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The Relationship between Anxiety Vulnerability Factors, Psychedelic Drug Use and Trait Anxiety

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Abstract

BACKGROUND: Distress tolerance (DT), anxiety sensitivity (AS), and intolerance of uncertainty (IU) are transdiagnostic vulnerability factors for emotional distress. Some have argued that AS and IU are components of DT but this hypothesis has not been properly addressed yet, and neither has their relationship to trait anxiety. Self-report studies and to lesser extent small clinical trials suggest that use of psychedelic drugs may help lower anxiety and depression, possibly because they increase the user's tolerance for distress either pharmacologically or psychologically. The primary aim of this study was to examine the relationship between trait anxiety, DT, AS, IU and psychedelic drug use. METHOD: A survey was posted online that included measures of IU, DT, AS, trait anxiety, the mystical quality of psychedelic drug use (MEQ), and questions about frequency of psychedelic drug use; 640 adults responded. RESULTS: Correlations between DT, AS and IU suggest they are overlapping constructs. Regression analysis showed that the relationship between DT, AS, IU and trait anxiety differed between the participants that had used psychedelic drugs and the ones that had not. The three transdiagnostic vulnerability factors were only weakly related to whether participants reported a transformative experience from psychedelic drug use. CONCLUSIONS: The mechanisms by which psychedelic drug use lessens anxiety and depression remains unclear but it is possible that they do so through changes in DT, AS and IU. Further study is needed.

Keywords: trait anxiety, intolerance of uncertainty, anxiety sensitivity, distress tolerance, psychedelic drugs, mystical experiences

Introduction

Background

The current master's thesis research had two related aims: to examine the relationship between trait anxiety and three anxiety vulnerability factors (intolerance of uncertainty, anxiety sensitivity and distress tolerance); and to examine the relationship between the mystical experience associated with psychedelic drug use and the anxiety constructs.

Trait anxiety. State and trait anxiety are different aspects of anxiety that are related to different genetic and environmental components. State anxiety is the environmentally reactive component of anxiety and it elicits an emotional response caused by environmental stressors. It includes both physiological arousal (such as increased sweating and heartbeat) and psychological symptoms (apprehension, worry, and tension) (Lau, Eley, Stevenson, 2006). Trait anxiety refers to individual differences in the predisposition to respond to threatening situations (Lau et al., 2006), and is often characterized as a personality disposition. It is expressed through the tendency to respond with state anxiety under 'threatening' circumstances. Thus, individuals with high levels of trait anxiety are more likely to respond through physiological and cognitive state anxiety manifestations when faced with a threatening situation.

Trait anxiety is a construct related to anxiety symptomatology and anxiety vulnerability factors. Chambers, Power and Durham (2004) found that patients diagnosed with Generalized Anxiety Disorder (GAD), social phobia and depressive disorders had very high scores on trait anxiety at a long-term follow-up, and trait anxiety recorded pre-treatment was also related to both anxiety and depression at long-term follow-ups. Muris, Schmidt, Merckelbach and Schouten (2001) conducted a study

on Dutch adolescents and found that trait anxiety accounts for unique variance in anxiety disorder symptoms, and, after controlling for other vulnerabilities, it was strongly connected to symptoms of social phobia and separation anxiety disorder. Due to such findings, the current study aims to control for a diagnosis of depressive disorder.

Anxiety vulnerabilities. Three anxiety vulnerability factors that have been established in the literature of anxiety symptomatology are: intolerance of uncertainty, distress tolerance, and anxiety sensitivity. Intolerance of uncertainty (IU) is defined as a cognitive bias that affects how a person perceives, interprets, and responds to uncertain situations on a cognitive, emotional and behavioural level. Individuals high in IU experience the possibility of a future negative event as threatening and unacceptable, regardless of the probability of the event actually happening (Buckner, Keough, & Schmidt, 2007). General Anxiety Disorder (GAD) and worry were the first forms of anxiety psychopathology thought to be associated with IU. Currently, IU is associated with a wide range of anxiety conditions: OCD, social anxiety symptoms, hoarding symptoms, as well as depression (Norr, Oglesby, Capron, Raines, Korte, & Schmidt, 2013). Norr et al. (2013) maintains that IU increases anxious cognitions leading to behaviours that maintain anxious pathology, and IU should be conceptualized as a general anxiety vulnerability, rather than a vulnerability for a specific disorder. Compulsive checking (part of OCD symptomatology), uncontrollable worry (GAD), and avoidance of social interactions may be viewed as futile attempts to gain certainty about the future (Buckner et al., 2007).

Anxiety sensitivity (AS) is another cognitive vulnerability factor in anxiety and it is defined as fear of the consequences of anxiety related symptoms. Muris et al. (2001)

found that in Dutch adolescents, anxiety sensitivity accounts for unique variance in anxiety disorder symptoms, but it is not correlated to depression when trait anxiety is controlled for. They concluded that anxiety sensitivity and trait anxiety each account for unique proportions of the variance in anxiety disorders symptomatology. Norr et al. (2013) found in adults that AS accounts for a significant proportion of the variance in social anxiety and OCD symptoms.

Distress tolerance (DT) is defined as an individual's ability to experience and endure negative emotional states (Zvolensky, Vujanovic, Bernstein & Leyro, 2010). DT is also described as a higher-order construct including domain-specific difficulties in tolerating negative emotions, physical states, frustration, ambiguity, and uncertainty (Zvolensky et al., 2010). In this way, AS and IU may be seen as domain specific difficulties for individuals with low tolerance for distress. Low levels of DT are associated with higher levels of depression, anxiety, eating disorders, and substance use (Buckner et al., 2007; Brandon et al., 2003; Norr et al., 2013). However the relationship between these three vulnerabilities remains underexplored. To date one study has looked at the relationship between these three vulnerability factors and found that after controlling for the effects of AS and IU, DT was no longer acted as a significant predictor of the severity of anxiety symptoms in adults seeking treatment for anxiety (Laposaa, Collimore, Hawley, & Rector, 2015). The authors concluded that DT, AS and IU are clearly related to anxiety severity across both clinical and non-clinical studies but there is also overlap between DT, AS and IU at a conceptual and empirical level and that further investigation of this overlap is needed in clinical and non-clinical samples. The current study aims to improve our understanding of the topic by exploring the relationship between these three vulnerability variables, and trait anxiety in a large

sample who were recruited online and not from a clinic as was done in the previous study by Laposaa et al. (2015).

Research on psychedelic drugs. Psychedelic drugs are psychoactive substances that powerfully alter perception, mood, and cognitive processes (Halpern, 2003). Scientists have considered psychedelic drugs to be a door to the human mind and a way of understanding altered states of consciousness that are characteristic of schizophrenia or other psychotic disorders (Albaught & Anderson, 1974). There is small but growing body of literature involving experimental (human and animals), cross-sectional and longitudingal surveys, as well as meta-analysis studies which have found an association between psychedelic drug use and lower frequency/severity of anxiety and depressive symptoms. They also found no evidence of long-lasting negative effects that are often found for other drugs used in a recreational context (Johansen & Krebs, 2015). The association between lower anxiety/depression and psychedelic drug use may arise from the effects these drugs have on brain structures that govern mood and/or the drugs influence the user's sensitivity to and tolerance for stressful stimuli, whether external or internal states (negative sensations, thoughts, images, emotions) but more research is needed. This study addresses the relationship between vulnerability factors for anxiety, trait anxiety and the use of the following psychedelics: LSD, psilocybin, 3,4-Methylenedioxymethamphetamine (MDMA), ayahuasca, ibogaine, peyote, ketamine and N,N-Dimethyltryptamine (DMT). I will now briefly summarize the literature on the relationship between mental health and psychedelic drug use and the proposed mechanisms by which they may have their beneficial effects.

Psychedelic drug use and the brain. Psychedelic drugs have their principal effect on the central nervous system through an agonist (or partial agonist) action at

serotonin 5-HT_{2A} receptors, with a contribution of 5-HT_{2C} and 5-HT_{1A} receptors. Serotonin is the neurotransmitter believed to maintain mood balance and alterations in serotonin activity have been found in individuals with depression and anxiety (Rambousek, Palenice, Vales, & Stuchlik, 2014). It appears that these drugs primarily target sites in the pre-frontal cortex and thalamus, regions that are considered essential for conscious activity and mindful mood management (Nichols, 2004; Halpern, 2003), as well as in the amygdala, which plays a crucial role in the perception and generation of emotions (Stuhrmann et al., 2013). Several studies have demonstrated that activation of 5-HT_{2A} receptors by classical psychedelics or by serotonin leads to a robust, glutamate-dependent increase in the activity of pyramidal neurons, preferentially those in layer V of the prefrontal cortex (PFC) which is believed to be brain region most responsible for mood regulation (Aghajanian & Marek, 1999). Use of psychedelics has been found to increase 5-HT_{2A} receptor density in the PFC in post-mortem samples and in patients with major depression, and this same density reduced after chronic treatment with various antidepressants (Vollenweider & Kometer, 2010). In humans, fronto-limbic 5-HT_{2A} receptor density is correlated not only with anxiety but also with an individual's difficulties in coping with stress (Frokjaer et al., 2008). These findings indicate that psychedelics are potent modulators of prefrontal network activity that involves a complex interaction between the serotonin and glutamate systems in prefrontal circuits, which together govern regulation of mood, anxiety, and stress.

