Psychiatric profiles of mothers who take Ecstasy/MDMA during pregnancy: reduced depression one year after giving birth and quitting Ecstasy.

John J.D. Turner+, Andrew C. Parrott*, Julia Goodwin+, Derek G. Moore+,
Sarah Fulton**, Meeyoung O. Min**, Lynn T. Singer**

University of East London, London E15 4LZ, United Kingdom+
Swansea University, Swansea SA2 8PP, United Kingdom*
Case Western Reserve University, Cleveland, Ohio, USA**

Corresponding Author:
Dr John J.D. Turner
School of Psychology, University of East London
London E15 4LZ
Tel: +44 (0) 20 8223 4462
Email: j.j.d.turner@uel.ac.uk

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Abstract

Background: the recreational drug MDMA (3,4-methylenedioxymethamphetamine) or 'Ecstasy' is associated with heightened psychiatric distress and feelings of depression. The Drugs and Infancy Study (DAISY) monitored the psychiatric symptom profiles of mothers who used Ecstasy/MDMA while pregnant, and followed them over the first year post-partum.

Methods: 28 young women who took MDMA during their pregnancy were compared with a polydrug control group of 68 women who took other psychoactive drugs while pregnant. The Brief Symptom Inventory (BSI) was completed for several periods: the first trimester of pregnancy, also 1, 4, and 12 months after childbirth. Recreational drug use was monitored at each time point.

Results: During the first trimester of pregnancy, MDMA using mothers reported higher depression scores than polydrug controls. One year after childbirth their BSI depression score were significantly lower, and now close to control group values. At the same time point their self-reported use of MDMA had become nearly-zero, in contrast to their continued of cannabis, nicotine and alcohol. Significant symptom reductions were also found with BSI obsessive-compulsive and interpersonal sensitivity, following Ecstasy/MDMA cessation

Conclusions: The findings from this unique prospective study of young recreational drug using mothers are consistent with previous reports of improved psychiatric health after quitting Ecstasy/MDMA.

Keywords: MDMA – Ecstasy – drug - depression – pregnancy

Introduction

MDMA (3,4-methylenedioxymethamphetamine) or "Ecstasy" is used as an illicit drug by subgroups of adolescents and young adults. Its recreational use is mainly associated with dance clubs, all-night raves, and house parties (Parrott et al, 2008; Winstock et al, 2001). Population surveys in the USA have revealed usage levels as high as 9.5% in college students (Johnston et al., 2005; Singer et al., 2004), while in the American National Survey on drug use and health, Ecstasy/MDMA was found to be used more by young women than men (Wu et al., 2010). Neuroimaging studies of abstinent MDMA users have revealed significantly lower levels of the serotonin transporter or 'SERT' (Kish et al, 2010; Erritizoe et al, 2011), and have been widely interpreted as suggesting serotonergic neurotoxicity (Ricaurte et al, 2000; Puerta et al, 2009; Benningfield and Cowan, 2013; Parrott, 2013a). Recreational use of MDMA is also associated with various neuropsychobiological problems, including memory deficits (Rogers et al, 2009; Zakzanis and Campbell, 2006; Montgomery et al, 2010), impairments in higher cognitive processing (Fox et al, 2002; Reay et al, 2006; Parrott, 2012, 2013b), sleep apnea (McCann et al, 2009), raised cortisol levels (Parrott, 2009; Parrott et al, 2012), psychosocial impairments (Topp et al, 1999), and various psychiatric problems (Schifano et al, 1998; MacInnes et al, 2000; Morgan et al, 2002; Verheyden et al, 2003; Singer et al, 2004; Milani et al, 2004; Brière et al, 2012).

Laboratory animal studies have shown adverse effects of MDMA upon the developing foetus (Skelton et al, 2008; Adori et al, 2010), raising concerns about potentially damaging effects when taken by female recreational users during pregnancy. To date there has been no controlled empirical data addressing this question, although there is some evidence for adverse birth consequences (McElhatton et al, 1999; review in Singer et al, 2012b). To investigate potential effects of foetal MDMA exposure on development, the National Institute on Drug Abuse in the United States (NIDA) funded the Drugs and Infancy Study (DAISY). This prospective study monitored a group of mothers who took recreational Ecstasy/MDMA while pregnant, and a control group of pregnant female polydrug-users. The two groups were followed over time in order to monitor the physical development and psychobiological well-being of their children. Over the first year of life, the children of MDMA-using mothers displayed significantly poorer gross psychomotor skills than control group children (Singer et al, 2012a, 2012b). The DAISY study

also assessed maternal well-being using the Brief Symptom Inventory, a self-report measure of psychiatric health for non-clinical populations, derived from the earlier Symptom Check List-90 (Derogatis and Nelisaratos, 1983).

