Protocol

Title: Mood effects of serotonin agonists Extended (“Effects of drugs on mood and behavior – MESA-E” on the consent form)

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Objectives: To study the effects of very low doses of lysergic acid diethylamide administered at 3-day intervals for two weeks, on affect and responses to emotional stimuli in young adults with depressed mood.

Background:

The purpose of this study is to determine the effects of very low, sub-hallucinogenic doses of lysergic acid diethylamide (LSD) on negative mood states in human volunteers. The serotonergic system is critically involved in the neurobiology of depression, and specifically $5HT_{2A}$ signaling is thought to underlie the effectiveness of standard selective-serotonin reuptake inhibitor (SSRI) antidepressants (Celada et al., 2004). LSD acts directly at $5HT_{2A}$ and other serotonin receptors, and may have mood-enhancing effects. In the 1950s and 1960s, over 1,000 studies were published supporting therapeutic effects of LSD in combination with psychotherapy (Savage, 1952; Vollenweider and Kometer, 2010). However, many of these early studies lacked adequate control groups, and did not isolate drug effects from effects of the psychotherapy itself. Recent preclinical studies show that LSD exerts antidepressant effects in animal models (Buchborn et al., 2014), and a small number of recent studies in humans have shown that moderate to high doses of the drug (200-800µg) are effective in reducing end-of-life anxiety in terminally ill patients, and may also be effective in the treatment of addictive disorders (Gasser et al., 2014; Krebs and Johansen, 2012). Anecdotal reports suggest that very low doses of LSD, below those that produce standard "hallucinatory" effects (100-200 µg), reduce depressed mood, and such "microdosing" is reported to improve cognitive function and positive outlook (Nichols, 2013). A Google search of "LSD microdosing" reveals over 900 blog posts and articles reporting that low doses of LSD (10-30 µg) improve mood and cognition, without

producing noticeable hallucinogenic effects. However, the idea that sub-threshold doses of LSD may have anti-depressant properties has never been tested in humans.

In an ongoing study (Protocol 15-1311) we are testing the effects of single low doses ("microdoses") of LSD on subjective ratings and behavioral markers of depression (e.g., negative processing bias) in young adults. In the ongoing study, participants receive single doses at one-week intervals, and we are examining their direct effects during the laboratory sessions. Thus far, the doses are well tolerated and initial findings are promising. We have identified a dose that would be suitable for repeated administration (i.e., one dose every 3 days), as described in the present protocol. Figure 1 shows the mean (and sem) ratings of "feel" a drug effect, scored from 0 (not at all) to 100 (strong drug effect), in 20 participants (unpublished data from Protocol 15-1311). The lines correspond to placebo (lowest) 6.3, 13, and 26 micrograms. The dose to be used here (13 micrograms) produces ratings of 'feeling a drug effect" of about 20 on a scale of 100. No adverse effects were reported at any of the three doses tested. Based on this and other unpublished reports (see attached review), in the present protocol we propose to test effects of a low dose (13 µg LSD) administered four times, once each day at 3-day intervals. Participants will participate in two, two-week phases in which they receive either drug or placebo at 3-day intervals. The two phases will be presented in counterbalanced order and will be separated by 2 weeks. Thus subjects will attend four 5-h laboratory sessions to consume the drug (or placebo) on Days 1, 4, 7 and 10, and a 1-hour nondrug followup session at day 13. After a 2-week washout period, this sequence will be repeated with the other substance (drug or placebo). Participants will complete mood questionnaires on the days between the sessions to monitor the subacute effects of the drug. We hypothesize that low doses of LSD will alleviate both subjective and behavioral dimensions of depression in adult volunteers, during the sessions and in the days following.

