

Original Article

Emotional breakthrough and psychedelics: Validation of the Emotional Breakthrough Inventory

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Abstract

Background: Psychedelic therapy is gaining recognition and the nature of the psychedelic experience itself has been found to mediate subsequent long-term psychological changes. Much emphasis has been placed on the occurrence of mystical-type experiences in determining long-term responses to psychedelics yet here we demonstrate the importance of another component, namely: emotional breakthrough.

Methods: Three hundred and seventy-nine participants completed online surveys before and after a planned psychedelic experience. Items pertaining to emotional breakthrough were completed one day after the psychedelic experience, as were items comprising the already validated Mystical Experience Questionnaire and the Challenging Experience Questionnaire. Emotional breakthrough, Mystical Experience Questionnaire and Challenging Experience Questionnaire scores were used to predict changes in well-being (Warwick-Edinburgh Mental Wellbeing Scale) in a subsample of 75 participants with low well-being baseline scores (≤45).

Results: Factor analyses revealed six emotional breakthrough items with high internal consistency (Cronbach's alpha=0.932) and supported our prior hypothesis that emotional breakthrough is a distinct component of the psychedelic experience. Emotional breakthrough scores behaved dose-dependently, and were higher if the psychedelic was taken with therapeutic planning and intent. Emotional breakthrough, Mystical Experience Questionnaire and Challenging Experience Questionnaire scores combined, significantly predicted subsequent changes in well-being (r=0.45, p=0.0005, n=75), with each scale contributing significant predictive value. Emotional breakthrough and Mystical Experience Questionnaire scores predicted increases in well-being and Challenging Experience Questionnaire scores predicted less increases.

Conclusions: Here we validate a six-item 'Emotional Breakthrough Inventory'. Emotional breakthrough is an important and distinct component of the acute psychedelic experience that appears to be a key mediator of subsequent longer-term psychological changes. Implications for psychedelic therapy are discussed.

Keywords

Psychedelics, catharsis, emotion, therapy

Introduction

Psychedelic therapy is a re-emerging paradigm within mental health research (Schenberg, 2018). It is hypothesised that both biological and psychological processes play a role in this treatment, potentially working synergistically to determine therapeutic outcomes (Carhart-Harris, 2018; Carhart-Harris et al., 2017b). From a purely psychological perspective, most studies to-date have focused on the involvement of the mystical-type experience in determining long-term responses to psychedelics (Bogenschutz et al., 2015; Dakwar et al., 2014; Erritzoe et al., 2018; Garcia-Romeu et al., 2014; Griffiths et al., 2016; Johnson et al., 2016; Klavetter and Mogar, 1967; Kurland et al., 1972; MacLean et al., 2011; O'Reilly and Funk, 1964; Pahnke et al., 1970; Richards et al., 1977; Roseman et al., 2017; Ross et al., 2016) and see Stace (1960) for some classical texts relevant to the mystical experience. Influential measures used to operationally define the mystical experience include factors within the altered states of consciousness questionnaire (Dittrich, 1998; Studerus et al., 2010) and the more recently validated Mystical Experience Questionnaire (MEQ) (MacLean et al., 2012; Pahnke and Richards, 1966). It is now a well-replicated finding that the quality of the acute psychedelic experience is a key determinant of longer-term responses to psychedelics – and the mystical type experience seems to be relevant and important in this regard. However, this does not imply that the construct is well-defined, or that it is the sole, or indeed, primary determinant of long-term psychological outcomes.

Another key component of the acute psychedelic experience that has been found to be influential in determining long-term responses is the challenging experience (CE) (Barrett et al., 2016). Perhaps the best available tool for measuring CEs is the recently validated Challenging Experience Questionnaire (CEQ). This scale was developed with the intention of quantifying challenging emotions such as grief, fear, paranoia, etc. (Barrett et al., 2016). Recent studies have suggested that higher scores of the CEQ and other measures of CE can predict worse longer-term mental health

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Leor Roseman, Department of Medicine, Imperial College London, Hammersmith Campus, Du Cane Road, London, W2 5PB, UK. Email: leor.roseman13@imperial.ac.uk outcomes, thus suggesting that CE might be counter-therapeutic and perhaps even iatrogenic (Barrett et al., 2016; Carbonaro et al., 2016; Haijen et al., 2018; Roseman et al., 2017), although there are some contradictory findings in this regard, suggesting a more complex relationship (Barrett et al., 2016; Carbonaro et al., 2016). A major limitation of the CEQ however, is that it measures different challenging emotions and/or memories without addressing their potential resolution, and consequently is not able to quantify the potential clinical value of accepting and/or overcoming the relevant challenges (Watts et al., 2017).

Here, we endeavoured to examine a third potential mediator of longer-term responses to psychedelics, based on the assumption that the MEO and CEO do not fully or clearly capture the phenomenon of overcoming challenging emotions/memories and thereby experiencing emotional release or breakthrough. The phenomenon of emotional breakthrough (EB) overlaps to some extent with the psychoanalytic notion of catharsis (Breuer and Freud, 1895; Jackson, 1994). We call the questionnaire we have constructed and validated here, the Emotional Breakthrough Inventory (EBI). Unlike the CEQ, which appears to be a 'negative' predictor of clinical outcomes (i.e. higher CEQ scores predict worse mental health outcomes), we theorised that EBI would serve as a positive predictor of mental health, i.e. higher scores would predict better mental health outcomes such as increases in well-being. The development and use of the EBI in intended to supplement the use of the CEQ and MEQ and motivate further critique of all of three measures and the real-world phenomena they are intended to capture.

