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Neuroticism is associated with challenging experiences with psilocybin mushrooms

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ABSTRACT

Objectives: Classic hallucinogens (e.g. psilocybin and LSD) have substantial effects on perception, cognition, and emotion that can often be psychologically challenging, however we know very little regarding the source of significant individual variability that has been observed in the frequency and intensity of challenging experiences (i.e. "bad trips") with psychedelics. Previous clinical and observational literature suggests that there may be an association between neuroticism and challenging psychedelic experiences.
Methods: Data from two online surveys of challenging experiences with psilocybin were analyzed. Multivariate analysis was used to estimate the associations between total score and scores from seven sub-factors (fear, grief, physical distress, insanity, isolation, death, and paranoia) of the Challenging Experience Questionnaire (CEQ), and scale scores from the Ten Item Personality Inventory (TIPI) in Study 1 (N = 1993) and the Big Five Inventory (BFI) in Study 2 (N = 981).
Results: CEQ scores were negatively associated with emotional stability scores (the inverse of neuroticism) in Study 1 and positively associated with neuroticism scores in Study 2.
Conclusions: Neuroticism may contribute to the strength of challenging experiences with psychedelics in uncontrolled settings.

1. Introduction

Classic hallucinogens (i.e. serotonin 2A receptor agonist hallucinogens, or psychedelics), including psilocybin, have substantial effects on perception, cognition, and emotion (as reviewed in Preller & Vollenweider, 2016). Significant individual variability has been observed in the effects of psychedelics on emotional state. A wide range of emotional states can accompany a psychedelic experience, including a range from strongly positive to extremely challenging emotional states, however we know little regarding the source of this variability. The strongest lines of evidence thus far point to the roles of set (the intentions and internal state of an individual), setting (the environment) (Leary, Litwin, & Metzner, 1963; Zinberg, 1986), and personality (Dittrich, 1994; Hemsley & Ward, 1985; Studerus, Gamma, Kometer, & Vollenweider, 2012) in predicting the effects of psychedelics. The current study investigates the association between traits in the Five Factor Model (FFM) of personality, and dimensions of challenging experiences (or "bad trips") with psychedelics as measured using the Challenging Experiences Questionnaire (CEQ) (Barrett, Bradstreet, Leoutsakos, Johnson, & Griffiths, 2016).

Substantial progress has been made in understanding the relationships between personality factors and emotional experience. The FFM has emerged as a widely accepted model of the general underlying structure of personality, and it has been applied to study various aspects of psychological functioning, including emotions (John, Naumann, & Soto, 2008). Whereas extraversion (relative to neuroticism) is associated more strongly with positive emotionality, neuroticism (relative to extraversion) is associated more strongly with negative emrotionality (Costa & McCrae, 1980; John et al., 2008).

The Challenging Experience Questionnaire (CEQ) is a self-report instrument that measures dimensions of challenging experience with psychedelics that are suggested by clinical and research literature (panic or fear, grief, isolation, feeling as though one is dying, feeling insane, physiological distress, and paranoia) (Barrett et al., 2016). The CEQ has advantages over other self-report measures of the subjective effects of psychedelics, when specifically considering challenging experiences. These questionnaires, such as the Altered States of Consciousness (OAV) questionnaire (Dittrich, 1975; Dittrich, 1998), the Addiction research center inventory (ARCI) (Haertzen, 1966), or the Hallucinogen Rating Scale (HRS) (Strassman, Qualls, Uhlenhuth, & Kellner, 1994) include a broadly defined or general measure of challenging experience (such as the Dread of Ego Dissolution scale of the OAV, or the LSD scale of the ARCI), measures of psychedelic experience that are not specific to challenging or non-challenging experience (such as the scales of the HRS),

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or more focused and refined measures of some aspect of challenging experience (such as the Anxiety and Impaired Cognition and Control factors of the 5D-ASC) (Studerus, Gamma, & Vollenweider, 2010) while not including items that index the full potential range of dimensions of challenging experience (e.g. "grief").