This psychiatric measure was included because previous research has shown higher symptom profiles in abstinent Ecstasy/MDMA users. Soar et al (2001) reviewed the medical case study literature, which indicated an increased risk of several psychiatric disorders, including depression and psychosis in MDMA users. Schifano et al (1998) noted that regular Ecstasy/MDMA users were at increased risk of developing various psychiatric problems, the most frequent being depression. MacInnes et al (2000) found significantly raised Beck Depression Inventory scores, in a non-clinical sample of abstinent regular Ecstasy/MDMA users. Singer et al (2004) found that abstinent Ecstasy users reported significantly higher BSI scores for anxiety, depression, and obsessive-compulsive disorder than non-users controls. Milani et al (2004) reported significant gender effects, with female Ecstasy/MDMA users reporting higher levels of BSI anxiety, depression and somatization scores. Verheyden et al (2003) investigated the reasons for quitting Ecstasy/MDMA, and found that most users in their large survey reported improved mental health after drug cessation. In the current DAISY, the BSI allowed us to prospectively monitor the psychiatric health of our pregnant mothers, and to investigate how any changes in drug usage were associated with their report of psychological distress on the BSI. Based on previous findings it might be predicted that elevated psychiatric symptoms would be evident in mothers who are continuing MDMA users, whilst those who discontinue use may show improvements. However, given its uniqueness, and the additional biopsychosocial changes associated with pregnancy and motherhood, the aims of the study were largely exploratory.

Methods.

Experimental Design. The data in the current report were collected as part of the maternal assessment component of DAISY, a prospective study primarily exploring the effects of recreational drug use, notably MDMA/Ecstasy, on infant social and cognitive development (Moore et al, 2010; Singer et al, 2012a and b). In a Mixed design, mothers who used MDMA/Ecstasy during pregnancy (MDMA/Ecstasy users) were compared with those who used other drugs but not MDMA/Ecstasy (Polydrug user controls), across measures of drug use and symptoms of mental distress at four distinct time periods: first trimester of pregnancy and then at 1, 4 and 12 months post-partum.

Participants. 96 pregnant UK women were prospectively recruited through midwife referral, leaflets describing the study at prenatal clinics, and advertisements in commercial pregnancy magazines. We sought pregnant women who were using recreational drugs during pregnancy, and listed ecstasy, tobacco, cannabis, alcohol and cocaine as examples. The majority of participants were therefore recreational 'polydrug' users. Exclusionary factors included: positive HIV status, moderate or severe intellectual disability, chronic medical disorder, or psychiatric diagnosis. In total there were 28 mothers in the MDMA-exposed group, who used MDMA (and other substances) during pregnancy, and 68 non-MDMA controls (some of who used substances during pregnancy but not MDMA). The majority of the sample were white, married or with a partner and educated to UK degree level. Their mean ages at the birth of their infants were 30.3 (S.D. 6.4) years of age in the MDMA exposed group and 28.4 (S.D. 6.2) in the controls. The groups did not differ on basic demographic profiles. Participants were informed of data confidentiality, and gave written informed consent. The study protocol was approved by ethics committees from the University of East London UK, Case Western Reserve University USA, and the National Health Service UK. For a fuller description of the participant sample and screening procedures, see Singer et al (2012a).