The most often-used approach in modern psychedelic therapy trials has its basis in work advanced by the collaboratory effort of Al Hubbard, Humphry Osmond and Abram Hoffer in the 1950s (Dyck, 2006; MacLean et al., 1961; Osmond, 1957). The focus of the so-called 'psychedelic' model is to use relatively high doses of a given psychedelic to promote the attainment of a powerful self-transcendent state that may be positively transformative in effect. The other major alternative therapeutic model, is the so-called 'psycholytic' (mind-loosening) model. This approach used lower doses of a psychedelic in concert with psychoanalytically oriented psychotherapy. Despite differences, mainly related to dose and number of sessions (i.e. higher doses but fewer sessions in psychedelic therapy), both of the psychedelic and psycholytic models emphasised the importance of emotional release.

One early account of Lysergic Acid Diethylamide's (LSD) therapeutic action stated that drug works to break emotional or memory blocks and 'in almost every case... terminates in psycho-catharsis, [causing] the patient to experience an exhilarating feeling of liberation' (Frederking, 1955: 263). Other psychedelic therapists, with allegiances to varying psychoanalytic schools, shared this appreciation of the importance of EB (Bonny and Pahnke, 1972; Cohen, 1959; Crocket et al., 1963; Eisner and Cohen, 1958; Fisher, 2015; Grof et al., 1980; Jensen, 1963; Katzenelbogen and Fang, 1953; Leuner, 1961; Martin, 1957; Richards, 2015; Sandison, 1955), and patients often make special reference to it in post-treatment reports (Belser et al., 2017; Gasser et al., 2014; Watts et al., 2017). EBs are often accompanied by and related to personal and interpersonal insights, and are therefore not necessarily transpersonal in the same way - or to the same extent – that mystical-type or peak experiences appear to be (Belser et al., 2017; Gasser et al., 2014; Grof, 1975; Loizaga-Velder, 2013; Richards, 2015; Watts et al., 2017).

The present study sought to develop and validate a brief EBI that is focused and concise in nature. Specifically, we assessed its internal, convergent, divergent and predictive validity. This was done using an online prospective survey in which participants answered questionnaires before and after drug intake in their own environment rather than e.g. in a laboratory. The sample was self-selecting and comprised mostly of healthy individuals, thus, to combat the issue of floor effects, a well-validated measure of psychological well-being was used as the primary dependent variable and index of post-psychedelic change in psychological/emotional health. We hypothesised that:

- H1: Scores on the EBI will increase in a dose-dependent
 manner
- H2: A therapeutic context (therapeutic intention before drug intake and a therapeutic setting) will be associated with higher EBI scores.
- H3: EBI scores will significantly discriminate from MEQ and CEQ scores.
- H4: EBI will predict changes in well-being.
- H5: A model incorporating EBI, MEQ and CEQ will predict changes in well-being, with EBI performing at least as well as the MEQ and CEQ.

Method

The study was approved by Imperial College Research Ethics Committee and the Joint Research Compliance Office at Imperial College London and carried out in accordance with principles of good clinical practice. Written informed consent was obtained from all subjects. The original survey has now closed but revised and still active versions of related surveys can be found here at www.psychedelicsurvey.com.

Software

Statistical analyses were conducted on SPSS 25 and Matlab 2017.

Design

The data presented in this article was collected as part of a larger prospective study (Haijen et al., 2018). Only elements of the design and data that are relevant to this article are presented here. Data was collected from psychedelic 'users' in a non-controlled, naturalistic and observational manner. Data was collected on-line, through the website and software platform psychedelicsurvey.com. The study was advertised via social media platforms. The baseline time-point was one week before a planned psychedelic experience and the key end-point was two weeks post the relevant experience. The following data were collected at baseline: demographics, intentions for the experience (see below), and the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) which served as the primary and sole dependent variable. Retrospective reports of the acute experience were answered one day after the relevant psychedelic experience. These included: EBI, MEQ, CEQ, dose and whether the

Table 1. Factor loadings from factor analysis of eight Emotional Breakthrough Inventory (EBI) items.

| Item | Factor 1 | Factor 2 |
|---|----------|----------|
| I faced emotionally difficult feelings that I usually push aside. | 0.788 | 0.192 |
| I experienced a resolution of a personal conflict/trauma. | 0.896 | -0.044 |
| I felt able to explore challenging emotions and memories. | 0.866 | -0.076 |
| I was resisting and avoiding challenging feelings throughout, without breakthrough. | 0.260 | 0.786 |
| I had an emotional breakthrough. | 0.872 | -0.151 |
| I was able to get a sense of closure on an emotional problem. | 0.889 | -0.185 |
| I felt emotionally stuck throughout, without breakthrough. | 0.249 | 0.845 |
| I achieved an emotional release followed by a sense of relief. | 0.848 | -0.194 |

The extraction method was principal component analysis (PCA). The six bold Items in Factor 1 reflect the final version of the EBI. The remaining bold items in Factor 2 where not used in the final version of EBI. Factor loadings >0.5 are in bold (n=379).

experience took place in a therapeutic setting (see below). Long-term outcomes were collected two weeks after the experience. The WEMWBS serving as the sole dependent variable for the present analysis. Data of 379 participants have been used for most of the analysis in this article, however, a subset of 75 participants with low well-being baseline scores (WEMWBS≤45) have been used for prediction of changes in well-being (more information below).

