (as by altering health-related behaviors or producing additional physiological effects). Comparing physiological or immunological effects of MDMA with effects from psychological stressors offers researchers the opportunity to examine what happens when physiological effects associated with the stress response appear in tandem with elevated mood and unchanged or reduced anxiety. It is possible that MDMA and acute stressors produce the same outcomes in healthy humans. However, it is also possible that comparisons of psychological stressors with MDMA may demonstrate that subjective feelings of distress may produce effects that would be absent under MDMA and present after a psychological stressor.

A better understanding of the stress response could also be reached by comparing brain activity after MDMA with brain activity after a specific stressor. Studies might compare MDMA with at least one other stressor, such as preparing for and performing a public speech. Anxiety and distress could be measured, along with cardiovascular and immune responses to the stimulus, and these could be correlated with brain activity. Similarities and differences between the two treatments could be measured across

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subjects or across conditions. Such research might be able to locate the processes involved in producing the subjective effects of stress, and the processes that might dampen these feelings in humans.

While some researchers might be interested in examining the effects of physiological "stress" in the absence of psychological stress, psychologists and neuroscientists studying emotion might also use MDMA to test hypotheses concerning the role of physiological feedback in the generation of emotion. Some models posit that emotions begin as non-conscious responses to things or situations, and that conscious experience of an emotion arises via feedback about somatic (bodily) processes that are already taking place in response to those stimuli (LeDoux, 1998; Damasio, 1999). MDMA may mimic some physiological and neuroendocrine cues associated with stressful events, but that this feedback is apparently not associated with subjective feelings of distress. Or it may be that increases and decreases in anxiety seen after MDMA follow the time course of specific physiological changes. Hypotheses concerning the relationship between specific physiological processes, emotion generation, and a person's awareness of his or her own emotions might be tested by comparing the effects of MDMA with the effects of other procedures known to alter mood, including mood induction or exercise. Brain activity could be imaged after MDMA and after another mood induction procedure, with brain activity then correlated with changes in self-reported mood and physiological state.

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Risks to Research Subjects and Difficulties involved in Conducting Research

The risks of administering nearly any pharmacological agent to humans are higher than the risks of participating in the typical cognitive or social psychological study. Hence it is important to weigh the risks of administering psychoactive substances like MDMA to humans against the potential benefits that might result from performing the research, and to reduce risks to participants whenever possible. Most risks to participants in typical social psychological studies of empathy and social interaction result from deception practiced by the experimenter. Psychologists sometimes mislead participants about the nature of the research, or about some aspect of the study, to keep people from learning what the research hypothesis is, and to engage the participant in a "real" situation rather than relying on self-reports about hypothetical behavior (Aronson et al. 1990). Researchers may not want people to know what their study is about because people might change how they respond if they knew the hypothesis, either to "help" the researcher or to make themselves look better. Risks posed to participants by deception include not being fully informed about the nature of the study and possible distress arising either from being deceived or from a participant behaving in a way that he or she may find painful or embarrassing. These risks are usually countered by providing each participant with information about the nature of the study and an opportunity to express feelings about participation upon completion of an experimental session. Studies of the stress response also involve psychological and physiological discomforts. However, the risks described above are comparatively minor compared to risks associated with drug challenge studies, which can include risks of experiencing potentially life-threatening adverse events. These include risks posed by the acute physiological effects described above and the potential for long-term effects to occur after administration of MDMA. While MDMA has not produced any serious adverse events in controlled studies to date, the typical psychological study possesses far fewer potential risks.