Drug usage. All women were individually interviewed about their substance use by fully trained female research assistants. The interview was an adaptation of the Maternal Post-Partum Interview, which was developed for earlier studies of maternal cocaine exposure (Singer et al.,

2002). Interview questions covered substances commonly used in the UK, and were based on the University of East London Recreational Drug Usage Questionnaire (Parrott et al, 2001). The list of drugs included tobacco/cigarettes, alcohol, cannabis, Ecstasy/MDMA, amphetamine, cocaine, LSD, benzodiazepines, hallucinogenic mushrooms, ketamine, and opiates. It may be noted that mephedrone (m-cathinone or m-cat) was not on this list, since the DAISY study was undertaken before m-cat was used as a recreational drug (Schifano et al, 2011). Mean usage for each drug per week was calculated by multiplying the frequency of use with the amount taken per occasion. The MDMA user group comprised women who reported taking MDMA during pregnancy or in the month prior to pregnancy. Those who reported MDMA use prior to this time were categorized as non-users, since the study was designed to assess foetal drug exposure.

Assessment battery. The study included a comprehensive battery of assessment measures, covering various aspects of child behaviour and physical health indices, maternal activities and psychological well-being (Singer et al, 2012a,b). This report describes the findings from the Brief Symptom Inventory (BSI; Derogatis and Nelisaratos, 1983) This questionnaire comprises 53 self-rating questions across nine psychiatric subscales for: depression, anxiety, phobic anxiety, hostility, somatic complaints, obsessive-compulsive behavior, interpersonal sensitivity, paranoid ideation, and psychosis/schizophrenia. The summary measure - the General Severity Index (GSI), provided a general index for overall psychiatric distress. The assessments covered four occasions: first trimester of pregnancy, 1 month post-partum, 4 months post-partum, and 12 months post-partum.

Statistical Analysis. Data that were positively skewed were transformed using natural logarithm prior to analysis. However the means and standard deviations are reported for the untransformed scores. Bivariate correlations were employed to calculate the inter-relationships between variables. Multicollinearity was assessed using tolerance and variance inflation factor. Repeated measures Analysis of Variance (ANOVA), using a mixed model approach, was implemented by SAS Proc Mixed with maximum estimation method to compare the substance use for both groups, MDMA-users during pregnancy (n=28) and non-users (n = 68), at the four different assessment times (during pregnancy, 4 weeks, 12 weeks and 52 weeks). As noted earlier, both groups contained polydrug users of various substances, both legal (tobacco, alcohol), and illegal (cannabis,

amphetamine, cocaine; Moore et al, 2010). Since the dependent variables were repeated measures and correlated within subjects, we used unstructured covariance matrix to account for these correlated responses. We included interaction terms between drug groups and time, to test for homogeneity of MDMA effects over time. For all BSI outcome measures, we employed repeated measures Analysis of Covariance (ANCOVA). The covariates included other substance usage that differed by MDMA status at $p<0.10$, and were correlated with the given outcome at $p<0.10$ on at least two time points; they were then entered into the longitudinal model. Different sets of covariates were adjusted on each psychological outcome, and included demographic variables and use of all other drugs.

Results

The socioeconomic and educational profiles of mothers enrolled in the study are described more fully elsewhere (Singer et al, 2012a). In brief, the cohort was primarily white, married or in a stable relationship, and represented a wide range of socioeconomic backgrounds, including many from middle and higher psychosocial groupings. The MDMA using mothers and polydrug control mothers were well matched on most variables (Singer et al, 2012a). Table 1 describes the group mean weekly rates of usage for five main types of drug used: alcohol, nicotine/cigarettes, cannabis/marijuana, cocaine, and Ecstasy/MDMA. Other psychoactive drugs were taken by a few individuals, and those data are described more fully elsewhere (Moore et al, 2010).

A Mixed ANOVA was conducted with group as the between conditions factor and time as the within conditions factor. The between group ANOVAs revealed that the two groups did not differ in overall use of alcohol, cigarettes, cannabis or cocaine, although the cocaine group effect

Table 1. Ecstasy/MDMA, alcohol, cigarettes, marijuana/cannabis, and cocaine usage patterns for 28 mothers who took Ecstasy/MDMA during pregnancy, and a control group of

68 polydrug users during pregnancy. Drug values represent mean weekly rates of usage, during first trimester of pregnancy and three times post-partum