Methods:

Design: Participants will be healthy adults who report moderate negative mood states, and some prior use of hallucinogen drugs or MDMA. The study will consist of two blocks of 4 laboratory sessions involving either low-dose LSD (13 ug) or placebo administration. Within each block, four 5-hour sessions will be conducted at 3-day intervals, with at least two weeks separating the blocks. At each 5-hour laboratory session participants will receive single low doses of LSD or placebo (13 ug in one block, placebo in the other). Following each block they will attend a 1-hour nondrug behavioral testing session. Screening, orientation, and study session procedures will take place in the Human Behavioral Pharmacology Laboratory suite in the L4 wing of 5841 S. Maryland Ave.

Subjects: Forty volunteers (20 male, 20 female; age range 18-35 years except undergraduates at U of C who must be 21 or older) who score in the minimal-to-moderate range (0-28) on the Beck Depression Inventory (BDI-II; Beck et al., 1996) will participate in the experiment. The BDI-II contains 21 questions, each scored from 0 to 3. Higher total scores indicate more severe depressive symptoms. The standardized cutoffs are: 0–13: minimal depression, 14–19: mild depression, 20–28: moderate depression and 29–63: severe depression. All subjects will have previous experience

with a hallucinogenic drug (e.g. psilocybin, LSD, mescaline, dimethyltryptamine or MDMA). Based on our previous rates of participants completing multi-session drug studies, to recruit 40 complete subjects we will need to consent 55 participants. Participants will be recruited without regard to race, religion or ethnicity through posters, advertisements and word-of-mouth referrals. Candidates will be screened in accordance with our general screening protocol, approved by the IRB under Protocol #13681B, which includes a physical, EKG, psychiatric screening interview and detailed drug use history questionnaire. The following populations are excluded for safety reasons: Individuals with a medical condition contraindicating study participation, as determined by our physician (e.g. liver or kidney disease), individuals with current or past drug abuse or dependence, individuals with serious psychiatric conditions (e.g., PTSD or Panic Disorder), any lifetime PTSD or psychotic disorder, or a first degree relative with a psychotic disorder, women who are pregnant, nursing, or planning to become pregnant in the next 3 months. The self-report questionnaires we use require fluency in English and a high-school education so lack of either of these are further exclusionary criteria. Individuals with a BMI below 19 or above 30 will also be excluded to minimize variability due to body weight. Women not on hormonal birth control will be scheduled only in the follicular phase of the menstrual cycle.

Drug and Doses: The 13 µg dose of LSD does not produce hallucinatory or perceptual effects. Other recent studies have used substantially higher doses (100 – 200 µg (Krebs and Johansen, 2012; Schmid et al., 2014) or 20-80 µg administered *intravenously* (Carhart-Harris et al. 2014) with no adverse effects. We will administer the drug in accordance with the published safety guidelines for hallucinogen research in humans (Johnson et al., 2008). The onset of action after oral LSD is 30 minutes, with a peak plasma concentration at 1.5-3 hours (Dolder et al., 2015). Our preliminary findings indicate that the subjective effects of the drug have returned to baseline by 4 hours (Figure 1 above). Doses will be separated by three days. The drug is obtained from Organix Inc, under IND 127547, and placed in solution with assistance from the U of Chicago Investigational Pharmacy Service. The drug is administered sublingually in a volume of 0.2 ml; placebo consists of 0.2 ml distilled water. See “Risks” for complete safety information.

Study Tasks:

1. International Affective Picture System (IAPS) – (Lang et al., 1999) Participants will view standardized positive, negative and neutral pictures from the IAPS. The negative and positive images will be matched on degree of valence and arousal. An Evaluative Space Grid rating will follow each picture to allow for ratings on both emotional valence (positive, negative, neutral), and arousal.
2. Dynamic Affect Recognition Evaluation – (DARE; Porges et al., 2007) Participants will view dynamically developing facial expressions depicting one of six emotions: Happiness, sadness, anger, fear, surprise or disgust. Participants will be instructed to respond as soon as they are able to identify the emotion depicted. The variables of interest are accuracy and latency to response.

