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Psychedelic Microdosing, Mindfulness, and Anxiety: A Cross-Sectional Mediation Study

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ABSTRACT

While anecdotal reports claim that psychedelic microdosing reduces anxiety and mood symptoms, evidence supporting these claims is scarce. This cross-sectional study investigated the association between microdosing and trait anxiety. Furthermore, it was investigated if trait mindfulness mediated this association. Participants completed anonymous online questionnaires and were divided into three groups: current microdosers (n = 186), former microdosers (n = 77) and microdosing-naïve controls (n = 234). Trait anxiety and trait mindfulness were measured using the State-Trait Anxiety Inventory – Trait subscale (STAI-T) and the 15-item Five-Facet Mindfulness Questionnaire (FFMQ-15) respectively. Current and former microdosers reported lower STAI-T scores compared to microdosing-naïve controls. Furthermore, associations of current and former microdosing with trait anxiety were mediated by trait mindfulness, with small effects of FFMQ-15 Total, Non-judging and Non-reactivity scores. However, in an exploratory analysis, all associations between microdosing and STAI-T scores became non-significant when participants with previous macrodose experience (n = 386) were excluded. Our findings suggest that RCT<apos;>s are warranted to test causal hypotheses concerning the effects of microdosing and the role of trait mindfulness in the effects of microdosing, while controlling for previous macrodose experience.

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Microdosing; psychedelics; anxiety; mindfulness; psilocybin; LSD

Introduction

Microdosing refers to the practice of regularly ingesting a sub-hallucinogenic dose of a psychedelic substance. Classical psychedelics are a group of compounds that share a common mechanism of action as 5-HT2A receptor agonists. A regular dose of a classical psychedelic can induce alterations in cognition, perception, and emotion (Halberstadt 2015; Nichols 2016), along with mystical experiences (Griffiths et al. 2011; Liechti, Dolder, and Schmid 2017) and ego dissolution (Nour et al. 2016). In contrast, a sub-hallucinogenic dose, typically one-tenth of a regular dose, does not induce these alterations or experiences (Fadiman 2011). Lysergic acid diethylamide (LSD) and psilocybin mushrooms are the most commonly microdosed psychedelics, at a frequency of two to four times per week (Hutten et al. 2019; Johnstad 2018; Rosenbaum et al. 2020). In recent years, microdosing attracted considerable attention in popular media, where it is reported to enhance productivity and reduce anxiety and mood symptoms (Garlick 2019; Glatter 2015; Nye 2017; Siebert 2020; Turk 2019; Waldman 2017). Current research concerning the effects of microdosing has focused on determining dose-effect relationships (Bershad et al. 2019; Holze et al. 2020; Hutten et al. 2020) or patterns of use and associated outcomes (Andersson and Kjellgren 2019; Hutten et al. 2019; Johnstad 2018; Webb, Copes, and Hendricks 2019). Findings have been inconclusive, with some studies observing that microdosing is associated with improved mental health (Anderson et al. 2019) and others observing increased anxiety in microdosers compared to controls (Bright et al. 2021; Hutten et al. 2020).

While the scientific evidence to support anecdotal claims concerning microdosing remains inconclusive, more is known of the effects of psychedelics in moderate to large (macro-) doses. Multiple clinical trials have investigated the effectivity of psychedelic-assisted psychotherapy and found promising results for the treatment of anxiety in patients with life threatening diseases (Gasser et al. 2014; Griffiths et al. 2016; Grob et al. 2011; Ross et al. 2016) and treatment resistant depression (Carhart-Harris et al. 2018, 2016; Osório et al. 2015). In addition, psychedelic use is associated with positive personality change (Dressler, Bright, and Polito 2021; MacLean, Johnson, and Griffiths 2011) and mindfulness (Madsen et al. 2020; Soler et al. 2016; Uthaug et al. 2019) in healthy individuals. While multiple studies have demonstrated the physiological safety and low abuse

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potential of macrodoses (Carhart-Harris et al. 2018; Johnson et al. 2018; Moreno et al. 2006), they are not without risks. They often induce intense experiences which can lead to what is commonly known as a "bad trip," characterized by acute anxiety, fear, panic, dysphoria, and paranoia (Strassman 1984). While implementation of appropriate safeguards mitigates these risks (Johnson, Richards, and Griffiths 2008; Studerus et al. 2011), microdosing may circumvent them entirely, as it does not induce the intense experiences that characterize a bad trip (Fadiman 2011). Should microdosing be able to reproduce the positive effects found in macrodose research in a safer way, it could be a valuable tool in the treatment of anxiety and depression. As macrodoses have been found to be effective in the treatment of anxiety (Gasser et al. 2014; Griffiths et al. 2016; Grob et al. 2011; Ross et al. 2016) and treatment resistant depression (Carhart-Harris et al. 2018, 2016; Osório et al. 2015), and some early reports suggest the same for microdosing (Hutten et al. 2019; Johnstad 2018), the first aim of this study was to investigate if current microdosers report lower trait anxiety compared to microdosing-naïve controls. In addition, as macrodose effects are often long-term (Carhart-Harris et al. 2018; Gasser et al. 2014; Griffiths et al. 2016; Grob et al. 2011; Ross et al. 2016) and may include changes in relatively stable traits such as openness and neuroticism (Dressler, Bright, and Polito 2021; MacLean, Johnson, and Griffiths 2011) and mindfulness (Madsen et al. 2020; Soler et al. 2016; Uthaug et al. 2019), the second aim of this study was to investigate if former microdosers also report lower trait anxiety compared to microdosing-naïve controls.

In recent years, the similarities between the phenomenology and neurophysiology of psychedelics and mindfulness meditation (MM) received increasing attention (Barrett and Griffiths 2018; Heuschkel and Kuypers 2020; Millière et al. 2018). MM refers to multiple meditation practices that find their origin in the Buddhist tradition and is used in mindfulness-based interventions such as mindfulness-based stress reduction (MBSR: Kabat-Zinn 1990) and mindfulness-based cognitive therapy (MBCT: Segal, Williams, and Teasdale 2002). Mindfulness is typically defined as a state in which one<apos;>s complete attention is directed toward the experiences occurring in the present moment in a non-judgmental, accepting manner (Baer et al. 2006; Bishop et al. 2004; Brown and Ryan 2003; Kabat-Zinn 1990). Trait or dispositional mindfulness refers to one<apos;>s general tendency to be mindful (Medvedev et al. 2017). Both mindfulness-based interventions and MM have been found to be moderately effective in improving anxiety and mood symptoms in healthy and clinical samples (Bohlmeijer et al. 2010; Eberth and Sedlmeier 2012; Hofmann et al. 2010). In addition, MM has been associated with increased openness (Hurk et al. 2011). Phenomenological similarities between the effects of psychedelics and MM include the ability to induce mystical experiences (Berkovich-Ohana and Glicksohn 2017; Reavley and Pallant 2009; Russ and Elliott 2017) and ego dissolution (Hanley, Nakamura, and Garland 2018). Furthermore, psychedelics and MM seem to have similar effects on the default mode network (DMN), a large scale intrinsic network that functionally integrates distant brain areas. DMN activity generally correlates with internally directed attention (Fox et al. 2005) and is associated with multiple types of self-referential processing such as internal dialogue and self-related judgments (Northoff et al. 2006), mind-wandering (Fox et al. 2015), rumination (Hamilton et al. 2015), and worry (Servaas et al. 2014). Abnormalities of the DMN have been associated with high trait anxiety (Imperatori et al. 2019) and multiple psychological disorders including depression (Berman et al. 2011; Greicius et al. 2007; Sheline et al. 2009), whereas psychological treatment of these disorders has been associated with adaptive changes in the DMN (Scult et al. 2019; Yuan et al. 2018). Both psychedelic states and MM have been associated with acute changes in DMN activity and functional connectivity (Carhart-Harris et al. 2012; Fox et al. 2016; Palhano-Fontes et al. 2015). In addition, changes in the DMN have been found in long-term MM practitioners (Brewer et al. 2011). As MM and psychedelic states show similarities in associated outcomes (Bohlmeijer et al. 2010; Eberth and Sedlmeier 2012; Hofmann et al. 2010), phenomenology (Berkovich-Ohana and Glicksohn 2017; Griffiths et al. 2011; Hanley, Nakamura, and Garland 2018; Liechti, Dolder, and Schmid 2017; Nour et al. 2016; Reavley and Pallant 2009; Russ and Elliott 2017) and neural correlates (Carhart-Harris et al. 2012; Fox et al. 2016; Palhano-Fontes et al. 2015), and as macrodoses have been associated with increased mindfulness (Madsen et al. 2020; Soler et al. 2016; Uthaug et al. 2019), the third aim of this study was to investigate if trait mindfulness mediates the association between microdosing and trait anxiety.

