Short Communication

Ketamine as a primary predictor of out-of-body experiences associated with multiple substance use

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\textbf{A B S T R A C T}

Investigation of “out-of-body experiences” (OBEs) has implications for understanding both normal bodily-self integration and its vulnerabilities. Beyond reported associations between OBEs and specific brain regions, however, there have been few investigations of neurochemical systems relevant to OBEs. Ketamine, a drug used recreationally to achieve dissociative experiences, provides a real-world paradigm for investigating neurochemical effects. We investigate the strength of the association of OBEs and ketamine use relative to other common drugs of abuse. Self-report data ($N = 192$) from an online survey indicate that both lifetime frequency of ketamine use and OBEs during ketamine intoxication were more strongly related to the frequency of OBEs and related phenomena than other drugs. Moreover, the apparent effects of other drugs could largely be explained by associated ketamine use. The present results, consistent with the role of NMDA receptors in OBEs, should encourage future studies of the role of neurochemical systems in OBEs.

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1. Introduction

Folk psychology traditionally subscribes to the theory that there is an intrinsic spatial unity between self and body (\textsuperscript{1}Blanke & Arzy, 2005). Out-of-body experiences (OBEs) present a challenge to this view, as well as a unique means to investigate the cognitive and neural mechanisms associated with bodily-self processes. An OBE is the experience of discrepancy between the location of one’s subjective sense of “self” and one’s own physical body. There are three common variants in which OBEs are experienced: (1) feeling of separateness, or taking leave of one’s physical body (out-of-body feeling, OBF: Cheyne & Girard, 2009), (2) seeing what one takes to be one’s own body as perceived from an external viewing station (out-of-body autoscopy, OBA: Cheyne & Girard, 2009), or (3) a combination of OBF and OBA (i.e., viewing one’s physical body from the perspective of a disembodied ‘self’; see also Blanke & Mohr, 2005). Thus, OBF and OBA are viewed as distinct OBE components that may occur separately or together. It is also important to note that OBEs are distinct from other forms of autoscopy, such as doppelgänger experiences (see Brugger, Regard, & Landis, 1997). Importantly, OBFS are taken to be more fundamental reflections of disruption of vestibular-motor integration and often precursors and possible instigators of OBFs (Cheyne & Girard, 2009).

OBE phenomena have been associated with various neurological conditions such as epilepsy, migraines, infections and also with psychiatric conditions such as schizophrenia, depression, anxiety, and dissociative disorders (\textsuperscript{1}Blanke et al., 2005). However, OBEs are found not only in clinical populations, but have been reported in approximately 10\% of the healthy population across different cultures (\textsuperscript{1}Blanke et al., 2005) and have been an important part of folklore, mythology and
精神异常体验报告跨越了几个世纪（Blanke et al., 2005; Todd & Dewhurst, 1955）。对OBEs的研究具有重要的科学意义，因为它涉及到对身体自我整合的理解，以及对自我存在本质的理解。此外，增强对认知和神经机制的理解对于理解身体自我解体和OBEs的体验具有重要的科学意义。

1.1. Neuroanatomy of OBEs

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对OBEs的神经解剖学研究大多数直接来自神经学领域，涉及脑损伤患者的病例研究（e.g., Blanke, Landis, Spinelli, & Seeck, 2004）和脑刺激技术的使用（e.g., Blanke, Landis, Spinelli, & Seeck, 2004）。这种损伤导致了大脑中产生OBEs，如脑部刺激和相关体验。例如，五项OBEs的研究被Blanke et al. (2004) 所报道，其中两项研究指出OBEs有脑损伤或功能障碍，这可能导致大脑的视点和相关体验的改变。此外，这种工作还导致了对TPJ在自我加工中的重要性及其影响的理解。

1.1.2. Neurochemistry of OBEs

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研究的前景模型（即脑部解离运动整合→ OBF→ OBA）也可能适用于其他具有与精神异常体验相关的药物使用（Blackmore, 1982; Bunning & Blanke, 2005; Curran & Morgan, 2000; Irwin, 1985; Muetzelfeldt et al., 2008; Overney, Arzy, & Blanke, 2009; Pomarol-Clotet et al., 2006; Tart, 1971）和近死体验（Nelson, Mattingly, & Schmitt, 2006, 2007）。

