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PSYCHOLOGICAL EFFECTS OF MDMA

Section A: The Effects of MDMA (3,4-methylenedioxmethamphetamine) on Emotions and Pro-Social Behaviour in a Therapeutic Setting and in Recreational Use: A Systematic Review.

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Summary of the MRP Portfolio

This thesis examines psychological effects of MDMA. It consists of two sections.

Section A is a systematic literature review investigating the psychological effects of MDMA on emotional processes and pro-social behaviours. It critically reviews the empirical studies investigating emotional and pro-social effects of MDMA in both recreational users and in a therapeutic setting. Limitations and future research directions are discussed.

Section B is an empirical paper reporting the findings from an online-based quantitative study exploring a range of individual and environmental factors and their role in shaping the psychological effects of 3,4-methylenedioxmethamphetamine (MDMA), as well as their function in reducing the risk of the drug abuse. The results and implications, as well as future research directions, are discussed.

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Major Research Project

Section A: Systematic Literature Review

The Effects of MDMA (3,4-methylenedioxmethamphetamine) on Emotions and Pro-Social Behaviours in Recreational Use and in a Therapeutic Setting: Systematic Review.

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Abstract

Although there are existing reviews published on psychological effects of MDMA, none have specifically explored the effects of MDMA on emotional processes and pro-social behaviour. The current review aims to critique the literature on emotional and pro-social effects of MDMA in both recreational users and in a therapeutic setting.

Searches were conducted on PsycInfo, PubMed, Medline, and Google Scholar for peer-reviewed articles to identify quantitative studies targeting the effects of MDMA on emotions and pro-social behaviour, including recreational and therapeutic use of MDMA.

Twenty-four studies were identified. Overall, the studies supported the hypotheses that MDMA alters emotional process by increasing positive emotions and diminishing negative emotions, and it increases sociability and pro-social behaviours by elevating the perceived value of social interactions and intimacy with others. MDMA was found to increase emotional empathy, whereas the relationship between MDMA and both cognitive empathy and emotional intelligence remains unclear.

The preliminary studies presented provide preliminary evidence that MDMA may be successful in treating treatment-resistant PTSD. Further research addressing both recreational and therapeutic use of MDMA is warranted.

Keywords: MDMA (Ecstasy), psychological effects, emotions, pro-social effects.

Introduction

MDMA

MDMA (3,4-methylenedioxmethamphetamine) is a synthetic psychoactive drug better known by its street name 'ecstasy' (Weir, 2000). MDMA is one of the most popular recreational drugs in the United Kingdom (UK, Home Office, 2012; Uosukainen, Tacke, & Winstock, 2015). Similar trends were reported across Europe, as well as the United States (US) and Australia (Thomas et al., 2012; United Nations Office on Drugs and Crime, 2012).

MDMA was first synthesised in 1912 by German pharmaceutical company Merck and was briefly tested on animals by the American Army as a potential brainwashing agent in 1953 (Holland, 2001). Two decades later in 1976, Sasha Shulgin, a chemist from the US, synthesized MDMA in his own laboratory and introduced the drug to a group of psychotherapists. MDMA was subsequently used in underground psychotherapeutic work in the late seventies and early eighties, with very promising outcomes (Greer & Tolbert, 1986). However, in the early eighties, MDMA was leaked from the medical community and became a popular recreational drug, which led to Drug Enforcement Administration (DEA) declare MDMA as a schedule I drug in 1985. This put an end to the psychotherapeutic use of MDMA due to its illegal status. Despite the government's attempts to cease the use, recreational use of the drug spread over to Europe and its popularity has been well documented since (United Nations Office on Drugs and Crime, 2012).

Recreational Use of MDMA

Recreational use of ecstasy, in particular at dance clubs, is a cultural phenomenon, which initiated in the late eighties. In the UK, those taking part in the use of ecstasy at dance clubs were referred to as the 'Chemical Generation'

(Hammersley, Khan, & Ditton, 2002). Rave parties involve all-night dancing fuelled by the stimulants, predominantly ecstasy, which is referred to as a 'club drug' (Weir, 2000). The popularity of ecstasy as a recreational drug has remained stable over the past three decades (United Nations Office on Drugs and Crime, 2012). Among young people aged 16-24, the use of ecstasy in the UK has increased since 2013/14 from 3.9 per cent to 5.4 per cent, although this figure increases by further 25 per cent when the respondents are attending nightclubs on a regular basis (Home Office, 2015). There are several issues regarding the widespread use of MDMA, which are highlighted below.

One of the main issues in relation to the recreational use of ecstasy is its purity and the exact content of the pills available on the underground market (Cole, Bailey, Sumnall, Wagstaff, & King, 2002; Parrott, 2004). Research shows variation in MDMA content of ecstasy tablets and presence of other adulterants, which poses serious methodological problems in research of this substance (Vogels et al., 2009). A large-scale study in the Netherlands (Brunt, Koeter, Niesink, & van den Brink, 2012) reported higher levels of subjective adverse effects as a result of consuming ecstasy tablets containing other drugs apart from MDMA.

MDMA was classified as a Class A drug in the US and the UK in 1985 implying it's high risk of addictive abuse potential and the lack of medical use (Holland, 2001). However, there is a lack of evidence in the literature for an MDMA dependence syndrome similar to the one observed in alcohol or opioids users (Degenhardt, Bruno, & Topp, 2010). Although increased tolerance as well as psychological aspects of dependence seem to be more prominent among MDMA users, physical characteristics such as withdrawal are less common (Degenhardt et al., 2010; Degenhardt & Hall, 2012; White et al., 2006). Furthermore, a relatively small

percentage of MDMA users report problems with their use, or seek treatment (Degenhardt et al., 2010). A recent international study on harms and benefits associated with psychoactive substances considered MDMA use less harmful and more beneficial than the majority of other substances studied, including alcohol, Tobacco and benzodiazepines (Morgan, Noronha, Muetzelfeldt, Fielding, & Curran, 2013).

MDMA has been in the public spotlight for the past 30 years due to its capability to become a therapeutic tool for psychotherapy on one side, and its potentially neurotoxic effect in humans, on the other (Chabrol, 2013; Holland, 2001; Sessa, 2007). Research on neurotoxicity of MDMA in humans raise concerns that it may lead to both short- and long-term adverse effects on cognitive functioning. In particular, these have been argued to include verbal memory deficits (Verheyden, Henry, & Curran, 2003) and relatively slow processing speeds (e.g. Halpern et al., 2011), and a range of executive impairments, including spatial working memory (e.g. Hanson, K. L., Luciana, 2004), verbal fluency (e.g. Bhattachary & Powell, 2001; Fox et al., 2002; Heffernan, Ling, & Scholey, 2001). On the contrary, other studies report the lack of deficits (e.g. Back-Madruga et al., 2003; Gouzoulis-Mayfrank, Thimm, Rezk, Hensen, & Daumann, 2003; Vollenweider, Gamma, Liechti, & Huber, 1998).

MDMA as a Therapeutic Agent

Entactogens are drugs that have been used to facilitate the psychotherapeutic process by enabling patients to access and process often painful and repressed emotional material (Nichols, 1986). MDMA was classified as an entactogen due to effects which Nichols (1985) described as intensely emotional and argued allows people to establish a deeper connection with their true self. In 2001, Metzner and

Adamson proposed the alternative name 'Empathogens' to highlight the drug's ability to enhance interpersonal relationships and feelings of empathy.

From the perspective of potential for clinical use as an entactogen, MDMA possesses unique effects on the human brain. Firstly, it acts as a mood enhancer due to its euphoric effects (Sessa & Nutt, 2015). Secondly, MDMA is the only anxiolytic drug without a sedative effect, which may prove to be particularly useful in the treatment of anxiety disorders (Sessa & Nutt, 2015). Thirdly, MDMA reduces defensiveness and enables bonding with others as well as improving social interactions and emotional regulation (Johansen & Krebs, 2009). All of the above characteristics are argued to make MDMA well-suited to act as a therapeutic agent (Parrott, 2007; Sessa, 2007).

PTSD Treatment

PTSD is a deliberating condition characterised by intrusive re-living of the traumatic events, associated with intense anxiety and excessive arousal as well as avoidance of any stimuli that might trigger the fear response, often leading to severe difficulties managing everyday life (APA, 2013). PTSD develops as a result of experiencing a life-threatening event, in particular among survivors of sexual abuse, war veterans and those who endured severe accidents.

Cognitive-behavioural therapy (CBT) provided a useful model for development and treatment of PTSD (Ehlers & Clark, 2000). The model implies that PTSD becomes persistent when the traumatic event and its squeal is experienced as a current threat causing distortions in processing the traumatic memory, which leaves it poorly integrated within the autobiographical memory store (Ehlers & Clark, 2000). The prefrontal cortex and the amygdala form an emotional regulation circuit, and have been found central in maintenance of the PTSD symptoms. People with PTSD

show dysfunctional connectivity in these regions associated with increased activity of the amygdala, which is a part of the brain responsible for the fear response. Prolonged exposure to safe but fear evoking triggers is one of the most commonly used techniques for treatment of PTSD (Bradley et al., 2005; Roth & Fonagy, 2005). This technique can lead to strengthening the connectivity in the prefrontal cortex and the inhibition of amygdala-induced fear responses (Amoroso, 2015; Krebs & Johansen, 2012). This results in improvement of emotional regulation and facilitates incorporation of corrective information into the trauma memory in the hippocampus (Amoroso, 2015).

Although, there is robust evidence that CBT is a safe and effective treatment for PTSD, up to 50% of patients undergoing this form of therapy do not improve (Kar, 2011). High rates of nonresponse to treatment and dropouts seem to be associated with greater severity of PTSD symptoms, in particular avoidance and hyperarousal as well as comorbid mental health problems such as depression and borderline personality disorder, and impaired social functioning (Kar, 2011). These factors suggest that CBT might not always be an acceptable form of treatment for more acutely distressed clients, therefore, implying the need for a more tolerable treatment alternative.

Some preliminary studies have suggested that MDMA may be effectively employed in treatment of PTSD (Amoroso, 2015; Johansen & Krebs, 2009). Imaging studies in healthy volunteers showed that MDMA reduced activity of amygdala and hippocampus, (Carhart-Harris et al., 2013; Gamma et al., 2000), which might be responsible for reduction in anxiety response to a recollection of traumatic content. In a clinical setting, MDMA has been experimentally observed to produce a state of improved insight, allowing non-threatening exploration of painful and repressed

memories associated with traumatic past experiences, by 'inhibiting the subjective fear response to an emotional threat' (Greer & Tolbert, 1998, p. 371).
Lowering of the anxiety response while engaging in a compassionate relating to the traumatic incidents during the MDMA-assisted psychotherapy session, seems to be instrumental in processing traumatic memories and allowing emotional learning (Amoroso, 2015).

The Effects of MDMA on Emotions and Pro-social Behaviour

Pro-social effects of MDMA, such as sociability, interpersonal closeness and feelings of empathy for others; and emotional effects described as improved mood, and feelings of euphoria and well-being, were reported by Sumnall, Cole and Jerome (2006) as the main reason for its use.

The empathy construct incorporates both cognitive and emotional elements (Blair, 2005). Cognitive empathy can be described as one's ability to identify emotional states in others, whereas the emotional aspect of empathy refers to the sensations and feelings as a response to feelings perceived in another person (Blair, 2005).

Emotional and pro-social effects of MDMA seem to contribute to both its recreational and therapeutic uses, although relatively little is known to date about the basic emotional processes responsible for these specific effects. MDMA may facilitate pro-social effects by directly producing positive emotional and pro-social subjective states, or by enhancing responses to positive emotions and diminishing responses to negative emotions (Hysek, Domes, & Liechti, 2012).

Developing a better understanding of the emotional and behavioural mechanisms by which MDMA is thought to produce these pro-social and emotional effects may be useful in expanding our understanding of recreational use as well as

the mechanisms of the therapeutic potential of the drug. Research on this topic has been limited by the legal status of MDMA as well as the methodological difficulties in assessing these effects (Kirkpatrick, Delton, Robertson, & de Wit, 2015). However, over the past decade, a considerable number of studies investigating emotional and pro-social effects of MDMA have been published.

Aims and Objectives of the Current Review

Aims. The primary aim of this review is to examine and summarise the existing research on emotional and pro-social effects of MDMA on humans. Furthermore, the review aims to provide a methodological critique of the literature and considers both research and clinical implications.

Scope. Although there are existing reviews published on psychological effects of MDMA, none specifically explored emotional and pro-social effects of the drug on humans. For example, most reviews address a wide range of short-term and long-term subjective effects of MDMA (Baylen & Rosenberg, 2006; Burgess, O'Donohoe, & Gill, 2000; Noller, 2009; Parrott, 2001; Vollenweider, Liechti, Gamma, Greer, & Geyer, 2002). Other reviews focus on neurotoxicity and adverse physical and mental health problems related to MDMA use in humans (Burgess et al., 2000; Gowing, Henry-Edwards, Irvine, & Ali, 2002; McGuire, 2000; Morgan, 2000; Parrott, 2002; Rivas-Vazquez & Delgado, 2002; Soar, Turner, & Parrott, 2001). None of the previous reviews investigated emotional effects of MDMA in both recreational users and in a therapeutic setting to allow a more comprehensive comparison of the effects.

Since this review focuses on emotional and pro-social effects of MDMA, only studies looking at emotional states and pro-social behaviours were selected. It is

beyond the scope of this review to investigate mental health problems related to MDMA use such as depression or anxiety (e.g. Daumann et al., 2004; Taurah, Chandler, & Sanders, 2014) as well as studies addressing cognitive deficits including memory problems and disinhibition (Gouzoulis-Mayfrank et al., 2000; e.g. Zakzanis, Young, & Campbell, 2003).

Method

Literature Search

This review was based on a search of four online databases: PsycInfo, PubMed, Medline, and Google Scholar. Searches for peer-reviewed articles published before 1st December 2015 (last database search) were conducted. A manual search of the references of relevant papers was also carried out.

The following search terms were selected: 'MDMA ***or*** 3,4-methylenedioxmethamphetamine ***or*** ecstasy ***or*** Molly ***or*** Adam' ***and*** 'emotion ***or*** emotion(al) processing or pro(-)social behaviour ***or*** sociability'. The search strategy was limited to articles published in English.

All papers included in this review met all of the following criteria:

1. The study focused primarily on exploring the effects of MDMA on emotions and pro-social behaviour.
2. The participants were recreational MDMA users or used MDMA as a therapeutic agent.
3. The study included at least one measure of emotional effects of MDMA or pro-social behaviour.
4. The study employed a quantitative methodology.

Based on titles and abstracts, a subset of 854 articles was screened, resulting in the selection of 89 manuscripts for a full-text review. The selected articles were

reviewed using the inclusion and exclusion criteria (see Figure 1 for search procedures). The final step of the screening identified 24 relevant studies. Refer to Appendix 1 for further details.