In summary, this cross-sectional study investigated the association between microdosing and trait anxiety and if this association is mediated by trait mindfulness. It was hypothesized that (1) current microdosers report lower trait anxiety compared to microdosing-naïve controls, (2) former microdosers report lower trait anxiety compared to microdosing-naïve controls, and (3) the associations of both current and former microdosing with trait anxiety are mediated by trait mindfulness.

Methods

Participants

Participants were recruited in October and November 2020 using posts on the online forum Reddit under the username /u/erivha (n = 641) and through a university research advertising website (n = 100). Participants aged ≥ 16 with and without microdosing experience were included. Participants with microdosing experience were included if they were currently following or had previously followed a microdosing regimen using psilocybin, LSD, DMT or mescaline. Examples of microdosing regimen include "once every three days" and "four days on, three days off." Participation was voluntary and student participants recruited through the university research advertising website received course credits as remuneration, whereas participants recruited through Reddit were not remunerated. Ethical approval was received from the Ethics Review Board of the Faculty of Social and Behavioral Sciences of the University of Amsterdam (ID: 2019-CP-11359).

Measures

After providing informed consent, participants answered questions concerning their demographic characteristics, microdosing experience, previous macrodose experience, current MM practice, trait anxiety, and trait mindfulness (Table 1).

Demographic characteristics included age, gender, highest educational qualification, and relationship status. Regarding microdosing experience, participants were asked "What is your microdosing experience?" (I have no microdosing experience, I irregularly microdose, I have previously followed a microdosing regimen, I am currently following a microdosing regimen). Next, participants were asked "What substance, if any, have you microdosed?" (I have no microdosing experience, Psilocybin, LSD, DMT, Mescaline, Other). Participants who selected "Other" were asked to specify which substance(s) they had microdosed. Regarding macrodose and mindfulness experience, participants were asked "Do you have previous moderate to large dose experience?" and "Do you currently practice mindfulness?" (Yes, No).

Trait anxiety was measured using the trait subscale of the State-Trait Anxiety Inventory (STAI-T: Spielberger et al. 1983), a 20-item self-report questionnaire which measures one<apos;>s proneness to anxiety. Sample items include "I wish I could be as happy as others seem to be," "I worry too much over something that really doesn<apos;>t matter" and "I am a steady person." Items are rated on a 4-point Likert scale, ranging from 1 (almost never) to 4 (almost always). The minimum and maximum scores are 20 and 80 respectively. A high score indicates a higher proneness to anxiety. The STAI-T has good psychometric properties, with Cronbach<apos;>s alpha values in the range of .86 to .95, and test–retest correlations ranging from .73 to .86 (Spielberger et al. 1983). In this study, Cronbach<apos;>s alpha value was .94.

Trait mindfulness was measured using the 15-item Five-Facet Mindfulness Questionnaire (FFMQ-15; Baer et al. 2008), a self-report questionnaire which measures the trait-like tendency to be mindful in daily life. It contains the following subscales: Observing, Describing, Acting with awareness, Non-judging, and Non-reactivity. Sample items include "I notice how foods and drinks affect my thoughts, bodily sensations, and emotions" (observing), "I believe some of my thoughts are abnormal or bad and I shouldn<apos;>t think that way" (non-judging) and "When I have distressing thoughts or images I just notice them and let them go" (non-reactivity). Items are rated on a 5-point Likert scale, ranging from 1 (never or very rarely true) to 5 (very often or always true). Minimum and maximum scores on each subscale are 3 and 15 respectively. High scores on a subscale indicate a higher tendency to be mindful in daily life. The FFMQ-15 has good psychometric properties, with Cronbach<apos;>s alpha values for the subscales ranging from .64 to .80 (Gu et al. 2016). In this study, Cronbach<apos;>s alpha values for the subscales ranged from .64 to .87.

Analysis

Participants were divided into three groups: current microdosers (Current MD), former microdosers (Former MD) and microdosing-naïve controls (No MD). First, differences between these groups were tested with an ANOVA for age and chi-squared tests for gender, highest educational qualification, relationship status, previous macrodose experience, and MM practice. Second, a linear regression was used to test the association between current microdosing (No MD vs Current MD) and STAI-T scores. If this association was significant, mediation by the FFMQ-15 total and subscale scores was first tested using joint significance tests as recommended by Yzerbyt et al. (2018). Mediation was assumed to be present if path a (microdosing experience to FFMQ-15 scores) and path b (FFMQ-15 scores to STAI-T scores) of the mediation model were significant. To test the size and significance of the indirect effect, percentile bootstrapping analyses were conducted using the PROCESS macro (Hayes 2013). These steps were repeated to test the association between

Table 1. Participant characteristics (n = 497).