1.2. Neurobiology of OBEs

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我们已经建立了一个神经生物学模型，即紊乱的前庭运动整合→ OBF→ OBA。这个模型是基于对OBEs的描述，即当OBEs在脑中产生时，这些OBEs有脑损伤或功能障碍，这可能导致大脑的视点和相关体验的改变。这个模型是由我们的工作支持的，该工作使用睡眠性瘫痪样本，其中OBFs被认为是更基本的体验。

The foregoing functional model (disrupted vestibular-motor integration → OBF → OBA) may also be applicable to other precipitating factors of OBEs, including neurochemical disruption associated with drug use (Blackmore, 1982; Bunning & Blanke, 2005; Curran & Morgan, 2000; Irwin, 1985; Muetzelfeldt et al., 2008; Overney, Arzy, & Blanke, 2009; Pomarol-Clotet et al., 2006; Tart, 1971) and near-death experiences (Nelson, Mattingly, & Schmitt, 2006, 2007).

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the majority of reports of drug use associated with OBEs were published 20–30 years ago, before ketamine was popular and available in the mainstream as a drug of abuse. Consequently, ketamine was omitted from reports of OBEs induced by drugs of abuse and its connection with reports of OBEs has only recently been of key interest (Curran & Morgan, 2000; Muetzelfeldt et al., 2008; Overney et al., 2009; Pomarol-Clotet et al., 2006). Moreover, there are relatively few investigations that have directly compared ketamine with other drug types, such as cannabis and LSD, which have traditionally been linked to OBEs. The purpose of this investigation was to assess the relative strengths of association among drugs of abuse with OBE-related experiences in a sample of multiple-substance users.

One long-standing neurochemical hypothesis proposes N-methyl-D-aspartate (NMDA) receptors as neural mediators for altered states of conscious awareness and body-self distortions. This model extends from Karl Jansen’s work, which introduced NMDA receptors as the basis of a potential neurochemical model for near-death experiences (Bianchi, 1997; Jansen, 1997). Near-death experiences have been linked to REM intrusions and ketamine use (Nelson et al., 2006, 2007). Individuals who report near-death experiences also report a high frequency of REM intrusions into waking consciousness, as indexed by sleep paralysis and hypnagogic and hypnopompic hallucinations (Nelson et al., 2006). Both disruptions of REM and NMDA-receptor function seem to be precipitating factors for near-death experiences, of which OBEs are a hallmark feature. We propose that near-death experiences, REM intrusions, and NMDA-receptor antagonism give rise to these anomalous experiences through similar disruptions of the neuromatrix. Ketamine, a dissociative anaesthetic drug that blocks brain NMDA receptors, has thus provided some insight in this domain. Most recently, Corazza and Schifano (2010) reported that in a group of 50 ketamine users reporting NDEs, which included a strong sense of detachment from their physical bodies, 45 (90%) of the cases occurred during the first few occasions of ketamine use.

Phenomenological research of acute and chronic ketamine use has consistently reported symptoms of dissociation, including out-of-body phenomena (Curran & Morgan, 2000; Muetzelfeldt et al., 2008; Pomarol-Clotet et al., 2006). Reports of body-self disruption and OBEs reported with ketamine use appear consistent, at least at a surface level, to those reported by neurological patients and in brain stimulation studies on self-processing (Arzy, Seeck, Ortigue, Spinelli, & Blanke, 2006; Brugger & Mohr, 2009).
Blanke & Mohr, 2005). Therefore, recreational ketamine use provides a useful paradigm to begin to investigate neurochemical systems involved in OBEs. Moreover, the observation that ketamine users tend to also consume a variety of other drugs provides an opportunity to examine the differential effects of ketamine and other recreational substances.