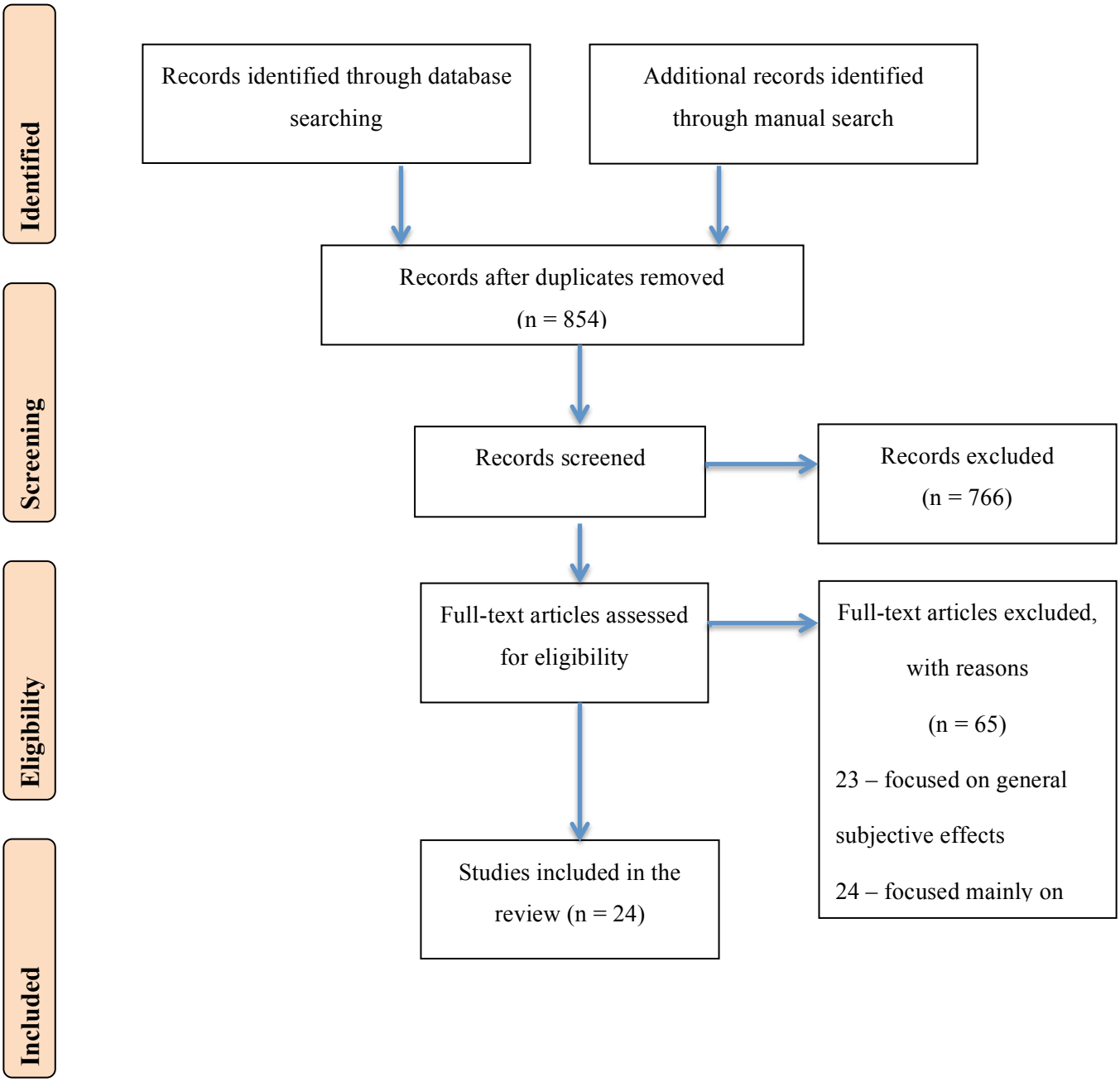

Figure 1. Flow Diagram of Search (PRISMA, Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009)

Structure of this Review

The structure of this review was organised to critically appraise psychological effects of MDMA in two types of setting; recreation and therapeutic. In the recreational setting group, there were 12 randomised controlled trials (RCTs), four naturalistic studies and three correlational studies. The therapeutic setting group included three RCTs (see Appendix 1 for summary tables).

The RCTs and naturalistic studies were critiqued according to the Critical Appraisal Skills Programme for reporting RCT (CASP, 2013), and correlational trials were evaluated according to the CASP guidelines for reporting Case Control Trials (Critical Appraisal Skills Programme (CASP, 2013a).

The following section of the review presents the general findings. This is followed by discussion of results, and consideration of research and clinical implications.

Results

Psychological Effects of MDMA in Recreational Users

Randomised controlled trials. This review will start with an exploration of the experimental literature, which has been divided into three sub-categories. Firstly, the effects of MDMA on positive and negative emotions are discussed. This is followed by an examination of the effects of the drug on sociability and pro-social behaviour, after which trials investigating the effects of MDMA on empathy are reviewed. All of the studies took place in a laboratory environment, where a dose of chemically pure MDMA was administered to participants by medical staff. The doses of MDMA ranged between 0.5 mg/kg to 1.5 mg/kg. The studies employed a randomised double-blind, within-participants design (see Appendix 1 for more details).

Positive and negative emotions. Eight RCT studies examined the acute effects of MDMA on the intensity of emotional experiences as well as the ability to identify emotions in others (Baggott, Kirkpatrick, Bedi, & de Wit, 2015; Bedi, Hyman, & de Wit, 2010; Bedi, Phan, Angstadt, & de Wit, 2009; Carhart-Harris et al., 2013; Hysek et al., 2012; Hysek, Schmid, et al., 2014; Hysek, Simmler, et al., 2014). See Table 1 in Appendix 1 for further details.

Results from all the reviewed trials support the hypotheses that MDMA would increase subjective positive emotions and decrease subjective negative emotions in their participants, as well as improve their ability to identify positive emotions in others. The emotional effects of MDMA were measured through self-reported ratings of affective states. The ability to recognise emotions in others were assessed by completing standardised images depicting emotional facial expressions and, in some cases, also vocal cues.

With regards to the ability to recognise negative emotions in others, the results are inconclusive. Two studies conducted by the same research group (Bedi et al., 2010, 2009) reported that MDMA decreased accurate identification of threat-related signals in others (i.e. the ability to recognise angry faces). Four other studies identified that the ability to identify all negative emotions in others such as anger, fear and sadness, was impaired (Hysek et al., 2012; Hysek, Schmid, et al., 2014; Hysek, Simmler, et al., 2014; Kirkpatrick, Lee, Wardle, Jacob, & de Wit, 2014). Hysek, Schmid, et al. (2014), reported gender differences with female participants displaying greater difficulty identifying negative emotions in others in comparison to male participants.

In a study by Baggott, Kirkpatrick, Bedi, and de Wit, (2015), participants completed a standardised talking task during which they discussed a significant

relationship, for example with a family member or a friend. They found that MDMA increased the use of words relating to both positive and negative emotions. Finally, in a British study (Carhart-Harris et al., 2013), participants' recall of most positive and negative autobiographical memories was assessed under the influence of MDMA. The results supported their hypothesis that MDMA use would result in participants rating their favourite memories as more positive and emotionally intense, and rating their most disliked memories as less negative.

Sociability and pro-social behaviour. Six RCTs measured the acute effects of MDMA on sociability and pro-social behaviour (Bedi et al., 2009; Frye, Wardle, Norman, & de Wit, 2014; Kirkpatrick & de Wit, 2015; Kirkpatrick et al., 2015, 2014; Wardle, Kirkpatrick, & de Wit, 2014). Refer to Table 1 in Appendix 1 for more details. All studies reported that MDMA had a positive impact on sociability and increased pro-social behaviour. The studies employed self-report measures of sociability.

MDMA was also found to enhance responses to rewarding social signals (Bedi et al., 2009) and decrease the perception of social rejection in a virtual social simulation task called 'Cyberball' (Frye et al., 2014). Another study suggested that MDMA increases a level of generosity, measured by a task in which participants make decisions whether they or someone else receives money (Kirkpatrick et al., 2015). However, this effect seemed to be mediated by the social proximity of the relationship (Kirkpatrick et al., 2015).

Three other studies run by the same research group also support the pro-social effect of MDMA. The drug was found to increase the desire to be with others (Kirkpatrick et al., 2014), and increased positive ratings of positive social pictures while reducing the positive ratings of non-social positive pictures (Wardle,

Kirkpatrick, & de Wit, 2014), suggesting that MDMA increases the relative value of social interactions and intimacy with other people. The third study was the first to investigate the role of the social contact and its impact on the effects of MDMA (Kirkpatrick & de Wit, 2015). Social contact with other participants (who were also currently experiencing effects of MDMA), in comparison to the contact with a research assistant or a solitary condition was found to reinforce some of the subjective and physiological effects of MDMA. Furthermore, the study found that MDMA increased the frequency of social interactions and self-reported perceived attractiveness of a person in the room (Kirkpatrick & de Wit, 2015). This study supported the role of the social context in shaping certain effects of MDMA.

Empathy. Three studies investigated how acute effects of MDMA might affect empathy (Bedi et al., 2010; Hysek, Schmid, et al., 2014; Kuypers et al., 2014; see Table 1 in Appendix 1). All three studies supported the hypothesis that MDMA increases empathy, with Bedi et al. (2010) reporting it increased self-rated empathogenic feelings.

Two studies measured emotional empathy and cognitive empathy through a set of standardised tasks, finding emotional empathy enhanced in the MDMA conditions. The results of the impact of the drug on cognitive empathy are inconclusive. Kuypers et al., 2014 reported that MDMA did not increase cognitive empathy as well as trust and reciprocity. However, Hysek, Schmid, et al. (2014), claimed that MDMA increased cognitive empathy but only among male participants, whereas there was no significant increase among female participants.

Overall methodological critique. Overall, all of the RCTs presented in this review were of satisfactory standards. However, there were a number of methodological issues.

The studies used randomised double-blind crossover (within-participants) design, which partially addresses the issue of systematic differences between the two conditions. However, one of the main issues in the majority of the trials is the lack of an active control group. Only four trials (Bedi, Hyman, & de Wit, 2010; Hysek, Schmid, et al., 2014; Kirkpatrick et al., 2014; Kuypers et al., 2014) used active control groups: methamphetamine, Ritalin, intranasal oxytocin, and pindolol, respectively. The rest of the trials used only non-active placebo, which might create certain issues of participants' bias due to distinctive, perceptible and strong effects of MDMA therefore making a truly double-blinded design difficult to achieve. Both participants and researchers were likely to be able to tell whether someone is under the influence of MDMA compared to a non-active placebo.

Another major methodological issue that needs elaborating on is the relatively poor ecological validity of the studies performed in the laboratory conditions. This seems to be a particular problem with regards to assessing ability to recognise emotions of others based on a standardised set of pictures of human's faces. Similarly, assessing the levels of pro-social behaviour and empathy based on standardised tasks might be far removed from participants' social context.

Furthermore, the majority of the studies did control for a gender bias, having between 50% to 78% of male participants. This seems to be the prominent issue with regards to the generalizability of the findings to the female population. Similarly, there was a large variability among studies with regards to the doses of MDMA administered to participants. This makes it difficult to compare the results between studies as certain pro-social and emotional effects might be dose-dependent. For example, one study (Kirkpatrick et al., 2014) found that pro-social effects of MDMA were prominent at a higher dose 1.5mg / kg but not at a lower dose of .75mg/kg.

Naturalistic studies.

Emotion recognition, sociability and self-compassion. This review will now present the evidence from naturalistic studies and a pseudo-experimental study (refer to Table 2 in Appendix 1 for more details).

One study (Yip & Lee, 2006) applied pseudo-experimental design to investigate long-term effects of 'ecstasy' on emotion recognition. Three studies (Hoshi, Bisla, & Curran, 2004; Kamboj et al., 2015; Stewart et al., 2014) applied naturalistic design to investigate the acute effects of MDMA on emotion recognition, sociability and self-compassion.

Yip and Lee (2006) completed pseudo-experimental, between-participants, non-randomised design. They compared 100 abstinent 'ecstasy' users with 100 matched non-users. Participants took part in an adapted version of a facial emotion recognition test (Matsumoto and Ekman's Japanese and Caucasian facial expressions of emotion, Biehl et al., 1997), and a test measuring prosodic emotion recognition, developed by the authors of the study (Yip & Lee, 2006). Findings suggest that emotion recognition among abstinent 'ecstasy' users was impaired compared with non-users' emotion recognition. The findings were only related to the ability to recognise sadness and disgust, leaving other types of emotion recognition intact (i.e. happiness, anger, surprise and fear). Furthermore, the findings suggest that the cumulative number of ecstasy tablets previously taken might be a stronger predictor of impaired recognition of sadness and disgust rather than the length of abstinence from 'ecstasy'. However, the authors did not present enough information on the duration of time since the participants used 'ecstasy' or relevant details on the pattern of drug use.

Hoshi et al. (2004), used an independent group, repeated measures design to compare recreational 'ecstasy' users (n = 16) and non-drug users (n = 21) at the time of ecstasy use in a dance club (ecstasy users) and four days later, when some users experience serotonin depletion and related mood disturbances (Parrott & Lasky, 1998). All participants completed measures of drug use, mood, aggression, impulsivity and subjective effects of the drug, and took part in a standardised facial expression recognition task. 'Ecstasy' users were better at correctly identifying fearful facial expressions and presented lower levels of self-reported aggression at the time of the drug use. However, this was not consistent on day four where the control group was more accurate in identifying fearful expressions and 'ecstasy' users presented higher levels of aggression. Diminished fear recognition on day four was positively correlated with the number of years of ecstasy use and a number of ecstasy tablets taken on day one.

Stewart et al. (2014) used the same design as described in the previous study, where 17 'ecstasy' users were compared with a control group of non-drug users (n = 22) at two points in time: on the night of drug use at participant's homes, and three days later. Participants were asked to rate the trustworthiness of 66 faces, to carry out three co-operative behaviour tasks and to complete mood self-ratings and a standardised measure of trait empathy. The results indicated that ecstasy increased the ratings of face trustworthiness and co-operative behaviour. On day three there were no group differences in ratings of trustworthiness and co-operative behaviour, suggesting that the group differences were associated with the acute effect of the drug. Overall, ecstasy users displayed higher levels of trait empathy than the controls.

Finally, a recent study by Kamboj et al. (2015) used a two-session, within-participants design with a group of 20 'ecstasy' users. Participants completed a range

of self-report questionnaires measuring mood and ecstasy-related subjective effects, attachment styles, and trait self-criticism and self-compassing scales. The measures were administered in participants' homes at three points in time: before and after ecstasy consumption and after a completion of a guided compassionate imaginary exercise while still under the influence of the drug. Results revealed that 'ecstasy' on its own increased self-compassion and reduced self-criticism, however, the effects were even greater after the compassionate imaginary exercise.

Overall methodological critique. The studies described above brought a unique understanding of the effects of 'ecstasy' on emotional processes and were of a higher ecological validity, however, there are a number of methodological problems that need addressing.

Firstly, two studies (Hoshi et al., 2004; Stewart et al., 2014) assessed ecstasy users at two points in time only: in the acute phase of ecstasy effects and in an ecstasy 'hangover' state which was four and three days after the ecstasy use, respectively. The lack of a neutral baseline testing session as observed in the third study by Kamboj et al. (2015), did not allow for a clear comparison of the ecstasy effects. On the contrary, Yip and Lee (2006) only collected the data at the time of abstinence of ecstasy without identifying the acute effects of 'ecstasy'.

Another significant methodological issue apparent in all four studies is the lack of control over dose and purity of the substance referred to as 'ecstasy'. It is difficult to predict the amount of MDMA contained in ecstasy tablets consumed by participants as well as consumption of other drugs before the testing session. Only one study (Hoshi et al., 2004) reported the number of tablets taken by participants during the study.

Furthermore, neither participants nor researchers were blind to treatment, creating a potential source of bias. Similarly, the fact that participants were tested in their own homes (Kamboj et al., 2015; Stewart et al., 2014) and in a club (Hoshi et al., 2004), might have increased expectancy of the drug effects, in particular, those related to empathy and pro-social behaviour. Apart from Yip and Lee's study (2006), the remaining three had relatively small sample sizes and a large proportion of males along with the gender mismatch between the groups, which were also potential sources of bias.

Correlational studies.

Emotional intelligence and emotion recognition and personality traits. This review will now focus on evaluating the evidence from three correlational studies (Craig, Fisk, Montgomery, Murphy, & Wareing, 2010; Reay, Hamilton, Kennedy, & Scholey, 2006; ter Bogt, Engels, & Dubas, 2006). See Table 3 in Appendix 1 for more details.

Reay et al. (2006), compared 15 polydrug ecstasy users with 15 non-ecstasy polydrug user controls. Participants completed a general drug questionnaire, emotional intelligence scale (Schutte et al., 1998) and the Tromso Social Intelligence Scale (Silvera, Martinussen, & Dahl, 2001) to evaluate emotional and social processing, respectively. The study found that 'ecstasy' polydrug users in comparison to non-ecstasy polydrug users, had worse outcomes on two subscales of social intelligence scale: social awareness and social skills, and also scored lower on the measure of emotional intelligence.

