Ecstasy users: Risk factors for depressive and anxiety symptomatology

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This thesis is submitted in partial fulfilment of the requirements for the degree of Doctor of Psychology (Clinical)

February 2010
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In accordance with Monash University Doctorate Regulation 17/ Doctor of Philosophy and Master of Philosophy (MPhil) regulations the following declarations are made:

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

This thesis includes one original paper published in a peer reviewed journal and two manuscripts submitted for publication. The core theme of the thesis is ecstasy and mood. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the School of Psychology under the supervision of Dr J. Sabura Allen and under the supervision of Dr Leanne Hides and Dr Dan Lubman of Orygen Youth Health Research Centre.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.
In the case of chapters four, five and six my contribution to the work involved the following:

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ACKNOWLEDGEMENTS

Firstly, my sincere thanks go to my supervisors, Dr J. Sabura Allen, Dr Leanne Hides and Dr Dan Lubman. Many of the strengths of this thesis are owed to your combined research and clinical knowledge in the area of mental health and substance use. Sabura, thank you for your unwavering support and guidance; reading my draft over your Christmas holidays is testament to your incredible dedication to your students, and for that I am immensely grateful. Leanne, thank you for sharing your expertise in the area of comorbidity. I am extremely grateful for your comprehensive and supportive guidance at all phases of this doctorate. Dan, thank you for your ideas, and your contagious enthusiasm, that always had the effect of refueling my conviction for this project, and for your guidance through the publication process.

I am hugely grateful to my fellow doctoral candidates. Your friendship and ongoing support enabled this academically and emotionally challenging course to be a truly enjoyable experience. Thank you to Rowan Ogeil and Lauren Douge for your feedback on one of the thesis chapters. I really appreciate your time and support.

To my family and friends, thank you for your love, support, encouragement and ongoing belief in my abilities. Thank you all for your understanding of my thesis-related absences and for your active interest in my research. Specifically, thank you to my parents for providing me with the opportunities that have got me to this point. I am immensely grateful for your unconditional love and support. Thank you to my family-in-law for their support and interest in this research, and in particular, to Alice, for proof reading my literature review.

Thank you to all the participants who gave their time, and in particularly for answering my telephone calls when that was probably the last thing you felt like after a late night out! Without their contribution, this thesis could not have come to fruition.

Finally, to my boyfriend, Tim, thank you for embarking upon this journey with me. It is hard to summarise all that you have done, especially over the last six months, from cooking to proof reading and IT support, your contribution is immeasurable. Without your unrelenting support, this thesis would not have been possible. Thank you and I love you.
THESIS DERIVED PUBLICATIONS


   Depressive and anxiety symptomatology in ecstasy users: the relative
   contribution of genes, trauma, life stress and drug use. *Psychopharmacology.*

   DOI 10.1007/s00213-009-1763-5


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ABSTRACT

Considerable research has been conducted looking at ecstasy and psychological functioning, particularly mood. However, the nature of the relationship between ecstasy and mood remains unclear. Few studies have examined what factors increase the likelihood that someone who uses ecstasy will experience mood symptoms in the short or long term. The current thesis aimed to develop a greater understanding of the relationship between ecstasy and mood by identifying risk factors for depressive and anxiety symptomatology in a sample of ecstasy users.

Constructed as a thesis by publication, the thesis begins with review of the relevant literature and an overall introduction to the research project and design. Three articles are then presented in a series of chapters. The first article, titled ‘Depressive and anxiety symptomatology in ecstasy users: The relative contribution of genes, trauma, life stress and drug use’ has been published in Psychopharmacology. The research presented in this article aimed to determine the relationship between ecstasy use and depressive/anxiety symptomatology, after controlling for known environmental and genetic (polymorphism of the serotonin transporter gene) risk factors for depression and anxiety disorders. The second article is titled ‘Subacute effects of ecstasy on mood: An exploration of associated risk factors’. This article has been submitted to Journal of Psychopharmacology. Using a prospective design, the research reported in this article aimed to explore potential risk factors for depressive and anxiety symptoms in the short term, including ecstasy use. The third article, titled ‘Coping style and ecstasy use motives as predictors of current mood symptoms in ecstasy users’ has been submitted to Journal of Affective Disorders. The primary aim of this article was to determine whether the severity of mood symptoms in ecstasy users was predicted by coping style or ecstasy use motives.

Data for the three papers were collected from two studies. Study one consisted of a community sample of 184 18-35 year olds who had taken ecstasy at least once in the past 12 months. Participants (87 males; 97 females) completed a semi-structured interview, self-report questionnaires and provided a saliva sample. Study 2 used a subsample of ecstasy users from study one to prospectively explore predictors of mood change over a one-week period. Individuals who took ecstasy during the follow up (n=35) were compared with those who abstained (n=21). Mood symptoms were assessed using the Mood and Anxiety Symptom Questionnaire, Kessler 10, a subjective mood rating, and the depression, anxiety and hostility items of the clinician-rated Brief Psychiatric Rating Scale.
Ecstasy use motives and coping style were measured with the Drinking/Drug Motives Questionnaire and the Coping Inventory for Stressful Situations, respectively. Timeline methods were used to collect information on lifetime and recent ecstasy use, as well as recent other drug use and life stress. Trauma exposure was assessed using the Composite International Diagnostic Interview (CIDI) - Trauma List. Participants also provided demographic, psychiatric and sleep behaviour information. Genomic deoxyribonucleic acid (DNA) was extracted from participant saliva samples.

The results of study one indicated that neither lifetime nor recent ecstasy use were associated with the severity of current mood symptoms, either alone or in combination with a genetic risk factor. Rather, lifetime trauma, recent stressful life events, coping style, ecstasy use motives and other drug use factors significantly predicted the severity of depressive and anxiety symptoms. Consistent with these findings, Study two (Article two) found that lowered mood and increased psychological distress were associated with self-reported quality of sleep and the number of stressful life events experienced during the one-week follow up, and not by ecstasy use. These results highlight the need to consider the role of environmental factors in the relationship between ecstasy use and mood symptoms, as well as the importance of coping skills training for managing stressful life events for people with co-occurring depressive/anxiety symptoms and substance use.
Ecstasy (3,4-methylenedioxymethamphetamine or MDMA) is one of the most popular recreational drugs in Australia, with up to 24% of Australian 20-29 year olds reporting lifetime ecstasy use (Australian Institute of Health and Welfare, 2008a). Although prevalence rates have stabilised in Australia in the last three years, the rates are still higher than those observed in Europe and North America (United Nations Office on Drugs and Crime, 2008, 2009). Ecstasy is taken for its acute effects, including feelings of euphoria, increased energy, and greater sociability and connectedness with others (Cohen, 1995; White, Degenhardt, Breen, Bruno, Newman, & Proudfoot, 2006). However, increasing popularity and reports that ecstasy is neurotoxic to the serotonin system of laboratory animals (Ricaurte, Yuan, & McCann, 2000) and possibly humans (McCann et al., 2008) has raised concern about the potential psychological consequences of ecstasy use.

Considerable research has explored the relationship between ecstasy use and clinical and subclinical psychopathology. The current thesis focuses on ecstasy and mood, specifically, the severity of depressive and anxiety symptomatology in ecstasy users. The term ‘ecstasy’ will be used throughout, aside from when MDMA is identified as the substance of interest (e.g., in MDMA administered laboratory studies or when biological assays confirm MDMA content).

To date, studies have largely focused on whether a relationship between ecstasy and mood symptoms exists. Numerous cross-sectional studies indicate that ecstasy users have higher rates of depressive and anxiety symptoms, compared to drug-naïve controls and that the severity of symptoms is related to the patterns of ecstasy use (i.e. lifetime severity or frequency of ecstasy use). However, the ecstasy literature is limited by a preponderance of cross-sectional designs, small sample sizes and poor control of other drug use. More recent research suggests that symptom severity is related to illicit drug use in general, not ecstasy per se. Further, other researchers propose the observed mood symptoms in ecstasy users may relate to premorbid mood differences, or that shared risk factors may be contributing to a heavier pattern of drug use and mood symptoms in this population. The current thesis takes the position that the relationship between ecstasy and mood is likely to be more complex than is currently depicted in the literature. Ecstasy users likely form a heterogeneous group whose consumption leads to differing consequences for different people (Sumnall & Cole, 2005).

Chapter 1 of the thesis provides a review of the relevant literature. Section 1 provides the context for exploring ecstasy use by summarising the social and legal history, prevalence
and patterns of ecstasy use, the pharmacology of MDMA and evidence for neurotoxicity. Section 2 reviews the evidence for a relationship between ecstasy and mood symptoms in the short (section 2.1) and long term (section 2.2). Section 3 reviews possible models to explain the relationship between ecstasy use and mood symptoms. Section 4 explores potential risk factors for more severe symptomatology in ecstasy users. The review concludes with a summary and provides a rationale for the current thesis (section 5).

The current thesis expanded upon the previous research literature on ecstasy and mood in a number of ways. First, the relative contribution of lifetime ecstasy use on current mood symptoms was investigated, while controlling for known environmental and genetic risk factors for depression, anxiety and substance use. Second, factors related to the experience of a negative mood change in the days following ecstasy use were explored using a prospective design. Third, the influence of coping style and ecstasy use motives on current mood symptoms was determined.

Chapter 2 summarises the rationale and overarching aims of the thesis and describes the aims and hypotheses for the three empirical papers. Chapter 3 provides a detailed description of the methodology, beyond that included in the empirical papers. Chapters 4, 5 and 6 make up the three empirical papers submitted for publication. The thesis concludes with an integrated general discussion (chapter 7) that draws together the findings from the three papers and discusses the limitations and clinical implications of the findings.
Chapter 1

Literature review
1. Background

1.1 History: Social and legal

MDMA was first patented in 1914 by the German pharmaceutical company Merck, for use in the synthesis of therapeutically active compounds (see Shulgin, 1990 for review of the history of MDMA). However, MDMA was not made commercially available (Cole & Sumnall, 2003b). The first animal toxicology studies were conducted in the 1950s at the University of Michigan, funded by the United States Army (Grob, 2000; Shulgin, 1990). In the mid-1970s MDMA began to be used as an adjunct to psychotherapy, used in the treatment of a range of conditions including anxiety, trauma-related distress, alcohol and drug abuse, and relationship difficulties (Greer & Tolbert, 1990; Shulgin, 1990). In 1978, Shulgin and Nichols published the first paper on the psychoactive properties of MDMA in humans (Shulgin & Nichols, 1978). Subsequently, it was proposed that MDMA and its related compound, MDA, should be identified as a new class of pharmaceuticals termed “entactogens” due to their unique effects not seen in typical stimulants or hallucinogens (Nichols, 1986).

In contrast, in 1977 the United Kingdom Home Office listed MDMA as a Class A Schedule 1 substance, indicating no medicinal uses (Cole & Sumnall, 2003a). Subsequently in 1985, following concern regarding the abuse potential of MDMA and preliminary findings that MDMA caused neuronal damage in laboratory animals (Ricaurte, Bryan, Strauss, Seiden, & Schuster, 1985), the United States Drug Enforcement Administration (DEA) classed MDMA as a Schedule 1 controlled substance. Amid the associated media attention, the recreational use of MDMA was on the rise. By the mid 1980s, ecstasy use had spread to Europe and had become the drug of choice at all night dance parties or “raves” (Cole & Sumnall, 2003a; Grob, 2000).

Ecstasy is typically sold in tablet form and occasionally in capsule or powder form. Tablets come in a variety of colours and shapes with printed designs or logos (see www.pillreports.com). However, the dose and purity of MDMA in tablets sold as ecstasy can vary widely. In a review of the literature, Parrott (2004) reported that ecstasy purity has varied over time, citing in particular, that in the mid 1990s lower purity of MDMA was observed. Tablets sold as ecstasy often contain other substances, including related compounds MDA and MDEA, and to a lesser extent amphetamine, PMA, caffeine, paracetemol, ephedrine and ketamine (Parrott, 2004; World Health Organisation, 1997). However, more recent reports indicate that 90 to 100% of tablets sold as ecstasy in Europe
contain MDMA (Parrott, 2004). Dose typically ranges between 80 and 150mg of MDMA per tablet (Green et al., 2003). However, Australian data suggests poorer purity and lower doses of MDMA (Quinn, Dunn, & Degenhardt, 2007).

Data on pill content in Australia largely comes from police seizures in different states. In the state of Victoria, the most recent published data (for the 2004-2007 period) indicate that MDMA was the most frequently identified drug in tablets seized by police, followed by methylamphetamine, MDA/MDEA and ketamine (Quinn et al., 2007). However, in recent years there has been an increase in seized tablets containing no active drug (Quinn, Breen, & White, 2004; Quinn et al., 2007). Of those tablets containing MDMA, the purity varies widely (0.5% to 75%). However, data from police seizures is based on all tablets seized. Whether these were all going to be sold as ‘ecstasy’ is unclear.

In a South Australian study investigating the reliability of pill testing kits, 65% of 84 pills presented for testing by rave attendees contained MDMA (Camilleri & Caldicott, 2005). The rave attendees submitting pills for testing all reported that the pills had been sold to them as ‘ecstasy’. After MDMA, ketamine was the second most common illicit substance detected (present in 26% of pills). Consistent with Victorian seizure data, ketamine was typically combined with another drug, most commonly methylamphetamine. The combination of methylamphetamine and ketamine, and in most cases caffeine, accounted for 17% of pills tested. Four pills (5%) contained MDA, five pills (6%) possibly contained LSD (analysis was not complete at time of writing), two pills (2%) contained a cold and flu preparation containing pseudoephedrine sulfate and chlorpheniramine maleate and one tablet (1%) contained ephedrine. Findings from the Ecstasy and Related Drugs Reporting System reported that ecstasy pills in Victoria typically contain between 80 and 100mg of MDMA, as reported by a key expert in law enforcement interviewed in the study (Johnston, Quinn, & Jenkins, 2007). However, it was not reported where this person obtained this information.

1.2 Patterns of use

Ecstasy is typically swallowed, and to a lesser extent snorted, smoked, shelved/shafted (i.e. vaginal/anal administration, respectively) or injected (Dunn et al., 2007; Topp, Hando, Dillon, Roche, & Solowij, 1999). Ecstasy users typically take one to two tablets per occasion (Johnston et al., 2006; Topp et al., 1999) with frequency of use varying from occasional to weekly use (Degenhardt et al., 2004). The most recent
Australian national household drug survey indicated that of those who had used ecstasy within the last 12 months, 8.3% reported weekly use, while 46.0% reported using ecstasy only once or twice a year (Australian Institute of Health and Welfare, 2008a). Today, ecstasy continues to be most commonly taken at dance parties or raves and to a slightly lesser extent at private parties and licensed bars and clubs (Australian Institute of Health and Welfare, 2008a; Degenhardt et al., 2004). Ecstasy users are typically polydrug users with high rates of other illicit drug use and the majority using other substances in combination with ecstasy (Degenhardt et al., 2004; Winstock, Griffiths, & Stewart, 2001). The most recent Australian National Household Drug Survey found ecstasy users (in the past 12 months) had used the following proportions of drugs concurrently with ecstasy: 85.4% used alcohol, 49.2% used cannabis, and 28.7% used meth/amphetamine (Australian Institute of Health and Welfare, 2008a).

1.3 Pharmacology and neurotoxicity

MDMA is a potent agonist and reuptake inhibitor, initiating the release of serotonin and to a lesser extent dopamine, norepinephrine, and acetylcholine (Liechti & Vollenweider, 2001; Fischer, Zernig, Schatz, Humpel, & Saria, 2000; Schmidt, Levin, & Lovenberg, 1987; Shulgin, 1986). Following the initial release of serotonin from presynaptic vesicles, MDMA prevents reuptake of serotonin from the synaptic cleft and inhibits tryptophan hydroxylase, preventing the synthesis of new serotonin (McKenna & Peroutka, 1990). These acute effects lead to the temporary attenuation of central serotonin (Schmidt, 1987). Repeated use of MDMA typically leads to reduced drug effects or tolerance, leading users to take more ecstasy to achieve the same effects (see Parrott, 2005 for review).

Serotonin plays an important role in the regulation of mood, emotion, sleep, sexual function, and appetite (Jans, Riedel, Markus, & Blockland, 2005). Serotonin dysfunction has been implicated in the aetiology of several mental illnesses including depression, anxiety, schizophrenia, obsessive-compulsive disorder and eating disorders (Heninger, 1995; Naughton, Mulrooney, & Leonard, 2000). Given MDMA’s known action upon the serotonergic system, concern has been raised that MDMA use may lead to problems in the regulation of mood and behaviour and contribute to the onset of psychopathology (Parrott, 2001; Taffe et al., 2003).

Consistent with serotonin neurotoxicity, long-term changes in the serotonin system of
various animal species after repeated doses of MDMA have been reported. Specifically, data from rats and non-human primates indicate long-term dose-dependent reductions in brain serotonin (5-HT) and its metabolite 5-HIAA and decreased density of brain 5-HT transporters (SERT) and 5-HT axons and nerve terminals (Green et al., 2003; O'Shea, Granados, Esteban, Colado, & Green, 1998; Ricaurte et al., 2000; Schmidt, Wu, & Lovenberg, 1986). This damage can persist for months in rats and years in non-human primates (Gouzoulis-Mayfrank & Daumann, 2006). However, criticisms regarding interspecies dosing, differing pharmacology across animal species, and confounding factors including routes of administration, experimental designs and dosing regimens have questioned the generalisability of these findings to humans (Easton & Marsden, 2006; Green, Gabrielsson, Marsden, Fone, 2009; Saunders, 1995).

Human studies of ecstasy users however, are producing a growing body of evidence for MDMA-induced serotonin damage (for reviews see Gouzoulis-Mayfrank & Daumann, 2006 and Reneman, de Win, van den Brink, Booij, & den Heeten, 2006). Specifically, a number of studies indicate that ecstasy users have reduced serotonin metabolites, blunted endocrine responses and reduced serotonin transporter (SERT) densities, suggestive of serotonin neurotoxicity (Buchert, et al., 2004; McCann et al., 2005, 2008; Reneman, et al., 2001; Semple, Ebmeier, Glabus, O'Carroll, & Johnstone, 1999). However, the mechanisms by which MDMA neurotoxicity occurs remain unclear (Dean, 2004).

Reduced serotonin transporter densities have been associated with heavier ecstasy use, including lifetime and last year use, and typical dose (Reneman et al., 2001, 2006). Greater differences have been found in females suggesting heightened vulnerability to serotonin neurotoxicity (Reneman et al., 2001). Despite these findings, there is some suggestion that these effects can be reversed following long-term abstinence (Selvaraj et al., 2009; Thomasius et al., 2003, 2006). However, methodological limitations such as predominantly cross-sectional designs, polydrug use and potential premorbid differences remain significant factors in interpreting findings from human neurotoxicity studies (Gouzoulis-Mayfrank & Daumann, 2006).

In contrast to the above findings, a recent well-designed prospective study found no changes in serotonin transporter densities or brain metabolites in ecstasy users prior to and after commencing ecstasy use (de Win et al., 2008). However, they found a number of group differences on other physiological measures between those that remained ecstasy-
naïve and those who went on to take ecstasy over the course of the study (mean lifetime pills=6, median=2). The authors suggested that the observed group differences indicated physiological changes relating to low doses of ecstasy.

However, whether the observed brain differences translate into changes in psychological functioning remains unclear. In an earlier study by de Win and colleagues, elevated depression scores were found in current and former ecstasy users with a positive association found between severity of depression and lifetime ecstasy use. However, they found no association between mood disorders or depressive symptoms and SERT binding, suggesting that MDMA-induced serotonin changes cannot fully explain the elevated mood symptoms observed in ecstasy users (de Win, et al., 2004).

2. Ecstasy and Mood

Given MDMA’s high affinity for serotonin and potential neurotoxicity, considerable research has been dedicated to exploring the relationship between ecstasy use and mood symptoms. Indeed, the aetiology of high prevalent psychiatric disorders, such as depression and anxiety, is strongly associated with serotonergic function. Data from the United States National Comorbidity Survey indicated that the most prevalent disorders in the general population for the past 12 months were anxiety (18.1%) and mood disorders (9.5%) (Kessler, Chiu, Demler, Merikangas, & Walters, 2005). Major depressive disorder was the most prevalent 12-month mood disorder (6.7%), while the most prevalent anxiety disorders were specific phobia (8.7%), social phobia (6.8%), posttraumatic stress disorder (35%) and generalised anxiety disorder (3.1%). Similar 12-month prevalence has been reported in Australia with the most recent National Survey of Mental Health and Wellbeing indicating that 14.4% of Australians aged 16–85 years had a 12-month anxiety disorder and 6.2% had a 12-month affective disorder (Australian Bureau of Statistics, 2007). Many of these disorders are associated with significant morbidity, increased mortality and comorbid psychopathology. Specifically, strong associations have consistently been found between depression and anxiety and substance use disorders (Burns & Teesson, 2002; Kessler et al., 2005; Merikangas et al., 1998). Consistent with this, epidemiological studies indicate that ecstasy users have significantly higher rates of mental disorders compared to non-illicit drug users and ecstasy-naïve drug users, with consistent associations found between ecstasy use and anxiety, depressive and substance use disorders (Keyes, Martins, & Hassin, 2008; Lieb, Schuetz, Pfister, von Sydow, & Witchen, 2002). Taken together, it is critical to understand the relationship between depression/anxiety and ecstasy use.
Human studies of ecstasy users have looked at both short-term (acute and subacute) and long-term effects related to ecstasy use. Acute effects relate to the period of intoxication, with the primary effects lasting three to five hours (Green et al., 2003). Subacute refers to the days following use with studies investigating subacute ecstasy effects from one to seven days post use (Curran & Travill, 1997; Curran, Rees, Hoare, Hoshi, & Bond, 2004; Hoshi, Pratt, Mehta, Bond, & Curran, 2006; Huxster, Pirona, & Morgan, 2006; Parrott & Lasky, 1998; Pirona & Morgan, 2009; Verheyden, Hadfield, Calin, & Curran, 2002).

Acute and subacute studies have included prospective designs, including laboratory studies whereby MDMA is administered in a controlled environment; field studies that observe ecstasy users before and/or after ecstasy consumption; and retrospective studies that have asked participants to report on their experiences of ecstasy use. In the current context, ‘long-term’ refers to mood symptoms that persist beyond the subacute period. Long-term studies have predominantly used cross-sectional designs whereby ecstasy users have been compared with control groups on severity of self-reported or clinician-rated psychopathology/symptomatology (e.g., Beck Depression Inventory [BDI]; Symptom Checklist-90-revised [SCL-90-R]; the Structured Clinical Interview for DSM-IV [SCID-I]) or retrospective studies, whereby ecstasy users report on the experience of symptoms that they attribute to ecstasy use. A small number of longitudinal studies have provided a valuable addition to the literature by investigating changes in mood symptoms in ecstasy users over time and comparing individuals that go on to take ecstasy with those that do not. The following sections review the literature on short- (section 2.1) and long-term mood symptoms associated with ecstasy use (section 2.2).

2.1 Acute and subacute mood effects. Acutely, ecstasy produces feelings of euphoria, increased energy, greater sociability and connectedness with others, moderate increased sensory perception and altered perception of time (Cohen 1995; Liechti, Baumann, Gamma, & Vollenweider, 2000a; White et al., 2006). Acute psychological and physical side effects include jaw clenching, thirst, reduced appetite, difficulty concentrating, confusion, insomnia, mild depersonalisation and derealisation, anxiety and restlessness (Liechti et al., 2000a; Verheyden, Henry, & Curran, 2003a). Other physical symptoms include pupil dilation and increased body temperature (Mas et al., 1999; Vollenweider, Gamma, Liechti, & Huber, 1998). It has also been reported that ecstasy enhances some aspects of sexual experience, including increased sexual desire, sensuality and satisfaction, but may reduce some aspects of sexual functioning including the ability to orgasm and maintaining an erection (Buffum & Moser, 1986; Zemishlany, Aizenberg, & Weizman,
In contrast to the desired acute effects, a large number of ecstasy users report experiencing negative psychological and physical side effects in the days following ecstasy use (subacute period). In a retrospective study of ecstasy users, the most commonly reported psychological side effects experienced whilst ‘coming down’ from ecstasy (i.e. during the acute recovery period) included irritability (60% of participants), trouble sleeping (52%), depression (50%), confusion (36%), anxiety (33%), and paranoia (31%) (Topp et al., 1999). Similarly, findings from prospective field and laboratory studies indicate that ecstasy use may result in lowered mood or increased aggression in the days following use (Curran & Travill, 1997; Curran et al., 2004; Hoshi et al., 2006; Huxster et al., 2006; Liechti, Gamma, & Vollenweider, 2001; Parrott & Lasky, 1998). These subacute mood effects are thought to be due to the [temporary] depletion of serotonin following the acute elevation caused by MDMA (Curran & Travill, 1997).

Liechti and colleagues conducted a series of well-designed human laboratory studies aimed at identifying the acute psychological and physiological effects of MDMA and the role of serotonin and dopamine in producing these effects (Liechti, Baumann, Gamma, & Vollenweider, 2000a; Liechti, Saur, Gamma, & Vollenweider, 2000b; Liechti & Vollenweider, 2000a, 2000b). Healthy participants who had never or rarely taken ecstasy were administered MDMA (range: 70-150mg) or placebo in a controlled environment. In addition to the acute physiological and subjective effects of MDMA, adverse subacute drug effects were measured 24 hours post ingestion using the List of Complaints measure. Up to a third of MDMA participants reported signs of depressed mood including irritability, brooding, difficulty concentrating, lack of energy and bad dreams. A small number of participants continued to report these subacute effects three days post administration of MDMA (Liechti et al., 2001).

However, ‘field’ studies suggest higher rates of subacute mood effects lasting up to four days following ecstasy use (Curran & Travill, 1997; Curran et al., 2004; Huxster et al., 2006; Hoshi et al., 2006; Parrott & Lasky, 1998). Using a retrospective design with a large sample of regular ecstasy users (n= 430), Verheyden et al. (2003a) found 83% of participants reported having experienced low mood in the days after ecstasy use. A similar association between ecstasy and low mood has been found in prospective studies with ecstasy users. Curran and Travill (1997) found an association between ecstasy use and
depressive symptoms (measured on the BDI), the day after and four days after ecstasy use, with some participants scoring in the mild to moderate clinical range for depression at day four (Curran & Travill, 1997). In contrast, the alcohol-using control group in this study showed only a mild increase in symptoms the day after drinking. Similarly, Parrott and Lasky (1998) found that ecstasy use was associated with significant increases in self-reported ratings on abnormal, sad, depressed, unpleasant and unsociable visual analogue mood scales in the days after ecstasy use, compared to baseline scores. Interestingly, increased aggression has also been found in the days after ecstasy use. Ecstasy users scored higher on self-report measures of aggression and depression and demonstrated a bias towards aggressive stimuli four days post ecstasy use, compared to a group of mostly ecstasy-naïve drug using controls, well-matched for lifetime other drug use (Curran et al., 2004; Hoshi et al., 2006). These mood effects were no longer present seven days post ecstasy use (Curran et al., 2004).

However, there are a number of methodological issues that may be confounding findings from subacute field studies. The subacute mood effects associated with ecstasy use may or may not be directly associated with ecstasy itself, but rather could be associated with other pre-existing or co-occurring factors. For example, some studies have not obtained a predrug baseline measure of mood (e.g., Curran & Travill, 1997), meaning that observed subacute mood effects may reflect premorbid differences. Other studies have not controlled for other drug use on the night of drug use or over the course of the follow up (e.g., Parrott & Lasky, 1998). This is important given that other drugs such as alcohol can have subacute negative effects on mood (McKinney & Coyle, 2005). In addition, ecstasy users frequently report taking other drugs whilst coming down from ecstasy, which has been associated with a greater number of self-reported ecstasy side effects (e.g., Topp et al., 1999).

Furthermore, many studies have not controlled for the potentially confounding factor of sleep (e.g., Curran et al., 2004; Curran & Travill, 1997; Hoshi et al., 2006; Parrott & Lasky, 1998). Given that sleep deprivation alone can cause negative mood effects (Keane & James, 2008), and that ecstasy users report experiencing sleep disturbance following use in both field (Curran et al., 2004) and laboratory studies (Liechti et al., 2001), it is imperative that sleep is included in studies looking at the subacute effects of ecstasy on mood.

Assessment measures may also be biased. For example, studies assessing depressed mood have relied on self-report measures which may be subject to reporter bias. Secondly, the
use of the BDI which contains items that are directly affected by ecstasy including sleep and appetite may spuriously inflate depressive scores in the days after use (Sumnall & Cole, 2005). However, one study continued to find a significant increase in BDI scores in the days after ecstasy use following removal of these items (Curran & Travill, 1997). Furthermore, the repeated administration of the BDI, as well as other self-report mood scales, has been criticised due to potential test-retest effects (Huxster et al., 2006).

Two well-designed studies aimed to address some of these methodological limitations by using an ecstasy-using control to reduce potential premorbid differences as well as controlling for sleep and other drug use prior to and throughout the follow up (Huxster et al., 2006; Pirona & Morgan, 2009). Huxster et al. (2006) recruited 38 regular ecstasy users (at least monthly use) and obtained baseline measures of psychopathology (SCL-R-90), personality (Impulsiveness, Venturesomeness, and Empathy Questionnaire), and drug use. Participants were subsequently telephoned daily for nine days and assessed using the Daily Rating Scale (DRS), a ten-item scale measuring depressive symptoms, subjective concentration and memory, sexual desire, craving for ecstasy and restless sleep. Half of the participants went on to take ecstasy during the follow-up period and half abstained. Subacute negative mood effects (depression, irritability, rumination, anxiety) were observed for the group who took ecstasy with scores returning to baseline three to four days post ecstasy use. These differences remained significant after controlling for alcohol use during the follow up, lifetime ecstasy use, baseline psychopathology scores, and restless sleep. In contrast, the subacute effects on cognition, as measured by two self-report questions on concentration and memory, were no longer significant after controlling for these variables.

Pirona and Morgan (2009) found that although participants who took ecstasy over the 4-day study period reported feeling more muddled, afraid, and sad the day after ecstasy use, this was no longer significant after controlling for hours of sleep obtained the preceding night. Furthermore, they found no significant differences between the ecstasy users and abstainers in BDI scores the day after and four days after taking ecstasy, contrasting with earlier studies using the same measure (e.g., Curran & Travill, 1997; Hoshi et al., 2006). In response to these conflicting findings, the authors discussed the limitations of the repeated administration of the BDI over a short time frame in terms of test-retest effects, as well as the possible confounding effects of the somatic items of the BDI which may the direct consequences of drug use (Sumnall & Cole, 2005). This study highlights the importance of
controlling for sleep variables when exploring the relationship between ecstasy use and mood.

In summary, field studies with recreational ecstasy users have found higher rates of subacute mood effects from ecstasy than controlled laboratory studies. This may be due to the methodological limitations of early field studies including lack of baseline mood measures, poor control of other drug use, as well as the possible confounding effects of disrupted sleep and other drug use. Two recent studies have cast doubt on previous research finding subacute mood effects following ecstasy use, as many of the observed subacute effects from ecstasy use on mood and cognition were no longer significant after controlling for these variables (Huxster et al., 2006; Pirona & Morgan, 2009). Despite this, it remains possible that some ecstasy users are more vulnerable to ecstasy-induced subacute mood effects than others. However, there is a lack of research on potential risk factors for subacute mood symptoms. Aside from gender and other drug use, no prospective studies have examined what variables increase the likelihood that someone will experience lowered mood, anxiety or increased aggression in the days following ecstasy use, after controlling for a number of important confounding variables such as sleep. By determining whether there is a relationship between susceptibility to subacute mood effects and premorbid factors, may shed light on who may be vulnerable to potential long-term psychological effects of ecstasy use. Potential risk factors for subacute mood effects will be discussed further in Section 4. First, the following section will review the relationship between ecstasy use and long-term mood symptoms.

2.2 Long-term mood symptoms. Retrospective and cross-sectional studies indicate that a large number of ecstasy users report experiencing mood symptoms, including depression, outside the subacute period that they attribute to ecstasy (Topp et al., 1999; Verheyden et al., 2003a) and that ecstasy users have more severe depressive and anxiety symptomatology compared to controls (Fingeret, Moellar, & Stotts, 2005; Gamma et al., 2000; Gamma, Buck, Berthold, & Vollenweider, 2001; Gerra et al., 2000; Hanson & Luciana, 2004; McCordle, Luebbers, Carter, Croft, & Stough, 2004; MacInnes et al. 2001; Morgan, McFie, Fleetwood, & Robinson, 2002; Parrott, Sisk, & Turner, 2000; Parrott, Milani, Parmar, & Turner, 2001; Roiser & Sahakian 2004; von Geusau, Stalenhoef, Huizinga, Snel, & Ridderinkhof, 2004; Wareing, Fisk & Murphy 2000). Consistent with this, a meta-analysis of 25 studies revealed a small but significant relationship between ecstasy and mood, after partially controlling for alcohol and cannabis use, with lifetime
ecstasy consumption predicting effect size (Sumnall & Cole, 2005).

In addition to lifetime ecstasy use, severity of depressive symptomatology has also been associated with greatest ecstasy dose (MacInnes et al., 2001) and typical ecstasy dose (Verheyden, Maidment, & Curran, 2003b). de Win and colleagues compared 15 moderate ecstasy users, 23 heavy ecstasy users (>50 lifetime pills), 16 former heavy ecstasy users (abstinent for more than 12 months) with 15 polydrug using controls. They found former heavy users had significantly higher BDI scores than the polydrug-using controls. However, there were no significant differences in mood disorders between heavy users and polydrug users, assessed using the Composite International Diagnostic Interview (CIDI). In contrast, a community sample of ecstasy users (n=402), found individuals who had taken ecstasy on more than 50 occasions were significantly more likely to meet criteria for a number of lifetime psychiatric disorders (Falck et al., 2006b). Using a computerised version of the Diagnostic Interview Schedule (CDIS), 35% of the sample met DSM-IV criteria for lifetime diagnosis of major depression, 13% generalised anxiety disorder and 11% posttraumatic stress disorder (PTSD), among others. Importantly, the majority experienced their first episode prior to using ecstasy (major depression = 72.5%; generalised anxiety disorder = 79.8%; PTSD = 59.1%). The authors concluded that while ecstasy did not seem to play a role in the first episode of disorder in the majority of cases, it may have contributed to subsequent episodes.

Likewise, retrospective studies have found a positive correlation between lifetime ecstasy use and long-term mood effects attributed to ecstasy use (Parrott et al., 2002; Soar, Turner, & Parrott, 2006). Specifically, Parrott and colleagues (2002) found that 65% of heavy users (> 100 occasions) reported experiencing depression when they were drug-free, which they attributed to their ecstasy use compared to 54% of moderate users (10-99 occasions) and 33% of novice users (1-9 occasions). A similar pattern was found for anxiety and mood fluctuation.

The large number of studies finding elevated depressive/anxiety symptomatology in ecstasy users and the positive correlation between the severity of symptoms and patterns of ecstasy use (e.g., lifetime use) has led some researchers to suggest there is a causal association between ecstasy use and these symptoms (e.g., McCardle et al., 2004; Parrott et al., 2002). However, the findings have been mixed. Several studies have found no relationship between severity of mood symptoms and patterns of ecstasy use including
lifetime ecstasy use, duration of ecstasy use, usual ecstasy dose, and time since last ecstasy use (Daumann et al., 2004; de Win et al., 2004; Falck et al., 2006a; Guillot & Greenway, 2006; Medina & Shear, 2007).

Furthermore, other drug use has generally been poorly controlled for (Curran, 2000; Sumnall & Cole, 2005). Given that ecstasy users typically consume larger amounts of other drugs compared to ecstasy-naive drug-using controls (Bobes, et al., 2002; Roiser, Rogers, Cook, & Sahakian, 2006), it is critical to control for other drug use as any group differences cannot be attributed to ecstasy use alone. Concurrent use of other drugs with ecstasy not only poses a methodological issue, but may increase the risk of immediate and long-term psychological and neurobiological problems (Parrott et al., 2006; Winstock et al., 2001). In light of these criticisms and in order to identify the specific association between ecstasy use and mood symptoms, more recent research has compared ecstasy users with ecstasy-naive drug-using controls.

The majority of studies employing a drug-using control have found no group differences on self-reported depression and anxiety scales, including the Beck Depression Inventory (BDI; e.g., Curran & Robjant, 2006; Verkes et al., 2001 and BDI-II e.g., Guillot & Greenway, 2006; Medina & Shear, 2007), the depression and anxiety subscales of the SCL-90-R (Daumann et al., 2004; Halpern et al., 2004; Thomasius et al., 2006), and the State Trait Anxiety Inventory (STAI; Medina & Shear, 2007; Verkes et al., 2001), as well as a clinician-rated and diagnostic measures (Hamilton Depression Rating Scale (HAM-D), SCID; Halpern et al., 2004). In a number of studies that have included multiple control groups, group differences emerged with drug-naive controls but not polydrug using controls (e.g., Roiser & Sahakian, 2004; Thomasius et al., 2003) highlighting that the elevated symptoms are not unique to ecstasy users. Furthermore, severity of mood symptoms is related to many other drug use factors, besides ecstasy. For example, in a study of regular dance music attendees, regression analysis indicated that current anxiety, as measured by the Beck Anxiety Inventory, was predicted by frequency of amyl nitrate use, cigarette use, and weekly alcohol consumption (Sumnall et al., 2004). Similarly, an Australian study looking at patterns of ecstasy use and associated harm found that a greater number of psychological side effects attributed to ecstasy use were associated with the number of drugs usually taken while coming down from ecstasy, extensive recent polydrug use and recent bingeing on stimulants (Topp et al., 1999).
In contrast to the above studies, one study found that ecstasy/cannabis users \((n=11)\) scored higher on measures of anxiety (BAI) and depression (BDI-II) compared to a cannabis-using control group \((n=15)\), but the group difference on depression only became significant after controlling for frequency of alcohol use \((p=.039)\) (Lamers, Bechara, Rizzo, & Ramaekers, 2006). In contrast, no significant differences in depression or anxiety scores were found between the cannabis-using and a non-illicit drug using control \((n=15)\). The authors reported that there were no significant differences in frequency of other drug use between the ecstasy/cannabis users and the cannabis group. Consequently, they argued that the elevated depression and anxiety symptoms may be specific to ecstasy users. However, this study only required participants to be drug free on the day of testing meaning that subacute mood effects may have affected the findings. Furthermore, small sample sizes may have restricted the power required to detect relevant differences in frequency of other drug use.

A unique study from Hong Kong that excluded regular users of other drugs including alcohol, tobacco and polydrug use from both the ecstasy-using and control groups found very low depressive symptomatology in both groups and no significant group differences on the BDI (Yip & Lee, 2005). However, the ecstasy-using group had used ecstasy for a relatively short period (two to three months) and the mean lifetime dose was relatively small \((36\) pills; maximum=60\), as compared with other studies \(e.g.,\) Bedi, Van Dam, & Redman, 2008; Sumnall, Wagstaff, & Cole, 2004). Given that other studies have found that severity of mood symptoms is related to a heavy pattern of ecstasy and other drug use, the strict exclusion criteria regarding drug use may explain why depressive symptomatology was so low in this sample, and the findings may not be generalisable to typical ecstasy users.

Despite the mixed findings in the literature regarding the relationship between individual drug use factors and mood symptoms \(e.g.,\) Falck et al., 2006a, de Win et al., 2004; Medina & Shear, 2007; Thomasius et al., 2006), the majority of studies controlling for other drug use suggest that the elevated symptoms of depression and anxiety in ecstasy users relates to a heavier pattern of drug use in general and not ecstasy use \textit{per se}. Different methodologies and statistical analyses are also likely contributing to the mixed findings with respect to individual substances. These include the measures of drug use used \(e.g.,\) lifetime quantity, occasions of use, frequency of use, recent use; the reliability of participants’ recall of their
drug use and how this information is obtained (e.g., single question estimates, frequency by quantity calculations, context-based timeline methods; see Bedi & Redman, 2006b); the use of correlations versus regressions; and limited power due to small sample sizes. With respect to the current thesis, the above literature highlights that polydrug use is an important variable and needs to be controlled for when exploring the relationship between ecstasy use and mood symptoms.

In addition to polydrug use, a number of limitations with the ecstasy literature have been reported (see Curran, 2000 for review). Few studies have assessed ecstasy users before and after the first use of the drug. Consequently, it is difficult to draw conclusions about the direction of causality with respect to the association between ecstasy use and heightened mood pathology/symptomatology. Similarly, a number of studies have not reported time since last ecstasy use or have not requested participants to abstain from ecstasy use prior to participation (e.g., Abdallah, Scheier, Inciardi, Copeland, & Cottler, 2007; Fingeret et al., 2005; Parrott, Milani, Parmar, & Turner, 2001). Given that ecstasy may lead to subacute mood effects including lowered mood, anxiety and aggression up to four days post ecstasy use (e.g., Curran et al., 2004), it is critical that ecstasy users are not currently affected by subacute mood effects when making conclusions about the long-term effects of ecstasy.

