

Recreational 3,4-methylenedioxy-N-methylamphetamine (MDMA) or 'ecstasy' and self-focused Compassion: Preliminary steps in the development of a therapeutic psychopharmacology of contemplative practices

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Abstract

3,4-methylenedioxy-N-methylamphetamine (MDMA) produces diverse pro-social effects. Cognitive training methods rooted in Eastern contemplative practices also produce these effects through the development of a compassionate mindset. Given this similarity, we propose that one potential mechanism of action of MDMA in psychotherapy is through enhancing effects on intrapersonal attitudes (i.e. pro-social attitudes towards the self). We provide a preliminary test of this idea. Recreational MDMA (ecstasy)-users were tested on two occasions, having consumed or not consumed ecstasy. Self-critical and self-compassionate responses to self-threatening scenarios were assessed before (T1) and after (T2) ecstasy-use (or no use), and then after compassionate imagery (T3). Moderating roles of dispositional self-criticism and avoidant attachment were examined. Separately, compassionate imagery and ecstasy produced similar sociotropic effects as well as increases and reductions in self-compassion and self-criticism respectively. Higher attachment-related avoidance was associated with additive effects of compassionate imagery and ecstasy on self-compassion. Findings were in line with MDMA's neuropharmacological profile, its phenomenological effects and proposed adjunctive use in psychotherapy. However, although conditions were balanced, the experiment was non-blind and MDMA dose/purity was not determined. Controlled studies with pharmaceutically pure MDMA are still needed to test these effects rigorously.

Keywords

MDMA, compassion-focused therapy, compassion, psychotherapy, self-criticism

Introduction

Recreational users of 3,4-methylenedioxy-N-methylamphetamine (MDMA), or 'ecstasy,' report a number of acute desirable effects. Principal among these is the experience of enhanced interpersonal relatedness, or a sense of connection to others [Bedi *et al.*, 2009, Dumont *et al.*, 2009]. Indeed, the experimental effects of MDMA are primarily reported in the social domain and these may relate to its unique and complex pharmacology as a broad-acting pro-monoamine-, vasopressin- and oxytocin-ergic compound [Broadbear *et al.*, 2013, Parrott, 2013]. The interaction between these neurotransmitter systems is implicated in social approach, reward and attachment in mammalian brain systems that evolved specifically to promote affiliation among conspecifics, enabling cooperation within large social groups [Depue *et al.*, 2005]. It is proposed that the evolution of complex social-cognitive capabilities in humans was accompanied by the development of self-referential cognitive processes, including the tendency toward critical self-evaluation [Gilbert, 2000]. High levels of self-criticism are a risk factor for psychopathology following stressful life events [Lassri *et al.*, 2013, Pinto-Gouveia *et al.*, 2013]. Increased self-criticism is also a core feature of various psychological disorders [Gilbert *et al.*, 2001]. By contrast, effects of self-soothing arise from the neural systems

responsible for affiliative bonding referred to above [Depue *et al.*, 2005], which are compromised in psychological disorders. Psychotherapists have long recognised the need to develop treatment strategies that subvert the cognitive processes responsible for negative self-referential thinking and for upregulating self-soothing processes [Linehan, 1993].

Recently, novel psychotherapeutic procedures, inspired by Eastern meditative practices which emphasise 'loving kindness' and compassion have been developed and show promise in the treatment of a range of disorders [Gilbert, 2014; Hofmann *et al.*, 2011], including psychosis [Laithwaite *et al.*, 2009; Braehler *et al.*, 2013] and personality disorder [Lucre *et al.*, 2013]. Other therapeutic approaches emphasise the evolutionary psychology of attachment and bonding and the capacity to counteract the influence of negative self-referential thinking through a variety of compassion-focused exercises [Gilbert, 2014]. For example, Compassion-Focused Therapy (CFT) involves the use of compassionate imagery (CI) to direct benevolent, nurturing, warmly-regarding and compassionate feelings towards the self [Gilbert, 2014].

Self-directed compassion is not only a potential antidote to maladaptive feelings of shame and guilt in psychopathology but may also have a role in promoting well-being and resilience in the absence of psychological disorder [Wallace et al., 2006]. Expert mediators show evidence of neural remodelling and alterations in neural [Lutz et al., 2008, Weng et al., 2013] and epigenetic [Kaliman et al., 2014] responses to social stress. During meditation, experts can achieve states of ecstasy and transcendence. However, as with other forms of 'mind training,' expertise is generally only achieved after intensive and prolonged practice. Alternatively, transcendence and profound personal insights can also be gained through the use of psychedelic drugs. While the legitimacy or authenticity of such insights might be questioned - particularly when effects are short-lived rather than transformative - it is also true that under certain conditions, including those of the controlled laboratory setting, some compounds (notably psilocybin) can produce lasting and positive personality changes after only a single dose [Griffiths et al., 2011]. Such 'restructuring' of the personality was previously only thought to be possible through prolonged and intensive psychotherapy. These observations, along with a reconsideration of evidence from non-controlled studies that predate the scheduling of these drugs, have resulted in a revival of interest in the use of psychedelics as therapeutic agents [Nutt et al., 2013].