	No MD (n = 234)	Current MD (n = 186)	Former MD (n = 77)
Age, *M* (SD)	26.4 (10.8)[a]	34.1 (10.9)[b]	30.3 (10.8)[c]
Gender, *n* (%)	[a]	[b]	[b]
Male	99 (42.3)	127 (68.3)	58 (75.3)
Female	130 (55.6)	53 (28.5)	18 (23.4)
Non-binary	5 (2.1)	6 (3.2)	1 (1.3)
Highest education, *n* (%)	[a]	[b]	[b]
Doctoral degree	3 (1.3)	4 (2.2)	3 (3.9)
Master's degree	21 (9.0)	29 (15.6)	12 (15.6)
Bachelor's degree	78 (33.3)	80 (43.0)	28 (36.4)
Vocational certificate	18 (7.7)	29 (15.6)	9 (11.7)
High school diploma	105 (44.9)	44 (23.7)	24 (31.2)
Primary education	8 (3.4)	0 (.0)	0 (.0)
No formal education	1 (.2)	0 (.0)	1 (1.3)
Romantic relationship, *n* (%)	[a]	[b]	[ab]
No	128 (55.4)	67 (36.0)	36 (46.8)
Yes	106 (45.3)	119 (64.0)	41 (53.2)
Microdosed substance, *n* (%)[1]			
Psilocybin	-	152 (81.7)	56 (72.7)
LSD	-	68 (36.6)	38 (49.4)
DMT	-	4 (2.1)	3 (3.9)
Mescaline	-	3 (1.6)	-
Previous macrodose, *n* (%)	[a]	[b]	[b]
No	145 (62.0)	38 (20.4)	12 (15.6)
Yes	89 (38.0)	148 (79.6)	65 (84.4)
Current MM practice, *n* (%)	[a]	[b]	[b]
No	164 (70.1)	70 (37.6)	36 (46.8)
Yes	70 (29.9)	116 (62.4)	41 (53.2)
STAI-T, *M* (SD)	49.8 (12.1)[a]	44.6 (11.3)[b]	45.5 (11.9)[b]
FFMQ-15 total, *M* (SD)	46.4 (8.3)[a]	51.5 (8.2)[b]	50.5 (8.9)[b]
Observing, *M* (SD)	9.6 (2.5)[a]	10.7 (2.4)[b]	10.5 (2.3)[b]
Describing, *M* (SD)	9.9 (2.7)[a]	10.7 (2.5)[b]	9.8 (2.8)[a]
Acting w/ awareness, *M* (SD)	8.7 (2.3)[a]	9.2 (2.2)[b]	9.2 (2.0)[ab]
Non-judging, *M* (SD)	9.5 (3.0)[a]	11.1 (3.1)[b]	10.7 (2.8)[b]
Non-reactivity, *M* (SD)	8.7 (2.5)[a]	9.9 (2.4)[b]	10.3 (2.5)[b]

No MD: microdosing-naïve controls; Current MD: current microdosers; Former MD: former microdosers; MM: mindfulness meditation; FFMQ-15: 15-Item Five Facet Mindfulness Questionnaire; STAI-T: State-Trait Anxiety Inventory – Trait Subscale. [a-c] Means in a row (or proportions across multiple rows for categorical variables) without a common superscript letter differ ($p < .05$).
[1]Percentage sum exceeds 100% as some participants had microdosed multiple substances.

former MD (No MD vs Former MD) and STAI-T scores and their mediation by the FFMQ-15 total and subscale scores. Third, exploratory regression and mediation analyses were conducted to investigate the role of macrodose experience in the observed associations between microdosing experience, FFMQ-15 scores and STAI-T scores.

While there is no straightforward way to determine sample size for mediation analyses (Pan et al. 2018), Fritz and MacKinnon (2007) investigated power calculations for the simple mediation model and provided guidelines for researchers in determining the necessary sample size to conduct a mediation analysis with .8 statistical power. These guidelines are based upon the expected effect sizes of path *a* and path *b* of the mediation model. As there are no previous reports on the association between microdosing and FFMQ-15 scores, the size of path *a* was conservatively assumed to be small. In a recent meta-analysis, large correlations (r = −.53) were found between the Five Facet Mindfulness Questionnaire and measures of anxiety (Carpenter et al. 2019). The size of path *b* was therefore conservatively assumed to be medium. With these expected effect sizes, the sample size needed for .8 power is n = 402 for joint significance testing and n = 398 for percentile bootstrapping.

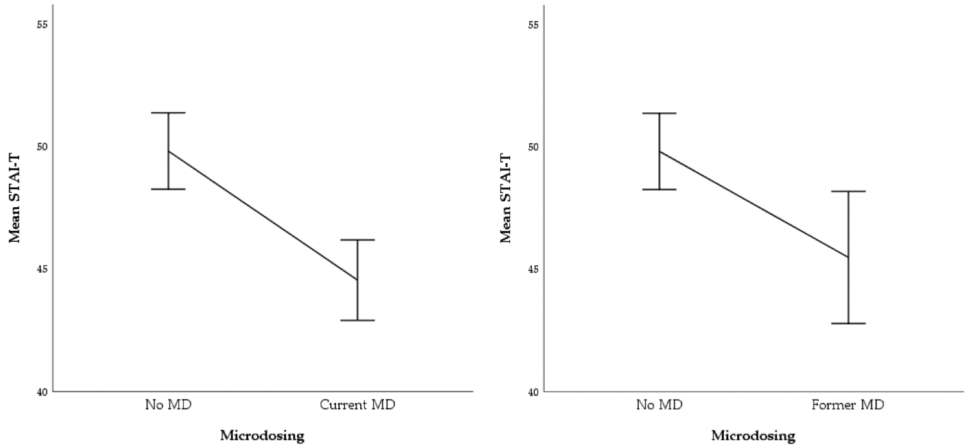

Figure 1. Association between current (left) and former (right) microdosing and STAI-T scores.

The significance level of all analyses was set to $\alpha = .05$ and all statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.

Results

Participant characteristics

Of the 741 participants that started the survey, 590 completed all questionnaires. Of these, 93 participants were excluded from further analyses because they microdosed irregularly, resulting in a total sample of 497 participants. Of these, 263 (52.9%) participants had microdosing experience. As shown in Table 1, No MD differed significantly from Current and Former MD in age, gender, highest educational qualification, previous macrodose experience and current MM practice. Current and Former MD only differed significantly in age.

Association between microdosing experience and STAI-T scores

Current MD vs No MD

There was a significant association between microdosing and STAI-T scores ($r = .22$, r^2 adjusted = .05, $F[1,418] = 20.74$) with Current MD being associated with lower STAI-T scores ($B = -5.26$, SE = 1.16, $p < .001$) compared to No MD (Figure 1).

Former MD vs No MD

There was a significant association between microdosing and STAI-T scores ($r = .15$, r^2 adjusted = .02, $F[1,309] = 7.49$) with Former MD being associated with lower STAI-T scores ($B = -4.33$, SE = 1.58, $p = .007$) compared to No MD (Figure 1).

Mediation of trait mindfulness

Current MD vs No MD

The association between Current MD and STAI-T scores was mediated by FFMQ-15 scores (Table 2). The regression coefficients for the associations of Current MD with FFMQ-15 total and all subscale scores (path *a*) were significant, as were the coefficients for the associations of FFMQ-15 total and all subscale scores with STAI-T scores (path *b*). The significance of the indirect effects was tested using bootstrapping procedures. Unstandardized indirect effects were computed for each of 5000 bootstrapped samples and the 95% confidence intervals were computed by determining the indirect effects at the 2.5^{th} and 97.5^{th} percentiles. None of the bootstrapped confidence intervals contained zero. Thus, the indirect effects for the FFMQ-15 total and all subscale scores were significant.

Former MD vs No MD

The association between Former MD and STAI-T scores was mediated by FFMQ-15 scores (Table 3). The regression coefficients for the associations of Former MD with FFMQ-15 total, observing, non-judging and non-reactivity scores (path *a*) were significant, as were the coefficients for the associations of these FFMQ-15 scores with STAI-T scores (path *b*). The significance of the indirect effects was tested using bootstrapping procedures. Unstandardized indirect effects were computed for each of 5000 bootstrapped samples and the 95% confidence intervals were computed by determining the indirect effects at the 2.5^{th} and 97.5^{th} percentiles. None of the bootstrapped confidence intervals contained zero. Thus, the indirect effects for FFMQ-15 total, observing, non-judging and non-reactivity scores were significant.