A further limitation relates to measurement. Many of the scales used for measuring depressive symptomatology in ecstasy users contain a number of somatic symptoms, such as loss of appetite and sleep disturbance, which can be direct consequences of ecstasy use and not necessarily due to depression (Sumnall & Cole, 2005). This may inadvertently increase ecstasy users’ scores on self-report mood measures leading to an exaggeration of the association between ecstasy use and depression. It is therefore important to use measures that are able to isolate emotional depressive symptoms.

Similarly, measures of lifetime ecstasy and other drug use have typically relied on participant self report. Participant recall may be inaccurate given the possibility of drug-induced memory impairment (Curran, 2000). Specifically, lifetime ecstasy use has typically been obtained using single question methods or quantity by frequency calculations (Bedi & Redman, 2006b). It has been found that single question methods may lead to an underestimation of lifetime use and that quantity by frequency may not provide accurate lifetime dosage estimates (Bedi & Redman, 2006b). In contrast, timeline methods that use contextual cues such as life events are thought to increase recall accuracy of past
drug use (Bedi & Redman, 2006b; Del Boca & Darkes 2003; Shillington, Cottler, Mager, & Compton, 1995). However this method has not been employed in the majority of studies exploring the relationship between severity of use and mood symptoms.

Finally, the other significant limitation of the literature to date, but one that has received far less attention, is the lack of studies looking at what factors are related to elevated mood symptoms in ecstasy users. In the meta-analysis cited above, the authors concluded that the relationship between ecstasy and mood is likely to be more complex than is currently depicted in the literature. Ecstasy users likely form a heterogeneous group whose consumption leads to differing consequences for different people (Sumnall & Cole, 2005). However, few studies have explored what factors are associated with elevated mood symptoms in ecstasy users. This issue will be expanded upon in section 4, but first, the following section will review the prospective literature relating to ecstasy and mood.

2.3 Longitudinal studies. Prospective studies overcome a key limitation of cross-sectional studies by allowing for the assessment of individuals prior to and following the commencement of ecstasy use. The results of a number of longitudinal studies suggest that the onset of mental disorders typically precedes the onset of ecstasy use (Falck et al., 2006b; Lieb et al., 2002), and that people with heightened depressive and anxiety symptomatology in childhood and adolescence are more likely to use ecstasy in later adolescence and young adulthood (Huizink, Ferdinand, van der Ende, & Verhulst, 2006). These findings are consistent with the drug literature in general, with longitudinal studies indicating that psychological distress in childhood or adolescence predicts future licit and illicit drug use (McGee, Williams, Poulton, & Moffitt, 2000; Shedler & Block, 1990).

Lieb et al. (2002) investigated the relationship between mental disorders and ecstasy use in a large sample of adolescents and young adults over a four-year period (n=2462). Sixty-nine percent of ecstasy users (used ecstasy on one or more occasions) had at least one mental disorder. The most common disorders that were associated with ecstasy use compared to the ecstasy-naive illicit drug users and non-illicit drug users were panic attacks/disorder, generalised anxiety disorder, posttraumatic stress disorder, major depression and eating disorders. Importantly, ecstasy users were more likely to have taken other illicit substances than ecstasy-naive illicit drug users. Ecstasy users were also more likely to have an alcohol use disorder or nicotine dependence than both the ecstasy-naive illicit drug users and those who had never taken illicit drugs. In fact, ecstasy users were
significantly more likely to meet diagnosis for most DSM-IV diagnoses compared to non-illicit drug users and ecstasy-naive illicit drug users. Specifically, ecstasy users were significantly more likely to have experienced major depressive disorder or an anxiety disorder than both of the other groups and were more likely to have posttraumatic stress disorder than the non-drug users. However, for the majority of cases (88.4%) the onset of the mental disorder preceded the first use of ecstasy. It remains possible that ecstasy may have played a role in the aetiology of mental disorders in the remaining cases. On the other hand, those with a history of mental disorder at the first assessment point were significantly more likely to go on to use ecstasy over the course of the study, compared to those with no psychiatric history. The authors concluded that although pharmacological research indicates that it may be possible for ecstasy to lead to psychopathology, they argued that it is more likely that mental disorders lead to ecstasy use, for example, through self-medication.

In support of this conclusion, Huizink et al. (2006) investigated whether scores on the childhood behaviour checklist (CBCL) at baseline (mean age = 9.9 years) predicted ecstasy use 14 years later (mean age = 24.5 years). Scores in the deviant range on the anxious or depressed subscales of the CBCL at baseline, but not the delinquent behaviour subscale, were associated with increased likelihood of ecstasy use 14 years later, after controlling for sex, age and socioeconomic factors. Consequently, the authors concluded that people with depression and anxiety symptoms may be particularly attracted to the positive effects of ecstasy such as euphoria, relaxation and closeness with others.

In contrast, an Australian birth cohort study found that delinquent and aggressive behaviour at age 14, but not depressive or anxiety symptoms in childhood and adolescence, predicted ecstasy use disorders at age 21 (Alati et al., 2008). Similarly, a longitudinal study found that baseline depression, impulsivity and sensation seeking (baseline age range=18-35 years) did not predict ecstasy use 12 to 24 months later (de Win, et al., 2006).

However there are significant methodological factors that may be contributing to these mixed findings. Alati et al. highlighted that as the mean age of first ecstasy use in Australia is closer to 23 years, their earlier age of onset sample may be biased towards those with a more harmful pattern of use and higher rates of antisocial behaviour. They acknowledged that if they assessed an older sample other predictors may have been significant, such as depressive and anxiety symptoms. Furthermore, this study was looking at ecstasy use
disorders, not simply ecstasy use, as in the study by Huizink et al. (2006).

Similarly, de Win et al. highlighted that all participants, including those that did not go on to use ecstasy within the 17 month follow up, were chosen based on the high probability that they would go on to use ecstasy. That is, all participants reported that they would “probably” or “certainly” use ecstasy in the near future. Therefore, it is unlikely that there would be significant differences between those who went on to use ecstasy within the next 17 months and those who did not when their level of interest were comparable. The participants also had to agree to laborious involvement in the study including brain scans and detailed neuropsychological testing where a high level of motivation would have been required. The mean level of depression for all the participants was particularly low (BDI mean = 3.9) which may have reduced the predictive power of this variable (de Win et al., 2006), as was the mean for lifetime ecstasy use in the ecstasy group (six tablets).

**Summary.** Despite some differences in findings, these longitudinal studies suggest that for many ecstasy users with elevated depressive and anxiety symptoms, these symptoms are likely to have preceded ecstasy use. Consequently, some authors of longitudinal studies have suggested that some users may be using ecstasy as a form of self-medication (Huizink et al., 2006; Lieb et al., 2002).

2.4 **Summary: Ecstasy and mood**

Several studies have found that ecstasy users have higher levels of depressive and anxiety symptoms, and that greater lifetime ecstasy use is related to more severe symptomatology. Large numbers of ecstasy users also report subacute and long-term psychological problems that they attribute to ecstasy use. These findings have resulted in the proposal that ecstasy use may cause mood symptoms, such as depression and anxiety, in the short and long term. However, long-term studies have suffered from a number of methodological limitations, including the use of predominantly cross-sectional designs and poor control of other drug use (see Curran, 2000 for review; Sumnall & Cole, 2005). More recent research suggests that the elevated symptoms observed in ecstasy use relates to a heavier pattern of polydrug use and not ecstasy use *per se*.

Furthermore, longitudinal studies indicate that people with heightened depressive and anxiety symptomatology in childhood and adolescence are more likely to use ecstasy in later adolescence and young adulthood (Huizink et al., 2006) and that the onset of mental
disorders in ecstasy users typically precedes the onset of ecstasy use (Lieb et al., 2002).
Consequently, it has been suggested that elevated depressive/anxiety symptoms in ecstasy
users may be associated with the use of ecstasy to cope with pre-existing mood symptoms
(Huizink et al., 2006; Lieb et al., 2002). However, it remains possible that some users may
be more vulnerable to experiencing ecstasy-related harm (i.e. due to pre-existing factors) or
other co-occurring factors may increase the risk of mood symptoms amongst ecstasy users.
The following section will expand upon the possible models for the relationship between
ecstasy and mood, drawing upon the wider comorbidity literature.

3. Models of comorbidity: Ecstasy and mood

The term comorbidity in the current thesis refers to the co-occurrence of a
substance use disorder/substance use and one or more mental health conditions, including
subclinical symptoms. A number of models for understanding the relationship between
mental illness and substance misuse have been proposed including: 1) substance use leads
to mental health problems; 2) mental health problems lead directly to substance use, that is,
the self medication hypothesis; 3) there is an indirect causal relationship between substance
use and mental health symptoms whereby one affects a third variable which in turn
increases the risk of the other; and 4) there are shared risk factors that are related to
increased likelihood of mental health problems and substance use (Degenhardt, Hall &
Lynskey, 2004).

Consistent with the first model that substance use leads to mental health problems, ecstasy
and other drug use may exacerbate existing mood symptoms or lead to depressive/anxiety
symptomatology, such as through biological mechanisms (e.g., serotonin neurotoxicity;
McCann et al., 2008). The results of studies finding an association between lowered mood
or anxiety and the onset or continuation of substance use support the self-medication
hypothesis (Huizink et al., 2006; Lieb et al., 2002). In support of the third model, mood
symptoms may be a consequence of or may be exacerbated by a pattern of polydrug use
and/or associated lifestyle factors such as sleep deprivation and poor nutrition (Degenhardt
et al., 2004; Parrott et al., 2001). Finally, shared risk factors (e.g. low socioeconomic
status) may also increase the risk of both depressive/anxiety symptomatology and ecstasy
and other drug use (Kessler, 2004; Merikangas, Risch, & Weissman, 1994). Clearly, the
relationship between depressive/anxiety symptomatology and ecstasy use is complex, and
a number of possible explanations for this relationship exist. The following section will
review the literature regarding factors found to be associated with depressive and anxiety
symptomatology in ecstasy users.

4. **Risk factors for mood symptoms**

Many researchers have suggested that premorbid differences may account for the elevated depressive symptoms among ecstasy users compared to controls (e.g., Gamma et al., 2001; Saunders, 1995). However, to date, few studies have considered the role of risk factors in understanding the association between ecstasy use and mood symptoms. Risk factors refer to variables that increase the likelihood of a negative outcome (Kraemer et al., 1997). For clarity, all variables reviewed in the following section will fall under the umbrella of risk factors, though it is acknowledged that the term ‘risk factor’ should be reserved for variables that precede the negative outcome (Kraemer et al., 1997).

4.1 **Non-drug related risk factors**

The following section summaries the potential non-drug related risk factors for mood symptoms in ecstasy users, including demographics, genetic and environmental variables and coping style.

*Demographic factors.* The current literature suggests that females are more susceptible than males to the acute and subacute psychological effects of ecstasy (see Allott & Redman, 2007 for review). In a retrospective study of 329 ecstasy users, females reported a greater number of short- and long-term psychological problems than males, including depression, which they attributed to ecstasy use (Topp et al., 1999). Gender differences on subacute mood have also been identified in a prospective study, whereby females were more likely to experience midweek low mood following weekend ecstasy use (Verheyden et al., 2002). These findings are consistent with findings that females are more sensitive to the serotonin-induced psychoactive effects of MDMA (e.g. experiencing perceptual changes) and are more likely to experience acute adverse effects (e.g. depressive and anxiety symptoms, jaw clenching) than males (Liechti et al., 2001). Similarly, two cross-sectional studies found that females scored significantly higher than males on self-report depression scales outside the subacute period (Falck et al., 2006a, 2008).

Females may be at heightened risk of ecstasy-related harm due to a number of factors, including gender-related differences in hormones, pharmacokinetics (e.g., metabolism), and brain structure (Allot and Redman, 2007). However, it is also possible that such long-term mood differences may reflect gender differences evident in the general population,
given the higher prevalence of depression and anxiety disorders observed amongst females than males (Australian Bureau of Statistics, 2007), as well as a gender bias in reporting mental health symptoms (Hankin & Abramson, 1999).

However, the findings are not conclusive. Hoshi et al. (2006) found no gender differences on an objective measure of aggression four days after ecstasy use. Similarly, Verheyden et al. (2003a) found no gender differences in the number of regular ecstasy users (n=466) reporting depression as a long-term consequence of ecstasy use. Although this study was limited by the use of a binary (yes/no) measure that did not capture the severity or frequency of symptoms, other studies that have used structured measures of current symptoms, have also found no gender differences in severity of self-reported depressive and anxiety symptomatology in ecstasy users (e.g., Fingeret et al., 2005; Medina & Shear, 2007; Roiser & Sahakian 2004). However these three studies all excluded participants with a psychiatric history, limiting the generalisability of their findings.

In a study of gender differences, Milani and colleagues administered an adapted version of the SCL-90 (with added positive items) to 768 young people in the UK and Italy (Milani, Parrott, Turner, & Fox, 2004). Participants were grouped into six groups based on drug use: nondrug users, alcohol and/or tobacco users, cannabis and/or alcohol and/or tobacco users, ecstasy-naïve polydrug users, light ecstasy polydrug users (<20 occasions), and heavy ecstasy polydrug users (>21 occasions). Females scored significantly higher than males on the depression, anxiety and somatisation subscales for the alcohol/tobacco group and on the depression scale for the cannabis/alcohol/tobacco and the light ecstasy polydrug users. Among the males, ecstasy polydrug users and ecstasy-naïve polydrug users scored significantly higher than nondrug users on the somatisation and anxiety subscales. There were no group differences for females. The authors reported that although scores on depression and somatisation increased in males as drug use became heavier, in females the severity of symptoms was consistent across the different drug using groups. The authors likened the findings to an earlier study that found that males were more likely to develop depression following the onset of drug use, while in females, depression was more likely to precede drug use (Brady, Grice, Dustan, & Randall, 1993). Consequently, the authors suggested that premorbid psychiatric factors may contribute to drug use in females while males may be more susceptible to experiencing psychopathology as a result of drug use.

However, a number of methodological problems have been raised concerning this study’s
design (see Cole, Sumnall, & Wagstaff, 2002). These include the use of the SCL-90 which was reported to be psychometrically flawed by the scale’s author (Derogatis, 1994), the possibility of subacute drug effects influencing results, and the potential effect of age differences between groups, with the mean age of the heavy ecstasy users being five years older than the nondrug users.

Indeed, the majority of participants in ecstasy studies are adolescents or young adults. Given that this age range coincides with the age of onset of many mental disorders, it is important to control for age when comparing groups (Cole et al., 2002). Age of first ecstasy use may also be an important risk factor. A younger age of ecstasy onset was related to higher scores on four subscales of the SCL-90-R, including depression (Daumann et al., 2004). It has been proposed that MDMA neurotoxicity may be more severe in adolescents than in adults (Jacobsen, Mencl, Pugh, Skudlarski, & Krystal, 2004). Another study found that females who endorsed the item “I get depressed” in relation to long-term effects of ecstasy use were significantly older than those who did not (Verheyden et al., 2003a). However, others have found no relationship between severity of mood symptoms and current age or age of first use of ecstasy (e.g., de Win et al., 2004; Verheyden et al., 2003b).

Other demographic factors that have been associated with elevated depressive symptoms include ethnicity and education. In a longitudinal study of young adult ecstasy users in the United States (n=402), ‘nonwhites’ and those with no university education had higher depression scores on the BDI than ‘whites’ and those with some university education (Falck, Wang, & Carlson, 2008). Taken together, demographic factors may be associated with elevated mood symptoms consistent with general population data (Australian Bureau of Statistics, 2007), but may also be associated with increased risk of ecstasy-related harm.

**Psychiatric history and genetic factors.** Personal or family psychiatric history may increase the likelihood that ecstasy users experience symptoms of depression or anxiety. Aetiological models for depression and anxiety in general population studies indicate a significant genetic component to these disorders (American Psychiatric Association, 2000; Kendler, Gardner, & Prescott, 2002; Kendler, Gardner, & Prescott, 2006), with the genetic component of depression estimated to be approximately 40-50% and 30-40% for anxiety disorders (Hettema, Neale, & Kendler, 2001; McGuffin et al., 2003).
With respect to ecstasy users, it has been suggested that people with a history of depression may be at heightened risk of experiencing adverse effects of ecstasy (Falck et al., 2006), and in particular, Parrott (2006) hypothesised that people with heightened psychiatric vulnerability, such as a history of depression, will be more likely to experience adverse subacute effects on mood. Despite these hypotheses, few studies have investigated the role of personal or family psychiatric history on mood symptoms in the short or long term. In fact, many subacute and long-term studies have excluded participants with a personal psychiatric history (Daumann, Pelz, Becker, Tuchtenhagen, & Gouzoulis-Mayfrank, 2001; Daumann et al., 2004; Fingeret et al., 2005; Gamma et al., 2001; Lamers et al., 2006; MacInnes et al., 2001; Medina & Shear, 2007; Roiser & Sahakian, 2004; Verheyden et al., 2002; Verkes et al., 2001; Yip & Lee, 2005) and in some cases also those with a family psychiatric history (Liechti et al., 2001; Sumnall et al., 2004). This may mean that the prevalence of depressive and anxiety symptomatology in ecstasy users may be higher than currently depicted in the literature.

Although some studies have collected data on personality trait factors and baseline psychopathology, these measures have been used to check the comparability between the ecstasy-using and control groups (e.g., Curran et al., 2004; Huxster et al., 2006). To date, no study has looked at whether there is a relationship between these premorbid factors and the likelihood of experiencing lowered mood, anxiety or increased aggression following ecstasy use.

In a study looking at problematic versus nonproblematic ecstasy use, Soar and colleagues (2006) found that ecstasy users that said “yes” to the question: “Have you experienced any problems, which you attribute to your ecstasy use?”, were more likely to have a personal or family history of psychopathology compared to nonproblematic users, and scored higher on measures of current psychopathology compared to nonproblematic ecstasy users, polydrug controls and illicit drug-naïve controls (Soar, Turner, & Parrott, 2006). The authors concluded that ecstasy-related psychopathology may be due to an interaction of premorbid vulnerability and heavy lifetime use. However, it may also be that ecstasy is exacerbating preexisting symptoms or that shared aetiological factors are contributing to both a heavy pattern of drug use and psychopathology.

More specifically, it has been hypothesised that a particular gene, the serotonin transporter, may play a role in vulnerability to ecstasy-induced neurotoxicity (Roiser, Cook, Cooper,
Rubinsztein, & Sahakian, 2005). The serotonin transporter gene is an obvious candidate for genetic studies exploring the aetiology of depression and anxiety, given the role of serotonin in the aetiology of these disorders (Laucht et al., 2009). The serotonin transporter gene regulates the magnitude and duration of serotonergic responses and thus contributes to many physical functions such as sleep, appetite, motor activity and psychological processes such as mood and cognition (Lesch et al., 1996). The coding of the serotonin transporter gene contains a polymorphism which produces two alleles: L (“long”) and S (“short”) (Lesch, et al., 1996). It has been found that the S allele is less efficient, resulting in reduced expression of the serotonin transporter and less reuptake of serotonin than the L allele (Lesch, et al., 1996). Consistent with this, individuals with the S allele have been found to have elevated risk for anxiety-related personality traits (Lesch et al., 1996) and depression (Furlong et al., 1998), particularly in the context of multiple stressful life events (Caspi et al., 2003). However, the findings have been mixed. A recent meta-analysis found that 5-HTTLPR genotype did not predict depression, either alone or in combination with stressful life events (Risch et al., 2009).

In a study examining the role of the serotonin transporter and psychological functioning in ecstasy users, Roiser et al. (2005) found that ecstasy users carrying the S allele of the serotonin transporter gene showed abnormal emotional processing, greater depressive symptomatology on the BDI, and were more likely to be classified as depressed (according to the BDI) than those without the S allele. This was not the case for the cannabis-using or non-illicit drug using controls. The authors concluded that ecstasy users carrying the S allele may be at greater risk of serotonin-related emotional dysfunction. Further research is clearly needed to identify whether a personal or family history of psychiatric disorder and more specifically, the S allele of the serotonin transporter, are associated with elevated mood symptoms amongst ecstasy users and whether these factors may increase the risk of ecstasy-related harm.

Life stress and trauma. Adverse life events, such as trauma and life stress, have been identified as a key environmental risk factor for depression, anxiety and substance (ab)use (Kendler et al., 2002, 2006; Kessler, 1997; McCauley, Kern, Kolodner, Dill, & Schroeder, 1997). Exposure to multiple adverse life events has also been shown to further increase the risk of psychopathology (Chapman et al., 2004; Copeland, Keeler, Angold, Costello, 2007), and childhood trauma is a particularly strong risk factor for co-occurring anxiety, mood, and substance use disorders (De Graaf, Bijl, Smit, Vollebergh, & Spijker, 2002). In a study looking at the psychosocial profile of ecstasy users, Singer and colleagues found
that ecstasy users reported more experiences of childhood abuse and neglect, were more likely to be depressed, and exhibited more severe levels of substance use than ecstasy-naïve drug-using controls (Singer, Linares, Ntiri, Henry, & Minnes, 2004). The authors hypothesised that these childhood experiences may have precipitated their later polydrug use. Similarly, life stress has been found to be associated with current depressive symptomatology among former chronic ecstasy users (MacInnes et al., 2001). This association may relate to ecstasy users having poorer coping strategies for dealing with life stress, thus increasing their risk of depression. Alternatively, it may reflect a more stressful life situation, possibly due to or being exacerbated by their drug use.

Coping style. Given the proposal that the more severe levels of depressive/anxiety symptoms in ecstasy users may be associated with the use of ecstasy to cope with pre-existing mood symptoms (Huizink et al., 2006; Lieb et al., 2002), coping style may be a particularly strong risk factor for mood symptoms amongst ecstasy users. However, there is a currently a lack of research exploring the coping styles of ecstasy users.

Coping refers to the way a person manages or responds to a stressful event (Lazarus & Folkman, 1984). The literature traditionally refers to two coping categories: problem or task-focused coping and emotion-focused coping (Endler & Parker, 1994; Lazarus & Folkman, 1984). Research findings have consistently found that task-focused coping (e.g., problem solving) is negatively associated with psychological distress, while emotion-focused coping, which relates to managing or regulating one’s emotional response to a stressful event (e.g., worrying, blaming oneself), has been associated with poorer psychological and behavioural adjustment, including depression and anxiety (Endler & Parker, 1994; McWilliams, Cox, & Enns, 2003) and substance use (Cooper, Russell, & George, 1988; Staiger, Melville, Hides, Kambouropoulos, & Lubman, 2009). A third coping category, avoidance, is also cited in the literature. Avoidance coping has been conceptualised as both denial of the problem (e.g., Lazarus & Folkman, 1984) and distracting oneself from the problem or seeking social support (Endler & Parker, 1994). Although there are mixed findings reported in the literature, emotion-focused and avoidant coping have been found to increase risk of psychological symptoms following trauma exposure (Gil, 2005; Spaccarelli, 1994). Given these findings, the experience of depression/anxiety symptoms among ecstasy users may be associated with an emotion-focused rather than task-focused coping style, particularly in those with a history of trauma.
The only known study that has looked at coping styles in ecstasy users compared how ecstasy users, ecstasy-naïve drug users (e.g., alcohol, cannabis, amphetamine users) and nondrug users cope with loneliness (Rokach & Orzech, 2003). They found that ecstasy users displayed different coping strategies compared to both control groups. Specifically, ecstasy users engaged in more distancing/denial and social support, compared to both groups; more increased activity and less internal reflection/acceptance and religion/faith than the nondrug users; and scored higher on self-development and understanding than the ecstasy-naive drug users. The finding regarding internal reflection contrasts with other research that has found that many ecstasy users report that ecstasy increased their self-awareness and introspection (Rodgers et al., 2006). Further, this study was limited by a number of factors. Data on drug-use variables (e.g., lifetime ecstasy and other drug use) or time since last use of drug were not reported. This limits conclusions about the relationship between extent of drug use and coping styles and suggests that subacute mood effects may have affected responses. Further, this study is limited to how drug users cope with loneliness, rather than looking at how they cope with stressful life events in general. Given that this is the only known study looking at coping in ecstasy users, and its limitations, further research in this area is clearly needed.

4.2 Patterns of drug use

Severity of use and lifestyle factors. Findings from retrospective and prospective studies indicate that patterns of drug use, such as frequency and severity of drug use, as well as the ecstasy-using environment, are associated with subacute and long-term mood effects. As outlined in section 2.2, severity of ecstasy and other drug use has been associated with more severe depression and anxiety symptoms. Although the findings have been mixed regarding severity of use of individual substances, including ecstasy, the literature suggests that a heavier pattern of drug use in general is associated with more severe mood symptoms.

In a retrospective study of 430 ecstasy users, Verheyden et al. (2003a) found that males reporting low midweek mood had been using ecstasy for longer and currently used ecstasy less frequently. Further, the number of substances taken whilst coming down from ecstasy has been associated with a greater number of self-reported ecstasy side effects (Topp et al., 1999), and significant correlations between mood the day after ecstasy use and baseline ecstasy measures have been reported (Curran et al., 2004; Huxster et al., 2006; Pirona &
Specifically, Pirona and Morgan (2009) found that higher scores on the ‘happy’ and ‘sociable’ scales and lower scores on the ‘anxiety’ scale were related to smaller usual doses of ecstasy. Higher scores on the ‘irritable’ and ‘aggressive’ scales were associated with younger age of first use, and higher ‘nervous’ scores the day after ecstasy use were related to greater lifetime ecstasy use. Similarly, Huxster et al. (2006) found that negative mood the day after ecstasy use correlated with frequency of ecstasy use per month, lifetime ecstasy use and negatively correlated with time since last use. With respect to aggression, Curran et al. (2004) found significant correlations between self-reported aggression four days after ecstasy use and frequency and years of ecstasy use. However, given that all of these analyses did not control for baseline mood scores, it is possible that premorbid differences impacted upon the findings and it remains unclear whether these variables are related to increased risk of experiencing these mood symptoms following ecstasy use.

In contrast, Verheyden et al. (2002) calculated change scores for mood, as measured with the BDI. They found that amongst females, the number of ecstasy tablets taken at day 0 positively correlated with mood change score from day 0 to day 4, consistent with animal studies indicating a dose-dependent relationship between MDMA and neurotoxicity (Green et al., 2003). However, as day 0 mood was measured on the night of drug use it is not clear whether a greater number of pills is associated with particularly low BDI scores at day 0, consistent with the positive subjective effect of ecstasy on mood, or are associated with particularly high scores on the BDI at day 4, consistent with subacute mood symptoms, or a combination of both.

In contrast to the above prospective findings, an Internet study by Parrott et al. (2006) found that retrospective reports of subacute effects on mood and cognition were generally independent of amount of ecstasy consumed. Rather, they found that participants who danced ‘all the time’ while on ecstasy reported significantly more problems in the days after ecstasy use, including depression, poor concentration, memory problems and difficulties in organisation, and significantly more long-term depression, memory problems and weight loss, compared with those who danced less. Similarly, those reporting feeling ‘strongly’ or ‘extremely’ ‘hot or overheating’ while on ecstasy reported significantly poorer concentration in the days following ecstasy use and more mood fluctuation and impulsivity in the long term. Importantly, these findings were generally independent of the amount of ecstasy consumed.
These findings are consistent with the animal literature indicating that MDMA neurotoxicity is greater under crowded conditions, high ambient temperatures and restricted water intake (Dafters, 1995; Malberg & Seiden, 1998). Consequently, it has been proposed that the similar hot, crowded conditions and at times, limited availability of water, at dance parties or raves may be associated with greater adverse side effects of ecstasy (Green et al., 2003; Parrott et al., 2006). Indeed, other studies indicate that ecstasy users report that ambient temperature and dancing influence the acute effects of ecstasy and some users manipulate these factors to enhance ecstasy’s effects (Bedi & Redman, 2006b). Consequently, lifestyle and ecstasy-use environmental factors may also impact upon the long-term effects on mood. Ecstasy is most commonly consumed at raves or all night dance parties where people dance for hours in a hot environment, often staying up all night leading to disrupted sleep patterns and insufficient rest (Degenhardt et al., 2004). Given that sleep deprivation can cause negative mood effects (Keane & James, 2008), these lifestyle factors alone may affect ecstasy users physical and psychological health (Parrott et al., 2001). As reported earlier, a recent study looking at the subacute effects of ecstasy on mood, found that the mood effects reported the day after ecstasy use were no longer significant after controlling for hours of sleep (Pirona & Morgan, 2009).

Recognising that lifestyle may be a potential confound in ecstasy research, Verkes et al. (2001) recruited rave attendees for their control group. They found no significant differences between the non-users, light ecstasy users (12-48 occasions in the last two years) and heavy ecstasy users (>48 occasions) on measures of depression (BDI) and anxiety (STAI). Similarly, Sumnall et al. (2004) investigated psychopathology in rave attendees in general, not simply ecstasy users. They found that severity of depressive and anxiety symptoms was related to a heavier pattern of drug use, and was not specific to ecstasy use alone.

Taken together, animal studies indicate that ecstasy dose and environmental factors increase MDMA-induced neurotoxicity. Consistent with this, there is some evidence of a relationship between ecstasy dose/environment and subacute mood effects in humans, and that a heavier pattern of drug use in general is likely to be associated with more severe mood symptoms in the long-term. However given the methodological limitations of the current literature, including poor control of pre-existing mood differences and co-occurring factors, more research is clearly needed to clarify whether dose and ecstasy environment
are risk factors for subacute and long-term mood effects. Associated lifestyle factors, such as disrupted sleep following all-night dance parties, may be associated with the observed mood symptoms in ecstasy users. Further, shared risk factors may increase the risk of both mood symptoms and a heavier pattern of drug use.

**Ecstasy use motives.** The reasons behind people’s use of ecstasy may also be associated with severity of mood symptomatology, as indicated in studies of other drug using samples. Specifically, drug use aimed at alleviating negative mood states (coping motives) has been associated with greater frequency and quantity of drug use, psychopathology, and substance-related problems (Boys & Marsden, 2003; Brodbeck, Matter, Page, & Moggi, 2007; Redman, 2008). Ecstasy is typically taken for its feelings of euphoria, increased energy to dance all night, to heighten perception of lights and music, and to enhance social interaction (Boys et al., 1999; Cohen, 1995; White et al., 2006). However, a significant number of ecstasy users report using ecstasy to feel better when down or depressed, to reduce worry, or to escape (Boys, Marsden & Strang, 2001; Ter Bogt & Engels, 2005; White et al., 2006).

Ter Bogt and Engels (2005) examined ecstasy use motives and consequences of ecstasy use amongst rave attendees. Data from the ecstasy users in their sample (n=372) indicated that the most common motives for ecstasy use were increased energy and euphoria, followed in decreasing order by sociability/flirtatiousness, sexiness, coping, self-insight and conformity. Motives were related to extent of ecstasy use and self-reported consequences of use. Specifically, high scores on the euphoria and sexiness motives were associated with heavier ecstasy use and those motivated by social/wanting to flirt reasons were using less ecstasy. High scores on euphoria, sexiness, and self-insight was associated with more self-reported positive effects of ecstasy use, while females using ecstasy to forget their problems and males using ecstasy to conform with their friends reported more negative effects of ecstasy use. However, this study was conducted at raves meaning that intoxication may have influenced responding. Furthermore, it is unclear how extent of ecstasy use and consequences of ecstasy use were measured in the regression analyses. That is, they did not state whether they combined ecstasy use variables (e.g., frequency, usual dose, length of use) or have used one parameter of use. Furthermore, the consequences of ecstasy appear to be measured by the total number of positive and negative side effects (e.g., depression/low mood; more) reported, rather than the severity of these side effects. Despite these limitations, these findings are consistent with other studies.
that demonstrate peoples’ subjective experiences of ecstasy differ depending on their
motives for use (Beck & Rosenbaum, 1994; Sumnall, Cole, & Jerome, 2006). For example,
Sumnall et al. (2006) found that those who used ecstasy purely for recreation had different
experiences than those who used ecstasy for a particular purpose, such as therapy.

In a study of 364 young polydrug users, Boys et al. (2001) investigated the perceived
functions of cannabis, amphetamines, ecstasy, LSD, cocaine and alcohol. Participants were
asked to respond yes/no to whether they had used each substance (if used more than once)
for the listed functions in the last year. The most common functions for ecstasy use were to
‘Help you keep going on a night out with friends’ (91.1%), ‘Enhance an activity such as
listening to music or playing a game or sport’ (79.6%), ‘Help you feel elated or euphoric’
(77.7%), ‘Help you to stay awake’ (72.0%) and ‘Get intoxicated’ (68.2%). Although
cannabis and alcohol were more highly endorsed as being used to ‘Make yourself feel
better when down or depressed’, almost half of the ecstasy users endorsed this item
(48.4%). Participants who reported having used ecstasy to feel elated/euphoric were
significantly older than those who had not, while those who had used ecstasy to ‘feel
better’, ‘increase confidence’ or to ‘stop worrying’ were significantly younger. Despite
collecting frequency data on drug use functions for the past year (coded 0 = never to 4 =
always), this is not reported.

5. Summary

There are a number of factors that may be associated with heightened mood
symptoms in ecstasy users. Risk factors may be non-drug related (i.e. demographic,
genetic, environmental) or relate to patterns of drug use (i.e. severity of ecstasy and other
drug use, the ecstasy-using environment). Specifically, it is possible that environmental
factors (e.g., life stress and trauma) may be associated with both mood symptoms and an
increased risk of ecstasy and other drug use, thus contributing to the elevated depressive
and anxiety symptomatology observed in ecstasy users; or that certain risk factors (e.g.
genetic predisposition) may interact with ecstasy use, leading to mood symptoms in
vulnerable individuals. Consistent with aetiological models for depression and anxiety, the
above review of the literature indicates that demographic, environmental and genetic
factors may all relate to severity of depressive/anxiety symptomatology in ecstasy users.
However, the relative contribution of ecstasy compared with genetic and environmental
risk factors for depression and anxiety have not been explored in either the subacute or
long-term literature.
The current thesis aimed to extend the current literature by focusing on risk factors for depression and anxiety symptoms in a large, heterogeneous sample of ecstasy users, while taking into consideration the methodological limitations of past research.
Chapter 2

Rationale, Aims and Hypotheses
2.1 Research Aims of the Thesis

The overarching aim of the present thesis was to increase understanding of the relationship between ecstasy and mood. To do so, the current research focused on identifying potential risk factors for depressive and anxiety symptoms amongst ecstasy users. A large number of studies have found an association between ecstasy use and mood symptoms. However, more recent studies suggest that mood symptoms relate to a pattern of polydrug use and not ecstasy per se. Secondly, given the predominance of cross-sectional designs in past research, many researchers have highlighted that pre-existing factors may be contributing to the more severe mood symptoms observed in ecstasy users. Specifically, it has been proposed that the association between ecstasy and mood may be due to the use of ecstasy to cope with pre-existing mood symptoms, consistent with longitudinal findings. However, few studies have examined what factors are associated with more severe mood symptoms amongst ecstasy users in the short and long term. Given ecstasy’s ongoing popularity and reports that ecstasy is neurotoxic to the serotonin system of laboratory animals and possibly humans, it is critical to understand what factors are related to the experience of mood symptoms in this population, and to explore who may be more vulnerable to experiencing ecstasy-related harm.

The aims of this thesis are:

1. To identify potential risk factors for current mood symptoms in ecstasy users. In doing so, the current thesis aimed to determine if ecstasy use is associated with current depressive and anxiety symptomatology, after controlling for known genetic and environmental risk factors for depression, anxiety and substance use.

2. To prospectively explore short-term risk factors for mood symptoms in a 7-day period. To this end, the research aimed to establish whether ecstasy use was associated with lowered mood, anxiety or aggression in the days following use, after controlling for potential confounds such as hours of sleep and other drug use. Second, this thesis aimed to explore potential risk factors associated with subacute mood symptoms following ecstasy use.

Together, it was hoped that this research would highlight the complex nature of the relationship between ecstasy use and depressive and anxiety symptomatology, while increasing understanding of the factors that may be associated with heightened vulnerability to experiencing mood symptoms among those that use ecstasy.
The specific hypotheses and analyses of the thesis are presented in the following three papers.

2.2 Aims and Hypotheses for Article One

Article One: ‘Depressive and anxiety symptomatology in ecstasy users: the relative contribution of genes, trauma, life stress and drug use’. Published in *Psychopharmacology.*

Article One aimed to identify (1) What variables were related to the severity of current mood symptoms in ecstasy users and (2) To determine whether ecstasy use was associated with the severity of current depressive and anxiety symptoms, after controlling for known genetic and environmental risk factors for depression, anxiety, and substance use. It was hypothesised that (1) patterns of ecstasy use (i.e. lifetime and recent ecstasy use) would be associated with the severity of current mood symptoms (i.e. depressive and anxiety symptomatology), but (2) any association between patterns of ecstasy use and severity of current mood symptoms would no longer be significant after controlling for other risk factors, including the serotonin transporter gene, lifetime trauma, recent life stress and other drug use.

2.3 Aims and Hypotheses for Article Two


Article Two expands upon the findings from Article One by prospectively exploring predictors of subacute mood effects (i.e. lowered mood, anxiety and aggression). Specifically, the aims of Article Two are (1) To investigate whether ecstasy use is associated with mood symptoms (i.e. lowered mood, anxiety or aggression) in the days following use, after controlling for potential confounds such as sleep deprivation and other drug use, and (2) To identify what factors are associated with negative mood change in a community sample of ecstasy users. It was hypothesised that 1) ecstasy use would be associated with a significant increase in depression, anxiety and aggression symptoms in the days after use, compared to baseline scores, 2) an increase in depression, anxiety or aggression in the days following ecstasy use would be related to pre-existing risk factors.
(i.e. gender, more severe baseline self-reported state depressive/anxiety symptomatology, and having a personal psychiatric history) and patterns of drug use (i.e. severity of drug use, ecstasy use environment (heat/exercise)), and 3) stressful life events and sleep disruption would significantly predict mood change in all participants.

2.4 Aims and Hypotheses for Article Three


Expanding on Article One, Article Three explores whether coping style or motives for use are significant predictors of current mood symptoms. Article Three also investigates whether ecstasy use motives and coping style help explain the relationship between the identified risk factors from Article One (trauma and life stress) and current mood symptoms. It was hypothesised that 1) coping motives for ecstasy use and emotion-focused coping would be associated with current depressive/anxiety symptomatology, 2) lifetime trauma would be related to coping motives and emotion-focused coping, 3) coping motives and emotion-focused coping would mediate the relationship between trauma and current mood symptoms, and 4) coping motives and emotion-focused coping would moderate the relationship between recent life stress and current mood symptoms.
Chapter 3

Expanded methodology
3.1 Participants

One hundred and ninety participants aged between 18 and 35 years who had taken ecstasy at least once in the last 12 months were recruited from the community in Melbourne, Australia. A subsample of 63 participants were subsequently recruited from this larger sample to participate in a brief prospective study (Study Two). All regular ecstasy users (at least monthly use over the last 6 months) and those planning to take ecstasy within one week of the baseline assessment were invited to participate in the prospective study. Participants were excluded from both studies if they were pregnant, were unable to converse fluently in English or if they had a history of a psychotic disorder.

3.2 Measures

Measures are explained within the body of each empirical article.

3.3 Procedure

Ethics approval was obtained from the Monash University Human Ethics Committee (SCERH; see Appendix 1). Participants were recruited via local universities’ job advertisement websites (Monash University, University of Melbourne, La Trobe University and Deakin University), posters placed around Monash University, Clayton campus, electronic newsletters received by Monash University staff and students (monash memo and ebulletin), a national dance music website (inthemix.com.au), an ecstasy test results website (pillreports.com), a local newspaper (Herald Sun) and a free street music magazine (Beat), as well as distributing flyers in cafes, music stores, and dance music events (see Appendix 2 for advertising material). Written permission was obtained from all venues prior to advertising (see Appendix 3). Finally, a ‘snowballing’ technique (Solowij, Hall, & Lee, 1992) was used to recruit the friends, family and acquaintances of individuals participating in the study and people known to the doctoral candidate.

Potential participants were initially screened for eligibility over the phone including age, ecstasy use, pregnancy and history of psychosis. Interested participants who met the eligibility criteria were sent the Study 1 Explanatory Statement to read (see Appendix 4). Potential participants were subsequently telephoned and given the opportunity to ask questions relating to the Explanatory Statement. No participant declined to participate after reading the Explanatory Statement. To reduce potential subacute drug effects, participants
were requested to abstain from: taking ecstasy for at least seven days prior to participating, using other recreational drugs for at least 24 hours (except tobacco and caffeine) and drinking alcohol within 12 hours of the interview. Participants completed a semi-structured interview (see Appendix 5 for interview pack), a set of self-report questionnaires (see Appendix 6 for questionnaire pack) and provided a saliva sample (see Appendix 7 for biohazard collection protocol). Participation took an average of one hour to complete.

Interviews were conducted at a mutually convenient location including private interview rooms at Monash University, Orygen Youth Health Research Centre or in a public location such as cafes, parks and libraries. For all interviews conducted in public places, participants were asked if they felt comfortable talking openly about their drug use and mental health in that location. To ensure confidentiality was maintained, participants provided verbal consent, not written, and were advised that submitting their questionnaire pack was confirmation of their consent (see Appendix 8 for Study One consent form). Participants were not required to give their name and no names or other identifying information were recorded on any interview or questionnaire form; participants were advised not to include any information regarding their drug use via email; all contact details and records of communication were deleted following participation; and saliva samples were destroyed after genetic analysis. Participants were reimbursed $25 for their time and travel-related expenses.