A similar study by Craig et al. (2010), compared 'ecstasy' polydrug users (n = 78) with cannabis-only users (n = 38) and non-drug users (n = 34). Participants completed a drug use questionnaire, Emotional Intelligence Measure (Schutte et al.,

1998), and Mood adjective checklist (Matthews, Jones, & Chamberlain, 1990). The results indicated that 'ecstasy' users did not differ from non-users on measures of emotional intelligence. Furthermore, adverse mood effects associated with ecstasy use were associated with lower levels of emotional intelligence. On the contrary, higher levels of emotional intelligence were associated with ecstasy-related precautions used when using the drug such as monitoring fluid intake, taking rest breaks when dancing.

The results of the two studies investigating emotional intelligence among polydrug ecstasy users are inconclusive. Both studies used the same measure of emotional intelligence (Schutte et al., 1998) and were carried out in the UK. Reay et al. (2006) used a very small sample size and reported significant differences in the levels of cannabis consumption between the groups. Even though the cannabis use was not directly related to emotional intelligence, it is conceivable that the interaction of the two drugs (ecstasy and cannabis) might have been responsible for the observed group differences; however, this was not empirically supported by either study.

Finally, a large study by ter Bogt et al. (2006) compared a sample of 381 MDMA users among which 170 were under the influence of MDMA when completing the survey, with a sample of party-goers who did not use MDMA (n = 160) and a national sample of 265 non-hard drug using adults. Participants completed a drug use questionnaire, and a Dutch adaptation of Goldberg's Big Five questionnaire (Goldberg, 1992), measuring five personality traits: agreeableness, extraversion, conscientiousness, emotional stability and openness. The results found MDMA use was associated with higher levels of extraversion and lower levels of conscientiousness. There were no significant differences in personality traits between people in the sample of MDMA users who were under the influence of MDMA while

filling out the questionnaires and sober MDMA users, which suggest that the acute effects of MDMA did not differentiate between the scores on the personality measure.

Overall Methodological Critique. There were several methodological problems identified in the studies described above. The correlational nature of the studies means that the results are uninformative with regards to the causality of the relationships and, therefore, should be interpreted cautiously. Reay et al. (2006) had a particularly small sample size, and all studies presented with an issue of gender imbalance with females participants being under-represented.

The studies relied on self-report measures, which could be a potential source of bias with participants not disclosing accurate information. The majority of participants were poly-drug users, which is a very common problem in this area of research as there are limited ways of controlling for poly-drug use. Finally, there are significant issues around drug purity, dose and presence of adulterants, in particular among participants who use ecstasy pills. Since the majority of participants were poly-drug users it is very difficult to obtain information that would directly apply to this specific drug, creating potential confounding variables and questioning the validity of the results presented across the studies. All those factors make it very difficult to conclude that any evidence is directly related to MDMA use.

Psychological Effects of MDMA in a Therapeutic Setting

Randomised controlled trials. The review will now move to focus onto the therapeutic setting of MDMA use and psychological effects resulting from preliminary MDMA-assisted therapy RCT studies published to date. Refer to Table 4 in Appendix 1 for more details.

All three trials (Bouso, Doblin, & Farré, 2008; Mithoefer et al., 2013; Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2011; Oehen, Traber, Widmer, &

Schnyder, 2013), investigated the therapeutic potential of MDMA in treating chronic and treatment-resistant PTSD. MDMA was used as an adjunct to a course of short-term psychotherapy and followed a treatment protocol described in the manual for MDMA-assisted psychotherapy in patients with PTSD (Mithoefer, 2013). Participants took part in non-drug preparatory psychotherapy sessions prior to the first MDMA experience, and the follow-up sessions, which were scheduled in-between MDMA-assisted psychotherapy sessions to ensure the integration of the experiences from the MDMA sessions. The therapeutic approach during the MDMA sessions was generally non-directive, following and encouraging the naturally occurring recollection and processing of traumatic experiences.

All studies used a double-blind, between-participants randomised and placebo-controlled design. Bouso et al. (2008) completed a pilot study with only six participants, among which four were allocated to MDMA treatment group (50-75mg) and two were in a non-active placebo control group. The study was specifically for women with treatment-resistant PTSD secondary to a sexual assault. The study was planned to include five increasing doses of MDMA, ranging from 50 to 150 mg, in 29 women. However, the study was prematurely terminated due to political pressure resulting in a very small group of six participants. Due to a small sample size, any statistical analysis comparing the two groups was not possible, allowing only for descriptive analysis. The study concluded that low doses of MDMA within the context of psychotherapy were found to be safe and the preliminary results have shown some promising signs of efficacy and reduced symptoms of PTSD.

A second RCT was reported in two separate papers (Mithoefer et al., 2011) with some interesting long-term effects reported from the follow-up data (Mithoefer et al., 2013). Participants were women, who were randomly allocated into the

MDMA-assisted therapy group (n = 12) or non-active placebo (n = 8). MDMA was administered on two separate sessions in two doses, 125mg and 62.5mg respectively. The results indicated a significant reduction in clinical symptoms of PTSD in the MDMA group, in comparison to the placebo group. This was assessed by an independent clinician, who was blind to treatment condition, using a standardised measure (Clinician-Administered PTSD Scale, CAPS, Blake et al., 1995). The clinical response rate in the MDMA group was 83%, in comparison to 25% in the placebo group. Furthermore, a long-term follow-up reported that the participants maintained treatment gains at up to six years post-treatment.

Finally, a RCT by Oehen et al. (2013) used a very similar design to the previous study but with an active placebo of the sub-therapeutic dose of MDMA (first dose: 25mg, second dose: 12.5mg). There were three MDMA sessions spread across the treatment period. There were eight participants, both male and female, in the MDMA group and four participants in the active placebo group. This study reported a lack of significant reduction in clinically rated CAPS scores (Blake et al., 1995) in the higher dose group compared to the active placebo group, but a significant reduction in a self-report measure of The Posttraumatic Diagnostic Scale (PDS; Foa, Cashman, Jaycox, & Perry, 1997). The follow-up data a year later showed further improvement on the CAPS scores in the MDMA group.

Across all RCTs, where MDMA was administered in a clinical setting, it was found to be safe for participants. Participants' heart rates and temperatures were measured regularly throughout the sessions to ensure safety. There were no drug-related serious adverse events reported in any of the clinical studies.

Overall Methodological Critique. The RCTs described above present strengths such as a prospective double-blind design, the use of standardised outcome measures,

and clearly defined inclusion and exclusion criteria. The majority of the participants were MDMA-naïve. This allowed for unique comparisons in terms of the drug effects. This kind of comparison is not usually observed in studies on recreational MDMA users.

Furthermore, the use of a blinded, independent evaluator in all studies and well-matched baseline scores on the PTSD measure in two studies (Mithoefer et al., 2011; Oehen et al., 2013) were also indisputable strengths of these innovative trials.

The studies also have several limitations and although they provide promising results they should be interpreted very cautiously and only be considered as a preliminary step in the exploration of MDMA as an adjunct to psychotherapy for PTSD. Firstly, the studies had very small sample sizes and the majority of participants were female. Although small samples are relatively common in pilot studies, they are often unable to detect smaller effect sizes, which seemed likely among severe cases of prolonged and treatment-resistant PTSD.

Secondly, the lack of active control groups in two trials, as well as the lack of assessment of the treatment fidelity in all trials, are the two major concerns with regards to the quality of the trials. Although, the studies provided information on therapists' backgrounds and details on treatment protocols, there was no mentioning in the reports whether the therapists received regular supervision.

Another significant weakness of the studies is the issue of transparency of the blinding to participants and therapists. It is quite likely that due to very strong and unique effects induced by MDMA, participants and therapists were no longer unaware of the group to which they had been assigned.

Discussion

The aim of this review was to summarise and critically acclaim the existing evidence on emotional and pro-social effects of MDMA on humans, focusing on two types of the setting of the drug use; recreational and therapeutic.

The RCTs using recreational users provided robust evidence that MDMA increases positive emotions while diminishing negative emotions. However, the evidence with regards to the ability to recognise negative emotions in others is mixed. All studies showed that the ability to recognise angry faces was impaired, with some also supporting the idea that identification of sadness and fear was also impaired (e.g. Hysek, Schmid, et al., 2014; Hysek, Simmler, et al., 2014). The discrepancies between the studies might be due to the differences in study designs, in particular, the use of different tests measuring facial recognition across studies.

The evidence from one pseudo-experimental study (Yip & Lee, 2006) and one naturalistic study (Hoshi et al., 2004) provided some contradicting results. Yip and Lee (2006), revealed a long-term emotion recognition impairment in abstinent ecstasy users. However, due to methodological weaknesses in the design of this study described earlier the results should be interpreted very cautiously. Hoshi et al. (2004), found that 'ecstasy' users were better at correctly identifying fearful facial expressions while under the influence of the drug but this effect diminished four days later.

The contradicting evidence from naturalistic and pseudo-experimental studies might be possibly explained by the design weaknesses, in particular, the lack of control over the purity and dose of the drug consumed by the participants. Therefore, this evidence should be considered very carefully. There is also some preliminary evidence that MDMA may increase the emotional value of positive memories at the

same time as diminishing the negative value of most disliked memories (Hysek et al., 2012). The studies have shown that MDMA increases sociability and pro-social behaviour by increasing the value of social interactions and intimacy with others. Similarly, MDMA increases emotional empathy, whereas the relationship between cognitive empathy and MDMA remains unclear. Hysek and Schmid, et al.'s 2014 finding of gender differences in cognitive empathy and ability to recognise negative emotions in others was interesting as it suggested women might be more susceptible to the effects of MDMA compared to men. Gender differences in the effects of MDMA have been previously reported, for example, women were found to experience more acute subjective effects (Liechti, Gamma, & Vollenweider, 2001) as well as more negative long-term effects than men (Ogeil, Rajaratnam, & Broadbear, 2013).

Alongside the two other naturalistic trials (Hoshi et al., 2004; Stewart et al., 2014), Kamboj et al.'s 2015 finding that increased self-compassion and reduced self-criticism following MDMA use was further enhanced following a compassionate imaginary exercise provided a unique perspective on the potentially confounding variables that have not been addressed in the studies so far. None of the studies addressed the role of participants' motivation and expectations of the drug on the effects reported by the participants, which was reported previously to have a significant impact on drug experiences (Zinberg, 1994). It is likely that the effects of the drug reported in a research laboratory will be somehow different to the effects of the drug reported in a recreational setting or a therapeutic setting. A study by Kirkpatrick and de Wit (2015) revealed that the social context, for example, the presence of another person under the influence of the drug, reinforces some of the

effects of MDMA. This appears to be a significant methodological omission in the majority of the studies reported in the literature to date.

With regards to emotional intelligence in the 'ecstasy' users, the results of two correlational studies are inconclusive (Craig et al., 2010; Reay et al., 2006). The lack of clarity on this matter might be related to the poor control over the potential confounding variables related to the poly-drug use among recreational users.

Finally, the three RCTs investigating the use of MDMA as an adjunct to psychotherapy revealed very promising results in treating treatment-resistant PTSD. This suggests that MDMA used in a therapeutic setting with the support of an experienced therapist might facilitate the emotional process, enabling participants to process traumatic material in a safer way. More importantly, the effects of the MDMA-assisted therapy seemed to have been long-lasting, with a low rate of relapse. Although, the results are very encouraging, the small sample sizes in these pilot studies limit the generalizability of the findings as well as the statistical analysis.

There are certain limitations of this review that have to be highlighted at this point. It was outside of the control of the author to thoroughly search for the grey literature, therefore the review did not provide sufficient measures to control for a publication bias increasing the chances of reporting results, which were statistically significant. Similarly, the search strategy was limited to articles published in English and the studies included in the review mostly relied on an English-speaking white male population. These characteristics limit the generalizability of the findings to a more diverse population.

Implications for Research and Practice

This review highlights the need for longitudinal studies, in order to control for a range of confounding variables, in particular, the polydrug use among participants.

The evidence from RCTs in the laboratory conditions is lacking ecological validity, therefore, the future studies should take into account the wider context of the MDMA experience. It is particularly important to think about the set and setting of the drug use as defined by Zinberg's model (Zinberg, 1994) and the relationship between those factors. In particular, how they can mediate the effects of MDMA on emotional processes.

Secondly, this review highlights the issue of purity of the drug investigated in the studies. Future naturalistic studies should consider controlling for purity and doses of the drug consumed by participants. It is also important to separate the findings related to chemically pure MDMA often used in clinical trials and laboratory studies, from studies addressing the street drug 'ecstasy' containing up to several other active substances (Cole et al., 2002; Vogels et al., 2009). Future studies should also focus on investigating if there are psychological differences in the effects between pure MDMA and drugs sold as 'ecstasy'.

Thirdly, there is a great need to investigate gender differences in the effects of MDMA or 'ecstasy'. This review revealed significant disproportions in gender ratio. The recreational context of the drug use is mostly represented by male participants, whereas, the studies addressing the therapeutic use of MDMA mostly relied on female participants. It is of a great importance to address the gender imbalance in future studies.

Since the preliminary studies investigating safety and efficacy of MDMA-assisted psychotherapy brought promising results, future trials are warranted. The upcoming studies should use larger sample sizes and address the issue of transparency of blinding to participants and therapists, by using an active placebo group. Although, one study did use a low dose of MDMA deemed not high enough to be potentially

therapeutic as an active placebo, it was found to cause some uncomfortable side effects on a small number of participants. Therefore, it would be better to use a substance that has somehow similar effects on participants but with minimal side effects.

Although the treatment model of MDMA-assisted therapy is still at its infancy and poses significant clinical and ethical dilemmas associated with its legal status and our limited understanding of its potential neurotoxic effects, there are certain advances it can bring to the find of clinical psychology. The potential use of MDMA in a controlled clinical setting provides an interesting avenue for developing a new psychotherapy approach to trauma and PTSD. This is particularly relevant for understanding neurological basis for treatment of trauma survivors. The use of MDMA alongside more traditional therapy models might alter the way therapy is delivered and potentially minimise engagement difficulties and facilitate development of the therapeutic alliance, as a catalyst of the therapeutic process (Adamson & Metzner, 1988). The preliminary studies are indicative of MDMA shifting an emphasis in treatment from cognitive processes to more emotionally loaded and experiential processes, where therapists are less active in their roles as MDMA experience unfolds (Danforth, Struble, Yazar-Klosinski, & Grob, 2016).

The traditional CBT model of trauma work assumes that the anxiety response and cognitive appraisal can be adapted through re-processing of traumatic memories (Ehlers & Clark, 2000). However, this process is often hindered by intolerable levels of anxiety and avoidance, which often results in high levels of treatment dropouts (Kar, 2011). MDMA-assisted therapy might be perceived by patients as a less threatening form of treatment due to its unique effects, which allow the client to feel

safe yet at the same time enabling connection with difficult feelings associated with trauma, as a result, aiding the processing of traumatic memories (Sessa & Nutt, 2015).

Conclusions

In conclusion, there have been a number of advances in the literature exploring the effects of MDMA on emotions and pro-social behaviour over the past decade. With regards to recreational use, there is robust early evidence that MDMA alters emotional process by increasing positive and diminishing negative emotions. Due to some contradicting results, it is unclear, however, how MDMA affects the ability to recognise emotions in others.

The studies to date also provided evidence that MDMA affects sociability and pro-social behaviours by elevating the value of social interactions and intimacy with others. MDMA was found to increase emotional empathy, whereas the relationship between cognitive empathy and emotional intelligence, and MDMA remains unclear. There is also some preliminary evidence that MDMA might increase self-compassion and help reduce self-criticism.

Regarding the use of MDMA in a therapeutic capacity, the preliminary studies provide some compelling evidence that the drug might be successful in treating treatment-resistant PTSD. Methodological issues have impacted the potential for interpretation and generalizability of findings, and further research addressing both recreational and therapeutic use of MDMA is warranted.