Item selection and face validity

The items of EBI were devised based on interview content from our previous psilocybin for treatment-resistant depression trial (Watts et al., 2017) and knowledge of the extensive literature and personal observations on the phenomenology of the psychedelic experience and its therapeutic application (Belser et al., 2017; Bonny and Pahnke, 1972; Cohen, 1959; Crocket et al., 1963; Eisner and Cohen, 1958; Fisher, 2015; Frederking, 1955; Gasser et al., 2014; Grof et al., 1980; Jensen, 1963; Katzenelbogen and Fang, 1953; Leuner, 1961; Martin, 1957; Richards, 2015; Sandison, 1955). Eight initial items were devised (Table 1), out of which two were 'negative' items that required reverse scoring. Items were rated using a visual analogue scale (VAS) (0-100, with incremental units of one) with zero defined as 'No, not more than usually', and 100 defined as 'Yes, entirely or completely'. Five experts (W Richards, R Watts, R Carhart-Harris, J Rucker and L Roseman) assessed the items and revised them if needed. Below are selected quotes that helped inform the construction of EBI items. These derive from interviews with patients (Watts et al., 2017) in our recent psilocybin for treatment-resistant depression trial (Carhart-Harris et al., 2017a). The quotes are from the qualitative analysis of Watts et al. (2017), although most were not included in that study.

- 'It felt like a relief, I was getting so emotional, I could feel it all coming out'
- 'One emotional song, and I lost control, the song was so sad I started crying uncontrollable, and was terrified by the depth of emotions'
- 'It was an emotional purging. The weight and anxiety and overwhelming depression have been lifted'
- 'It was an uncomfortable experience and it got to the point where I got really really angry with it, like something snapped

inside my head, and rather than be afraid of it I challenged it and at that point it kind of vanished, it went away'

- 'I was weeping, tears were flowing out of me. It wasn't a painful crying, it was like turning on the taps, like a washing, a washing out.'
- 'There was a lot of sadness, really really deep sadness: the loss the grief, it was love and sadness together, and letting go, I could feel the grief and then let it go because holding onto it was hurting me, holding me back. It was a process of unblocking'
- 'Excursions into grief, loneliness and rage, abandonment. Once I went into the anger it went 'pouf' and evaporated. I got the lesson that you need to go into the scary basement, once you get into it, there is no scary basement to go into [anymore]'
- 'I had lost my ability to grieve and cry. [During the dosing session] I cried and that was a cathartic experience for me, a very welcoming sweet experience'.

Other measures

MEQ (Pahnke et al., 1970; Pahnke and Richards, 1966). The MEQ was originally developed by Walter Pahnke and Bill Richards based on the anthropological research and theoretical writings of philosopher Walter Stace (1960). Stace studied reports of mystical-type experiences occurring in a variety of religions and identified common experiential components which he argued are universal, i.e. culturally independent and unspecific to any particular religion or philosophical framework (as in Maslow's peak experience (Maslow, 1959; Maslow, 1964), and Huxley's Perennial Philosophy (Huxley, 1945)). The MEQ has been revised since its original conception and now includes 30 questions (MacLean et al., 2012) rated according to a five-point Likert scale. It is divided into four subscales: (a) Mystical - which includes arguably the core features of mystical-type experience: named 'unity', 'noetic' and 'sacredness'; (b) Positive-mood; (c) Transcendence of time and space; and (d) Ineffability. The total MEQ score is calculated as the average of all 30 items and then multiplied by 20 to provide a 0-100 value.

CEQ. The CEQ was recently developed to measure the challenging experience (Barrett et al., 2016). The CEQ is derived from 'challenging' items from other psychedelic questionnaires: Hallucinogen Rating Scale (HRS) (Strassman et al., 1994), Altered State

of Consciousness questionnaire (ASC) (Dittrich, 1975, 1998), and States of Consciousness Questionnaire (SOCQ) (Griffiths et al., 2006; Pahnke et al., 1969). The CEQ has 26 questions, five-point Likert scale, and is divided into seven dimensions: (a) Isolation, (b) Grief, (c) Physical distress, (d) Fear, (e) Insanity, (f) Paranoia, and (g) Death. Total CEQ score was calculated as the average of all items and then multiplied by 20 to provide a 0–100 value.

WEMWBS. The WEMWBS (Tennant et al., 2007) was designed to measure the psychological well-being of a population. WEMWBS has 14 questions scored using a five-point Likert scale. Scores reflect feelings and thoughts in the two weeks prior to answering the questionnaire. In the present study, the WEMWBS was used to observe potential changes in well-being two weeks after drug intake compared to baseline. Many of the participants had high baseline WEMWBS scores – which created a potential ceiling effect limiting scope for the predicted increases in well-being. We therefore restricted the present analysis to just those subjects who had relatively low baseline well-being scores (\leq 45, n=75) (Taggart et al., 2015) and therefore greater potential for change (normative data based on the general population in England and Scotland showed a mean WEMWBS score of 50.7 (95% confidence interval (CI): 50.3–51.1)).

Drug type. Participants were asked what specific psychedelic they took. Options included: (a) psilocybin/magic mushrooms/truffles, (b) LSD/1P-LSD, (c) ayahuasca, (d) DMT/5-5-MeO-DMT, (e) *Salvia divinorum*, (f) mescaline, (g) iboga/ibogaine or (h) the option to give a free answer.

Drug dose. Drug dose was assessed using a previously implemented approach of estimating dosage in relation to LSD equivalents. The rationale for this is to provide a reference-standard dose that can be compared across different psychedelics (Nour et al., 2016). Options were: a low dose (equivalent to no more than 50 μg of LSD), a moderate dose (equivalent to no more than 100 μg of LSD), a high dose (equivalent to no more than 200 μg of LSD), a very high dose (equivalent to no more than 300 μg of LSD), or an extremely high dose (equivalent to more than 300 μg of LSD).

Therapeutic intention. At pre-drug baseline, participants answered the question 'Can you indicate what your motives are to undergo a psychedelic session/ceremony/experience?' A number of intentions were presented, and participants scored each of them on a four-point Likert scale with the options: 'not at all,' 'somewhat,' 'moderately,' or 'very much.' For this analysis we chose two intentions of interest as potential predictors of EBI scores: the intention to have the experience for (a) 'Therapeutic/personal growth', and (b) 'To confront difficult emotions'.