Association between psychedelic use and mental health. The exising research has observed that use of classic serotonergic-influencing psychedelics is not associated with withdrawal symptoms or addiction, damage to the brain or other organs, birth defects, risky or violent behaviour, and accident or suicide under the influence of

psychedelics is incredibly rare (Halpern, 2003; Krebs & Johansen, 2013; Nutt, King, Saulsbury & Blakemore, 2007; Nutt, King & Phillips, 2010). A series of studies have been carried out in the USA with nearly 200,000 participants focusing on the relationship between use of what are termed 'classic' psychedelic drugs (i.e. lysergic acid diethylamide (LSD), psilocybin, mescaline, peyote) and mental health (Krebs & Johansen, 2013, 2015; Hendricks, Thorne, Clark, Coombs & Johnson, 2015). These studies were using data from the nationally reprentative surveys of drug abuse carried out by the National Institute of Drug Abuse under mandate from the US government. These recurring surveys employ a mixture of standardized and unstandardized self-report measures of drug use, physical and mental health, and various sociodemographic variables including employment. These surveys found that lifetime use of any classic psychedelics was not significantly asssociated with serious psychological distress in the worst month of the past year (participants were asked to think back on the worst month they experiences in the previous year from a mental health perspective, relating to worry, stress, etc.) or with any of the eight past year psychiatric symptom indicators. However, past year use of LSD was associated with lower rates of serious psychological distress, and lifetime LSD use was significantly associated with a lower rate of outpatient mental health treatment and psychiatric medication prescription (Krebs & Johansen, 2013, 2015). Krebs and Johansen (2013, 2015) also found a series of marginally statistically significant effects between lifetime psychedelic drug use and past year mental health symptoms: younger people with lifetime psychedelic drug use had lower rate of past year symptoms of generalized anxiety disorder, psilocybin use was significantly associated with a lower rate of symptoms of panic attacks, and mescaline/peyote use was significantly associated with a lower rate of symptoms of agoraphobia (Krebs & Johansen, 2013). Hendricks et al. (2015) found that lifetime

psychedelic use was associated with significantly reduced odds of psychological distress, suicidal thinking, suicidal planning, and suicide attempt over the past year, whereas lifetime use of other drugs (cocaine, amphetamines) was associated with an increased likelihood of these outcomes.

It is important to point out that the absence of a significant association between psychedelic drug use and health-related difficulties found in the literature does not mean that these drugs are not necessarily harmful to any particular individual. One potential negative consequence of psychedelics is a condition termed Hallucinogen Persisting Perception Disorder (HPPD), where flashbacks similar to what users feel during a psychedelic 'trip' come back in a disturbing way, affecting day-to-day life (Halper, 2003; Halpern & Pope Jr., 2003). Halpern and Pope Jr. (2003) analysed twenty quantitative studies examining this phenomenon, and found that while HPPD is a genuine disorder, it is very rare among psychedelic drug users. Unfortunately, due to the different ways in which the included studied screened for HPPD, and their definition of flashback, the data do not permit us to estimate, even crudely, the prevalence of 'strict' HPPD, but studies examining subjects given LSD in research settings (where subjects were screened to exclude those with serious psychiatric or medical pathology) have consistently reported few instances of flashbacks. A history of mental disorders, especially psychosis, and the use of other drugs have been shown to increase the vulnerability of developing HPPD (Halpern, 2003). Of course it is possible that use of these drugs outside of controlled clinical settings may put an individual user at increased risk of physical or psychological harm even if the current evidence suggests that the risk is very low.

Psychological consequences of psychedelic drug use that might explain effects on mental health. Studies attempting to identify the psychological mechanisms by which psychedelic drug use might positively impact mental health have increased in the literature over the past few years. Gasser et al. (2014) carried out a study where LSD-assisted psychotherapy sessions was compared with regular psychotherapy in patients with anxiety associated with life-threatening diseases. Twelve months after finishing LSD plus psychotherapy, 77.8% reported sustained reductions in anxiety according to their scores on the trait anxiety questionnaire (STAI) and reduced fear of death and 66.7% reported improved quality of life. Patients who experienced a benefit from the combined treatment reported (subjectively perceived) changes in personality such as increased openness, deepened awareness and being more patient with themselves (Gasser et al., 2014). Interestingly, all of the patients in this controlled clinical trial described the intensified emotional experiences that accompanied the LSD use as positive, in spite of sometimes coping with difficult emotional experiences. Neither the experimental dose, nor the active placebo produced any drug-related severe adverse events, that is, no panic reaction, no suicidal crisis or psychotic state, and no medical or psychiatric emergencies requiring hospitalization. Nevertheless, the experimental dose subjects experienced more types of adverse short-term effects during the session (increased anxiety). Importantly, this was a very small scaled study, with only 12 participants. Whether these same patients would report similar positive experience if these drugs were used outside of a clinical trial is not known.

In light of their newest findings regarding brain connectivity and LSD, Carhart-Harris et al. (2016) proposed that, in many psychiatric disorders, behaviors and cognitions become automated and rigid, making the person more susceptible to stress and making emotion regulation more difficult. They argue that psychedelics might

induce disintegration and desegregation of the neural networks responsible for these behaviors and allow more balanced responses to stress and greater ease managing emotions. It is reasonable to hypothesise whether this effect represents an increase in distress tolerance, and possibly IU and AS, and the current study will attempt a first exploratory look at how psychedelic drug use might relate to these psychological vulnerabilities to anxiety. The exploratory study will look at the relationship between scores on self-report measures of anxiety, DT, AS, and IU and the frequency (and associated experience of) LSD, psilocybin, 3,4-Methylenedioxymethamphetamine (MDMA), ayahuasca, ibogaine, peyote, ketamine and N,N-Dimethyltryptamine (DMT) as being part of the psychedelic category.

Self-reports of illicit psychedelic drug use point towards LSD and psilocybin being significantly associated with experiences that can be characterized as mystical, transcendental or spiritual in nature, a relationship which appears to be dose-dependent (Lyvers & Meester, 2012). These mystical experiences are often reported to be transformative for the individual, i.e. altering the way they perceive themselves, others and the world (Griffiths, Richards, McCann & Jesse, 2006). The current study will examine the relationship between psychedelic drugs and the level of mystical experience associated with them in the context of the anxiety and vulnerability measures.

Griffiths et al. (2006) looked at the attribution of mystical experience to psilocybin use using the MEQ. Their participants were psychedelic-naïve adults reporting regular participation in religious or spiritual activities. The study was double-blind and involved two or three 8-hour drug sessions conducted at 2-month intervals. Compared to the control substance methylphenidate at 2 months, the volunteers rated

the psilocybin experience as having substantial personal meaning and spiritual significance and attributed to the experience sustained positive changes in attitudes and behaviour consistent with changes rated by community observers. At the 14-month follow-up, 58% (2 sessions group) and 67% (3 sessions group), respectively, of volunteers rated the psilocybin-occasioned experience as being among the five most personally meaningful and among the five most spiritually significant experiences of their lives; 64% indicated that the experience increased well-being or life satisfaction; 58% met criteria for having had a 'complete' mystical experience (Griffiths, Richards, Johnson, McCann & Jesse, 2008). Hence, it appears that the mystical experience rating increases with frequency of use, and it is also associated with more positive life-changes. The MEQ showed robust increases on all dimensions (Positive mood, transcendence, mysticism and innefability) after psilocybin use, and correlation and regression analysis showed a central role for these mystical-type experiences in the sustained high ratings of personal meaning and spiritual significance at follow-up.

Summary. According to a new World Health Organisation study (Chisholm et al., 2016) based on data from 36 low, middle and high-income countries, the number of people suffering from anxiety and depression worldwide increased from 416 million in 1990 to 615 million in 2013, and currently cost the global economy more than $1 trillion per year. It is estimated that every dollar spent on improving treatments for anxiety and depression accounts for a $4 return in better health and ability to work (Chisolm et al., 2016). Thus there is a clear need to identify factors that increase an individual's vulnerability to anxiety so that these might be targeted in treatment and to discover new treatments for anxiety and the mechanisms by which they act to reduce anxiety.

In order to gain a better understanding of the causes of anxiety and to develop better treatments, researchers have tried to identify any psychological factors that might increase the risk of developing an anxiety disorder (or help to maintain or worsen an anxiety disorder). This study focuses on three putative mediators for emotional disturbance (including anxiety) that emerge in the literature: DT, AS, and IU. Each of these vulnerability factors has been shown to be significantly correlated with anxiety and depression in clinical and non-clinical samples and with some limited evidence that changes in these vulnerability factors during treatment is associated with improved outcomes for anxiety and depression. DT, AS and IU appear to be overlapping constructs and it is possible that AS and IU are domain-specific areas of dysfunction in individuals with low DT but further research involving measurement of all three factors and anxiety simultaneously is required (Zvolensky et al., 2010). There is also a growing body of evidence that psychedelic drug use might be of benefit to patients with obsessive compulsive disorder (OCD), post-traumatic stress disorder (PTSD), end-of- life anxiety, depression and cluster headaches (Johansen & Krebs, 2015). It is possible that the benefits experienced from these drugs may have to do with the 'mystical' experiences that occur during their use, which in turn lead to a greater openness to negative experiences and emotional states. It seems reasonable to wonder if this greater openness to negative experiences might be related to the individuals levels of DT, AS and IU, and thus the level of mystical experiences as measured by the MEQ-30 might be related to scores on measures of DT, AS and IU. This research aims to look at the influence of anxiety vulnerabilities on trait anxiety, as well as the relationship between these anxiety constructs and self-reported psychedelic drug use in terms of type used, frequency, and subjective experience of the drugs in a population recruited over the internet.

Hypotheses and Research Questions

1. IU, AS and DT significantly and independently correlate with each other and with trait anxiety, with higher scores on IU and AS and lower scores on DT correlating with higher scores on trait anxiety.
2. Are scores on the measures of DT, AS, IU and trait anxiety related to the frequency of psychedelic use or the subjective experience of these drugs as measured by the MEQ-30?
3. Do IU, AS and DT, and a diagnosis of depressive disorders predict trait anxiety similarly in groups that have and groups that have not used psychedelic drugs?

Methods

Participants

Participants were recruited online, and there were no restrictions on backgrounds, age, gender, or education level. The final sample consisted of 640 participants. The questionnaire was posted on the same open forum sites as used in Carhart-Harris and Nutt's (2010) online study. Specifically, a large proportion of the participants found out about the questionnaire from websites that take a relatively favourable view of drug use: sites where individuals go in order to educate themselves and discuss psychedelic drugs. However no attempt was made to select participants based on whether they had or had not a positive/negative experience with these drugs; as with Carhart-Harris and Nutt (2010), all adults visiting these websites were invited to participate. So it is important to keep in mind that because the participants in this study were recruited from such websites and not a nationally representative sample, it is possible that the participants in this study were biased on some way as to their

views/experiences of psychedelic drugs. The country the participants were from and their mother-tongue were not investigated, but all the websites where the questionnaire was posted were in English and a good understanding of the language was necessary in order to be able to navigate them. . Participants received no form of compensation for their participation. Table 1 provides data on demographics.

Materials

The entire questionnaire was in English. It started with sociodemographic questions, and a question regarding self-reported psychiatric diagnosis in order to obtain statistics on the a diagnosis of depressive disorder.