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Major Research Project

Section B: Empirical Paper

Psychological effects of MDMA: the function of the drug, set and setting.

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Abstract

Zinberg's Interaction Model implies that the content of a drug-induced experience is a function of the pharmacological properties of the drug, the set (the user's characteristics e.g. motivation and personality), and the setting (the physical and social context). The current research investigated the function of the set and setting and their role in shaping the psychological effects of 3,4-methylenedioxmethamphetamine (MDMA), as well as their role in reducing the risk of drug abuse.

An online survey was distributed among adult MDMA polydrug users (n = 158) and MDMA-naïve controls (alcohol, nicotine and cannabis users, n = 138). Participants answered questions regarding their pattern of drug use, their motivation for MDMA use and the setting (e.g. clubbing, home with friends), as well as the subjective effects of MDMA. Participants also completed a range of self-report measures of self-reflection and insight, emotional intelligence, and personality, as well as a drug dependency measure.

MDMA users displayed higher levels of self-reflection and insight, openness to new experience and lower levels of neuroticism and conscientiousness, in comparison to non-MDMA users. The significant predictors of self-reflection and insight were openness, emotional intelligence, MDMA use, extraversion and neuroticism. When the analysis was rerun only for the MDMA group, the significant predictors of self-reflection and insight were openness, emotional intelligence and self-insight effects of MDMA. High levels of self-reported negative effects of MDMA were predictors of a problematic drug use.

These findings suggest that there might be a relationship between MDMA use and higher levels of self-reflection and insight; however, longitudinal studies are required

to further investigate the causality of this relationship. The results add to existing evidence that MDMA has potential for altering emotional experiences.

Key words: MDMA (Ecstasy), psychological effects, personality, emotional intelligence, insight

Introduction

3,4-methylenedioxmethamphetamine (MDMA) is a popular recreational psychoactive drug, often referred to as a 'club drug', with unique psychological effects on humans (Holland, 2001). Population-based studies continue to provide evidence of high rates of MDMA use among young people around the world (Barratt, Ferris, & Winstock, 2014; Morgan, Noronha, Muetzelfeldt, Fielding, & Curran, 2013).

MDMA is commonly called 'ecstasy' (Holland, 2001); however, research shows variation in the MDMA content of ecstasy tablets, and the presence of other adulterants (Cole, Bailey, Sumnall, Wagstaff, & King, 2002; Doblin et al., 2014; A. C. Parrott, 2004). Little is known about the association between the composition of ecstasy tablets, and the effects experienced by drug users.

Brunt, Koeter, Niesink, and van den Brink (2012) reported findings that ecstasy tablets with higher MDMA content showed stronger association with desirable subjective effects. However, due to difficulty determining the non-MDMA additions and adulterants in ecstasy tablets, it has not been possible to confidently attribute findings of such studies directly to MDMA.

Psychological effects of MDMA can enhance emotional bonding with others, as well as reducing anxiety and improving social interactions and emotional regulation (Johansen & Krebs, 2009). Frye, Wardle, Norman & de Wit (2014) reported that taking MDMA reduces social exclusion phenomena. Similarly, MDMA enhanced levels of shared empathy and pro-social behaviour in comparison to placebo (Hysek, Schmid, et al., 2014). Participants given MDMA were also found to be more likely to use words relating to friendship, support and intimacy, and compassion (Baggott, Kirkpatrick, Bedi, & de Wit, 2015; Bedi et al., 2014).

However, MDMA might also be associated with negative effects such as low mood, which is likely to be associated with serotonin depletion, lasting several days after consumption (Parrott, 2002). Furthermore, MDMA can be neurotoxic which raise concerns that MDMA use may lead to adverse effects on executive functions; in particular, verbal memory (eg. Hoshi, Bisla, & Valerie Curran, 2004) and decision-making (eg. Hanson, Luciana, 2004). On the contrary, other studies report a lack of adverse effects on these areas (Back-Madruga et al., 2003; Gouzoulis-Mayfrank et al., 2000).

Although there has been a recent increase in the number of studies investigating the effects of MDMA (Amoroso, 2015; Bedi, Hyman, & de Wit, 2010), the literature on factors altering the effects of MDMA remains limited. The current research aimed to investigate the function of the set and setting introduced by Zinberg (1994), their role in shaping the psychological effects of MDMA, and their function in reducing the risk of the drug abuse. The model implies that the content of a drug-induced experience is a function of the pharmacological properties of the drug, e.g. its dose and presence of adulterants; the set, defined as the user's characteristics e.g. one's motivation and personality, and the setting, defined as the physical and social context in which intoxication occurs (Zinberg, 1994). Elements of the set and setting concerning MDMA use are described in more depth in the following sections.

Set

In context of discussing individual characteristics relevant to MDMA use, the set is defined as a range of factors which may contribute to individual differences in the effects of MDMA (Zinberg, 1994). Individual qualities such as motivation for drug use (Sumnall, Cole, & Jerome, 2006), personality traits and emotional

intelligence have been identified as one of the most prominent elements of the set (Shewan, Dalgarno, & Reith, 2000; Shewan & Dalgarno, 2005).

Openness to experience (McCrae & Costa, 2004) was found to be associated with novelty seeking behaviour and attentiveness to inner feelings, whereas extraversion (McCrae & Costa, 2004) was found to be related to sociability and tendency to seek stimulation in the company of others. There is considerable evidence that high novelty seekers are at increased risk of abusing drugs in comparison to low novelty seekers (Bardo, Donohew, & Harrington, 1996).

Research on personality characteristics of MDMA users is limited. Only one study to date has investigated personality profiles of MDMA users; ter Bogt, Engels & Dubas (2006) linked MDMA use in a club setting to higher levels of extraversion and lower levels of conscientiousness. Taking into account the previous result, it seems plausible that, in comparison to the general population, MDMA users might be more likely to present a higher level of extraversion and openness to experience.

Similarly, MDMA users might be likely to become more attentive to their inner feelings in response to deceased levels of anxiety and defensiveness as a result of the drug use (Greer & Tolbert, 1986). This in turn might lead to emotional insight, as has previously been observed in qualitative accounts of MDMA users (Greer & Tolbert, 1986; Liester, Grob, Bravo, & Walsh, 1992). However, not all users report emotional insight as a result of MDMA use (Greer & Tolbert, 1998), which suggest that this particular effect might be associated with the individual's set', for example motivation for drug use to gain self-insight, emotional intelligence, and personality. Different reasons for MDMA use were associated with alterations in the type and degree of subjective effects of MDMA. For example, individuals taking MDMA to socialise reported significantly greater pro-social effects (Sumnall et al., 2006).

However, no previous studies have examined the relationship between personal qualities and motivation for drug use, and psychological effects of MDMA. Therefore, this study investigated the role of motivation for drug use in shaping the effects of MDMA. Specifically, this study examined whether being motivated to use MDMA by the desire to gain self-insight is associated with higher levels of self-reflection and insight.

Furthermore, research suggests that higher levels of emotional intelligence are significantly associated with users taking ecstasy-related precautions such as monitoring drug and fluid intakes, or taking breaks from dancing (Craig, Fisk, Montgomery, Murphy, & Wareing, 2010). Higher levels of emotional intelligence have also been associated with decreased levels of the adverse effects of MDMA (Craig et al., 2010). Therefore, the current study also explored relationships between emotional intelligence, motivation for drug use, the psychological effects of MDMA and the setting in which intoxication occurs. Taking into account previous evidence in the literature, it is likely that higher levels of emotional intelligence will be associated with lower levels of adverse effects of MDMA and higher levels of positive effects. The following section elaborates further on the concept of setting in terms of the social context of the drug experience.

Setting

Research investigating the effects of MDMA suggests that the drug can be used safely as a therapeutic tool alongside traditional psychotherapy for treatment-resistant PTSD (Mithoefer et al., 2013; Oehen, Traber, Widmer, & Schnyder, 2013). However, it can also become a drug of abuse in other environments such as dance clubs (Leung, Ben Abdallah, Copeland, & Cottler, 2010). The above implies the role of set and setting in shaping the effects of MDMA. The use of the drug in social

settings is very common and many users claim that they take MDMA predominantly to experience its pro-social effects (Sumnall et al., 2006). It has been shown that many other drugs, such as alcohol, are experienced as more pleasurable when the consumption occurs in a social context (Kirkpatrick & de Wit, 2015). A recent study (Kirkpatrick & de Wit, 2015) indicated that the pro-social effects of MDMA can also be reinforced by the presence of other people.

Previous research revealed that some people typically use MDMA outside of a club setting in order to gain self-insight and to overcome relationship or emotional difficulties (Almeida & Silva, 2003; Boeri, Sterk, & Elifson, 2004; Liester et al., 1992; Solowij, Hall, & Lee, 1992).

Risk of MDMA abuse

Finally, the study also investigated the risk factors of MDMA abuse. A study by Shewan et al., (2000) indicated that risk reduction coping strategies such as planning, preparation and monitoring of the drug effects, and use of social support networks among MDMA users were associated with participants' awareness of these risks, and of the set and setting. This in turn was associated with reduced risk of adverse effects of the drug. Furthermore, hedonistic motivation to drug use, e.g. taking the drug for fun or pleasure was associated with increased risk of drug abuse (Shewan et al., 2000). This study investigated potential predictors of problematic use of MDMA, taking into account all elements of the set and setting.

Aims and Rationale

Changes observed in emotional processing of social information under the influence of MDMA might underlie its possible psychotherapeutic benefits (Metzner & Adamson, 2001). Further investigation of such mechanisms could inform treatment design of MDMA-assisted psychotherapy.

Therefore, it seems paramount to further investigate possible differences in the effects of the drug depending on the set, namely the motivation and personality traits and the setting in which people take drugs. Investigating the setting of MDMA use is particularly important in order to gain better knowledge of the applicability of MDMA as therapeutic agent in psychotherapy.

Gaining a better understanding of different elements of the set and setting influencing MDMA effects might improve effectiveness of MDMA-assisted psychotherapy. Furthermore, there might be some scope to use the findings to inform a risk-reduction initiative among MDMA users and provide a better understanding of the risk factors among health professionals. In particular, the role of personality traits as well as emotional intelligence in shaping drug taking behaviours was examined. This is the first quantitative study to explore the relationship between personality, emotional intelligence, and self-reflection and insight, in the context of MDMA use.

Research Questions

This research addressed the below research question and hypotheses:

1. Which personality traits are associated with MDMA use? It is hypothesized that MDMA group will present higher levels of openness to experience and extraversion, than the comparison group.

2. Do elements of the set influence the psychological effects of MDMA (i.e. insight, self-reflection)? It is hypothesized that the use of MDMA for self-reflection will be significantly associated with higher levels of insight and self-reflection.

3. Does emotional intelligence affect the levels of positive and negative effects of MDMA? It is hypothesized that higher levels of Emotional Intelligence will be associated with more positive effects and less adverse effects of MDMA.

4. Does setting of MDMA use (e.g. home environment or dance setting) influence the effects of MDMA?

5. Is there a relationship between the setting of MDMA use (e.g. home environment or dance setting) and different motives for MDMA use?

6. What elements of the set and setting are associated with a reduction of risk of drug abuse?

Methods

Participants

The study used a between-group cross-sectional design. All participants were English-speaking and aged 18-65. MDMA-users were recruited from drug-related forums such as Erowid, Bluelight, and drug-related social groups on Facebook. Participants from the comparison group were recruited from non-drug related social groups and websites. Participants were not offered any incentive to take part in the study. A total of 604 participants took part in the study, of which 293 dropped out before completion. Of the remaining 311, 15 cases were excluded from the analysis due to a high percentage (45-65%) of their data missing.

The remaining 296 participants were assigned to one of the two groups based on their self-reported history of drug use: the MDMA group (n = 158), or the comparison group (MDMA-naïve participants, n = 138). Participants who had used MDMA or ecstasy at least once in the past 12 months, and at least three times in their

lifetime, were assigned to the MDMA group. Participants who had no previous experience of using MDMA or any other drugs apart from alcohol, nicotine, or marijuana were allocated to the comparison group.

The inclusion criteria (described above) were very generic to capture a wide variety of drug users. Many studies targeted participants who were abusing the drug, therefore arriving at a non-representative sample of MDMA users. Based on Cohen's guidelines (1992), with alpha-level of .05 and the recommended power of .8, the sample size of each group was large enough to detect a medium effect size r = .3.

Materials

The University of East London drug use questionnaire (UEL drug use questionnaire, Parrott, Sisk, & Turner, 2000). The questionnaire collects information about details of participants' own and their immediate family's psychiatric history as well as drug use history. MDMA users are also required to provide further information concerning patterns of their drug use: the duration of MDMA use; the last time taken.

The Motives Questionnaire (ter Bogt & Engels, 2005), measures motives for MDMA and includes 28 items concerning energy, euphoria, and self-insight (Enhancement Motives), sociability/flirtatiousness and sexiness (Social Motives), coping (Coping Motive), and conformism (Conformism Motive). All items have the form of "I take MDMA because/to/for…'' and had the format of five-point Likert scales (1 'definitely not,' 5 'definitely so'). The scale demonstrated good internal validity: .66 (ter Bogt & Engels, 2005).

Perceived Positive and Negative Effects Scales (ter Bogt & Engels, 2005). Positive effects of MDMA were measured with a subset of 24 items assessing the energising, mood enhancing, and entactogenic effects of MDMA users' experiences. Examples of

items are ‘euphoria, feel absolutely great, open, sensitive’. The scale demonstrated good internal validity: .91. Negative effects were measured with a subset of 11 negative psychological and physical effects. The scale demonstrated good internal validity .85 (ter Bogt & Engels, 2005).

The Self- Reflection and Insight Scale (SRIS; Grant, Franklin, & Langford, 2002). SRIS is a questionnaire asking subjects to rate the extent to which they agree or disagree with 20 statements on a five-point Likert-type scale. The test consists of three subscales: recognition of the need for reflection, the process of engaging in reflection and the presence of insight. The scale demonstrated good test-retest reliability .77 - .78, and construct validity: .87 - .91 (Grant et al., 2002).

The NEO Five-Factor Inventory (NEO-FFI, McCrae & Costa, 2004). NEO-FFI measures five basic personality factors: neuroticism, agreeableness, conscientiousness, extraversion and openness. The instrument uses a five-point Likert response format. Two-week retest reliability is uniformly high, ranging from .86 to .90 for the five scales (and internal consistency ranges from .68 to .86).

The Severity of Dependence Scale (SDS; Martin, Copeland, Gates, & Gilmour, 2006). SDS is a five-item scale measuring the degree of psychological dependence experienced by drug users. The statements are specifically related to impaired control, preoccupation and anxieties about drug use. The validity of the scale on different samples was between .81-.9, test-retest reliability .88 (Gossop et al., 1995).

The Trait Emotional Intelligence Questionnaire-Short Form (TEIQ-SF; Cooper & Petrides, 2010). TEIQ-SF consists of 30 items measuring global trait emotional intelligence (e.g., “I usually find it difficult to regulate my emotions”; “I’m usually able to influence the way other people feel”). The scale demonstrated good construct validity: between .83-.93, test-retest reliability .76 (Cooper & Petrides, 2010).

Procedure

Ethical approval was received from University Ethics Committee (see Appendix 3). Participants were provided with information about the purpose of the research before they decided to take part in the study. They were told that they could withdraw at any point of completing the survey. It was identified that participants could have experienced negative effects, discomfort or distress while participating in the survey, in particular when answering questions about the potential negative effects of the drug. In order to minimise any discomfort, participants were automatically redirected to a website ("Drugs Meter," n.d.), where they could find reliable information on drug harm reduction and how to access support if they recognised their drug use being problematic. They were also advised to contact their GP if they felt they needed some advice regarding their drug use. Also, the participants were encouraged to contact the researcher for any queries, thoughts or feedback with regards to the study.