Despite these limitations, neuroticism has been shown in the past to correlate positively with scores on the Dread of Ego Dissolution factor of the OAV in reference to altered states of consciousness that were induced by means that included psychedelic, non-psychedelic pharmacological, and non-pharmacological methods (Dittrich, 1994). Higher neuroticism scores have more specifically been linked to higher reported frequency of bad trips with psychedelics in a sample (N = 29) of poly-drug users receiving in-patient treatment for drug use disorders (Hemsley & Ward, 1985). In another study (N = 65), extroverted neurotics were shown to be more susceptible to acute negative effects of LSD than those with other personality types (Lienert & Netter, 1996). However, these studies were conducted in small samples, one of which was a sample of psychiatric patients (Hemsley & Ward, 1985). In contrast, a more recent pooled analysis found no such association between neuroticism and challenging experience (Studerus et al., 2012). In this report, 23 studies were pooled to investigate predictors of subjective effects of psychedelics. In an analysis of the 11 studies in this report that included personality measures (pooled N = 126), Studerus and colleagues found no association between psilocybin effects and the personality trait neuroticism-anxiety. This null result may be due to the fact that those with high neuroticism scores (>2 standard deviations above the mean for a normative sample) were excluded from the studies included in this pooled analysis. Thus, the pooled sample yielded neuroticism scores with a low mean and variance ("almost one SD below the mean of a normative sample") (Studerus et al., 2012). The failure to show a relationship between personality and challenging experiences in this pooled analysis may also be due to the highly controlled and structured laboratory environment that may reduce the likelihood or intensity of challenging experiences.

There is contradictory evidence from previous literature for an association between neuroticism and challenging experiences with psychedelics, and this has yet to be addressed in a large, naturalistic sample. Following is a report of analyses of questionnaire data from two online surveys of challenging experiences with psilocybin mushrooms to test the hypothesis that neuroticism is positively associated with the strength of challenging experiences.

2. Methods

2.1. Participants

2.1.1. Study 1

Responses from a total of 1993 participants who provided useable data for an online survey of challenging experiences with psilocybin (Barrett et al., 2016; Carbonaro et al., 2016) were included in the current analyses. Analysis of Study 1 data constitutes a secondary analysis of previously reported data (Barrett et al., 2016; Carbonaro et al., 2016). Participants were recruited to report on their single most psychologically difficult or challenging session or experience (worst "bad trip") via internet advertisements (70.4% of respondents indicated that they became aware of the study through websites that are frequented by individuals interested in psychedelics such as Erowid, an online information library on psychoactive substances, www.erowid.com), email invitation via emails that were sent by study staff to email distribution lists related to websites and groups that are frequented by individuals interested in psychedelics (6.6% of respondents indicated that they received an email for the survey as a member of a large email distribution list, and 5.0% of respondents indicated that they received a personal email regarding the survey from a friend), and word of mouth (6.7% of respondents indicated that they became aware of the survey via personal communication other than email, and 0.9% of respondents indicated that they heard about the survey at a conference or public presentation). 9.3% of respondents indicated that they became aware of the survey through means not otherwise specified, and 1.1% of participants indicated that they preferred not to indicate how they became aware of the survey. Participants in Study 1 were not provided compensation. Participants were included if they endorsed having had a difficult or challenging experience (i.e. a "bad trip") after ingesting an active dose of psilocybin mushrooms that produced moderate to strong psychoactive effects. Participants were excluded who did not read, write, and speak English fluently, who were <18 years of age at the time of completing the survey, who were not between the age of 18 and 70 years old at the time of the reported challenging experience, who encountered their challenging experience in the context of a research study, who were reporting on the experience of another person, who attributed their challenging experience to another substance in addition to psilocybin, or who reported having already completed the survey. Participants were also excluded if free-response comments provided at the end of the survey raised concerns about the validity of their reports. Participants were asked to refrain from completing the survey more than once.