Table 2. Summary of tests for mediation of the association between MD_1 and STAI-T scores (n = 420).

	a path				*b* path				*c′* path		Indirect effect	
Mediator	*B* (SE)	*β*	R^2	*F*	*B* (SE)	*β*	R^2	*F*	*B* (SE)	*r*	*B* (SE)	95% CI
Total FFMQ-15	5.16 (.81)	.30***	.09	40.72	−.93 (.05)	.67***	.44	331.83	−5.26 (1.16)	.20	−4.75 (.80)	−6.40, −3.22
Observing	1.08 (.24)	.21***	.04	19.92	−.98 (.23)	.20***	.04	18.14	−4.41 (1.17)***	.04	−.85 (.32)	−1.56, −.31
Describing	.77 (.26)	.15*	.02	8.94	−1.60 (.21)	.35***	.12	59.45	−4.11 (1.10)***	.05	−1.15 (.40)	−1.98, −.38
Acting w/awareness	.53 (.22)	.11*	.01	5.53	−1.51 (.25)	.29***	.08	37.09	−4.53 (1.12)***	.03	−.73 (.33)	−1.39, −.13
Non-judging	1.60 (.30)	.25***	.06	28.57	−2.78 (.13)	.73***	.53	470.47	−.86 (.84)	.18	−4.40 (.86)	−6.13, −2.72
Non-reactivity	1.19 (.24)	.24***	.05	24.69	2.59 (.20)	.54***	.29	168.29	−2.33 (1.02)*	.13	−2.93 (.66)	−4.26, −1.69

MD_1: No MD vs Current MD; FFMQ-15: 15-Item Five Facet Mindfulness Questionnaire; STAI-T: State-Trait Anxiety Inventory – Trait Subscale.
*p < .05. **p < .01. ***p < .001.

Table 3. Summary of tests for mediation of the association between MD_2 and STAI-T scores (n = 311).

	a path				*b* path				*c′* path		Indirect effect	
Mediator	*B* (SE)	*β*	R^2	*F*	*B* (SE)	*β*	R^2	*F*	*B* (SE)	*r*	*B* (SE)	95% CI
Total FFMQ-15	4.15(1.10)	.21***	.04	14.12	−.96 (.06)	.68***	.46	14.12	−.35 (1.20)	.14	−3.98 (1.11)	−6.21, −1.8
Observing	.93 (.32)	.16*	.02	8.43	−.87 (.28)	.18*	.03	8.43	−3.62 (1.59)*	.03	−.71 (.36)	−1.53, −.14
Describing	−.08 (36)	.01	−.00	.05	−1.58 (.24)	.35***	.12	.05	−4.46 (1.48)*	.00	.13 (.58)	−.98, 1.30
Acting w/awareness	.51 (.30)	.10	.01	2.88	−1.74 (.29)	.33***	.10	2.88	−3.48 (1.51)*	.03	−.85 (.50)	−1.93, .07
Non-judging	1.22 (.39)	.18*	.03	9.75	−2.94 (.16)	.73***	.53	9.75	−.77 (1.12)	.13	−3.56 (1.11)	−5.74, −1.42
Non-reactivity	1.57 (33)	.27***	.07	23.42	−2.77 (.22)	.58***	.34	23.42	−.03 (1.35)	.16	−4.36 (.98)	−6.37, −2.57

MD_2: No MD vs Former MD; FFMQ-15: 15-Item Five Facet Mindfulness Questionnaire; STAI-T: State-Trait Anxiety Inventory – Trait Subscale.
*p < .05. **p < .01. ***p < .001.

Exploratory analysis

Initial exploratory mediation analyses showed that when participants with previous macrodose experience (n = 386) were excluded, the association between microdosing experience and STAI-T scores (r = .05, r^2 adjusted < .01, F[1,202] = .57) became non-significant (B = 49.99, SE = 1.02, p < .453). Associations between microdosing experience and FFMQ-15 total scores (r = .10, r^2 adjusted < .01, F[1,181] = 1.78) also became non-significant (B = 46.17, SE = .66, p < .184). In addition, regression analyses showed that there was a significant association between previous macrodose experience and STAI-T scores (r = .15, r^2 adjusted = .02, F[1,495] = 11.84) with previous macrodose experience being associated with lower STAI-T scores (B = −3.76, SE = 1.09, p = .001) compared to macrodose-naïve controls. Furthermore, this association was mediated by FFMQ-15 total scores. The regression coefficient for the association between previous macrodose experience and FFMQ-15 total scores (path a) was significant (r = .21, r^2 adjusted = .04, F[1,495] = 22.89), with previous macrodose experience being associated with higher FFMQ-15 total scores (B = 3.73, SE = .78, p < .001), as was the coefficient for the association between FFMQ-15 total scores and STAI-T scores (path b) (r = .67, r^2 adjusted = .44, F[1,495] = 394.07), with higher FFMQ-15 total scores being associated with lower STAI-T scores (B = −.92, SE = .05, p < .001). The standardized indirect effect was (.21)(.67) = .14.

Discussion

The aim of this study was to investigate the association between microdosing and trait anxiety. In line with our hypotheses, we found that (1) current and (2) former microdosers reported lower trait anxiety compared to microdosing-naïve controls. In addition, these associations were (3) mediated by trait mindfulness, with non-judging and non-reactivity facets having small indirect effects. However, *post hoc* exploratory analyses showed that all associations of microdosing with both trait mindfulness and trait anxiety became non-significant when participants with previous macrodose experience were excluded. Furthermore, we found that participants with previous macrodose experience reported lower trait anxiety compared to psychedelic-naïve controls. This suggests that the differences in trait anxiety found between participants who have microdosed and microdosing-naïve controls in this study are perhaps explained by previous macrodose experience.

If we assume that the association between microdosing and trait anxiety is indeed explained by previous macrodose experience, this may support the idea that mystical experiences play an important role in the therapeutic effects of psychedelics. Mystical experiences are characterized by a sense of unity and sacredness, transcendence of time and space, paradoxicality, noetic quality (intuitive understanding of ultimate reality) and deeply felt positive mood (Griffiths et al. 2006). Greater acute effects of psychedelics on measures of mystical experiences are associated with positive effects in multiple domains including attitudes, prosocial behavior, depression, anxiety and satisfaction with life in healthy individuals (Davis et al. 2019; Griffiths et al. 2018, 2011; Uthaug et al. 2019). In addition, Griffiths et al. (2016) and Ross et al. (2016) investigated the role of mystical experiences in psilocybin treatment for patients with life-threatening cancer and found that the subjective intensity of a mystical experience mediates the treatment effect on anxiety and depression. One of the main differences between micro- and macrodoses of psychedelics is that a microdose is unable to induce mystical experiences (Fadiman 2011). If mystical experiences are indeed necessary for psychedelics to have therapeutic effects, that might explain why the observed associations between microdosing and trait anxiety became non-significant when participants with previous macrodose experience were excluded.

An alternative explanation of our findings that should be considered is the possible presence of a placebo effect in the reported outcomes of microdosing. Szigeti et al. (2021) and Marschall et al. (2021) found no differences in anxiety between microdosing and placebo groups. In addition, Kaertner et al. (2021) found that positive expectancy scores regarding the effects of microdosing at baseline predicted subsequent improvements in well-being. Furthermore, in a self-reported observational study, Politio and Stevenson (2019) found evidence for an expectancy bias in naïve and experienced microdosers. While these findings suggest the possible presence of a placebo effect, this notion is undermined by the fact that Politio and Stevenson (2019) found no association between expected and observed effects of microdosing. More placebo-controlled experimental research is needed to test causal hypotheses concerning the effects of microdosing.