An online survey containing all the above questionnaires was created and distributed among the MDMA users and controls. The data collection was carried out between March and September 2015. Participants were asked to answer questions regarding their pattern of MDMA and other drug use, set and setting of MDMA use, history of psychiatric illnesses, and the positive and negative effects. They also completed a range of psychological measures. On average, the participants spent 40 minutes competing the survey.

Results

Data Analysis

The analysis was conducted using IBM SPSS version 22. Parametric assumptions were checked before analysis. A normal distribution was assessed using

the Shapiro-Wilk test, box plots, skewness and kurtosis. Non-parametric tests were used for variables which did not meet the criteria for parametric analysis.

Missing Values Analysis has been applied to analyse the pattern of the missing data. In order to account for the data that has been randomly missing, multiple imputation procedure has been implemented. Chi^{2-}test and, in cases where chi^2-test's assumptions were violated, Fisher's exact test, were used to compare group differences in categorical socio-demographic variables and history of mental health illness. Independent samples t-test as well as Mann-Whitney u-test, in cases of not normally distributed variables, were used to compare group differences in age and all the psychological measures. Pearson's correlation coefficient was used to assess the relationships between different elements of the set and setting. Hierarchical multiple regression analysis was carried out to check for predictors of self-reflection and insight as well as the risk of drug dependence.

Cronbach's alpha was used to assess internal consistency of all scales and subscales of the questionnaires (Gliem & Gliem, 2003). As presented in Table 5 in Appendix 2, all questionnaires showed good levels of internal consistency.

Descriptive Statistics

Socio-demographic variables. Descriptive statistics concerning all demographic variables are presented in Table 1. Mann-Whitney u-test for age, and chi-square test for the remaining variables, were used to assess whether the groups differed on any of the demographic characteristics.

There were significant group differences in gender, with females representing 70% of the comparison group, and only 42% of the MDMA group, c^2 (1, N = 296) = 23.18, p < .001. Similarly, the control group had a higher percentage of participants in a relationship (70%, MDMA group = 57%), c^2 (1, N = 295) = 5.32, p = .021, as well

as some form of employment, c^2 (4, N = 296) = 18.89, p = .001. However, the MDMA group had greater numbers of students (22%, comparison group = 12%), which was reflected in the differences in the levels of education, where the same percentage of participants in the MDMA group had some years of college but no degree, c^2 (5, N = 296) = 20.15, p = .001.

There were no significant group differences in sexual orientation, c^2 (2, N = 295) = 4.96, p = .084, and age, p = .26 (SPSS version 22 does not report test statistics for Mann-Whitney u-test, therefore only p value is reported). However, histograms presented in Appendix 2, illustrated some important group differences. The most numerous subgroup in the MDMA group were young people in their early twenties, most likely accounting for the student population, whereas the comparison group was represented by young adults in their late twenties. These might account for the differences in education levels, employment status and the relationship status.

Table 1

Group comparison: demographic variables

	MDMA Group			Comparison group			Total		
	n	**M**	**(SD)**	**n**	**M**	**(SD)**	**n**	**M**	**(SD)**
Age (years)	158	29.80	(9.816)	138	29.66	(7.695)	296	29.73	(8.878)
	MDMA Group			**Comparison group**			**Total**		
	n	**%**		**n**	**%**		**n**	**%**	
Gender									
Male	91	57.6%		41	29.7%		132	44.6%	
Female	67	42.4%		97	70.3%		164	55.4%	
Total	158	100%		138	100%		296	100%	
Relationship status									
Single	67	42.7%		41	29.7%		108	36.6%	
In a relationship	90	57.3%		97	70.3%		187	63.4%	
Total	157	100%		138	100%		295	100%	
Sexual orientation									
Heterosexual	123	77.8%		120	87.6%		243	82.4%	
Gay or lesbian	8	5.1%		3	2.2%		11	3.7%	
Bisexual	27	17.1%		14	10.2%		41	13.9%	
Total	158	100%		137	100%		295	100%	
Employment									
Employed for wages	69	43.7%		93	67.4%		162	54.7%	
Self-employed	29	18.4%		11	8.0%		40	13.5%	
Looking for work	14	8.9%		8	5.8%		22	7.4%	
Not looking for work	10	6.3%		9	6.5%		19	6.4%	
A student	36	22.8%		17	12.3%		53	17.9%	
Total	158	100%		138	100%		296	100%	
Education									
High school or less	21	13.3%		7	5.1%		28	9.5%	
Some years of college, no degree	36	22.8%		19	13.8%		55	18.6%	
Bachelor's degree	59	56.7%		45	32.6%		104	35.1%	
Master's degree	28	17.7%		50	36.2%		78	26.4%	
Professional degree	8	5.1%		7	5.1%		15	5.1%	
Doctorate degree	6	3.8%		10	7.2%		16	5.4%	
Total	158	100%		138	100%		296	100%	

Mental Health and Substance Use. Chi2-test and, in cases where chi2-test assumptions were violated, Fisher's exact test, were used to assess group differences in history of mental health illness. Table 2 shows that there were no significant group differences in the prevalence of mental health illness, such as anxiety disorders, depression and obsessive-compulsive disorder (OCD), schizophrenia and addiction. Only 2% of the MDMA group received treatment for addiction to substances, in contrast with none in the comparison group. Similarly, the numbers of alcohol and tobacco users did not differ between the groups. However, the MDMA group had significantly higher numbers of cannabis users than the comparison group, 59% and 32%, respectively, c2 (1, N = 290) = 20.57, p < .001.

In terms of the MDMA use, less than 4% of participants from the MDMA group displayed some levels of MDMA dependence. The vast majority were classified as non-problematic drug users based on the Severity of Dependence Scale cut-off score of five and above being indicative of a problematic drug use (Topp & Mattick, 1997). See Table 8 in Appendix 2 for more details.

Table 3 presents the drug use profile in the MDMA group. The majority of the sample were light (up to 10 times in a life time, 36%) to moderate users (up to 40 times in a life time, 28%). Other frequently used drugs were cannabis, ecstasy, magic mushrooms, LSD and cocaine. Apart from cannabis, in which the vast majority of those who used it reported heavy use, the other commonly used drugs were categorised as having light to moderate use.

Table 2

Mental health history, alcohol, cannabis and tobacco: group differences

	MDMA Group n %	Comparison group n %	Total n %	Chi^2 test/ Fisher's Exact Test*	df	sig.
MDMA Dependence						
Yes	6 3.8%	-	6 3.8%	-	-	-
No	144 91.1%	-	144 91.1%			
Treatment for: Addiction						
Yes	4 2.7%	0 0%	4 1.4%	-*	-	0.124
No	146 97.3%	136 100%	282 98.6%			
Anxiety						
Yes	21 13.7%	22 16.2%	43 14.9%	0.342	1	0.621
No	132 86.3%	114 83.8%	246 85.1%			
Depression						
Yes	38 24.7%	34 24.8%	72 24.7%	0.001	1	1.000
No	116 75.3%	103 35.4%	219 75.3%			
OCD						
Yes	4 2.7%	1 0.7%	5 1.7%	-*	-	.374
No	146 97.3%	135 99.3%	281 98.3%			
Schizophrenia						
Yes	3 2%	0 0%	3 1%	-*	-	.249
No	147 98%	136 100%	283 99%			
Drink Alcohol						
Yes	129 82.7%	108 78.3%	237 80.6%	0.920	1	0.376
No	27 17.3%	30 21.7%	57 19.4%			
Smoke Cannabis						
Yes	90 59.2%	45 32.6	135 46.6%	20.572	1	0.000
	62 40.8%	93 67.4	155 53.4%			
Smoke Tobacco						
Yes	64 40.8%	42 30.4%	106 35.9%	3.404	1	0.069
No	93 59.2%	96 69.6%	189 64.1%			

Table 3

Drug use profile

	None		Light 1-10 x		Moderate 11-40x		Heavy 41-100x		Very heavy >100x	
Drug	n	%	n	%	n	%	n	%	n	%
MDMA	11	7%	57	36.1%	44	27.9%	35	22.1%	11	7%
Ecstasy	36	22.8%	44	27.8%	42	26.5%	21	13.3%	15	9.5%
Amphetamine	65	41.1%	44	27.8%	28	17.7%	8	5.1%	13	8.2%
Mephedrone	108	68.4%	36	22.8%	10	6.3%	2	1.3%	2	1.3%
Cocaine	47	29.7%	57	36.1%	32	20.3%	12	7.6%	10	6.3%
Crack	142	89.9%	15	9.5%	1	0.6%	-	-	-	-
LSD	44	27.8%	62	39.5%	32	20.3%	10	6.3%	10	6.3%
DMT	93	58.9%	49	31%	10	6.3%	6	3.8%	-	-
Cannabis	12	7.6%	4	2.5%	19	12%	24	15.2%	99	62.7%
Barbiturates	148	93.7%	5	3.2%	5	3.2%	-	-	-	-
Benzodiazepines	72	45.6%	45	28.5%	22	13.9%	9	5.7%	10	6.3%
Opiates	125	79.1%	20	12.7%	7	4.4%	2	1.3%	4	2.5%
Magic Mushrooms	35	22.2%	74	46.8%	38	24.1%	6	3.8%	5	3.2%
Steroids	156	98.7%	2	1.3%	-	-	-	-	-	-
Solvents	142	89.9%	8	5.1%	6	3.8%	1	0.6%	1	0.6%
Poppers	95	60.1%	38	24.1%	16	10.1%	6	3.8%	3	1.9%
Ketamine	82	51.9%	48	30.4%	19	12%	4	2.5%	5	3.2%
Prozac	144	91.1%	4	2.5%	3	1.9%	2	1.3%	5	3.2%
Viagra	136	86.1%	16	10.1%	3	1.9%	1	0.6%	2	1.3%
GHB	130	82.3%	22	13.9%	4	2.5%	2	1.3%	-	-
Legal Highs:										
Synthetic cannabis	119	75.3%	31	19.6%	6	3.8%	-	-	2	1.3%
pills	136	86.1%	16	10.1%	3	1.9%	1	0.6%	2	1.3%
others	134	84.8%	17	10.8%	4	2.5%	2	1.3%	1	0.6%

Inferential statistics

Set: Personality Traits. It has been hypothesised that MDMA users will be presenting with higher levels of openness to experience and extraversion than the comparison group. This hypothesis was tested using independent sample t-test (see Table 4). Due to running a series of independent t-tests, the Bonferroni correction was applied and α level was adjusted to .0045 (Field, 2009).

The MDMA group has shown higher levels of openness to experience than the control group, t (26991003) = 6.782, $p < .001$, $d = .79$; but did not differ with regards to the levels of extraversion. Additionally, independent t-test revealed that the MDMA group presented lower levels of neuroticism, t (51444913) = -2.99, $p = .003$, $d = -.347$; and conscientiousness t (34897668) = -3.09, $p = .002$, $d = -.36$, in comparison to the controls. There were no group differences in agreeableness.

Table 4

Psychological measures: groups comparison.

		N	Mean	SD	t-test	df	sig.	Cohen's d
SRIS_FULL_SCALE	MDMA	158	80.07	9.171	4.782	35751749	**.000**	**.555**
	Control	138	74.87	9.568				
Engaging in Self Reflection	MDMA	158	25.55	3.846	4.196	2626678	**.000**	**.486**
	Control	138	23.52	4.482				
Need for Self Reflection	MDMA	158	25.85	3.703	4.875	17851609	**.000**	**.606**
	Control	138	23.61	4.226				
Insight	MDMA	158	28.67	4.886	1.663	33919052	.096	
	Control	138	27.75	4.568				
TEIQ Emotional Intelligence	MDMA	158	151.87	25.088	1.808	19715479	.071	
	Control	138	146.57	25.398		73		
NEO FFI Full Scale	MDMA	158	145.35	13.024	.043	18499771	.965	
	Control	138	145.28	14.346				
NEO FFI Neuroticism	MDMA	158	21.76	10.407	-2.996	51444913	**.003**	**-.347**
	Control	138	25.34	10.211				
NEO FFI Extraversion	MDMA	158	28.45	6.590	1.925	26721827.	.054	
	Control	138	26.79	8.058		965		
NEO FFI Openness	MDMA	158	36.35	5.481	6.782	26991003	**.000**	**.786**
	Control	138	31.77	6.156				
NEO FFI Agreeableness	MDMA	158	31.16	5.639	.231	370958	.817	
	Control	138	31.01	6.203				
NEO FFI Conscientiousness	MDMA	158	27.63	7.476	-3.087	34897668	**.002**	**-.357**
	Control	138	30.37	7.828				

Self-reflection and insight. An independent sample t-test was used to check for group differences in self-reflection and insight (full scale). As presented in Table 4, the MDMA group showed higher levels of the overall self-reflection and insight, than the comparison group, t (35751749) = 4.78, p < .000. However, when the individual subscales were analysed, engagement in self-reflection and need for self-reflection remained significant but the groups did not differ on the insight subscale.

It has been hypothesised that the use of MDMA for self-reflection will be significantly associated with higher levels of insight and self-reflection among MDMA users. This hypothesis was tested using Pearson's correlation coefficient. There were significant positive correlations between self-insight motive for MDMA use and self-reflection and insight scale, r (156) = .37, p < .05. There was also a significant negative correlation between conformism motive and self reflection and insight scale, r (156) = .27, p < .001, and insight subscale, r (156) = .31, p < .001 (see Table 5 for more details).

The results suggest that MDMA users who declared using MDMA for gaining self-insight generally displayed higher levels of self-reflection and insight. On the contrary, participants who used MDMA due to conformity (i.e. peer pressure), presented with lower levels of self-reflection and insight.

Table 5

Pearson's correlation coefficients: motives for MDMA use and self-reflection and insight

	Euph.	Self - insight	Soc.	Sex	Coping	Conform	SRIS	Eng. in S.R.	Need For S.R.	Insight
Energy	.453**	-.164*	.141	.094	.228*	.229*	-.070	.026	-.017	-.169*
Euphoria		.077	.203*	.116	.196*	.083	-.042	-.025	-.092	.009
Self-insight			.262*	.175*	.061	-.241*	.365*	.258*	.301*	.245*
Sociability				.677**	.263**	.049	.077	.129	.117	-.045
Sexiness					.196*	.032	.107	.112	.064	.062
Coping						.270**	-.115	.033	.004	-.240*
Conformism							-.269**	-.119	-.120	-.314**
SRIS								.846**	.823**	.561**
Eng. In S.R.									.844**	.096
Need for S.R.										.055

**. Correlation is significant at the 0.01 level (2-tailed)

*. Correlation is significant at the 0.05 level (2-tailed)

Emotional intelligence. It was hypothesised that higher levels of emotional intelligence will be associated with more positive effects and less adverse effects of MDMA. Pearson's correlation coefficient was used to test this hypothesis. The higher the levels of emotional intelligence, the higher the levels of self-insight, $r(157) = .17$, $p < .05$, and sexiness effects of MDMA use, $r(157) = .20$, $p < .05$ (Table 6). The

strength of the relationship was low. There was no significant correlation between the negative effects of MDMA and emotional intelligence.

Table 6

Pearson's correlation coefficients: effects of MDMA and emotional intelligence

	EI	SDS	Neg.	Mood	En.	Danc.	Self-ins.	Comm.	Sex
EI									
SDS	-.265**								
Negative	-.127	.458**							
Mood	.090	-.015	.006						
Energy	.055	.085	.083	.534**					
Dancing	.072	.023	.112	.326**	.554**				
Self-Insight	.165*	-.142	-.016	.264**	.246**	.050			
Communication	.059	-.088	.030	.471**	.463**	.283**	.505**		
Sexiness	.200*	-.133	.067	.374**	.358**	.343**	.246*	.327**	
Openness	.099	.028	.025	.497**	.458**	.337**	.513**	.571**	.351**

**. Correlation is significant at the 0.01 level (2-tailed)

*. Correlation is significant at the 0.05 level (2-tailed)

Setting and effects of MDMA. For the purpose of this analysis, the four categories of the setting of the MDMA use were collapsed into two categories: home setting (including 'home with friends or partner' and home alone), and dance setting (including club setting and music festival setting).