Following the baseline assessment, all potential participants for the prospective study were given the Explanatory Statement to read (see Appendix 9). Potential participants were given the opportunity to ask any questions and the consent form was completed (see Appendix 10). No participant declined to participate after reading the Explanatory Statement. All consenting participants were asked if they were planning on taking ecstasy over the next week. If yes, the researcher arranged to contact the participant the day following planned ecstasy use and again two days later. If not, participants were telephoned on Sunday evening and again on Tuesday evening. If participants were unsure on whether they would take ecstasy or when they would take it, they were asked to text the researcher so that the researcher could contact them the day after use. Telephone interviews were conducted between 6pm and 8pm unless the participant was unavailable at this time (see Appendix 11 for telephone interview pack).

If it became evident that a participant was experiencing psychological distress they were provided with the contact details of a number of counselling services (see final page of
explanatory statement; Appendix 4) and risk procedures were implemented (see Appendix 7). One participant became distressed during the baseline interview when discussing recent stressful life events. Counselling options were discussed and the participant said she was fine to continue the interview. Furthermore, if a participant responded to the item on the Mood and Anxiety Questionnaire indicating the presence of recent thoughts of death or suicide, an assessment was conducted according to Appendix 7. Forty-three participants reported some thoughts of death or suicide over the last week. The majority of these were relating to thoughts of death, not suicide. All participants expressing suicidal ideation were assessed. The majority presented with a mild level of distress. Three participants presented with a moderate level of distress, with one participant requiring follow up the next day. No participants presented with a severe level of distress and based on risk assessment, no one was deemed at high risk of suicide.

3.4 Statistical analysis

Statistical analyses are described in the body of each empirical article.
CHAPTER 4

Depressive and anxiety symptomatology in ecstasy users: The relative contribution of genes, trauma, life stress and drug use

This chapter comprises of an article published in *Psychopharmacology*. This journal has a word limit of 15 typewritten pages of text. The format of the article is according to the guidelines for this journal.
4.1 Introduction to article one

The following research presented in this chapter reflects the overarching aim of the current thesis: to identify potential risk factors for current mood symptoms. Specifically, given findings of neurotoxicity and a relationship between severity of ecstasy use and subclinical and clinical psychopathology, this article reflects a specific aim to identify the relative contribution of lifetime ecstasy use on mood symptoms, while controlling for known genetic and environmental risk factors.
4.2 Declaration for Thesis Chapter Four

Declaration by candidate

In the case of Chapter Four the nature and extent of my contribution to the work was the following:

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<th>Nature of contribution</th>
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<tr>
<td>Conceptualisation of study design; data collection; data analysis; conceptualisation of paper; and write up.</td>
<td>80%</td>
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The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

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<th>Name</th>
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<tr>
<td>Dr Leanne Hides</td>
<td>Provided guidance on study design, measures selection, statistical analysis and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
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<tr>
<td>Dr J. Sabura Allen</td>
<td>Provided guidance on methodology, including measures selection. Read drafts and provided feedback</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr Richard Burke</td>
<td>Genetic analysis of saliva samples</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr Dan Lubman</td>
<td>Provided guidance on study design, statistical analysis and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
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Candidate’s Signature

Date

Declaration by co-authors

The undersigned hereby certify that:

1. the above declaration correctly reflects the nature and extent of the candidate’s contribution to this work, and the nature of the contribution of each of the co-authors.
2. they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
3. they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor
or publisher of journals or other publications, and (c) the head of the responsible
academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five
years from the date indicated below:

| Location(s) | Monash University, Melbourne, Australia |

[Please note that the location(s) must be institutional in nature, and should be indicated
here as a department, centre or institute, with specific campus identification where
relevant.]

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Depressive and anxiety symptomatology in ecstasy users: The relative contribution of genes, trauma, life stress, and drug use

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Funding acknowledgements: Rebecca Scott was supported by an Australian Postgraduate Award and the project was funded by Monash University, School of Psychology and Psychiatry. Drs Hides and Lubman are supported by the Colonial Foundation.

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Abstract

Rationale Previous research has identified elevated rates of depressive and anxiety symptoms among ecstasy users, however few studies have examined which factors increase the likelihood of experiencing such symptoms. Objectives The current study aimed to determine the relationship between ecstasy use and depressive/anxiety symptomatology after controlling for known environmental and genetic (polymorphisms of the serotonin transporter gene) risk factors for depression and anxiety disorders. Methods Participants consisted of a community sample of 184 18-35 year olds who had taken ecstasy at least once in the past 12 months. Participants completed an interview and questionnaires and provided a saliva sample. Mood symptoms were assessed using the Mood and Anxiety Symptom Questionnaire (MASQ). Timeline methods were used to collect information on lifetime and recent ecstasy use, as well as recent other drug use and life stress. Trauma exposure was measured using the Composite International Diagnostic Interview (CIDI)-Trauma List. Genomic DNA was extracted from participant saliva samples. Results Neither lifetime nor recent ecstasy use were associated with the severity of current mood symptoms, either alone or in combination with genetic risk factors. Rather, lifetime trauma, recent stressful life events, the frequency of tobacco use, and recent polydrug use significantly predicted the severity of depressive and anxiety symptoms. Conclusions These results highlight the need to consider the role of environmental factors when examining the relationship between ecstasy use and mood symptoms. Whether ecstasy exacerbates such symptoms in vulnerable individuals requires further investigation using prospective designs.

Key words: Ecstasy, MDMA, depression, anxiety, serotonin transporter, trauma, life stress, risk factors
Introduction

MDMA (3,4-methylenedioxymethamphetamine) or ‘ecstasy’ is a popular recreational drug, particularly among young people, with up to 24% of Australian 20-29 year olds reporting lifetime ecstasy use (Australian Institute of Health and Welfare 2008). Although prevalence rates have stabilised in Australia in the last three years, the rates are still higher than those observed in Europe and North America (United Nations Office on Drugs and Crime 2008, 2009). Ecstasy is taken for its acute effects, including feelings of euphoria, increased energy, and greater sociability and connectedness with others (Cohen 1995; White et al. 2006). Increasing popularity and reports that ecstasy is neurotoxic to the serotonin system of laboratory animals (Ricaurte et al. 2000) and possibly humans (McCann et al. 2008) has raised concern about the potential psychological consequences of ecstasy use. While several studies have found that ecstasy users have higher levels of depressive and anxiety symptoms (Lamers et al. 2006; McCardle et al. 2004; MacInnes et al. 2001), and that greater lifetime ecstasy use is related to more severe symptomatology (Sumnall and Cole 2005; Verheyden et al. 2003), other studies have found that symptom severity is related to illicit drug use in general, not ecstasy per se (Bedi et al. 2008; Sumnall et al. 2004).

While methodological differences across studies may have contributed to these mixed findings (Bedi et al. 2008; Curran 2000), limited research has explored the role of other risk factors for depression and/or anxiety on the relationship between ecstasy use and psychopathology. Causation models for depression and anxiety disorders indicate that both genetic and environmental factors contribute to their onset (Goldberg 1994; Kendler et al. 2002, 2006). Individuals with the S (“short”) allele of the serotonin transporter gene (5-HTTLPR) have been found to have elevated risk for depression (Furlong et al. 1998) and anxiety-related personality traits (Lesch et al. 1996), and there is some evidence that ecstasy users with the S allele also exhibit abnormal emotional processing and heightened depressive symptomatology (Roiser et al. 2005).

A broad range of environmental factors have been associated with increased risk of psychopathology. In particular, adverse life events, such as trauma and life stress, have been identified as a key environmental risk factor for depression, anxiety and substance (ab)use (Kendler et al. 2002, 2006; Kessler 1997, McCauley et al. 1997). Exposure to multiple adverse life events has also been shown to further increase the risk of psychopathology (Chapman et al. 2004; Copeland et al. 2007), and childhood trauma is a particularly strong risk factor for co-occurring anxiety, mood, and substance use disorders (De Graaf et al. 2002). In a study looking at the psychosocial profile of ecstasy users, Singer and colleagues found that ecstasy users reported more experiences of childhood abuse and neglect, were more likely to be depressed, and exhibited more severe levels of substance use than ecstasy-naïve drug-using controls (Singer et al. 2004). Life stress has also been found to be associated with current depressive symptomatology among former chronic ecstasy users (MacInnes et al. 2001).

The relationship between ecstasy use and mood symptoms remains poorly understood, despite evidence that ecstasy users report greater depressive and anxiety symptomatology compared to non-drug and ecstasy-naïve drug-using controls. The current study aims to determine if ecstasy use is associated with current depressive and anxiety symptomatology, after controlling for known genetic and environmental risk factors for depression, anxiety, and substance use. It was hypothesised that (1) lifetime and recent ecstasy use would be associated with the severity of current depressive and anxiety symptoms, but (2) any association between...
lifetime ecstasy use and severity of current depressive and anxiety symptoms would no longer be significant after controlling for other predictor variables, including 5-HTTLPR genotype, lifetime trauma, recent life stress and other drug use.

Materials and methods

Participants

Participants consisted of a community sample of 190 individuals aged between 18 and 35 years who had taken ecstasy at least once in the last 12 months. Participants were recruited from Melbourne, Australia, via advertisements in university job websites and newsletters, a national dance music website, a free street music magazine and a local newspaper. Flyers were also distributed in locations frequented by young people such as cafes, music stores, and dance music events. A ‘snowballing’ technique (Solowij et al. 1992) was also used to recruit the friends, family and acquaintances of individuals participating in the study. Participants were excluded if they were pregnant, were unable to converse fluently in English or if they had a history of a psychotic disorder.

Measures

Substance use. Lifetime ecstasy use was calculated using a context-based timeline method, which asked participants to recall when they first took ecstasy and then prompted them to identify contextual information (e.g., periods of work, study, travel, living arrangements, relationships) to assist recall of their patterns of ecstasy use along a timeline. Context-based timeline methods demonstrate adequate test-retest reliability amongst people with substance use disorders (Anglin et al. 1993) and the use of timelines with life events increases recall accuracy of past drug use (Del Boca and Darkes 2003; Shillington et al. 1995). Duration of ecstasy use was calculated by subtracting age of first use from current age. A score of zero was recoded to .5 for 12 participants who had recently initiated ecstasy use.

Participants were also asked to report lifetime use (Yes/No), age of first use, and the most frequent use (never used, less than monthly, monthly, 2-3 times a month, weekly, daily or almost daily) of alcohol, tobacco, cannabis, amphetamines, cocaine, hallucinogens, inhalants, opiates, benzodiazepines/sedatives, ketamine, and gamma-hydroxybutyric acid (GHB). The total number of substances consumed was used as a measure of lifetime polydrug use. Recent drug use was assessed using the Timeline Followback (TLFB) method for the preceding 28 days (Sobell and Sobell 1992). This method retrospectively assesses the frequency and quantity of recent substance use anchored against life events (see Life Stress measure below) to assist recall. The TLFB has well-established reliability and validity for assessing alcohol and illicit drug use (Fals-Stewart et al. 2000).

Mood symptoms. Current depressive and anxiety symptoms were measured using the 62-item Mood and Anxiety Symptom Questionnaire - Short Form (MASQ; Watson and Clark 1991). This self-report tool provides two scales of general distress (GD) symptomatology (GD Depressive and GD Anxious), a depression-specific scale (Anhedonic Depression) and an anxiety-specific scale (Anxious Arousal). Participants indicated how much they had experienced each symptom over the previous week (1 = not at all
to 5 = extremely). The MASQ demonstrates excellent convergent and discriminant validity between anxiety and depressive symptoms in both clinical and non-clinical samples (Watson et al. 1995) and has been found to have good sensitivity and specificity in predicting mood disorders in clinical samples (Buckby et al. 2007). All four subscales demonstrated very good internal consistency with the current sample (Cronbach’s $\alpha = .87 - .92$).

Serotonin transporter. Genomic DNA was extracted from participant saliva samples (Heils et al. 1996). 5-HTTLPR was determined by polymerase chain reaction using Gotaq HotStart polymerase (Promega), followed by identification of the ‘short’ (S) and ‘long’ (L) alleles. Genetic analyses were conducted at Monash University by one of the authors (R.B.).

Trauma. The Composite International Diagnostic Interview (CIDI)– Trauma List (World Health Organisation 1997) was used to identify the incidence of life events meeting DSM-IV criterion A for exposure to a traumatic event (American Psychiatric Association 2000). The first nine items relate to specific traumas experienced by the participant (e.g., physical assault). The last two items include an ‘other’ item for traumatic events not included in the previous nine items. The final item refers to experiencing ‘a great shock’ in response to someone close to them being exposed to a traumatic event. If participants respond yes to an item, they are asked if at the time they experienced feelings of ‘intense fear, helplessness or horror’. Participants were given a score of 1 if they responded ‘yes’ to both questions relating to each item, with a total possible lifetime trauma score of 11.

Life stress. Participants were asked if they had experienced any major stressful life events in the month preceding the interview while completing the TLFB. Life events were defined according to subject areas from the Psychiatric Epidemiological Research Interview (PERI)– Life Events Scale (Dohrenwend et al. 1978). Subject areas included employment and study (e.g., lost job; university exams), finances (e.g., went off benefits), relationships and family (e.g., break up of romantic relationship; family conflict), residence (e.g., moved house), health (e.g., physical illness) and crime and legal matters (e.g., victim of assault). Life events were only included if participants reported finding the event stressful. Events were tallied to provide a total recent stressful life events score. Participants also rated how stressed they felt in general over the past month (subjective stress; 1 = not stressed at all to 10 = extremely stressed).

Procedure

The study was approved by the Monash University Human Ethics Committee. Potential participants were initially screened via a brief telephone interview to ensure they met inclusion criteria. To minimise potential subacute drug effects, participants were requested to abstain from: taking ecstasy for at least seven days prior to participating, using other recreational drugs for at least 24 hours, with the exception of tobacco and caffeine, and drinking alcohol within 12 hours of the interview.

Individuals who provided informed consent to participate in the study were interviewed face-to-face for approximately one hour by a postgraduate clinical psychology student (R.S.), and were asked to provide a saliva sample for genetic analysis. All participants were reimbursed AUD$25 for their time and travel-related
expenses.

Results

Participation rate and data screening

Of the original 190 consenting participants, six participants were excluded due to recent drug use ($n=4$) and lack of English fluency ($n=2$). Seven outliers on the MASQ subscales were identified with a box plot and truncated to one above the outlier scores. There were seven missing data points for the 5-HTTLPR genotype due to failed or missing biological analyses. Following initial data screening, logarithmic transformations were used on lifetime ecstasy use, greatest number of ecstasy pills taken in a 12-hour period, recent polydrug use and recent ecstasy use to reduce skewness and kurtosis and improve normality. The serotonin transporter gene was dummy coded (gene_dummy1 and gene_dummy2). Interaction terms were then created with genotype by ecstasy use to be included in the regressions. Multivariate outliers were identified using Mahalanobis distance ($p < .001$). An alpha level of .01 was required for statistical significance for all analyses to account for the increased likelihood of type 1 error caused by the multiple comparisons made. All data were analysed using SPSS version 17 (SPSS Inc., Chicago, IL, USA).

Sample characteristics

The final data set contained 184 participants (87 males; 97 females) with a mean age of 23.3 ($SD=4.0$) years. The majority of participants identified themselves as Caucasian ($n=128; 72.3$%), followed by Asian ($n=12; 6.5$%), Indian ($n=11; 6.0$%), mixed ethnicity ($n=10; 5.4$%), and a small minority identified themselves as indigenous Australian ($n=2; 1.1$%). One hundred and ten participants (59.8%) were born in Australia and 169 (91.8%) reported English as the main language spoken at home. A large number of participants were currently enrolled in tertiary education ($n=122; 66.3$%), 51 were working full time (27.7%) and nine (4.9%) were unemployed. Ninety percent ($n=166$) of the sample had completed or were currently undertaking post-secondary school qualifications. Fifty-one (27.7%) participants reported that they had received one or more psychiatric diagnoses during their lifetime. The most commonly reported diagnosis was unipolar depression ($n=35; 19.0$%), followed by an anxiety disorder ($n=17; 9.2$%). Five (2.7%) participants reported a history of a substance use disorder (alcohol, methamphetamine and cocaine dependence) and one reported a diagnosis of posttraumatic stress disorder (PTSD; 0.5%). Fifteen (8.2%) reported that they had taken prescribed medication for a psychiatric or psychological problem in the past month.

Substance use

Self-reported lifetime and recent substance use are presented in Table 1. Participants had tried between 2 and 12 of the substances reported in Table 1 (Lifetime polydrug use; $M=7.4; SD=2.4$). Age at first ecstasy use ranged from 12 to 31 years, and duration of ecstasy use ranged from less than one year to 18 years ($M=4.2; SD=3.6$). Lifetime ecstasy use ranged from half a pill to 5332 pills ($M=172.4; SD=507.4$), and typical ecstasy dose ranged from half a pill to eight pills ($M=1.7; SD=.8$). With respect to recent drug use, participants had taken a mean of 2.3 other substances in the preceding 28 days, excluding ecstasy ($SD=1.4; range=0-9$).
Serotonin transporter

Forty-six participants were homozygous for the S allele of the 5-HTTLPR (SS=26.0%), 89 were heterozygous (SL=50.3%) and 42 were homozygous for the L allele (LL=23.7%).

Trauma and life stress

Rates of self-reported traumatic events are reported in Table 2. Twenty-nine percent of the sample reported no history of traumatic events, 22.8% reported one, 15.2% reported two, 10.9% reported three, and 21.7% reported four or more traumas in their lifetime (M=1.9, SD=1.8; range=0-10). Participants reported a mean of 1.3 stressful life events for the past month (SD=1.2; range=0-5), and subjective stress ratings for the past month ranged from one to nine (M=4.4; SD=1.9).

Mood

Seventeen participants (9.2%) met the proposed cut off of 76 on the depression-specific subscale of the MASQ indicative of current depression, as established in an Australian study of adolescents and young adults (Buckby et al. 2007).

Main analyses

Depressive and anxiety symptomatology: Correlational analyses

Pearson’s correlations between the four MASQ subscales (DV: dependent variables) and ecstasy use are presented in Table 3. A range of other demographic, drug use, genetic and environmental variables were included in the analysis to identify other predictor variables. Examination of the correlations indicated that log lifetime ecstasy use was not associated with the severity of current depressive and anxiety symptomatology. However, as previous research has found a relationship between lifetime ecstasy and severity of depressive and anxiety symptoms, this variable was included in subsequent regressions. Log of greatest number of ecstasy pills taken in a 12-hour period did not correlate with any MASQ subscale (r=0.00 to -.12, p >.05). Due to a high correlation between the two recent ecstasy use measures, these variables were combined to create an intensity of recent ecstasy use variable that was used in subsequent analyses (number of pills/days of ecstasy use). Lifetime frequency of tobacco use significantly correlated with Anxious Arousal and GD Anxious and was identified as a covariate. Age at first use of cannabis significantly correlated with Anxious Arousal (r=-.20, p<.01), indicating that a younger age of cannabis onset was associated with more severe current anxiety symptoms. No other correlations between frequency of use and age of onset of individual drugs and the DVs were found.

With respect to recent drug use, number of drug-using days in the last 28 days (excluding tobacco), and specifically, number of alcohol using days, ecstasy using days and number of ecstasy pills consumed in the last 28 days negatively correlated with Anhedonic Depression (r=-.19, -.19, -.23, -.25, respectively, p<.01), indicating that more severe current depressive symptoms were associated with less recent drug use and...
specifically, less ecstasy and alcohol use. Self-reported lifetime history of unipolar depression and/or an anxiety disorder significantly correlated with all of the DVs (Spearman’s Rho correlations). No other correlations between the DVs and demographic or genetic variables were found. However, as gender differences have consistently been observed in the general population with regards to depression and anxiety (Australian Bureau of Statistics 2007), gender was included as a covariate in all subsequent analyses.

Lifetime and log recent polydrug use were also entered as covariates in the regressions. Lifetime trauma and measures of both stressful life events and subjective life stress correlated with the DVs. Recent stressful life events was entered into the regression as this was considered to be a more objective measure of recent stress.

Depressive and anxiety symptomatology: Regression analyses

A series of hierarchical regression analyses were conducted to examine the relationship between ecstasy use and the severity of depressive and anxiety symptoms, as measured by the four MASQ subscales, after controlling for demographic, genetic and environmental risk factors, including other drug use. The predictor variables were entered in four steps (1) gender, history of unipolar depression and/or an anxiety disorder and 
$5$-HTTLPR genotype (gene_dummy1 and gene_dummy2); (2) environmental factors: recent stressful life events and lifetime trauma; (3) other drug use: lifetime polydrug use and tobacco frequency, and (4) ecstasy use and ecstasy by $5$-HTTLPR genotype interaction terms. The influence of lifetime and intensity of recent ecstasy use were examined in two separate sets of analyses.

**Lifetime ecstasy use.** One participant was identified as a multivariate outlier and was deleted from the analysis. Table 4 shows self-reported history of unipolar depression and/or an anxiety disorder significantly predicted the MASQ subscale scores. Neither gender nor $5$-HTTLPR genotype were significant predictors. Of the drug variables, frequency of tobacco use significantly predicted GD Anxious. Recent life stress was a significant predictor of the Anhedonic Depression, GD Depressive and GD Anxious subscales. Lifetime trauma was a significant predictor of Anxious Arousal. However, this was no longer significant after entering other drug use factors. After controlling for other variables, the extent of lifetime ecstasy use continued to have no association with the level of current depressive and/or anxiety symptomatology. The genotype X log lifetime ecstasy interaction was also nonsignificant. Substitution of stressful life events with recent subjective life stress produced comparable findings.

**Recent ecstasy use.** One participant was identified as a multivariate outlier and was deleted from the analysis. Consistent with the initial correlation, log recent ecstasy use was not predictive of any MASQ subscale after controlling for recent life stress, trauma, $5$-HTTLPR genotype, gender, history of depression/anxiety disorder and log recent polydrug use (see Table 5). The genotype X log recent ecstasy use interaction was also nonsignificant. In contrast to lifetime polydrug use, after excluding participants currently on psychotropic medication, log recent polydrug use was a significant predictor of GD Anxious with participants who had taken a greater number of drugs in the preceding 28 days reporting more severe current anxiety symptoms.

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1 When the regression analyses were conducted with only those participants with at least moderate lifetime ecstasy use (>20 pills; n=114), log lifetime ecstasy use continued to have no relationship with the MASQ subscales and the genotype X log lifetime ecstasy interaction continued to be nonsignificant.
Discussion

In this sample, we found that neither lifetime nor recent ecstasy use were associated with current mood symptoms either before or after controlling for other genetic and environmental risk factors for depression, anxiety and substance (ab)use. In contrast, lifetime frequency of tobacco and a younger age of cannabis onset were associated with more severe current anxiety symptoms. Furthermore, after excluding participants currently taking prescribed psychotropic medication, recent polydrug use was associated with current general distress anxiety symptoms. While, as expected, a lifetime history of unipolar depression and/or an anxiety disorder significantly predicted current mood symptoms, no other associations between demographic or genetic variables and psychopathology were found. Instead, lifetime history of trauma and recent stressful life events were significant predictors of the severity of current depressive and anxiety symptoms, as hypothesised. In addition, when stressful life events was substituted with the subjective stress measure, stress continued to be associated with general distress symptoms and the depressionspecific subscale of the MASQ. Together, these findings indicate that in this community sample of ecstasy users, current depressive and anxiety symptoms were related to environmental risk factors including other drug factors, rather than 5-HTTLPR genotype or recent or lifetime ecstasy use.

The lack of an association between ecstasy use and current depressive/anxiety symptomatology is contrary to our hypothesis. However, these findings are consistent with other studies finding no relationship between lifetime or recent ecstasy use and depressive and anxiety symptoms (Abdallah et al. 2007; Daumann et al. 2004; Medina and Shear 2007). Indeed, mixed results have been found with regard to the relationship between the severity of mood symptoms and the use of specific substances, (including ecstasy), and that a heavier pattern of drug use in general may be more strongly related to the severity of depressive and anxiety symptoms (e.g., Bedi et al. 2008; Sumnall et al. 2004). However, methodological differences between studies may be contributing to these mixed findings, including key differences in how drug use is defined (e.g., lifetime quantity, occasions of use, frequency of use, recent use) and measured (e.g., single question estimates, frequency by quantity calculations, context-based timeline methods; see Bedi and Redman 2006), as well as the statistical analyses and covariates used. Other limitations of these studies include the use of small sample sizes and the lack of appropriate control groups. Nonetheless, 17 (9.2%) ecstasy users in the current study met the diagnostic cut off for current depression on the MASQ (Buckby et al. 2007), which is an appreciably higher rate than Australian national data on the prevalence of depression in the previous 12 months (4.1%; Australian Bureau of Statistics 2007). Similarly, the rate of self-reported lifetime depression in the current sample (19.0%) is greater than the Australian lifetime prevalence for a depressive episode (11.6%; Australian Bureau of Statistics 2007). While the results of the current study provided no evidence that the level of ecstasy use was associated with the severity of depression or anxiety symptoms, there is clearly a higher prevalence of depressive symptoms and disorder in our sample of ecstasy users. Whether these results reflect a specific vulnerability among ecstasy users or are reflective of a vulnerability among drug users in general warrants further investigation. There may also be other yet to be identified premorbid variables contributing to both mood symptoms and a heavier pattern of drug use in some individuals, which may also be contributing to differences across studies. Importantly, the current findings do not negate that ecstasy use may lead to negative psychological outcomes for some individuals. Many ecstasy users report experiencing mood symptoms and disrupted functioning in the short and long term that they attribute to their ecstasy use (Topp et al. 1999). It is possible that these negative side effects may be independent from severity
of lifetime use.

The lack of significant associations between 5-HTTLPR genotype and genotype X ecstasy interaction with current mood symptoms contrasts with past findings with ecstasy users (Roiser et al. 2005). However, it is consistent with the results of a recent meta-analysis finding that 5-HTTLPR genotype did not predict depression, either alone or in combination with stressful life events (Risch et al. 2009). Furthermore, the same meta-analysis found a strong relationship between the number of stressful life events and risk of depression, consistent with the current findings.

While the results of the current study are new and require replication, they indicate that the experience of depressive and anxiety symptoms in ecstasy users was associated with factors related to environmental vulnerability rather than lifetime or recent ecstasy use, consistent with our hypotheses. Recent stressful life events were associated with more severe depression-specific and general distress symptoms. Lifetime trauma significantly predicted current anxiety symptoms but not depression-related symptoms, and a greater number of lifetime trauma experiences were associated with more severe anxiety symptoms. While it is difficult to determine the direction of the relationship between these variables due to the cross-sectional nature of the study, a history of trauma has been associated with increased risk for ecstasy and other drug use, as well as depressive/anxiety symptoms, in both community and clinical samples (McCauley et al. 1997; Singer et al. 2004; Creamer et al. 2001; Fergusson and Lynskey 1997; Simpson and Miller 2002; Lubman et al. 2007). Consistent with this, frequency of tobacco use was also associated with trauma in the current sample. This vulnerability may also increase the risk of further stressful life events in an individual’s immediate environment leading to increased risk of depressive and anxiety symptoms (Risch et al. 2009) and substance use (Staiger et al. 2009). This may explain why after controlling for recent stressful life events, trauma was no longer related to anxiety-related general distress symptoms. That is, life stress may mediate the relationship between trauma and current distress symptoms. Clearly, a prospective study is required to fully describe the complex relationship between these variables.

There are a number of limitations to the current study. These include the use of a cross-sectional design and the reliance upon retrospective self-report measures that may be subject to recall bias. It is also possible that the presence of current mood symptoms inflated recall of past adverse life events (Schraedley et al. 2002). The reliability of self-reported recent drug use was also not confirmed using biological analysis, although previous studies have indicated ecstasy and other drug users provide reliable data (Anglin et al. 1993; Bedi and Redman 2006). Furthermore, although detailed data was obtained on lifetime ecstasy use, the content of ecstasy tablets consumed was not determined. It is possible that participants unknowingly consumed other substances and not MDMA (Quinn et al. 2007). The measures of other drug use, including drug use frequency and the number of drugs tried (polydrug use), rather than the lifetime quantity of use, is a further limitation of the current study. These measures may not have been sensitive enough to reveal possible associations between other drug use factors and current symptoms. Although participants were required to abstain from ecstasy use for one week prior to the assessment, it is possible that subacute effects may have affected the data as the MASQ asks about mood symptoms in the past week. The effects of other drug use may also have impacted on our results, as only 12- and 24-hour abstinence periods were used for alcohol and other substances, respectively. However, consistent with other papers in this area (e.g., Bedi et al. 2008), a
24-hour abstinence period was implemented for cannabis to balance potential subacute and withdrawal drug effects and participant recruitment factors. Specifically, subacute cannabis effects can last for more than seven days (Pope et al. 2001) and abstinence periods longer than one day may lead to withdrawal symptoms (Kouri and Pope 2000). Furthermore, given that we aimed to have a representative sample of ecstasy users with a range of other drug-using habits, an abstinence period of 24 hours was used in order to include regular users of other drugs. No significant correlations were found between days since last use of individual drugs and the MASQ subscales. Finally, as the interviewer was one of the authors (R.S.), this introduces a potential reporting bias as she was not blind to drug use. However, given that many of the measures were self report scales, including those assessing depressive/anxiety symptomatology, this reduces the risk of bias.

The strengths of the current study include the recruitment of a large sample of ecstasy users with varying levels of use. Furthermore, lifetime ecstasy use was measured using a context-based timeline to aid recall as the use of timelines with life events increases recall accuracy of past drug use (Del Boca and Darkes 2003; Shillington et al. 1995). The inclusion of individuals with a psychiatric history, as well as those currently on psychotropic medications, is a further strength of the study as these individuals have often been excluded from previous research (e.g. Medina and Shear 2007; Roiser and Sahakian 2004). Furthermore, the use of the MASQ allowed for the examination of independent relationships between ecstasy use and depression-specific, anxiety-specific and general distress symptomatology. In contrast to commonly used depression scales, the depression-specific scale of the MASQ is less confounded by somatic symptoms such as sleep disturbance and loss of appetite (which are also related to substance misuse; Cole et al. 2002), and instead focuses on anhedonia and lack of positive affect. Finally, this is the first study to examine the relative contribution of genetic and environmental risk factors, including other drug use, on psychiatric symptomatology in a community sample of ecstasy users.

The current findings indicate that environmental risk factors, including a history of trauma and recent life stress, are more robust predictors of depressive and anxiety symptoms among ecstasy users than lifetime or recent ecstasy or 5-HTTLPR genotype. Secondly, frequency of tobacco use, recent polydrug use and a younger age of cannabis onset were associated with depressive/anxiety symptomatology. These findings further highlight the importance of controlling for other drug use in studies of ecstasy users, and emphasise the need to assess for and address environmental factors, such as a history of trauma and stressful life events, when treating ecstasy users with depression and/or anxiety. Indeed, it highlights the importance of providing coping skills training to people with depressive/anxiety symptoms and co-occurring substance use. These findings also provide one possible explanation for the mixed findings observed in the literature with respect to the relationship between depressive and anxiety symptomatology and ecstasy use. However the relationship between trauma, depression and anxiety, and drug use is complex. Whether ecstasy use exacerbates trauma or mood symptoms in people with a history of trauma or psychopathology needs further investigation. Prospective research exploring the relationship between these variables over both the short and long term is needed to fully understand the interaction between these variables.
Acknowledgements

Rebecca Scott was supported by an Australian Postgraduate Award and the project was funded by Monash University, School of Psychology and Psychiatry. Drs Hides and Lubman are supported by the Colonial Foundation. The authors wish to thank Dr Penelope Hasking and Dr Simon Moss for statistical assistance.
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Roiser JP, Cook LJ, Cooper JD, Rubinsztein DC, Sahakian BJ (2005) Association of a functional polymorphism in the serotonin transporter gene with abnormalemotional processing in ecstasy


Table 1

Drug use frequencies

<table>
<thead>
<tr>
<th>Substance</th>
<th>Ever used n (%)</th>
<th>Age at first use (years) Mean (SD)</th>
<th>Used in last 12 months n (%)</th>
<th>Used in last 28 days n (%)</th>
<th>Mean days of use in last 28 days Mean (SD; range)</th>
<th>Mean amount used in last 28 days Mean (SD; range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecstasy</td>
<td>184 (100)</td>
<td>19.05 (2.54)</td>
<td>184 (100)</td>
<td>78 (42.4)</td>
<td>1.68 (1.01; 1-6)</td>
<td>2.90 pills (3.02; 25-16)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>183(^b) (100)</td>
<td>13.52 (2.83)</td>
<td>180(^b) (97.8)</td>
<td>172 (93.5)</td>
<td>10.20 (6.36; 1-27)</td>
<td>67.70 units(^c) (55.34; 1-252)</td>
</tr>
<tr>
<td>Tobacco</td>
<td>174 (94.6)</td>
<td>14.52 (2.69)</td>
<td>144 (78.3)</td>
<td>98(^d) (54.4)</td>
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<td>-</td>
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<tr>
<td>Cannabis</td>
<td>176 (95.7)</td>
<td>16.04 (2.42)</td>
<td>152 (82.6)</td>
<td>76 (41.3)</td>
<td>6.61 (8.12; 1-27)</td>
<td>4.12g (11.85; .01-96.50)</td>
</tr>
<tr>
<td>Amphetamines</td>
<td>138 (75.0)</td>
<td>19.05 (2.56)</td>
<td>114 (62.0)</td>
<td>30 (16.3)</td>
<td>2.20 (1.97; 1-10)</td>
<td>.51g (.43; .02-1.38)</td>
</tr>
<tr>
<td>Cocaine</td>
<td>102 (55.4)</td>
<td>20.98 (3.27)</td>
<td>71 (38.6)</td>
<td>15 (8.2)</td>
<td>1.2 (.41; 1-2)</td>
<td>.62g (.50; .05-1.5)</td>
</tr>
<tr>
<td>Hallucinogens</td>
<td>119 (64.7)</td>
<td>19.71 (2.82)</td>
<td>74 (40.2)</td>
<td>12 (6.5)</td>
<td>1.58 (1.00; 1-4)</td>
<td>1.69 tabs(^e) (1.60; 25-6)</td>
</tr>
<tr>
<td>Inhalants</td>
<td>78 (42.4)</td>
<td>19.63 (3.28)</td>
<td>39 (21.2)</td>
<td>10 (5.4)</td>
<td>2.70 (2.71; 1-9)</td>
<td>23.65 inhales (38.55; 2-130)</td>
</tr>
<tr>
<td>Opiates</td>
<td>46 (25.0)</td>
<td>20.33 (3.42)</td>
<td>19 (10.3)</td>
<td>3 (1.6)</td>
<td>1.67 (1.15; 1-3)</td>
<td>.13g (.15; .03-3)</td>
</tr>
<tr>
<td>Benzodiazepines/Sedatives(^f)</td>
<td>67 (36.4)</td>
<td>21.06 (3.47)</td>
<td>44 (23.9)</td>
<td>9 (4.9)</td>
<td>1.44 (.73; 1-3)</td>
<td>25mg(^g) (17.32; 5-55)</td>
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<tr>
<td>Ketamine</td>
<td>64(^h) (36.0)</td>
<td>21.14 (3.19)</td>
<td>28(^h) (15.2)</td>
<td>4 (2.2)</td>
<td>1.5 (.58; 1-2)</td>
<td>.06g (.04; .03-11)</td>
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<tr>
<td>GHB</td>
<td>33(^i) (18.5)</td>
<td>21.55 (4.12)</td>
<td>12(^i) (6.5)</td>
<td>2 (1.1)</td>
<td>3.0 (1.41; 2-4)</td>
<td>29.95mls (28.21; 10-49.90)</td>
</tr>
</tbody>
</table>

\(^a\)Includes only those participants who have used the substance in the last 28 days, \(^b\) one missing data point, \(^c\) each unit equivalent to 10mg ethanol, \(^d\) four missing data points, \(^e\) one tab equivalent to one LSD tab or four magic mushroom shakes (Thailand), \(^f\) non-prescribed use, \(^g\) converted to diazepam equivalence, \(^h\) six missing data points
Table 2

*Lifetime prevalence of trauma experiences (n=184)*

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<th>Type of trauma</th>
<th>n</th>
<th>(%)</th>
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<td>Natural disaster</td>
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<td>12.0</td>
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<td>Witnessed assault/murder</td>
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<td>Physical assault</td>
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<td>Physical assault</td>
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<td>Threatened with a weapon</td>
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<tr>
<td>Torture/terrorists</td>
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<td>Other(^a)</td>
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<tr>
<td>Shock(^a)</td>
<td>60</td>
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\(^a\) Relates to participants endorsing both the occurrence of the event and at the time experiencing ‘intense fear, helplessness or horror’
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*p ≤.01, **p ≤.001; ¹Males = 0, Females = 1; ²No diagnosis = 0, Past or present diagnosis of unipolar depression and/or an anxiety disorder = 1 (Spearman’s Rho correlations); transformed data, total drug using days, excluding tobacco; ³Last month
### Table 4

**Lifetime drug use: Hierarchical regression models predicting MASQ subscales from genetic, environmental, and lifetime drug use factors (n = 183)**

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*p ≤ .05, **p ≤ .001; Males = 0, Females = 1; No = 0, Yes = 1

NB. When participants who had taken prescribed psychotropic medication within the last month (n = 15) were excluded, dep/anx diagnosis was no longer a significant predictor (p > .01) of Anhedonic Depression at steps 2, 3 and 4 and recent stress was no longer significant at steps 3 and 4. For GD anxious, frequency of tobacco use was no longer significant at step 4. There were no changes to Anxious Arousal and GD Depressive.
Table 5
Recent drug use: Hierarchical regression models predicting MASQ subscales from genetic, environmental, and recent drug use factors (n = 183)

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*p ≤ .01, **p ≤ .001; \(^a\) Males = 0, Females = 1, \(^b\) No = 0, Yes = 1.
NB. When participants who had taken prescribed psychotropic medication within the last month (\(n=15\)) were excluded, dep/anx diagnosis was no longer a significant predictor (\(p>.01\)) of Anhedonic Depression at steps 2, 3 and 4 and was no longer a significant predictor of GD Depressive at steps 3 and 4. For GD Anxious, trauma became nonsignificant at step 2 and recent polydrug use became a significant predictor at step 3. There were no changes to Anxious Arousal.
CHAPTER 5

Subacute effects of ecstasy on mood: An exploration of associated risk factors

This chapter comprises of an article submitted for publication in *Journal of Psychopharmacology*. This journal has no maximum word limit for full research reports. The format is according to the guidelines for this journal.
5.1 *Introduction to article two*

The empirical study presented in Chapter Four demonstrated that environmental risk factors, including life stress and other drug use, were more robust predictors of current mood symptoms than lifetime or recent ecstasy use. Consequently, Article Two aimed to expand upon these findings using a prospective design. The empirical study presented in this chapter aimed to determine what factors were related to the experience of mood symptoms in the short term, including ecstasy use, life stress and sleep. Secondly, this study aimed to explore whether pre-existing and patterns of drug use factors may increase the likelihood of someone experiencing mood symptoms in the days following ecstasy use. A subsample of participants presented in chapter four were interviewed at two further time points over the week following study one. Those that took ecstasy were compared with those that abstained. Factors relating to mood change over the follow up were explored.
5.2 Declaration for Thesis Chapter Five

Declaration by candidate

In the case of Chapter Five the nature and extent of my contribution to the work was the following:

<table>
<thead>
<tr>
<th>Nature of contribution</th>
<th>Extent of contribution (%)</th>
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</thead>
<tbody>
<tr>
<td>Conceptualisation of study design; data collection; data analysis; conceptualisation of paper; and write up.</td>
<td>80%</td>
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</tbody>
</table>

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

<table>
<thead>
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<th>Name</th>
<th>Nature of contribution</th>
<th>Extent of contribution (%) for student co-authors only</th>
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<tbody>
<tr>
<td>Dr Leanne Hides</td>
<td>Provided guidance on study design, measures selection, statistical analysis and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr J. Sabura Allen</td>
<td>Provided guidance on methodology, including measures selection and statistical analysis; and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr Dan Lubman</td>
<td>Provided guidance on study design and conceptualisation of manuscript</td>
<td>n/a</td>
</tr>
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</table>

Candidate’s Signature

Date

Declaration by co-authors

The undersigned hereby certify that:

(7) the above declaration correctly reflects the nature and extent of the candidate’s contribution to this work, and the nature of the contribution of each of the co-authors.

(8) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;

(9) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;

(10) there are no other authors of the publication according to these criteria;

(11) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(12) The original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

| Location(s)          | Monash University, Melbourne, Australia |

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

| Signature 1 | Date |
| Signature 2 |      |
| Signature 3 |      |
Subacute effects of ecstasy on mood: An exploration of associated risk factors

Rebecca M. Scott¹, Leanne Hides², J. Sabura Allen¹, and Dan I. Lubman²

Funding acknowledgements: Rebecca Scott was supported by an Australian Postgraduate Award and the project was funded by Monash University, School of Psychology and Psychiatry. Drs Hides and Lubman are supported by the Colonial Foundation.