Our findings should also be interpreted in light of the notable between-group differences that we observed in age, gender, and education. These can be attributed to the fact that the microdosing-naïve control group consisted mostly of female first-year bachelor students. This could have influenced the association between microdosing and trait anxiety, as female college students have been found to report slightly higher trait anxiety than their male counterparts (Spielberger et al. 1983). We might have found different associations between microdosing and trait anxiety if these demographic between-group differences were absent.

This study was not without limitations and its results should therefore be interpreted with caution. First, due to its cross-sectional design, our findings cannot be used to infer any causal associations. Second, microdosing was broadly operationalized, as participants were only asked if they had followed a microdosing regimen and which substances they had microdosed. The duration and frequency of these regimen, exact doses and frequency within each regimen, and time between subsequent regimen or since quitting remain unknown, possibly resulting in a highly heterogeneous microdosing sample. More research is therefore needed to investigate the effects of clearly defined specific microdosing regimen. Third, it should be noted that the construct validity of the STAI-T has been criticized in the past. Multiple confirmatory factor analyses have found the best fit with a bifactor model (Bados, Gómez-Benito, and Balaguer 2010; Balsamo et al. 2013; Bieling, Antony, and Swinson 1998). As these two factors correlate with measures of both anxiety and depression, it has been suggested that the STAI-T measures general negative affect, a factor underlying both mood and anxiety disorders. It is therefore possible that microdosing is associated with a broader range of outcomes than trait anxiety per se, and future research should include other measures of anxiety and depression when investigating the effects of microdosing.

The main strengths of this study are its sample size and statistical procedures, as microdosing samples are difficult to recruit. By following recommendations regarding mediation analysis by Fritz and MacKinnon (2007) and Yzerbyt et al. (2018), we can confidently conclude the presence of a mediation effect. Our sample size met the requirements for sufficient statistical power to compare current microdosers to microdosing-naïve controls. This was not true for the exploratory analysis that excluded participants with previous macrodose experience, but it is unsure if repeating that analysis on larger samples would result in effect sizes that are more meaningful than the present negligible one.

In conclusion, this study found an association between microdosing and trait anxiety that was partially mediated by trait mindfulness, with individuals who are currently microdosing and individuals who have previously microdosed reporting lower trait anxiety compared to microdosing-naïve controls. Randomized placebo-controlled trials are now warranted to test causal hypotheses concerning the effects of microdosing and the role of trait mindfulness in these effects, while controlling for previous macrodose experience.

Compliance with Ethical Standards

On behalf of all authors, the corresponding author states that there is no conflict of interest. Ethical approval was received from the Ethics Review Board of the Faculty of Social and Behavioral Sciences of the University of Amsterdam (ID:

2019-CP-11359). Participants were required to provide informed consent prior to being included in this study.

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References

Anderson, T., R. Petranker, D. Rosenbaum, C. R. Weissman, L. Dinh-Williams, K. Hui, E. Hapke, and N. A. S. Farb. 2019. Microdosing psychedelics: Personality, mental health, and creativity differences in microdosers. *Psychopharmacology* 236 (2):731–40. doi:10.1007/s00213-018-5106-2.

Andersson, M., and A. Kjellgren. 2019. Twenty percent better with 20 micrograms? A qualitative study of psychedelic microdosing self-rapports and discussions on YouTube. *Harm Reduction Journal* 16 (1):Article 63. doi:10.1186/s12954-019-0333-3.

Bados, A., Gómez-Benito, and G. Balaguer. 2010. The state-trait anxiety inventory, trait version: Does it really measure anxiety? *Journal of Personality Assesment* 92 (6):560–67. doi:10.1080/00223891.2010.513295.

Baer, R. A., G. T. Smith, J. Hopkins, J. Krietemeyer, and L. Toney. 2006. Using self-report assessment methods to explore facets of mindfulness. *Assessment* 13 (1):27–45. doi:10.1177/1073191105283504.

Baer, R. A., G. T. Smith, E. Lykins, D. Button, J. Krietemeyer, S. Sauer, E. Walsh, D. Duggan, and J. M. G. Williams. 2008. Construct validity of the Five Facet Mindfulness Questionnaire in meditating and nonmeditating samples. *Assessment* 15 (3):329–42. doi:10.1177/1073191107313003.

Balsamo, M., R. Romanelli, M. Innamorati, G. Ciccarese, L. Carlucci, and A. Saggino. 2013. The state-trait anxiety inventory: Shadows and lights on its construct validity. *Journal of Psychopathology and Behavioral Assessment* 35 (4):475–86. doi:10.1007/s10862-013-9354-5.

Barrett, F. S., and R. R. Griffiths. 2018. Classic hallucinogens and mystical experiences: Phenomenology and neural correlates. *Current Topics in Behavioral Neuroscience* 36:393–430. doi:10.1007/7854_2017_474.

Berkovich-Ohana, A., and J. Glicksohn. 2017. Meditation, absorption, transcendent experience, and affect: Tying it all together via the consciousness state space (CSS) model. *Mindfulness* 8 (1):68–77. doi:10.1007/s12671-015-0481-9.

Berman, M. G., S. Peltier, D. E. Nee, E. Kross, P. J. Deldin, and J. Jonides. 2011. Depression, rumination and the default network. *Social Cognitive and Affective Neuroscience* 6 (5):548–55. doi:10.1093/scan/nsq080.

Bershad, A. K., S. T. Schepers, M. P. Bremmer, R. Lee, and H. de Wit. 2019. Acute subjective and behavioral effects of microdoses of lysergic acid diethylamide in healthy human volunteers. *Biological Psychiatry* 86 (10):792–800. doi:10.1016/j.biopsych.2019.05.019.

Bieling, P. J., M. M. Antony, and R. P. Swinson. 1998. The state-trait anxiety inventory, trait version: Structure and content re-examined. *Behaviour Research and Therapy* 36 (7–8):777–88. doi:10.1016/S0005-7967(98)00023-0.

Bishop, S. R., M. Lau, S. Shapiro, L. Carlson, N. D. Anderson, J. Carmody, Z. V. Segal, S. Abbey, M. Speca, D. Velting, et al. 2004. Mindfulness: A proposed operational definition. *Clinical Psychology: Science and Practice* 11:230–41. doi:10.1093/clipsy.bph077.

Bohlmeijer, E., R. Prenger, E. Taal, and P. Cuijpers. 2010. The effects of mindfulness-based stress reduction therapy on mental health of adults with a chronic medical disease: A meta-analysis. *Journal of Psychosomatic Research* 68 (6):539–44. doi:10.1016/j.jpsychores.2009.10.005.

Brewer, J. A., P. D. Worhunsky, J. R. Gray, Y. Tang, J. Weber, and H. Kober. 2011. Meditation experience is associated with differences in default mode network activity and connectivity. *Proceedings of the National Academy of Sciences* 108 (50):20254–59. doi:10.1073/pnas.1112029108.

Bright, S., E. Gringart, E. Blatchford, and S. Bettinson. 2021. A quantitative exploration of the relationships between regular yoga practice, microdosing psychedelics, wellbeing and personality variables. *Australian Journal of Psychology* 73 (2):134–43. doi:10.1080/00049530.2021.1882266.