Therapeutic setting. Participants answered 'yes' or 'no' to the question 'Was the setting designed and/or prepared with a therapeutic objective in mind?' We hypothesised that those who answered 'yes' here would have higher EBI scores.

Factor analysis and definition of EBI

Scores for the original eight EBI items were subjected to an exploratory factor analysis using principal component analysis (PCA). The appropriate number of factors to be extracted was

determined by the scree plot criterion (Cattell, 1966). The PCA yielded two factors (Table 1), out of which only factor 1 with six items was used in further analysis. The internal consistency of the six items was assessed with Cronbach's alpha (Cronbach, 1951).

Discriminant validity

In order to test whether the EBI, and the construct it is intended to sample, is significantly different from the constructs indexed by the MEO and CEO, the items of all of the questionnaires were entered into one factor analysis (PCA, 62 items). If EB, and the EBI that samples EB, is insufficiently different from the other questionnaires and the constructs they sample, then the PCA would have been expected to yield just two factors - one containing items of the MEQ and the other containing items from the CEO, with EBI items loading onto one or both of these two factors. If, however, as predicted, the EBI can be discriminated from the MEQ and CEQ, then the PCA would be expected to discover three independent factors, one of which would contain items of the EBI. A correlation matrix including the EBI and subdimensions of MEQ and CEQ was also calculated to further explore similarities and differences between the three questionnaires and their components.

Predictive validity - changes in well-being

Pearson correlation of the EBI versus ΔWEMWBS was calculated to test whether the EBI could serve as a predictor of clinical changes (n=75). Furthermore, a multiple regression was calculated with Δ WEMWBS as the dependent variable and the EBI, MEQ and CEQ as independent variables (n=75). Beta coefficients were calculated for each of the questionnaires to assess the contribution of each of the questionnaires to explaining changes in the dependent variable (Δ WEMWBS). If significant beta coefficients were found for scores on all of the questionnaires, this would demonstrate the significant added value of each of the three questionnaires and the variance they can explain when combined. We hypothesised that the beta coefficients of EBI and MEQ would be positive predictors of changes (increases) in WEMWBS scores whereas CEQ scores would be negative predictors of changes in well-being.

Results

Demographics

See Table 2 for the demographics of 379 participants who completed EBI and of a subsample of 75 participants with WEMWBS_{baseline} \$\infty 45\$.

Factor structure

The eight original EBI items were entered into a PCA. The Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy was found to be 0.877, and Bartlett's test of sphericity was significant ($\chi^2_{(28)}$ =2005.9, p<0.0001) confirming that the data was suitable for factor analysis (Budaev, 2010). Inspection of the scree plot using Cattell's criterion (Cattell, 1966) supported

Table 2. Demographics.

| Total | | n=379 | n=75 |
|-------------------------------|---|-----------------|--------------|
| Gender | Male | 252 (66.5%) | 57 (76%) |
| | Female | 97 (25.6%) | 18 (24%) |
| | Other | 2 (0.5%) | 0 |
| | Blank | 28 (7.4%) | 0 |
| Age | | 30.6 ± 11.0 | 29 ± 9.4 |
| Educational level | Left school before age 16 years without qualifications | 7 (1.8%) | 3 (4%) |
| | Some high school/GCSE level (in UK) | 23 (6.1%) | 4 (5.3%) |
| | High school diploma/A-level education (in UK) | 47 (12.4%) | 10 (13.3%) |
| | University (or equivalent) | 74 (19.5%) | 18 (24%) |
| | Bachelor's degree (or equivalent) | 121 (31.2%) | 29 (38.7%) |
| | Post-graduate degree (e.g. masters or doctorate) | 79 (20.1%) | 11 (14.7%) |
| | Blank | 28 (7.4%) | 0 |
| Employment status | Student | 124 (32.7%) | 17 (22.7%) |
| . , | Unemployed | 33 (8.7%) | 14 (18.7%) |
| | Part-time job | 55 (14.5%) | 16 (21.3%) |
| | Full-time job | 133 (35.1%) | 27 (36%) |
| | Retired | 6 (1.5%) | 1 (1.3%) |
| | Blank | 28 (7.4%) | 0 |
| Nationality | United Kingdom | 74 (19.5%) | 19 (25.3%) |
| • | United States of America | 97 (25.6%) | 21 (28%) |
| | Denmark | 42 (11.1%) | 4 (5.3%) |
| | Germany | 21 (5.5%) | 0 |
| | Canada | 13 (3.4%) | 5 (6.6%) |
| | Other (38 other nationalities) | 104 (27.4%) | 26 (34.8%) |
| | Blank | 28 (7.4%) | (*) |
| Psychiatric history | Has been diagnosed with at least one psychiatric illness in the past ^a | 116 (30.6%) | 38 (50.7%) |
| | Never been diagnosed with a psychiatric illness | 235 (62%) | 37 (49.3%) |
| Previous psychedelic drug use | Never (psychedelic naïve) | 42 (11.1%) | 11 (14.6%) |
| | Once | 20 (5.3%) | 7 (9.3%) |
| | 2–5 times | 71 (18.7%) | 22 (29.3%) |
| | 6-10 times | 54 (14.2%) | 15 (20%) |
| | 11-20 times | 57 (15%) | 7 (9.3%) |
| | 21-50 times | 63 (16.6%) | 8 (10.6%) |
| | 51–100 times | 19 (5%) | 4 (5.3%) |
| | More than 100 times | 25 (7%) | 1 (1.3%) |
| | Blank | 28 (7.4%) | (12 /9) |

Absolute frequencies and means \pm standard deviations are presented in the table. Numbers in the brackets show the percentages of the absolute frequencies. The column with n=379 is the whole population in this paper, while the column with n=75 is of the subpopulation with Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) \leq 45. Psychiatric illnesses include major depressive disorder, bipolar disorder, schizophrenia, anxiety disorder, substance abuse disorder, alcohol dependence, hallucinogen persisting perception disorder, psychotic disorder, personality disorder, attention deficit hyperactivity disorder, obsessive compulsive disorder and eating disorder.

a two-factor model (Table 1). The first component explained 57.1% of the variance and the second explained 18.3%. Other components explained <8% of the variance. Commonality values (the variance of a variable which is explained by the factors) ranged from 65.7–82.5%. Factor 1 comprised of six items, and factor 2 comprised of the two negative, reverse scored items. Originally, we theorised that all items would load into one single factor with the negative items negatively loading on to this. Results revealed that this is not the case, however, and instead the two negative items load onto a sufficiently distinct factor. We therefore decided not to use these two negative items in the final version of EBI.