Similarly, the mixed-profile psychedelic/stimulant drug MDMA has been tested in a number of small-scale clinical trials as an adjunct to psychotherapy [Mithoefer et al., 2011, Mithoefer et al., 2013, Oehen et al., 2013]. While these studies show that MDMA is a promising therapeutic agent, it is most commonly used as a recreational drug (i.e. ecstasy). A recent Australian survey suggested approximately one in four 20-29 year olds has tried the drug and 10% have used it in the past month [Australian Institute of Health and Welfare, 2011]. Its pro-social effects include feelings of love [Bedi et al., 2010], sense of connection and compassion; [Sumnall et al., 2006] which have been widely documented in controlled studies and amongst recreational users, who frequently report using ecstasy specifically to obtain these effects [Morgan et al., 2013]. These perceptual, psychedelic and transcendental effects [Dumont et al., 2006] particularly motivate its use amongst those seeking spiritual awakening and enlightenment, with some users combining Eastern meditative practices with ecstasy to achieve insights and transcendent states [Watson et al., 1991]. Alternatively, some recreational users take the drug to help them cope with adverse life events, namely as a form of self-medication [Moonzwe et al., 2011], although the extent and nature of psychological changes that accompany such use remains unclear.

It is of interest to determine whether the unique sociotropic effects of MDMA extend to intrapersonal attitudes, particularly self-criticism and self-compassion. In line with the proposed use of MDMA as an adjunct to psychotherapy and the apparently overlapping phenomenological effects of MDMA and compassion-oriented practices, it is of particular interest to examine the combined effects of MDMA and CI on self-criticism and self-compassion. Here we use a within-subjects, repeated measures, naturalistic experimental design to test the effects of CI and ecstasy in recreational ecstasy users. Ecstasy-use has typically been associated with the dance scene, and naturalistic studies have tended to focus on determining whether ecstasy is associated with acute neurotoxic effects (i.e. cognitive impairment) by examining users' performance in the presence and absence of

the drug [Rogers et al., 2009]. In contrast, using the same research strategy, our aim is to determine whether subjectively positive or therapeutically-relevant effects related to self-attitude can also be attributed to ecstasy (and by implication, to MDMA) by studying its effects in recreational users. Our hypotheses were broad-based: ecstasy's well-characterised pro-affiliative effects were expected to extend to improvements in self-attitudes (reduced self-criticism and/or enhanced self-compassion). In line with MDMA's ability to enhance psychological treatment effects, we predicted that effects of CI - a psychological procedure used in a *bona fide* psychotherapy (Gilbert, 2010) - would be enhanced by ecstasy.

We also examine whether any interaction between CI and ecstasy is moderated by attachment characteristics. This is of particular interest because attachment security provides the basis for care-related behaviours and feelings; conversely those with problematic forms of adult attachment, that is, avoidant or anxious styles of relating in close relationships, may experience barriers to (self-) compassion [Mikulincer et al., 2005] and, in the context of mood disorders, may benefit from compassion-oriented treatments to overcome these barriers [Gilbert, 2014]. Adult attachment patterns have implications for adaptive interpersonal functioning but can also resemble personality styles that are a predisposition for depression [Blatt, 1974]. Moreover, the only other study examining the neuropharmacology of self-compassion found that the effects of oxytocin were moderated by attachment-related avoidance [Rockliff et al., 2011]. The same study found similar moderating effects of trait self-criticism. Since the effects of ecstasy may be partially mediated by oxytocin, it is of interest to also investigate the moderating role of trait self-criticism in the current study.

It should be noted that ecstasy is a recreational drug and that much of what is sold as ecstasy contains varying amounts of MDMA along with other compounds. A recent analysis of ecstasy tablets showed that 70% contained only MDMA whereas 7% contained a mixture of MDMA and other stimulant compounds [Brunt et al., 2012]. Studies on the neurotoxicity or 'beneficial' effects of MDMA in which ecstasy rather than pharmaceutical-grade MDMA is examined must therefore be considered in the context of the relative impurity of the drug being investigated.

Methods

Participants

Ecstasy users were recruited from the local community through word of mouth and snowball sampling. Participants who became aware of the study and were interested in participating were invited to contact the team for further information. Participants were screened via telephone interview to exclude those with history of self-declared psychotic illness, current mental health problems requiring treatment, serious physical illness requiring treatment, pregnancy or breast-feeding.

A power calculation based on an assumption of medium effects ($f=0.25$) in a repeated measures ANOVA interaction (Time x Session), with $\beta=0.8$, $\alpha=0.05$, assuming strong correlations ($r=0.7$) between primary repeated measures variables across time, suggested a sample size of $n=18$. Twenty participants began and completed the study (7 women; 13 men). Of the women participants, five used hormone-based contraception, two did not. Participants generally did not practice meditation ($n=16$), although

some meditated with differing frequencies (<1/week: n=2; >1/week: n=2).

All gave written, informed consent at the start of the first session during which they were made aware that they could withdraw from the study at any time without needing to give a reason. The study was approved by the UCL Graduate School Research Ethics Committee.

Design and Procedure

A naturalistic within-subjects design was used, with all participants completing one session in which they took ecstasy recreationally prior to a compassionate imagery (CI) task, and a second session (control) in which they took no drug prior to CI. Testing sessions took place between 6-14 days apart. Participants informed the experimenter of their plans to use ecstasy (usually when they were *not* intending to go to a party or clubbing) and the experimenter arranged the control session to occur either before or after the CI + ecstasy session, at the convenience of the participant while ensuring session balance across participants. The order of the CI + ecstasy session, and the control session was balanced such that 10 participants completed the CI + ecstasy session first.