The current study investigated the relative strength of association between ketamine use and OBE-related experiences in comparison to other common drugs of abuse including alcohol, amphetamines, cannabis, LSD/hallucinogens, and MDMA (ecstasy), which have been sampled in previous OBE studies (Luke & Kittenis, 2005; Muetzelfeldt et al., 2008). Under the heuristic that NMDA-receptor disruption may be an important precipitating factor in OBE-related phenomena, we hypothesized that the frequency of ketamine use and having been under its influence at the time of the experience(s) would predict the frequency of vestibular sensations and OBEs, particularly OBFs, over and above the variance explained by use of other drugs.

2. Materials and methods

2.1. Participants

Individuals with a history of recreational drug use were recruited via flyers posted on campus at Ryerson University, flyers posted at the TRIP! Agency, and advertisements posted on the TRIP! website and TRIP! Facebook, as well as through word-of-mouth and snowball sampling, which resulted in postings and recruitment on RaveLinks and BlueLight website forums. TRIP! is a local non-profit harm-reduction agency in Toronto, Canada. The recruitment methods were based on similar procedures used by leading groups in the UK (Curran & Morgan, 2000; Muetzelfeldt et al., 2008) and in accordance with requirements from the Ethics Review Board at Ryerson University. Before completing the online survey, individuals were provided with study information and consent procedures explaining the voluntary and anonymous nature of participation. No inclusion/exclusion criteria were imposed at the outset, as it was of interest to assess the range of potential participants using recreational substances. Additionally, participants’ data were removed for (1) failure to provide consent at the beginning of the survey, (2) repeated submissions (assessed via a self-report item and/or time-based IP address), (3) failing to answer any of the questions pertaining to unusual bodily sensations (i.e., OBE and related items), and/or (4) failure to complete demographic and drug history questions. Based on these criteria, we present data from 192 respondents out of a total of 300 surveys collected between September 2009 and February 2010. This final sample comprised approximately 63% males. Ages ranged from 14 to 48 years with a median of 21 years. Half of these respondents were recruited through the TRIP! agency (51%), 40% responded to Ryerson community ads, and 9% to postings on other rave-related websites.

2.2. Questionnaire

This study focuses on survey responses regarding OBE-related phenomena and drug history derived from a larger survey assessing dissociative states (the relevant items may be viewed at http://www.surveymonkey.com/s/2Y3PQYB).

Five questions regarding unusual bodily-self sensations were sampled from the Waterloo Unusual Sleep Experiences Scale (WUSES) used in our previous investigation of OBEs associated with sleep paralysis (Cheyne & Girard, 2009): (1) Have you ever had the subjective experience that felt like you had temporarily left your physical body? (OBF); (2) Have you ever had the subjective experience that you were able to see your own physical body as if from an outside vantage point? (OBA); (3) Have you ever had the illusion that you sat-up, or moved an arm or a leg, or walked around the room, only to discover later that you had not moved at all? (illusory movements); (4) Have you ever had the subjective experience of an “elevator” feeling of moving rapidly up or down (even though you were not actually moving up or down)? (elevator sensations); (5) Have you ever had the subjective experience that you were falling, flying and/or spinning and turning rapidly (i.e., independent of being on an aircraft)? (vestibular-motion sensations). Each of these five questions were followed up with questions including (a) the frequency of the experience on a seven-point scale (never, once, several times in a life, several times in a year, monthly, weekly and several times in a week), (b) vividness/intensity of the experience on a four-point scale with a score of 0 indicating “vague and suggestive, more like a hint of something” and a score of 4 indicating “clear and distinct impression, as clear as any everyday experience”, (c) whether the respondent was under the influence of a drug at the time of the experience (yes/no), and if so, (d) whether it was alcohol, cannabis, LSD/hallucinogens, MDMA (ecstasy), ketamine (special K) and/or another, or if not, (e) whether the experience was due to bereavement, illness, extreme situations or other (a text box was provided to specify other reasons for the experience in question).

The questions regarding history of drug use were based on those used by Curran and Morgan (2000) to measure poly-drug use: recreational use of alcohol, cannabis, LSD/hallucinogens, MDMA (ecstasy), ketamine (special K), and other drugs; age of initiation; total years of use; age of peak use; time since last use of substance (month/years); current frequency of use; and total current amount/dosage typically used. The majority of the survey involved five-point scales and checkboxes; in addition, text boxes were provided for additional comments.