3. Cyberball (Williams and Jarvis 2006). This task simulates social acceptance and exclusion. Subjects participate in two 4-min computer games in which they play "catch" with two computer avatars. In each game subjects are included (63 ± 3% of the tosses) and then excluded (10 ± 3% of the tosses). They complete questionnaires assessing their mood and estimate the percentage of tosses (0-100%) they receive, and to rate their desire to play again (0-100).
4. N-back Task – This continuous performance task is a standard measure of working memory. Individuals with major depression have been shown to exhibit slower reaction times and reduced accuracy on this task, and who routinely use very low doses of LSD report experiencing cognitive enhancement. We will also include a questionnaire assessing how well the participants think they performed on this task, to obtain a measure of meta-cognition of agency.
5. Digit Symbol Substitution Test (DSST) – This task requires subjects to match as many numbers to symbols as they can in a 90 second interval.

Subjective Measures:

1. Profile of Mood States – (POMS: McNair et al., 1971) The POMS is a validated measure consisting of 72 adjectives commonly used to describe momentary mood states. The POMS is highly sensitive to the effects of drugs, and will be used to assess mood effects of the drug during the study sessions.
2. Positive and Negative Affect Scale (PANAS; Watson, Clark and Tellegen, 1988). The PANAS will be used to monitor subjects' mood states on the days between sessions.
3. Drug Effects Questionnaire - (DEQ: Fischman and Foltin, 1991) The DEQ is a validated measure consisting of questions on a visual analog scale about the subjective effects of drugs. Subjects are asked to rate the extent they feel a drug effect, whether they like or dislike the drug effect, and if given a choice would they want to take more of the drug. This will also be used to assess the pharmacodynamics of the drug effect during the study.
4. Visual Analogue Scale (VAS) – This includes adjectives assessing commonly reported effects of LSD, such as "stimulated", "happy", "closeness", "openness", and "trust" (Schmid et al., 2014). This will also be used to assess the effect of the drug during the sessions.
5. 5 Dimensions of Altered States of Consciousness (5D-ASC) scale (Dittrich, 1998) assesses altered states of consciousness in five domains, and is sensitive to LSD administration (Schmid et al. 2014). This will be completed once at the end of each drug session.
6. The Columbia Suicide-Severity Rating Scale (C-SSRS; Posner et al. 2008) defines 5 subtypes of suicide ideation and will be administered at the start of each session for safety reasons.

Physiological Measures:

Blood pressure and heart rate will be monitored every 30 min using portable blood pressure cuffs, to track the cardiovascular effects of the drug, and ensure participant safety.

Procedure

Orientation: Participants who meet criteria will first be scheduled for an orientation session. During this session, subjects will be informed that during the sessions, they may be given a placebo, a stimulant drug used to treat ADHD (e.g. methylphenidate), a sedative drug used to treat sleep disorders (e.g. diazepam), or a "hallucinogenic" drug (e.g. LSD). This procedure minimizes expectancy effects that may obscure the true pharmacological effects of drugs. We and others (Mitchell et al, 1996; Kirk et al, 1998; Metric et al, 2009; 2012; Heinz et al, 2013) have demonstrated that participants' expectancies can strongly influence responses to drugs, and this is especially true for this current project. That is, there is a strong expectation among users about the effectiveness of microdosing. This sentiment is evident in numerous accounts and claims on the internet. Until now, these claims have not been put to the test. If our participants know or expect to be receiving this particular drug then it will be impossible to determine whether the results were due to their expectancies or to the pharmacological effects of the drug. Even with these instructions, there is a possibility that expectations will influence the outcome, but as researchers we need to make a best effort. At the end of the study we will ask subjects what they thought they received, before providing them with the information. Participants will be given an oral description of the study procedures and the written consent form. After the experimenter reviews this information and the consent form with the subject, and answers any questions he/she may have, subjects will answer questions confirming their understanding of the study, and sign the informed consent document. The subject will then practice completing the tasks and questionnaires to be used in the study. This will help reduce practice effects across the study sessions. Abstention from recent drug and alcohol use will verified by breathalyzer and urine drug tests. Women will also be urine tested for pregnancy.