An explorative analysis has been carried out to check whether the setting of MDMA use can influence the effects of MDMA. Pearson's correlation coefficient was used to detect relationships between different variables of set and setting. There have been significant positive correlations between dance setting and energy and

euphoria effect, r (155) = .23, p = .003 as well as dancing effect, r (155) = .39, p < .001. Suggesting that those participants who used MDMA in a dance setting were experiencing stronger energy and euphoria effects of MDMA.

Home setting was positively correlated with emotional intelligence, r (155) = .17, p = .030, and conscientiousness, r (155) = .23, p = .005, and negatively correlated with dancing effect, r (155) = -.36, p < .001. Participants who declared using MDMA in a home setting reported weaker dancing effects, and presented with higher levels of emotional intelligence and conscientiousness.

Setting and motives for MDMA use. Pearson's correlation coefficient has been used to check whether there was a relationship between the setting of MDMA use and the motives. There were significant positive correlations between dance setting and energy motive, r (156) = .37, p < .001, and euphoria motive, r (156) = .24, p = .002; and a significant negative correlation with self-insight motive, r (155) = -.16, p = .045. Home setting was significantly and positively associated with self-insight motive, r (156) = .21, p = .010, and negatively associated with energy motive, r (156) = -.33, p < .001. The strengths of the relationships were low to moderate. The results suggest that among those whose motivation to use MDMA was to experience dancing and energy and euphoria were more likely to use MDMA in a dance setting. Conversely, participants whose motivation was to experience self-insight were more likely to use MDMA in a home setting.

Risk of Drug Abuse. An explorative analysis was carried out to investigate which elements of the set and setting may be associated with risk of drug abuse. Firstly, Pearson's correlation coefficient was used. There were significant positive relationships between MDMA severity of dependence scale (SDS) and negative effects of MDMA, r (154) = .46, p < .001, conformism motive, r (154) = .16, p =

.048, and neuroticism, r (156) = .29, p < .001. There were negative relationships between SDS and emotional intelligence, r (155) = -.27, p = .001, and conscientiousness, r (156) = -.25, p = .002. All the significant correlations were of moderate effect size or below.

Secondly, a hierarchical multiple regression analysis was carried out to find out the predictors of SDS. The hierarchical multiple regression was chosen to test the effects of certain predictors (Tabachnick & Fidell, 2001), specifically negative effects of MDMA.

The sample size of 158 was large enough for seven independent variables to be included in the analysis (Tabachnick & Fidell, 2001). The assumptions of linearity and homoscedasticity were checked using residual and scatter plots. The assumption of singularity was met and Pearson's correlations coefficients revealed the lack of perfect multicollinearity. The assumptions of independent errors were tested with the Durbin-Watson test.

The variables were entered into the model in three steps. The first step included: emotional intelligence, conscientiousness, neuroticism and conformism motive. In the second step, negative effects of MDMA was added to the existing model. In the third step, age and gender were added to the model. Table 7 presents the regression statistics. The model in step 1 explained almost 12% of the variance in SDS; R^2 = .115, adjusted R^2 = .088, F (4, 131) = 4.24, p = .003. Adding negative effects of MDMA to the model in step two explained additional 19% of the SDS variance and this change in R^2 was significant F (1, 130) = 34.50, p < .001. In step three, age and gender were added but the model did not improve the ability to predict the SDS, R^2 change = .003, F (2, 128) = .29, p = .744. Negative effects of MDMA was the only significant predictor of severity of dependence from MDMA.

Table 7

Hierarchical regression: severity of dependence and self-reflection and insight

Severity of Dependence Scale (SDS)					Self-Reflection and Insight (Both groups)					Self-Reflection and Insight (MDMA group)			
	B	SE B	β	Sig.		B	SE B	β	Sig.	B	SE B	β	Sig.
Step 1					Step 1								
Emotional intelligence	-.001	.008	-.019	.892	Openness	.630	6.435	.412	.000	.491	.122	.301	.000
Conscientiousness	-.026	.019	-.132	.162	Emotional Intelligence	.187	.081	.489	.000	.211	.047	.583	.000
Neuroticism	.029	.020	.198	.149	Agreeableness	.005	.095	.003	.959	-	-	-	-
Conformism Motive	.075	.054	.118	.168	Neuroticism	.146	.076	.157	.056	.200	.099	.229	.046
Step 2					Extraversion	-.170	.090	-.132	.060	-.013	.130	-.010	.919
Emotional intelligence	-.008	.007	-.137	.282	Step 2								
Conscientiousness	-.024	.017	-.121	.152	Openness	.539	.087	.352	.000	.393	.122	.241	.002
Neuroticism	.003	.018	.024	.848	Emotional Intelligence	.198	.035	.518	.000	.189	.046	.521	.000
Conformism Motive	.031	.049	.048	.528	Agreeableness	.040	.095	.025	.675	-	-	-	-
Negative effects	4.151	.707	.450	.000	Neuroticism	.179	.076	.193	.020	.162	.097	.185	.097
Step 3					Extraversion	-.208	.090	-.160	.022	-.012	.126	-.009	-.924
Emotional intelligence	-.009	.008	-.155	.239	MDMA use/self-insight effects*	2.808	1.072	.147	.009	2.756*	.858*	.236*	.002*
Conscientiousness	-.025	.017	-.126	.143	Step 3								
Neuroticism	.001	.019	.005	.967	Openness	.534	.088	.349	.000	.393	.123	.240	.001
Conformism Motive	.030	.049	.048	.537	Emotional Intelligence	.199	.036	.519	.000	.187	.047	517	.000
Negative effects	4.213	.729	.457	.000	Agreeableness	.050	.096	.031	.606	-	-	-	-
Age	.007	.012	.044	.573	Neuroticism	.151	.080	.164	.058	.143	.103	.163	.171
Gender	.122	.227	.042	.591	Extraversion	-.226	.091	-.175	.013	-.024	.128	-.018	.849
					MDMA use/self-insight effects*	2.933	1.090	.154	.008	2.789	.868	.238	.002*
					Age	-.084	.056	-.080	.131	-.031	.066	-.034	.635
					Gender	.565	1.027	.030	.583	.521	1.277	.030	.684

Additional Analysis

Predictors of self-reflection and insight. The results revealed higher levels of the overall self-reflection and insight among the MDMA group, in contrast with the comparison group. Therefore, further analysis was carried out to investigate whether the use of MDMA, as well as emotional intelligence and personality traits, were associated with higher levels of self-reflection and insight.

Firstly, Pearson's correlation coefficient was used to determine the strengths of the relationships between the variables. Secondly, a hierarchical multiple regression analysis was carried out to identify the predictors of SRIS.

Analysis identified significant positive relationships between SRIS and openness, r (156) = .49, $p < .001$, emotional intelligence, $r = .38$, $p < .001$, MDMA use, r (156) = .27, $p < .001$, and agreeableness, r (156) = .22, $p < .001$, and extraversion r (156) = .12, $p = .045$; and a negative relationship between SRIS and neuroticism, r (156) = -.21, $p < .001$.

A hierarchical multiple regression was chosen in order to control for the effects of certain predictors (Tabachnick & Fidell, 2001), specifically MDMA use. Prior to conducting the analysis, all relevant assumptions were tested as discussed in the previous section (Field, 2009).

The variables were entered into the model in three steps. The first step included: openness, emotional intelligence, agreeableness, neuroticism and extraversion. In the second step, MDMA use was added to the existing model. In the third step, age and gender were added to the model. Table 7 presents the regression statistics.

The analysis revealed that the model in step 1 explained 33.5% of the variance in SRIS; $R^2 = .335$, adjusted $R^2 = .322$, F (5, 256) = 25.75, $p < .001$. Adding MDMA

use to the model in step two explained an additional 2% of the SRIS variance and this change in R^2 was significant F (1, 255) = 6.87, p = .009. When all eight variables were added to the model in step three, age and gender were not significant predictors of SRIS and the model in step three did not improve the ability to predict the SRIS, R^2 change = .007, F (2, 253) = 1.34, p = .265. The significant predictors of SRIS were openness, emotional intelligence, MDMA use, extraversion and neuroticism. Together all five predictors accounted for 35% of the variance in SRIS; R^2 = .35, adjusted R^2 = .34, F (6, 255) = 23.09, p < .001.

Predictors of self-reflection and insight among MDMA users. A further hierarchical regression analysis has been carried out to find out which elements of the set and setting were predictors of self-reflection and insight among MDMA users only.

The variables were entered into the model in three steps. The first step included: openness, emotional intelligence, neuroticism and extraversion. In the second step, self-insight effects was added to the existing model. In the third step, age and gender were added to the model. See table 7 for the regression statistics.

The analysis revealed that the model in step 1 explained almost 32% of the variance in SRIS; R^2 = .32, adjusted R^2 = .30, F (4, 133) = 15.38, p < .001. Adding self-insight effects to the model in step two explained an additional 5% of the SRIS variance and this change in R^2 was significant F (1, 132) = 10.31, p = .002. Similarly to the previous analysis, age and gender were not significant predictors of SRIS and the model in step three did not improve the ability to predict the SRIS, R^2 change = .002, F (2, 130) = .202, p = .817. The significant predictors of SRIS among MDMA users were openness, emotional intelligence and self-insight effects of MDMA.

Together, all predictors accounted for 36.6% of the variance in SRIS; $R^2 = .37$, adjusted $R^2 = .33$, $F\ (5, 132) = 15.38$, $p < .001$.

Discussion

Set

The aim of the study was to explore the role of the set and setting in shaping the psychological effects of MDMA, as well as their function in reducing the risk of drug abuse. MDMA users presented higher levels of openness to experience and lower levels of neuroticism, and conscientiousness, in comparison to the controls. However, there were no group differences in extraversion and agreeableness. These results were partially in line with a study by ter Bogt et al. (2006), where MDMA users reported lower levels of conscientiousness but higher levels of extraversion. However, this study was completed on a specific sample of MDMA users who were visitors of a rave party, which may be at least partially responsible for the differences reported by the studies.

MDMA users reported higher levels of engagement in self-reflection and need for self-reflection but the groups did not differ on the levels of insight. Furthermore, the results indicated participants who reported the use of MDMA to obtain self-reflection and insight displayed greater ability to self-reflect and insightfulness. However, participants who stated the use of MDMA due to conformity (i.e. peer pressure) reported lower levels of self-reflection and insight.

The study did not support the hypothesis that higher levels of emotional intelligence might be associated with lower levels of the negative effects of MDMA. However, the results indicated that participants with higher levels of emotional intelligence are more likely to experience self-insight and sexiness effects of MDMA.

The result of lower levels of neuroticism among MDMA users was unexpected as there were no previous results that would suggest those differences. Neuroticism reflects distress proneness and tendencies toward the experience of negative affects. It has been documented that women score higher on the traits of neuroticism and agreeableness in comparison to men (Costa Jr., Terracciano, & McCrae, 2001). It is possible that the differences reported in this study might be due to gender differences between the groups, with the majority of the comparison group being women.

Setting

In terms of the setting of MDMA use, some differences were observed in MDMA effects and personality qualities, depending on the environment in which participants used the drug. Dance settings (i.e. clubs or music festivals) were associated with higher levels of energy and euphoria, as well as reported effects of MDMA on participant's dance subscale score on the Perceived Positive Effects Scale (ter Bogt & Engels, 2005). Taking MDMA in a home setting was associated with lower levels of the dancing effects of MDMA.

There was also a weak but significant positive correlation between home environment and emotional intelligence and conscientiousness. This suggests that the dance setting might be reinforcing certain effects of MDMA, in this case, the effects associated with dancing, energy and euphoria. Whereas people with certain personal qualities such as higher levels of emotional intelligence and conscientiousness might be preferring more a intimate setting for MDMA use, such as a home environment. These findings are supported by a previous study by Sumnall, Cole, & Jerome, (2006), which also reported that subjective MDMA experience might be influenced by the elements of the setting.

Self-Reflection and Insight

Higher levels of self-reflection and insight were associated with higher levels of openness, emotional intelligence and MDMA use, agreeableness and extraversion, as well as with lower levels of neuroticism. Among those variables, the significant predictors of SRIS were openness, emotional intelligence, MDMA use, extraversion and neuroticism. When the analysis was rerun only for the MDMA group, the significant predictors of SRIS were openness, emotional intelligence and self-insight effects of MDMA. These findings suggest that there is a relationship between MDMA use and higher levels of self-reflection and insight. It is likely that MDMA may increase self-reflection and insightfulness, however, due to the cross-sectional nature of this study it is impossible to imply a direction of this relationship. The results are in line with several qualitative studies which suggested that MDMA use led to increased self-insight (e.g. Adamson & Metzner, 1988; Greer & Tolbert, 1986). At this point, it is important to acknowledge the role of other individual factors, in particular, personality traits and emotional intelligence, which might facilitate the process of psychological insight into one's emotional state.

Problematic Use

Regarding the factors associated with the risk of developing a problematic use of MDMA, in this study, higher levels of negative effects of MDMA and neuroticism, as well as the use of MDMA due to conformity, were associated with increased levels of drug dependence. These results contradict findings from a previous study by Scott, Hides, Allen, & Lubman (2013) where coping motives, but not conformity motives, were associated with heavier ecstasy use.

Higher levels of emotional intelligence and conscientiousness were associated with lower levels of drug abuse. Among all those variables, only negative effects of

MDMA were identified as a significant predictor of the drug dependence syndrome. This might suggest that higher levels of reported negative effects of MDMA could be a significant indicator of problematic drug use, which may lead to a development of a drug dependence syndrome.

MDMA users did not exhibit increased levels of addiction than the comparison group. In fact, less than 3% of the MDMA group received treatment for addiction to some form of psychoactive substance. Similarly, the numbers of alcohol and tobacco users did not differ between the groups. However, the MDMA group had significantly greater numbers of cannabis users than the comparison group. Cannabis was also the most frequently used drug among MDMA users.

The vast majority of the MDMA users were classified as non-problematic MDMA users and less than 4% displayed some symptoms of MDMA dependence. The majority of the sample were light-to-moderate MDMA users. These findings indicated that the self-reported use of MDMA among this group of users put them in a relatively low risk category with regards to developing a dependence syndrome (Degenhardt, Bruno, & Topp, 2010). As identified in previous studies, the majority of MDMA users appeared to decrease or stop using MDMA as part of a natural trajectory (Smirnov et al., 2013; Verheyden, Henry, & Curran, 2003). However, these results have to be interpreted cautiously since the study included only self-report measures of drug dependency.

Mental Health

This study revealed the lack of differences between the MDMA users and non-MDMA users in the self-reported prevalence of mental health illness, such as anxiety disorders, depression, obsessive-compulsive disorder, and schizophrenia. Using standardised measures to assess current mental health among participants was

outside the remit of this study. However, there are a number of studies indicating increased levels of mental health problems among users, in particular among heavier MDMA polydrug users (e.g. Milani, 2011; Singer, Linare, Ntiri, Henry, & Minnes, 2004; Soar, Turner, & Parrott, 2006; Turner et al., 2014). It is conceivable that the lack of observed group differences in the prevalence of mental health could be due to heterogeneity among MDMA users on wider factors associated with mental health. As pointed out by Soar et al. (2006) it is likely that socio-economic variables, as well as pre-existing mental health problems, are factors which need to be taken into account when interpreting the results. Since almost all MDMA users are polydrug users, it is not possible to isolate the effects of MDMA on mental health. Several studies indicated that mental health difficulties found in MDMA polydrug users were associated with other drug use such as alcohol, marijuana, opioids, and inhalants (e.g. Daumann et al., 2004; Falck, Wang, Carlson, & Siegal, 2006; Medina & Shear, 2007).

Methodological Considerations

There are a number of limitations to the current study. Firstly, the cross-sectional design does not allow determination of causality, and limits possible conclusions about the direction of the relationships between analysed variables (Tabachnick & Fidell, 2001).