2.3. Data analysis

Descriptive statistics based on responses to individual questions were used to characterize the nature of phenomenological experiences and drug use history in the sample. Unfortunately, the open self-report format used to gauge current amount/dosage of use failed to provide useful data; participants either neglected to provide dose information or the
information was vague in many cases. Thus, we were unable to assess the relations between dose and intensities of experiences in this report.

Pearson's product-moment correlation coefficients ($r$) were used to assess the relations among lifetime frequencies of drug use and unusual bodily experiences, as well as point-biserial correlations between being under the influence of each drug at the time of experience and the lifetime frequency of each unusual bodily experience. Follow-up linear regression analyses were used to provide an assessment of the relative predictive power of each drug per experience on these variables. Parallel analyses replacing frequencies of drug use with intensity/vividness ratings revealed a similar, but less robust pattern of results (data not shown).

Due to differing response rates across analyses, we placed an emphasis on effect size in evaluating the strength of relations. In particular, we highlight in our results those associations of medium ($r > .20$) or large ($r > .30$) magnitude, according to the empirical guidelines provided by Hemphill (2003).

### 3. Results

#### 3.1. Descriptives

Reports of past and current frequency of recreational drug use are summarized in Table 1. In all cases, distributions were positively skewed except for lifetime frequency of using alcohol and cannabis, which were significantly negatively skewed (most having used more than 90 times in a life). Results indicate that a majority of the sample comprised poly-drug users: almost all reported having used cannabis (99%) and alcohol (97.9%), followed by ecstasy (90.1%), LSD (81.8%), ketamine (66.7%), and amphetamines (63%) at least once. Indeed, 47% of the sample reported having used all six of these substances. Ninety-three participants also endorsed “other” drugs, including cocaine (46%), magic mushrooms (psilocybin; 16%), salvia divinorum (14%), DMT (dimethyltryptamine; 14%), 2C phenethylamines (14%), DXM (dextromethorphan; 9%), and NO2 (7%). It is noted that some of these are hallucinogenic but were reported under “other” vs. “LSD/hallucinogens”, which likely reflects reports of hallucinogen use in addition to LSD. On average, the sample reported initial and peak drug use during adolescence (Table 1). It was also notable that among those reporting current use, 6% reported using ketamine and 23.4% cannabis on a daily basis.

Reports of unusual bodily sensations were also frequent (Fig. 1). The majority (72.6%) of the sample reported having experienced an OBF and 41.7% an OBA at least once; these overall rates of OBF phenomena are comparable to other reports of drug-induced dissociative experiences (Tart, 1971) and support our earlier findings that OBFs appear more fundamental (Cheyne & Girard, 2009). In this regard, it is also noted that the mean reported frequencies for OBFs (~several per life) were significantly greater than for OBAs (~once in a life), $t(184) = 9.92, p < .001$. Frequencies of other OBE-related phenomena having been experienced at least once were similarly high in this sample: 40.7% illusory movement, 62.4% elevator sensations, and 65.2% vestibular-motion sensations.

#### 3.2. Correlation and regression analyses

As predicted, lifetime frequency of ketamine use was most strongly associated with the lifetime frequency of OBFs, as well as illusory movements, elevator, and vestibular-motion experiences (see Table 2). The rank of correlations for lifetime frequencies can be summarized (drugs listed by effect size) as the following: (1) OBF revealed a large correlation with lifetime frequency of ketamine and a medium relation with ecstasy; (2) OBA was moderately associated with lifetime frequency of amphetamine use; (3) elevator sensations were only strongly correlated with ketamine use; (4) illusory movement was moderately correlated with ketamine, ecstasy, and cannabis use; (5) vestibular-motion sensations (flying, falling, spinning) revealed only small correlations across drug types (Table 2). Due to skewed distributions among several variables,
Spearman’s Rho ($p$) correlations were also computed. The overall pattern across the correlation matrix remained very similar. The only notable differences were that the nonparametric coefficients for MDMA also reached a medium size with elevator and vestibular-motion sensations. The list-wise sample size was constrained to 75 participants for follow-up regression analyses on these relations, and none reached overall significance (all $R^2 < .15$). Nonetheless, individual Beta weights indicated ketamine as a significant predictor of OBFs and elevator sensations, both $W = .29, p < .05$; there were no other significant independent predictors.