The State-Trait anxiety inventory (STAI). The STAI is a commonly used measure of trait and state anxiety (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). For the purpose of this study, only the trait anxiety section (Y2) was used. It is used in clinical settings to diagnose anxiety. There are 20 questions related to trait anxiety, such as "I am content; I am a steady person." All items are rated on a 4-point scale (e.g., from "Almost Never" to "Almost Always"). Scores are obtained by summing up all items. Higher scores indicate greater anxiety. Internal consistency coefficients for the scale have ranged from .86 to .95; test-retest reliability coefficients have ranged from .65 to .75 over a 2-month interval (Spielberger et al., 1983). Considerable evidence attests to the construct and concurrent validity of the scale (Sylvers, Lilienfeld, & LaPrairie, 2011).

Intolerance of uncertainty scale (IUS-12). The original intolerance of uncertainty scale had 27 items and the psychometric properties of the English version was examined by Buhr and Dugas (2002). The English version had excellent internal

consistency and good test–retest reliability, over a five-week period, and convergent and divergent validity when assessed with symptom measures of worry, depression, and anxiety.

Carleton, Norton and Asmundson (2007) used two undergraduate samples and evaluated a psychometrically stable 12-item two-factor English version of the IUS. The reduced measure (IUS-12) retained exemplary internal consistency, while correlating extremely well with the original IUS and related measures of anxiety and worry. The IUS-12 also demonstrated a stable two-factor structure, representing both anxious and avoidance components of intolerance of uncertainty. The current study used this short version of the IUS-12. The first factor involves fear and anxiety based on future events and it is defined as Prospective, while the second factor describes uncertainty inhibiting action or experience; therefore, it might be best described as Inhibitory Anxiety. Each item is rated on a Likert scale from 1 (not at all characteristic of me) to 5 (entirely characteristic of me).The scores on the IUS- 12 are obtained through a sum of scores, either for each separate factor (prospective and inhibitory), or for the total IU. Higher scores imply more IU.

Distress tolerance scale (DTS). The DTS is a 15 item scale developed by Simons and Gaher (2005) that is rated on a Likert-scale from 1 (strongly agree) to 5 (strongly disagree). Confirmatory factor analysis of the DTS indicates a higher-order General Distress Tolerance factor comprised of all items and corresponding to the total score, and four lower-order factor scale: (1) *Tolerance* – made up of 3 items (e.g., "Feeling distressed and upset is unbearable to me"); (2) *Appraisal* – made up of 6 items (e.g., "My feelings of distress or upset are not acceptable"); (3) *Absorption* – made up of 3 items (e.g., "When I feel distressed or upset, all I can think about is how bad I feel"); and (4)

Regulation – made up of 3 items (e.g., "I'll do anything to avoid feeling distressed or upset") (Simons & Gaher, 2005). Exploratory analysis showed good test–retest reliability for the second order scale over a 6-month interval (intra-class r = .61). Higher scores imply higher capacity to withstand emotional distress, and lower scores imply participants are less capable of dealing with distress (distress intolerance). Scores for each of the four factors are calculated by computing average scores of all the items related to each specific factors, and a general distress tolerance score is calculated by averaging all items. While reading the results, it is worth keeping in mind that higher scores on the DTS are a positive indicator, implying participants cope with distress better.

Anxiety sensitivity inventory (ASI-3). In 1998, Taylor and Cox proposed the Anxiety Sensitivity Index–Revised (ASI-R) as a broad measure of AS, but because of its unstable factor structure (Taylor et al., 2007), another revision took place. The most recent version, the Anxiety Sensitivity Index–3 (ASI-3) was proposed by Taylor and colleagues in 2007. The ASI-3 was found to be superior to its predecessors ASI and ASI-R. Taylor et al. (2007) demonstrated that the ASI-3 measures the construct more precisely—the ASI-3 has a higher reliability and construct validity than the ASI. In contrast to the ASI-R, the internal structure of the ASI-3 is stable across diverse samples. According to these results, the ASI-3 may be considered a reliable and valid measure of the most robust dimensions of the AS construct. Kemper, Lutz, Bähr, Rüddel, and Hock (2012) found that ASI-3 has good construct validity in a clinical sample as well.

The 18-item ASI-3 assumes a hierarchical three-factor structure of the construct and yields measures of Somatic Concerns (e.g., "It scares me when my heart beats rapidly"), Social Concerns (e.g., "It is important for me not to appear nervous"), and

Cognitive Concerns (e.g., "When I cannot keep my mind on a task, I worry that I might be going crazy") for the first-order level, and Global AS for the second-order level. The scale has scores ranging from 0 (very little) to 4 (very much), where higher scores imply more anxiety sensitivity. The scores for each of the three factors are computed by summing up scores on individual items related to one of the three factors. A global AS score is computed by summing up scores on all items.

Questionnaire regarding psychedelic drug use. The questions related to psychedelic drug use were created by the author and have not been validated. In the first question, participants were asked if they had ever taken any of the following psychedelic drugs: psilocybin (magic mushrooms or magic truffles), LSD, DMT, MDMA, ayahuasca, ibogaine, peyote, mescaline or ketamine. If their answer was "no", the questionnaire ended there, and they were thanked for their participation. If they answered "yes", they were then asked to select which of the nine previously mentioned psychedelics they had taken. Next, they were asked about the frequency of use of each specific psychedelic drug, and the answer options were: never, once, 2 to 5 times, 6 to 10 times, 11 to 20 times, 21 to 49 times, and over 50 (scored from 0 to 6). Higher scores imply higher frequency of use of a specific psychedelic.

Revised mystical experiences questionnaire (MEQ-30). The original 43-item Mystical Experience Questionnaire (MEQ) was developed to evaluate the occurrence and character of individual, discrete mystical experiences occasioned by classic hallucinogens (Griffiths et al., 2006). The recently developed 30-item version was developed and validated through factor analysis of retrospective accounts of profound experiences with psilocybin-containing mushrooms (MacLean et al., 2012). That analysis yielded a four factor structure for the MEQ30. Barrett, Johnson and Griffiths

(2015) validated the MEQ30 with data from five experimental psilocybin studies in which participants received a moderate to high dose of psilocybin (⩾20 mg/70 kg). The four-factor MEQ30 model demonstrated good construct validity, acceptable model fit (CFI >0.90, SRMR <0.09) and excellent reliability, calculated using Cronbach's alpha (αmystical=0.97, αpositive mood=0.92, α transtime/space=0.86, α ineffability = 0.90). Factor loadings for the four-factor MEQ30 model show high loading of each item onto its intended factor, and support the internal validity of the instrument. These findings support the use of the MEQ30 as an efficient measure of individual mystical experiences.

To summarize, the four factors of the MEQ30 are: mystical, positive mood, transcendence of time and space, and ineffability. It is rated on a six-point scale [0=none, not at all; 1=so slight, cannot decide; 2=slight; 3=moderate; 4=strong (equivalent in degree to any previous strong experience or expectation of this description); and 5=extreme (more than ever before in my life and stronger than 4)]. The final factor scores are calculated by averaging the scores on items related to the four separate subscales, while the total score is computed by averaging the scores on all the four subscales.

Design

The study is a non-experimental, correlational study. It is a cross-sectional investigation, largely exploratory in nature with no a priori assumptions about the size, direction or significance of relationships between DT, AS and IU and psychedelic drug use or scores on the MEQ-30. The dependent variable is trait anxiety. The independent variables were measures of DT, AS, IU, trait anxiety, mystical experience during drug use, frequency of psychedelic drug use, and a self-reported diagnosis of depressive

disorder. The online survey also included questions about sociodemographic variables (age, gender, education level and ethnicity) but they were only included in order to obtain a picture of the participants' characteristics and were not included in the analyses. The study was approved by my supervisor and the course leader at the Department of Psychology, Lund University.

Procedure and Instruments

The questionnaire was conducted online on the SoGoSurvey platform. Considering that the study was interested in participants that engage in psychedelic use as well as a normal population, advertising the study was done both on sites related to psychedelic drug use and on neutral websites: shared on personal Facebook pages, University-related Facebook pages, drug-related Facebook pages (Erowid Centre, Zenda project, Enpsychedelica, Psychedelic Adventure, Psychedelic Society, Students for Sensible Drug Policy, Beckley Foundation), Reddit (psychedelic drugs subreddits, psychology subreddits, sampling and data gathering subreddits, mental health related subreddits), and websites related to information and safety of drug use (shroomery.com).

The questionnaire started with an information and consent form that had to be signed, and continued with demographic questions related to age, gender, level of education, ethnicity, and psychiatric diagnosis (in order to obtain a self-reported diagnosis of depressive disorder). The anxiety vulnerabilities scales followed: short version of the Intolerance of Uncertainty scale (IUS-12, 12 items), Distress Tolerance Scale (DTS, 15 items), and the Anxiety Sensitivity index-3 (ASI-3, 18 items). Participants then completed the 'Trait' section of the Spielberg State and Trait Anxiety Inventory for Adults (STAI), followed by the questions related to psychedelic drug use. The last

questionnaire was the Revised Mystical Experience Questionnaire (MEQ30, 30 items). A debriefing page outlining the purpose of the study ended the questionnaire. Completing the entire questionnaire took between 10 and 15 minutes.

Ethical questions

The data is stored in an encrypted file in an anonymous format (no identifiable information) on the researcher's computer for the duration of three years so as to not be able to be traced back to an individual participant. The individual's data has not been, and will never be reported, only data based on the group of participants. Participants were made aware of the steps taken to ensure their confidentiality in order for them to feel safe answering the questionnaires. All participants were informed that they can withdraw from the experiment at any time.

Participation in this project was not expected to cause injury, pain, discomfort, or have any other negative outcomes. The information sheet provided the contact information of the researcher in case participants had any questions or worries related to their participation. The study has two potential ethical concerns.. Firstly, completing questionnaires related to anxiety and depression could potentially trigger unwanted negative emotions, but there is no evidence in the literature on this effect. Secondly, asking questions regarding psychedelic drug use can be problematic due to the fact that they are illegal and people might be reticent to answer truthfully. The anonymization process was highlighted a number of times to put their mind at ease. The participants were made aware of the nature of the questions they would be asked, and told they can withdraw at any time.