2.1.2. Study 2

Responses from a total of 981 participants who provided useable data for an online survey of challenging experiences with psilocybin mushrooms (Barrett et al., 2016) were included in the current analysis. Participants were recruited in a fashion similar to Study 1. 61.3% of respondents indicated that they became aware of the study through a website. 4.7% of respondents indicated that they received an email for the survey as a member of a large email distribution list. 5.0% of respondents indicated that they received a personal email regarding the survey from a friend. 10.3% of respondents indicated that they became aware of the survey via personal communication other than email. 0.9% of respondents indicated that they heard about the survey at a conference or public presentation. 15.9% of respondents indicated that they became aware of the survey through means not otherwise specified, and 2.0% of participants indicated that they preferred not to indicate how they became aware of the survey. Respondents completed a separate online survey from the survey in Study 1. Inclusion and exclusion criteria for this survey were identical to those in Study 1. On the first page of the survey, participants were informed to not continue if they had previously completed a survey of "bad trips" or challenging experiences with psilocybin. On the second page of the survey, participants were asked to confirm that they had not previously completed this or any similar survey. Participants in Study 2 were not compensated for their participation.

2.2. Materials

2.2.1. Challenging Experience Questionnaire (CEQ; Barrett et al., 2016)

The CEQ is a 26-item questionnaire that consists of seven factors of challenging experience with psilocybin mushrooms: *fear*, *grief*, feeling of losing your sanity (*insanity*), feel as though you are dying (*death*), feelings of *isolation*, *physiological distress*, and *paranoia*. In Study 1, several hallucinogen-sensitive questionnaires from which the CEQ was derived (Hallucinogen Rating Scale, HRS; the States of Consciousness Questionnaire, SOCQ; and the 5-Dimensional Altered States of Consciousness questionnaire, 5D-ASC) were administered, and the CEQ items from these questionnaires were included in the analyses for Study 1. In Study 2, the CEQ was administered as a stand-alone questionnaire (i.e. without the additional items from the HRS, SOCQ, and 5D-ASC). Responses to the stand-alone CEQ were included in the analyses for Study 2. Strict factorial invariance has been previously demonstrated for the CEQ between the stand-alone version and the version derived from the HRS, SOCQ, and 5D-ASC within the two datasets utilized in the current analysis (Barrett et al., 2016).

2.2.2. Ten Item Personality Inventory (TIPI; Gosling, Rentfrow, & Swann, 2003)

The TIPI is a brief, 10-item questionnaire that measures factors of the Five Factor Model (FFM) of personality, and it has been shown to correlate well with the Big Five Inventory (Gosling et al., 2003). The five factors of the TIPI are: extraversion, emotional stability (the inverse of neuroticism), openness, conscientiousness, and agreeableness. Each factor consists of two items, one of which is reverse scored. Factor score estimates for the TIPI were computed as the average of the two items for each factor (after reverse-scoring the appropriate item). TIPI factor score estimates were included in the analysis for Study 1.

2.2.3. Big Five Inventory (BFI; John et al., 2008)

The BFI is a 44-item questionnaire that measures the factors of the FFM of personality. The five BFI factors are: extraversion, neuroticism (the inverse of emotional stability), openness, conscientiousness, and agreeableness. Factor score estimates for the BFI were computed as the average of the items contributing to each scale (after reverse-scoring appropriate items). Factor score estimates for the BFI were included in the analysis for Study 2.

2.2.4. Intentions for taking psilocybin

Participants in Study 1 were asked to respond to the item "Your psychological intention for taking psilocybin (check all that apply):" using the following response options: 1) "I took psilocybin only because other people were taking psilocybin (i.e., I felt peer pressure), but I did not have a serious intention", 2) "Curiosity without any other serious intention", 3) "Recreational (e.g. to enjoy the experience, which may or may not involve a social recreational event such as a concert)", 4) "A serious intention for psychological self-exploration (e.g., resolve a personal issue or to increase self-understanding)", 5) "A serious intention to explore spirituality or the sacred (e.g. to contemplate God, as you understand the word, or the nature of ultimate reality, and so on)", or 6) "Other (please specify)". Responses to this item were analyzed in relation to TIPI factor score estimates in Study 1 (described below), to determine whether neuroticism was associated with individual intentions to take psilocybin mushrooms.