¹School of Psychology and Psychiatry. Monash University, Victoria 3800, Australia
²Orygen Youth Health Research Centre, Centre for Youth Mental Health, University of Melbourne, Poplar Road (Locked Bag 10), Parkville, Victoria 3052, Australia

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Abstract

Ecstasy use may result in lowered mood, anxiety or aggression on the days after use. However, few studies have investigated what factors may increase the risk of subacute mood symptoms. The current study aimed to determine what factors were related to short-term mood symptoms. Ecstasy users (used at least once in the last 12 months) who subsequently took ecstasy ($n=35$) were compared with those that abstained ($n=21$) on measures of mood, sleep, stress and drug use. Measures were administered prior to ecstasy use and one and three days after ecstasy use, or equivalent day for abstainers. Mood symptoms were assessed using the Kessler 10, a subjective mood rating, and the clinician-rated depression, anxiety and hostility items of the Brief Psychiatric Rating Scale. Timeline followback methods were used to collect information on drug use and life stress. Sleep was assessed using self-report. Ecstasy use was not associated with subacute depressive, anxiety or aggressive symptoms. Rather, lowered mood and increased psychological distress were associated with self-reported quality of sleep and number of stressful life events experienced during the 3-day follow up. These findings suggest the importance of sleep and environmental factors in understanding short-term mood effects in ecstasy users.

Key words: ecstasy, mood, subacute, risk factors, sleep, stress
Ecstasy and subacute mood effects

Ecstasy (3,4-methylenedioxymethamphetamine, MDMA) is a popular recreational drug, particularly amongst young people. Ecstasy is taken for its acute effects, including feelings of euphoria, increased energy, and greater sociability and connectedness with others (Cohen, 1995; White et al., 2006). Its acute psychological effects occur between 20 to 60 minutes post ingestion, peaking at 60 to 90 minutes and lasting three to five hours (Green et al., 2003), and are largely attributed to serotonin release (Liechti and Vollenweider, 2001). Following the initial release of serotonin from presynaptic vesicles, ecstasy prevents reuptake of serotonin from the synaptic cleft and reduces tryptophan hydroxylase preventing the synthesis of new serotonin (McKenna and Peroutka, 1990). Given that serotonin plays an important role in the regulation of mood, emotion, sleep and appetite and ecstasy use may lead to its temporary depletion for several days (Curran et al., 2004), a number of studies have investigated the short-term consequences of ecstasy use on psychological functioning.

Findings from a series of well-designed laboratory studies, indicate that up to a third of healthy participants who have never or rarely taken ecstasy report signs of depressed mood including irritability, brooding, difficulty concentrating, lack of energy and bad dreams 24 hours after being administered MDMA (range: 70-150mg) (Vollenweider et al., 1998, 1999; Liechti and Vollenweider, 2000a, b; Liechti et al., 2000a, b, 2001). A small number of participants continued to report these subacute effects three days post use (Liechti et al., 2001). However, findings from non-laboratory studies of recreational ecstasy users suggest higher rates of subacute mood effects. Indeed, Verheyden et al. (2003) found that 83% of participants (n=430) reported experiencing low mood in the days after ecstasy use. Similar associations have been found between ecstasy and mood (elevated depression, anxiety and aggression) in prospective studies comparing ecstasy users with non-using controls (mostly ecstasy-naïve), with subacute mood effects persisting for up to four days post ecstasy use (Curran and Travill, 1997; Parrott and Lasky, 1998; Verheyden et al., 2002; Curran et al., 2004).
Given the evidence of increased mood symptomatology following ecstasy use, the identification of factors associated with an increased risk of ecstasy-induced subacute mood effects may provide valuable information regarding who may be more vulnerable to ecstasy-related harm.

The empirical literature highlights a number of potential risk factors for ecstasy-induced subacute mood effects including gender, psychiatric vulnerability, patterns of drug use, and environmental factors. However, there is a lack of prospective studies exploring whether these factors are associated with subacute mood symptoms. In a review of the literature, Parrott (2006) proposed a diathesis-stress model for understanding how ecstasy may interact with internal and external factors to produce adverse psychiatric outcomes. While highlighting that regular ecstasy users presenting with psychiatric symptoms often exhibited symptoms prior to ecstasy onset, Parrott (2006) proposed that heightened psychiatric vulnerability (e.g. a history of depression) may be a risk factor for ecstasy-induced subacute mood effects (Parrott, 2006). However, this hypothesis remains largely unexplored as many subacute studies have excluded participants with a psychiatric history (Liechti et al., 2001; Verheyden et al., 2002; Pirona and Morgan, 2009).

With respect to gender, females have been found to attribute a greater number of short- and long-term psychological problems including depression to ecstasy use (Topp et al., 1999) and to be more likely to experience midweek low mood following weekend ecstasy use than males (Verheyden et al., 2002). This is consistent with research finding females are more sensitive to the serotonin-induced psychoactive effects of ecstasy (e.g. experiencing perceptual changes) and are more likely to experience acute adverse effects (e.g. depressive and anxiety symptoms, jaw clenching) than males (Liechti et al., 2001). In
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contrast, Hoshi et al. (2006) found no gender differences on subacute mood, as measured by the Beck Depression Inventory.

Patterns of drug use may also impact upon subacute mood change. For example, the number of substances taken whilst ‘coming down’ from ecstasy (i.e. during the acute recovery period) has been associated with a greater number of self-reported ecstasy side effects (Topp et al., 1999). A similar association has been found in prospective studies, with positive correlations between severity of ecstasy use and mood symptoms the day after use being reported (Curran et al., 2004; Huxster et al., 2006; Pirona and Morgan, 2009). Specifically, Verheyden et al. (2002) found a relationship between severity of subacute mood effects and number of ecstasy pills consumed in females, consistent with animal studies indicating a dose-dependent relationship between MDMA and neurotoxicity (Green et al., 2003). Despite the authors collecting data on trait depression, it remains possible that pre-existing mood differences may have contributed to these findings, as pre-drug baseline mood measures were not obtained (Allott and Redman, 2007).

In terms of lifetime drug use factors, greater lifetime ecstasy use and younger age of first use have been associated with more severe subacute mood symptoms (i.e., more ‘irritable’, ‘aggressive’ and ‘nervous’) (Pirona and Morgan, 2009). Similarly, Huxster et al. (2006) found that negative mood the day after ecstasy use correlated positively with lifetime ecstasy use as well as the frequency of ecstasy use per month, and correlated negatively with time since last use. Curran et al. (2004) found significant correlations between ecstasy use (frequency of use, years of use) and self-reported aggression four days after use. However, it is possible that premorbid differences in mood symptoms may have impacted on these findings, as these studies failed to control for baseline mood differences when exploring these relationships.
In contrast to the above findings, an Internet study by Parrott et al. (2006) found that retrospective reports of subacute effects on mood and cognition were generally independent from amount of ecstasy consumed. Rather, they found that participants who danced ‘all the time’ while on ecstasy reported significantly more problems in the days after ecstasy use, including depression, compared to those who danced less. In addition, those reporting feeling ‘strongly’ or ‘extremely’ ‘hot or overheating’ while on ecstasy reported significantly poorer concentration in the days following ecstasy use. These findings are consistent with the animal literature indicating that MDMA neurotoxicity is greater under crowded conditions, high ambient temperatures and restricted water intake (Dafters, 1995; Malberg and Seiden, 1998). Consequently, it has been proposed that the similar hot, crowded conditions and at times, limited availability of water, at dance parties or raves may be associated with greater adverse side effects of ecstasy (Green et al., 2003; Parrott et al., 2006). Indeed, other studies indicate that ecstasy users report that ambient temperature and dancing influence the acute effects of ecstasy and some users manipulate these factors to enhance ecstasy’s effects (Bedi and Redman, 2006). Taken together, the above studies suggest that patterns of drug use including ecstasy dose and the ecstasy-using environment may be risk factors for subacute mood effects.

In addition to these pre-existing and patterns of drug use factors, the confounding factor of sleep disruption was recently highlighted in two well-designed studies. Using an ecstasy-using control group and controlling for other drug use over the follow up period, Pirona and Morgan (2009) found the effects of ecstasy use on negative mood (feeling muddled, afraid, and sad) one day after ecstasy use were no longer significant after controlling for the hours of sleep obtained. In a similar study by the same research group, Huxster et al. (2006) reported that while the subacute effects of ecstasy use on mood remained after controlling for sleep, the effect of ecstasy on cognition (self-reported concentration, memory) was no longer significant after controlling for restless sleep.
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Finally, we recently found that stressful life events, a history of trauma and other drug use factors were more robust predictors of current mood symptoms than ecstasy and genetic factors in a cross sectional study of 184 ecstasy users who had used ecstasy at least once in the last 12 months (Scott et al., 2010). These findings are consistent with the broader depression and anxiety literature whereby adverse life events are a significant risk factor in the onset of these disorders (Goldberg, 1994; Kendler et al., 2002, 2006). However, prospective research is yet to determine the relative contribution of these variables on short-term changes in mood among ecstasy users.

The current prospective study aims to build on the findings of previous research by exploring what factors are associated with negative mood change following ecstasy use, as well as determining if ecstasy use is associated with lowered mood, anxiety or aggression in the days following use, after controlling for potential confounds such as hours of sleep and other drug use. Based on the existing literature, it was hypothesised that 1) ecstasy use would be associated with a significant increase in depressive, anxiety and aggressive symptoms in the days following use; 2) an increase in depression, anxiety or aggression in the days following ecstasy use would be related to pre-existing factors (i.e. female gender, more severe baseline depressive/anxiety symptoms, personal psychiatric history), patterns of drug use (e.g., ecstasy dose and other drug use) and the ecstasy-use environment (heat/exercise), stressful life events and sleep factors; and 3) stressful life events and sleep disruption would significantly predict mood change in all participants (ecstasy users and abstainers).

Method

Participants

A subsample of 63 participants were recruited from a larger study of 184 ecstasy users aged 18 to 35 years who had used ecstasy at least once in the last 12 months (see Scott et
al., 2010). All regular ecstasy users (at least monthly use over the last 6 months) and those planning to take ecstasy within one week of the baseline assessment were invited to participate. Thirty-five participants voluntarily took ecstasy following the baseline assessment (ecstasy users) and 21 chose to abstain from taking ecstasy (abstainers).

Recruitment took place in Melbourne, Australia using advertisements on universities’ and dance music websites, newsletters, music magazines and newspapers. Flyers were also distributed in cafes, music stores, and at dance music events. A ‘snowballing’ technique was used to recruit friends, family and acquaintances of individuals participating in the study (Solowij et al., 1992). Exclusion criteria were current pregnancy, poor English fluency and history of a psychotic disorder.

Procedure

The study was approved by the Monash University Human Ethics Committee. Potential participants were initially screened via a brief telephone interview to ensure they met inclusion criteria. Participants were requested to abstain from taking ecstasy for at least seven days prior to baseline testing, other recreational drugs for at least 24 hours (with the exception of tobacco and caffeine), and alcohol for at least 12 hours. Individuals who provided informed consent to participate were interviewed face-to-face for approximately one hour by a doctoral candidate in clinical psychology (R.S.). Following the baseline assessment (baseline), all consenting participants for the current study were asked if they were planning on taking ecstasy over the next week. If yes, the researcher arranged to contact the participant the day following planned ecstasy use (Day 1) and again two days later (Day 3). If not, participants were telephoned on Sunday evening (Day 1) and again on Tuesday evening (Day 3). Telephone interviews were conducted between 6pm and 8pm unless the participant was unavailable at this time. All participants were reimbursed AUD$25 for their time and travel-related expenses for the baseline interview.
Baseline measures

Demographics and lifetime drug use. Participants provided information on age, occupation, education, ethnicity, personal psychiatric history, including treatment and current medication. Participants provided substance use information including age at first use, lifetime polydrug use (the total number of drugs tried; maximum possible score=12), and the most frequent use (never used, less than monthly, monthly, 2-3 times a month, weekly, daily or almost daily) of alcohol, tobacco, cannabis, ecstasy, amphetamines, cocaine, hallucinogens, inhalants, opiates, benzodiazepines/sedatives, ketamine, and gamma-hydroxybutyric acid (GHB). A context-based timeline method was used to estimate total lifetime number of ecstasy pills consumed (Bedi and Redman, 2006). The Timeline Followback (TLFB; Sobell and Sobell, 1992) was used to retrospectively assess frequency and quantity of substances used over the past 28 days and over the course of the study.

Mood symptoms: Self report

Mood and Anxiety Symptom Questionnaire - Short Form (MASQ; Watson and Clark 1991). This 62-item self-report measure of general distress and depressive and anxiety symptoms has excellent convergent and discriminant validity between anxiety and depressive symptoms in both clinical and non-clinical samples (Watson et al., 1995). Participants indicated how much they had experienced each symptom over the past week (1 = not at all to 5 = extremely).

Kessler-10 (K10; Kessler et al., 2002). The K10 is a widely used 10-item self-report measure of psychological distress associated with depressive and anxiety symptoms and has been found to be valid and reliable in detecting the presence of depressive and anxiety disorders (Andrews and Slade, 2001). A cut-off score of ≥17 was used to indicate the presence of psychological distress. The standard instructions were modified so that
participants reported on how they had been feeling over the present day.

*Subjective mood.* Participants rated their mood on a scale from one to ten (1 = worst they have ever felt, 10 = best they have ever felt) for the present day.

*Mood symptoms: Clinician rated*

*Brief Psychiatric Rating Scale (BPRS) (Ventura et al., 1993).* The anxiety, depression and hostility components of the BPRS were used to provide a clinician rating of mood symptoms for the present day (1 = not present to 7 = extremely severe). The BPRS has been found to have excellent inter-rater reliability (Ventura et al., 1993) and to be an effective measure of psychiatric symptoms in various substance-using populations (Steer & Schut, 1979; Westermeyer et al., 1995).

*Stressful life events.* Participants were asked to report any stressful life events that had occurred over the last 28 days and between each testing point. Stressful life events could relate to any area of life including employment and study (e.g., lost job; university exams), finances (e.g., went off benefits), relationships and family (e.g., break up of romantic relationship; family conflict), residence (e.g., moved house), health (e.g., physical illness) and crime and legal matters (e.g., victim of assault). Life events were only included if participants reported finding the event stressful. Events were tallied to provide a total recent stressful life events score for Day 1 and Day 3 (events occurring since baseline). Participants also gave a subjective rating of stress for the present day (1 = not stressed at all to 10 = extremely stressed).

*Sleep.* Hours of sleep for the preceding night were calculated based on participant report of time they fell asleep and awoke. If participants reported periods of being awake within this timeframe, the duration of wakefulness was subtracted from the hours of sleep.
Participants rated how restless their sleep was the previous night compared to normal (1 = not restless at all to 10 = extremely restless).

Medication. Participants were asked if they were currently on psychiatric medication, if they had made any changes to their medication in the last 28 days or if they had made any changes to or had missed any medication over the follow up.

Ecstasy factors. Those that went on to take ecstasy provided ecstasy-specific information including what the tablet(s) looked like, what time they were consumed, what drugs were taken in combination with ecstasy, and rated how much they believed they had taken MDMA after being described the common psychological and physiological effects of MDMA (1 = definitely not MDMA to 10 = definitely was MDMA). Participants were also asked to rate how positive their ecstasy experience was (1 = extremely negative to 10 = extremely positive), how much time they spent dancing or doing exercise whilst on ecstasy (1 = not at all to 5 = all the time) and if they felt hot or were over heating while on ecstasy (1 = not at all to 5 = extremely).

Summary of assessments

• Baseline: Consent form, demographics, lifetime drug use, MASQ, K10, subjective mood rating, BPRS, TLFB for past 28 days, stressful life events for past 28 days, last night sleep hours, last night restless sleep, medication

• Day 1: K10, subjective mood, BPRS, TLFB, stressful life events, last night sleep hours, last night restless sleep, medication, ecstasy factors (for ecstasy users only)

• Day 3: K10, subjective mood, BPRS, TLFB, stressful life events, last night sleep hours, last night restless sleep, medication

Statistical analysis
All data were analysed with PASW version 18 (SPSS Inc., 2009). Individuals with missing data (i.e. those who were not contactable at Day 1 or Day 3) were compared with the other participants on baseline data including demographics, lifetime ecstasy and other drug use, and psychopathology, to ensure those who were not contactable did not differ on these variables. Ecstasy users and abstainers were also compared on these variables to determine if there were any group differences that needed to be controlled for in the subsequent analyses. Tests for group differences were conducted using independent samples t-tests for parametric continuous data, Mann-Whitney U tests for nonparametric data and Pearson Chi Square analysis for categorical data.

Two-way repeated measures ANCOVAs with ecstasy use group (ecstasy use on day 0: yes/no) as the between subjects factor and time (baseline, day 1, day 3) as the repeated measure were conducted on K10 and subjective mood ratings. Potential confounding variables were treated as covariates. Kruskal-Wallis tests for group differences were conducted on the BPRS change scores for the depression, anxiety and hostility items (baseline score minus follow up score). Separate analyses were conducted for Day 1 and Day 3 for all between-subjects comparisons due to missing data.

Change scores for the K10 and subjective mood were calculated by subtracting each individual’s day 1 and day 3 scores from their baseline scores. A negative mood change at day 1 or day 3 was defined by at least a 20% increase in K10 score or at least a 20% decrease in subjective mood score, compared to the relative baseline scores. Given the small sample size and that the focus of the current research was to identify predictors of depressive and anxiety symptoms, participants with change scores indicating no change or a positive change in mood from baseline were combined to form one group. 20% change scores were not calculated for the BPRS due to the narrow distribution of possible scores. Pearson’s correlations were conducted to explore relationships with negative mood change.
Ecstasy and subacute mood effects (yes/no). An alpha level of .01 was adopted to indicate statistical significance for the correlational analyses due to the multiple comparisons made.

Results

Sample characteristics and follow up

Of 63 consenting participants, 56 participants were contactable and provided follow up data for day 1 (n=55, 98.2%) and/or day 3 (n=47, 83.9%). The characteristics of the final sample are presented in Table 1. At day 1, one ecstasy user could not be contacted. At day 3, five ecstasy users and four abstainers could not be contacted. No group differences were found between those who were contactable at both time points (n=46) and those who were not (n=10) on gender, lifetime ecstasy use and polydrug use, baseline mood scores (K10 and MASQ) or self-reported past diagnosis of unipolar depression and/or an anxiety disorder. However, those who were not contactable at both time points were significantly younger (t=3.90, df=54, p<.001). In order to identify potential confounding variables to include as covariates in the group comparisons, the following analyses for group differences between the ecstasy users and the abstainers were conducted.

No group differences were found between ecstasy users and abstainers on ethnicity, education, self-reported past diagnosis of unipolar depression and/or an anxiety disorder, or on any of the baseline mood measures (see Table 2 for mood measures). However, there were significant group differences in age (t=-3.07, df=54, p<.01) with ecstasy users being older, and gender (χ²(1,56)=4.31, p=.05) with a greater proportion of males taking ecstasy over the follow up. Consequently, age and gender were included as covariates in subsequent analyses.

Table 3 summarises ecstasy and polydrug use information. No significant group differences between ecstasy users and abstainers were found on lifetime ecstasy use (log
transformed), typical or greatest ecstasy dose or lifetime polydrug use. However, significant differences were found in the duration of ecstasy use ($t=-2.25, df=54, p=.03$), with those that took ecstasy reporting a longer duration of ecstasy use. Significant group differences were found for lifetime frequency of cannabis ($U=236.00, N_1=21, N_2=35$, $p=.02$) and cocaine use ($U=221.00, p=.01$), and a trend was found for frequency of GHB use ($U=278.00, p=.08$), with those that took ecstasy reporting a higher frequency of use of these substances. Of note, there were no group differences in lifetime ecstasy frequency ($U=309.50, p=.25$).

Follow up drug use and sleep

Day 0. Thirty ecstasy users (85.7%) and 10 abstainers (47.6%) consumed alcohol on day 0 and 12 ecstasy users (34.3%) and 3 abstainers (14.3%) used cannabis. Six ecstasy users (17.1%) used amphetamines, one used LSD, one used GHB, one used cocaine, and one used a benzodiazepine. Ecstasy users had taken a significantly greater number of substances at day 0 than abstainers ($t=9.58, df=54, p<0.001$; Total drugs taken: ecstasy users $M=2.51, SD=0.66$; abstainers $M=.71, SD=0.72$). Consequently, total drugs taken was treated as a covariate. Group comparisons of amount of alcohol and cannabis consumed revealed trends towards the ecstasy users consuming more alcohol ($t=-1.88, df=54, p=0.07$) and cannabis ($t=-1.81, df=54, p=0.08$). Group comparisons of other individual drugs were not conducted due to the low rates of use. Ecstasy users consumed an average of 1.91 ecstasy pills ($SD=1.23$; range: 0.5-5). There was no significant gender difference in number of ecstasy pills taken at day 0 (females $M=1.70$, males $M=2.08$). The mean time since the last ecstasy pill was consumed was 21.74 hours ($SD=6.64$; range: 12.5-40) with two participants being assessed two days post ecstasy use due to not being contactable at day 1.

Day 1. Six ecstasy users and three abstainers reported consuming alcohol and seven
Ecstasy and subacute mood effects

Ecstasy users reported using cannabis on day 1 since waking. One participant reported not having slept since day 0 but they had not consumed any substances since 9pm on day 0. Significant group differences were found for hours of sleep \((t=3.87, df=53, p<0.001)\) but not for restless sleep \((t=1.21, df=52, p=0.23)\) with ecstasy users reporting having fewer hours of sleep (ecstasy users: \(M=5.85, SD=2.14\); ecstasy abstainers: \(M=8.06, SD=1.93\)). Therefore hours of sleep was entered as a covariate in subsequent analyses.

Day 1 to day 3. Seventeen ecstasy users (56.7%) and six abstainers (35.3%) consumed alcohol and nine ecstasy users (30%) and two abstainers (11.8%) used cannabis between days 1 and 3, inclusive. One ecstasy user used amphetamines, one used LSD and one used ecstasy again. Ecstasy users had taken a significantly greater number of substances than abstainers (Total drugs taken: \(t=-3.08, df=54, p<0.01\)). Significant group differences were found in amount of alcohol \((t=-2.02, df=47, p=0.05)\) and cannabis consumed \((t=-2.32, df=47, p=0.03)\) with ecstasy users consuming more alcohol and cannabis than abstainers over these three days. No other group comparisons for individual substances were conducted due to the low rates of use. No significant group differences on hours of sleep or restless sleep were found for the night preceding day 3.

Association between ecstasy use and subacute negative mood effect: Ecstasy users versus abstainers

K10. K10 scores showed no main effect of group (Day 1: \(F(1,53)=0.09, p=0.77\); Day 3: \(F(1,45)=0.00, p=0.98\)), or group X time interaction (Day 1: \(F(1,53)=1.02, p=.32\); Day 3: \(F(1,45)=0.29, p=0.59\)). There was a significant main effect of time at day 1 \(F(1,53)=4.94, p=0.03\) but not at day 3 \(F(1,45)=0.04, p=0.85\) with participants reporting lower K10 scores at day 1 compared to baseline. Secondary analyses of the individual items ‘depressed’ and ‘nervous’ on the K10 revealed no significant group differences.
**K10 with covariates.** The main effect of time at day 1 was no longer significant after controlling for gender \((F(1,52) = 0.73, p=0.40)\), age \((F(1,52) = 0.76, p=0.39)\), hours of sleep at day 0 \((F(1,52) = 0.07, p=0.80)\), total drugs taken at day 0 \((F(1,52) = 1.61, p=0.21)\) or duration of ecstasy use \((F(1,52) = 1.80, p=0.19)\). Following the addition of these covariates, there continued to be no main effect of group or group X day interaction at day 1 or day 3.

**Subjective mood.** There were no main effects of group (Day 1: \(F(1,52) = 0.22, p = 0.64\); Day 3: \(F(1,45) = 0.54, p = 0.47\)) or group X day interaction (Day 1: \(F(1,52) = 0.23, p = 0.64\); Day 3: \(F(1,45) = 0.79, p = 0.38\)). There was a significant main effect of time with participants reporting lower scores at day 1 \((F(1,52) = 4.60, p = 0.04)\) and day 3 compared to baseline \((F(1,45) = 6.52, p = 0.01)\).

**Subjective mood with covariates.** The time effect for day 1 remained significant after controlling for gender \((F(1,51) = 5.53, p=0.02)\), age \((F(1,51) = 5.59, p=0.02)\) and duration of ecstasy use \((F(1,51) = 7.76, p<0.01)\). Furthermore, there was a significant age X time interaction \((F(1,51) = 3.93, p=0.05)\). However, at day 1, the time effect was no longer significant after controlling for hours of sleep at day 0 \((F(1,51) = 0.55, p=0.46)\). At day 3, the time effect remained significant after controlling for gender \((F(1,44) = 5.59, p=0.02)\), duration of ecstasy use \((F(1,44) = 6.98, p=0.01)\), but not after controlling for age \((F(1,44) = 3.42, p=0.07)\), hours of sleep at day 2 \((F(1,44) = 1.50, p=0.23)\) or other drug use (total drugs taken at day 0 and during days 1-3, days 1-3 alcohol consumption, days 1-3 cannabis consumption: \(Fs= 2.38, 0.00, 1.68, 3.66\), respectively, \(p>0.05\)). Following the addition of the covariates, there continued to be no main effect of group or group X day interaction.
Ecstasy and subacute mood effects

**BPRS clinician ratings.** Consistent with the self-report data, there were significant group differences on BPRS depression, anxiety and hostility change scores ($\chi^2s(1) = 0.02$-$2.14$, $p=0.14$-$0.88$).

**Follow up mood: clinically significant symptoms**

Raw scores indicated that five ecstasy users (14.3%) at baseline, four at day 1 (11.8%) and seven at day 3 (23.3%) had scores indicative of psychological distress ($K10\geq17$). Among the abstainers, four participants (19.0%) had scores indicative of psychological distress at baseline, compared to three (14.3%) at day 1 and two (11.8%) at day 3 with one abstainers’s score indicating a high level of psychological distress ($\geq30$) at day 3. Table 4 presents the number of ecstasy users and abstainers reporting at least a 20% change in mood at day 1 and day 3, compared to baseline scores.

**Correlational analyses: Exploration of potential risk factors**

**Demographics and baseline mood and psychopathology.** No associations were found between short-term negative mood change (yes/no) and gender, age, self-reported history of unipolar depression and/or an anxiety disorder or baseline mood symptoms, as measured by the MASQ, with either the combined sample or when including only those that took ecstasy. However, amongst the ecstasy-using group, there were trends toward more severe anxiety-related symptoms at baseline, as measured by the MASQ Anxious Arousal and GD Anxious subscales, and subjective lowered mood at day 1 ($r=0.43$, $p=0.02$ and $r=0.39$, $p=0.02$, respectively).

**Lifetime drug use factors.** Negative mood change (yes/no) did not correlate with lifetime
ecstasy use, duration of ecstasy use, age at first ecstasy use, lifetime polydrug use, or frequency of drug use, when looking at the total sample. However, when looking at the ecstasy users only, a significant association was found between lifetime frequency of hallucinogen use and increased psychological distress at day 3 ($r=0.50, p<0.01$) with more frequent hallucinogen use being associated with increased distress.

Days 0, 1 and 2 drug use. When looking at the combined sample and the ecstasy users alone, no significant associations between negative mood change and any drug use variables at day 0 were found, including number of ecstasy pills taken, total number of drugs used or amount of alcohol or cannabis consumed. Similarly, no correlations were found between mood change and amount of alcohol and cannabis used between days 1 and day 3.

Ecstasy factors at day 0. Of those that did take ecstasy, no significant associations were found between negative mood change and feeling hot/over heating or time spent dancing/doing exercise while on ecstasy, rating of ecstasy experience, or how confident the participant was that they had consumed MDMA.

Sleep. Hours slept the night preceding day 3 moderately correlated with day 3 K10 change score ($r=-0.49, p=0.003$) with fewer hours of sleep being associated with increased psychological distress. Similarly, restless sleep strongly correlated with day 3 subjective mood change ($r=0.53, p=0.001$) with higher restless sleep scores being associated with lowered mood at day 3. There was a trend towards restless sleep at day 2 being associated with an increase in psychological distress at day 3, as measured by the K10 ($r=0.36, p=0.04$).
Stress. Stressful life events reported at day 3 (occurring since baseline) moderately correlated with day 3 K10 change score ($r=0.41$, $p=0.004$) with a greater number of stressful life events being associated with increased psychological distress. No other significant correlations between lowered mood and stressful life events were found.
Discussion

The current study aimed to explore potential risk factors for short-term mood symptoms in a community sample of ecstasy users, while also exploring potential factors that may increase the risk of subacute mood effects following ecstasy use. Two main findings emerged. First, contrary to our hypothesis, ecstasy use was not associated with self-report or clinician-rated subacute depressive, anxiety or aggressive symptoms. Rather, associations were found between lowered mood/increased psychological distress and self-reported quality and hours of sleep and number of stressful life events experienced during the 3-day follow up. These prospective findings are consistent with our previous cross-sectional study, with stressful life events being significantly associated with current mood symptoms in a community sample of 184 ecstasy users (Scott et al., 2010). Second, amongst those who did consume ecstasy over the follow up, the experience of negative mood symptoms was not associated with pre-existing risk factors (i.e. severity of baseline depressive and anxiety symptoms, a history of depression and/or anxiety disorders, being female) or patterns of ecstasy use (i.e. ecstasy dose or ecstasy-related environmental factors), contrary to our hypotheses.

The current findings are inconsistent with previous research reporting an association between ecstasy use and lowered mood, increased anxiety and/or aggression in the days following a use (Curran and Travill, 1997; Parrott and Lasky, 1998; Curran et al., 2004). The current findings indicated no group differences between those that took ecstasy and those that abstained, as measured by self-report and clinician-rated scales. Average scores on the K10 for the ecstasy-users and abstainers at all time points were comparable to normative data from an Australian national survey (K10 mean score =14.2; Andrews and Slade, 2001). Furthermore, only one participant had a score on the K10 suggestive of a high level of distress (> 30; Commonwealth of Australia; 2005), and this individual had
not used ecstasy during the course of the study. These findings suggest that any subacute mood effects following ecstasy use are likely to be modest, consistent with more recent research (Huxster et al., 2006; Pirona and Morgan, 2009).

A key difference between earlier subacute research and more recent studies, including the current study, is the use of an ecstasy-using control group whereby individuals who subsequently used ecstasy during the follow up were compared with those who abstained from taking ecstasy. Consistent with the current findings, a recent study using an ecstasy-using control group, found no effect of ecstasy on depressive symptoms (as measured by the Beck Depression Inventory), and that self-reported mood symptoms, measured on visual analogue scales (feeling muddled, afraid, and sad) the day after ecstasy use, were no longer significant after controlling for hours of sleep (Pirona and Morgan, 2009). Similarly, Huxter et al. (2006) reported that although the effect of ecstasy use on subacute mood remained, the subacute effects on self-reported cognition were no longer significant after controlling for quality of sleep.

The current finding that self-reported hours and rating of restless sleep were associated with changes in mood are consistent with the findings of these more recent studies, and suggest that the negative subacute mood effects of ecstasy found in previous studies may be confounded by sleep factors. Indeed, sleep deprivation alone can cause negative mood effects (Keane & James, 2008), and ecstasy users report experiencing sleep disturbance following use in both field (Curran et al., 2004) and laboratory studies (Liechti et al., 2001). Consistent with this, the ecstasy users in the current sample reported sleeping for significantly fewer hours on the night of drug use, compared with the abstainers. Ecstasy is most commonly consumed at raves or all night dance parties where people dance for hours in a hot environment, often staying up all night leading to disrupted sleep patterns and insufficient rest (Degenhardt et al., 2004). It has been proposed that these lifestyle factors
alone may affect ecstasy users’ physical and psychological health (Parrott et al., 2001). The effect of age in the current sample is interesting. Younger participants tended to report lower subjective mood ratings, particularly at day 1. This suggests that younger individuals may experience greater mood fluctuation and be more vulnerable to day of the week effects on mood (Egloff et al., 1995).

The relationship between stressful life events and elevated psychological distress in the current study is consistent with aetiological models for depression and anxiety disorders indicating that stressful life events is a key environmental risk factor in the onset of these disorders (Goldberg, 1994; Kessler, 1997; Kendler et al., 2002, 2006). Although beyond the scope of the current study, it is possible that ecstasy users may more vulnerable to experiencing depressive and anxiety symptoms in the face of stressful life events. It is also possible that some individuals may be using ecstasy and other substances to cope with stressful life events, consistent with other research indicating that some ecstasy users report using ecstasy to alleviate negative mood states (Boys et al., 2001; White et al., 2006). Future research would benefit from looking at the relationship between ecstasy use motives, expectancies of use and the experience of subacute mood symptoms.

The lack of significant associations between subacute mood change and pre-existing factors (i.e. gender, baseline psychopathology) or patterns of ecstasy use (i.e. ecstasy dose and ecstasy-related environmental factors) was unexpected. Despite other studies suggesting that females may be more vulnerable to subacute mood symptoms (Verheyden et al., 2002), the current findings are consistent with those by Hoshi et al. (2006) who found not gender effect of ecstasy on mood, as measured by the Beck Depression Inventory. However, the current findings indicated a trend towards more severe baseline anxiety symptoms and the experience of subacute psychological distress following ecstasy use. It remains possible that some individuals are more likely to experience subacute
Ecstasy and subacute mood effects lowered mood, and that this relates to a more complex interaction of variables not captured by the correlational analysis in the current study. The low rates of self-reported history of depression and/or anxiety disorders reported in the current sample may have limited the power available to detect potential relationships. Further prospective studies with larger sample sizes are required to further understand the relationships between these variables.

Although the use of an ecstasy-using control is a strength of the current study, the groups significantly differed on a number of baseline variables and drug use over the follow-up. Ecstasy users were older, were more likely to be male, had used ecstasy for longer and used other drugs more frequently. Over the follow-up, the ecstasy users consumed a greater number of substances and greater amounts of alcohol and cannabis. These findings highlight the importance of controlling for other drug use when exploring subacute mood effects following ecstasy use. However, interestingly, no associations were found between negative mood effects and patterns of drug use, including ecstasy dose at day 0. This contrasts with the finding by Verheyden et al. (2002), who reported an association between ecstasy dose at day 0 and mid-week mood in females. Secondary analyses with females only in the current sample continued to find no association between ecstasy dose and subacute mood. However, as Verheyden et al. (2002) did not control for baseline mood, this finding may reflect pre-existing mood differences (Allott and Redman, 2007). In contrast, the current study controlled for baseline mood by correlating ecstasy dose with change in mood from baseline to follow up.

An important limitation of the current study relates to the participant follow-up rate at day 3. Although missing data was a factor in both the ecstasy users and abstainers at day 3, it remains possible that participants who were not contactable for the entire follow-up (n=7) and the ecstasy users who were not contactable at day 3 (n=5) were less willing to receive the follow-up phone call as they were experiencing subacute mood symptoms. Secondly,
sleep was measured using self-reported hours and rating of restless sleep. Future research would benefit from including standardised and/or objective measures of sleep to reduce potential reporter bias. Thirdly, given that some participants had consumed substances on days 1 and 3, they may have been intoxicated when interviewed. This may have impacted upon mood, masking potential subacute mood effects. However, analyses revealed that controlling for amount of alcohol and cannabis used on day 1 and day 3 did not alter the results of the group comparisons. Fourthly, the tablets consumed by the ecstasy users were not analysed for content. It is possible that the ecstasy users did not consume MDMA, reducing the chance of finding subacute mood changes relating to the temporary serotonin depletion following MDMA use. In the state of Victoria, the most recent published data (for the period 2004-2007) indicate that MDMA is the most frequently identified drug in tablets seized by police, followed by methylamphetamine, MDA/MDEA and ketamine (Quinn et al., 2007). However, of those tablets containing MDMA, purity varies widely (0.5% to 75%) and in recent years there has been an increase in seized tablets containing no active drug (Quinn et al. 2004, 2007). Despite this, the majority of ecstasy users in the current sample (91.4%) rated the likelihood that they had consumed MDMA as highly likely to definitely.