Statistical Analysis

The SPSS software was used for statistical analysis. Statistical analysis literature maintains that for large sample sizes, parametric tests can be performed on data that is not normally distributed (Ghasemi & Zahediasl, 2012). The standardized self-report measures used in this study followed a largely normal distribution and parametric statistics were used throughout. Previous research reports pairwise correlations in the moderate to large range between the DTS, ASI-3 (or earlier version), and the IUS-12 (or the 27-item original), and STAI, as well as self-report measures of anxiety and depression, i.e. all r's $\geq$ 0.40. Using the *G-Power* programme, with an alpha set to 0.05, power set to 95%, and assuming the pairwise correlation between the vulnerability measures and between the vulnerability measures and trait anxiety were all $\geq$ r = .40 in the population, G-Power estimated that a total of 71 participants would be required to detect similarly sized correlations between the anxiety vulnerability measures and trait anxiety in the current study. Considering the large number of planned analyses in this study and the associated risk of increased Type 1 error, the plan was to recruit as many participants as possible and a minimum of 300. This number was exceeded (total N = 640).

Percentage and frequency analyses were run on the demographic variables age, gender, education level, ethnicity, psychiatric diagnosis, and psychedelic drug use (Table 1). Descriptive statistical tests, specifically mean, standard deviation, and range, were performed on all subscales and total scores of the trait anxiety, DTS, ASI-3, IU12, and MEQ (Table 2). A series of ANOVA's were run to compare the means of participants on STAI, DTS, ASI-3, IUS-12 and MEQ that have taken psychedelics and participants that have never taken psychedelics.

A series of Pearson's pairwise correlations were performed (two-tailed) to assess the relationships between DTS, ASI-3, IUS-12 and trait anxiety, and among each other. Pairwise correlations between frequency of use of each separate psychedelic and MEQ, trait anxiety, DTS, ASI-3, IUS-12 (including their subscales) were performed in order to understand the relationship between psychedelic drugs, the mystical experience associated with them, and the anxiety measures. Finally, two multiple linear regressions were run with trait anxiety as a dependent variable: one in the group that had never taken psychedelics, assessing the predicting value of DTS, ASI-3, and IUS-12 subscales and a diagnosis of depression, and one in the psychedelic taking group, assessing the relative contributions of subscale scores of the DTS, ASI-3, IUS-12, MEQ, frequency of psychedelic drug use, and a diagnosis of depression.

Results

Descriptive statistics

Sociodemographic data (age, gender, education level, ethnicity, any diagnosis of mental health disorders, psychedelic drug use). Table 1 presents sociodemographic data (frequency and percentages). The participants are preponderantly white males between 18 and 25 years of age, with an undergraduate diploma. There is a large discrepancy between ethnicity groups, with people of white ethnicity being by far the largest group (552 participants). A self-reported diagnosis of depression is included in the regression analysis.

Table 1. Sociodemographic characteristics of the sample (N=640)

Variable	Group	Frequency	Percent
Age	under 18	38	5.94
	18-25	420	65.63
	26-40	152	23.75
	41-60	28	4.38
	over 60	1	0.16
Gender	Male	457	71.41
	Female	153	23.91
	Other	12	1.88
Education level	High-school diploma	280	43.75
	Undergraduate degree	227	35.47
	Master's degree	48	7.50
	Doctoral Degree	5	0.78
	Some high school, no diploma	35	5.47
	Vocational/ technical school	28	4.38
Ethnicity	White	552	86.25
	Hispanic or Latino	30	4.69
	Black or African American	4	0.63
	Asian/ Pacific Islander	17	2.66
	Native American/ American Indian	4	0.63
	Middle Eastern	5	0.78
	Other	11	1.72
Mental Health Diagnosis	Yes	248	38.75
	No	392	61.25
	Anxiety Disorder	143	22.3
	Depressive Disorder	154	24.1

	Neurodevelopmental Disorder	52	8.1
	Bipolar disorder	23	3.6
	Trauma Stressor Disorder	14	2.2
	OC Disorder	13	2
Psychedelics used	Yes	568	88.75
	No	72	11.25
	Psilocybin	452	70.60
	LSD	446	69.70
	DMT	187	29.20
	MDMA	394	61.60
	Ayahuasca	36	5.60
	Ibogaine	4	0.60
	Peyote	21	3.30
	Mescaline	65	10.20
	Ketamine	160	25.00

Table 2 presents descriptive statistics for DTS, IUS-12, ASI-3, trait anxiety and MEQ in three separate groups: for all participants, for the psychedelic-using group, and for the group that never used psychedelics. Having higher scores on the IUS, ASI and trait anxiety is a negative outcome because it implies higher anxiety vulnerability levels, but higher scores on DT is a positive outcome. A series of ANOVAs were carried out comparing scores on the IUS-12, DTS, ASI-3, and STAI in participants who did (N=568) and did not report psychedelic drug use (N=72). No significant differences were observed on any of the scales.

Table 2. Descriptive statistics for self-report measures of distress tolerance, intolerance of uncertainty,

anxiety sensitivity, trait anxiety and mystical experiences (N = 640).

	Total (n=640)		Psychedelic users (n=568)		Non-psychedelic users (n= 72)	
Scale (range of scores)	Mean	SD	Mean	SD	Mean	SD
STAI-Trait anxiety (1-72)	47.38	12.61	47.41	12.65	47.18	12.34
IUS total (1-53)	31.29	9.45	31.29	9.63	31.31	7.93
IUS prospective (1-30)	19.31	5.38	19.25	5.44	19.77	4.91
IUS inhibitory (1-23)	11.98	5.20	12.04	5.31	11.54	4.25
DTS total (1-4)	3.23	0.93	3.24	0.93	3.20	0.88
DTS tolerance (1-4)	3.33	1.04	3.34	1.04	3.22	0.99
DTS absorption (1-4)	3.14	1.17	3.14	1.18	3.15	1.11
DTS regulation (1-4)	3.16	1.01	3.17	1.01	3.11	0.96
DTS appraisal (1-4)	3.31	1.05	3.31	1.06	3.32	1.01
ASI total (1-69)	21.55	14.76	21.48	14.77	22.11	14.83
ASI social concerns (1-24)	10.21	5.70	10.17	5.76	10.52	5.25
ASI cognitive concerns (1-24)	6.09	6.11	6.02	6.02	6.59	6.76
ASI physical concerns (1-24)	5.25	5.58	5.28	5.65	5.00	4.97
MEQ total (1-5)			3.38	0.94		
MEQ transcendence (1-5)			2.97	1.17		
MEQ positive mood (1-5)			4.04	0.80		
MEQ ineffability (1-5)			4.15	0.96		
MEQ mystical (1-5)			3.12	1.22		

Note: n for IU, DT, AS and trait anxiety variables = 693, n for MEQ variables= 551; SD= standard deviation; STAI= State-Trait anxiety inventory, DTS= Distress Tolerance Scale, IUS= Intolerance of uncertainty Scale-12, ASI= Anxiety Sensitivity Inventory-3, MEQ= Mystical Experiences Questionnaire.

Correlations

There is a significant medium negative correlation between gender and psychedelic use, $r(620) = -.30$, $p < .01$, which implies that men report higher numbers of psychedelics used. Table 3 shows the correlations between the IUS-12, DTS, ASI-3, trait anxiety and MEQ scores. Each scale's sub-scales are highly correlated, bringing support to the validity of the scales. The four anxiety measures are also highly positively correlated (for IU, AS, and trait anxiety), respectively negatively correlated (for DT) among each other, which points towards them being related underlying construct of psychiatric symptomatology. There are also small correlations between the MEQ total score and its subscales (except transcendence and ineffability) and trait anxiety.

Table 3. Correlation table of anxiety vulnerabilities, trait anxiety and scores on the mystical experiences questionnaire

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. STAI-Trait anxiety	-												
2. IUS total	.68**	-											
3. IUS prospective	.49**	.90**	-										
4. IUS inhibitory	.72**	.89**	.59**	-									
5. DTS total	-.69**	-.61**	-.47**	-.61**	-								
6. DTS tolerance	-.55**	-.53**	-.44**	-.51**	.89**	-							
7. DTS absorption	-.68**	-.55**	-.41**	-.58**	.91**	.77**	-						
8. DTS regulation	-.42**	-.41**	-.32**	-.41**	.77**	.58**	.55**	-					
9. DTS appraisal	-.73**	-.61**	-.47**	-.63**	.90**	.74**	.82**	.58**	-				
10. ASI total	.67**	.61**	.49**	.61**	-.66**	-.56**	-.60**	-.47**	-.67**	-			
11. ASI social concerns	.62**	.57**	.46**	.56**	-.56**	-.46**	-.52**	-.37**	-.58**	.83**	-		
12. ASI cognitive concerns	.60**	.52**	.40**	.52**	-.62**	-.53**	-.55**	-.44**	-.63**	.87**	.58**	-	
13. ASI physical concerns	.48**	.47**	.39**	.46**	-.50**	-.42**	-.46**	-.39**	-.49**	.84**	.55**	.62**	-
14. MEQ total	-.13**	-0.08	-0.07	-0.08	0.04	0.04	0.05	-0.02	0.06	-0.02	-0.03	0	-0.01
15. MEQ transcendence	-0.06	-0.08	-0.07	-0.06	0	0	0.01	-0.01	0.02	0	-0.03	0.02	0.01
16. MEQ positive mood	-.14**	-0.08	-0.06	-0.08	0.05	0.04	0.08	-0.03	.08*	-0.06	-0.05	-0.05	-0.06

17. MEQ ineffability	-0.03	0	0	0.01	0.04	0.03	0.03	0.03	0.04	0.01	0.04	0	0
18. MEQ mystical	-.13**	-0.08	-0.07	-0.07	0.04	0.05	0.06	-0.03	0.06	-0.01	-0.02	0	0

Note: STAI= State-Trait anxiety inventory, DTS= Distress Tolerance Scale, IUS= Intolerance of uncertainty Scale-12, ASI= Anxiety Sensitivity Inventory-3; MEQ= Mystical experiences questionnaire; * p< 0.05., ** p<0.01., *** p< .001.

Table 4 presents correlations between frequency of psychedelic drugs used and scores on the MEQ and its subscales. Higher frequency of psychedelics used during one's lifetime (except ibogaine and peyote, likely due to the very small number of participants that have used them: 4, respectively 21) is positively correlated (low and medium) to higher MEQ total scores, as well as to the transcendence and mystical subscales. This points towards the mystical and transcendent experience of psychedelics being of utmost importance in determining more frequent use, likely due to the positive and spiritual experience associated with it.