2.3. Analysis

Structural equation modeling was used to conduct multivariate analysis of responses to the CEQ and the FFM measures in each study. Factor score estimates from the TIPI were used as the FFM measures in Study 1, and factor score estimates from the BFI were used as the FFM measures in Study 2. The first analysis (Analysis 1) for each study included a measurement model with each CEQ item loading only onto the intended latent variable for the given item, and a structural model with the factor score estimates for each FFM scale predicting each CEQ latent variable (*fear*, *grief*, *insanity*, *isolation*, *death*, *physiological distress*, and *paranoia*). In these analyses, Bonferroni correction was applied to correct for 35 comparisons (7 CEQ factors, each predicted by 5 FFM factor score estimates), yielding a significance threshold of $p < 0.0014$. A second analysis (Analysis 2) was conducted for each study that consisted of each FFM factor score estimate predicting a second-level CEQ total latent variable (with all seven CEQ latent variables loading onto this second-level CEQ total latent variable). Bonferroni correction for the 5 comparisons in this analysis (1 CEQ latent variable predicted by 5 FFM factor score estimates) yielded a significance threshold of $p < 0.01$.

A combination of fit indices was used to assess structural equation model fit, including the *comparative fit index* (CFI) (Bentler, 1990) the *standardized root mean square residual* (SRMR) (Hu & Bentler, 1999), and the *root mean square error of approximation* (RMSEA) (Browne & Cudeck, 1993). Values of SRMR and RMSEA < 0.1, and CLI > 0.90 (Browne & Cudeck, 1993; Hu & Bentler, 1999) indicate acceptable model fit. Consideration of a combination of fit indices, with "good fit" values of SRMR < 0.09, and CLI > 0.90, have been shown to minimize both Type I and Type II error (Hu & Bentler, 1999). Structural equation modeling was conducted using the *sem* function in the *lavaan* toolbox (Rossell, 2012) in R (R Core Team, 2015).

A series of logistic regressions was also conducted on Study 1 data, regressing the binary response for each of the intentions for taking psilocybin mushrooms on standardized scores for the TIPI emotional stability dimension to determine the likelihood, based on emotional stability, that an individual would endorse a given intention for taking psilocybin mushrooms. Bonferroni correction for the 5 comparisons across these analyses (odds ratios for neuroticism predicting each of 5 intentions) yielded a significance threshold of $p = 0.01$. Additional structural equation models were fit, extending Analysis 1 to include each intention as a moderator of the relationship between the TIPI emotional stability dimension and each CEQ latent variable (Analysis 3), and extending Analysis 2 to include each intention as a moderator of the relationship between the TIPI emotional stability dimension and the CEQ total latent variable (Analysis 4), to determine whether intention to take psilocybin mushrooms moderated the relationship between personality and challenging experiences.

3. Results

3.1. Study 1

Emotional stability (the inverse of neuroticism) as measured by the TIPI was significantly and negatively associated with scores on each of the CEQ latent variables, except for the *death* latent variable which was not associated with emotional stability but rather was positively associated with scores on openness (Analysis 1; Table 1). Scores on the CEQ total latent variable (Analysis 2) were also significantly negatively associated with emotional stability ($B = -0.250$, $SE = 0.030$, $Z = -8.380$, $p < 0.0001$), but no other TIPI scales. Model fit indices for Analysis 1 (CFI = 0.915, SRMR = 0.041, RMSEA = 0.057 [95% CI: 0.054–0.059]) and for Analysis 2 (CFI = 0.913, SRMR = 0.043, RMSEA = 0.055 [95% CI: 0.053–0.058]) indicated acceptable model fit.

Individuals with less emotional stability (greater neuroticism) were more likely to endorse having taken mushrooms due to peer pressure (odds ratio for emotional stability = 0.887, $z = -2.863$, $p < 0.005$), and less likely to have taken mushrooms due to serious intentions for psychological self-exploration (odds ratio for emotional stability = 1.043, $z = 2.496$, $p < 0.05$) or spiritual exploration (odds ratio for emotional stability = 1.047, $z = 2.625$, $p < 0.01$). "Other" was indicated as an intention to take psilocybin mushrooms by 187 respondents (9.4% of the respondents). Of the 187 free responses provided when "Other" was selected, only one respondent indicated that they felt coerced into taking psilocybin mushrooms ("I had been very curious for a while, but I was not prepared when I took it and was pressured into taking it"). Structural equation models for Analyses 3 and 4 did not reveal any significant relationship between neuroticism and CEQ factor or CEQ total scores that were moderated by intention to take psilocybin mushrooms.