Participants were asked to refrain from any drugs (except caffeine and nicotine) for 24 hours prior to each session and provided a urine drug-screen at the start of each of the two sessions. Testing sessions were conducted individually in a quiet room in participants' homes. On both testing sessions state measures of affect (the PANAS and TPAS; see below) were administered along with a scenario-based measure (the SCCS, see below) which required participants to imagine life-events intended to induce negative self-referential thinking and then immediately rate themselves on a number of self-compassion- and self-criticism-related dimensions at three time points: T1 (baseline), T2 (40 + 13 mins) after T1, and T3 (~20 min after T2; see Figure 1). Immediately after T1, participants took their ecstasy via their normal route of administration. Assessment at T2 (i.e. administration of PANAS, TPAS and SCCS) occurred after participants indicated that they were experiencing 'peak effects' of ecstasy (relative to previous experiences with the drug). Immediately after T2 assessment, participants underwent the CI task, after which they completed the same measures again (T3). As such, assessment of affect, self-compassion and self-criticism at T2 occurred only in the presence of ecstasy (CI + ecstasy session) or its absence (control session), whereas assessment of these constructs at T3 represented the combined assessment of ecstasy and CI effects (CI + ecstasy session) or CI effects alone (control session).

Seven participants insufflated ecstasy and 13 took it orally; differences in timing of self-judged 'peak effects' account for the variability in T2 with respect to T1 (the T1 and T2 interval did not differ between insufflating and orally ingesting participants).

During the control session, participants completed a closely matched procedure, with two main exceptions: they did not consume any substance, and they completed additional trait questionnaires (between T1 and T2).

State Measures

The choice of measures in this experiment was informed by a previous study examining the effects of oxytocin on CI

[Rockliff et al., 2011] and consisted of pre-/post- state measures to assess effects of CI + ecstasy on affective state and self-attitudes. In addition ecstasy-specific subjective measures were used to assess subjective changes in state following drug ingestion.

Ecstasy-related Mood and Symptoms Scale: A set of visual analogue scales specifically assessed ecstasy-related mood and symptoms, including compassion and empathy. Items included euphoria, energetic, jaw clenching, trust, wanting to be with others, closeness to others, compassion for others, compassion for self, empathy, sensitivity to colour, self-confidence. Anchors (e.g. not at all [euphoric] and very [euphoric]) were used at the extremes of the scales (0 and 10).

Drug experience/ expectancy: On the CI + ecstasy session, participants rated the (expected) strength of effect of their ecstasy ('How strongly will it affect you/is the effect?'), and its purity ('How pure is the MDMA?') on a 7 point drug expectation/experience scale (1=not at all, 7=extremely) before and after taking the drug.

Experience of Compassionate Imagery Questions: Participants responded to items about their experience of CI on Likert scales (1=low-10=high), particularly of receiving compassion: resistance, momentary tension, 'effort creating,' clarity, 'feeling moved' and sadness in response to CI. An additional question assessed the 'ease' with which participants experienced their image, which was intended to embody wisdom, kindness, warmth and care. These items and their scoring are described by Rockliff and colleagues [Rockliff et al., 2011].

Positive and negative affect: The 10-item version of the Positive and Negative Affect Schedule (PANAS) was used [Thompson, 2007]. Each of the five positive and five negative items (single-word adjectives) were rated on Likert scales (1=not at all-5=very much so). Participants were instructed to rate their current feelings. Additionally the Types of Positive Affect Scale (TPAS) [Gilbert et al., 2008] assesses the extent to which people experience different types of positive affect. The TPAS consists of 18 words, which individuals rate on a 5 point scale to indicate the extent to which each word characterises them. There are three subscales for different forms of positive affect: activating, relaxed and safeness/contentment. Participants were instructed to respond to items in relation to how they felt right now.

State self-compassion and self-criticism: The Self-Compassion and Criticism Scale (SCCS; [Falconer et al., 2015] is a situational measure of self-compassion and self-criticism. It consists of five scenarios which are potentially self-threatening and which participants are instructed to vividly imagine, as if they were occurring at the current moment. After imagining each scenario, participants immediately rate their reaction towards themselves. While the scenarios would normally produce negative self-referential thinking, participants can also respond with varying degrees of self-soothing, reassurance, and compassion (self-compassion items) as well as harshness, contempt and self-criticism (self-criticism items) on 7-point Likert scales (1 = not at all to 7 = highly). Psychometrically, the SCCS is separated into two orthogonal scales (self-criticism and self-compassion). The scales have excellent or good reliability with Cronbach's alphas of 0.91 and 0.87 respectively [Falconer et al., 2015], and recent research suggests that the SCCS scale is a useful tool in repeated measures designs that examine the effects of experimental compassion-focused interventions [Falconer et al., 2014].

Mood, trait and drug-use measures

Depression: The Beck Depression Inventory II (BDI-II) [Beck et al., 2005] consists of 21 sets of 4 statements (scored from 0 – 3) relating to symptoms of depression. Participants select the statement that best describes how they have felt over the previous two weeks. Higher total scores indicate more severe symptoms of depression.