Table 4. Correlations between frequency of psychedelics drugs use and scores on the mystical experience questionnaire

	MEQ total	MEQ transcendence	MEQ positive mood	MEQ ineffability	MEQ mystical
Psilocybin	.26**	.24**	.10*	.10*	.28**
LSD	.25**	.19**	.12**	.18**	.25**
DMT	.20**	.25**	0.08	.11*	.18**
MDMA	.18**	.18**	.20**	0.03	.16**
Ayahuasca	.16**	.15**	0.08	0.06	.15**
Ibogaine	0.06	0.06	0.01	-0.02	0.07
Peyote	0.05	0.06	0.04	0.04	0.04
Mescaline	.10*	.12**	0.02	0.00	.10*
Ketamine	.15**	.19**	.10*	0.04	.13**

Note: Categories of answers on frequency of psychedelic drugs questions in order of associated score: never, once, 2-5 times, 6-10 times, 11-20 times, 21-49 times, over 50 times (higher scores= more frequent use), MEQ= Mystical Experience Questionnaire; * p< 0.05., ** p<0.01., *** p< .001.

Table 5 presents the correlations between the frequency of use of each separate psychedelic drug and the scores (subscales and total scores) on the IUS-12, DTS, ASI-3 and trait anxiety. Trait anxiety, and total and subscale scores of IUS-12 and ASI-3 (except physical concerns) scores have a marginally significant negative correlation with frequency of psilocybin, LSD and DMT use. DTS total and subscale scores (except appraisal) have a marginally significant positive correlation with

frequency of LSD use. Unfortunately, no conclusion can be drawn regarding the direction of this relationship, considering smaller anxiety scores could determine more frequent psychedelic use and not the other way around, but it does appears that more frequent psychedelic use does not determine worse outcomes on anxiety variable scores.

Table 5. Correlations between frequency of psychedelics drug used and scores on the anxiety variables and all their subscales

	Psilocybin	LSD	DMT	MDMA	Ayahuasca	Ibogaine	Peyote	Mescaline	Ketamine
STAI- Trait anxiety	-.11**	-.09*	-.09*	0.00	-0.05	0.03	-0.01	0.01	0.00
IUS total	-.13**	-.15**	-.15**	-0.06	-0.06	-0.02	-0.05	-0.05	-0.04
IUS prospective	-.15**	-.14**	-.17**	-0.07	-0.08	-0.03	-0.02	-0.04	-0.06
IUS inhibitory	-0.08	-.13**	-.09*	-0.03	-0.04	-0.01	-0.07	-0.05	-0.01
DTS total	.09*	.11*	0.08	0.01	0.07	-0.03	0.03	-0.03	0.02
DTS tolerance	.11*	.12**	0.06	0.04	0.06	-0.01	0.01	-0.02	0.04
DTS absorption	0.08	.12**	.09*	-0.02	0.03	0.00	0.03	-0.04	0.02
DTS regulation	0.05	.09*	0.04	0.01	0.07	-0.06	0.05	-0.03	-0.03
DTS appraisal	.09*	0.06	0.08	0.01	0.07	-0.04	0.01	-0.02	0.04
ASI total	-.12**	-.11**	-.12**	0.04	-.09*	0.07	-0.03	-0.02	0.00
ASI social concerns	-.11*	-.11**	-.11*	0.03	-0.08	0.03	0.00	-0.01	0.04
ASI cognitive concerns	-.14**	-.11*	-.11*	0.05	-.09*	0.06	-0.03	-0.01	-0.05
ASI physical concerns	-0.06	-0.06	-0.08	0.02	-0.07	.09*	-0.04	-0.02	0.01

Note: Categories of answers on frequency of psychedelic drugs questions in order of associated score: once, 2-5 times, 6-10 times, 11-20 times, 21-49 times, over 50 times, never. STAI= State-Trait anxiety inventory, IUS= Intolerance of uncertainty Scale-12, DTS= Distress Tolerance Scale, ASI= Anxiety Sensitivity Inventory-3; * p< 0.05., ** p<0.01., *** p< .001.

Multiple Regression

Table 6 presents the results of the stepwise multiple regression analysis that assessed the predicting value of the subscales of IUS-12, DTS, ASI-3, and a diagnosis of depressive disorder, towards the outcome variable trait anxiety in the group of participants that never used psychedelics. Considering there is little theoretical background regarding the comparative importance of each of the anxiety vulnerabilities in predicting trait anxiety, a stepwise regression was chosen in order to assess the importance of each variable every step of the way. This method of regression removes all variables that independently do not have a predicting value on the outcome variable, thus the four variables included in the table below all have a significant predicting value on trait anxiety. The multiple regression model, with the four predictors included, produced $R^2 = .677$, $F(4, 65)= 34.099$, $p < .001$., which implies the model is statistically significant. The predicting variables account for 67.7% variability in trait anxiety.

Table 6. Multiple regression table for trait anxiety as DV and all the anxiety vulnerability subscales, and depressive disorder diagnosis as predictor variables, for the group that never used psychedelics

	M1			M2			M3			M4		
	B	SE	Beta	B	SE	Beta	B	SE	Beta	B	SE	Beta
(Constant)	38.93	1.46		27.75	2.67		40.57	5.35		37.93	5.24	
AS cognitive concerns	1.23	0.16	0.69***	0.84	0.16	0.47***	0.62	0.17	0.34**	0.43	0.18	0.24*
IUS inhibitory				1.19	0.25	0.43***	0.99	0.25	0.36***	0.85	0.25	0.30**
DTS absorption							-2.89	1.06	-0.26**	-2.86	1.02	-0.26**
AS social concerns										0.52	0.20	0.23*
R2	0.470			0.605			0.644			0.677		
F	60.393***			52.213***			39.872***			34.099***		
R2 change	0.470			0.134			0.040			0.033		
F change	60.393***			22.732***			7.402***			6.611***		

Note: Dependent variable: STAI (State-Trait anxiety inventory) Trait Anxiety; DTS= Distress Tolerance Scale, IUS= Intolerance of Uncertainty Scale, ASI= Anxiety Sensitivity Inventory; M= Model; * p< 0.05., ** p<0.01., *** p< .001.

Table 7 presents the results of the multiple regression analysis that assessed the predictive value of different variables towards the outcome variable trait anxiety in the psychedelic user group. Stepwise regression was again chosen due to the lack of theoretical background regarding the predictive value of anxiety vulnerabilities, psychedelic drug use, and mystical experiences associated with it, on trait anxiety. Initially, all DTS, IUS-12, ASI-3 and MEQ subscales were included, as well as depressive disorder diagnosis, and frequency of psychedelic drug use. Only the eight variables included in the table had a p-value significant at the 0.001 and 0.05 level, thus being meaningful additions to the model as predictors of trait anxiety. Considering all the regression coefficients are significant and large, we can conclude that the changes in the predictor variables

determine changes in the outcome variable (trait anxiety). The multiple regression model, with the eight predictors included, resulted in $R^2 = .708$, $F(8, 496) = 150.518$, $p < .001$., which implies the model is statistically significant. Additionally, it shows that IU Inhibitory, DT Appraisal, Absorption and Regulation, AS for cognitive and social concerns, a diagnosis of depressive disorder, and MEQ Positive Mood account for 70.8% of variability in trait anxiety in a psychedelic-using group.

Table 7. Multiple regression table for trait anxiety as DV and all the anxiety vulnerability subscales, MEQ subscales, and depressive disorder diagnosis as predictor variables, for the psychedelic users group

	M1			M2			M3			M4		
	B	SE	Beta	B	SE	Beta	B	SE	Beta	B	SE	Beta
(Constant)	76.48	1.25		52.39	2.14		47.07	2.29		45.98	2.25	
DTS appraisal	-8.81	0.36	-0.73***	-5.41	0.41	-0.45***	-4.53	0.43	-0.38***	-4.30	0.42	-0.36***
IUS inhibitory				1.06	0.08	0.44***	0.91	0.08	0.38***	0.88	0.08	0.37***
ASI social concerns							0.41	0.07	0.19***	0.39	0.07	0.18***
Depressive disorder										3.59	0.76	0.12***
MEQ positive mood												
DTS absorption												
ASI cognitive concerns												
DTS regulation												
R2	0.540			0.656			0.677			0.690		
F	590.713***			479.394***			349.407***			278.671***		
R2 change	0.540			0.116			0.020			0.014		
F change	590.713***			169.819***			31.389***			22.171***		

Note: Dependent variable: STAI (State-Trait anxiety inventory) Trait Anxiety; DTS= Distress Tolerance Scale, IUS= Intolerance of Uncertainty Scale-12, ASI= Anxiety Sensitivity Inventory-3; * p< 0.05., ** p<0.01., *** p< .001.

Table 7 (continued)

	M5			M6			M7			M8		
	B	SE	Beta	B	SE	Beta	B	SE	Beta	B	SE	Beta
(Constant)	50.80	2.75		51.89	2.76		50.57	2.80		48.63	2.89	
DTS appraisal	-4.26	0.42	-0.36***	-3.11	0.56	-0.26***	-2.80	0.58	-0.23***	-3.16	0.59	-0.26***
IUS inhibitory	0.87	0.08	0.37***	0.84	0.08	0.35***	0.82	0.08	0.34***	0.82	0.08	0.35***
ASI social concerns	0.40	0.07	0.18***	0.39	0.07	0.18***	0.34	0.07	0.15***	0.34	0.07	0.15***
Depressive disorder	3.44	0.76	0.12***	3.34	0.75	0.11***	3.42	0.75	0.12***	3.44	0.75	0.12***
MEQ positive mood	-1.21	0.41	-0.07**	-1.23	0.40	-0.08**	-1.23	0.40	-0.08**	-1.12	0.40	-0.07**
DTS absorption				-1.40	0.47	-0.13**	-1.37	0.47	-0.13**	-1.53	0.47	-0.14***
ASI cognitive concerns							0.17	0.07	0.08*	0.18	0.07	0.08*
DTS regulation										0.98	0.39	0.08*
R2	0.696			0.701			0.705			0.708		
F	228.263***			194.733***			169.285***			150.518***		
R2 change	0.005			0.005			0.003			0.004		
F change	8.937**			8.935**			5.660*			6.364*		

Note: Dependent variable: STAI (State-Trait anxiety inventory) Trait Anxiety; DTS= Distress Tolerance Scale, IUS= Intolerance of Uncertainty, Scale-12, ASI= Anxiety Sensitivity Inventory-3; M= Model; * p< 0.05., ** p<0.01., *** p< .001.