3.2. Study 2

Neuroticism as measured by the BFI was significantly and positively associated with scores on each of the CEQ latent variables except for the *death* latent variable, which was not significantly associated with any CEQ latent variables (Analysis 1; Table 2). Scores on the CEQ total latent variable (Analysis 2) were also significantly associated with neuroticism ($B = 0.259$, $SE = 0.042$, $Z = 6.091$, $p < 0.0001$), but no other BFI scales. Model fit indices for Analysis 1 (CFI = 0.911, SRMR = 0.045, RMSEA = 0.061 [95% CI: 0.058–0.064]) and for Analysis 2 (CFI = 0.905, SRMR = 0.051, RMSEA = 0.059 [95% CI: 0.056–0.062]) indicated acceptable model fit.

Table 1
Challenging Experience Questionnaire (CEQ) latent variable scores associated with Ten Item Personality Inventory (TIPI) factor score estimates in Study 1.

CEQ latent variable	TIPI scale	Parameter estimate	SE	Z	p†
Fear = …	Extraversion	0.011	0.026	0.438	0.662
	Emotional stability	**−0.207**	**0.028**	**−7.490**	**<0.0001**
	Agreeableness	0.041	0.026	1.562	0.118
	Conscientiousness	−0.020	0.026	−0.752	0.452
	Openness	0.017	0.026	0.661	0.509
Grief = …	Extraversion	0.019	0.026	0.735	0.463
	Emotional stability	**−0.208**	**0.028**	**−7.406**	**<0.0001**
	Agreeableness	0.046	0.027	1.724	0.085
	Conscientiousness	−0.067	0.027	−2.481	0.013
	Openness	0.082	0.027	3.105	0.002
Physical distress = …	Extraversion	0.004	0.027	0.142	0.887
	Emotional stability	**−0.143**	**0.029**	**−5.002**	**<0.0001**
	Agreeableness	0.024	0.027	0.880	0.379
	Conscientiousness	0.030	0.027	1.079	0.281
	Openness	0.050	0.027	1.856	0.063
Insanity = …	Extraversion	−0.010	0.027	−0.363	0.716
	Emotional stability	**−0.133**	**0.028**	**−4.678**	**<0.0001**
	Agreeableness	0.002	0.027	0.091	0.928
	Conscientiousness	−0.027	0.027	−0.994	0.320
	Openness	0.057	0.027	2.119	0.034
Isolation = …	Extraversion	−0.032	0.027	−1.189	0.235
	Emotional stability	**−0.133**	**0.028**	**−4.678**	**<0.0001**
	Agreeableness	−0.023	0.027	−0.849	0.396
	Conscientiousness	−0.063	0.027	−2.308	0.021
	Openness	0.044	0.027	1.626	0.104
Death = …	Extraversion	−0.069	0.025	−2.774	0.006
	Emotional stability	−0.065	0.026	−2.468	0.014
	Agreeableness	0.029	0.025	1.168	0.243
	Conscientiousness	0.035	0.025	1.404	0.160
	Openness	**0.087**	**0.025**	**3.506**	**<0.0001**
Paranoia = …	Extraversion	0.051	0.031	1.632	0.103
	Emotional stability	**−0.146**	**0.033**	**−4.396**	**<0.0001**
	Agreeableness	−0.095	0.031	−3.034	0.002
	Conscientiousness	−0.038	0.032	−1.195	0.232
	Openness	0.044	0.031	1.396	0.163

† Effects in bold typeface were significant after Bonferroni correction ($p < 0.0014$).

Table 2
Challenging Experience Questionnaire (CEQ) latent variable scores associated with Big Five Inventory (BFI) factor score estimates in Study 2.