Study Session: The study consists of two 2-week blocks, each with 4 sessions, conducted at 3-day intervals. The blocks can be separated by 2-4 weeks. The timeline of each session is summarized below. On study session days, participants will arrive at 9am, and consume a standardized snack. Research assistants will conduct urine and breath screening for recent alcohol and drug use, and a pregnancy test (for women). We will then take pre-drug measures of subjective mood, drug effects, body temperature, and cardiovascular variables; these measures are repeated every 30 min throughout the session (see below). Participants will ingest the drug or placebo at 9:30am. While waiting for the drug effect to reach peak, they will be allowed to relax and watch a movie or read a book, but will not be allowed to do work. At 2 hrs after drug ingestion subjects will complete behavioral tasks, lasting about 1 hour, coinciding with the peak effect of the drug. They will complete the tasks in a counterbalanced order. The subjects will then be given a standardized lunch. Research assistants will check on participants every half hour, and they will be in an adjacent room with a video monitor

throughout the sessions. A psychiatrist will be on call and on the premises throughout each session. A procedure is in place to handle adverse drug responses (see SOP below). Participants will remain in the lab until 2 pm, or if needed until effects of the drug return to baseline, as measured by both subjective report and cardiovascular variables. Our laboratory is located in a hospital setting, with medical assistance readily available. In the unlikely event that subjects are still affected by the drug at 2:00 pm, we can retain them in our comfortable testing rooms (couches, tv, blankets) until the effects dissipate. A research assistant will be in the adjacent room at all times, and will obtain approval from the physician before releasing the subject. Sessions will be separated by 3 days.

Timeline
9:00am – Arrival, snack, breath and urine tests
9:15am – subjective and cardiovascular measures
9:30am – Drug administered
10:30am - subjective and cardiovascular measures
11:00am - subjective and cardiovascular measures
11:30am – Tasks, counterbalanced
1:00pm – subjective and cardiovascular measures
1:15pm- Standardized lunch
1:30pm - subjective and cardiovascular measures
2:00pm - subjective and cardiovascular measures, end of session questionnaire; Leave Laboratory

Post drug session. Three days after each block of four sessions subjects will attend a 1-hour non-drug laboratory session to assess their post-drug mood and behavioral responses. During this session they will complete the DASS, BDI, the IAPS ratings, and the n-back memory test. During the second post-drug session (i.e., after the second 4-session blocks) will also complete an end-of-study questionnaire, on which they will be asked to report which type or types of drugs they think they received at each session. They will also re-complete the State of Consciousness Questionnaire (Griffiths et al., 2006). Finally, participants will be told about the study hypotheses, methods and the types of drugs that they received, and will be given a chance to ask any final questions in person, via phone, or via email.

Data Analysis

The effects of the drug will be assessed using three-way repeated measures analysis of variance (ANOVA), with drug (drug vs placebo), session (days 1-4) dose and time (within sessions) as within-subject factors. We hypothesize LSD will reduce depressed mood, compared to placebo, that this effect will increase over the 4 drug administration days, and that it will be evident three days after the 4^{th} drug administration. Our primary mood measure will be negative affect scores on the PANAS. Behavioral tasks will also be analyzed with two-way repeated measures ANOVAs, with drug, session and stimulus valence (negative, positive, neutral) as within-subjects factors.