Discussion

Overview

The current study aimed to look at the influence of anxiety vulnerabilities on trait anxiety, as well as the relationship between these anxiety constructs and psychedelic drug use in terms of type used, frequency, and subjective experience of the drugs. The participants were preponderantly white males between the ages of 18 and 25 with a high-school or undergraduate degree. Slightly less than half had a mental health diagnosis, depression and anxiety being the most common. Most had taken psychedelics at least once during their lifetime, but this is probably sample bias due to the nature of the websites where the questionnaire was posted. Psilocybin and LSD were the most commonly used psychedelics. Correlation analysis revealed that having used psychedelics was moderately correlated to being a male.

The relationship between the three anxiety vulnerability factors and trait anxiety

The anxiety vulnerability total scores were highly correlated to their subscales, which brings support their construct validity. IUS-12, ASI-3 and all their subscales were all strongly positively correlated amongst themselves, as well as to trait anxiety. Consistent with the model described by Zvolensky et al. (2010), as well as with previous empirical studies reporting pairwise correlations between the DTS and various versions of the ASI and IUS in clinical and non-clinical samples (Carleton et al., 2007; Carleton, Collimore, & Asmundson, 2010; Laposa et al., 2015; Norr et al., 2013), the current study found that participants who reported higher trait anxiety also reported significantly lower levels of

tolerance for distress, significantly greater sensitivity to anxiety symptoms, and significantly higher levels of intolerance of uncertainty.

For example, Laposa et al. (2015) reported pairwise correlations between total scores on the DTS and ASI-3 of -0.39, a somewhat smaller number than the one observed in this study (r = -0.66). Laposa et al.'s (2015) participants where all treatment seeking individuals with an anxiety disorder, thus it is possible that other variables might have been present that determined a lower correlation between DT and AS. Another previous study by Norr et al (2013) reported a correlational value of -0.53 when controlling for negative affect and -0.44 when controlling for trait anxiety, values that are closer to the ones of the current study, and the existing difference most likely being due to the control variables included by the authors of that study. Correlations between the DTS and IUS have been reported in the range of -0.44 to -0.53 (Laposa et al., 2015; Norr et al., 2013): the observed correlation in this study for total scores of the two constructs (-0.61) being toward the higher end of that range, but nevertheless not very different. Correlations between AS and IU has previously been reported in the range of 0.43 to 0.71 (Laposa et al., 2015; Carleton et al., 2010; Norr et al, 2013) and the current study found a correlation between IU and AS total scores of 0.61, which is in the expected range. Carleton et al.'s (2010) study found the correlations between the subscales of ASI-3 and IUS-12 (r between 0.43 and 0.71) to be slightly higher than the current study (r between 0.39 and 0.56). A possibility for this slight discrepancy is the fact that their sample consisted of mostly females, while the current study's sample consisted of mostly males, which could potentially explain the slightly higher correlation scores in their samples, females usually scoring higher on anxiety constructs (Bahrami & Yousefi, 2011).

Relationship between psychedelic use and anxiety constructs

No study to date has looked at the correlations between psychedelic drug use and the three anxiety vulnerability factors and trait anxiety, and the current exploratory study was intended to begin to fill this gap in knowledge. Consistent with expectations, participants who reported a higher frequency use of psilocybin, LSD and DMT reported lower scores on the measures of intolerance of uncertainty, anxiety sensitivity and trait anxiety. Participants who reported a higher frequency use of Psilocybin and LSD reported slightly higher scores on the measure of distress tolerance (indicating greater tolerance for distress). It is important to point out that these correlations, while statistically significant, were in the small range. Additionally, no assumption about causation or the direction of the effect can be made from a correlational, cross-sectional study employing no control group such as the current study. Moreover, as will be discussed later, including frequency of psychedelic drug use in the regression analysis did not explain a significant proprortion of the variance in trait anxiety. None of the other psychedelics included in the current study were significantly correlated with either DT, AS, IU or trait anxiety.

In conclusion, no strong conclusion can be drawn regarding the relationship between psychedelic drugs and the four anxiety constructs,

Mystical experiences, frequency of psychedelic drug use, and anxiety constructs

Higher frequency of psychedelics used during one's lifetime was positively correlated (low and medium) to higher mystical experience scores. This can be explained in two different ways: having more enhanced mystical experiences after taking psychedelics

makes people more likely to continue taking psychedelics, or that by taking more psychedelics, people start coping better with the negative aspects of the trip which leads to more enhanced mystical experiences. Significant, but very low, negative correlations existed between some mystical experience subscales and trait anxiety (higher scores of mystical experiences were correlated with lower scores on trait anxiety). Nevertheless, the effect is very small, and the direction of the effect is unclear.

Carhart-Harris et al. (2016): found that participant ratings of “ego-dissolution” and “altered meaning” during an LSD "trip" correlated strongly with a decreased connectivity between the parahippocampus and retrosplenial cortex, which they attribute to the role this brain circuit has in the maintenance of “self” and “ego” and its processing of “meaning.”. This finding, as well as the correlation they found between decreased posterior cingulate cortex alpha power and ego-dissolution, is consistent with previous research on psilocybin. (Carhart-Harris et al., 2012). But is it this "loss of ego" and associated mystical experience that determines the beneficial therapeutic effects of psychedelics, or is it the chemical component of psychedelics? According to Majić, Schmidt and Gallinat (2015), while modern psychopharmacologic drug development primarily targets biological mechanisms, psychedelics have been assumed to exert their therapeutic actions by facilitating different types of therapeutically useful states of consciousness. The current study did show tentatively, according to the regression model further explained in the next section, that a more profound mystical experience, especially one characterized by high scores on the positive mood subscale of the mystical experience questionnaire, has a small significant predicting value on trait anxiety. Considering that the participants that had less mystical experiences still ingested the same chemical components but their anxiety scores

were not as good, one can assume that the mystical experience itself had a beneficial impact on anxiety. Nevertheless, due to the study being cross-sectional instead of longitudinal, we cannot discount the possibility that people had psychedelic experiences that were less mystical due to underlying anxiety issues (they could not relax enough and let go in order to enjoy the experience to the full extent).

The predicting value of anxiety vulnerabilities, diagnosis of depression, and mystical experiences on trait anxiety

To date, there are no studies looking at the regression model of the three anxiety vulnerability factors with trait anxiety as a dependent variable. The study with the closest aim to this is Norr et al'. (2013): their outcome variable was the Social Interaction Anxiety Scale, trait anxiety and gender were used as controls and predicted 26% of the variance, and IU, DT and AS, plus Discomfort Intolerance, predicted 10% of the variance. Nevertheless, DTS was found not to be significantly associated with Social Interaction Anxiety anymore when AS and IU where controlled for. Their second regression model, with non-hoarding OCD symptoms as an outcome variable and trait anxiety as a control, found that the four aforementioned anxiety vulnerability factors accounted for 21% of the variance, but when taking separately, distress tolerance again was not a significant predictor. A third regression model with worry as an outcome variable found that only IU was a significant predictor out of the four anxiety vulnerability factors. Laposa et al. (2015) ran different regression with Social Interaction Anxiety Scale, Penn State Worry Questionnaire, and Yale-Brown Obsessive-Compulsive Scale as outcome variables, and IU, DT and AS as predictors. When IU and AS were included in the regression model first, DT

was not significant anymore. These results point towards DT being indeed a higher order construct that includes AS and IU. Due to the overlap resulted from this hierarchical model, when entered into a regression model together, IU and AS cover the predictive value of DT and possibly add a small variance of their own, and render DT insignificant.

In the current study, two separate multiple regressions were run: one for the psychedelic-naïve group, and one for the group that have taken psychedelics. For the psychedelic naïve group, in order of importance, AS cognitive concerns, IU inhibitory, DT absorption and AS social concerns were found to predict 67.7% of the variance in trait anxiety scores. It appears that trait anxiety is affected by various subscales out of the three anxiety vulnerability factors, with AS having the slightly bigger impact. AS related to physical concerns and prospective IU (fear based on future events) did not have a significant impact on trait anxiety; while AS related to cognitive and social concerns and inhibitory IU (suffering from uncertainty that inhibits actions and experiences) did. Being consumed/ absorbed by the experience of distress (DTS Absorbed) also predicted trait anxiety, but none of the other DTS subscales did. These results are mostly in line with Norr et al.'s (2013) and Laposa et al.'s (2015) findings of DT losing its predicting value when AS and IU are introduced in the model, bringing further support to it being a higher order construct. Nevertheless, the absorption subscale of DT still had a significant impact, which could imply DT absorption is an underlying anxiety construct that is not covered by the AS and IU subscales.

In the psychedelic user group, a stepwise regression including the three anxiety vulnerabilities, frequency of psychedelic drug use, and the mystical experience associated

with the psychedelic drug use was performed. IUS Prospective, DTS tolerance and ASI Physical Concerns were excluded by SPSS, which is consistent with the first regression performed, and so was the frequency of use of all psychedelics and all MEQ sub-scales except Positive mood. As the correlation analyses showed a marginally significant relationship between drug use and trait anxiety, it was not surprising that the frequency of psychedelic drug use was not predictive of trait anxiety. The regression model indicated that, in order of their importance, DT Appraisal, IU Inhibitory, AS Social Concerns, Depressive Disorder, MEQ Positive mood, DT Absorption, AS Cognitive concerns, and DT Regulation account for 70.8% of variability in trait anxiety.

All the four anxiety vulnerability subscales that had a predicting effect in the first regression have a significant predicting effect in the second regression as well. Interestingly, it appears that DT is a more important predictor of trait anxiety in the psychedelic-using group: beside DT absorption, DT appraisal (a lack of acceptance of distress, being ashamed of being distressed, and perceiving other's ability to deal with distress as better than one's own) and regulation (going through a lot of effort to avoid negative emotions and utilizing rapid means of alleviating them) also have significant effects. Actually, it appears that DT appraisal is the most important predictor of trait anxiety in the second regression.

The most note-worthy additions in the regression model of the psychedelic-using group are a diagnosis of depression and MEQ positive mood. It appears that the use of a psychedelic drug with the experience being characterized by the user as "mystical and involving positive mood" was a significant predictor of less trait anxiety. Having a diagnosis

of depression was also a significant predictor of higher trait anxiety scores. Thus, the question arises: why does DT and a diagnosis of depression only predict trait anxiety in the psychedelic-using group and not the groupr reporting no use of psychelics? One possibility is that a diagnosis of depression in this study is based on self-report, and the results would have been different if the diagnosis was assessed through a standardized self-report measure of depression. Owing to the length of the survey, the author took the decision not to include a standardized self-report measure of depression and this is a weakness of this study.