Internal consistency

After discarding the two negative items, the resulting six-item EBI displayed a very high internal consistency (Cronbach's alpha=0.932) (Cronbach, 1951). The average of the six items showed a high correlation with factor 1 score (r=0.996, p<0.0001) and therefore the average of the six items was used as the total EBI score in further analysis. The mean of EBI scores was significantly higher than 0 (EBI=43 \pm 31.5, skewness=0.165, kurtosis=-1.3, p<0.0001, one sample t-test, t=379). The mean MEQ score was 57 \pm 22.63. The mean CEQ score was 19.7 \pm 16.4. See violin plots (Hintze and Nelson, 1998) of EBI, MEQ and CEQ in Figure 1.

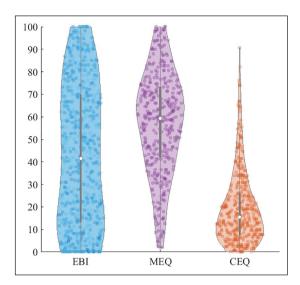


Figure 1. Violin plots of Emotional Breakthrough Inventory (EBI), Mystical Experience Questionnaire (MEQ) and Challenging Experience Questionnaire (CEQ). Total scores of each questionnaire are spread along the y axis. Violin plots are similar to box plots but show also probability density in different values (the width of the plot). The white circle and the thick line are a boxplot in which the white circle is the median and the thick line is the interquartile range (n=379).

Predictive validity – dose, therapeutic intention and setting

As predicted, EBI scores significantly (positively) correlated with (estimated) drug dose (r_s =0.192, p=0.0001, one-tail, n=379). Baseline ratings of therapeutic intention and ratings of willingness to confront difficult emotions significantly correlated (positively) with EBI scores (r_s =0.256 and r_s =0.279, respectively, p<0.0001, one-tail, n=351). Participants who endorsed the view that the setting for their experience was designed with a therapeutic objective in-mind had higher EBI scores (EBI=47.9±30.1, n=144) than those who felt the setting for their experience was not therapeutic in nature or design (EBI=31.6±29.1, n=168) (p<0.0001, Cohen's d=0.55, independent samples t-test, one-tail).

Discriminant validity

To demonstrate that the EBI is a novel measure that can be discriminated from the MEQ and CEQ, all of the 62 items from MEQ, CEQ and EBI were entered into a single factor analysis (PCA) (Table 3). The KMO measure of sampling adequacy was 0.941, and Bartlett's test of Sphericity was significant ($\chi^2_{(1891)}$ =19829, p<0.0001) confirming that the data was suitable for factor analysis (Budaev, 2010). Inspection of the scree plot using Cattell's criterion (Cattell, 1966) supported a model of three factors. The first component explained 31.3% of the variance, the second explained 15.4% of the variance, and the third explained 6.1% of the variance. Other components explained <4% of the variance in the sample. Commonality values ranged from 43.7–81.5%. The first factor contained high loadings from MEQ items, and relatively high loading from EBI items as well.

The second factor contained high loadings from CEQ items alone, and the third factor contained high loading from EBI items alone (without any MEQ or CEQ items). These results suggest that for some subjects, EB was accompanied by mystical-type phenomena (and vice versa), whilst for others, EB was distinct from either classical challenging and/or mystical-type phenomena. Note that the relatively low percentage of variance explained by component 3 is probably due to the relatively few EBI items when compared with the MEQ and CEQ (i.e. six in the EBI versus 26 and 30 the CEQ and MEQ, respectively).

A correlation matrix containing all of the EBI items plus subscales of the MEQ and CEQ is presented in Figure 2. It is apparent that the EBI correlates strongly with all MEQ dimensions and also with the grief dimension of CEQ (a relationship between EBI and grief is also suggested in the factor analysis (Table 3)). Correlations between a given subscale of the MEQ and its other subscales are higher than those with the EBI, suggesting that despite some commonalities, the EBI and MEQ are still measuring sufficiently distinct phenomena.