Human Subjects Information

Recruiting methods: We will place print ads in newspapers and on online job search sites such as craigslist.org, Facebook, and flyers in the Chicago area. Volunteers who respond to our ads are screened using our standard screening protocol for all studies in the Human Behavioral Psychopharmacology Laboratory, which is separately approved by the IRB under Protocol #13681B

Obtaining consent: Consent for the screening session only is obtained at the screening according to procedures outlined in Protocol #13681B. Written informed consent for the study procedures is obtained at the orientation session, after a verbal explanation of study procedures, check of comprehension, and an opportunity for the participant to ask any questions they may have. Consent is verbally re-verified at the beginning of each study session.

Risk to subjects:

1. Diagnostic procedures and questionnaires: Some of the questions asked during the screening may be considered sensitive information, including drug use history and psychiatric history. We have rigorous procedures in place to ensure confidentiality of data, including locked cabinets for confidential files, subject coding, secure computer systems, and rigorous training of personnel. Please see screening protocol #13681B for full information on steps taken to protect information gathered as part of the screening.

2. Study drug: The possible side effects of LSD include: dizziness, weakness, tremors, nausea, drowsiness, paraesthesia, blurred vision, dilated pupils and increased tendon reflexes, increase in blood pressure, although these effects are minimal even at doses much higher than we plan to administer. The risk of these effects is low at the 13 microgram dose used in this study (Passie et al., 2008). In addition, to protect against, or minimize any possible risks with LSD, we will administer the drug according to the guidelines set forth by Johnson et al. 2008. Subjects are carefully screened to exclude those who are physically or psychiatrically at risk (e.g., current AXIS I disorders or history of psychosis). The studies are conducted in a hospital, where emergency assistance, including the psychiatry resident on-call, and the psychiatrist connected with the study are close at hand. A research assistant will be present throughout the procedures and will monitor heart rate, blood pressure, and respiratory rate throughout the sessions. In addition, on-call physicians will be available in the case of medical emergencies. Subjects will be provided with transportation home after the sessions. Subjects will be told that small amounts of the drugs or their metabolites will be detectable in the body for several weeks and to advise the experimenter if they intend to undergo a drug screening within one month of participating in the study.
The PI holds an IND to study LSD (IND127547) and we submitted an amendment to the original protocol on September 29, 2018, to conduct this study.

3. Tasks: Some of the tasks (emotional pictures, pictures of facial expressions) employ stimuli that are designed to elicit short-term positive and negative emotional reactions.

Although the pictures used are designed to elicit emotional reactions, these reactions are typically brief, and similar methods to have previously been used in a wide range of studies without evidence of any long-term adverse reactions. Further, participants are screened for any psychiatric conditions that might make them vulnerable to experiencing adverse reactions to brief alterations in mood. Any participants who are unduly distressed will be counseled by a trained staff member.

Benefits to subjects: There is no direct benefit to the participants, although we hope that the information learned from this study will contribute to our knowledge of potential novel treatments for mood disorders. Additionally, participating in research may be an educational experience for participants, and we attempt to facilitate this by providing a thorough debriefing including an explanation of study hypotheses and procedures at the conclusion of participation.

Subject time commitment and compensation: The study sessions (8 sessions) are estimated to last 5 hrs each, plus two 1-hour followup sessions for a total of 42 hours spent in study sessions. Participants are compensated $40 for each study session, $10 for each of the 1-hour sessions and a bonus of $110 for completion of all study sessions, giving a total of $450.

Data and Safety Monitoring: The PI and the psychiatrist associated with the study will monitor data collection and safety at weekly staff meetings. During these meetings, the PI will review and respond appropriately to (1) data collection and storage practices and (2) any adverse or unexpected effects from the study drugs. Both the study physician and PI will monitor the safety of study participants on an ongoing basis. The physician connected with this study will be on call during the experimental sessions and for 24 hours after sessions. Subjects will be given telephone numbers for the study physician and investigators in case they experience unpleasant effects after leaving the laboratory. If a serious or unexpected adverse event were to occur, the staff member most closely involved with the subject at that time or the physician would notify the PI immediately. The PI would then take appropriate action and communicate with all necessary offices within the University and the FDA.