DT appears to somehow stop overlapping with AS and IU subscales in the group of people that have taken psychedelics. A possible explanation for this could be found in Carhart-Harris et al.'s latest neuroimaging study on LSD (2016): they propose that psychedelics induce disintegration and desegregation of the neural networks responsible for emotional regulation and stress management. I propose that such a disintegration might determine a more balanced response to stress, anxiety-inducing stimuli, and negative aspects of day-to-day life, potentially due to an enhancement and maybe even a transformation of DT due to psychedelic use, and it is because of this effect that DT has a significant predicting value on trait anxiety in the psychedelic-using group compared to the psychedelic-naïve group. While this is an informed speculation at best, I propose it is a research avenue worth pursuing by future studies.

Limitations

The current study suffers from a number or limitations. First, it was correlational, cross-sectional, and lacked a control group, with decreases the validity and reliability of the

results, and no causal relationships can be drawn. The direction of the relationship between trait anxiety, anxiety vulnerabilities, and psychedelic drug use is unknown, and the possibility of a third variable with a strong impact on the scores cannot be excluded. Second, it had a strong selection bias due to the nature of the websites where the survey was posted, many of which had users with a positive view on drugs. Third, web-based questionnaires are inherently unreliable. Fourth, the psychiatric diagnosis was only assessed through self-report, thus the variable of having a depressive disorder that was included in the regression is not completely reliable. Future studies should aim to assess symptomatology either with a very inclusive questionnaire such as the Structured Clinical *Interview* for DSM-5 (*SCID*-5), or focus on specific symptomatology, for example using Beck Depression Inventory. In light of these limitations, and considering the small correlational effects, no conclusions can be drawn regading the relationship between psychedelic drugs and anxiety constructs.

When performing regression analysis, the IVs should not be correlated, but in the current analysis this was not the case, because the three anxiety vulnerability subscales were all slightly correlated. Nevertheless, the collinearity condition index did not surpass 30 for any of the variables, and most were under 10.

A limitation that was out of the control of the current study's researcher is the lack of consensus in the literature regarding the three anxiety vulnerability constructs. For example, various different measures representing distinct construct maintain to represent distress tolerance, and this makes generalizations across the literature and studying the transdiagnostic potential of the construct problematic (Bardeen, Fergus, & Orcutt, 2013).

The current study used the newer and improved scales/ inventories from the literature that have also been tested for variability and reliability.

Future directions

While this study was cross-sectional, future longitudinal studies should observe the long-term effects of suffering from these vulnerabilities on developing trait anxiety, and ultimately, anxiety disorders. Identifying ways to address the development of anxiety disorders when they are in their incipient stages, thus preventing them instead of waiting until aggressive treatment is the only option, is of utmost importance. Identifying people at risk due to their high scores on anxiety vulnerabilities followed by preventive treatments, would determine better mental health outcomes for the people in question, less suffering, as well as societal cost savings. Further attempt should be made to understand the hierarchical model between these anxiety constructs, and a proposed recommendation would be to control for different individual characteristics of the participants.

If proven safe and efficient, treatment with psychedelics would only include a few doses over a long time span instead of daily use, and the cost for one dose is very small. While the 'trip' itself is quite long and requires clinician supervision, it is still a smaller time commitment to both the patient and the clinician compared to cognitive behavioural therapy, and can be further reduced if the same clinician oversees more patients going through the therapy simultaneously, either as a group or in separate rooms, but at the same time. Since they are not addictive, there is a much smaller chance of the patients becoming dependent compared to other psychiatric drugs. Thus, psychedelic therapy for anxiety

disorders has the potential to be less time-consuming, cheaper, and possibly even more efficient than the current treatment plans (Nutt, 2013).

Future research should also attempt to find out if it is the chemical components of psychedelics are the reason for a positive change in mental health diagnosis, or if psychedelics are just "aids" that enhance the effects of therapy. A type of therapy that has the potential to work well in combination with psychedelic intervention is mindfulness. Mindfulness is defined as "paying attention in a particular way: on purpose, in the present moment and non-judgmentally" and is a type of meditation that has now been integrated in many mental health therapies (Josefsson, Lindwall, & Broberg, 2014). Various studies have found mindfulness-based therapy to be effective in various contexts: patients diagnosed with anxiety disorders (Vøllestad, Nielsen, & Nielsen, 2012; Josefsson et al., 2014), improving anxiety and stress in children and adolescents (Kallapiran, Koo, Kirubakaran, & Hancock, 2015), reducing anxiety in patients with cancer (Zhang, Wen, Liu, Peng, Wu, & Liu, 2015) and improving PTSD symptoms (Banks, Newman, & Saleem, 2015). Mindfulness meditation has also been found to be connected with mystical experiences (Mysticism Scale, not MEQ), although there is little quantitative research on the topic (de Castro, 2015). Thus, we propose a future double-blind, randomized clinical trial where participants suffering from anxiety disorder, or having high scores on anxiety vulnerability constructs with potential to develop into full-blown disorder, would (a) take psychedelics in combination with mindfulness therapy, (b) take psychedelics without any other intervention, or (c) take part in normal mindfulness therapy. An interesting follow-up question from such a study is whether combining mindfulness with the psychedelic

intervention would determine higher MEQ scores (which would be assessed at various times), and a more positive mental health outcome following the treatment.

Conclusion

In conclusion, DT, AS and IU are three putative mediators or vulnerabilities for emotional distress that show moderate to strong relationships with symptoms of trait anxiety. A clear hierarchical model cannot be drawn in light of the current results, especially considering the differences between the naïve and psychedelic-using group. While the first regression brought support to the notion of DT being a higher order construct that includes AS and IU, in the psychedelic using group DT was a significant predicting factor in itself and not overlapping with AS and IU. Nevertheless, it appears all three anxiety vulnerability factors and their subscales are highly intertwined, and a tentative conclusion, until a better model appears, is that the hierarchy among them varies depending on the individual characteristics of the participants (psychedelic users, age, gender, etc.). Future studies should look at the effect individual characteristics have on the predictive value of the anxiety vulnerabilities on trait anxiety, and determine how psychedelics affect anxiety vulnerabilities and how this can be used in psychedelic-assisted therapies.

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References

Aghajanian, G. K., & Marek, G. J. (1999) Serotonin, via 5-HT2A receptors, increases EPSCs in layer V pyramidal cells of prefrontal cortex by an asynchronous mode of glutamate release. *Brain Research, 825*, 161–171.

Albaugh, B.J., & Anderson, P.O. (1974). Peyote in the treatment of alcoholism among American Indians. *American Journal of Psychiatry,* 131(11), 1247-1250.

Andlin-Sobocki, P., Jönsson, B., Wittchen, H.-U., & Olesen, J. (2005). Cost of disorders of the brain in Europe. *European Journal of Neurology, 12*, *Supplement 1*, 1-27. http://dx.doi.org/10.1111/j.1468-1331.2005.01202.x

Bahrami, F., & Yousefi, N. (2011). Females are more anxious than males: a metacognitive perspective. *Iran Journal of Psychiatry and Behavioural Science, 5*(2), 83-90.

Banks, K., Newman, E., & Saleem, J. (2015). An Overview of the Research on Mindfulness-Based Interventions for Treating Symptoms of Posttraumatic Stress Disorder: A Systematic Review. *Journal of Clinical psychology, 71*(10), 935-963, http://dx.doi.org/10.1002/jclp.22200

Bardeen, J. R., Fegus, T. A., & Orcutt, H. K. (2013). Testing a Hierarchical Model of Distress Tolerance. *Journal of Psychopathology and Behavioural Assessemnet, 35*, 495–505. http://dx.doi.org/10.1007/s10862-013-9359-0

Barrett, F. S., Johnson, M. W., & Griffiths, R. R. (2015). Validation of the revised Mystical Experience Questionnaire in experimental sessions with psilocybin. *Journal of*

Psychopharmacology, 29(11), 1182–1190. http://dx.doi.org/10.1177/0269881115609019

Brandon, T. H., Herzog, T. A., Juliano, L. M., Irvin, J. E., Lazev, A. B., & Simmons, V. N. (2003). Pretreatment task persistence predicts smoking cessation outcome. *Journal of Abnormal Psychology, 112*(3), 448–456.

Buckner, J. D., Keough, M. E., & Schmidt, N. B. (2007). Problematic alcohol and cannabis use among young adults: The roles of depression and discomfort and distress tolerance. *Addictive Behaviors, 32*(9), 1957-1963. http://dx.doi.org/10.1016/j.addbeh.2006.12.019

Buhr, K., & Dugas, M. J. (2002). The intolerance of uncertainty scale: psychometric properties of the English version. *Behaviour Research and Therapy, 40*(8), 931–945. http://dx.doi.org/10.1016/S0005-7967(01)00092-4

Carhart-Harris, R. L., & Nutt, D. J. (2010). User perceptions of the benefits and harms of hallucinogenic drug use: A web-based questionnaire study. *Journal of Substance Use, 15*(4), 283–300. http://dx.doi.org/10.3109/14659890903271624

Carhart-Harris, R. L., Erritzoe, D., Williams, T., Stone, J. M, Reed, L. J., Colasanti, A.,…, & Nutt, D. J. (2012) Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences of the USA, 109*(6), 2138–2143. http://dx.doi.org/10.1073/pnas.1119598109

Carhart-Harris, R. L., Muthukumaraswamy, S., Roseman, L., Kaelen, M., Droog, W., Murphy, K.,… & Nutt, D.J. (2016). Neural correlates of the LSD experience revealed by multimodal neuroimaging. *Proceedings of the National Academy of Sciences of the United States of America,* Advance online publication. http://dx.doi.org/10.1073/pnas.1518377113

Carleton, R. N., Norton, P. J., & Asmundson, G. J. G. (2007). Fearing the unknown: A short version of the Intolerance of Uncertainty Scale. *Journal of Anxiety Disorders, 21*, 105–117. http://dx.doi.org/10.1016/j.janxdis.2006.03.014

Carleton, R. N., Collimore, K. C., & Asmundson, G. J. G. (2010). ‘‘It’s not just the judgements—It’s that I don’t know’’: Intolerance of uncertainty as a predictor of social anxiety. *Journal of Anxiety Disorders, 24*, 189–195. http://dx.doi.org/10.1016/j.janxdis.2009.10.007

de Castro, J. M. (2015). Meditation has stronger relationships with mindfulness, kundalini, and mystical experiences than yoga or prayer. *Consciousness and Cognition, 35*, 115–127. http://dx.doi.org/10.1016/j.concog.2015.04.022