CEQ latent variable	BFI scale	Parameter estimate	SE	Z	p†
Fear = …	Extraversion	0.024	0.037	0.671	0.502
	Neuroticism	**0.212**	**0.039**	**5.393**	**<0.0001**
	Agreeableness	0.042	0.037	1.120	0.263
	Conscientiousness	−0.003	0.036	−0.094	0.925
	Openness	0.002	0.035	0.067	0.947
Grief = …	Extraversion	0.022	0.037	0.597	0.550
	Neuroticism	**0.158**	**0.039**	**4.049**	**<0.0001**
	Agreeableness	−0.042	0.037	−1.147	0.251
	Conscientiousness	−0.033	0.036	−0.916	0.359
	Openness	0.081	0.035	2.297	0.022
Physical distress = …	Extraversion	0.055	0.040	1.384	0.166
	Neuroticism	**0.188**	**0.042**	**4.511**	**<0.0001**
	Agreeableness	0.054	0.039	1.362	0.173
	Conscientiousness	−0.021	0.038	−0.539	0.590
	Openness	−0.026	0.037	−0.706	0.480
Insanity = …	Extraversion	0.003	0.039	0.069	0.945
	Neuroticism	**0.203**	**0.041**	**4.948**	**<0.0001**
	Agreeableness	0.019	0.039	0.492	0.623
	Conscientiousness	−0.014	0.038	−0.384	0.701
	Openness	0.007	0.037	0.183	0.855
Isolation = …	Extraversion	0.030	0.037	0.807	0.420
	Neuroticism	**0.145**	**0.038**	**3.785**	**<0.0001**
	Agreeableness	−0.031	0.036	−0.846	0.397
	Conscientiousness	−0.019	0.035	−0.550	0.582
	Openness	0.110	0.035	3.169	0.002
Death = …	Extraversion	0.000	0.036	0.003	0.997
	Neuroticism	0.040	0.038	1.064	0.288
	Agreeableness	0.004	0.036	0.115	0.908
	Conscientiousness	0.005	0.035	0.150	0.881
	Openness	0.011	0.034	0.324	0.746
Paranoia = …	Extraversion	0.013	0.043	0.311	0.756
	Neuroticism	**0.163**	**0.045**	**3.640**	**<0.0001**
	Agreeableness	−0.063	0.042	−1.478	0.139
	Conscientiousness	−0.027	0.041	−0.654	0.513
	Openness	0.068	0.040	1.685	0.092

† Effects in bold typeface were significant after Bonferroni correction ($p < 0.0014$).

4. Discussion

In a large internet survey sample (N = 1993), using the 10-item TIPI that measures emotional stability (the inverse of neuroticism) as well as a form of the CEQ that is derived from items of the HRS, SOCQ, and 5D-ASC (Study 1), we have demonstrated that increased neuroticism is associated with greater strength of challenging experience with psilocybin mushrooms. We replicated this finding in a separate large internet survey sample (N = 981) using the 44-item BFI that measures neuroticism (the inverse of emotional stability) as well as a stand-alone form of the CEQ (Study 2). Although openness was positively associated with scores on the *death* latent variable of the CEQ in Study 1, this relationship was not upheld in Study 2, suggesting that this may not be a reliable relationship.

4.1. Neuroticism and psychedelic experiences

Neuroticism is reflected in a propensity toward negative emotionality and poor coping with stress (John et al., 2008). Neuroticism is associated with vulnerability to psychopathology, potentially through supporting negative interactions with the environment, and a tendency toward negative reactivity to environmental stressors (Widiger & Smith, 2008). Our data suggest this tendency may extend to pharmacological stressors as well. A consistent preparation instruction to volunteers in therapeutic psychedelic research sessions is to "let go", or minimize negative reactivity to the strong and challenging psychological experiences that can be encountered during a psychedelic experience. Although the clinical benefits of such instructions have not been empirically tested, if true, it follows that psychedelic experiences may be more challenging in general for those who are high in neuroticism because they might have more difficulty in "letting go." This is consistent with findings relative to negative schizotypy, which is a related construct to neuroticism. Those high in negative schizotypy typically experience negative, distressing, and generally unpleasant reactions to altered states of consciousness (Rock, Abbott, Childargushi, & Kiehne, 2008; Schofield & Claridge, 2007). This should be considered in contrast to positive schizotypy, which is associated with not only pleasant and enriching reactions to altered states of consciousness, but also generally positive health outcomes (Mohr & Claridge, 2015).