Predictive validity - changes in well-being

The difference in WEMWBS from baseline (38.8±5.3) to two weeks after the experience (47.9 ± 7.2) was significant (Cohen's d=1.44, p<0.0001, n=75, paired sample t-test). Emotional breakthrough scores significantly correlated with changes in wellbeing (Δ WEMWBS) two weeks after the psychedelic experience (compared with well-being scores at baseline), r=0.294, p=0.005, one-tail, n=75. A multiple regression analysis with Δ WEMWBS as dependent variable and EBI, MEQ and CEQ values as independent variables yielded a strong predictive model (r=0.45, p=0.0005, one-tail, n=75). The standardised beta coefficients for the EBI, MEQ and CEQ were all significant, with the EBI performing as well as the other measures (β_{EBI} =0.29, p=0.017; p=0.038; $\beta_{\text{CEO}} = -0.35, \quad p = 0.002;$ $\beta_{\text{MEO}}=0.24$, Independent Pearson's correlations between the MEQ and CEQ and Δ WEMWBS were r=0.274, and r=-0.147, respectively. The tolerance measures (collinearity) of EBI, MEQ and CEQ were 0.631, 0.634, 0.814, respectively (tolerance >0.2 means that the independent variables are relatively independent from each other). As a further exploratory analysis, the same regression model was applied to the wider sample regardless of WEMWBS baseline scores. Out of the total sample, 253 participants had completed the WEMWBS at two weeks after the experience. The difference in WEMWBS from baseline (49.5±8.6) to two weeks after the experience (52.7 ± 7.3) for this population was significant as well though with smaller effect size (Cohen's d=0.4. p<0.0001, n=253, paired sample t-test). A multiple regression analysis with Δ WEMWBS as dependent variable and EBI, MEQ and CEQ values as independent variables for these 253 participants yielded a marginally significant result in the same direction as the smaller subsample (r=0.153, p=0.059, one-tail, n=253). The standardised beta coefficients for the EBI, MEQ and CEQ were all marginally significant (β_{EBI} =0.115, p=0.063; $\beta_{\text{MEO}} = 0.075, \quad p = 0.15;$ $\beta_{\text{CEO}} = -0.086$, p = 0.01; one-tail). Independent Pearson's correlations between the EBI, MEQ and CEQ and Δ WEMWBS were r=0.119, r=0.106 and r=-0.019, respectively. Overall, the results of the larger subsample of 253 participants were in a similar direction yet less significant compared to the subsample of 75 participants, and this is probably

Table 3. Factor analysis of Emotional Breakthrough Inventory (EBI), Mystical Experience Questionnaire (MEQ) and Challenging Experience Questionnaire (CEQ). All of the 62 items of the EBI, MEQ and CEQ have been included in a principal component analysis (PCA) which resulted in three factors. The first factor has high loadings of items from MEQ and EBI. The second factor has high loadings of items from CEQ. The third factor has high loading of items from EBI. This analysis, together with the correlation matrix in Figure 2, reveals that EBI is discriminate from MEQ and CEQ. Factor loadings >0.5 are in bold (*n*=379).

| Questionnaire | Subscale | Question | Factor 1 | Factor 2 | Factor 3 |
|---------------|------------|--|----------|----------|----------|
| EBI | | I faced emotionally difficult feelings that I usually push aside. | 0.524 | 0.306 | 0.528 |
| | | I experienced a resolution of a personal conflict/trauma | 0.543 | 0.036 | 0.656 |
| | | I felt able to explore challenging emotions and memories. | 0.552 | -0.055 | 0.613 |
| | | I had an emotional breakthrough. | 0.585 | 0.041 | 0.631 |
| | | I was able to get a sense of closure on an emotional problem. | 0.515 | -0.057 | 0.678 |
| | | I achieved an emotional release followed by a sense of relief. | 0.606 | -0.104 | 0.576 |
| MEQ | Mystical | Freedom from the limitations of your personal self and feeling a unity or bond with what was felt to be greater than your personal self. | 0.755 | -0.309 | -0.009 |
| | | Experience of pure being and pure awareness (beyond the world of sense impressions). | 0.776 | -0.3 | -0.057 |
| | | Experience of oneness in relation to an 'inner world' within. | 0.789 | -0.257 | -0.056 |
| | | Experience of the fusion of your personal self into a larger whole. | 0.778 | -0.271 | -0.055 |
| | | Experience of unity with ultimate reality. | 0.801 | -0.284 | -0.061 |
| | | Feeling that you experienced eternity or infinity. | 0.761 | -0.191 | -0.127 |
| | | Experience of oneness or unity with objects and/or persons perceived in your surroundings. | 0.65 | -0.3 | -0.078 |
| | | Experience of the insight that 'all is one'. | 0.756 | -0.321 | -0.084 |
| | | Awareness of the life or living presence in all things. | 0.681 | -0.337 | -0.082 |
| | | Gain of insightful knowledge experienced at an intuitive level. | 0.705 | -0.28 | 0.216 |
| | | Certainty of encounter with ultimately reality. | 0.682 | -0.283 | -0.02 |
| | | You are convinced now, as you look back on your experience, that in it you encountered ultimate reality. | 0.653 | -0.294 | 0.07 |
| | | Sense of being at a spiritual height. | 0.715 | -0.299 | 0.007 |
| | | Sense of reverence. | 0.624 | -0.255 | -0.015 |
| | | Feeling that you experienced something profoundly sacred and holy. | 0.65 | -0.243 | -0.008 |
| | Positive | Experience of amazement. | 0.675 | -0.291 | -0.203 |
| | mood | Feelings of tenderness and gentleness. | 0.596 | -0.374 | 0.091 |
| | | Feelings of peace and tranquillity. | 0.554 | -0.521 | -0.004 |
| | | Experience of ecstasy. | 0.522 | -0.396 | -0.097 |
| | | Sense of awe or awesomeness. | 0.654 | -0.344 | -0.144 |
| | | Feelings of joy. | 0.522 | -0.451 | -0.098 |
| | Time and | Loss of your usual sense of time. | 0.632 | -0.059 | -0.234 |
| | space | Loss of your usual sense of space. | 0.648 | -0.049 | -0.288 |
| | ., | Loss of usual awareness of where you were. | 0.547 | 0.058 | -0.319 |
| | | Sense of being 'outside of' time, beyond past and future. | 0.742 | -0.05 | -0.204 |
| | | Being in a realm with no space boundaries. | 0.711 | -0.181 | -0.14 |
| | | Experience of timelessness. | 0.736 | -0.114 | -0.239 |
| | Ineffabil- | Sense that the experience cannot be described adequately in words. | 0.71 | -0.045 | -0.123 |
| ity | | Feeling that you could not do justice to your experience by describing it in words. | 0.711 | -0.074 | -0.086 |
| | | Feeling that it would be difficult to communicate your own experience to others who have not had similar experiences. | 0.649 | -0.031 | -0.086 |
| CEQ | Isolation | Isolation and loneliness. | 0.298 | 0.647 | -0.001 |
| | | Feeling of isolation from people and things. | 0.255 | 0.623 | -0.025 |
| | | I felt isolated from everything and everyone. | 0.252 | 0.628 | -0.002 |
| | Grief | Sadness. | 0.356 | 0.542 | 0.365 |
| | | Feelings of grief. | 0.416 | 0.502 | 0.378 |
| | | I felt like crying. | 0.423 | 0.339 | 0.388 |
| | | Feelings of despair. | 0.396 | 0.662 | 0.118 |
| | | Despair. | 0.366 | 0.691 | 0.09 |
| | | | 0.500 | 0.071 | 0.00 |