Adult Attachment: The 'close relationships' version of the Revised Adult Attachment Scale was used [Collins, 1996]. This consists of 18 statements, with three subscales ('close,' 'depend' and 'anxiety'). Each statement is rated on a 5 point Likert scale, indicating the extent to which it is characteristic of how the participant generally feels in important close relationships in their life (1=not at all characteristic of me-5 = very characteristic of me). The close subscale measures how comfortable an individual is with closeness, tapping attachment-related avoidance. The normative value for this subscale is 3.20, based on a large-scale cluster analysis of different attachment styles [Collins, 1996]. This subscale was of particular interest in this study given the moderating role of attachment-related avoidance in oxytocin's effects on self-compassion [Rockliff et al., 2011]. Participants were classified as relatively low on attachment avoidance (mean score + SD: 3.30 + 0.70) or high on attachment avoidance (mean score + SD: 4.57 + 0.37) based on a median split of their scores, which were significantly different ($t(18)=5.073, p<0.001$).

Trait self-criticism: Dispositional self-criticism – the persistent tendency toward negative self-evaluation was assessed using the 'inadequate self' subscale of the Forms of Self-Criticizing/attacking and Self-Reassuring Scale [Gilbert et al., 2004]. Responses are given on a 5 point Likert scale (0= not at all like me, 4=extremely like me). Participants were classified as 'high' and 'low' scorers on self-criticism based on a median split of scores as per Rockliff et al [Rockliff et al., 2011] who showed that self-criticism as measured by the inadequate-self subscale moderated the response of oxytocin on experiences of self-compassion.

Drug-use: Participants were asked about their drug-use using a semi-structured interview designed for young UK drug users [Freeman et al., 2012]. Alcohol, tobacco, ecstasy, cannabis, cocaine, ketamine, hallucinogens, mephedrone and amphetamine were rated for their most recent consumption (days ago), length of use (years), days per month use and 'amount per session' (various units) were recorded for each drug type. Participants were considered 'regular users' of a particular drug if they used the drug at least twice a month. Objective assessment of drug use was conducted using a drug screen urine test cup (Alere, Abingdon, Oxfordshire, UK) which assesses for the presence of a range of illicit and prescription pharmaceuticals on each session.

Compassionate imagery

Participants completed a guided CI exercise, by listening to three MP3 recordings through headphones. The recordings corresponded to: (i) description of an ideal compassionate being, (ii) relaxation through rhythmic breathing and (iii) active engagement with the ideal compassionate being in imagery. The exercise was based on the type used in CFT and is described at length in CFT manuals (e.g. Gilbert, 2010). A brief outline is provided here (the script is available from the corresponding

author). Participants listened to a recording outlining the nature of compassionate mental imagery which provided details about the nature of an ideal 'compassionate being,' and were told its qualities included unconditional positive regard, deep commitment, wisdom, acceptance and strength of mind. The description was deliberately permissive, such that participants could generate any type of compassionate figure, according to their preference. After a pause to allow for questions, participants were guided through five minutes of 'rhythmic breathing' and awareness. After this, participants were asked to develop an image of an ideal compassionate being and then receiving compassion from this being, focusing sequentially on various qualities of (or feelings arising from) deep commitment, strength and dependability, wisdom and understanding, acceptance, warmth, loving kindness, care and concern, and compassion flowing from the compassionate being. The total duration of the entire (three recordings) CI procedure was 18 min and was the same on both sessions.

Prior to, and immediately after CI, participants completed state questionnaires (PANAS, TPAS, SCCS) as well as the experience of compassionate imagery questions. Note, participants were not given any specific instructions to bring compassionate images or feelings to mind while completing these question(na)ires.

Statistical analyses.

Data were analysed using 2 x 3 repeated measures ANOVA, with Session (CI + ecstasy) and Time (T1, T2 and T3) as within subject factors and positive/negative mood states and state self-compassion and self-criticism as dependent variables. Repeated measures ANOVAs (2 x 3 x 2) were also used to assess effects of ecstasy-use on self-compassion and -criticism respectively, with dispositional self-criticism and attachment-related avoidance status (high and low) as a between subjects factor. Paired samples t-tests were used in planned comparisons to analyse 'experience of compassionate imagery' items and for follow-up analyses of significant interactions. Exploratory correlations were conducted using Spearman's Rho (ρ)

Where assumptions of sphericity were violated, Greenhouse Geisser corrections were applied and adjusted degrees of freedom reported.

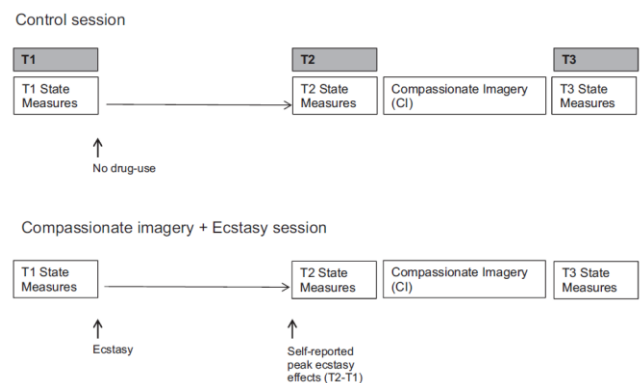


Figure 1: Timeline of the experimental procedure permitting a comparison of the effects of compassionate imagery and ecstasy, both alone and in combination. State measures were assessed at T1, T2, and T3, at which point participants completed the Ecstasy-Related Mood and Symptoms Scale, the Positive and Negative Affect Schedule and the Self-Compassion and Criticism Scale. The Experience of Compassionate Imagery Questions were completed only at T3.