Why might those high in neuroticism willingly choose to take a psychedelic drug if they understood that the effects could be challenging? It is plausible that individuals high in neuroticism may have succumbed to peer pressure to take psilocybin in some instances. Although those with higher neuroticism (lower emotional stability) in Study 1 were more likely than those with lower neuroticism (higher emotional stability) to have taken psilocybin mushrooms due to peer pressure, the odds ratio was only moderate at best (0.88). Further, no relationship between neuroticism and challenging experience was shown to be moderated by having taken psilocybin mushrooms due to peer pressure or coercion. Thus, though coercion and peer pressure may be expected to be a reasonable factor in the relationship neuroticism and challenging experiences, it does not appear to be central to this relationship.

4.2. Limitations and considerations

The cross-sectional nature of these data does not allow us to understand or investigate the direction of causality between neuroticism and challenging experiences, if there is any causal relationship between them. It may be that people who are highly neurotic may have more intense challenging experiences (due, for instance, to constitutional differences), or it may be that having a very challenging experience in some cases may lead to an increase in neuroticism. The latter case may be somewhat similar in type, but opposite in direction, to findings of increases in openness that have been observed after mystical experiences with psilocybin (MacLean, Johnson, & Griffiths, 2011), or after "ego-dissolution" that was reported with LSD (Lebedev et al., 2016). Nonetheless, these findings are consistent with previous studies suggesting a link between neuroticism and challenging experiences (Hemsley & Ward, 1985; Lienert & Netter, 1996), although these studies were not designed to investigate causality either.

Inconsistencies between the current survey report and a recent empirical report that failed to identify a relationship between neuroticism and the subjective effects of psychedelics (Studerus et al., 2012) may be due to a number of factors, including aspects of screening, preparation, interpersonal support provided during drug sessions, and integration provided after drug sessions. Within empirical studies, individuals who are high in neuroticism may be either explicitly (as in Studerus et al., 2012) or implicitly screened out of the study. Also, aspects of the environment such as interpersonal support that may mitigate challenging experiences are present by design in experimental laboratory settings (as in Griffiths, Richards, McCann, & Jesse, 2006; Johnson, Richards, & Griffiths, 2008; Studerus et al., 2012), but are variable and in many cases absent during experiences analyzed in the current report (Carbonaro et al., 2016).

4.3. Future directions and implications for clinical use of psychedelics

Under supportive conditions, and with proper screening, preparation, and integration, psychedelic experiences may have therapeutic effects (Bogenschutz et al., 2015; Carhart-Harris et al., 2016; Griffiths et al., 2016; Grob et al., 2011; Johnson, Garcia-Romeu, Cosimano, & Griffiths, 2014; Ross et al., 2016). However, the clinical indications that are being targeted with psychedelics, including mood disorders and addiction, are conditions in which high neuroticism may be of greater prevalence than otherwise healthy populations. Even within optimized conditions of set and setting (Johnson et al., 2008), participants can still encounter challenging experiences (Barrett et al., 2016; Griffiths et al., 2006; Griffiths et al., 2011; Studerus, Kometer, Hasler, & Vollenweider, 2011). Future research may benefit from further investigation of the role of personality in predicting response to psychedelics, not only in terms of Five Factor Model personality traits, but also in terms of other aspects of personality that have been related to psychopathology, including alexithymia and behavioral inhibition/behavioral activation models, which may have particular import in terms of predicting challenging experiences. Although it is not clear that challenging experiences will necessarily reduce the therapeutic efficacy of a psychedelic experience, it is possible that more preparation time before sessions or more integration time after sessions would be increase therapeutic efficacy in those who are high in neuroticism. Future studies should determine whether individuals who are high in neuroticism may be more prone to challenging experiences in clinical settings, and whether this has any effect on clinical and therapeutic outcomes with psychedelics.

Declaration of conflicting interest

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