Drug type	Maternal Group	First trimester of pregnancy	1 month post-partum	4 months post-partum	12 months post-partum	ANOVA Group Time GxT
Ecstasy (tablets)	Polydrug controls	0.00 +- 0.00	0.00 +- 0.00	0.02 +- 0.16	0.01 +- 0.02	No between-group analysis
	Ecstasy users	0.82 +- 1.57	0.01 +- 0.03	0.03 +- 0.13	0.06 +- 0.09	E users : time p<.0001
Alcohol (units)	Polydrug controls	6.94 +- 16.90	3.11 +- 10.66	6.48 +-10.89	13.75 +-24.02	n.s .0001 .02
	Ecstasy users	12.07 +- 16.62	1.33 +- 1.80	5.30 +- 5.70	6.01 +- 5.99	
Cigarette (numbers)	Polydrug controls	28.15 +-48.10	23.45 +- 50.13	27.27 +- 40.02	32.88 +-48.14	n.s .0001 .003
	Ecstasy users	44.78 +- 49.50	17.88 +-30.79	17.59 +- 22.23	28.68 +-34.37	
Cannabis (joints)	Polydrug controls	7.44 +- 19.24	3.36 +- 7.87	3.12 +-7.51	5.26 +-12.95	n.s .0001 n.s.
	Ecstasy users	10.28 +- 20.81	6.86 +- 17.36	6.20 +- 16.12	7.35 +-15.46	
Cocaine (grams)	Polydrug controls	0.02 +-0.18	0.001 +- 0.01	0.01 +- 0.07	0.02 +- 0.14	.057 .013 .03
	Ecstasy users	0.23 +- 0.85	0.01 +- 0.04	0.02 +- 0.06	0.02 +- 0.05	

Table 2. Psychiatric symptoms on the Brief Symptom Inventory during and after pregnancy: for 28 mothers who took Ecstasy/MDMA during pregnancy, and a non-user control group of 68 polydrug users during pregnancy.

Group	Time 1 Early-Mid Pregnancy	Time 2 Postpartum 1 month	Time 3 Postpartum 4 months	Time 4 Postpartum 12 months	Paired Comparisons Time1 v Time4
General Symptoms					
Polydrug controls	0.61	0.51	0.54	0.50	-
Ecstasy users	0.79	0.71	0.81	0.56	-
Depression					
Polydrug controls	0.50	0.45	0.57	0.50	-
Ecstasy users	0.87	0.74	0.80	0.51	$p<0.05$
Anxiety					
Polydrug controls	0.55	0.46	0.48	0.34	$p<0.05$
Ecstasy users	0.74	0.68	0.69	0.56	-
Hostility					
Polydrug controls	0.71	0.65	0.66	0.59	-
Ecstasy users	0.74	0.80	1.24	0.55	-
Psychoticism					
Polydrug controls	0.31	0.25	0.36	0.30	-
Ecstasy users	0.52	0.51	0.62	0.42	-
Somatization					
Polydrug controls	0.58	0.36	0.27	0.32	$p<0.001$
Ecstasy users	0.78	0.50	0.51	0.39	$p<0.01$
Paranoid Ideation					
Polydrug controls	0.61	0.48	0.64	0.66	-
Ecstasy users	0.75	0.70	066	0.73	-
Obsessive-Compuls.					
Polydrug controls	1.08	1.10	0.98	0.89	-
Ecstasy users	1.20	1.23	1.31	0.82	$p<0.05$
Interper-sensitivity					
Polydrug controls	0.74	0.64	0.64	0.73	-
Ecstasy users	0.92	0.85	0.96	0.57	$p<0.05$
Phobic Anxiety					
Polydrug controls	0.27	0.20	0.30	0.20	-
Ecstasy users	0.47	0.39	0.52	0.37	-

The ANOVA for the time factor was significant for all five drugs (all p=0.01 or smaller), with lower rates of usage during the weeks after giving birth. The ANOVA group by time interactions were significant for alcohol and cigarettes ($F[3,88]=4.06$, $p<0.005$ and $F[3,88]=3.61$, $p<0.02$ respectively), with the MDMA mothers using slightly more than controls during the first trimester of pregnancy, but slightly less than controls across all other time periods (Table 1). The group x time interaction was not significant for cannabis, though Ecstasy/MDMA using mothers appeared to be taking slightly more cannabis than controls across all time points (Table 1). The group x time interaction was significant for cocaine ($F[3,88]=3.48$, $p<0.05$), with most usage during the first session by Ecstasy users (Table 1).