The comparison groups were significantly disproportional in gender, relationship status and education. While the sampling method did not allow for these to be controlled for in the design of the study, statistically controlling within the analysis enabled some degree of confidence that these variables did not significantly account for the results. However, lack of standardised measures of mental health problems means it was not possible to assess group differences in experiences of mental health. These variables therefore could potentially have confounded the

results, meaning conclusions of this study have to be interpreted cautiously. Issues with the ecological validity of self-report measures of substance use, in absence of validation through biological analysis, need to be taken into account when interpreting the findings.

As discussed by many other studies involving polydrug users, work in this area is affected by methodological constraints. Due to the illegal status of MDMA and the lack of regulations of the content and the purity of the substances sold on the streets for recreational use, it is difficult to assess whether the participants actually used MDMA or some other chemically related substances available on the market. Therefore, it has not been possible, either in previous cross-sectional research or the current study, to confidently relate the findings from a sample of polydrug users to one particular drug (Gouzoulis-Mayfrank & Daumann, 2006). It is also difficult to assess the dose and collect an overall drug use history when relying on self-report measures as the only source of data.

Despite the limitations described above, the study also posses some strengths. Firstly, this study used a large sample size and managed to recruit a diverse population of MDMA users. Secondly, the study was the first one to address the role of personal qualities and motivation in shaping the effects of MDMA, allowing a more comprehensive account of the effects of MDMA to emerge.

Clinical Implications

The unique psychological effects of MDMA reported by this study might have certain clinical implications for treatment of trauma survivors. Although there are successful models of treatment for PTSD such as cognitive-behavioural therapy (CBT) and eye-movement desensitization and reprocessing (EMDR; Cukor, Spitalnick, Difede, Rizzo, & Rothbaum, 2009; Kar, 2011), a review of the treatment

literature indicated that these therapies have relatively large dropout and nonresponse rates (Schottenbauer, Glass, Arnkoff, Tendick, & Gray, 2008). Due to high prevalence rates of PTSD (Dorrington et al., 2014), there is a need for a more successful and acceptable treatment for this condition. Preliminary results of the MDMA-assisted therapy for PTSD provide some tentative evidence that MDMA might be a safe and acceptable treatment for PTSD, and provided rationale for further randomised controlled trials to test its efficacy (e.g. Chabrol, 2013; Oehen et al., 2013).

This study supported the hypothesis that the effects of MDMA differ with regards to set and setting of use providing some overarching explanations to both recreational and therapeutic uses. The results might suggest that the therapeutic effects of MDMA reported in the literature (Amoroso, 2015) might be associated with certain elements of the setting such as the presence of a couple of therapists in the room as well as client's attitude to treatment and personality. These elements should be taken into consideration in clinical trials of MDMA-assisted psychotherapy, which have recently gained momentum (Mithoefer et al., 2013; Mithoefer, Wagner, Mithoefer, Jerome, & Doblin, 2011; Oehen et al., 2013). The finding that openness to experience, extraversion as well as emotional intelligence, and the individual's motivation to experience insight might be associated with increased levels of self-reflection and insight, might in turn be useful in developing effective therapeutic interventions employing MDMA.

Regarding the problematic use of MDMA, this study identified that high levels of negative effects of MDMA might be a strong predictor of a development of a dependence syndrome. This information might be used by substance misuse programmes aimed at increasing awareness of drug use among young people, as well

as for drug and mental health workers supporting people who might be at risk of developing a problematic pattern of drug use.

Future Research

In order to address the methodological issues identified above, there is a need for longitudinal and prospective research designs. This could lead to a better understanding of the relationships between MDMA use and their psychological effects. Most importantly, it would provide more reliable evidence for the interactions between the various substances of abuse.

Future research investigating the set and setting of MDMA use should focus more on a wider range of factors influencing the drug-induced experience. Due to the complexity of the model, it is particularly important to investigate the interactions between different variables.

Since this study provided some preliminary evidence that MDMA use is associated with increased insight and self-reflection, it is important to investigate this further, which may be best facilitated by a prospective research design to provide more robust data, to further contribute to understanding of whether MDMA can actually facilitate psychological insight. More importantly, future studies should take into account a range of settings of MDMA use, alongside personal predispositions. Further research should also focus more precisely on the risk factors associated with the abuse of MDMA. It is likely that the risk of drug abuse is associated with socio-economic status and therefore future research studies should aim to recruit a more heterogeneous sample of MDMA users than the current study.

Conclusion

This study adds to the existing literature supporting the relationship between various elements of the set and setting of MDMA use. It has provided preliminary explorations of the role of personality traits and emotional intelligence as well as motivation for drug use in shaping the effects of MDMA. The study also tentatively indicates that use of MDMA might be associated with some positive psychological outcomes, such as self-reflection and insight. At this stage, it is not possible to draw any definite conclusions, or to determine causality, however, it is important to consider a multifactorial model of interactions between a wide range of variables involving the set and setting of MDMA use. The results are consistent with the theory that MDMA has a potential for altering emotional experiences. Further research utilising a prospective design is warranted.

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SECTION C: Appendices

Appendix 1. Summaries of the studies included in the review

Table 1

Summaries of RCT trials: Psychological Effects of MDMA in Recreational Users.

Authors/ Year	Sample details	Drugs administered	Study Design	Key Findings
Baggott, Kirkpatrick, Bedi, & de Wit (2015)	35 adults (66% male), with light-to-moderate 'ecstasy' experience, age: 18–35. USA	MDMA1.5 mg/kg or placebo	Two-session, within-subjects, randomised double-blind study. Participants completed a five-minute standardized talking task during which they discussed a personal relationship e.g. a friend or a family member.	- MDMA increased use of social and sexual words, as well as words relating to both positive and negative emotions.
Bedi, Hyman, & de Wit (2010)	21 adults (57% male) with previous 'ecstasy' experience, age: 18-3	MDMA 0.75 mg/kg , 1.5 mg/kg methamphetamine 20 mg,	double-blind, within-subjects randomized conditions four sessions: participants received MDMA methamphetamine and placebo.	MDMA increased 'empathogenic' feelings, but accurate identification of threat-related signals in others was reduced.

	USA	placebo	- self-report ratings of relevant affective states, and identified emotions from images of faces, pictures of eyes, and vocal cues.	
Bedi, Phan, Angstadt, & de Wit (2009)	nine adults (78% male) age: 18-29 with previous 'ecstasy' experience USA	MDMA 0.75 mg/kg, 1.5 mg/kg, placebo	three-session, within-participants, randomised double-blind design. Participants underwent fMRI[1] while viewing standardized images depicting emotional facial expressions and completed self-report measures of sociability.	MDMA increased self-reported sociability, and diminished responses to threatening stimuli but not to fearful facial expression. MDMA enhanced responses to rewarding social signals.
Carhart-Harris et al. (2013)	19 adults (74% male) with previous MDMA experience. UK	100mg of MDMA-HCl, placebo	two-session, within-participants, double-blind, randomised, placebo-controlled design. Participants underwent fMRI[1] while they were probed to recall favourite and worst autobiographical memories.	MDMA increased self-reported ratings of favourite memories as significantly more vivid, emotionally intense and positive. MDMA diminished the negative self-rating of worst memories.

Frye, Wardle, Norman, & de Wit (2014)	36 adults (18 female), age: 18-35 with light to moderate drug use. USA	MDMA 0.75 mg/kg, 1.5 mg/kg, placebo	three-session, randomised within-participants, double-blind design. Participants took part in a virtual social simulation task called "Cyberball" in which they experienced acceptance and rejection. Participants complete self-report measures of mood and self-esteem.	MDMA decreased perceptions of rejection in a simulated social situation.
Hysek, Domes, & Liechti (2012)	48 adults (24 male) with limited or no previous experience of MDMA use. Age: 18-44 Switzerland	MDMA 125mg, placebo	Two-session, randomised double-blind, placebo-controlled, within-subjects design. Participants completed self-reported measures of mood and subjective effects, and completed a task involved identification of complex emotions based on the eye region of faces.	MDMA enhanced identification of mental state decoding for positive emotions, impaired mind reading for negative emotions and had no effect on mind reading for neutral stimuli (e.g., reflective).
Hysek, Schmid, et al. (2014)	32 adults (16 male) with limited or no previous experience of MDMA use. Age: 20-31.	MDMA 125mg, placebo	Two-session, randomised double-blind, placebo-controlled, cross-over design. Participants completed self-reported measures of mood and subjective effects, empathy,	- MDMA increased explicit and implicit emotional empathy and pro-social behaviour in men. - MDMA did not increase cognitive empathy

	Switzerland		social behaviour measure, as well as completed tasks assessing cognitive and emotional aspects of empathy and facial emotion recognition.	in women. - MDMA reduced the ability to identify negative emotions, including fear, anger and sadness, particularly in women.
Hysek, Simmler, et al. (2014)	16 adults (8 male) with limited or no previous experience of MDMA use. Age: M^3=24.8, SD^4=2.6 Switzerland	1. Placebo + placebo, 2. Ritalin 60mg + placebo, 3. Placebo + MDMA 125mg, 4. Ritalin 60mg + MDMA 125mg	Four-session, randomised double-blind, placebo-controlled, crossover design. Participants completed self-reported measures of mood and subjective effects, and completed facial emotion recognition task.	- MDMA increased positive mood more than Ritalin. - Ritalin improved the recognition of sad and fearful faces while MDMA reduced the recognition of negative emotions.
Kirkpatrick, Delton, Robertson, & de Wit (2015)	Study 2: 32 adults (23 male) aged 18–30, who had used MDMA 4–80 times in their lifetime. USA	MDMA 0.5 mg/kg, 1.0 mg/kg and placebo	Three-session, randomised double-blind, placebo-controlled, within-subjects design. Participants took part in a task measuring generosity where they make decisions about whether they or another person will receive money.	MDMA produces pro-social effects such as generosity, but these appear to depend on the social proximity of the relationships.

Kirkpatrick & de Wit, (2015)	32 adults (24 male) MDMA users, aged: 18-35 USA	1. MDMA 0.5 mg/kg 2. MDMA 1.0 mg/kg 3. placebo	Three-session, randomised double-blind, placebo-controlled, mixed within- and between-subjects design. Participants were randomly assigned to one of three conditions: 1. Solitary, 2. Research assistant present, 3. Other participant present. Participants completed subjective effects questionnaires and were video recorded to measure their social-interactions.	The social contact reinforces some of the effects of MDMA. MDMA increased social interactions and ratings of the attractiveness of another person in the room.
Kirkpatrick, Lee, Wardle, Jacob, & de Wit (2014)	65 adults (40 male) with light-to-moderate past MDMA experience, aged: 18-35 USA	1. Placebo + placebo, 2. Placebo + intranasal oxytocin 20 or 40 IU, 3. MDMA 0.75 mg/kg + Placebo 4. MDMA 1.5 mg/kg + placebo	Four-session, randomised double-blind, placebo-controlled, within-subjects design. Participants completed measures of emotion recognition and sociability and subjective effects.	MDMA impaired recognition of angry and fearful facial expressions, and the larger dose (1.5 mg/kg) increased desire to be with others, compared with placebo.

Kuypers et al. (2014)	20 adults (12 male) poly-drug MDMA users, aged between 18–26 years. Netherlands	(1) pindolol + MDMA 75mg + placebo; (2) placebo + MDMA 75mg + placebo (3) placebo + placebo + oxytocin (4) placebo + placebo + placebo.	Four-session, randomised double-blind, placebo-controlled, within-subjects design. Participants completed tests measuring cognitive and emotional empathy and social interaction, defined as trust and reciprocity.	MDMA selectively enhanced emotional empathy but did not increase cognitive empathy, trust and reciprocity.
Wardle, Kirkpatrick, & de Wit (2014)	101 adults (58 male) aged 18-35 with light-to-moderate past MDMA experience. USA	MDMA 0.75mg/kg, and 1.5 mg/kg, Placebo.	Data from two studies using similar within-subjects, double-blind randomised designs. Participants rated positive and negative responses to standardized positive, negative and neutral pictures with and without social content.	MDMA increased positive ratings of positive social pictures, but reduced positive ratings of non-social positive pictures. The pro-social effects of MDMA increase the value of social contact and closeness with others.

Table 2

Summaries of naturalistic studies: Psychological Effects of MDMA in Recreational Users

Authors/ Year	Sample details	Drugs administered	Study Design	Key Findings
Hoshi, Bisla, & Curran (2004)	16 'Ecstasy' users (10 male) and 21 controls-other drugs users (6 male), age: 20-32. UK	'Ecstasy' users took M =3.06, SD =1.12 ecstasy tablets on a day of drug use.	An independent group, repeated measures design was used to compare 'ecstasy' users and non-drug users at two points in time: at the time of drug use in a club and four days later. Participants completed measures of drug use, mood state, aggression, impulsivity and subjective effects of the drug, as well as a facial expression recognition task.	- 'Ecstasy' users were better at recognising fearful facial expressions than controls at the time of drug use but less accurate than controls on day four. - fear recognition on day four was negatively correlated with number of years of ecstasy use and number of ecstasy tablets taken on one occasion. - 'Ecstasy' users scored lower on aggression scale than controls on day 0 and higher on day 4.
Kamboj et al.	20 adults (7 men) with	MDMA taken	Two-session, naturalistic within-subjects	MDMA increased self-compassion and

(2015)	previous experience of MDMA use. Age: M= 25.50, SD= 3.59 UK	recreationally versus no drug. Dose and purity not determined.	design. Participants completed MDMA-related mood and symptoms measures, depression, attachment style and trait-self-criticism scales. Self-criticism and self-compassion scales were administered before and after ecstasy use and then after completing a guided compassionate imagery exercise.	reduced self-criticism Higher attachment-related avoidance was associated with additive effects of compassionate imagery and ecstasy on self-compassion.
Stewart et al. (2014)	39 adults: 17 ecstasy users (12 male, age M=22.76 SD=3.17), 22 controls – non users (9 male, age M=23.00 SD=5.28). UK	MDMA taken recreationally versus no drug. Dose and purity not determined.	An independent group, repeated measures design was used to compare 'ecstasy' users and non-drug users at two points in time: on the night of drug use and three days later. Participants rated the trustworthiness of 66 faces, carried out three co-operative behaviour tasks and completed mood self-ratings.	Ecstasy increased face trustworthiness and cooperative behaviour; on day 3 there were no group differences on any task. Trait empathy ratings were significantly higher in the ecstasy users
Yip & Lee (2006)	200 adults: 100 abstinent ecstasy users (50 male) and 100 matched non-users.	N/A	Pseudo-experimental, between-subject non-randomised design.	Abstinent Ecstasy users were impaired on overall emotion recognition, in particular recognition of sadness and disgust.

China

Table 3

Summaries of correlational studies: Psychological Effects of MDMA in Recreational Users

Authors/ Year	Sample details	Drugs administered	Study Design	Key Findings
Craig, Fisk, Montgomery, Murphy, & Wareing (2010)	78 MDMA/polydrug users (35 female), 38 cannabis only users (27 female), 34 non-drug users (28 female). UK	N/A	Retrospective correlational study, comparing MDMA polydrug users with cannabis users and non-users. Participants completed measures of drug use, EI[2], mood and parenting styles and IQ measures.	- 'Ecstasy'-polydrug users did not differ from non-users on EI. - Adverse mood effects associated with ecstasy use were significantly related to lower EI. - Higher EI was significantly associated with ecstasy-related precautions used when taking this drug.
Reay, Hamilton,	30 adults: 15 polydrug 'ecstasy' users (9 male,	N/A	Retrospective correlational study, comparing current ecstasy polydrug users,	MDMA polydrug users scored significantly worse on social awareness

Kennedy, & Scholey (2006)	age M=25 SD=5.8) and 15 polydrug non-ecstasy user controls (7 male, age M=21.3 SD=5.8) UK		with non-ecstasy plydrug-users. Participants completed s general drug use questionnaire, emotional intelligence scale, social intelligence scale.	and social skills subscales of social intelligence scale. MDMA can impair social and emotional processing.
ter Bogt, Engels, & Dubas (2006)	265 non-hard drug using adults; 541 MDMA-users, Aged: 18-27	N/A	Retrospective between participants correlational study. Participants completed a substance use questionnaire and personality traits measure assessing agreeableness, extraversion, conscientiousness, emotional stability, and openness.	MDMA-using party visitors reported higher levels of extraversion and both MDMA and non-MDMA-using partygoers showed less conscientiousness.