References:

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Beck depression inventory-II. San Antonio.

Buchborn, T., Schröder, H., Höllt, V., Grecksch, G., 2014. Repeated lysergic acid diethylamide in an animal model of depression: Normalisation of learning behaviour and hippocampal serotonin 5-HT2 signalling. Journal of Psychopharmacology 28, 545-552.

Carhart-Harris, R., Kaelen, M., Whalley, M., Bolstridge, M., Feilding, A., Nutt, D., 2014. LSD enhances suggestibility in healthy volunteers. Psychopharmacology 232, 785-794.

Celada, P., Puig, M.V., Amargós-Bosch, M., Adell, A., Artigas, F., 2004. The therapeutic role of 5-HT1A and 5-HT2A receptors in depression. Journal of Psychiatry and Neuroscience 29, 252.

Dittrich, A, 1998. The standardized psychometric assessment of altered states of consciousness (ASCs) in humans. Pharmacopsychiatry, 31 80–84.

Dolder, P.C., Schmid, Y., Haschke, M., Rentsch, K.M., Liechti, M.E., 2015. Pharmacokinetics and concentration-effect relationship of oral LSD in humans. International Journal of Neuropsychopharmacology, pyv072.

Fischman, M.W., Foltin, R.W., 1991. Utility of subjective effects measurements in assessing abuse liability of drugs in humans. British journal of addiction 86, 1563-1570.

Gasser, P., Holstein, D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., Brenneisen, R., 2014. Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. The Journal of nervous and mental disease 202, 513.

Griffiths, R.R., Richards, W.A., McCann, U., Jesse, R., 2006. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. Psychopharmacology 187, 268-283.

Haertzen, C.A., 1970. Subjective effects of narcotic antagonists cyclazocine and nalorphine on the Addiction Research Center Inventory (ARCI). Psychopharmacologia 18, 366-377.

Johnson, M.W., Richards, W.A., Griffiths, R.R., 2008. Human hallucinogen research: guidelines for safety. Journal of psychopharmacology.

Krebs, T.S., Johansen, P.-Ø., 2012. Lysergic acid diethylamide (LSD) for alcoholism: meta-analysis of randomized controlled trials. Journal of Psychopharmacology 26, 994-1002.

Lang, P.J., Bradley, M.M., Cuthbert, B.N., 1999. International affective picture system (IAPS): Technical manual and affective ratings. Gainesville, FL: The Center for Research in Psychophysiology, University of Florida.

McNair, D., Lorr, M., Droppleman, L., 1971. POMS, Profile of mood states. San Diego, CA: Educational and Industrial Testing Services.

Nichols, D.E., 2013. Serotonin, and the past and future of LSD. MAPS Bull 23, 20-23.

Passie, T., Halpern, J.H., Stichtenoth, D.O., Emrich, H.M., Hintzen, A., 2008. The pharmacology of lysergic acid diethylamide: a review. CNS Neuroscience & Therapeutics 14, 295-314.

Posner, K., et al, 2008. Columbia-Suicide Severity Rating Scale (C-SSRS). New York: New York State Psychiatric Institute.

Savage, C., 1952. LYSERGIC ACID DIETHYLAMIDE (LSD-25) A Clinical-Psychological Study. American Journal of Psychiatry 108, 896-900.

Schmid, Y., Enzler, F., Gasser, P., Grouzmann, E., Preller, K.H., Vollenweider, F.X., Brenneisen, R., Müller, F., Borgwardt, S., Liechti, M.E., 2014. Acute Effects of Lysergic Acid Diethylamide in Healthy Subjects. Biological psychiatry.

Vollenweider, F.X., Kometer, M., 2010. The neurobiology of psychedelic drugs: implications for the treatment of mood disorders. Nature Reviews Neuroscience 11, 642-651.