The Ecstasy using mothers reported taking an average of 0.84 Ecstasy tablets/week during the first trimester of pregnancy. In terms of previous lifetime usage (Singer et al, 2012a), they reported first using Ecstasy at a mean age of 20.2 years (range 14-29 years), had taken it on an average of 171 times/lifetime (range 6 – 936 times), and typically ingested an average of 3 tablets per occasion (range 1 – 8 tablets), with an average maximum usage per occasion of 7.4 Ecstasy tablets (range 2 – 20 tablets). Turning to their usage around the time of pregnancy, the mean total amount of MDMA used during pregnancy and in the month prior was 25 tablets (range 0.45 – 180 tablets). Within the polydrug control group, several women had used ecstasy/MDMA previously, but were currently non-users (Singer et al, 2012a).

The Brief Symptom Inventory findings are summarized in Table 2. The main focus of interest here is the difference in psychiatric well-being between the first and last sessions. Over that time period, control group mothers showed a significant decline in BSI symptoms for somatization ($p<0.001$), and anxiety ($p<0.05$). Over the same period, the Ecstasy/MDMA subgroup mothers showed significant declines in BSI symptoms for somatization ($p<0.001$), depression ($p<0.05$), interpersonal sensitivity ($p<0.05$), and obsessive-compulsive disorder ($p<0.05$; Table 2).

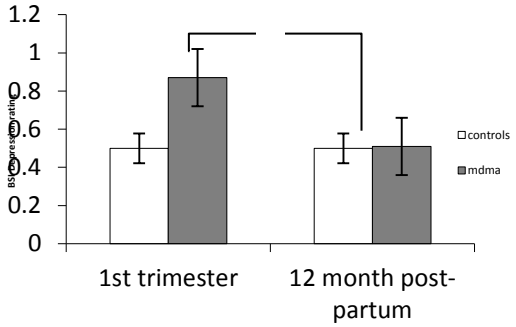

Figure 1: Brief Symptom Inventory ratings of depression during the first trimester and at 12 months post-partum, in women reporting MDMA/ecstasy use during pregnancy, and control women taking other recreational drugs during pregnancy.
** $p < 0.05$; Error bars indicate ±1SE*
was statistically borderline (Table 1; Group effect for Ecstasy was not calculated, since it was used to define these two groups).

Discussion

The young mothers in the Drugs and Infancy (DAISY) study provide a unique cohort in several respects. Although recreational polydrug users, they were predominantly middle class with middle socioeconomic status, and in stable interpersonal relationships. Hence unlike many studies of illicit drug users, they were not socially disadvantaged. The study covered an extended time period of nearly two years, and is the first study of pregnant Ecstasy/MDMA users (to our knowledge). The cohort of almost one hundred mothers was comparatively large, especially for a prospective study with repeated assessments. One of the main aims of the DAISY study was to investigate the effects of recreational Ecstasy/MDMA usage during pregnancy, on subsequent child development. The main findings were that the children of Ecstasy/MDMA using mothers displayed significant

psychomotor problems in comparison to control group children; this is described elsewhere (Singer et al, 2012a,b).

The study design allowed us to monitor changes in maternal reports of psychological well-being over time, in particular any alterations in their psychiatric status from the first to the last assessment. In this respect, both groups of mothers showed significantly higher somatization scores during the first trimester of pregnancy, when compared to 12 months post-partum (Table 2). The control group mothers also showed a significant reduction in BSI symptoms of anxiety, while the MDMA subgroup showed a very similar trend (Table 2). The first trimester of pregnancy is a period of pronounced somatic-body changes, and intuitively explains the higher somatization scores in both groups of women. Thus, the reduced BSI somatization scores one year post-partum may reflect a return to physical normality in both groups of women. The first trimester of pregnancy is also a period of general anxiety, with natural concerns and worries over becoming pregnant. This may help to explain the comparatively higher BSI anxiety scores during the first trimester, and the reduced scores at the final session (Table 2).