Despite these limitations, the study has a number of strengths. These include the use of an ecstasy-using control group, reducing potential premorbid differences associated with ecstasy and other drug use factors and baseline mood symptoms; the potentially confounding factors of self-reported sleep and other drug use over the follow up were controlled for; mood was measured using both self-reported measures and clinician-rated, supporting the reliability of the current findings; and finally, this is the first known prospective study to investigate the potential role of pre-existing psychopathology and baseline mood symptoms, as well as ecstasy-environment factors on the likelihood of experiencing low mood or anxiety following ecstasy use.
The results of the current study indicate that self-reported hours and quality of sleep and stressful life events are more strongly associated with short-term negative mood effects amongst ecstasy users than ecstasy use *per se*. Further, these findings suggest that pre-existing factors, (i.e. premorbid psychopathology and female gender) and patterns of drug use (i.e. ecstasy dose and the ecstasy-use environment) do not increase the likelihood of subacute mood effects following ecstasy use. However, further research with larger sample sizes is clearly needed to verify the current findings. The current findings contrast with earlier research indicating that ecstasy use may lead to clinically significant depressive symptoms (e.g. Curran and Travill, 1997), but are in keeping with recent research indicating that any subacute effects from ecstasy are likely to be modest (Huxster et al., 2006; Pirona and Morgan, 2009). Finally, the current findings have a number of potential implications for minimising the harm associated with ecstasy use such as consuming ecstasy earlier in the night to reduce the impact on sleep and subsequent mood effects.
Acknowledgements

Rebecca Scott was supported by an Australian Postgraduate Award and the project was funded by Monash University, School of Psychology and Psychiatry. Drs Hides and Lubman are supported by the Colonial Foundation.
Ecstasy and subacute mood effects

References


Dafters RI (1995) Hyperthermia following MDMA administration in rats: effects of ambient temperature, water consumption, and chronic dosing. Physiol Behav 58:


Ecstasy and subacute mood effects


Watson D, Clark LA (1991) The Mood and Anxiety Symptom Questionnaire. Iowa City: University of Iowa,


Table 1

Demographic and substance use information

<table>
<thead>
<tr>
<th></th>
<th>Ecstasy users (n=35)</th>
<th>Ecstasy abstainers (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (m/f)</td>
<td>20/15*</td>
<td>6/15*</td>
</tr>
<tr>
<td>Age mean (SD)</td>
<td>24.17 (5.19)**</td>
<td>21.14 (2.08)**</td>
</tr>
<tr>
<td>Caucasian n (%)</td>
<td>29 (82.9)</td>
<td>16 (76.2)</td>
</tr>
<tr>
<td>Post secondary school education n (%)</td>
<td>30 (85.7)</td>
<td>18 (85.7)</td>
</tr>
<tr>
<td>History of depression/anxiety disorder n (%)</td>
<td>7 (20.0)</td>
<td>4 (19.0)</td>
</tr>
<tr>
<td>Currently on psychiatric medication</td>
<td>0 (0)</td>
<td>1 (4.8)</td>
</tr>
</tbody>
</table>

*Within the last month, *p ≤ .05, **p ≤ .01
Table 2
Descriptive data for mood measures: mean (SD)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Day 1</th>
<th>Day 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ecstasy users (n=35)</td>
<td>Ecstasy abstainers (n=21)</td>
<td>Ecstasy users (n=34)</td>
</tr>
<tr>
<td>K10</td>
<td>13.43 (2.60)</td>
<td>14.14 (4.17)</td>
<td>12.85 (3.08)</td>
</tr>
<tr>
<td>Subjective mood</td>
<td>7.06 (1.21)</td>
<td>7.10 (1.45)</td>
<td>6.70 (1.51)</td>
</tr>
<tr>
<td>BPRS depression</td>
<td>1.11 (.40)</td>
<td>1.48 (.87)</td>
<td>1.29 (.68)</td>
</tr>
<tr>
<td>BPRS anxiety</td>
<td>1.57 (1.04)</td>
<td>1.90 (1.30)</td>
<td>1.47 (1.11)</td>
</tr>
<tr>
<td>BPRS hostility</td>
<td>1.17 (.51)</td>
<td>1.24 (.54)</td>
<td>1.12 (.41)</td>
</tr>
<tr>
<td>Anhedonic Depression</td>
<td>53.60 (9.03)</td>
<td>50.48 (11.14)</td>
<td>-</td>
</tr>
<tr>
<td>Anxious Arousal</td>
<td>22.57 (4.88)</td>
<td>25.67 (8.92)</td>
<td>-</td>
</tr>
<tr>
<td>GD Depressive</td>
<td>20.86 (6.74)</td>
<td>21.71 (6.78)</td>
<td>-</td>
</tr>
<tr>
<td>GD Anxious</td>
<td>17.89 (4.55)</td>
<td>19.86 (8.25)</td>
<td>-</td>
</tr>
</tbody>
</table>
Table 3

Ecstasy and polydrug use information: mean (SD; range)

<table>
<thead>
<tr>
<th></th>
<th>Ecstasy users (n=35)</th>
<th>Ecstasy abstainers (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age first ecstasy use (years)</td>
<td>18.60 (3.34; 15-31)</td>
<td>17.90 (1.95; 12-21)</td>
</tr>
<tr>
<td>Lifetime ecstasy use (pills)</td>
<td>422.39 (1001.85; 3.5-5332)</td>
<td>149.07 (354.63; 8.25-1645.45)</td>
</tr>
<tr>
<td>Typical ecstasy dose (pills)</td>
<td>1.90 (0.84; 1-4)</td>
<td>1.79 (0.90; 0.75-4)</td>
</tr>
<tr>
<td>Greatest ecstasy dose(^a) (pills)</td>
<td>5.04 (3.39; 1-15)</td>
<td>4.02 (2.37; 1.5-11)</td>
</tr>
<tr>
<td>Last month(^b) ecstasy use (days)</td>
<td>1.40 (1.38; 0-6)</td>
<td>1.33 (1.32; 0-4)</td>
</tr>
<tr>
<td>Last month(^b) ecstasy use (pills)</td>
<td>2.75 (3.59; 0-16)</td>
<td>2.57 (3.68; 0-13.5)</td>
</tr>
<tr>
<td>Ecstasy duration (years)</td>
<td>5.57 (4.59; 1-18)*</td>
<td>3.29 (2.30; 0.5-12)*</td>
</tr>
<tr>
<td>Polydrug total(^c)</td>
<td>8.0 (2.24; 4-12)</td>
<td>7.52 (2.09; 4-11)</td>
</tr>
</tbody>
</table>

\(^a\)Within a 12 hour period, \(^b\)28 days, \(^c\) total drugs tried \(^p\) ≤ .05
Table 4

Number of ecstasy users and abstainers indicating negative mood change\(^a\)

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th></th>
<th>Day 3</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ecstasy users</td>
<td></td>
<td>Abstainers</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n) (%)</td>
<td></td>
<td>(n) (%)</td>
<td></td>
</tr>
<tr>
<td><strong>K10</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased(^a) distress</td>
<td>5 (14.7)</td>
<td>2 (9.5)</td>
<td>6 (20)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>No change</td>
<td>22 (64.7)</td>
<td>12 (57.1)</td>
<td>17 (56.7)</td>
<td>13 (76.5)</td>
</tr>
<tr>
<td>Decreased(^b) distress</td>
<td>7 (20.6)</td>
<td>7 (33.3)</td>
<td>7 (23.3)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td><strong>Subjective mood</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lowered(^a) mood</td>
<td>7 (21.2)</td>
<td>7 (33.3)</td>
<td>13 (43.3)</td>
<td>4 (23.5)</td>
</tr>
<tr>
<td>No change</td>
<td>23 (69.7)</td>
<td>10 (47.6)</td>
<td>15 (50)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Improved(^b) mood</td>
<td>3 (9.1)</td>
<td>4 (19)</td>
<td>2 (6.7)</td>
<td>3 (17.6)</td>
</tr>
</tbody>
</table>

\(^a\) \(\geq 20\%\) increase (K10) or decrease (subjective mood) in mood score, compared with baseline score

\(^b\) \(\geq 20\%\) decrease (K10) or increase (subjective mood) in mood score, compared with baseline score
CHAPTER 6

Coping style and ecstasy use motives as predictors of current mood symptoms in ecstasy users

This chapter comprises of an article submitted for publication in *Journal of Affective Disorders*. This journal has a word limit of 4000-5000 words, excluding references and up to 6 tables/figures. The format is according to the guidelines for this journal.
6.1 Introduction to article three: As reported in articles one and two, stressful life events are associated with both current mood symptoms and an increase in symptoms in the short-term, consistent with aetiological models for depression and anxiety. In line with the overarching aim of the thesis, the research presented in this chapter aimed to explore coping style and ecstasy use motives as potential risk factors for current mood symptoms. Secondly, based on consideration of the data, a new line of data analysis was undertaken, taking into consideration the findings presented in article one. Specifically, as raised in article two, it is possible that ecstasy users may be particularly vulnerable to experiencing mood symptoms in the face of stressful life events with coping skills deficits being implicated in the aetiology of comorbid mental illness and substance misuse. Secondly, it has been proposed that some individuals are using ecstasy to cope with mood symptoms. However, there is a lack of research looking at the coping skills of ecstasy users and the relationship between ecstasy use motives and mood symptoms. The empirical paper presented in this chapter aimed to identify whether coping motives and an emotion-focused coping style were risk factors for current mood symptoms. Furthermore, this paper expands upon the findings from article one by investigating the role of coping in explaining the relationship between environmental risk factors (i.e. trauma and stressful life events) and current mood symptoms.
6.2 Declaration for Thesis Chapter Six

Declaration by candidate

In the case of Chapter Six the nature and extent of my contribution to the work was the following:

<table>
<thead>
<tr>
<th>Nature of contribution</th>
<th>Extent of contribution (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conceptualisation of study design; data collection; data analysis; conceptualisation of paper; and write up</td>
<td>80%</td>
</tr>
</tbody>
</table>

The following co-authors contributed to the work. Co-authors who are students at Monash University must also indicate the extent of their contribution in percentage terms:

<table>
<thead>
<tr>
<th>Name</th>
<th>Nature of contribution</th>
<th>Extent of contribution (%) for student co-authors only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr Leanne Hides</td>
<td>Provided guidance on study design, measures selection, statistical analysis and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr J. Sabura Allen</td>
<td>Provided guidance on methodology, including measures selection and statistical analysis; and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
</tr>
<tr>
<td>Dr Dan Lubman</td>
<td>Provided guidance on study design and write up, including reading drafts and providing feedback</td>
<td>n/a</td>
</tr>
</tbody>
</table>

Candidate’s Signature   Date

Declaration by co-authors

The undersigned hereby certify that:

(13) the above declaration correctly reflects the nature and extent of the candidate’s contribution to this work, and the nature of the contribution of each of the co-authors.

(14) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;

(15) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;

(16) there are no other authors of the publication according to these criteria;
(17) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(18) the original data are stored at the following location(s) and will be held for at least five years from the date indicated below:

| Location(s) | Monash University, Melbourne, Australia |

[Please note that the location(s) must be institutional in nature, and should be indicated here as a department, centre or institute, with specific campus identification where relevant.]

| Signature 1 |   | Date |
| Signature 2 |   |      |
| Signature 3 |   |      |
Coping style and ecstasy use motives as predictors of current mood symptoms in ecstasy users

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Abstract

**Background:** It has been proposed that the elevated depressive/anxiety symptoms in ecstasy users may be due to the use of ecstasy to cope with pre-existing symptoms. However, little is known about the coping styles of ecstasy users. This study aimed to determine whether current mood symptoms would be predicted by coping style or ecstasy use motives in an ecstasy using sample. An additional aim was to examine whether ecstasy motives and coping style help explain the previously identified relationship between trauma/stressful life events and current mood symptoms in this sample. **Methods:** A community sample (n=184) of 18-35 year olds who had taken ecstasy at least once in the past 12 months completed the Mood and Anxiety Symptom Questionnaire, the Drinking/Drug Motives Questionnaire, the Coping Inventory for Stressful Situations, and timeline methods were used to collect information on lifetime ecstasy, recent drug use and life stress. Trauma exposure was measured using the Composite International Diagnostic Interview - Trauma List. **Results:** Coping motives for ecstasy use and an emotion-focused coping style were significant predictors of current depressive/anxiety symptoms. Emotion-focused coping mediated the relationship between history of trauma and current anxiety symptoms and moderated the relationship between recent stressful life events and current depressive symptoms. **Limitations:** Cross-sectional design and reliance on participant self-report. **Conclusions:** These findings highlight the importance of interventions targeting the functional aspects underlying substance use and to emphasise coping skills training for managing stressful life events for people with co-occurring depressive/anxiety symptoms and substance use.

Key words: ecstasy, mood, coping, substance use motives, trauma, life stress
Population based studies continue to indicate higher rates of ecstasy (3,4-methylenedioxymethamphetamine or MDMA) use in Australia, compared with international figures, including those observed in the US, UK and Europe (United Nations Office on Drugs and Crime, 2009). Ecstasy is particularly popular among young adults with 1 in 9 (11.2%) 20 to 29 year olds in Australia having used ecstasy in the past 12 months (Australian Institute of Health and Welfare, 2008). Ecstasy is taken for its acute effects, including feelings of euphoria, increased energy, and greater sociability and connectedness with others (Cohen, 1995; White et al., 2006). However, many individuals report using ecstasy to alleviate negative mood states (Boys et al., 2001; White et al., 2006).

Longitudinal studies indicate that people with heightened depressive and anxiety symptomatology in childhood and adolescence are more likely to use ecstasy in later adolescence and young adulthood (Huizink et al., 2006) and that the onset of mental disorders in ecstasy users typically precedes the onset of ecstasy use (Lieb et al., 2002). Consequently, it has been suggested that elevated depressive/anxiety symptoms in ecstasy users may be associated with the use of ecstasy to cope with pre-existing mood symptoms (Huizink et al., 2006; Lieb et al., 2002). The current study focused on the exploration of coping styles and ecstasy use motives in predicting mood symptoms.

The co-occurrence of depressive/anxiety symptomatology and ecstasy use is likely to be complex with a number of possible explanations for this relationship. Ecstasy and other drug use may exacerbate existing mood symptoms or lead to depressive/anxiety symptomatology through biological and/or environmental mechanisms, such as serotonin neurotoxicity (McCann et al., 2008) and greater risk of exposure to adverse life events, consistent with a drug-using lifestyle. Secondly, lowered mood or anxiety may lead to the onset or continuation of substance use through self medication (Huizink et al., 2006).
Thirdly, shared risk factors may increase the risk of both depressive/anxiety symptomatology and ecstasy and other drug use (Kessler, 2004; Merikangas et al., 1994).

Given the limited research in this area, we recently investigated the relative contribution of known risk factors for depression, anxiety and substance use on current mood symptoms in a community sample of ecstasy users (Scott et al., 2010). We found that trauma exposure, recent life stress and other drug use factors, but not genetic or ecstasy use factors, were significant predictors of current depressive and anxiety symptomatology. This finding was consistent with the work of MacInnes et al. (2001), who found that life stress was associated with severity of depressive symptomatology in a group of former ecstasy users. Further, in a study looking at their psychosocial profile, young ecstasy users reported more experiences of childhood abuse and neglect, were more likely to have clinically significant symptoms of depression and reported a heavier pattern of polydrug use, compared to ecstasy-naive drug using controls (Singer et al., 2004). The authors concluded that a history of trauma may have played a role in the onset of later drug use. Indeed, one possible explanation for the high rates of substance use disorders found in people with a history of trauma is that substances are being used to alleviate negative mood states and trauma related symptoms (e.g., hyperarousal) in the context of coping skills deficits (Staiger et al., 2009; Stewart and Conrad, 2003).

Coping refers to the way a person manages or responds to a stressful event (Lazarus and Folkman, 1984). Research findings have consistently found that task-focused coping (e.g., problem solving) is negatively associated with psychological distress, while emotion-focused coping, which relates to managing or regulating one’s emotional response to a stressful event (e.g., worrying, blaming oneself), has been associated with poorer psychological and behavioural adjustment, including depression and anxiety (Endler and
Parker, 1994; McWilliams et al., 2003) and substance use (Cooper et al., 1988; Staiger et al., 2009). The use of an emotion-focused or avoidant coping style (e.g., mental and behavioural disengagement) has also been found to increase risk of psychological symptoms following trauma exposure (Gil, 2005; Spaccarelli, 1994). To date, research on coping in ecstasy users is limited to one study looking at how ecstasy users, ecstasy-naïve drug users (e.g., alcohol, cannabis, amphetamine users) and nondrug users cope with loneliness (Rokach and Orzeck, 2003). There are no known studies looking at the general coping styles of ecstasy users, and in particular, whether coping style can help explain the relationship between trauma/stressful life events and current mood symptoms in this population.

Consistent with the self-medication hypothesis (Khantzian, 1997), a significant number of ecstasy users report using ecstasy to feel better when down or depressed, to reduce worry, or to escape (Boys et al., 2001; Ter Bogt and Engels, 2005; White et al., 2006). Ter Bogt and Engels (2005) examined ecstasy use motives and consequences of ecstasy use amongst rave attendees. Data from the ecstasy users in their sample (n=372) indicated that the most common motives for ecstasy use were increased energy and euphoria, followed in decreasing order by sociability/flirtatiousness, sexiness, coping, self-insight and conformity. Motives were related to extent of ecstasy use and self-reported consequences of use. Specifically, high scores on the euphoria and sexiness motives were associated with heavier ecstasy use and those motivated by sociability/flirtatiousness used less ecstasy. High scores on euphoria, sexiness, and self-insight were associated with more self-reported positive effects of ecstasy use, while females using ecstasy to forget their problems and males using ecstasy to conform with their friends reported more negative effects of ecstasy use. Indeed, drug use aimed at alleviating negative mood states (coping motives) has been associated with greater frequency and quantity of drug use, psychopathology, and substance-related problems (Boys and Marsden, 2003; Brodbeck et al., 2007; Redman,
Furthermore, coping motives have been associated with history of stressful and traumatic life events (Brodbeck et al., 2007; Redman, 2008) and have been found to mediate the relationship between childhood abuse and neglect and substance use problems (Grayson and Nolen-Hoeksema 2005; Schuk and Widom, 2001). Together these findings indicate that individuals with a history of trauma may be more likely to (ab)use substances in order to self-medicate aversive symptoms (Stewart and Conrod, 2003) and in turn may be more vulnerable to substance-related harm.

Many researchers have suggested that premorbid factors may increase the risk of depressive/anxiety symptoms and ecstasy use. However, few studies have considered the role of potential risk factors for depressive/anxiety symptomatology and substance use in studies of ecstasy users. Further, it has been proposed that the elevated depressive/anxiety symptoms in ecstasy users may be associated with the use of ecstasy to cope with pre-existing mood symptoms (Huizink et al., 2006; Lieb et al., 2002), yet there is currently a lack of research looking at the coping styles of ecstasy users and the relationship between ecstasy use motives and current mood symptoms. Consequently, the current study aimed to 1) investigate whether coping style or ecstasy use motives predict current depressive/anxiety symptomatology in a community sample of ecstasy users, and 2) investigate whether ecstasy use motives and coping style help explain the relationships between environmental risk factors (trauma and life stress) and current mood symptoms in this sample. It was hypothesised that 1) coping motives for ecstasy use and emotion-focused coping would predict current depressive/anxiety symptomatology, 2) people with a history of trauma would be more likely to report coping motives for ecstasy use and would be more likely to engage in an emotion-focused coping style, 3) coping motives and emotion-focused coping would mediate the relationship between history of trauma and current mood symptoms, and 4) coping motives and emotion-focused coping would
moderate the relationship between recent life stress and current mood symptoms.

Method

Participants

The method has been described in detail elsewhere (Scott et al., 2010). Briefly, 190 participants aged between 18 and 35 who had taken ecstasy at least once in the last 12 months were recruited from the community in Melbourne, Australia. Participants were recruited using the ‘snowball’ technique (Solowij et al., 1992), as well as through advertising with local universities, a national dance music website, a local newspaper and a free street music magazine, and distributing flyers in cafes, music stores, and dance music events. Exclusion criteria were current pregnancy, lack of English fluency and a history of a psychotic disorder.

Measures

Substance use. Participants provided substance use information including age at first use, most frequent use, and the total number of drugs tried were tallied to provide a lifetime polydrug use score (maximum possible score=12). A context-based timeline method was used to estimate total lifetime number of ecstasy pills consumed (Bedi and Redman, 2006). Recent frequency and quantity of drug use was assessed using the Timeline Followback for the preceding 28 days (TLFB; Sobell and Sobell, 1992).

Mood symptoms. Current depressive and anxiety symptomatology were measured using the 62-item Mood and Anxiety Symptom Questionnaire – Short Form (MASQ; Watson and Clark, 1991). This self-report measure provides two subscales of general distress (GD) symptomatology (GD Anxious and GD Depressive), a depression-specific scale (Anhedonic Depression) and an anxiety-specific subscale (Anxious Arousal). Participants indicated how much they had experienced each symptom over the previous week (1 = not
Motives. Ecstasy use motives were assessed using the 20-item Drinking/Drug Motives Questionnaire (DMQ-R/DUMM (Drug Use Motives Measure) (Cooper, 1994; Mueser et al., 1995, respectively). Thinking of all the times they had taken ecstasy, participants rated how often they had taken ecstasy for enhancement (e.g., to get high; because it’s fun), social (e.g., to be sociable; because it helps you enjoy a party), coping (e.g., because it helps when you feel depressed or nervous; to forget your worries), and conformity (e.g., to fit in with a group you like; so you won’t feel left out) motives, with 5 items pertaining to each subscale. This scale has demonstrated acceptable levels of internal consistency and construct validity in assessing motives for alcohol and other substance use in the general population and clinical samples (Cooper, 1994; Mueser et al., 1995).

Coping. Coping was assessed using the Coping Inventory for Stressful Situations (CISS; Endler and Parker, 1994). This 48-item measure of task-focused (e.g., focus on the problem and see how I can solve it; outline my priorities), emotion-focused (e.g., become very tense; get angry; become very upset; blame myself for being too emotional about the situation), and avoidance-focused (e.g., phone a friend; watch TV) coping has demonstrated good reliability and validity in both community and clinically depressed populations (Endler and Parker 1994; McWilliams et al., 2003).

Trauma. Exposure to traumatic life events was assessed with the 11-item Composite International Diagnostic Interview – trauma list (CIDI; World Health Organisation, 1997). The CIDI trauma list outlines life events that meet DSM-IV criterion A for posttraumatic stress disorder (exposure to a traumatic event; American Psychiatric Association, 2000).
Recent life stress. Participants were asked if they had experienced any major stressful life events in the month preceding the interview while completing the TLFB. Life events were defined according to subject areas from the Psychiatric Epidemiological Research Interview (PERI) – Life Events Scale (Dohrenwend et al., 1978). Events were tallied to provide a total recent stressful life events score. Participants also rated how stressed they felt in general over the past month (subjective stress; 1 = not stressed at all to 10 = extremely stressed).

Procedure

The study was approved by the Monash University human ethics committee. Potential participants were initially screened in a brief telephone interview to ensure they met the inclusion criteria. To minimise potential subacute drug effects, participants were required to abstain from ecstasy use for seven days prior to participating, other recreational substance use for 24 hours, with the exception of alcohol (for 12 hours only) and tobacco and caffeine. Participants completed all questionnaires in a one hour face-to-face interview with a postgraduate clinical psychology student (R.S.). All participants provided informed consent and were reimbursed AU$25.

Statistical analysis

Pearson’s correlations were conducted to establish whether there were significant relationships between lifetime ecstasy and polydrug use, recent drug use, trauma, recent life stress, ecstasy use motives, coping styles, and the MASQ subscales (dependent variables). Hierarchical regression analyses were then performed to assess whether trauma, ecstasy use motives and coping styles predicted current mood symptoms, after controlling for covariates. Mediated regressions were conducted to establish whether ecstasy use motives and coping styles mediated the relationship between trauma and current mood symptoms. Finally, moderated regressions were used to establish whether coping styles or
ecstasy use motives moderated the relationship between recent stressful life events and current mood symptoms.

Following initial data screening, outliers were truncated to one above or below the outlier scores. Logarithmic transformation was used on lifetime ecstasy use to reduce skewness and improve normality. Due to significant findings in past research, gender and log lifetime ecstasy use were entered as covariates. Similarly, frequency of tobacco use and recent polydrug were identified as covariates in previous analyses with this sample (Scott et al., 2010) and were included in subsequent analyses. One way analyses of variance and correlations were conducted to identify any additional covariates to be included. No significant relationships between the main variables of interest and demographic and recent substance use variables were found, with the exception of negative correlations between recent ecstasy use, alcohol use and number of drug-using days with Anhedonic Depression. Internal consistency was established for all scales used with the current sample. All coefficients ranged from good to very good (Cronbach’s αs = .74-.92). Two participants were identified as multivariate outliers using Mahalanobis distance (p<.001) and were deleted from all regression analyses. An alpha level of .01 was adopted to indicate statistical significance in all analyses given the increased likelihood of type I error caused by the multiple comparisons made. All data were analysed using SPSS version 17 (SPSS Inc., Chicago, IL, USA).

Results

Sample characteristics

Of 190 consenting participants, four were excluded due to non-compliance with the abstention criteria and two for lack of English fluency. Sample characteristics of the final data set (n=184) including demographics, substance use variables and prevalence of trauma and stressful life events are reported in a previous paper (Scott et al., 2010). These are
summarised in Table 1. There was considerable variation in extent and duration of ecstasy use within the sample. However, polydrug use was the norm, with the majority of the sample having tried alcohol (100%), cannabis (95.7%), tobacco (94.6%), amphetamines (75.0%) and hallucinogens (64.7%). Mean scores for ecstasy use motives indicate that enhancement motives were the most highly endorsed ($M=4.27; SD=.83$), followed by social ($M=3.49; SD=.92$), coping ($M=2.06; SD=.98$), and conformity ($M=1.54; SD=.69$) motives. For the coping scale, the mean score for task-focused coping was 53.58 ($SD=10.29$), emotion-focused was 40.94 ($SD=10.79$) and avoidance was 47.05 ($SD=10.03$). Females scored significantly higher on emotion-focused coping than males ($F(1,183)=6.22, p=.01$; males: $M=38.87, SD=10.25$; females: $M=42.79, SD=10.98$). No other significant gender differences were found for motives or coping scale scores.

**Correlational analysis**

Pearson’s correlations between the MASQ subscales and demographic, drug use variables, trauma, recent life stress, ecstasy use motives and coping styles are presented in Table 2. As expected, coping motives for ecstasy use and an emotion-focused coping style moderately correlated with all MASQ subscales and there was a strong association between emotion-focused coping and GD depressive ($r=0.50$). Conformity motives had a small association with both GD subscales and Anxious Arousal, while social motives had a small association with GD anxious. Enhancement motives were not related to the MASQ subscales. Task-focused coping had a small negative association with both depression subscales, while avoidance coping was not associated with current mood symptoms. Trauma was moderately associated with emotion-focused coping and had a small association with coping motives and current anxiety symptoms. Recent stressful life events and subjective stress correlated with all MASQ subscales with small-moderate associations. Coping motives moderately correlated with emotion-focused coping. Task-focused coping was weakly associated with an older age of first ecstasy use. Log lifetime
ecstasy use had small positive correlations with enhancement, social and coping motives but was not associated with any of the coping scales. Of the drug variables, only frequency of tobacco use weakly correlated with the MASQ subscales (Anxious Arousal and GD Anxious).

Regression analyses

*Motives for ecstasy use.* A series of hierarchical regression analyses were conducted to determine which ecstasy use motives significantly predicted current depressive/anxiety symptomatology (see Table 3). Covariates were included at Step 1 (gender, log lifetime ecstasy use, tobacco frequency, recent polydrug use), followed by ecstasy use motives at Step 2 (enhancement, social, coping and conformity). At Step 1, no covariate was a significant predictor. However, when participants who had taken psychotropic medication within the last month were excluded (*n*=14), recent polydrug use became a significant predictor of GD Anxious, with a greater number of drugs consumed in the past 28 days being associated with more severe general distress anxiety symptoms. At Step 2, coping motives significantly predicted all MASQ subscales. When participants who had taken psychotropic medication within the last month were excluded, high scores on enhancement motives became associated with less severe current depressive symptoms.

*Coping styles.* A second series of regression analyses were conducted to establish which coping styles predicted current depressive and anxiety symptomatology, after controlling for covariates (see Table 4). Covariates were included at Step 1, followed by coping styles at Step 2 (task, emotion and avoidance). At Step 2, task and avoidance coping were negatively related to Anhedonic Depression, however task was no longer significant after excluding those currently taking psychotropic medication. Emotion-focused coping significantly predicted all MASQ subscales with higher emotion-focused
coping scores being associated with more severe current depressive/anxiety symptomatology.

**Mediation analysis.** Using the criteria outlined in Baron and Kenny (1986), regression analyses were conducted to establish whether coping motives and emotion-focused coping mediated the relationship between trauma and current depressive and anxiety symptomatology. Covariates were entered at Step 1. At Step 2, trauma was a significant predictor of the Anxious Arousal and GD Anxious subscales of the MASQ (Scott et al., 2010; see Table 5). Consistent with criterion 2, trauma was a significant predictor of emotion-focused coping ($\Delta R^2 = .09, p < .001$), but not coping motives ($\Delta R^2 = .02, p = .06$), after controlling for covariates. However, after controlling for emotion-focused coping, trauma was no longer associated with Anxious Arousal and GD Anxious (see Table 6), indicating that emotion-focused coping mediated the relationship between trauma and current anxiety-related symptoms.

**Moderation analysis.** Multiple regression analyses were conducted to determine whether the relationship between recent stressful life events and current mood symptoms was affected by coping motives or emotion-focused coping. Covariates were entered at Step 1 ($F$ statistic: Anhedonic=1.24; Anxious Arousal=1.43; GD Depressive=0.82; GD Anxious=2.65). To represent the interaction between stressful life events and coping motives and emotion-focused coping, the variables were first centred and multiplied together. Given that stressful life events, emotion-focused coping and coping motives had been identified as significant predictors in earlier analyses, these were entered together with the interaction terms at Step 2 ($F$ change: Anhedonic=11.22; Anxious Arousal=6.79; GD Depressive=21.86; GD Anxious=0.06). At step 2, stressful life events
was a significant predictor of Anhedonic Depression, GD Depressive and GD Anxious\(^2\) (\(\beta_s=0.17, 0.31, 0.32\), respectively). Emotion-focused coping significantly predicted Anhedonic Depression, Anxious Arousal, GD Depressive and GD Anxious (\(\beta_s=0.32, 0.21, 0.43, 0.28\)). Coping motives significantly predicted Anxious Arousal and GD Anxious (\(\beta_s=0.21\) and 0.19) but was no longer a significant predictor of Anhedonic Depression and GD Depressive after entering the interaction terms (\(\beta_s=0.14\) and 0.10). The stressful life events X emotion-focused coping interaction was a significant predictor of Anhedonic Depression (\(\beta=0.21\)) but not Anxious Arousal, GD Depressive or GD Anxious (\(\beta_s=0.09, 0.11, -0.01\)). Using equations derived from the standardised \(\beta\) values, the relationship between stressful life events and emotion-focused coping was explored to establish the direction of the relationship. Accordingly, when emotion-focused coping is high there is a strong positive relationship between stressful life events and Anhedonic Depression. However, when emotion-focused coping is low there was no association between recent stressful life events and current depressive symptoms. None of the stress X coping motives interactions were significant.

**Discussion**

Consistent with our hypotheses, ecstasy users who reported using ecstasy to cope and those engaging in high levels of emotion-focused coping reported more severe levels of current depressive/anxiety symptoms. Results also indicated that the relationship between trauma and current anxiety symptoms was explained by coping style. Specifically, ecstasy users with a history of trauma were more likely to use an emotion-focused coping style, which in turn was associated with more severe anxiety symptoms. In addition, the relationship between recent stressful life events and current depressive symptoms was moderated by emotion-focused coping. That is, an association between current depressive

\(^2\) As reported elsewhere (Scott et al., 2010)
symptomatology and recent stressful life events occurred only in the context of elevated emotion-focused coping.

These findings are consistent with previous research that emotion-focused coping relates to increased risk for depressive and anxiety symptomatology (Endler and Parker, 1994; McWilliams et al., 2003). Secondly, while enhancement and social motives for ecstasy use were the most highly endorsed, only coping motives were related to more severe depressive/anxiety symptoms and greater lifetime ecstasy use, consistent with past research (Brodbeck et al., 2007; Redman, 2008). These findings suggest that coping motives may be a risk factor for a heavier pattern of drug use and that both an emotion-focused coping style and coping motives may be risk factors for depressive/anxiety symptomatology in ecstasy users. Given that those with high emotion-focused coping were more likely to endorse coping motives suggest that some ecstasy users may be using ecstasy to self medicate in the context of coping skills deficits.

As hypothesised, emotion-focused coping helped explain the relationship between trauma and current mood symptoms, consistent with past research that emotion-focused coping style increases risk of psychological symptoms following trauma exposure (Gil, 2005; Spaccarelli, 1994). It has been proposed that childhood trauma impacts upon the developing brain, including areas involved in affect-regulation, thus increasing risk of psychiatric disorder and substance abuse (Teicher et al., 2002). It is also possible that affect-regulation or adaptive coping skills may not have been acquired in childhood environments associated with elevated risk of trauma.

Contrary to our hypotheses, trauma did not significantly predict coping motives, after controlling for gender and drug use factors. Although a significant number of ecstasy users report using ecstasy to cope with negative affect (Boys et al., 2001), ecstasy may not be the
drug of choice to alleviate trauma related symptoms such as hyperarousal. Indeed, alcohol and other depressants may be more likely to be used to self-medicate trauma-related symptoms (Hien et al., 2005). Given the intoxicating effects of ecstasy, ecstasy may serve to temporarily alleviate depressed mood and obtain closeness with others, rather than reducing trauma-related hyperarousal or anxiety symptoms.

A number of propositions have been put forward to explain the relationship between ecstasy and mood. Although the cross-sectional nature of the study’s design does not make it possible to make conclusions about the direction of causality, the current findings suggest that some ecstasy users may be using ecstasy to cope with pre-existing mood symptoms. Indeed, those with a self-reported history of unipolar depression and/or an anxiety disorder \((n=42)\) scored significantly higher on coping motives for ecstasy use. Furthermore, the majority of these individuals (80%) reported that mood symptoms preceded the first ecstasy use, consistent with other studies (de Win et al., 2004; Lieb et al., 2002). However, it remains possible that ecstasy use may also lead to depressive or anxiety symptoms in vulnerable individuals, exacerbate pre-existing mood symptoms, or that shared risk factors are contributing to both mood symptoms and ecstasy/other drug use.

The lack of a consistent directional relationship between depression and substance use disorders highlights the likelihood that multiple pathways of associations exist (Swendsen and Merikangas, 2000). Similarly, it is likely that all of these propositions are also applicable to ecstasy and mood. Prospective studies are required to further understand the interactions between these variables.

Coping motives were associated with recent subjective life stress but not stressful life events, suggesting that individuals using ecstasy to alleviate negative mood states may be in a chronic state of heightened stress, even in the absence of specific stressful life events,
or have a high level of trait anxiety. This finding, along with the finding that emotion-focused coping was related to all MASQ subscales, while task and avoidance coping were only related to the depression-specific subscale of the MASQ, highlight the importance of teaching emotion-regulation strategies to individuals presenting with psychological distress and substance use, and highlight the particular relevance for teaching alternative coping strategies such as distraction, problem solving and seeking social support for those experiencing depression-specific symptoms, such as anhedonia. Indeed, coping motives were associated with heavier lifetime ecstasy use, suggestive of limited alternative coping strategies. In contrast, emotion-focused coping was not related to lifetime ecstasy use, indicating that it may not be a risk factor for a heavy pattern of ecstasy use, although it may be a risk factor for the onset and ongoing use of substances in general. In contrast, task-focused coping was associated with a later onset of ecstasy use suggesting that it may be a protective factor against early onset drug use.

As reported elsewhere (Scott et al., 2010), there are a number of limitations to the current study that need to be acknowledged. These include the use of a cross-sectional design using retrospective self-report measures. It is possible that the presence of current mood symptoms inflated recall of past adverse life events (Schraedley et al., 2002). Recent and lifetime drug use were not confirmed using biological analysis. It is possible that subacute drug effects may have impacted upon self-reported mood symptoms reported for the past week. However, consistent with other studies in this area (e.g., Bedi et al., 2008), a 24-hour abstinence period was implemented for cannabis to balance potential subacute and withdrawal drug effects (Pope et al., 2001; Kouri and Pope 2000) and to allow for the inclusion of wide range of drug users with respect to frequency of use. No significant correlations between days since last use of individual substances and current mood symptoms were found.
The strengths of the current study include the recruitment of a large inclusive sample of ecstasy users with varying levels of drug use, including those with psychiatric history and currently taking psychotropic medication. Furthermore, the use of the MASQ allowed for the examination of independent relationships between ecstasy use motives and coping styles and depression-specific, anxiety-specific and general distress symptomatology. Finally, this study expanded on previous research identifying risk factors for depressive/anxiety symptomatology in ecstasy users and is the first known study to examine the coping styles and associated mood symptoms in a community sample of ecstasy users.

Role of Funding Sources
Rebecca Scott was supported by an Australian Postgraduate Award and the project was funded by Monash University, School of Psychology and Psychiatry. Drs Hides and Lubman are supported by the Colonial Foundation. Monash University and the Colonial Foundation had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Conflict of Interest
All authors declare that they have no conflicts of interest.

Acknowledgements
The authors wish to thank Dr Simon Moss for statistical assistance.


Bedi, G., Van Dam, N.T., Redman, J. (2008). Ecstasy (MDMA) and high prevalence symptomatology: somatic anxiety symptoms are associated with polydrug, not ecstasy, use. J Psychopharmacol, 0, 1-8.


and validation of a four-factor model. Psychol Assess. 6, 117-128.


Table 1

**Sample characteristics: demographics, drug use, and trauma prevalence (n = 184)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (SD; range)</td>
<td>23.3 (4.0; 18-35)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Males</td>
<td>47.3%</td>
</tr>
<tr>
<td>Females</td>
<td>52.7%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>White/Caucasian</td>
<td>72.3%</td>
</tr>
<tr>
<td>Asian</td>
<td>6.5%</td>
</tr>
<tr>
<td>Indian</td>
<td>6.0%</td>
</tr>
<tr>
<td>Mixed ethnicity</td>
<td>5.4%</td>
</tr>
<tr>
<td>Indigenous Australian</td>
<td>1.1%</td>
</tr>
<tr>
<td>Other</td>
<td>8.7%</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Tertiary student</td>
<td>66.3%</td>
</tr>
<tr>
<td>Full time employment</td>
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<tr>
<td>Part time employment</td>
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<tr>
<td>Unemployed</td>
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<td>Lifetime psychiatric diagnosis</td>
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<tr>
<td>Any diagnosis</td>
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</tr>
<tr>
<td>Unipolar depression</td>
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</tr>
<tr>
<td>Anxiety disorder</td>
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</tr>
<tr>
<td>SUD&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.7%</td>
</tr>
<tr>
<td>PTSD&lt;sup&gt;b&lt;/sup&gt;</td>
<td>.5%</td>
</tr>
<tr>
<td>Currently&lt;sup&gt;c&lt;/sup&gt; taking psychiatric medication</td>
<td>8.2%</td>
</tr>
<tr>
<td>Age at first ecstasy use (M; SD; range)</td>
<td>19.1; 2.5 (12 - 31)</td>
</tr>
<tr>
<td>Duration of ecstasy use (years) (M; SD; range)</td>
<td>4.2; 3.1 (&lt;1 - 18)</td>
</tr>
<tr>
<td>Lifetime ecstasy use (pills) (M; SD; range)</td>
<td>172.4; 507.4 (.5 - 5332)</td>
</tr>
<tr>
<td>Lifetime polydrug use (M; SD; range)</td>
<td>7.4; 2.4 (2-12)</td>
</tr>
<tr>
<td>Recent stressful life events (M; SD; range)</td>
<td>1.3; 1.2; (0-5)</td>
</tr>
<tr>
<td>Trauma exposure (no.) (M; SD; range)</td>
<td>1.9; 1.8 (0-10)</td>
</tr>
<tr>
<td>0</td>
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<tr>
<td>1</td>
<td>22.8%</td>
</tr>
<tr>
<td>2</td>
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<td>3</td>
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<td>4+</td>
<td>21.7%</td>
</tr>
</tbody>
</table>

<sup>a</sup>Substance use disorder, <sup>b</sup>Posttraumatic stress disorder, <sup>c</sup>Taken within the last month
Table 2
Correlations of the MASQ subscales, drug use, trauma, recent life stress, motive scales and coping styles (n = 184)

<table>
<thead>
<tr>
<th>Measure</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
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<th>17</th>
<th>18</th>
<th>19</th>
<th>20</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1. Anhedonic Depression</td>
<td></td>
<td>.19*</td>
<td>.60**</td>
<td>.32**</td>
<td>-.08</td>
<td>.11</td>
<td>-.10</td>
<td>-.06</td>
<td>-.08</td>
<td>-.05</td>
<td>-.15</td>
<td>.08</td>
<td>.26**</td>
<td>.33**</td>
<td>-.16</td>
<td>-.02</td>
<td>.31**</td>
<td>.10</td>
<td>-.26**</td>
<td>.40**</td>
<td>-.11</td>
</tr>
<tr>
<td>2. Anxious arousal</td>
<td></td>
<td>.43**</td>
<td>.74**</td>
<td>-.11</td>
<td>.01</td>
<td>-.14</td>
<td>.05</td>
<td>.03</td>
<td>.18*</td>
<td>.08</td>
<td>.26**</td>
<td>.18*</td>
<td>.27**</td>
<td>-.02</td>
<td>.15</td>
<td>.33**</td>
<td>.21*</td>
<td>-.15</td>
<td>.32**</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>3. GD depressive</td>
<td></td>
<td>.62**</td>
<td>-.04</td>
<td>.12</td>
<td>-.10</td>
<td>-.07</td>
<td>-.03</td>
<td>.01</td>
<td>-.00</td>
<td>.17</td>
<td>.41**</td>
<td>.46**</td>
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<td>.32**</td>
<td>.23*</td>
<td>-.18*</td>
<td>.51**</td>
<td>.08</td>
<td></td>
<td></td>
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<tr>
<td>4. GD anxious</td>
<td></td>
<td>.02</td>
<td>.05</td>
<td>-.07</td>
<td>.01</td>
<td>.10</td>
<td>.19*</td>
<td>.16</td>
<td>.26**</td>
<td>.38**</td>
<td>.43**</td>
<td>.04</td>
<td>.23*</td>
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<td>.25**</td>
<td>-.03</td>
<td>.40**</td>
<td>.07</td>
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<td>5. Age</td>
<td></td>
<td>-.16</td>
<td>.43**</td>
<td>.37**</td>
<td>.40**</td>
<td>.06</td>
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<td>.10</td>
<td>-.03</td>
<td>.01</td>
<td>.18*</td>
<td>.12</td>
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<td></td>
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<tr>
<td>6. Gender</td>
<td></td>
<td>.2</td>
<td>-.30**</td>
<td>-.30**</td>
<td>-.17</td>
<td>-.15</td>
<td>-.03</td>
<td>.17</td>
<td>.18*</td>
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<td>.12</td>
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</tr>
<tr>
<td>7. Age at first ecstasy use</td>
<td></td>
<td>-.34**</td>
<td>-.13</td>
<td>-.27**</td>
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<td>.00</td>
<td>.07</td>
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<td>-.10</td>
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</tr>
<tr>
<td>8. Log lifetime ecstasy use</td>
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<td>.65**</td>
<td>.41**</td>
<td>.37**</td>
<td>.13</td>
<td>-.25**</td>
<td>-.16</td>
<td>.21*</td>
<td>.19*</td>
<td>.24**</td>
<td>-.02</td>
<td>-.15</td>
<td>-.08</td>
<td>-.14</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
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<td>15. Enhancement motives</td>
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<td>17. Coping motives</td>
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</tbody>
</table>

*p ≤ .01, **p ≤ .001, a males = 0, females = 1, b total number of drugs consumed in lifetime (excluding ecstasy), c total number of drugs consumed in last 28 days, d last month
Table 3
Ecstasy motives: Hierarchical regression models predicting MASQ subscale scores (n = 182)

<table>
<thead>
<tr>
<th></th>
<th>Anhedonic Depression</th>
<th>Anxious Arousal</th>
<th>GD Depressive</th>
<th>GD Anxious</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>β</td>
<td>ΔR²</td>
<td>F</td>
<td>β</td>
</tr>
<tr>
<td>Step 1</td>
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<td></td>
</tr>
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<td>Gender^a</td>
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<td>1.24</td>
<td>.03</td>
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<tr>
<td>Log lifetime ecstasy use</td>
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<td>-.03</td>
<td>-</td>
<td>-.08</td>
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<td>Tobacco frequency</td>
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<td>.18</td>
<td></td>
<td>.02</td>
</tr>
<tr>
<td>Recent polydrug use^b</td>
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<td>.02</td>
<td></td>
<td>.02</td>
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<tr>
<td>Step 2</td>
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<td>Recent polydrug use^b</td>
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<td>Coping motives</td>
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<td>.30**</td>
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<td>Conformity motives</td>
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<td>.08</td>
<td>.07</td>
<td>.07</td>
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</table>

*p ≤ .01, **p ≤ .001, ^a males = 0, females = 1, ^b total number of drugs consumed in last 28 days
NB: When participants who had taken psychotropic medication in the last month were excluded (n=14), enhancement motives became a significant predictor (β = .24) of Anhedonic Depression. For GD Anxious, recent polydrug use became a significant predictor at step 1 (β = .24) and step 2 (β = .27) and log lifetime ecstasy use became a significant predictor at step 2 (β = .25). There were no changes to Anxious Arousal and GD Depressive.
Table 4
Coping styles: Hierarchical regression models predicting MASQ subscale scores (n = 182)

<table>
<thead>
<tr>
<th></th>
<th>Anhedonic Depression</th>
<th>Anxious Arousal</th>
<th>GD Depressive</th>
<th>GD Anxious</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>( \beta )</td>
<td>( \Delta R^2 )</td>
<td>( F )</td>
<td>( \beta )</td>
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<td><strong>Step 1</strong></td>
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<td>Gender</td>
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<td>.03</td>
<td>1.24</td>
<td>.10</td>
</tr>
<tr>
<td>Log lifetime ecstasy use</td>
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<td>-.03</td>
<td>-.08</td>
<td>-.11</td>
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<tr>
<td>Tobacco frequency</td>
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<td>.18</td>
<td>.02</td>
<td>.15</td>
</tr>
<tr>
<td>Recent polydrug use</td>
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<td>-.15</td>
<td></td>
<td>.15</td>
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<td><strong>Step 2</strong></td>
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<td>.01</td>
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<td>Tobacco frequency</td>
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<td>Recent polydrug use</td>
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<td>.06</td>
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<td>-.04</td>
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</table>

*\( p \leq .01 \), **\( p \leq .001 \), *males = 0, females = 1, \( \text{total number of drugs consumed in last 28 days} \)

NB. When participants who had taken psychotropic medication in the last month were excluded \( n=14 \), task coping was no longer a significant predictor of Anhedonic Depression \( \beta=-.14 \). For GD Anxious, recent polydrug use became a significant predictor at step 1 \( \beta=.24 \) and step 2 \( \beta=.22 \). There were no changes to Anxious Arousal and GD Depressive.
Table 5

Mediation analysis Step 1: Trauma as a predictor of MASQ subscale scores (n = 182)

<table>
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<tr>
<th></th>
<th>Anhedonic Depression</th>
<th>Anxious Arousal</th>
<th>GD Depressive</th>
<th>GD Anxious</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>β</td>
<td>ΔR²</td>
<td>F</td>
<td>β</td>
</tr>
<tr>
<td>Step 1</td>
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<tr>
<td>Gender&lt;sup&gt;a&lt;/sup&gt;</td>
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<td>Log lifetime ecstasy use</td>
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<td>-.03</td>
<td>-.08</td>
<td>-.11</td>
</tr>
<tr>
<td>Tobacco frequency</td>
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<td>.18</td>
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<td>.02</td>
</tr>
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<td>Recent polydrug use&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>.05</td>
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<td>.22*</td>
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*p ≤ .01, **p ≤ .001, <sup>a</sup>males = 0, females = 1, <sup>b</sup>total number of drugs consumed in last 28 days

NB. When participants who had taken psychotropic medication in the last month were excluded (n=14), recent polydrug use became a significant predictor at step 1 (β = .24) and step 2 (β = .22). There were no changes to the other subscales.
Table 6
Mediated regression Step 3 and 4: Trauma as a predictor of the MASQ anxiety subscale scores after controlling for emotion coping (n = 182)

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<td></td>
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<td>Gender</td>
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<td>.03</td>
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<td>Lifetime ecstasy use</td>
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<td>-.03</td>
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<td>Tobacco frequency</td>
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<tr>
<td>Recent polydrug use²</td>
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<tr>
<td>Gender</td>
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<td>Emotion coping</td>
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<td>.28**</td>
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</table>

*p ≤ .01, **p ≤ .001, ′males = 0, females = 1, ″total number of drugs consumed in last 28 days
NB. When participants who had taken psychotropic medication in the last month were excluded (n=14), recent polydrug use became a significant predictor at step 1 (β =.24), step 2 (β =.23) and step 3 (β =.22). There were no changes to Anxious Arousal.
Chapter 7

Integrated discussion
7.1 Chapter Overview

This discussion will discuss and integrate the key findings of the three research articles contained in this thesis. This discussion will include how the current findings relate to the existing ecstasy literature, including models for understanding the relationship between ecstasy and mood, as well as to the broader substance use and comorbidity literature. The clinical implications of the findings will also be discussed. The chapter concludes with a review of the strengths and limitations of the thesis and directions for future research.