Brown, K. W., and R. M. Ryan. 2003. The benefits of being present: Mindfulness and its role in psychological well-being. *Journal of Personality and Social Psychology* 84 (4):822–48. doi:10.1037/0022-3514.84.4.822.

Carhart-Harris, R. L., D. Erritzoe, T. Williams, J. M. Stone, L. J. Reed, A. Colasanti, R. J. Tyacke, R. Leech, A. L. Malizia, K. Murphy, et al. 2012. Neural correlates of the psychedelic state as determined by fMRI studies with psilocybin. *Proceedings of the National Academy of Sciences.* 109 (6):2138–43. doi:10.1073/pnas.1119598109.

Carhart-Harris, R. L., M. Bolstridge, J. Rucker, C. M. J. Day, D. Erritzoe, M. Kaelen, M. Bloomfield, J. A. Rickard, B. Forbes, A. Feilding, et al. 2016. Psilocybin with psychological support for treatment-resistant depression: An open-label feasibility study. *Lancet Psychiatry* 3 (7):619–27. doi:10.1016/S2215-0366/2816/2930065-7.

Carhart-Harris, R. L., M. Bolstridge, C. M. J. Day, J. Rucker, R. Watts, D. E. Erritzoe, M. Kaelen, B. Giribaldi, M. Bloomfield, S. Pilling, et al. 2018. Psilocybin with psychological support for treatment-resistant depression: Six-month follow-up. *Psychopharmacology (Berl.)* 235 (2):399–408. doi:10.1007/s00213-017-4771-x.

Carpenter, J. K., K. Conroy, A. F. Gomez, L. C. Curren, and S. G. Hofmann. 2019. The relationship between trait mindfulness and affective symptoms: A meta-analysis of the Five Facet Mindfulness Questionnaire (FFMQ). *Clinical Psychology Review* 74:101785. doi:10.1016/j.cpr.2019.101785.

Davis, A. K., S. So, R. Lancelotta, J. P. Barsuglia, and R. R. Griffiths. 2019. 5-Methoxy-N, N-dimethyltryptamine (5-MeO-DMT) used in a naturalistic setting is associated with unintended improvements in depression and anxiety. *The American Journal of Drug and Alcohol Abuse* 45 (2):161–69. doi:10.1080/00952990.2018.1545024.

Dressler, H., S. Bright, and V. Polito. 2021. Exploring the relationship between microdosing, personality and emotional insight: A prospective study. *Journal of Psychedelic Studies* 5 (1):9–16. doi:10.1556/2054.2021.00157.

Eberth, J., and P. Sedlmeier. 2012. The effects of mindfulness meditation: A meta-analysis. *Mindfulness* 3 (3):174–89. doi:10.1007/s12671-012-0101-x.

Fadiman, J. 2011. *The psychedelic explorer's guide*. Rochester: Park Street Press.

Fox, M. D., A. Z. Snyder, J. L. Vincent, M. Corbetta, D. C. Van Essen, and M. E. Raichle. 2005. The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proceedings of the National Academy of Sciences* 102 (27):9673–78. doi:10.1073/pnas.0504136102.

Fox, K. C. R., R. N. Spreng, M. Ellamil, J. R. Andrews-Hanna, and K. Christoff. 2015. The wandering brain: Meta-analysis of functional neuroimaging studies of mind-wandering and related spontaneous thought processes. *Neuroimage* 111:611–21. doi:10.1016/j.neuroimage.2015.02.039.

Fox, K. C. R., M. L. Dixon, S. Nijeboer, M. Girn, J. L. Floman, M. Lifshitz, M. Ellamil, P. Sedlmeier, and K. Christoff. 2016. Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. *Neuroscience and Biobehavioral Reviews* 65:208–28. doi:10.1016/j.neubiorev.2016.03.021.

Fritz, M. S., and D. P. MacKinnon. 2007. Required sample size to detect the mediated effect. *Psychological Science* 18 (3):233–39. doi:10.1111/j.1467-9280.2007.01882.x.

Garlick, H. 2019. *'It makes me enjoy playing with the kids': Is microdosing mushrooms going mainstream?* Accessed December 3, 2020. https://www.theguardian.com/science/2019/may/03/psychedelic-drugs-women-taking-tiny-doses-hattie-garlick.

Gasser, P., D. Holstein, Y. Michel, R. Doblin, B. Yazar-Klosinski, and T. Passie. 2014. Safety and efficacy of lysergic acid diethylamide-assisted psychotherapy for anxiety associated with life-threatening diseases. *Journal of Nervous & Mental Disease* 202 (7):513–20. doi:10.1097/NMD.0000000000000113.

Glatter, R. 2015. *LSD microdosing: The new job enhancer in Silicon Valley*. Acessed December 3, 2020. https://www.forbes.com/sites/robertglatter/2015/11/27/lsd-microdosing-the-new-job-enhancer-in-silicon-valley-and-beyond/?sh=753e46ce188a.

Greicius, M. D., B. H. Flores, V. Menon, G. H. Glover, H. B. Solvason, H. A. Kenna, A. L. Reiss, and A. F. Schatzberg. 2007. Resting-State Functional Connectivity in Major Depression: Abnormally Increased Contributions from Subgenual Cingulate Cortex and Thalamus. *Biological Psychiatry* 62 (5):429–37. doi:10.1016/j.biopsych.2006.09.020.

Griffiths, R. R., W. A. Richards, U. McCann, and R. Jesse. 2006. Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology (Berl)* 187 (3):268–83. doi:10.1007/s00213-006-0457-5.

Griffiths, R. R., M. W. Johnson, W. A. Richards, B. D. Richards, U. McCann, and R. Jesse. 2011. Psilocybin occasioned mystical-type experiences: Immediate and persisting dose-related effects. *Psychopharmacology* 218 (4):649–65. doi:10.1007/s00213-011-2358-5.

Griffiths, R. R., M. W. Johnson, M. A. Carducci, A. Umbricht, W. A. Richards, B. D. Richards, M. P. Cosimano, and M. A. Klinedinst. 2016. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized doubleblind trial. *Journal of Psychopharmacology* 30 (12):1181–97. doi:10.1177/0269881116675513.

Griffiths, R. R., M. W. Johnson, W. A. Richards, B. D. Richards, R. Jesse, K. A. MacLean, F. S. Barrett, M. P. Cosimano, and M. A. Klinedinst. 2018. Psilocybin-occasioned mystical-type experience in combination with meditation and other spiritual practices produces enduring positive changes in psychological functioning and in trait measures of prosocial attitudes and behaviors. *Journal of Psychopharmacology* 32 (1):49–69. doi:10.1177/0269881117731279.

Grob, C. S., A. L. Danforth, G. S. Chopra, M. Hagerty, C. R. McKay, A. L. Halberstadt, and G. R. Greer. 2011. Pilot study of psilocybin treatment for anxiety in patients with advanced-stage cancer. *Archives of General Psychiatry* 68 (1):71–78. doi:10.1001/archgenpsychiatry.2010.116.

Gu, J., C. Strauss, C. Crane, T. Barnhofer, A. Karl, K. Cavanagh, and W. Kuyken. 2016. Examining the factor structure of the 39-item and 15-item versions of the Five-Facet Mindfulness Questionnaire before and after Mindfulness-Based Cognitive Therapy for people with recurrent depression. *Psychological Assessment* 28 (7):791–802. doi:10.1037/pas0000263.