As expected given the closer proximity of the measures, correlations among being under the influence of a drug at the time of experience and the frequency of unusual bodily experiences were generally much greater than those above regarding lifetime frequencies of drug use, with 30% reaching a large and an additional 50% a medium effect size (Table 2). The exceptions to this rule were for the correlations of amphetamine with OBF, OBA, elevator, and illusory movement, as well as for cannabis and MDMA with OBA. The pattern of correlations using Spearman’s rho remained consistent with the Pearson $r$-values in Table 2, but with an overall slight increase in the magnitude of correlations. In sum, sizable correlations were observed across most drugs and experiences surveyed. In this regard, regression analyses are more central to the aims of the current study in determining the relative unique contributions of each drug to these experiences among the poly-drug using sample. That is, the regression analyses supersede the bivariate correlations, as the latter do not account for the influence of other drugs on their associations with OBE-related experiences.

Regression analyses indicated that being under the influence of a drug at the time of experience accounted for over one third of the variance in predicting frequency of OBFs, elevator sensations, and illusory movement, a quarter of the variance in OBA frequency, and 17% of that explaining frequency of vestibular-motion phenomena (Table 3). As predicted, concurrent use of ketamine was a significant predictor of the frequency of experience for all five OBE-related experiences, over and...
Consistent with the hypothesis that disruption of NMDA-receptor function is a primary neurochemical factor precipitating OBEx and related phenomena, the current study demonstrates that the NMDA-receptor antagonist ketamine is a primary predictor of drug-induced OBE-related experiences, above and beyond other common drugs of abuse. Moreover, these results suggest that the correlations of certain other drugs with OBE-related phenomena are, in part, an artifact of their association with ketamine in poly-drug use. With specific reference to ketamine, results indicated that both the frequency of lifetime ketamine use and, in particular, having been under the influence of ketamine at the time of the experience were most strongly correlated with the frequency of OBE-related unusual bodily-self experiences (Tables 2 and 3). Although bivariate analyses supported sizable correlations across most drugs with unusual bodily experiences, regression analyses confirmed that ketamine use accounted for most of the drug-related variance in predicting experience frequencies. Over half (58%) of those reporting the fundamental experience of OBFs reported being under the influence of ketamine at the time, whereas no other drugs revealed such a positive association with acute exposure independently of their association with ketamine. Moreover, ketamine use was also the strongest predictor of OBA, as well as illusory movement, elevator, and other motion-related vestibular sensations. Together, these findings support theoretical models emphasizing the role of the vestibular system in OBEs (see Cheyne & Girard, 2009) and the primacy of OBFs in OBEs (i.e., as supported by the greater lifetime frequencies reported for OBFs than OBAs; Fig. 1).

Although the current results support the hypothesis of the primary role of ketamine, it is noted that cannabis for illusory movements and MDMA for elevator sensations emerged as additional predictors of at least medium effect size (accounting for approximately half the variance of ketamine). Indeed, while phenomenological research of acute and chronic ketamine users has consistently reported symptoms of dissociation and out-of-body phenomena (Curran & Morgan, 2000; Morgan & Curran, 2006; Muetzelfeldt et al., 2008; Pomarol-Clotet et al., 2006), there is some prior evidence for a role of cannabis. For example, Overney et al. (2009) reported on the emergence of OBEs in a neurological patient treated with cannabis. To our knowledge, MDMA has not been linked to OBEs. Future work should explore the commonalities and dissimilarities in the phenomenological and neurochemical nature of out-of-body phenomena associated with these substances. Indeed, ketamine and cannabis are both associated with disruption of the glutamate system and may interact through effects on NMDA receptors (Hallak et al., 2010; Kuepper et al., 2010). Future research should also explore how ketamine and other drug exposure influences different experiences, such as different experiences pertaining to emergence of OBAs and/or OBFs.