There is concern that administering MDMA to humans could expose participants to long-term health risks. People who repeatedly use ecstasy have lower scores on measures of memory and executive function, often defined as planning and decision-making (see for example Croft et al. 2000; Gouzoulis-Mayfrank et al. 2003; Morgan 1999; Thomasius et al. 2003). Several reviews have examined and critiqued this body of research (Baggott et al. 2001; Cole and Sumnall 2003; Gamma 2000), but the fact remains that many studies continue to find differences between at least some groups of ecstasy users and non-ecstasy user controls. Furthermore, a spate of studies published in 2003 and 2004 suggest that moderate ecstasy use is not associated with impaired memory or executive function (Gouzoulis-Mayfrank et al. 2003; Halpern et al. 2004). Studies using radioactive drugs attracted to the serotonin transporter have also found fewer serotonin transporter sites in the brains of current ecstasy users (see for example Buchert et al. 2004; McCann et al. 1998; Reneman et al. 2001), though it is notable that more recent studies report a comparably small decline in transporter sites when compared with initial reports. Hence the potential for long-term effects to occur with regular, frequent use of illicit ecstasy cannot be dismissed. However, even before the appearance of recent studies finding little or no effects in moderate users, a number of researchers and commentators, including the editors of a major neuropsychological journal, have concluded that the risks involved in conducting controlled clinical trials with MDMA are

minimal (Aghajanian and Lieberman, 2001: Lieberman and Aghajanian, 1999; Vollenweider et al. 1999; Vollenweider et al. 2001). These authors have noted that as of now, no studies exist that examine the effects in non-human animals of one or two administrations MDMA in doses equivalent to those used in humans (Aghajanian et al. 2001; Vollenweider et al. 1999). Furthermore, researchers in Switzerland have failed to find changes in serotonin transporter sites or in measures of cognitive function in individuals who had received a single dose 1.5 mg/kg or 1.7 mg/kg MDMA as part of a research study (Ludewig et al. 2003; Vollenweider et al. 2000). Altogether, these findings seem to suggest that there is little or no risk of experiencing cognitive deficits for people given one or two doses of MDMA in controlled settings.

Because most lack the necessary equipment and training, it is likely that psychologists interested in using MDMA as a basic research tool in humans will have to work within a team of psychiatric or medical researchers . . . the teamwork required of investigators from different disciplines may enrich a research project and may allow each worker to gather relevant data from one study.

While the risks described above should not be considered lightly by researchers interested in human research with MDMA, they are not unique to MDMA or other entactogens. Substances posing similar risks to research participants have been employed by several research teams, including the psychostimulants amphetamine, methamphetamine and cocaine (e.g. Gouzoulis-Mayfrank et al. 1999a; Gouzoulis-Mayfrank et al. 1999b; Justice and DeWit, 1999; Rush et al. 1999) and fenfluramine (e.g. Mortimore and Anderson, 2000). Like MDMA, psychostimulants activate the sympathetic system and may produce psychological distress in some cases. Furthermore, studies in non-human animals suggest that fenfluramine possess the same risks to the serotonin system as MDMA (Schecter, 1990; Series et al. 1994, see also Whitaker-Azmitia and Peroutka, 1990), and methamphetamine may harm the dopamine system (see for example Clemens et al. 2003; Fornai et al. 2003; Miller and O'Callaghan 1996; Seiden and Kleven 1989). Despite these findings, fenfluramine is frequently used as a pharmacological challenge, and was even used in studies comparing ecstasy users with non-users (Gerra et al. 1998; Gerra et al. 2000; Gijsman et al. 2002). Investigators who administer psychoactive drugs to humans reduce risk by including only healthy participants who lack a history of major mental or physical illness, and by monitoring for cardiovascular effects if it is deemed necessary. In some studies, participation is further restricted to individuals with previous experience with the drug the researchers are studying (Rush et al. 1999). After taking these steps, the risks facing participants in human MDMA studies should be greatly reduced.

Other Challenges to Conducting Basic Human Research with MDMA

There are other obstacles to conducting the research described above. Equipment for measuring blood pressure and heart rate is often unavailable in the typical psychological laboratory outside the realm of psychiatric research, and it is likely that only psychiatrists and clinical psychologists currently possess training on how to intervene in cases of intense psychological distress. Because most lack the necessary equipment and training, it is likely that psychologists interested in using MDMA as a basic research tool in humans will have to work within a team of psychiatric or medical researchers. Working in such teams may slow the pace of research and make it more difficult. On the other hand, the teamwork required of investigators from different disciplines may enrich a research project and may allow each worker to gather relevant data from one study.