Halberstadt, A. L. 2015. Recent advances in the neuropsychopharmacology of serotonergic hallucinogens. *Behavioral Brain Research* 277:99–120. doi:10.1016/j.bbr.2014.07.016.

Hamilton, J. P., M. Farmer, P. Fogelman, and I. H. Gotlib. 2015. Depressive rumination, the default-mode network, and the dark matter of clinical neuroscience. *Biological Psychiatry* 78 (4):224–30. doi:10.1016/j.biopsych.2015.02.020.

Hanley, A. W., Y. Nakamura, and E. L. Garland. 2018. The Nondual Awareness Dimensional Assessment (NADA): New tools to assess nondual traits and states of consciousness occurring within and beyond the context of meditation. *Psychological Assessment* 30 (12):1625–39. doi:10.1037/pas0000615.

Hayes, A. F. 2013. *Introduction to mediation, moderation, and conditional process analysis: A regression-based approach*. New York: Guildford Press.

Heuschkel, K., and K. P. C. Kuypers. 2020. Depression, mindfulness, and psilocybin: Possible complementary effects of mindfulness meditation and psilocybin in the treatment of depression. A review. *Frontiers in Psychiatry* 11:11. doi:10.3389/fpsyt.2020.00224.

Hofmann, S. G., A. T. Sawyer, A. A. Witt, and D. Oh. 2010. The effect of mindfulness-based therapy on anxiety and depression: A meta-analytic review. *Journal of Consulting and Clinical Psychology* 78 (2):169–83. doi:10.1037/a0018555.

Holze, F., M. E. Liechti, N. R. P. W. Hutten, N. L. Mason, P. C. Dolder, E. L. Theunissen, U. Duthaler, A. Feilding, J. G. Ramaekers, and K. P. C. Kuypers. 2020. Pharmacokinetics and pharmacodynamics of lysergic acid diethylamide microdoses in healthy participants. *Clinical Pharmacology and Therapeutics* 109 (3):658–66. doi:10.1002/cpt.2057.

Hurk, P. A. M. V. D., T. Wingens, F. Giommi, H. P. Barendregt, A. E. M. Speckens, and H. T. van Schie. 2011. On the relationship between the practice of mindfulness meditation and personality-An exploratory analysis of the mediating role of mindfulness skills. *Mindfulness* 2 (3):194–200. doi:10.1007/s12671-011-0060-7.

Hutten, N. R. P. W., N. L. Mason, P. C. Dolder, and K. P. C. Kuypers. 2019. Motives and side-effects of microdosing with psychedelics among users. *International Journal of Neuropsychopharmacology* 22 (7):426–34. doi:10.1093/ijnp/pyz029.

Hutten, N. R. P. W., N. L. Mason, P. C. Dolder, E. L. Theunissen, F. Holze, M. E. Liechti, A. Feilding, J. G. Ramaekers, and K. P. C. Kuypers. 2020. Mood and cognition after administration of low LSD doses in healthy volunteers: A placebo controlled dose-effect finding study. *European Neuropsychopharmacology* 41:81–91. doi:10.1016/j.euroneuro.2020.10.002.

Imperatori, C., B. Farina, M. Adenzato, E. M. Valenti, C. Murgia, G. Della Marca, R. Brunetti, E. Fontana, and R. B. Ardito. 2019. Default mode network alterations in individuals with high-trait-anxiety: An EEG functional connectivity study. *Journal of Affective Disorders* 246:611–18. doi:10.1016/j.jad.2018.12.071.

Johnson, M. W., W. A. Richards, and R. R. Griffiths. 2008. Human hallucinogen research: Guidelines for safety. *Journal of Psychopharmacology* 22 (6):603–20. doi:10.1177/0269881108093587.

Johnson, M. W., R. R. Griffiths, P. S. Hendricks, and J. E. Henningfield. 2018. The abuse potential of medical psilocybin according to the 8 factors of the controlled substances act. *Neuropharmacology* 142:143–66. doi:10.1016/j.neuropharm.2018.05.012.

Johnstad, P. G. 2018. Powerful substances in tiny amounts: An interview study of psychedelic microdosing. *Nordic Studies on Alcohol and Drugs* 35 (1):39–51. doi:10.1177/1455072517753339.

Kabat-Zinn, J. 1990. *Full catastrophe living: The program of the stress reduction clinic at the University of Massachusetts Medical Center*. New York, NY: Delta, Random House Publishing Group.

Kaertner, L. S., M. B. Steinborn, H. Kettner, M. J. Spriggs, L. Roseman, T. Buchborn, M. Balaet, C. Timmermann, D. Erritzoe, and R. L. Carhart-Harris. 2021. Positive expectations predict improved mental-health outcomes linked to psychedelic microdosing. *Scientific Reports* 11 (1). doi:10.1038/s41598-021-81446-7.

Liechti, M. E., P. C. Dolder, and Y. Schmid. 2017. Alterations of consciousness and mystical-type experiences after acute LSD in humans. *Psychopharmacology* 234 (9–10):1499–510. doi:10.1007/s00213-016-4453-0.

MacLean, K. A., M. W. Johnson, and R. R. Griffiths. 2011. Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *Journal of Psychopharmacology* 25 (11):1453–61. doi:10.1177/0269881111420188.

Madsen, M. K., P. M. Fisher, D. S. Stenbæk, S. Kristiansen, D. Burmester, S. Lehel, T. Páleníček, M. Kuchař, C. Svarer, B. Ozenne, et al. 2020. A single psilocybin dose is associated with long-term increased mindfulness, preceded by a proportional change in neocortical 5-HT2A receptor binding. *European Neuropsychopharmacology* 33:71–80. doi:10.1016/j.euroneuro.2020.02.001.

Marschall, J., G. Fejer, P. Lempe, L. Prochazkova, M. Kuchar, K. Hajkova, and M. van Elk. 2021. Psilocybin microdosing does not affect emotion-related symptoms and processing: A preregistered field and lab-based study. *Journal of Psychopharmacology* 36 (1):97–113. doi:10.1177/02698811211050556.

Medvedev, O. N., C. U. Krageloh, A. Narayanan, and R. J. Siegert. 2017. Measuring mindfulness: Applying generalizability theory to distinguish between state and trait. *Mindfulness* 8 (4):1036–46. doi:10.1007/s12671-017-0679-0.

Millière, R., R. L. Carhart-Harris, L. Roseman, F. Trautwein, and A. Berkovich-Ohana. 2018. Psychedelics, meditation, and self-consciousness. *Frontiers in Psychology* 9. doi:10.3389/fpsyg.2018.01475.

Moreno, F. A., C. B. Wiegand, E. K. Taitano, and P. L. Delgado. 2006. Safety, tolerability, and efficacy of psilocybin in 9 patients with obsessive-compulsive disorder. *The Journal of Clinical Psychiatry* 67 (11):1735–40. doi:10.4088/JCP.v67n1110.

Nichols, D. E. 2016. Psychedelics. *Pharmacological Reviews* 68 (2):264–355. doi:10.1124/pr.115.011478.

Northoff, G., A. Heinzel, M. de Greck, F. Bermpohl, H. Dobrowolny, and J. Panksepp. 2006. Self-referential processing in our brain–A meta-analysis of imaging studies on self. *NeuroImage* 31 (1):440–57. doi:10.1016/j.neuroimage.2005.12.002.