Despite the need for further investigations, the primary role that ketamine displayed across the five sampled experiences supports our systems-based model of OBE phenomena. This work builds upon previous research regarding precipitating factors that induce OBEs such as direct TPJ disruption, REM sleep disruption, and sleep paralysis (Blanke et al., 2005; Cheyne & Girard, 2009). The associations of ketamine across OBE phenomena and related anomalous vestibular and motor experiences is consistent with the reliable associations among these phenomena seen in our work with individuals experiencing OBEs during sleep paralysis. We have proposed that REM-induced anomalous or disrupted integration of somatosensory information may give rise to unusual vestibular-motor sensations and experiences (see Cheyne & Girard, 2009). When of sufficient intensity these experiences may then give rise to emergence of OBEs, in the fundamental form of OBFs and subsequent OBAs. The current results suggest that ketamine use may similarly disrupt sensory integration to precipitate OBE phenomena.

Losing contact with the external world is one of the most characteristic effects of ketamine. This disrupted transmission of sensory input is partially due to blockade of NMDA receptors. NMDA receptors play a central role in the transmission of data from all sensory modalities (Jansen, 1997; Øye, Paulsen, & Maurset, 1992). Thus, we propose that ketamine affects the
availability of sensory information critical for its successful integration, such as that mediated by the TPJ. We view such disruption of the neurosignature, the pattern of activation across the neuromatrix (distributed neural systems processing and integrating bodily processes such as vestibular sensations, motor plans, efference copy, and proprioception), as the final common pathway underlying OBE phenomena (Cheyne & Girard, 2009).

Although the present study provides strong support in favour of ketamine use as a primary predictor of drug-induced OBE phenomena, it is important to consider limitations regarding the internal and external validity of the findings. The current survey was effective in eliciting 300 responses within half of a year. Possibly because participation was based on intrinsic motivation, however, only two thirds provided complete and useable reports. Moreover, self-report internet-based methodology constrains the ability to verify authenticity of submissions. Participants comprised a poly-drug using sample recruited primarily through ads targeted at drug users within the rave and club scene, and analyses focused on six particular drug types. Thus, the relative rates of drug use and unusual experiences, and the comparative relations across types must be interpreted in the context of the sample and correlational analyses. Nonetheless, the strength and distinctiveness of the results may be taken to encourage future laboratory-based research. In such future work, it will also prove useful to better quantify dose–response effects of ketamine and other drugs on the intensities of experiences.

Future research should also extend the investigation of anomalous experiences beyond the unusual bodily experiences presently reported to address the specificity of the current findings with regard to the nature of experiences, not just associations with specific drugs. In this regard, it is of potential interest that the vestibular experiences accompanying OBEs studied here and in our previous sleep-paralysis work have been related to self-motion. Vestibular sensations may encompass both the feeling of being stationary and the environment moving. Thus, it may prove informative to directly explore how/whether different drugs or other anomalous or neurological conditions contribute to experiencing vestibular sensations of self and environmental motion.

In addition to extending our understanding of the role of neurochemical systems involved in OBEs and bodily-self processing, continued research on the effects of ketamine is particularly important as its use is increasingly prevalent in today's society. In Canada, the 2009 Ontario Student Drug Use and Health Survey reported that 1.6% of high school students had used ketamine in the past year (Paglia-Boak, Mann, Adlaf, & Rehm, 2009). A more recent study by TRIP! indicated a rate of approximately 70.5% of rave goers in Toronto had reported using ketamine (Wilkins, Girard, & Salazar-Campbell, 2010). Importantly, this estimate more than doubles a rate of about 30% reported for ketamine in a similar TRIP! study conducted in 2004, despite similar rates of consumption across the other drug types (Guimond, Gnaim, & Strike, 2008). Finally, further investigations may provide insight into potential treatment for individuals affected by deficient self-processing and aid our understanding of the mechanisms behind related psychiatric manifestations such as paranoia, persecution, alien control, and hallucinations. Indeed, recent leading neurochemical models of schizophrenia are based on ketamine/NMDA-receptor antagonist exposure (Fletcher & Honey, 2006).

Disclosure statement

There are no conflicts of interest to declare. All study procedures were approved by the Research Ethics Board at Ryerson University.

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References