Chambers, J. A., Power, K. G., & Durham, R. C. (2004). The relationship between trait vulnerability and anxiety and depressive diagnoses at long-term follow-up of Generalized Anxiety Disorder. *Journal of Anxiety Disorders, 18*(5), 587–607. http://dx.doi.org/10.1016/j.janxdis.2003.09.001

Gasser, P., Holstein D., Michel, Y., Doblin, R., Yazar-Klosinski, B., Passie, T., & Brenneisen, R. (2014). Safety and Efficacy of Lysergic Acid Diethylamide-Assisted Psychotherapy

for Anxiety Associated With Life-threatening Diseases. *The Journal of nervous and mental disease, 202*(7), 513-520. http://dx.doi.org/10.1097/NMD.0000000000000113

Ghasemi, A., & Zahediasl, S. (2012). Normality Tests for Statistical Analysis: A Guide for Non-Statisticians. *International Journal of Endocrinology and Metabolism, 10*(2), 486–489. http://dx.doi.org/10.5812/ijem.3505

Griffiths, R. R., Richards, W. A., McCann, U., & Jesse, R. (2006) Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Journal of Psychopharmacology, 187*, 268–283. http://dx.doi.org/10.1007/s00213-006-0457-5

Griffiths, R. R., Richards, W. A., Johnson, M. W., McCann, U., & Jesse, R. (2008). Mystical-type experiences occasioned by psilocybin mediate the attribution of personal meaning and spiritual significance 14 months later. *Journal of Psychopharmacology, 22*(6), 621–632. http://dx.doi.org/10.1177/0269881108094300

Griffiths, R. R., Johnson, M. W., Richards, W. A., McCann, U., & Jesse, R. (2011). Psilocybin occasioned mystical-type experiences: immediate and persisting dose-related effects. *Journal of Psychopharmacology, 218*, 649–665. http://dx.doi.org/10.1007/s00213-011-2358-5

Halpern, J.H. (2003). Hallucinogens: An update. *Current Psychiatry Reports, 5,* 347-354.

Hapern, J.H., Pope Jr., H.G.P. (2003). Review: Hallucinogen Persisting perception disorder. What do we know after 50 years? *Drug and Alcohol Dependence, 69,* 109-119.

Hendricks, P. S.,Thorne, C. B., Clark, C. B., Coombs, D. W., & Johnson, M. W. (2015). Classic psychedelic use is associated with reduced psychological distress and suicidality in the United States adult population. *Journal of Psychopharmacology, 29*(3), 280– 288, http://dx.doi.org/10.1177/0269881114565653

Faul, F., Erdfelder, E., Lang, A.-G. & Buchner, A. (2007). G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods, 39*, 175-191.

Frokjaer, V. G., Mortensen, E. L., Nielsen, F. A., Haugbol, S., Pinborg, L. H., Adams, K. H.,... & Knudsen, G. M. (2008). Frontolimbic serotonin 2A receptor binding in healthy subjects is associated with personality risk factors for affective disorder. *Biological Psychiatry, 63*, 569–576. http://dx.doi.org/10.1016/j.biopsych.2007.07.009

Johansen, P., & Krebs, T. S. (2015). Psychedelics not linked to mental health problems or suicidal behavior: A population study. *Journal of Psychopharmacology, 29*(3)*,* 270-27. http://dx.doi.org/10.1177/0269881114568039

Josefsson, T., Lindwall, M., & Broberg, A.G. (2014). The Effects of a Short-term Mindfulness Based Intervention on Self-reported Mindfulness, Decentering, Executive Attention, Psychological Health, and Coping Style: Examining Unique Mindfulness Effects and Mediators, *Mindfulness, 5*, 18-35, http://dx.doi.org/10.1007/s12671-012-0142-1.

Kallapiran, K., Koo, S., Kirubakaran, R., & Hancock, K. (2015). Review: Effectiveness of mindfulness in improving mental health symptoms of children and adolescents: a meta-analysis. *Child and Adolescent Mental Health, 20*(4), 82–194, http://dx.doi.org/10.1111/c.

Kemper, C. J., Lutz, J., Bähr, T., Rüddel, H., & Hock, M. (2012). Construct Validity of the Anxiety Sensitivity Index–3 in Clinical Samples. *Assessment, 19*(1), 89–100. http://dx.doi.org/10.1177/1073191111429389

Krebs T.S., & Johansen P-Ø. (2013). Psychedelics and Mental Health: A Population Study. *PLoS ONE 8*(8). http://dx.doi.org/10.1371/journal.pone.0063972.

Laposaa, J. M., Collimorec, K. C., Hawleya, L. L., & Rector, N. A. (2015). Distress tolerance in OCD and anxiety disorders, and its relationship with anxiety sensitivity and intolerance of uncertainty. *Journal of Anxiety Disorders, 33.* http://dx.doi.org/10.1016/j.janxdis.2015.04.003

Lau, J. Y. F., Eley, T. C., & Stevenson, J. (2006). Examining the State-Trait Anxiety Relationship: A Behavioural Genetic Approach. *Journal of Abnormal Child Psychology, 34*(1), 19–27. http://dx.doi.org/10.1007/s10802-005-9006-7

Lyvers, M., & Meester, M. (2012). Illicit Use of LSD or Psilocybin, but not MDMA or Nonpsychedelic Drugs, is Associated with Mystical Experiences in a Dose-Dependent Manner, *Journal of Psychoactive Drugs, 44*(5), 410-417. http://dx.doi.org/10.1080/02791072.2012.736842

MacLean, K. A., Leoutsakos. J. M., Johnson, M. W., & Griffiths, R. R. (2012) Factor analysis of the Mystical Experience Questionnaire: a study of experiences occasioned by the hallucinogen psilocybin. *Journal for the Scientific Study of Religion, 51*, 721–737. http://dx.doi.org/10.1111/j.1468-5906.2012.01685.x

Muris, P., Schmidt, H., Merckelbach, H., & Schouten, E. (2001). Anxiety sensitivity in adolescents: factor structure and relationships to trait anxiety and symptoms of anxiety disorders and depression. *Behaviour Research and Therapy, 39*(1), 89–100. http://dx.doi.org/10.1016/S0005-7967(99)00179-5

Nichols, D. E. (2004). Hallucinogens. *Pharmacology and Therapeutics, 101*, 131-181.

Norr, A. M., Oglesby, M. E., Capron, D. W., Raines A. M., Korte, K. J., & Schmidt, N. B. (2013) Evaluating the unique contribution of intolerance of uncertainty relative to other cognitive vulnerability factors in anxiety psychopathology. *Journal of Affective Disorders, 151*(1), 136-142. http://dx.doi.org/10.1016/j.jad.2013.05.063

Nutt, D. (2013, June 12th). Medical breakthroughs missed because of pointless drug bans. *The Conversation.* Retrieved from: https://theconversation.com/medical-breakthroughs-missed-because-of-pointless-drug-bans-15072. Accessed on 17/04/16.

Nutt, D., King, L.A., Saulsbury, W., & Blakemore, C. (2007), Development of a rational scale to assess the harm of drugs of potential misuse. *Lancet, 369,* 1047-53.

Nutt, D.J., King, L.A., & Phillips, L.D. (2010) Drug harms in the UK: a multicriteria decision analysis*. Lancet, 376*, 1558–65.

Rambousek, L., Palenicek, T., Vales, K., & Stuchlik, A. (2014). The effect of psilocin on memory acquisition, retrieval, and consolidation in the rat. *Frontiers in Behavioral Neuroscience, 8*(180). http://dx.doi.org/10.3389/fnbeh.2014.00180

Simons, J. S., & Gaher, R. M. (2005). The Distress Tolerance Scale: Development and Validation of a Self-Report Measure. *Motivation and Emotion,* 29(2). http://dx.doi.org/10.1007/s11031-005-7955-3

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press

Stuhrmann, A., Dohm, K., Kugel, H., Zwanzger, P., Redlich, R., Grotegerd, D…, & Dannlowski, U. (2013). Mood-congruent amygdala responses to subliminally presented facial expressions in major depression: Associations with anhedonia. *Journal of Psychiatry and Neuroscience, 38*(4), 249–258. http://dx.doi.org/10.1503/jpn.120060

Sylvers, P., Lilienfeld, S. O., & LaPrairie, J. L. (2011). Differences between trait fear and trait anxiety: Implications for psychopathology. *Clinical Psychology Review, 31*, 122–137. http://dx.doi.org/10.1016/j.cpr.2010.08.004

Taylor, S., & Cox, B. J. (1998). An expanded anxiety sensitivity index: Evidence for a hierarchic structure in a clinical sample. *Journal of Anxiety Disorders*, *12*, 463-483. http://dx.doi.org/10.1016/S0887-6185(98)00028-0

Taylor, S., Zvolensky, M. J., Cox, B. J., Deacon, B., Heimberg, R. G., Ledley, D. R., . . . & Cardenas, S. J. (2007). Robust dimensions of anxiety sensitivity: Development and

initial validation of the Anxiety Sensitivity Index-3. *Psychological Assessment*, *19*, 176-188. http://dx.doi.org/10.1037/1040-3590.19.2.176

Vollenweider, F.X., & Kometer, M. (2010). The neurobiology of psychedelic drugs: implications for the treatment of mood disorders. *Nature, 11*, http://dx.doi.org/10.1038 /nrn2884.

Vøllestad, J., Nielsen, M. B., & Nielsen, G. H. (2012). Mindfulness- and acceptance-based interventions for anxiety disorders: A systematic review and meta-analysis. *British Journal of Clinical Psychology, 51*, 239–260. http://dx.doi.org/10.1111/j.2044-8260.2011.02024.x.

Zhang, M-F., Wen, Y-S., Liu, W-Y., Peng, L-F., Wu, X-D., & Liu, Q-W. (2015). Effectiveness of Mindfulness-based Therapy for Reducing Anxiety and Depression in Patients with Cancer: A Meta-analysis. *Medicine, 94*(45), e0897-0, http://dx.doi.org/10.1097/MD.0000000000000897.

Zvolensky, M.J., Vujanovic, A.A., Bernstein, A., & Leyro, T. (2010). Distress tolerance: Theory, measurement, and relations to psychopathology. *Current Directions in Psychological Science, 19,* 406-410.