Results

Demographics, trait questionnaire scores and drug use

Participants' mean age was 25.50 + 3.59 years. They had 16.5 + 1.64 years of education and negligible levels of depression (BDI score= 6.66+ 4.80). All reported regular use of alcohol, and most were regular users of both tobacco and ecstasy. Cannabis, cocaine and ketamine use was less frequent (Table 1). Urinalysis was generally consistent with self-report drug use. On the control session urinalyses results were either negative (i.e. drug-free; n=6), THC-positive (n=7) or benzodiazepine positive (n=2); three samples could not be interpreted. On the CI + ecstasy session participants were either negative (n=12) or THC positive (n=7); one participant was positive for opioids.

	Number tried/regular users	Days since last use	Days per month	Years used	Amount per session
Alcohol	20/20	3.03 (1.95)	14.33 (5.88)	11.33 (3.79)	6.94 (2.61)
Tobacco	20/15	0.13 (0.35)	25.27 (9.89)	8.20 (4.54)	4.37 (2.63)
Ecstasy	20/13	11.65 (7.50)	1.54 (0.43)	7.04 (3.47)	0.71 (0.82)
Cannabis	20/9	3.28 (2.22)	17.94 (10.66)	7.44 (3.84)	9.72 (6.06)
Cocaine	20/6	13.92 (10.45)	1.83 (1.37)	5.92 (1.56)	0.96 (0.68)
Ketamine	19/2	4.50 (0.71)	6.25 (6.72)	4.00 (2.83)	0.50 (0.00)
Hallucinogens	15/1	1250 (1032)	-	-	-
Mephedrone	17/0	-	-	-	-
Amphetamine	15/0	-	-	-	-

Alcohol=UK units (1=8g pure alcohol); cigarettes=number per day; ecstasy=number of pills; cannabis= days taken to smoke 3.5g; cocaine and ketamine=grams

Table 1: Participants' historic and current drug use.

Drug experience and expectancy ratings

On the CI + ecstasy session, participants' ratings of their ecstasy experience on the expectancy/experience questions did not vary from the pre-(expected) to post-(experienced) interval for rated strength (pre: 4.70 ± 0.98, post: 4.38 ± 1.09, $p > 0.2$), or rated purity (pre: 4.80 ± 0.95, post: 4.85 ± 1.18, $p > 0.5$).

Ecstasy-related mood and symptoms

Main effects of Time were found for all 11 ecstasy-related mood and symptom factors (energy, euphoria, jaw clenching, sensitivity to colours, trust, wanting to be with others, compassion for others, closeness to others, empathy, self-confidence and self-compassion; F values ≥ 3.63 , p values ≤ 0.036 , $\eta^2 > 0.16$). There were also main effects of session for euphoria, jaw clenching, and sensitivity to colours reflecting higher values on the CI + ecstasy session (F values ≥ 4.39 , p values ≤ 0.05).

A Time (T1, T2, T3) x Session (CI + ecstasy, control) interaction for euphoria [$F(2, 38)=27.80$, $P < 0.001$, $\eta^2=0.59$] reflected an increase in euphoria at T2 compared to T1 on the CI + ecstasy session. A similar pattern of interactions was observed for jaw-clenching [$F(2, 38)=20.37$, $p < 0.001$, $\eta^2=0.52$] and sensitivity to colours [$F(1.50, 38)=13.72$, $p < 0.001$, $\eta^2=0.38$].

An interaction between Time and Session for 'wanting to be with others' [$F(2,38)=4.60$, $p=0.027$, $\eta^2=0.17$] appeared to

reflect parallel, independent effects of ecstasy and CI. Specifically, scores on this attribute increased between T1 and T2 on the CI + ecstasy session reflecting the expected sociotropic effect of ecstasy ($t(19)=3.65$, $p=0.002$). In addition, a similar increase was observed between T2 and T3 on the control session, reflecting the effect of CI alone ($t(19)=3.214$, $p=0.005$).

All other interactions were non-significant (F values < 3.1 , p values > 0.05).

None of the 11 ecstasy-related mood and symptom factors increased significantly between T2 and T3 (all p values ≥ 0.05) on the CI + ecstasy session.

Effects of ecstasy and compassionate imagery on positive affect

There were no main effects of Time or Session on the 'active' positive affect subscale of the TPAS (F values < 3.14 , $p > 0.05$). However there was a significant interaction between Time and Session [$F(2,38)=3.98$, $p=0.027$, $\eta^2=0.17$], primarily reflecting a trend reduction in active positive affect between T1 and T2 [$t(19)=2.035$, $p=0.056$] on the control session and a trend increase between T1 and T2 on the CI + ecstasy session [$t(19)=2.017$, $p=0.058$] (Table 2).

No main effects or interactions were found for the relaxed or warm subscales (F values < 1.5 , p values > 0.25) of the TPAS or the positive affect subscale of the PANAS (F values < 2.0 , p values > 0.2).