7.2 Key findings

The current thesis aimed to address a previously understudied area of ecstasy research, by investigating potential risk factors for depressive and anxiety symptomatology in a community sample of ecstasy users. Findings from the cross-sectional study, presented in chapters 4 and 6, indicated that neither lifetime nor recent ecstasy use was associated with the severity of current mood symptoms, either alone or in combination with 5-HTTLPR genotype. Rather, lifetime trauma, recent stressful life events, coping style, ecstasy use motives and other drug use factors significantly predicted the severity of depressive and anxiety symptoms. Consistent with these findings, the prospective study, reported in chapter 5, found that lowered mood and increased psychological distress were associated with self-reported restless sleep and the number of stressful life events experienced over the follow up, and not by ecstasy use. These findings are consistent with aetiological models for depression and anxiety, indicating that adverse life events are a key risk factor in the development of depression and anxiety disorders (Kendler et al., 2002, 2006; Kessler 1997). They are also consistent with recent research finding subacute mood effects among ecstasy users were associated with other variables such as sleep disruption and other drug use rather than ecstasy use variables. The following section will discuss how the current findings relate to the risk factors identified in the clinical research literature.

7.3 Risk factors for depressive and anxiety symptomatology

7.3.1 Non-drug related risk factors

Demographic. Neither gender nor age were significant predictors of the severity of current mood symptoms or subacute mood effects during the 7-day follow up period. This contrasts with past research finding that females report more short and long-term psychological problems that they attribute to ecstasy (Topp et al., 1999) and that females were more likely to experience midweek low mood following weekend ecstasy use
(Verheyden et al., 2002). Two key differences between the current prospective study and that by Verheyden et al. may explain these conflicting findings. First, the current study did not find an effect of ecstasy on subacute mood. Consequently, the current findings are less likely to reveal a gender effect. Second, it is possible that pre-existing depression symptoms may have contributed to the observed gender difference in the Verheyden et al. study, as they did not control for baseline mood scores. Consistent with the current findings, Hoshi et al. (2006) found no gender differences in subacute mood effects, as measured by the BDI. In addition, a number of cross-sectional ecstasy studies have not observed gender differences in mood symptoms (e.g. de Win et al., 2004; Fingeret et al., 2005) and a review of gender differences in ecstasy users concluded there was no clear evidence for gender differences in long-term psychological symptoms in ecstasy users (Allott & Redman, 2007).

The lack of association between age at first ecstasy use and current symptoms is contrary to some studies (e.g. Daumann et al., 2004) but consistent with others (e.g. de Win et al., 2004). In contrast to ecstasy use, a younger age of first cannabis use was related to more severe current anxiety symptoms in the current sample, as reported in article one. This is consistent with findings that an earlier age of drug onset is related to poorer mental health, particularly depression, anxiety and conduct disorder (Teesson, Degenhardt, Lynskey, & Hall, 2005). The association between an earlier age of cannabis onset and anxiety symptoms may reflect a greater vulnerability to drug-related harm due to the extensive neuromaturational processes occurring during adolescence (Lubman, Yucel, & Hall, 2007). Alternatively, it may be associated with pre-existing mental health symptoms or other risk factors (e.g., parental conflict/separation, childhood sexual abuse) increasing the risk of early-onset drug use (Lynskey et al., 2003).

*Psychiatric history and genetic factors.* Consistent with our hypotheses, a past diagnosis of unipolar depression and/or an anxiety disorder was a significant predictor of current mood symptoms in Article One. In contrast, it was not a significant predictor of subacute mood effects, as reported in Article Two. This was unexpected as it has been proposed that people with a history of depression would be more likely to experience adverse subacute effects on mood (Parrott, 2006). However, given the lack of significant association between ecstasy and mood in the current study, it is not surprising. The proposal that people with a history of depression would be more likely to experience
adverse subacute effects on mood (Parrott, 2006) was not able to be adequately explored as the low rates of self-reported history of depression and/or anxiety disorders reported in the current sample (n=7) may have limited the power available to detect potential effects. There was a trend towards more severe baseline anxiety symptoms and the experience of subacute psychological distress following ecstasy use. However, this was a simple correlation and did not control for other confounding variables such as sleep. Further research with larger samples is required to test this hypothesis.

As described in Article One, the lack of significant associations between 5-HTTLPR genotype and genotype X ecstasy interaction with current mood symptoms contrasts with past findings with ecstasy users (Roiser et al., 2005). However, it is consistent with the results of a recent meta-analysis finding that 5-HTTLPR genotype did not predict depression, either alone or in combination with stressful life events (Risch et al., 2009). Unfortunately, the small sample size meant that 5-HTTLPR genotype on subacute mood effects could not be explored in the current thesis. However, as reported in a letter submitted to the editor (see Appendix 12), the distribution of genotype frequency in the current sample was significantly different to that reported in a New Zealand birth cohort (Caspi et al., 2003) with greater SS genotypes and fewer LL genotypes in the current sample. These findings suggest that the SS genotype may be a risk factor for commencing ecstasy use. Individuals with the SS genotype may be particularly attracted to the mood enhancing properties of ecstasy, given that the S allele is associated with reduced expression of the serotonin transporter and less reuptake of serotonin. While the current findings indicated no association between 5-HTTLPR genotype and current depressive and anxiety symptomatology, it remains possible that individuals with the SS genotype may experience more adverse effects (e.g., depressed mood) from ecstasy in the short- and/or long-term. Indeed, the S allele has been associated with poorer treatment response and greater adverse side effects from SSRIs (Serretti, Kato, De Ronchi, & Kinoshita, 2007; Smits et al., 2007), which, like ecstasy, affect the serotonin transporter. Clearly the potential role of the 5-HTTLPR genotype, and the SS genotype in particular, on depressive and anxiety symptomatology requires further exploration using large sample sizes.

Stressful life events and trauma. A history of trauma and recent stressful life events were significant risk factors for current mood symptoms in the current sample. This is consistent with aetiological models identifying adverse life events as a key risk factor for depression, anxiety and substance (ab)use (Kendler et al., 2002, 2006; Kessler 1997,
McCauley et al., 1997). In addition, the prospective study found that stressful life events were associated with negative mood change in the short term, supporting the robustness of findings regarding the relationship between stressful life events and mood symptoms in this sample. These findings are consistent with the ecstasy research literature, with one study finding that ecstasy users reported more experiences of childhood abuse and neglect than ecstasy-naïve drug-using controls (Singer et al., 2004) and that life stress has been found to be associated with current depressive symptomatology among former chronic ecstasy users (MacInnes et al., 2001).

In summary, a previous history of depression and/or an anxiety disorder, a history of trauma and recent stressful life events were found to be significant risk factors for current mood symptoms in this heterogeneous sample of ecstasy users. Consistent with the cross-sectional findings, stressful life events were also associated with negative mood change in a short-term prospective study. In contrast, demographic and genetic factors, including gender, current age, age of ecstasy onset and 5-HTTLPR genotype were not associated with current mood symptoms and no gender differences were found in the experience of mood symptoms following ecstasy use.

7.3.2 Patterns of drug use

Severity of drug use. No relationship was found between severity of ecstasy use (i.e. lifetime use, most frequent use and recent use) and current mood symptoms. Further, ecstasy dose and other drug use factors were not related to the experience of subacute mood effects following ecstasy use, contrasting with animal studies indicating a dose-dependent relationship (Green et al., 2003) and subacute research with humans finding a relationship between severity of subacute mood effects and number of ecstasy pills consumed (Verheyden et al., 2002). However, many subacute studies finding relationships between ecstasy dose and subacute mood have not controlled for baseline mood, meaning that pre-existing differences may have confounded these findings (e.g. Huxster et al., 2006; Pirona & Morgan, 2009). In one study that did calculate mood change from baseline to follow up, the baseline mood measure was taken on the night of drug use, rather than when the individuals were drug free (e.g. Verheyden et al., 2002).

However, as the content of tablets consumed by the current sample were not analysed for MDMA content, varying dose and purity of MDMA consumed may also have confounded the current findings. Despite this, the cross-sectional findings are consistent with other
studies finding no relationship between lifetime or recent ecstasy use and depressive and anxiety symptoms (Abdallah et al., 2007; Daumann et al., 2004; Medina & Shear, 2007) and that a heavier pattern of drug use in general may be more strongly related to the severity of depressive and anxiety symptoms (e.g., Bedi et al., 2008; Sumnall et al., 2004). In line with this, tobacco frequency was associated with severity of current anxiety symptoms, consistent with findings that smoking is highly prevalent amongst those with anxiety disorders (see Morissette, Tull, Gulliver, Kamholz, & Zimering, 2007 for review). Taken together, the current findings are in line with recent findings that mood symptoms are related to a heavier pattern of drug use in general, and not to ecstasy use per se.

*Ecstasy-use environment.* No statistically significant associations between ecstasy environmental factors (i.e. dancing or heat) and subacute mood effects were found, contrasting with past research (Parrott et al., 2006). A key difference between the current study and that by Parrott et al. (2006) is that the current study employed a prospective design, contrasting with Parrott et al.’s (2006) retrospective design. Prospective designs are less subject to recall bias, which is a strength of the current study. However, it remains possible that ecstasy-environment factors may play a role on subacute mood, for the reasons outlined in the literature review (see section 4.2). However, due to small sample size, the current study only conducted a correlation analysis, meaning that amount of ecstasy consumed was not controlled for. Given that MDMA-induced neurotoxicity in animals is dose-dependent (Green et al., 2003), it is possible that heat and dancing moderate the relationship between amount of ecstasy consumed and subacute mood effects, increasing the risk of subacute lowered mood in the context of larger amounts of ecstasy being ingested. Tolerance may also play a significant role here as ecstasy users consistently report having to take more ecstasy over time in order to achieve similar effects (Parrott, 2005).

*Sleep.* Consistent with recent research highlighting the confounding factor of sleep (Huxster et al., 2006; Pirona & Morgan, 2009), the current research indicated that restless sleep was a significant risk factor for negative mood change in the short term. This supports the proposal that associated lifestyle factors alone may affect ecstasy users psychological health (Parrott, 2001). Indeed, the current findings support recent research that the previously well-cited phenomenon of subacute mood, or ‘Tuesday bluesday’ is more strongly associated with disrupted sleep than ecstasy use, and suggests that findings from earlier studies may have been confounded by sleep factors (i.e. Curran & Travill,
In summary, the current thesis found no relationship between severity of ecstasy use and current mood symptoms, alone or in combination with 5-HTPPR genotype. Rather, tobacco frequency and a younger age of cannabis onset predicted current mood symptoms. Similarly, in the prospective study no significant associations were found between number of ecstasy pills, number of drugs taken or amount of alcohol and cannabis consumed and subacute negative mood effects. Furthermore, there were no significant associations with subacute negative mood and ecstasy-environment factors (heat/dancing). Rather, self-reported hours and quality of sleep significantly were significantly associated with negative mood effects over the follow up.

7.4 Ecstasy use and mood symptoms: Is there a relationship?

While the results from both studies provide no evidence that the severity of ecstasy use is associated with the severity of depression or anxiety symptoms, a higher rate of depressive symptoms and disorder was found in the current sample, compared with general population data, as highlighted in Article One. This suggests that there is a relationship between ecstasy and mood. However, the current findings indicate that it may be independent from severity of use. The following section will discuss the current findings with respect to current models for understanding co-occurring psychiatric disorders/symptomatology and substance use with a particular focus on ecstasy and mood.

7.4.1 Ecstasy use and mood symptoms: Models of comorbidity

As outlined in the literature review (see section 3), a number of explanations for comorbidity have been proposed. These include: 1) substance use leads to mental health problems, 2) mental health problems lead directly to substance use, i.e. the self medication hypothesis, 3) that there is an indirect causal relationship between substance use and mental health symptoms whereby one affects a third variable which in turn increases the risk of the other, and 4) there are shared risk factors that are related to increased likelihood of mental health problems and substance use (Degenhardt et al., 2004). The following section will review these proposed models with respect to the ecstasy literature and the current findings.

Substance use leads to mental health problems. Given that ecstasy is neurotoxic to
the serotonin system of laboratory animals (Ricaurte et al., 2000) and possibly humans (McCann et al., 2008), it has been proposed that ecstasy use may lead to depression and anxiety, particularly in vulnerable individuals (Parrott, 2006). Specifically, Parrott (2006) proposed that a heavier pattern of ecstasy and other drug use will interact with various predisposing factors such as genetic vulnerability leading to poor psychiatric outcomes such as depression. However, the lack of association between severity of ecstasy use and current mood symptoms in the current sample, alone and in combination with 5-HTTLPR genotype, suggests that this theory alone cannot sufficiently explain the elevated depression observed in the current ecstasy-using sample. The current results are consistent with findings gleaned from a longitudinal study finding no association between mood disorders or depressive symptoms and SERT binding (de Win et al., 2004) suggesting that MDMA-induced serotonin changes cannot fully explain the elevated mood symptoms observed in ecstasy users. Despite this, the current findings suggest that 5-HTTLPR genotype is not a vulnerability factor for depressive or anxiety symptomatology in ecstasy users. However, given the important role of genetics in the aetiology of depression and anxiety, it remains possible that ecstasy may lead to mood symptoms in some individuals and genetic and other predisposing factors are likely to be important in identifying who may be more vulnerable. Given that this is a relatively new line of research in the ecstasy literature, further research is required to clarify the potential role of 5-HTTLPR genotype.

**Self-medication hypothesis.** Longitudinal studies indicate that people with heightened depressive and anxiety symptomatology in childhood and adolescence are more likely to use ecstasy in later adolescence and young adulthood (Huizink et al., 2006) and the onset of mental disorders in ecstasy users typically precedes the onset of ecstasy use (Lieb et al., 2002). Consequently, it has been suggested that elevated depressive/anxiety symptoms in ecstasy users may be associated with the use of ecstasy to cope with pre-existing mood symptoms (Huizink et al., 2006; Lieb et al., 2002). Consistent with past research, coping motives for ecstasy use was associated with more severe mood symptoms in the current sample. Given that those with high emotion-focused coping were more likely to endorse coping motives suggests that some ecstasy users may be using ecstasy to self medicate in the context of coping skills deficits and pre-existing symptoms, particularly given that those with a self-reported history of unipolar depression and/or an anxiety disorder (n=42) scored significantly higher on coping motives for ecstasy use and the majority of these individuals (80%) reported that mood symptoms preceded the first ecstasy use, consistent with other studies (de Win et al., 2004; Lieb et al., 2002).
The role of a third variable. The current findings suggest that adverse life events, such as trauma and stressful life events, may be an important third variable in explaining the relationship between ecstasy and mood. Drug use may increase risk of exposure to trauma or decrease one’s ability to cope with stressful life events and in turn, lead to an increased risk of mood symptoms (Risch et al., 2009). Indeed, the current findings suggest that coping style may be an important third variable in explaining the relationship between drug use and mood symptoms. Specifically, mood symptoms in the context of poor coping skills may contribute to the onset and continuation of ecstasy and other drug use, as indicated by the significant associations between coping motives, emotion-focused coping, lifetime ecstasy use and current mood symptoms, as reported in Article Three (see Table 2 for correlation matrix).

Findings from the prospective study, reported in Article Two, suggest the role of sleep as a possible third variable in explaining the relationship between ecstasy and subacute mood symptoms. Given ecstasy’s stimulant properties, a common side effect of ecstasy is insomnia (Liechti & Vollenweider, 2000b) and ecstasy is often taken at all night dance parties leading to disrupted sleep patterns (Degenhardt et al., 2004). Consistent with this, the current thesis found that those who took ecstasy reported having slept for significantly fewer hours than those who abstained, and both hours and quality of sleep were significantly associated with negative mood effects over the follow up. These findings support the proposal that lifestyle factors associated with ecstasy use may contribute to the observed mood symptoms in ecstasy users.

Shared risk factors increase the risk of mood symptoms and ecstasy use. Causation models for depression and anxiety disorders indicate that adverse life events, such as trauma and life stress, is a key environmental risk factor for depression, anxiety and substance (ab)use (Kendler et al., 2002, 2006; Kessler, 1997; McCauley et al., 1997). Furthermore, exposure to multiple adverse life events has been shown to further increase the risk of psychopathology (Chapman et al., 2004; Copeland et al., 2007). Notably, childhood trauma has been found to be a particularly strong risk factor for co-occurring anxiety, mood, and substance use disorders (De Graaf et al., 2002). Indeed, one study that has assessed for trauma in ecstasy users found that ecstasy users reported more experiences of childhood abuse and neglect, were more likely to be depressed, and exhibited more severe levels of substance use than ecstasy-naïve drug-using controls (Singer et al., 2004).
The authors hypothesised that trauma may have played a role in the onset of ecstasy and other drug use.

Consistent with these findings, the current thesis indicated that life stress and trauma were robust predictors of current mood symptoms, with stressful life events also being associated with negative mood change in a brief prospective study. Further, although trauma did not significantly correlate with severity of recent or lifetime ecstasy use, it was associated with more frequent tobacco use, indicating that a history of trauma is a shared risk factor for both mood symptoms and regular tobacco use. Interestingly, the number of recent stressful life events negatively correlated with lifetime ecstasy use, which suggests that those who reported more stressful life events or those who subjectively experience more life events as stressful were using less ecstasy. One possible explanation for this finding is that the current sample had high trait anxiety leading them to report greater stressful life events and also to not consume large amounts of ecstasy due to higher levels of concern regarding potential harm. Another possible explanation is that individuals with higher vulnerability to stressful life events have experienced more negative outcomes from ecstasy use. Further research is required to clarify the nature of this relationship.

Finally, coping style is likely to be a shared risk factor. Emotion-focused coping has been associated with poorer psychological and behavioural adjustment, including depression and anxiety (Endler & Parker, 1994; McWilliams et al., 2003) and substance use (Cooper et al., 1988; Staiger et al., 2009). Consistent with this, the findings, as presented in Article Three, found significant associations between emotion-focused coping and current mood symptoms. In contrast, no association was found between the severity of ecstasy use, measured by lifetime, recent and frequency of use, and emotion-focused coping, which was unexpected. Consequently, it is possible that coping style relates to the initiation of drug use rather than to a heavier pattern of use. Consistent with this, task-focused coping was negatively associated with age at first use, suggesting that a task-focused coping style may be protective against early-onset ecstasy and other drug use.

Summary of theory. The predominantly cross-sectional nature of the current thesis limits possible conclusions about the direction of causality with respect to ecstasy and mood. Despite this, the findings suggest that some people are using ecstasy to cope which in turn is associated with more severe current depressive and anxiety symptomatology, in support of the self-medication hypothesis. Secondly, shared risk factors such as trauma and
life stress are likely to contribute to both mood symptoms and drug use. Findings from the prospective study cast doubt on the significance of ecstasy causing mood effects in the short-term, but supports recent research highlighting the role of self-reported sleep disruption on subacute mood. Further, the lack of findings regarding potential risk factors associated with ecstasy-related mood symptoms following use, does not support the proposal that ecstasy use may also lead to depressive or anxiety symptoms in vulnerable individuals or exacerbate pre-existing mood symptoms. However, the small sample size in the current thesis limited the potential for exploring vulnerability factors such as psychiatric history. Further, it remains possible that ecstasy use may exacerbate symptoms in the long-term, particularly when used more frequently or in large doses. Indeed, the lack of a consistent directional relationship between depression and substance use disorders highlights the likelihood that multiple pathways of associations exist (Swendsen and Merikangas, 2000). It is likely that all comorbidity models are also applicable to ecstasy and mood.

7.5 Clinical implications

The current findings relating to the relationship between trauma, stressful life events, substance use and coping highlight the need to provide coping skills training for people presenting with comorbid depressive/anxiety symptoms and substance use. There is increasing support for integrated treatment approaches that include simultaneous treatment of mental health and substance use by the same clinician, particularly for comorbid PTSD and substance use disorder (Ouimette, Moos & Brown, 2003). Further, integrated treatments that focus on providing coping skills to manage current trauma symptoms have found greater improvements in trauma and other mental health symptoms compared to treatment as usual (Hien, Cohen, Miele, Litt, & Capstick, 2004; Morrissey et al., 2005). There is preliminary evidence indicating the efficacy of integrated cognitive behaviour therapy for young people with co-occurring alcohol dependence and depression (Deas, Randall, Roberts, & Anton, 2000; Moak et al., 2003). Furthermore, several randomised control trials of integrated treatments for depression and substance use problems are currently being undertaken in Australia (Dawe & McKetin, 2004). Given that co-occurring mood, anxiety and substance use disorders are associated with increased treatment seeking, disability and poorer treatment outcomes (Burns & Teeson, 2002; Lubman et al., 2007), it is critical that we increase understanding of the nature of comorbidity and effective forms of intervention.
Australian data indicate that ecstasy was the principal drug of concern reported in 0.7% of closed treatment episodes in 2006-2007 (Australian Institute of Health and Welfare, 2008b). Given these low numbers, it has been proposed that interventions with ecstasy users will be “largely opportunistic” and therefore should take the form of brief interventions (Baker, Gowing, Lee, & Proudfoot, 2004). Brief interventions aim to identify a specific problem, increase motivation to change a target behaviour, and with respect to drug use, reduce risks of drug-related harm. Brief interventions can be used in isolation or prior to more intensive treatment (Baker et al., 2004). Baker et al. (2004) suggested a number of potential locations for brief interventions with ecstasy users, such as emergency departments within hospitals, (e.g. when ecstasy users present with acute adverse drug reactions), support services at dance parties, primary health care services (e.g. GPs), legal settings, (e.g. following charges of drug possession), and computer-based interventions. However they highlight that further research is required regarding the efficacy of brief interventions targeting ecstasy use, including the structure and context of delivery, as to date, evidence largely comes from tobacco and alcohol abuse.

In accordance with the current findings, brief interventions may include psychoeducation around the association between coping and increased symptoms. Psychoeducation may include information regarding the relationship between coping motives and coping style and mood symptoms, and specifically, the distinction between emotion and task-focused coping (Carver, Scheier, & Weintraub, 1989). Ecstasy users should be informed of the impact of sleep on subacute mood effects, and advised to take ecstasy earlier in the night to reduce sleep disruption. This is consistent with the proposal that the most important coping skill is to look after oneself, including eating a balanced healthy diet, sleeping regularly, treating physical illnesses, and exercising (Linehan, 1993). Time permitting, further coping skills could also be introduced, such as problem solving for dealing with stressful life events. More intensive treatment may be required for the small percentage of users with problematic use. Psychological treatments for cocaine and amphetamine abuse are likely to be effective for ecstasy also (Baker et al., 2004). However, as ecstasy users are typically polydrug users, they may present for treatment with a different identified drug of concern and require more intense interventions directed at these (Baker et al., 2004).

In addition to the direct clinical implications relating to ecstasy users themselves, the current findings have important implications for health providers. Ecstasy users typically access help for ecstasy-related problems from primary care services such as GPs.
Specifically, an Australian study found that one fifth of their ecstasy-using sample had sought assistance from a health professional for an ecstasy-related problem (GPs =11%) (Topp et al., 1999). Given the prevalence of ecstasy use, primary care services would benefit from ecstasy-related information and brochures on reducing ecstasy-related harm. The current findings highlight that these should include information on the impact of lifestyle factors (e.g. sleep) on psychological functioning, including mood. Further, it should highlight that those using ecstasy to cope may benefit from learning alternative coping strategies for dealing with stressful life events and with mental health issues. Indeed, the high rate of depression in the current sample highlights the need for primary care services to be aware of the elevated risk of depression in ecstasy users and highlights the importance of psychiatric assessment in those presenting with concerns regarding their drug use.

7.6 Limitations and strengths. The current thesis is limited by a number of factors, many of which are outlined in the empirical papers. First, all participants had commenced ecstasy use prior to the study, which restricts potential conclusions regarding direction of causality. Secondly, the current thesis, like the majority of research in this area, used purposive sampling to recruit participants (defined as the targeted recruitment of particular groups; Topp, Barker, & Degenhardt, 2004). This may mean that the data presented is not representative of all ecstasy users. However, an Australian study indicated that the characteristics and patterns of drug use observed in ecstasy users were comparable across those recruited through purposive sampling methods and those recruited in a general population household survey (Topp et al., 2004). Further, the patterns of use reported by the current sample are comparable to other studies in this area (e.g., Topp et al., 1999; Degenhardt et al., 2004).

The thesis predominantly relied upon retrospective self-report measures that may be subject to recall bias. It is also possible that the presence of current mood symptoms inflated recall of past adverse life events (Schraedley, Turner, & Gotlib 2002). The reliability of self-reported recent drug use was also not confirmed using biological analysis, although previous studies have indicated ecstasy and other drug users provide reliable data (Anglin, Hser, & Chou, 1993; Bedi & Redman, 2006b). Furthermore, biological analysis is limited in the information it can provide. MDMA can only be biochemically detected up to 24 to 48hrs after use, meaning that some users may still be experiencing subacute mood effects in the absence of MDMA or its metabolites being
biochemically detectable (Allott & Redman, 2007). On the other hand, cannabis can be detected up to one month since last use, when subacute effects are no longer apparent (Pope, Gruber, Hudson, Huestis, & Yurgelun-Todd, 2001). Although detailed data was obtained on lifetime ecstasy use, the content of ecstasy tablets consumed was not determined. As with all related studies, it is possible that participants unknowingly consumed other substances and not MDMA (Quinn et al., 2007).

The measures of other drug use in the cross-sectional study, including drug use frequency and the number of drugs tried (polydrug use), rather than the lifetime quantity of use, is a further limitation of the current study. These measures may not have been sensitive enough to reveal possible associations between other drug use factors and current symptoms. The context-based timeline method was used as the use of timelines with life event cues are thought to increase recall accuracy. However, this method is time consuming. Given that the aim of the thesis was not to determine the relative contribution of individual substances on current symptoms but rather, it aimed to determine whether lifetime ecstasy use was associated with symptom severity after controlling for other known risk factors, detailed data was not obtained on lifetime other drug use.

Although participants were required to abstain from ecstasy use for one week prior to study one, it is possible that subacute effects may have affected the data as the MASQ asks about mood symptoms in the past week. The effects of other drug use may also have impacted on our results, as only 12- and 24-hour abstention periods were used for alcohol and other substances, respectively. However, consistent with other papers in this area (e.g., Bedi et al., 2008), a 24-hour abstinence period was implemented for cannabis to balance potential subacute and withdrawal drug effects as well as participant recruitment factors. Specifically, subacute cannabis effects can last for more than seven days (Pope et al., 2001) and abstention periods longer than one day may lead to withdrawal symptoms (Kouri & Pope, 2000). Furthermore, given that we aimed to have a representative sample of ecstasy users with a range of other drug-using habits, an abstention period of 24 hours was used in order to include regular users of other drugs. No significant correlations were found between days since last use of individual drugs and the MASQ subscales. Finally, as the interviewer was the current doctoral candidate, this introduces a potential reporting bias as she was not blind to drug use. This is particularly relevant in the prospective study. However, given that many of the measures were self-report scales, including those assessing depressive/anxiety symptomatology, this reduces the risk of bias.
Notwithstanding these limitations, the thesis provides a unique and valuable contribution to the current literature on ecstasy and mood. It includes the first published study examining the relative contribution of genetic and environmental risk factors on psychiatric symptomatology in a community sample of ecstasy users. The exploration of risk factors for mood symptoms in the short term using a prospective design is a unique area of research and provides further support for the reliability of the cross-sectional findings. The thesis includes the first study looking at coping style in ecstasy users, in the context of many researchers suggesting that some individuals may be using ecstasy to self-medicate pre-existing symptoms. In doing so, this thesis increases understanding of a subset of mechanisms by which ecstasy and mood symptoms may co-occur (i.e. the self-medication hypothesis). Further strengths of the current thesis include the recruitment of a large sample of ecstasy users with varying levels of ecstasy and other drug use.

Furthermore, lifetime ecstasy use was measured using a context-based timeline to aid recall, as the use of timelines with life events increases recall accuracy of past drug use (Del Boca & Darkes, 2003; Shillington et al., 1995). The inclusion of individuals with a psychiatric history, as well as those currently on psychotropic medications, is a further strength of the study by increasing the generalisability of the current findings and that these individuals have often been excluded from previous research (e.g. Medina & Shear 2007; Roiser & Sahakian 2004). Furthermore, the use of the MASQ allowed for the examination of independent relationships between ecstasy use and depression-specific, anxiety-specific and general distress symptomatology. In contrast to commonly used depression scales, the depression-specific scale of the MASQ is less confounded by somatic symptoms such as sleep disturbance and loss of appetite (which are also related to substance misuse; Cole et al., 2002), and instead focuses on anhedonia and lack of positive affect. The prospective study was strengthened by the use of both self-report and clinician rating scales, supporting the reliability of the findings.

7.7 Directions for future research. As highlighted in this thesis, the aetiology of depression and anxiety is complex. The current thesis focused on variables that were both highlighted in the ecstasy literature and identified as important risk factors for depression, anxiety and substance use. Clearly, there are a number of other factors that may be increase the likelihood that someone who users ecstasy also experiences mood symptoms. Specifically, there is currently a lack of research exploring the relationship between personality and
mood symptoms in ecstasy users. Neuroticism plays a widely recognised role in the aetiology of depression (Kendler et al., 2006; see Enns & Cox, 1997 for review) and ecstasy users have scored higher on measures of novelty seeking and impulsivity, with higher impulsivity scores relating to greater severity of ecstasy and other drug use (Morgan, 1998; Moellar et al., 2002). In contrast, a number of studies have found no association between impulsivity and ecstasy use (Clark, Roiser, Robbins & Sahakian, 2009; Roiser, Rogers, Sahakian, 2007). Despite these mixed findings, further research on personality may provide valuable insights into who may be more vulnerable to ecstasy-related harm, such as those high on the personality traits neuroticism or sensitivity to reward (see Gray’s motivational systems, 1981), and why some ecstasy users continue to take ecstasy, despite reporting ecstasy-related problems (e.g. those high on impulsivity or low sensitivity to punishment).

A number of directions for future research were also highlighted in the previous chapters. These include the need for research to explore whether ecstasy use exacerbates trauma or mood symptoms in people with a history of trauma or psychopathology. Specifically, prospective research exploring the relationship between adverse life events, mood symptoms and ecstasy use over both the short and long term is needed to fully understand the interaction between these variables.

Given the significant associations between coping motives and coping style with current mood symptoms, and the role of these factors in explaining the relationship between adverse life events and mood symptoms in the current sample, future research would benefit from looking at the relationship between motives for and expectancies of use on the experience of adverse side effects from ecstasy use. Findings from the wider substance use literature indicate that although substance use may temporarily relieve mood symptoms, symptoms are likely to get worse with ongoing problematic use (Commonwealth of Australia, 2005). Further, as a coping strategy, substance use does not deal with the factors contributing to the maintenance of mental health problems. Consistent with this, it is likely that ecstasy users motivated by coping reasons may experience worsening mood symptoms with ongoing ecstasy use.

The frequency data on 5-HTTLPR genotype highlight an interesting area for future research looking at the relationship between genotype and patterns and consequences of ecstasy use. Although beyond the scope of the current thesis due to sample size limitations,
it is possible that individuals with the S allele may experience more subacute mood effects. This may lead to a shorter duration of ecstasy use.

Finally, in order to understand the complex interactions between risk factors, mood symptoms and drug use, longitudinal studies are critical. The predominance of cross-sectional research to date limits potential conclusions regarding direction of causality. However, Green et al. (2003) highlights the ethical limitations of conducting prospective studies when preclinical data suggest that MDMA is neurotoxic. Furthermore, a richer understanding of risk factors for mood symptoms is likely to come from sampling drug users more widely, rather than focusing on recruiting particular drug-using groups such as ecstasy users (Stockwell, 2007). This would allow for the investigation of shared risk factors for problematic drug use, as well as being able to explore the specific contribution of ecstasy use on mood symptoms, relative to other risk factors, including other drug use.

7.8 Conclusion. The current thesis found that neither lifetime nor recent ecstasy use were associated with the severity of current mood symptoms, either alone or in combination with 5-HTTLPR genotype. Rather, lifetime trauma, recent stressful life events, coping style, ecstasy use motives and other drug use factors significantly predicted the severity of depressive and anxiety symptoms. Consistent with these findings, the prospective study found that lowered mood and increased psychological distress were associated with quality of sleep and number of stressful life events experienced over the follow up, and not with ecstasy use. These results highlight the need to consider the role of environmental factors when examining the relationship between ecstasy use and mood symptoms, and further emphasise the importance of coping skills training for managing stressful life events for people with co-occurring depressive/anxiety symptoms and substance use.
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1 May 2007  

CF07/1061 - 2007/0273: Ecstasy users: Vulnerability factors for depression and anxiety symptomatology  

Dear Researchers,  

Thank you for your attendance at meeting C2/2007 of the Standing Committee on Ethics in Research Involving Humans on 24 April 2007 and for the further information provided regarding the above application. The items requiring attention have been resolved to the satisfaction of the Standing Committee on Ethics in Research Involving Humans (SCERH). Accordingly, this research project is approved to proceed.  

Terms of approval  
1. This project is approved for five years from the date of this letter and this approval is only valid whilst you hold a position at Monash University.  
2. It is the responsibility of the Chief Investigator to ensure that all information that is pending (such as permission letters from organisations) is forwarded to SCERH, if not done already. Research cannot begin at any organisation until SCERH receives a letter of permission from that organisation. You will then receive a letter from SCERH confirming that we have received a letter from each organisation.  
3. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval and to ensure the project is conducted as approved by SCERH.  
4. You should notify SCERH immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.  
5. The Explanatory Statement must be on Monash University letterhead and the Monash University complaints clause must contain your project number.  
6. Amendments to the approved project: Changes to any aspect of the project require the submission of a Request for Amendment form to SCERH and must not begin without written approval from SCERH. Substantial variations may require a new application.  
7. Future correspondence: Please quote the project number and project title above in any further correspondence.  
8. Annual reports: Continued approval of this project independent on the submission of an Annual Report. Please provide the Committee with an Annual Report determined by the date of your letter of approval.  
9. Final report: A Final Report should be provided at the conclusion of the project. SCERH should be notified if the project is discontinued before the expected date of completion.  
10. Monitoring: Projects may be subject to an audit or any other form of monitoring by SCERH at any time.  
11. Retention and storage of data: The Chief Investigator is responsible for the storage and retention of original data pertaining to a project for a minimum period of five years.  

All forms can be accessed at our website www.monash.edu.au/research/ethics/human/index.html  

We wish you well with your research.

Mrs Lyn Johannessen  
Acting Human Ethics Officer (on behalf of SCERH)  

Cc: Dr Daniel Ian Lubman, Dr Leanne Hides, Ms Rebecca Scott
PLEASE NOTE: To ensure speedy turnaround time, this correspondence is now being sent by email only. If you would prefer a hard copy on letterhead, please contact the Human Ethics Office (9905 2076 or scerh@adm.monash.edu.au) and a hard copy will be posted to you.

We would be grateful if first-named investigators could ensure that their co-investigators are aware of the content of the correspondence.

Dr J. Sabura Allen
School of Psychology, Psychiatry and Psychological Medicine
Faculty of Medicine, Nursing and Health Sciences
Clayton Campus

27 August 2007

CF07/1061 - 2007/0273: Ecstasy users: Vulnerability factors for depression and anxiety symptomatology

Dear Researchers,

Thank you for submitting your Request for Amendment form with respect to the above named project.

This is to advise that the requested amendments dated 17 July 2007 have been considered by the Standing Committee on Ethics in Research Involving Humans, however, the Committee requires further information to review for proposed amendments as follows:

1. The change to the recruitment strategy is approved.
2. However, for reasons of the personal safety of both the researcher and the participant, SCERH does not give approval for interviews to be held in private homes. Please confirm that arrangements will be made for the interviews to be held in a public place.

We apologise for the delay in responding to your request for amendment.

Thank you for keeping the Committee informed.

Dr Souheir Houssami
Executive Officer, Human Research Ethics (on behalf of SCERH)

Cc: Dr Daniel Ian Lubman, Dr Leanne Hides, Ms Rebecca Scott,
PLEASE NOTE: To ensure speedy turnaround time, this correspondence is now being sent by email only. SCERH will endeavour to copy all investigators on correspondence relating to this project, but it is the responsibility of the first-named investigator to ensure that their co-investigators are aware of the content of the correspondence.

Dr Janice Allen
Sch Psychol Psychiatry & Psych Medicine
Faculty of Med Nursing & Health Sciences
Clayton Campus

25 February 2008

CF07/1061 - 2007000273: Ecstasy users: Vulnerability factors for depression and anxiety symptomatology

Dear Researchers,

Thank you for submitting your Request for Amendment form with respect to the above named project.

This is to advise that the requested amendments dated 10 November 2007 have been approved taking into account your responses to the Committee’s concerns and the project can proceed according to your approval given on 1 May 2007.

Thank you for keeping the Committee informed.

Dr Souheir Houssami
Executive Officer, Human Research Ethics (on behalf of SCERH)

Cc: M. Dan L Lubman; Dr Leanne Hides; Miss Rebecca Margaret Scott
--
Ms Coral Lindupp
Senior Administrative Officer
Human Ethics Office
Building 3E, Room 111
Monash University, Clayton 3800
Phone: 9905 2076
eemail: scerh@adm.monash.edu.au
PLEASE NOTE: To ensure speedy turnaround time, this correspondence is now being sent by email only. SCERH will endeavour to copy all investigators on correspondence relating to this project, but it is the responsibility of the first-named investigator to ensure that their co-investigators are aware of the content of the correspondence.

Dr Janice Allen  
Sch Psychol Psychiatry & Psych Medicine  
Faculty of Med Nursing & Health Sciences  
Clayton Campus  
26 June 2008

CF07/1061 - 2007000273: Ecstasy users: Vulnerability factors for depression and anxiety symptomatology

Dear Researchers,

Thank you for submitting your Request for Amendment form with respect to the above named project.