The Ecstasy/MDMA using mothers showed a different pattern of change compared to controls on three BSI subscales, i.e., for depression, obsessive compulsive disorder, and interpersonal sensitivity (Table 2). The Ecstasy subgroup mothers reported feeling more depressed than control mothers at time point 1, with a statistically borderline between-group difference ($p = 0.058$, two-tail). One year post-partum the depression scores for the MDMA group had reduced significantly ($p<0.05$), to become almost identical to the control group (Figure 1). The BSI depression scores for the control group mothers remained broadly unchanged over this period. The MDMA group also showed significant BSI reductions for interpersonal sensitivity, and obsessive-compulsive disorder (Table 2). In order to examine the potential reasons for these changes, the changing patterns of drug usage over time should be noted. The Ecstasy/MDMA group mothers had reduced their usage of Ecstasy to near-zero after giving birth (Table 1); hence one year post-partum they had become former MDMA users. Their BSI improvement may reflect this cessation of Ecstasy/MDMA use.

There is an extensive empirical literature demonstrating higher rates of psychiatric distress in current Ecstasy/MDMA users, and psychiatric gains following drug cessation. Schifano et al (1998) gave structured psychiatric interviews to young Ecstasy/MDMA users at an addiction centre in Italy, and reported that around half the sample reported symptoms of psychiatric distress, especially depression, but also psychotic disorder, impulse control disorder, bulimia, and panic disorder. MacInnes et al (2000) compared young Ecstasy/MDMA users and polydrug controls, with participants screened to exclude anyone with a prior psychiatric history. On the Beck Depression Inventory, the Ecstasy users displayed significantly higher depression scores than non-user controls. In a survey of over 700 young people from the UK and Italy, the SCL-90 symptom profiles of the Ecstasy polydrug users were significantly higher than non-user controls (Parrott et al, 2001). In an American study of abstinent MDMA users compared to non-user controls who visited raves (Singer et al, 2004), the Ecstasy/MDMA users reported significantly higher BSI depression, anxiety, and obsessive-compulsive disorder, than the controls. Brière et al (2012) prospectively found that taking-up recreational Ecstasy/MDMA in Canadian schoolchildren, led to increased depression one year later. There are also indications that psychiatric health can improve after quitting. Morgan et al (2002) reported that current Ecstasy/MDMA users had elevated scores on many SCL-90 subscales, whereas former Ecstasy users had scores intermediate between current Ecstasy users and non-user controls. Verheyden et al (2003) interviewed former users about reasons for quitting Ecstasy/MDMA. Over half reported that 'mental health problems due to MDMA' were the *main reason* for quitting drug use, that using Ecstasy had led to feelings anxiety and depression, and that they feared for their mental health in the longer-term. Over 70% of their participants reported 'improved mental health' after quitting.

An important potential confound for Ecstasy/MDMA research is the use of other recreational drugs, since many Ecstasy users take a range of psychoactive drugs (Scholey et al, 2004; Parrott, 2001, Parrott et al, 2007; Sala and Braida, 2004). In the DAISY study we collected systematic drug usage data at all four time points. As noted above, the use of Ecstasy/MDMA was largely restricted to the first trimester of pregnancy. In contrast, the use of alcohol, tobacco and cannabis was continued throughout the study. There is some indication of a decline in all drug use in the Ecstasy/MDMA group, with significant group/time interactions for alcohol and cigarettes especially. As such, it could be argued that the depression effect in the Ecstasy/MDMA users is in part due to changes in

alcohol and/or cigarette use, as both have been linked to higher depression scores (Raimo and Schuckit, 1998; Munafo and Araya, 2010). However, usage rates at baseline were broadly similar to one year post-partum in both groups (Table 1), hence the changes in psychiatric status noted here (Table 2), cannot easily be attributed to alcohol, tobacco, or cannabis usage. The usage pattern for cocaine was however very similar to Ecstasy/MDMA, with almost total cessation after the first trimester (Table 1). Hence the selective reductions in particular psychiatric symptoms, may reflect the cessation of Ecstasy/MDMA and/or cocaine usage.