	T 1 (Baseline)	T 2	T 3
TPAS (Active)			
Control	18.55 (6.86)	16.95 (6.78)	15.95 (6.00)
CI-ecstasy	18.65 (5.64)	21.75 (6.46)	19.95 (6.07)
TPAS (Relaxed)			
Control	16.80 (3.91)	16.70 (4.00)	17.30 (4.77)
CI-ecstasy	15.20 (3.24)	14.40 (5.42)	15.65 (6.64)
TPAS (Safe)			
Control	11.75 (2.63)	12.05 (1.93)	11.50 (2.82)
CI-ecstasy	10.85 (2.94)	11.45 (3.35)	12.10 (2.81)
PANAS (Positive)			
Control	14.75 (3.85)	14.70 (3.96)	15.00 (3.34)
CI-ecstasy	14.95 (2.70)	16.50 (3.07)	15.30 (4.38)
PANAS (Negative)			
Control	8.00 (3.39)	7.60 (2.95)	6.60 (2.70)
CI-ecstasy	7.75 (2.59)	7.05 (2.26)	6.20 (1.70)

Mean (\pm SD) sub-scale scores from the Types of Positive Affect Scale (TPAS) and Positive and Negative Affect Schedule (PANAS) at three within-session testing time points (T1, T2 and T3) on the control session and CI-ecstasy session.

Table 2: Positive and negative affect over time in the control and CI-ecstasy sessions.

Effects of ecstasy and compassionate imagery on negative affect

There was a main effect of Time [$F(2,38)=9.361$, $p < 0.001$, $\eta^2=0.33$] reflecting a gradual reduction in scores on the negative affect subscale of the PANAS on both testing sessions (Table 2) but no main effect of Session and no Session x Time interaction (F values < 1.00 , p values > 0.4).

Effects of ecstasy and compassionate imagery on state self-criticism and self-compassion

There was a main effect of Time [$F(1,424, 27.059)=19.039, p<0.001, \eta^2=0.50$] and Session [$F(1,19)=5.135, p=0.035, \eta^2=0.21$] and a Time x Session interaction [$F(2,38)=5.377, p=0.009, \eta^2=0.22$] on the self-criticism scale of the SCCS. As can be seen in Figure 2 this interaction reflects reduced self-criticism in response to ecstasy between T1 and T2 (i.e. an effect of ecstasy alone; $p=0.001$) on the CI + ecstasy session and a similar reduction in response to CI between T2 and T3 on the control session (i.e. an effect of CI alone, $p=0.015$). On the CI + ecstasy session there was an additional decrease in self-criticism between T2 and T3 (i.e. after CI; $p=0.027$; Figure 2, top panel, reflecting a combined effect of CI + ecstasy). Self-criticism scores were not associated with the effects of ecstasy on the 'active' subscale of the TPAS at either of these time-points (p values $< 0.2, p>0.4$), suggesting that these effects on positive affect and self-criticism were independent.

There was a main effect of Time [$F(1,39, 26.34)=14.19, p<0.001, \eta^2=0.43$] and Session [$F(1,19)=17.106, p=0.001, \eta^2=0.47$] but no Time x Session interaction [$F(2,38)=2.15, p=0.131$] on self-compassion scores (Figure 2, bottom panel). An exploratory 2 X 2 ANOVA using only T1 and T2 did show an interaction between Time and Session [$F(1,19)=4.52, p=0.047, \eta^2=0.19$], suggesting an effect of ecstasy alone on self-compassion but no additional effect of CI on the CI + ecstasy session.

Experience of Compassionate Imagery

Except for the 'feeling moved [by receiving compassion]' item, which was higher in the CI + ecstasy session [$t(19)=2.17, p=0.043$], other items of the Experience of Compassionate Imagery yielded no other difference between sessions (t values $< 2.06, p$ values >0.05).

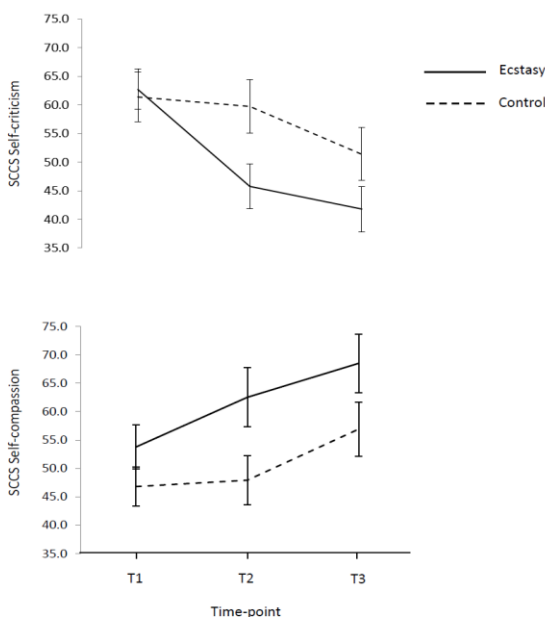


Figure 2: Top Panel: Mean SCCS self-criticism scores + SEM at three time points corresponding to pre- (T1) and post-ecstasy (T2) and post-CI (T3) on the CI-ecstasy session and at similar intervals on the control session when CI occurred between T2 and T3 and no ecstasy was consumed. Bottom Panel: Mean SCCS

self-compassion scores + SEM. In both panels, the ecstasy. A session data is represented by the solid black line and the control data by the dashed line.