This is to advise that the following amendments dated 13 June 2008, have been approved and the project can proceed according to your approval given on 1 May 2007.

1. Amend the inclusion criteria.

Thank you for keeping the Committee informed.

Professor Ben Canny  
Chair, SCERH

Cc: M. Dan L Lubman; Dr Leanne Hides; Miss Rebecca Margaret Scott

Human Ethics  
Monash Research Office  
Building 3E, Room 111  
Monash University, Clayton 3800  
Phone: 9905 5490  
email: scerh@adm.monash.edu.au
Are you aged between 18 and 29 AND have taken ECSTASY in the last year?

If yes, we need your help for our study about what factors increase the likelihood that someone who uses ecstasy experiences symptoms of anxiety or feeling down.

**Project Title** - Ecstasy Users: Vulnerability Factors for Depression and Anxiety Symptomatology

**What you need to do**
Participation will take approximately **an hour and a half** and will involve coming into Monash University, Clayton Campus or ORYGEN Research Centre, Parkville to complete an interview and questionnaires. Participants will be paid **$25.00** for their time and will remain **anonymous**.

For more information please contact:
Becca Scott
Doctor of Psychology (Clinical) Candidate
Monash University
Email: Becca.Scott@med.monash.edu.au
Ph: [Redacted]
Have you taken ecstasy in the last year? Are you aged 18-29 years?
If yes, we need your help for our study about what factors increase the
likelihood that someone who uses ecstasy experiences symptoms of anxiety or
feeling down.

Project Title - Ecstasy Users: Vulnerability Factors for Depression and Anxiety
Symptomatology

What does it involve? An interview and questionnaire
How long will it take? Approximately an hour and a half
Where: Monash University, Clayton Campus or
ORYGEN Research Centre, Parkville
Payment: $25.00

YOUR PARTICPATION WILL BE ANONYMOUS

Please contact: Becca Scott, Monash University,
Becca.Scott@med.monash.edu.au or ph:

MONASH University
Have you taken **ECSTASY** in the last year? Are you aged 18-35 years?

If yes, we need your help with a study about what increases the risk of experiencing depression or anxiety in ecstasy users.

**Payment: $25.00**

YOUR PARTICIPATION WILL BE ANONYMOUS

Please call or text Becca (______) if you’re interested in participating

MONASH University
Ecstasy and Mood research participants required

Research participants are required for a study at Monash University looking at ecstasy and mood.

Some healthy researchers in this field argue that ecstasy users may be using it to overcome symptoms such as depression, while others argue that people with a history of depression are more likely to use ecstasy. However, only a relatively small amount of research exists on what factors make ecstasy users more likely to experience depression or anxiety.

A study is currently being undertaken by Becca Scott, a psychology doctoral student at Monash University regarding this question.

People aged 18 to 25 years who have taken ecstasy in the last year are being recruited for participation. For more information on this study or if you would like to participate please contact Becca Scott via email – Becca.Scott@med.monash.edu.au
Research Participants Wanted!! - Melbourne

Research participants wanted - Ecstasy users.

If you are aged 18 to 35 years old and have taken ecstasy six or more times in the last six months, we need your help for our study looking at what factors increase the likelihood that someone who uses ecstasy experiences symptoms of anxiety or feeling down.

Participation involves an interview and completing questionnaires. This will take approximately an hour (max 1.5hrs) and participants will receive $25 for their time. The interview will include background information such as demographics, current psychological symptoms, medications, stressful life events, whether you or a family member have experienced mental illness, whether you have experienced a traumatic event in your life and for females, your current stage of the menstrual cycle.

You will also be asked a series of questions regarding your drug use. This will include questions around age at first use and frequency and extent of use with respect to a range of substances including ecstasy, amphetamines, GHB, ketamine, cannabis, alcohol and prescribed and homeopathic medication.

The questionnaire packet will include items on psychological symptoms, motives for ecstasy use, severity of ecstasy dependence and how you cope with stressful situations.

Finally, we will ask you to provide a saliva sample. This sample will be used to look at genetic predisposition to depression and anxiety.

The project has been approved by the Monash University Human Ethics Committee (Project number: CF07/1061 - 2007/0273). Participants confidentiality will be protected because names will not appear on interview data or questionnaire packets, but rather packets will be identified by identification numbers.

Participants' contact details and associated identification numbers will only be accessible to the principal investigators. Furthermore, participants' contact information will be destroyed directly after their participation and at no point will they be asked to give their name.

Advertisement placed on careers websites of Monash University, Deakin University, La Trobe University and University of Melbourne
Research participants needed for ecstasy study

Published: 19 March 2008

If you are aged 18 to 35 years and have taken ecstasy in the last year, we need your help for our study looking at what factors increase the likelihood that someone who uses ecstasy experiences symptoms of anxiety or feeling down.

What does it involve? An interview and completing questionnaires
How long will it take? Approximately an hour (max 1.5hrs)
Where: Various locations around Melbourne including Monash University, Clayton
Payment: $25

Your participation will be anonymous

For more information on this study or if you would like to participate please contact Becca Scott, Doctor of Psychology (Clinical) candidate via email: Becca.Scott@med.monash.edu.au or ph: If you know anyone else who may fit our criteria we would really appreciate you passing on our details.
Research participants wanted! 'Ecstasy users: Vulnerability factors for depression and anxiety symptomatology'

If you are aged 18 to 35 years old and have taken ecstasy in the last year, we need your help for our study looking at what factors increase the likelihood that someone who uses ecstasy experiences symptoms of anxiety or feeling down.

What does it involve? An interview and completing questionnaires
How long will it take? Approximately an hour (max 1.5hrs)

Where: Various locations around Melbourne including Monash University, Clayton
Payment: $25.00

YOUR PARTICIPATION WILL BE ANONYMOUS

For more information on this study or if you would like to participate please contact Becca Scott, Doctor of Psychology (Clinical) candidate via email: Becca.Scott@med.monash.edu.au or ph: [redacted].
APPENDIX 3: PERMISSION LETTER

MONASH University

Ecstasy Users: Vulnerability factors for Depression and Anxiety Symptomatology

Permission letter

To whom it may concern,

My name is Becca Scott and I am conducting a research project as part of a Doctorate of Clinical Psychology at Monash University. This research is being supervised by Dr. J. Sabura Allen of Monash University and Dr. Dan Lubman and Dr. Leanne Hides of ORYGEN Research Centre. The study aims to examine what factors increase ecstasy users’ vulnerability to experiencing symptoms of anxiety and depression.

For the purpose of the study we require English speaking participants aged between 18 and 35 years who have taken ecstasy at some time in the last 12 months. Recent Australian statistics indicate that 21% of people aged 20 to 24 years old have tried ecstasy on at least one occasion. This suggests that a wide range of people have tried ecstasy. In order to recruit an appropriate range of people, we are using a variety of recruitment methods. One method is to put flyers in cafes, music shops and dance music venues such as nightclubs. We are seeking assistance from those who own or manage such venues to allow us to leave flyers advertising our study for people who visit these venues.

If you would like to assist us please complete the following:

I give permission for flyers advertising the project titled ‘Ecstasy Users: Vulnerability factors for Depression and Anxiety Symptomatology’ to be placed in:

________________________________(please write name of café/shop/music venue)

Name __________________________________________________________

Signature _______________________________________________________

Designation _____________________________________________________
(e.g., manager/owner)

Thank you for your assistance.

Becca Scott
Doctor of Psychology (Clinical) Candidate
Monash University

Australian Institute of Health and Welfare (2005)
Ecstasy Users: Vulnerability factors for Depression and Anxiety Symptomatology

Study 1

Explanatory Statement

My name is Becca Scott and I am conducting a research project as part of a Doctorate of Clinical Psychology at Monash University. This research is being supervised by Dr. J. Sabura Allen of Monash University and Dr. Dan Lubman and Dr. Leanne Hides of ORYGEN Research Centre. The study aims to examine what factors increase ecstasy users’ vulnerability to experiencing symptoms of anxiety and depression.

Background

Current research indicates that higher rates of depressive and anxiety symptomatology exist amongst ecstasy users. Some leaders in this field argue that ecstasy use leads to adverse outcomes such as depression, while others argue that people with a history of depression are more likely to use ecstasy. However, only a relatively small amount of research exists on what factors make ecstasy users more likely to experience depression or anxiety. This study proposes to further our knowledge about ecstasy users by exploring factors that predict current depressive and anxiety symptomatology amongst ecstasy users by looking at severity of drug use, ecstasy dependence, motives for use, personality, life events, coping style and genetic predisposition to depression and anxiety. Furthermore, we aim to look at what factors may influence how much ecstasy people take.

Who is eligible to participate in this study?

For the purpose of the study we require English speaking participants aged between 18 and 35 years who have taken ecstasy at least once in the last 12 months. As we will be looking at a number of factors including mood, personality and genetic predisposition to depressive and anxiety symptoms, we require a wide range of participants with differing backgrounds, experiences with and motives for taking ecstasy. Due to the purpose of the study certain individuals will be ineligible to participate. This includes people with a history of a psychotic disorder and those who are currently pregnant.

This Explanatory Statement contains detailed information about the research project. Its purpose is to explain to you as openly and clearly as possible all the procedures involved in this project before you decide whether or not to take part in it. Please read this Explanatory Statement carefully. Feel free to ask questions about any information in the Explanatory Statement and feel free to discuss the project with a relative or friend.
Possible benefits of participating
You may not directly benefit from your participation in this project. However, your participation will assist us in furthering our knowledge regarding the effects of ecstasy use. Greater knowledge in this area will enable people to make more informed decisions about whether they want to take ecstasy, continue taking it or cease using it.

What does the research involve?
Participating in this study includes an interview and the filling out of a number of questionnaires. I will be administering both components. The interview will include background information such as demographics, current psychological symptoms, medications, stressful life events, whether you or a family member have experienced mental illness, whether you have experienced a traumatic event in your life and for females, your current stage of the menstrual cycle. You will also be asked a series of questions regarding your drug use. This will include questions around age at first use and frequency and extent of use with respect to a range of substances including ecstasy, amphetamines, GHB, ketamine, cannabis, alcohol and prescribed and homeopathic medication. The questionnaire packet will include items on psychological symptoms, motives for ecstasy use, severity of ecstasy dependence and how you cope with stressful situations. Finally, we will ask you to provide a saliva sample by spitting into a bottle. This sample will be used to look at genetic predisposition to depression and anxiety. At any time throughout the study, I will be glad to clarify instructions or answer any questions regarding any of the materials, including this Explanatory Statement. You may refuse to answer any questions without stating a reason or withdraw your participation at any time. Finally, we request that you refrain from taking ecstasy for at least one week prior to participating and that you do not consume any other illicit drugs within 24 hours of participating.

How much time will the research take?
The interview and questionnaires should take no more than an hour and a half to complete.

Inconvenience or discomfort
To participate in this research you will be required to either come into the Clayton campus of Monash University or the ORYGEN Research Centre in Parkville or you can arrange to meet with me in a public place at a Melbourne location convenient to you. As the research involves providing information regarding personal issues such as whether you have experienced a mental illness or a traumatic event, your current and past drug use and psychological symptoms, this may evoke negative emotions or emotional memories for you. You may stop at any time if you find it too upsetting. If this research raises any issues for you, you may wish to contact one of the counselling services listed at the end of this Explanatory Statement, as well as the last page of the questionnaire packet. If you do begin to feel upset we will stop or postpone the interview until later, you can discuss your issues and distress with me and I will encourage you to contact a support person and/or a counselling or support service.

Payment
Upon completion you will be given $25 in cash as compensation for your time.

Confidentiality
Firstly, in order to protect your privacy please do not email me any sensitive information or information regarding your drug use, as email is not confidential. All discussions of
private information and information regarding your drug use will be discussed in person or on the phone.

Your anonymity will be protected because names will not appear on interview data or questionnaire packets, but rather packets will be identified by identification numbers. Participants’ contact details and associated identification numbers will only be accessible to the principal investigators. Furthermore, your contact information will be destroyed directly after your participation and at no point will you be asked to give your name.

The anonymous data will be stored at the university under lock and key for at least five years, as prescribed by the university regulations, but there will be no information connecting you to your data. The information being collected from you will be combined with information collected from other participants. This information will be used to differentiate between groups of people rather than individuals. No findings which could identify any individual research participant will be published. Confidentiality will be maintained at all times except where the interviewer is ethically bound to break this confidentiality. Exceptions to confidentiality include, (a) if you disclose that you are at risk of harming yourself, (b) if you disclose that you are at risk of harming others, and (c) if there is a court order for the information. In this last instance, in the extremely unlikely event that the data is subpoenaed, any information held by the researchers would have to be submitted to the court or police. However, as your personal information will have been destroyed, data collected in this study will not include your name or contact details. If subpoenaed, it is extremely unlikely that any information collected in this study could be linked to you under such circumstances.

Results
After the collection of data is completed, the study outcomes will be available at: http://www.med.monash.edu.au/psych/questionnaires/rscott/. No individual participant will be identified; rather the results will include information of how groups of individuals responded on average and any associations found between the variables. The same is true for the final thesis and associated publications and conference presentations. No individual participant will be identifiable.

Participation is Voluntary
Your participation is voluntary and if you agree to participate you may withdraw your consent up until the point of handing in your questionnaire, without stating a reason. You may do this by simply telling me that you wish to withdraw from the study. Not participating in the research will not disadvantage you in any way. If you have any questions pertaining to your participation at any point after today, please contact me or Dr. Sabura Allen (contact details below).

Thank you for considering participating in this project.

Becca Scott
Doctor of Psychology (Clinical) Candidate
Contact details:

Becca Scott, BA, BScHONS (Psychology)
Doctor of Psychology (Clinical) Candidate
Department of Psychology
Telephone: [redacted]
Email: becca.scott@med.monash.edu.au

Chief Investigator:
Dr Sabura Allen, BA, MS, PhD
Department of Psychology
Telephone: 9905 4725
Email: sabura.allen@med.monash.edu.au

You can complain about this research if you don’t like something about it. To complain about this research, you need to phone 9905 2052. You can then ask to speak to the secretary of the Human Ethics Committee and tell him or her that the number of the project is CF07/1061 - 2007/0273. You could also write to the secretary. That person’s address is:

The Secretary
The Standing Committee on Ethics in Research Involving Humans
PO Box No 3A
Monash University Vic 3800

Telephone +61 3 9905 2052 Fax +61 3 9905 1420
Email: SCERH@adm.monash.edu.au
Available Services

If you need help with any drug or alcohol problems or would like further information regarding drugs and alcohol, you can contact any of the following resources:

- Direct Line (confidential drug and alcohol counselling and referral line, 24 hours, 7 days), Ph: 1800 888 236 (Victoria only) or go to: http://www.health.vic.gov.au/drugs/directline.htm for information on this service.
- DrugInfo Clearinghouse (Australian Drug Foundation) Ph: 1300 85 85 84 or go to: http://www.druginfo.adf.org.au/
- Turning Point Alcohol and Drug Centre. For clinic appointments, referrals or information about clinical services at Turning Point, call the Intake Team between 9.30am and 5.00pm, Monday to Friday. Ph: 03 8413 8444

If you are experiencing any distress or psychological symptoms, you can contact any of the following counselling or clinical psychology services:

- Monash University Counselling Service, Clayton Campus Ph: 03 9905 3156
  Monash University After Hours Telephone Counselling Service 03 9621 2600
- Monash University Clinical Psychology Centre Ph: 03 9548 7011
- Lifeline Ph: 13 11 14
- Talk to your GP about services in your area
APPENDIX 5: INTERVIEW PACK – STUDY ONE

STUDY 1

INTERVIEW PACK

Participant number: ____________________________

Day: ________  Day: ________  Month: ________  Year: ________

Day: ________  Day: ________  Month: ________  Year: ________
SECTION A: DEMOGRAPHIC AND PSYCHIATRIC HISTORY

1. Age ............ years

2. Sex:
   Male ..........0
   Female.......1

3. Height ............cm/feet

4. Weight ............kg/stone

5. Present Occupation: _________________________
   5(a)
   Not employed ............ 0
   Full time .................. 1
   Part time/casual ........... 2
   Student ................... 3
   Home duties ................. 4

6. Marital Status:
   Single .................. 0
   Defacto ................. 1
   Married ................. 2
   Separated ............ 3
   Divorced ............. 4
   Widowed ............. 5

7. What are your current living arrangements?
   Alone ................... 0
   With partner .......... 1
   With family ............ 2
   Share accommodation .... 3
   Other ..................... 4
   Specify: _________________

8. What is the highest level of formal education you have obtained?
   High school .......... 0 (Specify grade ____________)
   Trade qualification .... 1
   TAFE .................. 2
   Undergraduate .......... 3
   Postgraduate .......... 4
9. What is the main language you speak at home (or first language if participant lives alone)?
   English..........................1  
   Other.........................2  (Specify________________)

10. What is your country of birth:
   Australia ......................1  
   Other.........................2  (Specify________________)

11. What is the country of birth of your biological mother and father?
   Mother __________________
   Father __________________

12. What ethnic group do you identify with?
   ____________________________________________________________

13. Have you ever taken medication for a psychiatric problem?
   No.........................0  
   Yes .........................1

    Specify name and circle all that apply below:                Specify what participant was medicated for:

    None.........................0
    Antipsychotic..................1
    Benzodiazepines ..............2
    Antidepressant...............3
    Other .........................4
    Specify:____________________
14. Have you ever been diagnosed with a psychiatric problem?

No ......................... 0
Yes .......................... 1
Specify:  

15. [If yes to 13] Have you taken any medication in the past month for a psychiatric problem?

No ......................... 0  Go to Q16
Yes .......................... 1

If Yes:

<table>
<thead>
<tr>
<th>(a) Name?</th>
<th>(b) Taken for how long? (days)</th>
<th>(c) Dose?</th>
</tr>
</thead>
<tbody>
<tr>
<td>i)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ii)</td>
<td></td>
<td></td>
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<td>iii)</td>
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<td>iv)</td>
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<td>v)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>vi)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

16. Have you gone to a psychiatric facility, emergency department or hospital for a psychiatric problem in the past month?

No ......................... 0  Go to Q17
Yes .......................... 1

If Yes:

<table>
<thead>
<tr>
<th>(a) Where?</th>
<th>(b) For how long? (days)</th>
<th>(c) Medication?</th>
</tr>
</thead>
<tbody>
<tr>
<td>i)</td>
<td></td>
<td></td>
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<tr>
<td>ii)</td>
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<td>iii)</td>
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<tr>
<td>vi)</td>
<td></td>
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</tr>
</tbody>
</table>

Now I would like to ask some questions about your family

17. Do you know if anyone in your immediate family has been diagnosed with a psychiatric problem like depression, anxiety or psychosis?

No ......................... 0
Yes .......................... 1
Unknown .................. 9
Specify:  

...........................................................................................................................................................................
Q: Now I’m going to ask you some more questions about your use of drugs…
<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Yes</th>
<th>No</th>
<th>( q_1 )</th>
<th>( q_2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Cannabis (e.g., marijuana, hash)</td>
<td></td>
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</tr>
<tr>
<td>Amphetamines (e.g., speed, ice)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Cocaine (e.g., coke)</td>
<td></td>
<td></td>
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<tr>
<td>Hallucinogens (e.g., LSD, mushrooms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ecstasy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inhalants (e.g., Chroming petrol, paint, glue)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Opiates (e.g., heroin, codeine)</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Benzos/Sedative (non-prescribed use)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Ketamine</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>GHB</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
INTERVIEWER INSTRUCTIONS for MONTHLY TIMELINE FOLLOWBACK

Fill today’s date in as DAY 28. Write in the day signifying the beginning and end of each 1-week period (e.g. Monday to Monday) on each weekly calendar.

[with the following information, complete last 3 columns of substance use table]

“I’m going to ask you about your drug and alcohol use over the past 4 weeks”
Show the participant the calendars of the past 4 weeks

“First I’d like to know if there were any events that happened during this time”
Make a note of key events in the participant’s life (in the upper right hand of the boxes), starting with the current week.

“Have you had any Social Activities – like socializing with friends, birthdays, anniversaries, parties, or holidays over the past 4 weeks?, Lets start with the first week”

“Have you been studying or working over this time?”

“Have you changed your living arrangements in the past 4 weeks?”

**Stressful Life Events**

“Have you started, stopped, changed or had any problems with .......... in the past 4 weeks?”
School/Study
Employment (include serious difficulties at work, promotion/demotion, loss of job)
Finances (include income, bills, loans, went on/off benefits)
Relationships (include family/partner/friends/children/others; include serious relationship problems, divorce/break up, loss of confidant other than partner)

“Have you changed your living arrangements in the last 4 weeks?”
Living Arrangements (include change in residence, new resident, renovations)

“Have you had any problems with Health or Crime and Legal Matters since we last spoke?”
Health (include physical health/illness/injury, contact with health professionals)
Crime and Legal Matters: (include victim of assault/robbery; accidents; law suit, committed/accused of any crime)

“Have any of these events occurred in the last 6 months?”
specify

________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
________________________________________________________________________
“On a scale from 1 to 10, with 1 being not stressed at all and 10 being extremely stressed, how stressed would you say you were today?” ______

“And how stressed would you say you have been in general over the last month on a scale from 1 to 10?” ______

“And how stressed would you say you have been in general over the last 6 months on a scale from 1 to 10?” ______

[For females] “As menstrual cycle affects mood in some women, can you please tell me when your last period started, using this calendar?”

“Now I’m going to ask you about your drug and alcohol use over the past 4 weeks”.

Go to WEEK 4 and continue back to WEEK 1. Circle those that apply. If none discontinue.

If participant is unable to determine days of use in a week of any substance, use non-directive questioning to determine general information (i.e. did you have about the same amount that week?, more than half”, less than half?)

NOTE: Standard Drinks Units
### WEEK 4

“Did you use any ...Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?”

Circle those that apply. If none discontinue.

**FREQ:** “How many days did you use ________ that week?”

**QUAN:** “How much ________ did you use each day?”

<table>
<thead>
<tr>
<th>DAY</th>
<th>Alcohol: ___ SDU’s</th>
<th>Heroin: ___ g ___ Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: ___ mg ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>23</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: ___ mg ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>24</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: ___ mg ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>25</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
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<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: ___ mg ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>26</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
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<td></td>
<td>What type did you use?</td>
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<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>27</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
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</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td>28</td>
<td>Alcohol: ___ SDU’s</td>
<td>Heroin: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
</tr>
<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: ___ mg ___ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
<tr>
<td><strong>TOTALS</strong></td>
<td>Alcohol: _____ Days _____ SDU’s</td>
<td>Heroin: _____ Days _____ g _____ Pts</td>
</tr>
<tr>
<td></td>
<td>Cannabis: _____ Days _____ g/oz</td>
<td>Speed/Ice: _____ Days _____ g _____ Pts</td>
</tr>
<tr>
<td></td>
<td>LSD: _____ Days _____ Tabs/Pills</td>
<td>Ecstasy: _____ Days _____ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>Benzos: _____ Days _____ Tabs/Pills</td>
<td>Inhalants: _____ Days _____ Sniffs/Cans/Bags</td>
</tr>
</tbody>
</table>
### WEEK 3

“Did you use any ... Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?”

Circle those that apply. If none discontinue.

FREQ: “How many days did you use ________ that week?”

QUAN: “How much ________ did you use each day?”

<table>
<thead>
<tr>
<th>DAY</th>
<th>Day 15</th>
<th>Day 16</th>
<th>Day 17</th>
<th>Day 18</th>
<th>Day 19</th>
<th>Day 20</th>
<th>Day 21</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Alcohol: ___ SDU's</td>
<td>Heroin: ___ g ___ Pts</td>
<td></td>
<td>Alcohol: ___ g/oz</td>
<td>Speed/Ice: ___ g ___ Pts</td>
<td></td>
<td>Alcohol: ___ g/oz</td>
</tr>
<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: ___ Sniffs/Cans/Bags</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### TOTALS

Alcohol: ____ Days ____ SDU's | Heroin: ____ Days ____ g ____ Pts
Cannabis: ____ Days ____ g/oz | Speed/Ice: ____ Days ____ g ____ Pts
LSD: ____ Days ____ Tabs/Pills | Ecstasy: ____ Days ____ Tabs/Pills
Benzos: ____ Days ____ Tabs/Pills | Inhalants: ____ Days ____ Sniffs/Cans/Bags
"Did you use any ... Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?"

Circle those that apply. If none discontinue.

FREQ: “How many days did you use ________ that week?”

QUAN: “How much________ did you use each day?”

<table>
<thead>
<tr>
<th>DAY</th>
<th>WEEK 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>“Did you use any ... Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?”</td>
</tr>
<tr>
<td></td>
<td>Circle those that apply. If none discontinue.</td>
</tr>
<tr>
<td></td>
<td>FREQ: “How many days did you use ________ that week?”</td>
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<tr>
<td></td>
<td>QUAN: “How much________ did you use each day?”</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>DAY</th>
<th>Alcohol: ___ SDU’s</th>
<th>Heroin: ___ g ___ Pts</th>
</tr>
</thead>
<tbody>
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<td>Cannabis: ___ g/oz</td>
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<td></td>
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<td>Benzos: ___ mg ___ Tabs/Pills</td>
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<td></td>
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<td>Inhalants: ___ Sniffs/Cans/Bags</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TOTALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol: ______ Days ______ SDU’s</td>
</tr>
<tr>
<td>Cannabis: ______ Days ______ g/oz</td>
</tr>
<tr>
<td>LSD: ______ Days ______ Tabs/Pills</td>
</tr>
<tr>
<td>Benzos: ______ Days ______ Tabs/Pills</td>
</tr>
</tbody>
</table>
### WEEK 1

“Did you use any Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?”

Circle those that apply. If none discontinue.

**FREQ:** “How many days did you use ________ that week?”

**QUAN:** “How much ________ did you use each day?”

<table>
<thead>
<tr>
<th>DAY</th>
<th>Alcohol: ___ SDU’s</th>
<th>Heroin: ___ g ___ Pts</th>
<th>Speed/Ice: ___ g ___ Pts</th>
<th>Joints/Cones/Bongs</th>
<th>LSD/Ecstasy ___ Tabs/Pills</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
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<td>3</td>
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<td>4</td>
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<tr>
<td>5</td>
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<tr>
<td>6</td>
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<tr>
<td>7</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**TOTALS**

<table>
<thead>
<tr>
<th>Alcohol: ____ Days ____ SDU’s</th>
<th>Heroin: ____ Days ____ g ____ Pts</th>
<th>Speed/Ice: ____ Days ____ g ____ Pts</th>
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<th>LSD/Ecstasy ____ Days ____ Tabs/Pills</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis: ____ Days ____ g/oz</td>
<td></td>
<td></td>
<td></td>
<td>Ecstasy: ____ Days ____ Tabs/Pills</td>
</tr>
<tr>
<td>LSD: ____ Days ____ Tabs/Pills</td>
<td></td>
<td></td>
<td></td>
<td>Benzos: ____ Days ____ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Inhalants: ____ Sniffs/Cans/Bags</td>
</tr>
</tbody>
</table>
“How many ecstasy pills do you typically take in a single session?”

“What is the greatest number of ecstasy pills you have taken in a 12 hour period?”

“So you’ve taken _____ ecstasy pills in the last 4 weeks. How does that compare to how many you take in the average month?” (circle)
A lot more  A little more  About the same  A little less  A lot less

“Based on that and thinking about since you first started taking ecstasy and the times you took more and times you took less, how many pills do you think you have taken in the average month______ or year______”

“Finally, what would you say was your drug of choice?” specify ________

MEDICATION

“Are you taking any prescribed medication?” YES/NO
(specify type and dose)___________________

“Have you taken your prescribed medication everyday?” YES/NO (circle)

“Are you taking any homeopathic medication?” YES/NO
(specify type and dose)___________________

“Have you taken your homeopathic medication everyday?” YES/NO (circle)

“Have you commenced/ceased or changed your medication in the last 4 weeks?” YES/NO (circle), If yes, specify _______________

“Now I am going to ask you some questions about sleep and your mood today.”

SLEEP

“What time did you go to sleep last night?” _______

“What time did you wake up?” _______

“How does this differ from your usual sleep pattern?” more sleep, less sleep, the same (circle, ≥ 1hr is sign different)

“How restless was your sleep last night compared to normal?” (1 = not restless at all, to 10 = extremely restless) _______

SELF REPORTED MOOD:

“How would you rate your overall mood today out of 10, 1 being the worst you have ever felt and 10 being the best you’ve ever felt” _______
Brief Psychiatric Rating Scale: Anxiety, Depression and Hostility

**Anxiety**

Reported apprehension, tension, fear, panic or worry. Rate only the patient's statements, not observed anxiety which is rated under Tension.

- **Have you been worried a lot today? Have you been nervous or apprehensive?**
- **Are you concerned about anything? How about finances or the future?**
- **When you are feeling nervous, do your palms sweat or does your heart beat fast (or shortness of breath, trembling, choking)?**

(If patient reports anxiety or autonomic accompaniment, ask the following):

- **How much of the time have you been........... (use patient’s description)?**
- **Has it interfered with your ability to perform your usual activities/work?**

<table>
<thead>
<tr>
<th>N/a</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>very mild</td>
<td>mild</td>
<td>moderate</td>
<td>moderately severe</td>
<td>severe</td>
<td>extremely severe</td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td>Reports some discomfort due to worry OR infrequent worries that occur more than usual for most normal individuals.</td>
<td>Worried frequently but can readily turn attention to other things.</td>
<td>Worried most of the time and cannot turn attention to other things easily but no impairment in functioning OR occasional anxiety with autonomic accompaniment but no impairment in functioning.</td>
<td>Frequent periods of anxiety with autonomic accompaniment OR some areas of functioning are disrupted by anxiety or worry.</td>
<td>Anxiety with autonomic accompaniment persisting for most of the day OR many areas of functioning are disrupted by anxiety or constant worry.</td>
<td>Anxiety with autonomic accompaniment persisting throughout the day OR most areas of functioning are disrupted by anxiety or constant worry.</td>
<td></td>
</tr>
</tbody>
</table>
**Depression**

Include sadness, unhappiness, anhedonia and preoccupation with depressing topics (can't attend to TV or conversations due to depression), hopelessness, loss of self-esteem (dissatisfied or disgusted with self or feelings of worthlessness). Do not include vegetative symptoms, e.g. motor retardation, early waking or the amotivation that accompanies the deficit syndrome.

- How has your mood been today? Have you felt depressed (sad, down, unhappy, as if you didn't care)?
- Are you able to switch your attention to more pleasant topics when you want to?
- Do you find that you have lost interest in or get less pleasure from things you used to enjoy, like family, friends, hobbies, watching TV, eating?

[If subject reports feelings of depression, ask the following]
- How long do these feelings last?
- Has it interfered with your ability to perform your usual activities/work?

<table>
<thead>
<tr>
<th>N/a</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>very mild</td>
<td>mild</td>
<td>moderate</td>
<td>moderately severe</td>
<td>severe</td>
<td>extremely severe</td>
</tr>
<tr>
<td>N</td>
<td></td>
<td>Occasionally feels sad, unhappy or depressed.</td>
<td>Frequently feels sad or unhappy but can readily turn attention to other things.</td>
<td>Frequent periods of feeling very sad, unhappy, moderately depressed, but able to function with extra effort.</td>
<td>Frequent periods of deep depression OR some areas of functioning are disrupted by depression.</td>
<td>Deeply depressed most of the day OR many areas of functioning are disrupted by depression.</td>
<td>Deeply depressed all day OR most areas of functioning are disrupted by depression.</td>
</tr>
</tbody>
</table>
Hostility
Animosity, contempt, belligerence, threats, arguments, tantrums, property destruction, fights and any other expression of hostile attitudes or actions. Do not infer hostility from neurotic defenses, anxiety or somatic complaints. Do not include incidents of appropriate anger or obvious self-defense.

- How have you been getting along with people today (family, co-workers, etc.)?
- Have you been irritable or grumpy today? (How do you show it? Do you keep it to yourself?)
- Were you ever so irritable that you would shout at people or start fights or arguments? (Have you found yourself yelling at people you didn't know?)
- Have you hit anyone today?

<table>
<thead>
<tr>
<th>N/a</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>very mild</td>
<td>mild</td>
<td>moderate</td>
<td>moderately severe</td>
<td>severe</td>
<td>extremely severe</td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td>Irritable or grumpy, but not overtly expressed.</td>
<td>Argumentative or sarcastic.</td>
<td>Overtly angry on several occasions OR yelled at others excessively.</td>
<td>Has threatened, slammed about or thrown things.</td>
<td>Has assaulted others but with no harm likely, e.g. slapped or pushed, OR destroyed property, e.g. knocked over furniture, broken windows.</td>
<td>Has attacked others with definite possibility of harming them or with actual harm, e.g. assault with hammer or weapon.</td>
<td></td>
</tr>
</tbody>
</table>
**K10+ Scale**

“The following questions also ask about how you have been feeling **today**”

“On a scale of 1 to 5 with 1 being none of the time and 5 being all of the time, about how often did you feel…

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>A little</th>
<th>Some</th>
<th>Most</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) tired out for no good reason?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>b) nervous?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>c) so nervous nothing could calm you down?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>d) hopeless?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>e) restless or fidgety?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>f) so restless that you could not sit still?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>g) depressed?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>h) depressed that nothing could cheer you up?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>i) that everything was an effort?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>j) worthless?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
**Clinical Interview Diagnostic Instrument – Trauma List (CIDI-TL)**

Script: “Now I’m going to ask you about some really traumatic things that may have happened to you – things like being in a life threatening situation. I’m going to ask you to respond yes or no to whether any of the following things have happened to you and if they have I’m going to ask you if at the time you experienced feelings of intense fear, helplessness or horror. I’m not going to ask you to give me anymore details other than that. If at anytime you don’t want to answer a question you can do so without giving me a reason. If you feel distressed at anytime please let me know”.

<table>
<thead>
<tr>
<th>Event</th>
<th>YES/NO</th>
<th>If YES: At the time, did you experience feelings of intense fear, helplessness or horror?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Have you ever had to fight a war?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you been involved in a life-threatening accident?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you ever been involved in a fire, flood or natural disaster?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you ever witnessed someone being badly injured or killed?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Has someone ever touched your body in a way you didn’t like them to or in a way that made you uncomfortable?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>If YES: Would you say you have ever been sexually abused?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>If YES: Would you say you have been raped?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Or coerced into sex?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Have you ever been seriously physically attacked or assaulted?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>If YES: Would you say you have ever been physically abused?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Have you ever been emotionally abused?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you ever been threatened with a weapon, held captive or kidnapped?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you ever been tortured or the victim of terrorists?</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>Have you ever experienced any other extremely stressful or upsetting event?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Eg. Being taken away from your family</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>IF YES: Briefly, what was the most stressful or upsetting experience of this sort that ever happened to you?</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Have you ever suffered a great shock because one of the events on the list happened to someone close to you?</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>
APPENDIX 6: QUESTIONNAIRE PACK – STUDY ONE

STUDY 1

QUESTIONNAIRE PACK

<table>
<thead>
<tr>
<th>Participant number:</th>
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</table>

<table>
<thead>
<tr>
<th>Day:</th>
<th>Day:</th>
<th>Month:</th>
<th>Year:</th>
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<tbody>
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</tbody>
</table>

* Please note there are questions on both sides of the page *
Below is a list of feelings, sensations, problems, and experiences that people sometimes have. Read each item and then mark the appropriate choice in the space next to that item. Use the choice that best describes how much you have felt or experienced things this way *DURING THE PAST WEEK*, including today. Use this scale when answering:

<table>
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<tr>
<th></th>
<th>1</th>
<th>2</th>
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<th>4</th>
<th>5</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Not at all</td>
<td>A little bit</td>
<td>Moderately</td>
<td>Quite a bit</td>
<td>Extremely</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td>Felt sad</td>
<td></td>
<td></td>
<td>22. Felt like I was having a lot of fun</td>
</tr>
<tr>
<td>2</td>
<td></td>
<td>Startled easily</td>
<td></td>
<td></td>
<td>23. Blamed myself for a lot of things</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Felt cheerful</td>
<td></td>
<td></td>
<td>24. Hands were cold or sweaty</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>Felt afraid</td>
<td></td>
<td></td>
<td>25. Felt withdrawn from other people</td>
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<tr>
<td>5</td>
<td></td>
<td>Felt discouraged</td>
<td></td>
<td></td>
<td>26. Felt keyed up, “on edge”</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>Hands were shaky</td>
<td></td>
<td></td>
<td>27. Felt like I had a lot of energy</td>
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<tr>
<td>7</td>
<td></td>
<td>Felt optimistic</td>
<td></td>
<td></td>
<td>28. Was trembling or shaking</td>
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<tr>
<td>8</td>
<td></td>
<td>Had diarrhoea</td>
<td></td>
<td></td>
<td>29. Felt inferior to others</td>
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<tr>
<td>9</td>
<td></td>
<td>Felt worthless</td>
<td></td>
<td></td>
<td>30. Had trouble swallowing</td>
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<tr>
<td>10</td>
<td></td>
<td>Felt really happy</td>
<td></td>
<td></td>
<td>31. Felt like crying</td>
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<tr>
<td>11</td>
<td></td>
<td>Felt nervous</td>
<td></td>
<td></td>
<td>32. Was unable to relax</td>
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<tr>
<td>12</td>
<td></td>
<td>Felt depressed</td>
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<td></td>
<td>33. Felt really slowed down</td>
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<tr>
<td>13</td>
<td></td>
<td>Was short of breath</td>
<td></td>
<td></td>
<td>34. Was disappointed in myself</td>
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<tr>
<td>14</td>
<td></td>
<td>Felt uneasy</td>
<td></td>
<td></td>
<td>35. Felt nauseous</td>
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<tr>
<td>15</td>
<td></td>
<td>Was proud of myself</td>
<td></td>
<td></td>
<td>36. Felt hopeless</td>
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<tr>
<td>16</td>
<td></td>
<td>Had a lump in my throat</td>
<td></td>
<td></td>
<td>37. Felt dizzy or lightheaded</td>
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<tr>
<td>17</td>
<td></td>
<td>Felt faint</td>
<td></td>
<td></td>
<td>38. Felt sluggish or tired</td>
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<tr>
<td>18</td>
<td></td>
<td>Felt unattractive</td>
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<td></td>
<td>39. Felt really “up” or lively</td>
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<tr>
<td>19</td>
<td></td>
<td>Had hot or cold spells</td>
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<td>40. Had pain in my chest</td>
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<tr>
<td>20</td>
<td></td>
<td>Had an upset stomach</td>
<td></td>
<td></td>
<td>41. Felt really bored</td>
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<tr>
<td>21</td>
<td></td>
<td>Felt like a failure</td>
<td></td>
<td></td>
<td>42. Felt like I was choking</td>
</tr>
<tr>
<td></td>
<td>1 Not at all</td>
<td>2 A little bit</td>
<td>3 Moderately</td>
<td>4 Quite a bit</td>
<td>5 Extremely</td>
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<td>43.</td>
<td>Looked forward to things with enjoyment</td>
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<td>44.</td>
<td>Muscles twitched or trembled</td>
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<td>45.</td>
<td>Felt pessimistic about the future</td>
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<tr>
<td>46.</td>
<td>Had a very dry mouth</td>
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<tr>
<td>47.</td>
<td>Felt like I had a lot of interesting things to do</td>
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<td>48.</td>
<td>Was afraid I was going to die</td>
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<td>49.</td>
<td>Felt like I had accomplished a lot</td>
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<td>50.</td>
<td>Felt like it took extra effort to get started</td>
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<td>51.</td>
<td>Felt like nothing was very enjoyable</td>
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<td>52.</td>
<td>Heart was racing or pounding</td>
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<td>53.</td>
<td>Felt like I had a lot to look forward to</td>
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<td></td>
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<tr>
<td>54.</td>
<td>Felt numbness or tingling in my body</td>
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<tr>
<td>55.</td>
<td>Felt tense or &quot;high-strung&quot;</td>
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<td>56.</td>
<td>Felt hopeful about the future</td>
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<td>57.</td>
<td>Felt like there wasn't anything interesting or fun to do</td>
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<td>58.</td>
<td>Seemed to move quickly and easily</td>
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<td>59.</td>
<td>Muscles were tense or sore</td>
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<td>60.</td>
<td>Felt really good about myself</td>
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<td>61.</td>
<td>Thought about death or suicide</td>
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<td>62.</td>
<td>Had to urinate frequently</td>
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</table>
Below is a list of the same feelings, sensations, problems, and experiences that were in the above questionnaire. This time, instead of rating the items in terms of how much you have felt or experienced things this way during the past week, rate each item in terms of how much these feelings or experiences are generally like you or are common experiences for you. Use this scale when answering:

<table>
<thead>
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<th>1</th>
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<tr>
<td>Not at all</td>
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<td>Quite a bit</td>
<td>Extremely</td>
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1. Feel sad
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3. Feel cheerful
4. Feel afraid
5. Feel discouraged
6. Hands are shaky
7. Feel optimistic
8. Have diarrhoea
9. Feel worthless
10. Feel really happy
11. Feel nervous
12. Feel depressed
13. Are short of breath
14. Feel uneasy
15. Am proud of myself
16. Have a lump in my throat
17. Feel faint
18. Feel unattractive
19. Have hot or cold spells
20. Have an upset stomach
21. Feel like a failure
22. Feel like I am having a lot of fun
23. Blame myself for a lot of things
24. Hands are cold or sweaty
25. Feel withdrawn from other people
26. Feel keyed up, “on edge”
27. Feel like I had a lot of energy
28. Am trembling or shaking
29. Feel inferior to others
30. Have trouble swallowing
31. Feel like crying
32. Am unable to relax
33. Feel really slowed down
34. Am disappointed in myself
35. Feel nauseous
36. Feel hopeless
37. Feel dizzy or lightheaded
38. Feel sluggish or tired
39. Feel really “up” or lively
40. Have pain in my chest
41. Feel really bored
42. Feel like I was choking
### MASQ – 2 (TRAIT)

<table>
<thead>
<tr>
<th></th>
<th>1 Not at all</th>
<th>2 A little bit</th>
<th>3 Moderately</th>
<th>4 Quite a bit</th>
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<tr>
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<tr>
<td>57.</td>
<td>Feel like there isn't anything interesting or fun to do</td>
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<tr>
<td>48.</td>
<td>Am afraid I am going to die</td>
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<td>Have to urinate frequently</td>
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Sensitivity to Punishment (SP) and Sensitivity to Reward (SR) Questionnaire
(Torrubia, Avila, Molto, & Grande, 1995)

Answer each question by placing a cross in the circle for each question. There are no right or wrong answers, or trick questions. Work quickly and don’t think too much about the exact meaning of the question. **Remember to answer ALL the questions and to give only ONE response to each question.**

1. Do you often refrain from doing something because you are afraid of it being illegal?  
   ![YES](O) ![NO](O)

2. Does the good prospect of obtaining money motivate you strongly to do some things?  
   ![YES](O) ![NO](O)

3. Do you prefer not to ask for something when you are not sure you will obtain it?  
   ![YES](O) ![NO](O)

4. Are you frequently encouraged to act by the possibility of being valued in your work, in your studies, with your friends or with your family?  
   ![YES](O) ![NO](O)

5. Are you often afraid of new or unexpected situations?  
   ![YES](O) ![NO](O)

6. Do you often meet people that you find physically attractive?  
   ![YES](O) ![NO](O)

7. Is it difficult for you to telephone someone you do not know?  
   ![YES](O) ![NO](O)

8. Do you like to take some drugs because of the pleasure you get from them?  
   ![YES](O) ![NO](O)

9. Do you often renounce your rights when you know you can avoid a quarrel with a person or an organization?  
   ![YES](O) ![NO](O)

10. Do you often do things to be praised?  
    ![YES](O) ![NO](O)

11. As a child were you troubled by punishments at home or in school?  
    ![YES](O) ![NO](O)

12. Do you like being the centre of attention at a party or social meeting?  
    ![YES](O) ![NO](O)

13. In tasks that you are not prepared for, do you attach great importance to the possibility of failure?  
    ![YES](O) ![NO](O)

14. Do you spend a lot of your time on obtaining a good image?  
    ![YES](O) ![NO](O)

15. Are you easily discouraged in difficult situations?  
    ![YES](O) ![NO](O)

16. Do you need people to show their affection for you all the time?  
    ![YES](O) ![NO](O)
17. Are you a shy person?   O  O

18. When you are in a group, do you try to make your opinions the most intelligent or the funniest?   O  O

19. Whenever possible, do you avoid demonstrating your skills for fear of being embarrassed?   O  O

20. Do you often take the opportunity to pick up people you find attractive?   O  O

21. When you are in a group, do you have difficulties selecting a good topic to talk about?   O  O

22. As a child, did you do a lot of things to get people's approval?   O  O

23. Is it often difficult for you to fall asleep when you think about things you have done or must do?   O  O

24. Does the possibility of social advancement move you to action, even if this involves not playing fair?   O  O

25. Do you think a lot before complaining in a restaurant if your meal is not well prepared?   O  O

26. Do you generally give preference to those activities that imply an immediate gain?   O  O

27. Would you be bothered if you had to return to a store when you noticed you were given the wrong change?   O  O

28. Do you often have trouble resisting the temptation of doing forbidden things?   O  O

29. Whenever you can, do you avoid going to unknown places?   O  O

30. Do you like to compete and do everything you can to win?   O  O

31. Are you often worried by things that you said or did?   O  O

32. Is it easy for you to associate tastes and smells to very pleasant events?   O  O

33. Would it be difficult for you to ask your boss for a raise (salary increase)?   O  O

34. Are there a large number of objects or sensations that remind you of pleasant events?   O  O

35. Do you generally try to avoid speaking in public?   O  O

36. When you start to play a poker machine, is it often difficult for you to stop?   O  O
37. Do you, on a regular basis, think that you could do more things if it was not for your insecurity or fear? O O

38. Comparing yourself to people you know, are you afraid of many things? O O

39. Does your attention easily stray from your work in the presence of an attractive stranger? O O

40. Do you often find yourself worrying about things to the extent that performance in intellectual abilities is impaired? O O

41. Are you interested in money to the point of being able to do risky jobs? O O

42. Do you often refrain from doing something you like in order not to be rejected or disapproved of by others? O O

43. Do you like to put competitive ingredients in all your activities O O

44. Generally, do you pay more attention to threats than to pleasant events? O O

45. Would you like to be a socially powerful person? O O

46. Do you often refrain from doing something because of your fear of being embarrassed? O O

47. Do you like displaying your physical abilities even though this may involve danger? O O
Coping in Stressful Situations (CISS)

The following are ways people react to various difficult, stressful or upsetting situations. Please circle a number from 1 to 5 for each item. Indicate how much you engage in these types of activities when you encounter a difficult, stressful or upsetting situation. Try to think of specific situations that you have experienced to help you recall how you typically react.