The potential benefits of conducting psychological or human neuroscience studies with MDMA have already been listed above, and include learning more about emotions, social cognition, and the link between emotions and the immune system. This knowledge could help clinical psychologists and psychiatrists find ways of helping people who are anxious or under stress, and it may help us learn more about how to ease or reduce conflict between people. If MDMA is found to have therapeutic uses, this research will also provide therapists and psychiatric researchers with an understanding of the processes that lie behind its efficacy as an adjunct to psychotherapy. These benefits are worth the minimal risks faced by carefully selected participants in a study involving the administration of one or two doses of MDMA.

Reuniting Brain, Cognition-Emotion and Behavior

Perhaps the greatest benefit to be gained from basic research studies examining the effects of MDMA in humans is the potential to draw together researchers operating in several different fields or disciplines, including clinical psychology, social psychology and psychophysiology. While researchers in each area study human thoughts, feelings and actions, each area of research operates at a

specific level of analysis and uses a specific set of research tools, making communication across research domains both difficult and infrequent. Investigating the effects of MDMA on how we think, feel and act, and investigating the paradoxical effects of MDMA on mood and physiology offer opportunities for bridging across these domains. As a result of the potential (and necessity) for collaboration across research domains, the hypotheses and models that might arise from human research with MDMA are liable to inform broad areas of neuroscience and psychology. Both psychotherapists and social psychologists are likely to appreciate more information about the empathic experience. Clinical psychologists might better understand relationships between "psychological" and "neurochemical" sources of emotion and awareness of emotion, and researchers interested in psychoneuroimmunology might learn more about the nature of the stress response. A clearer and more accurate model of empathy or of emotion generation and perception might, in turn, assist in improving behavioral or psychotherapeutic interventions that increase empathy or alleviate depression.

References

To read the references for this article, please see
http://www.maps.org/news-letters/mdma_basic_resarch_refs.html

Neurocognitive Profile of Long-Term Ecstasy Users: Proposed Research

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There is some evidence that MDMA causes neuropsychological deficits in long-term users. The most examined of these are memory, attention, executive functions and the speed of information processes. Although the research field concerning the neurocognitive aspects of MDMA is growing, there is little consensus about where the changes in these domains come from. Some researchers suggest that these are premorbid differences in the subjects, others say that it has to do with the lifestyle of the typical ecstasy users (excessive, all-night rave parties and their side effects) and others argue that it is the result of a neurotoxic effect of MDMA. There are a number of fMRI and PET studies, which examine the relation between changes in brain functions or neuropharmacological markers and changes in different neuropsychological aspects. However, there is, as far as I know, only one MRI study (Cowan R.L. et al., Drug and Alcohol Dependence 72, 2003) which was done together with MDMA. This study was not specifically intended to investigate the relationship between changes in neuropsychological markers and the according anatomical areas.

Our proposed study has several purposes. First, we hope to examine the neurocognitive profile of long-term ecstasy users in several aspects (TAP, VLMT, DCS and so on). Thereby we try to rule out some of the well known confounding variables, like the consumption of Cannabis and others. Second, with our MRI design, which includes diffusion tensor imaging (DTI), we would like to examine the relationship between changes in the cognitive domains (if there are any) to changes in the anatomy. We would also like to investigate if there are changes in the white matter concentration. Specifically, we are interested in areas which are responsible for the mentioned neurocognitive domains. Third, we want to examine/replicate the results of Cowan et al., which no one has yet attempted.

The study design is not yet fully complete. We would like to have three different groups: long-term MDMA users, who have been abstinent for some time (former users), long-term users who are still active consumers (current users), and a control group which matches the other two groups. There are already some people who are interested in participating in the study, but because the procedure will take several hours, we need to offer compensation in order to recruit subjects. I am asking for donations in order to reach our goal of enrolling thirty people, ten in each group. We are seeking a total of about $4000. Of course, we appreciate every little donation.

If you have any questions concerning the study design, the purpose, or other things,
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