Moderating role of attachment-related avoidance

There was no moderating role of attachment-related avoidance with respect to state self-criticism (F values $<2, p$ values >0.1). However, as shown in Figure 3, there was a 3-way Session x Time x Group interaction for state self-compassion [$F(2,36)=3.91, p=0.029, \eta^2=0.18$]. In the CI + ecstasy session, state self-compassion increased significantly both between T1 and T2 (reflecting an effect of ecstasy; $p=0.037$) and between T2 and T3 (reflecting an additional effect of CI; $p=0.021$) in the high attachment-related avoidance group but not in the low attachment group (p values >0.1). In the control session, there was an increase in self-compassion between T2 and T3 (i.e. after CI) in both the high attachment-related avoidance ($p=0.02$) and low attachment-related avoidance group ($p=0.047$).

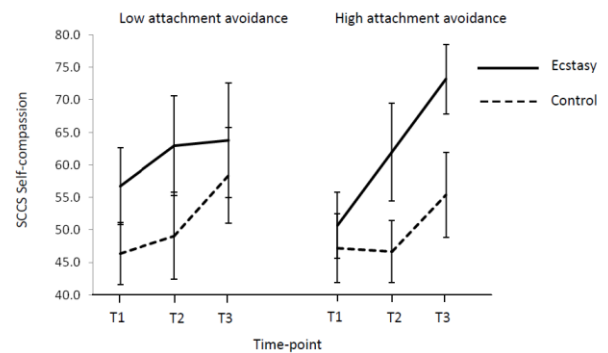


Figure 3: Moderating effect of avoidant attachment on self-compassion at three time-points (T1, T2, T3) on the CI-ecstasy and control sessions, as per Figure 2.

Moderating role of trait self-criticism

The other moderator of interest was dispositional self-criticism. There was a Group (low/high self-criticism) x Session interaction [$F(1,18)=10.28, p=0.005, \eta^2=0.36$] but no other interactions involving Group (F values $<1, p$ values >0.4). For self-compassion, there were no significant interactions involving group (F values $<3.76, p>0.05$).

Discussion

In this study we examined the effects of recreational ecstasy-use and compassionate imagery (CI) on self-criticism and self-compassion. As such we extended the investigation of ecstasy effects beyond the widely-documented interpersonal domain to affiliative self-attitudes. While anecdotal reports suggest potent effects of ecstasy on self-forgiveness and self-compassion [Leneghan, 2013, Power, 2013] systematic studies of these effects have been lacking.

The current findings were in line with our broad predictions: while there was a (10-point) decrease in self-criticism during the control session, there was a two-fold (21-point) larger decrease when CI occurred after ecstasy-use. There was a similar,

though less pronounced additional effect of ecstasy on self-compassion. Moreover, the effects of ecstasy on CI were moderated by adult attachment characteristics such that those with greater attachment-related avoidance appeared to show enhanced self-compassion following ecstasy, and CI thereafter. Interestingly, while ecstasy had the expected sociotropic effect, with increased levels of 'wanting to be with others' after ecstasy, CI also produced this effect in the absence of ecstasy (in the control session), despite compassion being directed towards *the self* rather than others.

The effects of ecstasy (\pm CI) on self-criticism and -compassion did not appear to reflect generalised improvements in mood. For instance, of the positive affect measures used here, only the 'active' subscale of the TPAS showed a Session by Time interaction, in line with ecstasy's dopamine-dependent stimulant properties [Green *et al.*, 2003]. Neither were these two effects (on positive affect and self-criticism) correlated suggesting that effects of ecstasy and CI on state self-criticisms and self-compassion are unlikely to simply reflect demand characteristics or expectancy effects alone. The moderating influence of attachment-related avoidance in particular is difficult to explain largely on the basis of expectancy. As such, while not biochemically verified, the effects of ecstasy-use are consistent with pharmacologically-induced modulation of self-processing.

Aberrant processing of 'the self' characterises a number of psychiatric disorders [Northoff, 2007]. In particular, negative self-referential processing -'self-criticism'-underlies the aetiology and maintenance of this variety of psychopathologies (e.g. eating disorders, depression, social anxiety, body dysmorphic disorder, schizophrenia, personality disorders) and can be regarded as an important transdiagnostic factor [Gilbert *et al.*, 2005, Schanche, 2013]. Finding effective ways of dealing with self-criticism therefore remains a priority for psychiatry and clinical psychology. Various lines of research support the use of self-compassion-enhancing strategies to overcome the effects of self-criticism. Yet for some individuals the initial experience of self-compassion, even in therapeutic settings, can be challenging. In particular, those with high levels of self-hatred tend to exhibit a *fear of compassion* [Gilbert *et al.*, 2011], and those with high levels of trait self-criticism and attachment-related anxiety tend to respond to CI with physiological activity resembling threat responses [Rockliff *et al.*, 2008]. For these individuals, compassion is a frightening and alien experience. As such, improved methods for overcoming barriers to self-soothing (e.g. by reducing self-critical responding) continue to be needed.