Table 4

Summaries of RCT trials: Psychological Effects of MDMA in a Therapeutic Setting.

Authors/ Year	Sample details	Drugs administered	Study Design	Key Findings
Bouso, Doblin, Farré, Alcázar, & Gómez-Jarabo (2008)	6 women with chronic and treatment resistant PTSD[5] secondary to a sexual assault, aged 29-49 with no previous experience with MDMA. Spain	MDMA 50 mg and 75mg, non-active placebo	a double-blind, between-subjects, randomized and placebo-controlled within each dose condition. Participants had three psychotherapy sessions with two therapists (a man and a woman) before the MDMA experimental session and three sessions after the MDMA session. Participants completed measures of PTSD, anxiety and depression pre-, post-therapy and at a follow-up.	MDMA administered as an adjunct to psychotherapy were found to be safe. There were promising signs of efficacy and reduced PTSD symptomatology.

Oehen, Traber, Widmer, & Schnyder (2013)	12 participants (10 females) with chronic and treatment resistant PTSD. Mean age = 41.4 Switzerland	MDMA 125 mg, plus 62.5 mg supplemental dose Active placebo MDMA low dose 25 mg, plus 12.5 mg supplemental dose	randomized, double-blind, between-subjects active-placebo controlled trial. Participants had three MDMA experimental sessions, combined with weekly non-drug psychotherapy sessions. Participants completed PTSD scales at baseline, three weeks after the second and third MDMA session, and at the 2-month and 1-year follow-ups.	There was no statistically significant reductions in clinician rated PTSD scores, but there was clinically and statistically significant self-reported improvement. Clinician rated scores improved at the 1-year follow-up. There were no drug-related serious adverse events.
Mithoefer, Wagner, Mithoefer, Jerome, & Doblin (2011) and Mithoefer et al. (2013)	20 adults (17 females) with chronic and treatment resistant PTSD[5] secondary to a sexual assault, mean age 40. USA	MDMA 125mg and optional supplementary dose of 62.5mg, non-active placebo.	a double-blind, between-subjects, randomized and placebo-controlled. Participants had two preparatory psychotherapy sessions and received two MDMA experimental sessions, and integrative follow-up non-drug psychotherapy in-between MDMA sessions. Participants completed measures of PTSD, anxiety and depression pre-, post-therapy and at a follow-up.	The rate of clinical response was 10/12 (83%) in the MDMA group in comparison to 2/8 (25%) in the placebo group. There were no drug-related serious adverse events. The gains were maintained by the large majority of the participants between 17 to 74 months after the original study. Only two participants relapsed.

Appendix 2. Additional data from the analysis

Table 5

Cronbach's Alpha levels of internal consistency

Self-Reflection and Insight Scale – Full SRIS	α .841
SRIS: Engaging in self-reflection	α .859
SRIS: Need for self-reflection	α .856
SRIS: Insight	α .702
Trait Emotional Intelligence Questionnaire-Short Form (TEIQ-SF)	α .914
The NEO Five-Factor Inventory (NEO-FFI) Full Scale	α .642
NEO-FFI: Neuroticism	α .908
NEO-FFI: Extraversion	α .820
NEO-FFI: Openness to Experience	α .744
NEO-FFI: Agreeableness	α .720
NEO-FFI: Conscientiousness	α .856
Substance Dependence Scale- Ecstasy (SDS)	α .760
SDS- MDMA	α .755
Negative Effects Scale	α .703
Positive Effects Scale (PES)	α .878
PES: Energy	α .878
PES: Euphoria	α .819
PES: Self-insight	α .977
PES: Sociability	α .886
PES: Sexiness	α .918
PES: Coping	α .846
PES: Conformism	α .751

Table 6

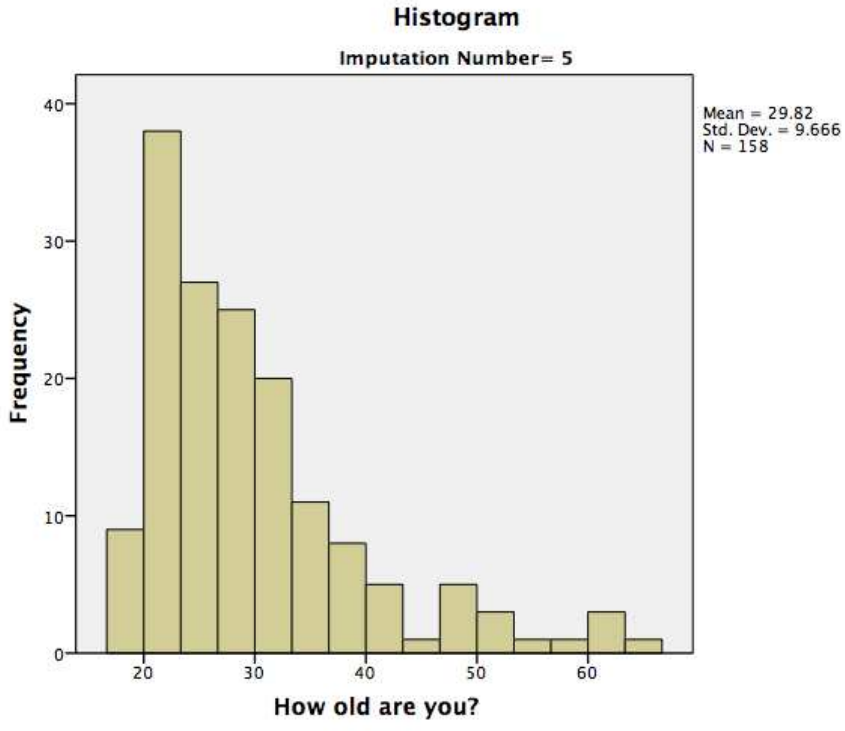
Demographic variables

Relationship status			
Single	64 40.8%	40 29.8%	104 35.3%
In a relationship	66 42%	56 40.6%	122 41.4%
Engaged	5 3.2%	8 5.8%	13 4.4%
Married	10 6.4%	28 20.3%	38 12.9%
Widowed	1 0.6%	0 0%	1 0.3%
Divorced	2 1.3%	1 0.7%	3 1%
Civil union	4 1.3%	0 0%	4 1.4%
Domestic partnership	5 3.2%	5 3.6%	10 3.4%
Total	157 100%	138 100%	295 100%
Employment			
Employed for wages	69 43.7%	93 67.4%	162 54.7%
Self-employed	29 18.4%	11 8.0%	40 13.5%
Looking for work	14 8.9%	8 5.8%	22 7.4%
Not looking for work	5 3.2%	4 2.9%	9 3.0%
A homemaker	2 1.3%	3 2.2%	5 1.7%
A student	36 22.8%	17 12.3%	53 17.9%
Retired	2 1.3%	2 1.4%	4 1.4%
Unable to work	1 0.6%	0 0%	1 0.3%
Total	158 100%	138 100%	296 100%

	6 3.8%	1 0.3%	7 2.4%
	15 9.5%	6 4.3%	21 7.1%
	36 22.8%	19 13.7%	55 18.6%
	5 3.2%	1 0.7%	6 2.0%
	54 34.2%	44 31.9%	98 33.1%
	28 17.7%	50 36.2%	78 26.4%
	8 5.1%	7 5.1%	15 5.1%
	6 3.8%	10 7.2%	16 5.4%
	158 100%	138 100%	296 100%

Histograms: Age

MDMA Group



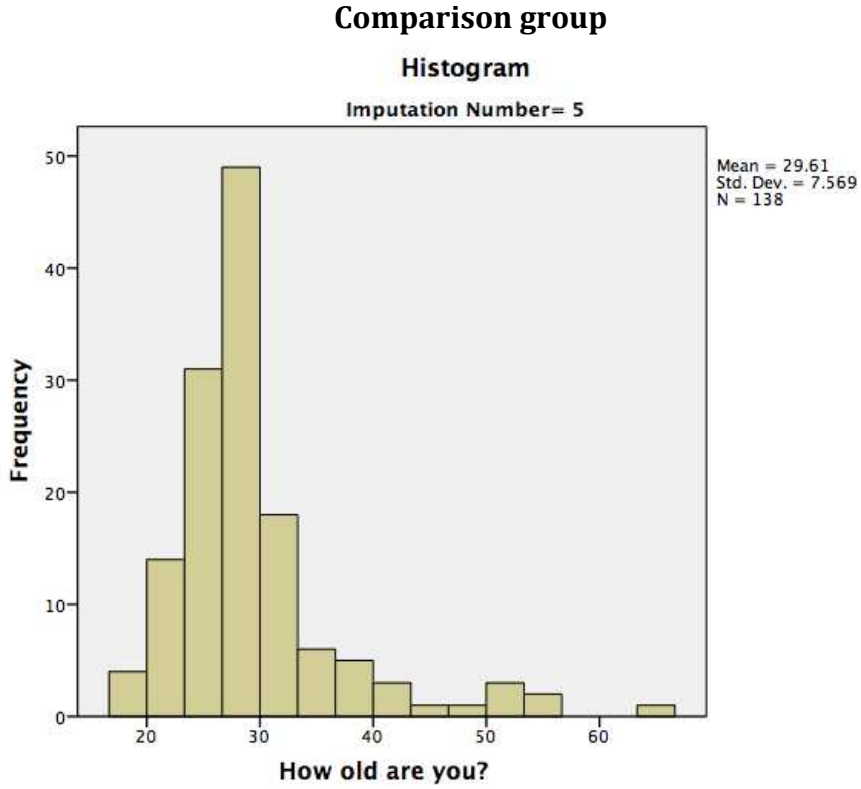


Table 7

The setting of MDMA use

The setting of MDMA use	n	M	SD
At home with friends/partner	157	33.23	29.960
At home on my own	157	3.55	11.191
Clubbing	158	31.46	27.643
Music festival	157	18.99	21.599
Psychotherapy session	158	0.82	6.178
Other	158	4.21	14.140

Table 8

Substance Dependence Scale: scores

SDS MDMA Score			Frequency	Percent	Valid Percent	Cumulative Percent
Original data	Valid	.00	100	63.3	66.7	66.7
		1.00	27	17.1	18.0	84.7
		2.00	10	6.3	6.7	91.3
		3.00	5	3.2	3.3	94.7
		4.00	2	1.3	1.3	96.0
		5.00	3	1.9	2.0	98.0
		6.00	2	1.3	1.3	99.3
		11.00	1	.6	.7	100.0
		Total	150	94.9	100.0	
	Missing	System	8	5.1		
	Total		158	100.0		

Appendix 3. Ethics Materials

Research Review Panel Approval Letter

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Ethics Panel Approval Letter

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Participants Information Sheet and Consent form

Psychological effects of MDMA (3,4-methylenedioxmethamphetamine): the function of the drug, set and setting.

Hi, my name is Monika Wieliczko and I am a trainee clinical psychologist at Canterbury Christ Church University in the UK. I am conducting research investigating a range of psychological and social factors that might influence the effects of MDMA on humans.

Before you decide to take part in this study, it is important for you to understand why the research is being done and what it would involve. Please take time to read the following information carefully.

Background

The broad aim of this project is to look at factors influencing drug experience, including individual and social aspects. The study focuses on both positive and negative psychological effects resulting from MDMA as well as risk reduction factors among polydrug users. Understanding the role of personality and motivation to drug use as well as the wider context of the environment in which intoxication occurs, might help us understand why the effects of the drug differ among people.

Procedures

Participation in the study is entirely voluntary. It is up to you to decide whether or not to do this. If you do decide to take part, I would ask you to sign a consent form. However, you are free to withdraw from

the study at any time.

If you decide to take part in this study, I will ask you to abstain from **taking drugs for 7 days** prior to the study to make sure you are not under the influence of any substances while participating in the study.

You will be asked to complete an online survey. Items in the survey cover topics related to your pattern of MDMA and/or other drugs use, and the effects of the drugs. You would be also asked to complete questionnaires measuring a range of psychological traits. The whole process would take approximately **20-30 minutes**.

Data Storage, Retention, Destruction and Future Use

All data collected in this study will be anonymised. Upon completion of the survey you will be asked to give consent to include your data in further analyses by pressing 'send' button. You are free to withdraw your data from the study at that point. Once you have given consent and pressed 'send', we cannot withdraw your data at a later stage because of the anonymised nature of the study.

Electronic data will be stored in a secure data file for a minimum of 10 years and shredded after data collection and entry is complete.

Ethical Issues

The questions in the survey may influence the way you feel about taking drugs in general, either in a positive or negative way, or may have no effect. Please discuss any concerns you might have with Monika Wieliczko, at any point during the research process.

Result Reporting

The survey data will be analysed and written up as academic research. The data will be anonymous. A short report of the main findings will be made available to you if you request it by contacting me directly.

If you have any questions at any time about the study, please do not hesitate to contact Monika Wieliczko m.j.wieliczko@gmail.com

CONSENT FORM

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason. ☐

3. I understand that any information given by me may be used in future reports, articles or presentations by the research team. ☐

4. I understand that my name will not appear in any reports, articles or presentations. ☐

5. I agree to take part in the above study. ☐

Letter to ethics committee

Dear Ethics Committee,

I write to update you on the progress of my research project 'Psychological effects of MDMA (3,4-methylenedioxmethamphetamine): the function of the drug, set and setting.'

I include a summary of the study and research findings. A similar summary has been distributed among those participants who requested information about the results.

I am planning to disseminate the findings in a number of ways. The paper will be submitted to a peer-reviewed journal for publication. I will be also presenting my results at the Interdisciplinary Conference on Psychedelic Research in June 2016 in Amsterdam.

If you wish to receive a copy of the paper following publication please let me know.

Feel free to contact me with any outstanding queries related to the project.

Kind regards

Monika Wieliczko

Trainee Clinical Psychologist

Research Summary for Ethics Committee

Psychological effects of MDMA (3,4-methylenedioxmethamphetamine): the function of the drug, set and setting.

Aims

Zinberg's Interaction Model implies that the content of a drug-induced experience is a function of the pharmacological properties of the drug, the set (the user's characteristics e.g. motivation and personality), and the setting (the physical and social context). The current research investigated the function of the set and setting and their role in shaping the psychological effects of 3,4-methylenedioxmethamphetamine (MDMA), as well as their role in reducing the risk of drug abuse.

Methods

An online survey was distributed among adult MDMA polydrug users (n = 158) and MDMA-naïve controls (alcohol, nicotine and cannabis users, n = 138). Participants answered questions regarding their pattern of drug use, their motivation for MDMA use and the setting (e.g. clubbing, home with friends), as well as the subjective effects of MDMA. Participants also completed a range of self-report measures of self-reflection and insight, emotional intelligence, and personality, as well as a drug dependency measure.

Results

MDMA users displayed higher levels of self-reflection and insight, openness to new experience and lower levels of neuroticism and conscientiousness, in comparison to non-MDMA users. The significant predictors of self-reflection and insight were openness, emotional intelligence, MDMA use, extraversion and neuroticism. When the analysis was rerun only for the MDMA group, the significant predictors of self-reflection and insight were openness, emotional intelligence and self-insight effects of MDMA. High levels of self-reported negative effects of MDMA were predictors of a problematic drug use.

Conclusions

These findings suggest that there might be a relationship between MDMA use and higher levels of self-reflection and insight; however, longitudinal studies are required to further investigate the causality of this relationship. The results add to existing evidence that MDMA has potential for altering emotional experiences.

Appendix 4. Questionnaires used in the study

NEO-FFI

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Drug Use Questionnaire

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Severity of Dependence Scale

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Trait Emotional Intelligence Questionnaire –Short Form

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Self Reflection and Insight Scale

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MDMA Motives Questionnaire

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Effects of MDMA use Questionnaire

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