Nour, M. M., L. Evans, D. Nutt, and R. L. Carhart-Harris. 2016. Ego-dissolution and psychedelics: Validation of the Ego-Dissolution Inventory (EDI). *Frontiers in Human Neuroscience* 10:10. doi:10.3389/fnhum.2016.00269.

Nye, C. 2017. *Microdosing: The people taking LSD with their breakfast*. Available at: https://www.bbc.com/news/health-39516345. Accessed December 3, 2020

Osório, F. D. L., R. F. Sanches, L. R. Macedo, R. G. Dos Santos, J. P. Maia-de-Oliveira, L. Wichert-Ana, D. B. de Araujo, J. Riba, J. A. Crippa, and J. E. Hallak. 2015. Antidepressant effects of a single dose of ayahuasca in patients with recurrent depression: A preliminary report. *Revista Brasileira de Psiquiatria* 37 (1):13–20. doi:10.1590/1516-4446-2014-1496.

Palhano-Fontes, F., K. C. Andrade, L. F. Tofoli, A. C. Santos, J. A. S. Crippa, J. E. C. Hallak, S. Ribeiro, and D. B. De Araujo. 2015. The psychedelic state induced by ayahuasca modulates the activity and connectivity of the default mode network. *PLOS ONE* 10 (2):e0118143. doi:10.1371/journal.pone.0118143.

Pan, H., S. Liu, D. Miao, and Y. Yuan. 2018. Sample size determination for mediation analysis of longitudinal data. *BMC Medical Research Methodology* 18 (1). doi: 10.1186/s12874-018-0473-2.

Politio, V., and R. J. Stevenson. 2019. A systematic study of microdosing psychedelics. *PLOS ONE* 14 (2). doi: 10.1371/journal.pone.0211023.

Reavley, N., and J. F. Pallant. 2009. Development of a scale to assess the meditation experience. *Personality and Individual Differences* 47 (6):547–52. doi:10.1016/j.paid.2009.05.007.

Rosenbaum, D., C. Weissman, T. Anderson, R. Petranker, L. Dinh-Williams, K. Hui, and E. Hapke. 2020. Microdosing psychedelics: Demographics, practices, and psychiatric comorbidities. *Journal of Psychopharmacology* 34 (6):612–22. doi:10.117/0269881120908004.

Ross, S., A. Bossis, J. Guss, G. Agin-Liebes, T. Malone, B. Cohen, S. E. Mennega, A. Belser, K. Kalliontzi, J. Babb, et al. 2016. Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: A randomized controlled trial. *Journal of Psychopharmacology* 30 (12):1165–80. doi:10.1177/0269881116675512.

Russ, S. L., and M. S. Elliott. 2017. Antecedents of mystical experience and dread in intensive meditation. *Psychology of Consciousness: Theory, Research, and Practice* 4:38–53. doi:10.1037/cns0000119.

Scult, M. A., D. M. Fresco, F. M. Gunning, C. Liston, S. H. Seeley, E. Garcia, and D. S. Mennin. 2019. Changes in functional connectivity following treatment with emotion regulation therapy. *Frontiers in Behavioral Neuroscience* 13. doi:10.3389/fnbeh.2019.00010.

Segal, Z. V., J. M. G. Williams, and J. D. Teasdale. 2002. *Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse*. New York: Guilford.

Servaas, M. N., H. Riese, J. Ormel, and A. Aleman. 2014. The neural correlates of worry in association with individual differences in neuroticism. *Human Brain Mapping* 35 (9):4303–15. doi:10.1002/hbm.22476.

Sheline, Y. I., D. M. Barch, J. L. Price, M. M. Rundle, S. N. Vaishnavi, A. Z. Snyder, M. A. Mintun, S. Wang, R. S. Coalson, and M. E. Raichle. 2009. The default mode network and self-referential processes in depression. *Proceedings of the National Academy of Sciences* 106 (6):1942–47. www.pnas.orgcgidoi10.1073pnas.0812686106.

Siebert, A. 2020. *Microdosing psychedelics is trendy, but does it work? Here's what science says*. Accessed December 3, 2020. https://www.forbes.com/sites/amandasiebert/2020/11/13/microdosing-psychedelics-is-trendy-but-does-it-work-heres-what-science-says/?sh=298ec05dcf7c.

Soler, J., M. Elices, A. Franquesa, S. Barker, P. Friedlander, A. Feilding, J. C. Pascual, and J. Riba. 2016. Exploring the therapeutic potential of ayahuasca: Acute intake increases mindfulness-related capacities. *Psychopharmacology* 233 (5):823–29. doi:10.1007/s00213-015-4162-0.

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

Strassman, R. J. 1984. Adverse reactions to psychedelic drugs: A review of the literature. *Journal of Nervous and Mental Disease* 172 (10):577–95. doi:10.1097/00005053-198410000-00001.

Studerus, E., M. Kometer, F. Hasler, and F. X. Vollenweider. 2011. Acute, subacute and long-term subjective effects of psilocybin in healthy humans: A pooled analysis of experimental studies. *Journal of Psychopharmacology* 25 (11):1434–52. doi:10.1177/0269881110382466.

Szigeti, B. L. K., A. Blemings, F. Rosas, A. Feilding, D. J. Nutt, R. L. Carhart-Harris, and D. Erritzoe. 2021. Self-blinding citizen science to explore psychedelic microdosing. *eLife* 10. doi:10.7554/eLife.62878.

Turk, V. 2019 *Inside the first placebo-controlled studies testing if microdosing LSD actually works*. Accessed December 3, 2020. https://www.wired.co.uk/article/microdosing-lsd-psilocybin-placebo-trials.

Uthaug, M. V., R. Lancelotta, K. van Oorsouw, K. P. C. Kuypers, N. Mason, J. Rak, A. Šuláková, R. Jurok, M. Maryška, T. Páleníček, et al. 2019. A single inhalation of vapor from dried toad secretion containing 5-methoxy-*N,N*-dimethyltryptamine (5-MeO-DMT) in a naturalistic setting is related to sustained enhancement of satisfaction with life, mindfulness-related capacities, and a decrement of psychopathological symptoms. *Psychopharmacology* 236 (9):2653–66. doi:10.1007/s00213-019-05236-w.

Waldman, A. 2017. *A really good day: How microdosing made a mega difference in my mood, my marriage, and my life*. New York: Alfred A. Knopf.

Webb, M., H. Copes, and P. S. Hendricks. 2019. Narrative identity, rationality, and microdosing classic psychedelics. *International Journal of Drug Policy* 70:33–39. doi:10.1016/j.drugpo.2019.04.013.

Yuan, M., H. Zhu, C. Qiu, Y. Meng, Y. Zhang, Z. Ren, Y. Li, C. Yuan, M. Gao, S. Lui, et al. 2018. Altered regional and integrated resting-state brain activity in general social anxiety disorder patients before and after group cognitive behavior therapy. *Psychiatry Research: Neuroimaging* 272:30–37. doi:10.1016/j.pscychresns.2017.12.004.

Yzerbyt, V., D. Muller, C. Batailler, and C. M. Judd. 2018. New recommendations for testing indirect effects in mediational models: The need to report and test component paths. *Journal of Personality and Social Psychology* 115 (6):929–43. doi:10.1037/pspa0000132.