(Continued)

Table 3. (Continued)

| Questionnaire | Subscale | Question | Factor 1 | Factor 2 | Factor 3 |
|---------------|----------|--|----------|----------|----------|
| | Physical | Feeling my heart beating. | 0.379 | 0.22 | -0.093 |
| | distress | Feeling my body shake/tremble. | 0.324 | 0.301 | -0.14 |
| | | I felt shaky inside. | 0.374 | 0.425 | -0.115 |
| | | I felt my heart beating irregularly or skipping beats. | 0.348 | 0.184 | -0.073 |
| | | Pressure or weight in my chest or abdomen. | 0.255 | 0.283 | -0.012 |
| | Fear | I had the feeling something horrible would happen. | 0.414 | 0.686 | -0.155 |
| | | Experience of fear. | 0.419 | 0.684 | -0.188 |
| | | Anxiousness. | 0.298 | 0.61 | -0.136 |
| | | Panic. | 0.414 | 0.655 | -0.201 |
| | | I felt frightened. | 0.429 | 0.702 | -0.158 |
| | Insanity | Fear that I might lose my mind or go insane. | 0.407 | 0.61 | -0.203 |
| | | I was afraid that the state I was in would last forever. | 0.419 | 0.54 | -0.235 |
| | | I experienced a decreased sense of sanity. | 0.414 | 0.48 | -0.206 |
| | Paranoia | I had the feeling that people were plotting against me. | 0.233 | 0.31 | -0.204 |
| | | Experience of antagonism toward people around me. | 0.167 | 0.368 | -0.069 |
| | Death | I had the profound experience of my own death. | 0.501 | 0.229 | -0.126 |
| | | I felt as if I was dead or dying. | 0.463 | 0.408 | -0.161 |

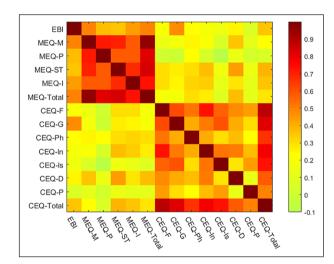


Figure 2. Correlation matrix of Emotional Breakthrough Inventory (EBI), Mystical Experience Questionnaire (MEQ) subscales and Challenging Experience Questionnaire (CEQ) subscales, and CEQ subscales. High Pearson's correlations are observed for EBI with MEQ subscales, and with CEQ_{Grief}. Yet, correlations between any given MEQ subscale and the other MEQ subscales are higher than with the EBI. This analysis, together with the factor analysis in Table 3, suggest that EBI is distinct from MEQ and CEQ (n=379). CEQ-D: Death; CEQ-F: Fear; CEQ-G: Grief; CEQ-In: Insanity; CEQ-Is: Isolation; CEQ-P: Paranoia; CEQ-Ph: Physical distress; MEQ-I: Ineffability; MEQ-M: Mystical;

MEQ-P: Positive mood; MEQ-ST: Transcendence of space and time.

due to a ceiling effect at the baseline of WEMWBS in the larger subsample. These results confirm that each of the questionnaires contribute added value to the model, whilst being significantly distinct from each other. A natural conclusion from this is that a prediction model containing measures of all three constructs will perform better than a model that neglects any one of them.

Discussion

Here we sought to devise and carry out validation work on a new scale intended to describe an important and hitherto under-quantified component of the psychedelic experience, the EB. We anticipate that this scale will serve as a useful 'state' predictor of the longer-term psychological outcomes after a psychedelic experience - supplementing already existing state predictor measures such as the MEQ and CEQ. We call this new scale the 'EBI'. Results revealed that (as measured by the EBI) emotional breakthrough is dose dependent and sufficiently different from the mystical-type and challenging experience as indexed by the MEQ and CEQ respectively. Consistent with a major prior hypothesis, we found that (like the MEQ) the EBI significantly predicts post-psychedelic changes in well-being (greater EB, greater increases in well-being) and we also discovered that the EBI does not render either the CEQ or MEQ redundant but rather a multi-factorial predictor model that combines all three measures performs better than any alternative that neglects any one of them. The combined EBI, MEQ and CEQ model is able to predict close to 20% of the variance in well-being changes after a psychedelic experience, a not inconsiderable amount given the relatively 'well' nature of this sample and uncontrolled study design. We also found that both therapeutic intention and therapeutic setting can predict the intensity of EB, suggesting that, as with other components of the acute psychedelic experience, EB is highly influenced by the context in which the psychedelic is taken (Carhart-Harris et al., 2017b; Hartogsohn, 2016, 2017). Taken together, these results support the addition of the EBI to the arsenal of tools used to quantitatively describe the psychedelic experience and predict its longer-term psychological effects.