There are several ways in which CNS stimulant drugs like MDMA can enhance psychiatric distress. In acute terms MDMA is a powerful mood intensifier, but it can boost positive *and* negative feeling states. Thus, increased levels of happiness and euphoria are often accompanied by emotional tension. This intensification of both positive and negative moods has been reported in studies of recreational users, and in placebo-controlled laboratory studies (Parrott et al, 2011; Kirkpatrick et al, 2012). It has also been noted in the psychotherapeutic situation. Two clients undergoing 'MDMA-assisted psychotherapy' experienced a resurgence of previous psychiatric problems following acute MDMA administration, with one client needing psychotherapy for a year afterwards to resolve the MDMA-induced problems (Greer and Tolbert, 1986; review: Parrott, 2007). In sub-acute terms, MDMA use is typically followed by a period of neurochemical recovery, when low moods and feelings of depression predominate; indeed, the 'mid-week blues' can often last for several days, and may reach clinical levels in some individuals (Curran and Travill, 1997). Since the positive mood intensification under MDMA is brief (several hours), and the post-MDMA period of mood recovery is more prolonged (several days), the average weekly mood of Ecstasy users will often *be lower* than in non-users (Parrott and Lasky, 1998). Such effects are supported in the animal literature by the acute and subacute impact of MDMA on 5-HT, notably delays in recovery of this transmitter, in brain regions regulating emotion (Colado et al, 1999), and similar pattern reductions in other functional serotonergic factors, such as SERT and tryptophan hydroxylase (see Adori et al, 2011). In addition, in chronic terms, abstinent Ecstasy/MDMA users report higher levels of stress, and lower levels of happiness, than non-user controls (Scholey et al, 2011). When used repeatedly, sympathomimetic drugs such as amphetamine, cocaine and MDMA, can adversely affect the HPA axis, and impair homeostatic control via the stress hormone cortisol (Seyle, 1955). Indeed, acute MDMA use can increase cortisol levels by 800% in young dance

clubbers (Parrott et al, 2008). While sub-chronically, recent Ecstasy/MDMA users display a 400% increase of cortisol in 3-month hair samples (Parrott et al, 2012). Hence recreational MDMA is both an acute *and* chronic stressor for the HPA axis (Parrott, 2009). There is also evidence that premorbid factors, may heighten the likelihood of clinical problems in disadvantaged individuals; this interactive 'diathesis-stress' model for recreational Ecstasy/MDMA is described more fully elsewhere (Parrott, 2006). The possible causative factors (including neurotoxicity, recovery and/or HPA axis changes) for the effects observed here in the current data, and in much of the literature, still need considerable further empirical investigation.

There are several limitations to the DAISY study. We relied on self-reported drug use and cannot therefore be certain that 'Ecstasy' comprised 'MDMA'. However data collection occurred during 2003-2006, which corresponded with a period of high MDMA purity in the UK. This was apparent in another study we undertook during 2006, which showed very high concordance between self-rated Ecstasy and MDMA use detected in saliva samples (Parrott et al, 2008). The second weakness was the absence of a non-user control group, since many studies have found that polydrug users are more impaired than non-users (Parrott et al, 2001; Morgan et al, 2002). Thirdly, although the DAISY study was designed as a prospective study, this was only partially achieved (Moore et al, 2010); hence with missing data points retrospective ratings were sometimes required (Singer et al, 2012a). Finally, the overall BSI difference scores were not large (Table 2). However we were not expecting strong drug effects, since our participants were psychiatrically normal, and their use of most drugs was similar at the first and last time points. Furthermore, although the group mean reduction of 0.2 on the BSI depression subscale may have been comparatively slight, it would still be beneficial for the individual user. It would also reduce the likelihood of individuals with prior vulnerability factors from developing more severe psychiatric problems (Parrott, 2006).

In summary, recreational stimulant drugs such as MDMA, cocaine and amphetamine, are well-known to be associated with enhanced psychiatric distress. The DAISY study found that women who took Ecstasy/MDMA during their first trimester of pregnancy reported slightly higher psychiatric symptom profiles than a control group of polydrug using mothers. One year after giving birth, their psychiatric symptom profiles improved to values near the control group (Table 2, Figure 1). The main explanatory factor proposed for this gain in psychiatric well-being was the cessation

of Ecstasy/MDMA usage, coupled with the parallel reduction in cocaine use. Hence this study has confirmed that a reduction in stimulant drug usage can have beneficial effects on well-being. Finally, we should also note that the DAISY study investigated the effects of MDMA use during pregnancy, on the child's subsequent development. It revealed that the children of MDMA-using mothers had various impairments in gross psychomotor skill (Singer et al, 2012a,b). Hence an important message for young females and their partners is to stop taking MDMA before pregnancy. This will protect the developing child, and enhance maternal well-being.

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