The unique subjective and interpersonal-affiliative effects of ecstasy seem to be accompanied by a facilitation of positive *intrapersonal* relating, potentially allowing individuals who typically attempt to ward off compassionate feelings, to apprehend the hated, feared or wounded parts of the personality with gentleness and understanding. This type of approach- motivation towards enfeebled aspects of the self simply mirrors intentional empathic behaviour *between* individuals directed at relieving *another's* suffering [Bartal *et al.*, 2011]. Such positive affiliative behaviour recruits a well-characterised set of neural systems and processes [Depue *et al.*, 2005] involved in affiliative and consummatory reward and positive social memory, primarily mediated by vasopressin, oxytocin, dopamine, and their interaction. Importantly,

these neurotransmitter systems are also strong positive regulatory targets of MDMA [Broadbear *et al.*, 2013].

Those with higher levels of attachment-related avoidance (i.e. discomfort in close or intimate relationships) showed the clearest evidence of additive effects of ecstasy and CI, specifically on state self-compassion. Avoidance of affectionate bonds in adulthood may result in loneliness and social isolation, which in turn are associated with psychological and physical disorders [Bartholomew, 1990]. These findings therefore suggest that those with this particular 'developmental vulnerability' may experience the greatest positive effects from the therapeutic or recreational [Watson *et al.*, 1991] combination of ecstasy and cognitive behavioural self-compassion enhancing practices. Attachment avoidance was of specific interest here because it moderated the effects of oxytocin on experiential aspects of self-focused CI [Rockliff *et al.*, 2011]. In particular, those who were *less* avoidant (i.e. more comfortable in close relationships) appeared to experience greater positive effects of CI following intranasal oxytocin. Those findings are in the opposite direction to those found here (we have found greater positive effects of CI in the presence of ecstasy in those with high attachment avoidance), although they are in keeping with the occasionally contradictory and paradoxical findings with intranasal oxytocin in humans, which are strongly influenced by contextual factors [Churchland *et al.*, 2012]. Alternatively, the current findings are in line with the broad psychopharmacological effects of MDMA which may rely on dopaminergic influences on affiliative processing, potentially via interaction with oxytocin and vasopressin [Depue *et al.*, 2005]. They are also consistent with the apparent 'antidepressant' effects of ecstasy seen in individuals with a vulnerability to depression [Majumder *et al.*, 2012], possibly as a form of self-medication [Sessa, 2014].

While MDMA enhances psychotherapeutic outcome in treatment-resistant PTSD in small-scale trials, its mechanism-of-action is unknown. In particular it is unclear which psychological process(es) interact with MDMA and whether additional psychological procedures, such as CI, may optimise MDMA-assisted psychotherapy. Our findings suggest this may be a possibility, especially since CI could easily be incorporated into the existing MDMA-psychotherapeutic model [Mithoefer *et al.*, 2011] and is *experientially consistent* with MDMA-induced states. This is a critical consideration for combination psychological-pharmacological treatments, since additive or synergistic interactions are only likely to be achieved when this kind of consistency is present.

We are aware of the need to be cautious in generalising these findings to either non-drug using healthy populations, or those seeking treatment for psychological disorders. Clearly, the best evidence for efficacy of psychiatric treatments comes from well-controlled, randomised, double-blind trials. In the UK, trials of schedule I drugs, such as MDMA, continue to occur in a highly restrictive and regulated context, are expensive, and would only be approved on the basis of a compelling rationale for testing [Nutt *et al.*, 2013]. In order to determine whether such a compelling rationale might exist, we decided to first test our hypotheses in a group of recreational ecstasy users. There are however, significant limitations to this approach. In this study we relied on convenience sampling so our participants may be non-representative in terms of response to MDMA. Since neither participants nor experimenters

were blind to treatment our study also has the same limitations as an open-label trial with respect to expectancy. In addition however, contextual factors associated with naturalistic drug-use (e.g. participants were tested in their own homes) may have increased expectancy of certain psychological effects (e.g. empathy and compassion). Several participants tested positive for recreational / medicinal compounds (THC, benzodiazepines and opioids). Of course, cannabinoids and benzodiazepines with long half-lives may have been detectable in urine but consumed some time prior to testing. However, except for self-declaration (no consumption within the previous 24 hours), we were unable to ensure that testing was unaffected by the presence of these compounds. Participants did not show all of the effects expected of MDMA (e.g. on compassion for others, closeness to others, trust). The absence of these effects may reflect insufficient statistical power or insufficiency of true MDMA-mediated effects arising from ecstasy that contained other ingredients [Brunt et al., 2012].

An additional ecstasy-alone condition would have helped to increase confidence that effects at time point 3 (T3) were really due to the *combined* effects of ecstasy and CI rather than ecstasy alone. In particular, it is possible that the effects of ecstasy intensify over T2 and T3 and this alone could have resulted in the effects on self-compassion and self-criticism on the session when ecstasy was taken prior to CI. However, none of the ecstasy-related mood and symptom factors increased significantly between T2 and T3 on the CI + ecstasy session. This might suggest that these effects had reached a steady state at T2.

Finally, since ecstasy likely contains varying levels of other psychoactive compounds, the effects observed here cannot unequivocally be attributed to MDMA alone. As such we cannot yet claim our findings are a strong basis for supporting the combined therapeutic use of MDMA and compassion-focused psychotherapeutic procedures. Future naturalistic studies should seek to verify the chemical composition of the formulations used by recreational-users. However, the most robust rest of these hypotheses would be through double-blind, placebo controlled procedures with pharmaceutical-grade MDMA, ideally including a suitable active control (e.g. methylamphetamine; Bedi et al., 2010).

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Conflicts of interest

The authors have no conflicts of interest to declare.

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