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<tr>
<td>Not at all</td>
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<tr>
<td>25.</td>
<td>“Freeze” and not know what to do</td>
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<td>26.</td>
<td>Take corrective action immediately</td>
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<td>27.</td>
<td>Think about the event and learn from my mistakes</td>
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<td>28.</td>
<td>Wish that I could change what had happened or how I felt</td>
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<td>29.</td>
<td>Visit a friend</td>
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<td>30.</td>
<td>Worry about what I am going to do</td>
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<td>31.</td>
<td>Spend time with a special person</td>
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<td>32.</td>
<td>Go for a walk</td>
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<td>33.</td>
<td>Tell myself that it will never happen again</td>
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<td>34.</td>
<td>Focus on my general inadequacies</td>
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<td>35.</td>
<td>Talk to someone whose advice I value</td>
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<td>36.</td>
<td>Analyse my problem before reacting</td>
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<td>37.</td>
<td>Phone a friend</td>
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<td>38.</td>
<td>Get angry</td>
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<td>39.</td>
<td>Adjust my priorities</td>
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<td>40.</td>
<td>See a movie</td>
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<td>41.</td>
<td>Get control of the situation</td>
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<td>42.</td>
<td>Make an extra effort to get things done</td>
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<td>43.</td>
<td>Come up with several different solutions to the problem</td>
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<td>44.</td>
<td>Take some time off and get away from the situation</td>
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<td>45.</td>
<td>Take it out on other people</td>
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<td>46.</td>
<td>Use the situation to prove that I can do it</td>
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<td>47.</td>
<td>Try to be organised so I can be on top of the situation</td>
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<td>48.</td>
<td>Watch TV</td>
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**SUBSTANCE USE MOTIVES**

*(Based on DRINKING/DRUG USE MOTIVES MEASURE)*

Below is a list of reasons people use drugs or alcohol. Thinking of all the times you take ecstasy, how often would you say that you take ecstasy for each of the following reasons? *(Circle one item for each reason)*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Almost never/ never</th>
<th>Some of the time</th>
<th>Half of the time</th>
<th>Most of the time</th>
<th>Almost always/ always</th>
</tr>
</thead>
<tbody>
<tr>
<td>S4</td>
<td>To be sociable</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
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<tr>
<td>F6</td>
<td>To fit in with a group you like</td>
<td>1</td>
<td>2</td>
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<tr>
<td>E7</td>
<td>To get high</td>
<td>1</td>
<td>2</td>
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<tr>
<td>C9</td>
<td>To forget about your problems</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>E10</td>
<td>Because it’s fun</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
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<tr>
<td>S12</td>
<td>Because it makes social gatherings more fun</td>
<td>1</td>
<td>2</td>
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<tr>
<td>S13</td>
<td>Because it helps you enjoy a party</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>C15</td>
<td>Because you feel more self-confident and sure of yourself</td>
<td>1</td>
<td>2</td>
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<tr>
<td>C16</td>
<td>Because it helps when you feel depressed or nervous</td>
<td>1</td>
<td>2</td>
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<tr>
<td>E18</td>
<td>Because you like the feeling</td>
<td>1</td>
<td>2</td>
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<tr>
<td>F21</td>
<td>Because your friends pressure you to do it</td>
<td>1</td>
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<tr>
<td>F22</td>
<td>To be liked</td>
<td>1</td>
<td>2</td>
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<tr>
<td>F23</td>
<td>So you won’t feel left out</td>
<td>1</td>
<td>2</td>
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<tr>
<td>S24</td>
<td>To celebrate a special occasion with friends</td>
<td>1</td>
<td>2</td>
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<tr>
<td>C25</td>
<td>To forget your worries</td>
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<td>E26</td>
<td>Because it gives you a pleasant feeling</td>
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<tr>
<td>E28</td>
<td>Because it’s exciting</td>
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<tr>
<td>C29</td>
<td>To cheer you up when you are in a bad mood</td>
<td>1</td>
<td>2</td>
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<tr>
<td>F37</td>
<td>So that others won’t hassle you about not doing it</td>
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<tr>
<td>S43</td>
<td>Because it improves parties and celebrations</td>
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</table>
SEVERITY OF USE SCALE

Q: During the past 12 months...

1. Did you ever think your use of ecstasy was out of control?  
   (please circle the appropriate response)

   Never or almost never 0  
   Sometimes 1  
   Often 2  
   Always or nearly always 3

2. Did the prospect of missing a pill make you very anxious or worried?  
   (please circle the appropriate response)

   Never or almost never 0  
   Sometimes 1  
   Often 2  
   Always or nearly always 3

3. How much did you worry about your use of ecstasy?  
   (please circle the appropriate response)

   Not at all 0  
   A little 1  
   Quite a lot 2  
   A great deal 3

4. Did you wish you could stop?  
   (please circle the appropriate response)

   Never or almost never 0  
   Sometimes 1  
   Often 2  
   Always or nearly always 3

5. How difficult would you find it to stop or go without ecstasy?  
   (please circle the appropriate response)

   Not difficult 0  
   Quite difficult 1  
   Very difficult 2  
   Impossible 3
Attribution

The following questions refer to how much you attribute any experiences of low mood, depression and anxiety to your use of ecstasy.

1. a) Have you ever experienced low mood or felt depressed or anxious in the days following ecstasy use? (please circle) Y N
   b) If yes, how much do you attribute your experience of low mood, depression or anxiety to your ecstasy use? (please rate on the scale below)

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<tbody>
<tr>
<td>Not at all due to ecstasy</td>
<td>Slightly due to ecstasy</td>
<td>Moderately due to ecstasy</td>
<td>Mostly due to ecstasy</td>
<td>Entirely due to ecstasy</td>
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</table>

2. a) Have you ever experienced periods of low mood, felt depressed or anxious other than when you have taken ecstasy within the last week? (please circle) Y N
   b) If yes, how much do you attribute your low mood, depression or anxiety to your ecstasy use? (please rate on the scale below)

<table>
<thead>
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<tbody>
<tr>
<td>Not at all due to ecstasy</td>
<td>Slightly due to ecstasy</td>
<td>Moderately due to ecstasy</td>
<td>Mostly due to ecstasy</td>
<td>Entirely due to ecstasy</td>
</tr>
</tbody>
</table>

*Thank you very much for your participation. If participating in this study has raised any issues for you, please feel free to discuss these with me or contact one of the services on the following page.*

Becca Scott
Doctor of Psychology (Clinical) Candidate
Monash University
Available Services

If you need help with any drug or alcohol problems or would like further information regarding drugs and alcohol, you can contact any of the following resources:

- Direct Line (confidential drug and alcohol counselling and referral line, 24 hours, 7 days), Ph: **1800 888 236** (Victoria only) or go to: [http://www.health.vic.gov.au/drugs/directline.htm](http://www.health.vic.gov.au/drugs/directline.htm) for information on this service.
- Turning Point Alcohol and Drug Centre. For clinic appointments, referrals or information about clinical services at Turning Point, call the Intake Team between 9.30am and 5.00pm, Monday to Friday. Ph: 03 8413 8444

If you are experiencing any distress or psychological symptoms, you can contact any of the following counselling or clinical psychology services:

- Monash University Counselling Service, Clayton Campus Ph: 03 9905 3156
  Monash University After Hours Telephone Counselling Service 03 9621 2600
- Monash University Clinical Psychology Centre Ph: 03 9548 7011
- Lifeline Ph: 13 11 14
- Talk to your GP about services in your area
APPENDIX 7: BIOHAZARD COLLECTION AND RISK ASSESSMENT

1. Protocol for collection and handling of saliva
   a. Participants will hold the bottle, not the researcher, while they spit into it.
   b. The researcher will wear latex gloves when handling the saliva bottle during collection of the sample.
   c. The researcher will wipe down the bottle after collection of the saliva sample to ensure that no saliva is left on the outside of the bottle.

2. Potential risks to participants include experiencing psychological distress. This potential risk will be dealt with in the same manner across all testing locations. That is, if the research participant identifies their distress during testing to the research investigator, they will provide support at the time. The investigator will be trained to respond to a range of reactions (mild to severe) in the unlikely event that such distress occurs.

   These include:
   
   *Mild distress*—provide support by listening to participants concerns and encouraging s/he follows up by contacting services.
   *Moderate distress*—provide support, encourage follow-up, and arrange to contact research participant to ensure resolution.
   *Severe distress*—provide support, contact crises services and arrange for an assessment.

   In addition, it will be made clear to participants that they are free to withdraw from participation up until handing in their questionnaires in Study 1.
Ecstasy Users: Vulnerability factors for Depression and Anxiety Symptomatology

Study 1

Consent Form

I freely agree to take part in the above Monash University research project. I have had the project explained to me, and I have read the Explanatory Statement that I can keep as a record. I understand that agreeing to take part means that I am willing to complete an interview with Becca Scott and to complete questionnaires and provide a saliva sample to be used for genetic analysis. I understand that at any time throughout the study I may refuse to answer any questions without stating a reason. I understand that if my responses indicate severe distress or symptoms of depression or anxiety I will be contacted by Becca Scott to encourage me to seek psychological counselling or support.

I understand that any information I provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project or to any other party except when the researchers are legally or ethically required. I understand that my participation is voluntary, that I can choose not to participate in part or all of the project, and that I can withdraw at any stage of participation, prior to submission of the completed questionnaire, without being penalised or disadvantaged in any way.

I also agree to being asked to participate in a follow-up study. I further understand that I am free to decline participation at that time for any reason.

Please tick if you consent to the following:

☐ I consent to partake in an interview conducted by Becca Scott and also to complete a questionnaire package.
☐ I consent to providing a saliva sample.
☐ I consent to being asked to participate in the follow-up.

Please note that handing in your completed questionnaire package will confirm your consent to participate in this study.

To be completed by Rebecca Scott, student researcher:

Date: ___/___/____
Participant number: ________
Ecstasy Users: Vulnerability factors for Depression and Anxiety Symptomatology

Study 2

Explanatory Statement

Firstly, thank you very much for participating in the first part of my study. As part of my thesis I am conducting a follow-up study with a sub-sample of those who participated in Study 1. This involves looking at the effects of ecstasy in the days following use.

Background and purpose of the current study
Research indicates that ecstasy may result in lowered mood in the days after use and there is some suggestion that certain people are more susceptible than others to experiencing this drop in mood. Despite this, an investigation of what factors increase the likelihood that someone will experience these effects, while observing people before and after taking ecstasy, is absent from the current research literature. Using the data from Study 1, we are investigating what factors (amount of ecstasy consumed, personality, genetic predisposition, coping style etc) make it more likely that a person will experience a drop in mood in the days following taking ecstasy. By determining what factors increase vulnerability to short-term mood effects may shed light on who may be vulnerable to potential long-term psychological effects of ecstasy use.

Who is eligible to participate in this study?
All participants from study 1 will be asked if they are planning on taking ecstasy over the next week. Those who are planning on taking ecstasy and those who have taken ecstasy at least six times in the last six months will be asked if they would like to participate in the follow up study (study 2).

As in the Explanatory Statement for Study 1 this Explanatory Statement contains detailed information about Study 2 of the research project. Its purpose is to explain to you as openly and clearly as possible all the procedures involved before you decide whether or not to take part in it. Please read this Explanatory Statement carefully. Feel free to ask questions about any information in the Explanatory Statement and feel free to discuss the project with a relative or friend.

Possible benefits of participating
Your participation in the follow-up will further add to our knowledge regarding the effects of ecstasy and will give us valuable insight into who is more vulnerable to experiencing short-term mood effects following ecstasy use. Greater knowledge in this area will enable people to make more informed decisions about using ecstasy and may assist health professionals to better understand the potential after effects of ecstasy use.

What does the research involve?
Participating in the follow-up involves two brief telephone interviews over one week. If you consent to participating in the follow-up I will be asking you if you are planning on taking ecstasy over the next week. If you are, I will phone you the day after you plan to
take ecstasy between 6pm and 8pm. If you are not planning on taking ecstasy, I will phone you on Sunday between 6pm and 8pm. The phone interview will include a series of questions on your drug use over the days since you participated in Study 1, your sleep, stress, mood and psychological symptoms. If you have taken ecstasy I will also ask about the impact of taking ecstasy on your functioning that day and about your experience of taking ecstasy. Two days later I will call you again between 6pm and 8pm and ask you the same questions.

**Your use of ecstasy**
Although we are studying the possible effects that the use of ecstasy might have on people, we do not encourage or require you to use ecstasy at any time. If you elect to participate in the initial research or the follow up period, any information we obtain from you will be significant whether you take ecstasy or not.

**How much time will the research take?**
Each phone interview will take approximately 10 minutes.

**Inconvenience or discomfort**
As in Study 1, the research involves providing information regarding personal issues such as your current drug use and psychological symptoms. This may cause you distress, however the risk of this is low. If this research raises any issues for you, you may wish to contact one of the counselling services listed at the end of this Explanatory Statement. Furthermore, as we are looking at lowered mood in the days following use you may be experiencing low mood or psychological symptoms when I talk to you on the phone and consequently the phone interview may be challenging for some people.

**Payment**
There is no additional payment over and above the payment you received for your participation in Study 1.

**Confidentiality**
As in Study 1 your anonymity will be protected because names will not appear on interview data, but rather your data will be identified by identification numbers. Participants’ contact details and associated identification numbers will only be accessible to the principal investigators. Furthermore, your contact information will be destroyed directly after your participation and at no point will you be asked for your name. The data will be stored at the university under lock and key for at least five years, as prescribed by the university regulations. The information being collected from you will be combined with information collected from other participants. This information will be used to differentiate between groups of people rather than individuals. No findings which could identify any individual research participant will be published. Confidentiality will be maintained at all times except where the interviewer is ethically bound to break this confidentiality. Exceptions to confidentiality include, (a) if you disclose that you are at risk of harming yourself, (b) if you disclose that you are at risk of harming others, and (c) if there is a court order for the information. In this last instance, in the extremely unlikely event that the data is subpoenaed, any information held by the researchers would have to be submitted to the court or police. However, as your personal information will have been destroyed, data collected in this study will not include your name or contact details. If subpoenaed, it is extremely unlikely that any information collected in this study could be linked to you under such circumstances.
Results
After the collection of data is completed, the study outcomes will be available at: http://www.med.monash.edu.au/psych/questionnaires/rscott/. No individual participant will be identified; rather the results will include information of how groups of individuals responded on average and any associations found between the variables. The same is true for the final thesis and associated publications and conference presentations. No individual participant will be identifiable.

Participation is voluntary
Your participation is voluntary and if you agree to participate you may withdraw your consent, without stating a reason, up until your completion of the final phone interview. This includes being able to withdraw your data from Study 1. You may do this by simply telling me that you wish to withdraw from the study. Following completion of your participation, your data will be pooled with the data from other participants and there will be no identifying information linking you to your data. Not participating in the research will not disadvantage you in any way. If you have any questions pertaining to your participation at any point after today, please contact me or Dr. Sabura Allen (contact details below).

Thank you for considering participating in this project.

Becca Scott, BA, BScHONS (Psychology)
Doctor of Psychology (Clinical) Candidate
Department of Psychology
Telephone: 
Email: becca.scott@med.monash.edu.au

Chief Investigator:
Dr. Sabura Allen, BA, MS, PhD
Department of Psychology
Telephone: 9905 4725
Email: sabura.allen@med.monash.edu.au

You can complain about this research if you don’t like something about it. To complain about this research, you need to phone 9905 2052. You can then ask to speak to the secretary of the Human Ethics Committee and tell him or her that the number of the project is: CF07/1061 - 2007/0273. You could also write to the secretary. That person’s address is:

The Secretary
The Standing Committee on Ethics in Research Involving Humans
PO Box No 3A
Monash University Vic 3800
Telephone +61 3 9905 2052 Fax +61 3 9905 1420
Email: SCERH@adm.monash.edu.au

Department of Psychology
Faculty of Medicine,
Nursing and Health Sciences
Building 17
Clayton Campus
Monash University
Victoria 3800, Australia
Telephone: +61 3 9905 3968
Fax: +61 3 9905 3948
Available Services

If you need help with any drug or alcohol problems or would like further information regarding drugs and alcohol, you can contact any of the following resources:

- Direct Line (confidential drug and alcohol counselling and referral line, 24 hours, 7 days) Ph: 1800 888 236 (Victoria only) or go to http://www.health.vic.gov.au/drugs/directline.htm for information on this service.
- DrugInfo Clearinghouse (Australian Drug Foundation) Ph: 1300 85 85 84 or go to: http://www.druginfo.adf.org.au/
- Turning Point Alcohol and Drug Centre. For clinic appointments, referrals or information about clinical services at Turning Point, call the Intake Team between 9.30am and 5.00pm, Monday to Friday. Ph: 03 8413 8444

If you are experiencing any distress or psychological symptoms, you can contact any of the following counselling or clinical psychology services:

- Monash University Counselling Service, Clayton Campus Ph: 03 9905 3156
- Monash University After Hours Telephone Counselling Service 03 9621 2600
- Monash University Clinical Psychology Centre Ph: 03 9548 7011
- Lifeline Ph: 13 11 14
- Talk to your GP about services in your area
Do you freely agree to take part in the follow-up study of this Monash University research project? YES □

Have you had the project explained to you in full and have you read the Explanatory Statement that you can keep as a record? YES □

Do you understand that agreeing to take part means that you are willing to complete a series of telephone interviews with student researcher, Becca Scott? YES □

Do you understand that you are not required or expected to take ecstasy over the follow up period and that neither the researchers nor Monash University are endorsing or encouraging ecstasy use in any way? YES □

Do you understand that at any time throughout the study you may refuse to answer any questions without stating a reason? YES □

Do you understand that if your responses indicate severe distress or symptoms of depression or anxiety I will encourage you to seek psychological counselling or support? YES □

Do you understand that any information you provide is confidential, and that no information that could lead to the identification of any individual will be disclosed in any reports on the project or to any other party, except when the researchers are legally or ethically required? YES □

Do you understand that you participation is voluntary, that you can choose not to participate in part or all of the project, and that you can withdraw at any stage of participation, prior to the completion of the final telephone interview, without being penalised or disadvantaged in any way? YES □

To be completed by Rebecca Scott, student researcher:

Date: __/___/___
Participant number: _______
STUDY 2

TELEPHONE INTERVIEW PACK

Participant number: 

Day: | Day: | Month: | Year: 
---|---|---|---

Day 1 | Day 3 (circle)
TIMELINE FOLLOWBACK – 24 hours and 72 hours post ecstasy use

“I’m going to ask you about your drug and alcohol use since we last spoke”

“We’re there any events that happened during this time – like birthdays, accidents, anniversaries, parties – things like that?”

Note events in the right hand side of the boxes.

Stressful Life Events

“You might remember that I asked you about whether you had experienced any stressful life events over the last month. Now I’m going to ask if you’ve experienced any of those since we last spoke?”

Have you started, stopped, changed or had any problems with ………… since [insert day]?

School/Study
Employment (include serious difficulties at work, promotion/demotion, loss of job)
Finances (include income, bills, loans, went on/off benefits)
Relationships (include family/partner/friends/children/others; include serious relationship problems, divorce/break up, loss of confidant other than partner)

Have you changed your living arrangements since we last spoke?

Living Arrangements (include change in residence, new resident, renovations)

Have you had any problems with Health or Crime and Legal Matters since we last spoke?

Health (include physical health/illness/injury, contact with health professionals)
Crime and Legal Matters: (include victim of assault/robbery; accidents; law suit, committed/accused of any crime)

“On a scale from 0 to 10, with 0 being not stressed at all and 10 being extremely stressed, how stressed would you say you were today?” ______

“Have you been drinking more caffeine or smoking more cigarettes than usual?”

Caffeine: YES/NO _____ cups/day
Cigarettes: YES/NO _____ cigarettes/day
“Since (insert day) have you used any … Alcohol, Cannabis/Marijuana, Speed, Ice, Cocaine, Ecstasy, Heroin, Methadone, LSD, Sleeping tablets or sedatives (eg. Valium or normison), or Inhalants that week?”
Circle those that apply. If none discontinue.
FREQ: “How many days did you use ______ that week?”
QUAN: “How much ______ did you use each day?”
ROUTE: “How did you use it?: smoked (joint or bong) /inhaled, mouth/eating, snort/sniffed, IV?”

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<th>Alcohol: _____ SDU’s</th>
<th>Heroin: _____ g _____ Pts</th>
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<tbody>
<tr>
<td>1</td>
<td>Cannabis: _____ g/oz</td>
<td>Speed/Ice: _____ g _____ Pts</td>
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<tr>
<td></td>
<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: _____ mg _____ Tabs/Pills</td>
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<tr>
<td></td>
<td>Leaf/Hydro/Buds/Hash</td>
<td>Inhalants: _____ Sniffs/Cans/Bags</td>
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<tr>
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<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
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<td></td>
<td>What type did you use?</td>
<td>Benzos: _____ mg _____ Tabs/Pills</td>
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<td>Inhalants: _____ Sniffs/Cans/Bags</td>
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<td>Speed/Ice: _____ g _____ Pts</td>
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<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
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<td>What type did you use?</td>
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<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
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<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: _____ mg _____ Tabs/Pills</td>
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<td>LSD/Ecstasy _____ Tabs/Pills</td>
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<td>Speed/Ice: _____ g _____ Pts</td>
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<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
</tr>
<tr>
<td></td>
<td>What type did you use?</td>
<td>Benzos: _____ mg _____ Tabs/Pills</td>
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<td>Cannabis: _____ g/oz</td>
<td>Speed/Ice: _____ g _____ Pts</td>
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<td>Joints/Cones/Bongs</td>
<td>LSD/Ecstasy _____ Tabs/Pills</td>
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<td></td>
<td>What type did you use?</td>
<td>Benzos: _____ mg _____ Tabs/Pills</td>
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<td></td>
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**TOTALS**

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<tr>
<th>Item</th>
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<tr>
<td>Alcohol</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>Heroin</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>Cannabis</td>
<td>_____</td>
<td>_____</td>
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<tr>
<td>Speed/Ice</td>
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<tr>
<td>LSD</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>_____</td>
<td>_____</td>
</tr>
<tr>
<td>Benzos</td>
<td>_____</td>
<td>_____</td>
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<tr>
<td>Inhalants</td>
<td>_____</td>
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Now I’m going to ask you some questions about your ecstasy experience last night?

“Can you remember what the ecstasy tablet looked like?”
Specify ________________________________

“About what time did you take your first and last ecstasy tablet?”
First:__________ Last:_____________

“Some common effects of MDMA are: increased energy, feelings of euphoria, increased sociability and warmth towards other, jaw clenching or chewing your mouth, and changes in sensory perception. Based on that and on your past experiences of ecstasy how confident are you that what you took was MDMA? Rate on scale from 0 to 10 with 0 = definitely not MDMA, 3 pretty sure it wasn’t MDMA, 5 = you’re not sure, 7 = pretty sure it was MDMA, 10 = definitely was MDMA.”

1  2  3  4  5  6  7  8  9  10

“Did you any other drugs in combination with ecstasy? (e.g. smoking cannabis as you came down from ecstasy)?”

Finally, how positive was your ecstasy experience last night on a scale from 0 to 10 with 0 being an extremely negative experience, 5 being a neutral experience and 10 being an extremely positive experience.

1  2  3  4  5  6  7  8  9  10

NOTE: Standard Drinks Units
MEDICATION: (Ask those that apply)
And since (insert day)…
“Have you taken your prescribed medication everyday?” YES/NO (circle)
“Have you commenced/ceased or changed your medication since you did the interview with me?” YES/NO (circle)
“Have you taken your homeopathic prescribed medication everyday?” YES/NO (circle)
“Have you commenced/ceased or changed your medication since you did the interview with me?” YES/NO (circle) Specify _______________________

“Now I’m going to ask you some questions about your sleep and your mood?”

SLEEP: “What time did you go to sleep last night?” _______
“What time did you wake up?” _______
“How does this differ from your usual sleep pattern? more sleep, less sleep, the same” (circle)
“How restless was your sleep last night compared to normal? (0 = not restless at all, to 10 = extremely restless)” _______

SELF REPORTED MOOD:
“How would you rate your overall mood today out of 10, 0 being the worst you have ever felt and 10 being the best you’ve ever felt” ______
**Brief Psychiatric Rating Scale: Anxiety, Depression and Hostility**

**Anxiety**
Reported apprehension, tension, fear, panic or worry. Rate only the patient's statements, not observed anxiety which is rated under Tension.
- Have you been worried a lot *today*? Have you been nervous or apprehensive?
- Are you concerned about anything? How about finances or the future?
- When you are feeling nervous, do your palms sweat or does your heart beat fast (or shortness of breath, trembling, choking)?

**[If patient reports anxiety or autonomic accompaniment, ask the following]**
- How much of the time have you been .......... (use patient 's description)?
- Has it interfered with your ability to perform your usual activities/work?

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<th>N/a</th>
<th>1</th>
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<th>4</th>
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<th>6</th>
<th>7</th>
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<tbody>
<tr>
<td>N o t a s s e s s e d</td>
<td>N o t p r e s e n t</td>
<td>Reports some discomfort due to worry OR infrequent worries that occur more than usual for most normal individuals.</td>
<td>Worried frequently but can readily turn attention to other things.</td>
<td>Worried most of the time and cannot turn attention to other things easily but no impairment in functioning OR occasional anxiety with autonomic accompaniment but no impairment in functioning.</td>
<td>Frequent periods of anxiety with autonomic accompaniment OR some areas of functioning are disrupted by anxiety or worry.</td>
<td>Anxiety with autonomic accompaniment persisting for most of the day OR many areas of functioning are disrupted by anxiety or constant worry.</td>
<td>Anxiety with autonomic accompaniment persisting throughout the day OR most areas of functioning are disrupted by anxiety or constant worry.</td>
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<tr>
<td>v e y m i l d</td>
<td>m i l d</td>
<td>m o d e r a t e</td>
<td>m o d e r a t e l y s e v e r e</td>
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<td>e x t r e m e l y s e v e r e</td>
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Depression
Include sadness, unhappiness, anhedonia and preoccupation with depressing topics (can’t attend to TV or conversations due to depression), hopelessness, loss of self-esteem (dissatisfied or disgusted with self or feelings of worthlessness). **Do not include** vegetative symptoms, e.g. motor retardation, early waking or the amotivation that accompanies the deficit syndrome.

- **How has your mood been today?** Have you felt depressed (sad, down, unhappy, as if you didn’t care)?
- **Are you able to switch your attention to more pleasant topics when you want to?**
- **Do you find that you have lost interest in or get less pleasure from things you used to enjoy, like family, friends, hobbies, watching TV, eating?**

[If subject reports feelings of depression, ask the following]
- **How long do these feelings last?**
- **Has it interfered with your ability to perform your usual activities/work?**

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<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>N o t a s s e s s e d</td>
<td>Not at all</td>
<td>Occasionally feels sad, unhappy or depressed.</td>
<td>Frequently feels sad or unhappy but can readily turn attention to other things.</td>
<td>Frequent periods of feeling very sad, unhappy, moderately depressed, but able to function with extra effort.</td>
<td>Frequent periods of deep depression OR some areas of functioning are disrupted by depression.</td>
<td>Deeply depressed most of the day OR many areas of functioning are disrupted by depression.</td>
<td>Deeply depressed all day OR most areas of functioning are disrupted by depression.</td>
</tr>
<tr>
<td>v e r y m i l d</td>
<td>mild</td>
<td>moderate</td>
<td>moderately severe</td>
<td>severe</td>
<td>extremely severe</td>
<td></td>
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</tbody>
</table>
Hostility
Animosity, contempt, belligerence, threats, arguments, tantrums, property destruction, fights and any other expression of hostile attitudes or actions. Do not infer hostility from neurotic defenses, anxiety or somatic complaints. **Do not include** incidents of appropriate anger or obvious self-defense.
- How have you been getting along with people today (family, co-workers, etc.)?
- Have you been irritable or grumpy **today**? (How do you show it? Do you keep it to yourself?)
- Were you ever so irritable that you would shout at people or start fights or arguments? (Have you found yourself yelling at people you didn't know?)
- Have you hit anyone today?

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<th>N/a</th>
<th>1</th>
<th>2</th>
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<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
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<tbody>
<tr>
<td>N/a</td>
<td>Very mild</td>
<td>Mild</td>
<td>Moderate</td>
<td>Moderately severe</td>
<td>Severe</td>
<td>Extremely severe</td>
<td></td>
</tr>
<tr>
<td>Not assessed</td>
<td>Irritable or grumpy, but not overtly expressed.</td>
<td>Argumentative or sarcastic.</td>
<td>Overtly angry on several occasions OR yelled at others excessively.</td>
<td>Has threatened, slammed about or thrown things.</td>
<td>Has assaulted others but with no harm likely, e.g. slapped or pushed, OR destroyed property, e.g. knocked over furniture, broken windows.</td>
<td>Has attacked others with definite possibility of harming them or with actual harm, e.g. assault with hammer or weapon.</td>
<td></td>
</tr>
</tbody>
</table>
K10+ Scale

“The following questions also ask about how you have been feeling today”

“On a scale of 1 to 5 with 1 being none of the time and 5 being all of the time, about how often did you feel…

<table>
<thead>
<tr>
<th>Question</th>
<th>None</th>
<th>A little</th>
<th>Some</th>
<th>Most</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) tired out for no good reason?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>b) nervous?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>c) so nervous nothing could calm you down?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>d) hopeless?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>e) restless or fidgety?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>f) so restless that you could not sit still?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>g) depressed?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>h) depressed that nothing could cheer you up?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>i) that everything was an effort?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>j) worthless?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

ATTRIBUTION

“How much do you attribute your mood experiences you have just described to you taking ecstasy last night (or three days ago)?”

<table>
<thead>
<tr>
<th>Score</th>
<th>Not at all due to ecstasy</th>
<th>Slightly due to ecstasy</th>
<th>Moderately due to ecstasy</th>
<th>Mostly due to ecstasy</th>
<th>Entirely due to ecstasy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
Functioning [for people who have taken ecstasy]

“Now I am going to ask you about whether taking ecstasy affected your functioning today?”

1. "Is there anything you didn't do today because you took ecstasy last night? YES/NO (circle)

2. “How much did taking ecstasy last night (or three days ago) affect your ability to fulfill your work (or study) obligations today? ” (circle)

<table>
<thead>
<tr>
<th>Not at all (e.g., went to work and functioned as normal)</th>
<th>A little</th>
<th>Moderately</th>
<th>A lot</th>
<th>Totally (e.g., didn’t go to work/uni)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

3. “How much did taking ecstasy last night (or three days ago) affect your ability to fulfill your social obligations today? As in, did you do everything you planned to do with your friends today?” (circle)

<table>
<thead>
<tr>
<th>Not at all (e.g., partook in all planned social activities as normal)</th>
<th>A little</th>
<th>Moderately</th>
<th>A lot</th>
<th>Totally (e.g., didn’t engage in any social activities that they normally would have)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
4. “How much did taking ecstasy last night (or three days ago) affect your ability interact with significant otherstoday, such as your partner, family?” (circle)

<table>
<thead>
<tr>
<th></th>
<th>Not at all (e.g., Didn’t treat them any different to normal)</th>
<th>A little</th>
<th>Moderately</th>
<th>A lot</th>
<th>Totally (e.g., couldn’t face talking to them)</th>
<th>N/A Didn’t see them (but not due to ecstasy factors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Romantic Partner</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>n/a</td>
</tr>
<tr>
<td>Family</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>n/a</td>
</tr>
<tr>
<td>Friends</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>n/a</td>
</tr>
<tr>
<td>Colleagues</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>n/a</td>
</tr>
</tbody>
</table>

5. “How much did taking ecstasy last night (or three days ago) affect your ability to fulfil your practical home obligations today, such as cleaning, food shopping etc?” (circle)

<table>
<thead>
<tr>
<th></th>
<th>Not at all (e.g., did all house tasks as normal)</th>
<th>A little</th>
<th>Moderately</th>
<th>A lot</th>
<th>Totally (e.g., couldn’t do anything around the house that I wanted or planned to do)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
APPENDIX 12: Letter to the editor submitted to *The American Journal of Psychiatry*

Differences in 5-HTTLPR frequencies among ecstasy users

REBECCA M. SCOTT, BSc(HONS), DAN I. LUBMAN, PHD., LEANNE HIDES, PHD., J. SABURA ALLEN, PHD., and RICHARD BURKE, PHD. Melbourne, Australia.

TO THE EDITOR. As published in your journal, Roiser et al. [1] examined the role of 5-HTTLPR genotype on emotional processing and depressive symptomatology in ecstasy users. Although they found significant differences on these measures, they found no difference in 5-HTTLPR genotype frequency between their ecstasy sample and groups of cannabis users and drug-naive controls.

Recently, we recruited 177 ecstasy users (83 males; mean age=23.3 years, SD=4.0) from the community in Melbourne, Australia [2]. Lifetime ecstasy use ranged from half a pill to 5332 pills (median=37). Forty-six participants were homozygous for the S allele (SS=26.0%), 89 were heterozygous (SL=50.3%) and 42 were homozygous for the L allele (LL=23.7%). The distribution of genotype frequency was significantly different to that reported in a New Zealand birth cohort (n=847) [3] (SS=17%, SL=51%, LL=31%) ($\chi^2=6.42, df=2, p<.05$), with greater SS genotypes and fewer LL genotypes in the current sample.

These findings suggest that the SS genotype may be a risk factor for commencing ecstasy use. Individuals with the SS genotype may be particularly attracted to the mood enhancing properties of ecstasy, given that the S allele is associated with reduced expression of the serotonin transporter and less reuptake of serotonin. While we found no relationship between 5-HTTLPR genotype and current depressive and anxiety symptomatology [2], it remains possible that individuals with the SS genotype may experience more adverse effects (e.g., depressed mood) from ecstasy in the short- and/or long-term. Indeed, the S allele has been associated with poorer treatment response and greater adverse side effects from SSRIs [4,5], which, like ecstasy, affect the serotonin transporter. Although relating to cross-sectional assessment, the current data highlight an interesting area for future research looking at 5-HTTLPR genotype and patterns and consequences of ecstasy use.

References

APPENDIX 13: Confirmation of acceptance of article one for publication

From v.curran@ucl.ac.uk
Sent Tuesday, December 15, 2009 3:58 am
To becca.scott@med.monash.edu.au
Cc
Bcc
Subject Psychopharmacology - Psych-2009-00427.R1: Paper accepted

14-Dec-2009

Manuscript No. Psych-2009-00427.R1
Title: Depressive and anxiety symptomatology in ecstasy users: The relative
collection of genes, trauma, life stress, and drug use
By: Scott, Rebecca; Hides, Leanne; Allen, J. Sabura; Burke, Richard; Lubman, Dan

Dear Ms. Scott,

We are pleased to inform you that your manuscript Psych-2009-00427.R1, entitled
"Depressive and anxiety symptomatology in ecstasy users: The relative
collection of genes, trauma, life stress, and drug use", has been accepted for
publication in Psychopharmacology.

The manuscript will now be forwarded to the publisher, from whom you will shortly
receive information regarding the correction of proofs and fast online publication.

Should you have any questions regarding publication of your paper, please contact
the responsible production editor, Mr. Anthony de Ocampo at
anthony.deocampo@springer.com.

Best wishes and thanks,

Valerie

Prof. H Valerie Curran
Principal Editor
Psychopharmacology

Reviewer: 1
Comments of Reviewer for the attention of authors.
I have considered the revised manuscript and the authors’ responses to my original
comments. I am satisfied with their answers and pleased that they have made some
important additions to the MS. On the basis of their response I would recommend
acceptance.