Wardle, M.C., Garner, M.J., Munafò, M.R., de Wit, H., 2012. Amphetamine as a social drug: effects of d-amphetamine on social processing and behavior. Psychopharmacology 223, 199-210.

Williams, J.M.G., Broadbent, K., 1986. Distraction by emotional stimuli: Use of a Stroop task with suicide attempters. British Journal of Clinical Psychology 25, 101-110.

Williams, J.M.G., Mathews, A., MacLeod, C., 1996. The emotional Stroop task and psychopathology. Psychological bulletin 120, 3.

Mitchell, S. H., Laurent, C. L., & de Wit, H. (1996). Interaction of expectancy and the pharmacological effects of d-amphetamine: Subjective effects and self-administration. *Psychopharmacology, 125*, 371-378. PMID: 8826542

Kirk, J. M., Doty, P., & de Wit, H. (1998). Effects of expectancies on subjective responses to oral delta-9-tetrahydrocannabinol. *Pharmacol, Biochem Behavior, 59*, 287-293. PMID: 9476972

Metrik, J., D. Rohsenow, P.M. Monti, J. McGeary, T.A.R. Cook, H. de Wit, M. Haney, C. Kahler (2009) Effectiveness of a marijuana expectancy manipulation: Piloting the balanced placebo design for marijuana. *Experimental Clinical Psychopharmacology*, 17, 217-225. PMC2810847

Metrik, J., C.W. Kahler, B. Reynolds, J.E. McGeary, P.M. Monti, M. Haney, H. de Wit, D.J. Rohsenow (2012) Balanced-placebo design with marijuana: Drug and expectancy effects on impulsivity and risk taking. *Psychopharmacology*, 223, 489-99. PMCID: PMC2810847

Heinz, A.J., H. de Wit, T.C. Lilje, J.D. Kassel (2013) The combined effects of alcohol, caffeine and expectancies on subjective experience, impulsivity and risk-taking. *Experimental and Clinical Psychopharmacology.* 21, 222-234. PMCID: PMC4354945

Standard Operating Procedure for psychiatric symptoms in MESA study (IND12747)
August 7, 2018
H. de Wit, PI

The studies will be conducted in a comfortable, living-room like environment located in the Department of Psychiatry, at the University of Chicago Hospital. The rooms are quiet, and have couches, subdued lighting and carpets. Subjects are encouraged to bring calming music or reading material. A research assistant or post doctoral fellow will be present during all sessions, in a room adjacent to the participant. Participants can contact the research assistant at all times. The psychiatrist connected with the study will be on call, and notified in advance that a session is scheduled. The psychiatrist can be telephoned (home and work numbers) or paged. If he is not available he will delegate this responsibility to a colleague. The emergency room is a 5 minute walk from the laboratory.

The research assistant will check on the subject at least every 30 minutes to obtain cardiovascular measures and administer questionnaires. If the subject describes discomfort that does not require further assistance, the research assistant will visit the subject every 10 minutes.

The research assistant will page the psychiatrist immediately if any of the following events occur:

1. If the subject's heart rate increases to 120 bpm or higher or if blood pressure rises over 180/105.

2. If the subject exhibits psychotic symptoms, or severe depression, or expresses thoughts or intentions to hurt self or others.

If the intentions to hurt self or others are immediate, the research assistant will call Hospital Security to transport the subject to the Emergency Room. A wheelchair is available, and the ER is a 5 minute walk from the testing rooms.

Treatment for drug-induced psychiatric symptoms will be treated mainly by reassurance, and if necessary, with a 1 mg lorazepam tablet. Lorazepam will be available in the laboratory but only administered with instruction from the psychiatrist or the PI.

At the scheduled end of the sessions (2:00 pm), subjects will be queried about residual drug effects, and the research assistant, in consultation with the PI and the psychiatrist, will determine whether the subject can be released. The research assistant will remain with the subject until it is safe for the participant to leave. Subjects will not be permitted to drive after sessions, and will be provided with transportation home.