Modern phenomenological analyses (Belser et al., 2017; Gasser et al., 2014; Watts et al., 2017) and therapists' accounts (Bonny and Pahnke, 1972; Cohen, 1959; Crocket et al., 1963; Eisner and Cohen, 1958; Fisher, 2015; Grof et al., 1980; Jensen, 1963; Katzenelbogen and Fang, 1953; Leuner, 1961; Martin,

1957; Richards, 2015; Sandison, 1955) have tended to recognise the importance of EB within the context of psychedelic experiences and psychedelic therapy; however, a validated quantitative measure of this phenomenon is arguably overdue and there is a significant contemporary need for it. Perhaps due to the relative dearth of psychedelic research since the 1960s and a particular bias common among those few research teams working within the current resurgent era, contemporary researchers have tended to place significant emphasis on the mystical-type experience, in part due to well-replicated findings that its occurrence is predictive of relevant psychological outcomes, such as improvements in well-being (Haijen et al., 2018) changes in personality (MacLean et al., 2011), and improvements in clinical outcomes in patient populations (Roseman et al., 2017).

The present work has demonstrated the added value of measuring EB for predicting subsequent psychological outcomes after a psychedelic experience. However, are there other 'state' and perhaps 'contextual' factors that are also important determinants of longer-term responses to psychedelics – and might there be alternative dependent variables that are differentially influenced by state and contextual predictors? Indeed, these variables may also interact in non-linear ways. We have previously emphasised (Carhart-Harris et al., 2017b), and sought to measure and demonstrate, the influence of contextual factors such as the presence of others, associated therapeutic alliance, a therapeutic intention and setting and a willingness to surrender or 'let-go' to the psychedelic experience on longer-term psychological outcomes, and found them to be important (Haijen et al., 2018). Like 'state' predictors of long-term responses, it is logical to see these factors as mediators of the relevant changes, as they are temporal antecedents of them. Other factors we predict may be important for influencing long-term changes include psychological insight and psychological integration. Insight is a phenomenon that may occur acutely in a state-like fashion (like EB) but could only be more protracted, crystallising in the days to weeks following a psychedelic experience. Integration is another protracted phenomenon that may have no clear end-point as such.

Much more work is needed to understand the neurobiology of the entire psychedelic psychotherapy process and this will naturally require brain imaging at various time points: before, during and after a specific psychedelic experience. Further discussion of this topic is beyond the remit of the present article, only to say that there is some evidence that the magnitude of increased brain entropy, a known biomarker of the psychedelic state, has been found to be predictive of subsequent psychological changes (increased trait 'openness') over a consistent time-scale as was measured here in relation to well-being (Lebedev et al., 2016).

Finally, we advocate looking at other dependent variables than just well-being. Well-being is a useful index of mental health in general populations (Tennant et al., 2007) but it may be that certain psychiatric disorders and/or symptom clusters behave differently in their relation to predictor variables. This is something we intend to investigate more fully in future analyses plus new and on-going studies.

Our novel analysis is part of an effort to elucidate the importance of the psychological mechanism of psychedelics alongside their pharmacological uses, and by doing so to emphasise the importance of the context in which these drugs are taken. That is to say that affirming that the experience mediates the clinical outcomes, means that the regular clinical context will have to be

modified to accommodate psychedelics as an effective psychopharmacological intervention within psychiatry. On that note, there is a lesson from history we would like to bring to readers' attention before closing: psychedelic therapy was once a relatively widely practised intervention in Western psychiatry before opinion shifted against it (Baum, 2016; Grinspoon and Bakalar, 1979). As the pharmacological revolution in psychiatry gathered momentum in the 1960s and the thalidomide scandal occurred at a related time, regulations on experimental medicines tightened, as did the methods for assessing their safety and efficacy (Oram, 2012). Within this climate, some efforts were made to extricate the basic pharmacological action of LSD from the psychotherapeutic manner in which it was typically administered, e.g. by giving the drug in a psychologically 'sterile' environment (Ludwig, 1985). In at least one published study, patients treated with LSD were placed in a belt that restrained them to their bed (Johnson et al. 1969). Unsurprisingly, such efforts to 'neutralise' context (which is, of course, a misnomer) tended to reveal that LSD without contextual support does not nearly have the same therapeutic value and safety profile as LSD given with the rapeutic support (Oram, 2012, 2014). These results, combined with the spread of unfounded but nonetheless affecting misinformation about LSD (Dishotsky et al., 1971) plus a tightening of legislation on drugs of potential misuse, best exemplified by the 1970 Controlled Substances Act (1970), signalled the demise of psychedelic psychotherapy. The present study's analyses confirm the findings of other analyses (Dimascio and Klerman, 1960; Haijen et al., 2018; Hyde, 1960; Lasagna, 1963; Leary et al., 1963; Studerus et al., 2012) that context is an essential component of the psychedelic model (Carhart-Harris et al., 2017b; Hartogsohn, 2017; Leary et al., 1963) and that if one wishes to promote a positive therapeutic response to a psychedelic, then heeding and optimising the role of certain contextual components is entirely necessary, whereas neglecting them is bad practice if not unethical. Our hope is that psychedelic therapy of the future can be done in a way and a context that encourages and allows the free release of emotion, e.g. using tools such as music (Barrett et al., 2018; Bonny and Pahnke, 1972; Kaelen et al., 2017), empathic listening and purposefully designed supportive environments, even if this presents a significant challenge to the conventions of mainstream medicine:

[Practicing psychedelic therapy here] has transformed the entire hospital, because the whole atmosphere engendered by LSD has spread throughout the hospital and, in fact, forms an essential part of the hospital culture. If LSD is given in a large institutional setting, treatment will be ineffective unless this transformation has occurred.

British psychiatrist Ronald Sandinson (1916–2010) cited in Abramson (1960: 15)

Three limitations of the present study should be noted. First, the present study's population contained mostly healthy experienced psychedelic users, and therefore the results do not necessarily apply to clinical population (Haijen et al., 2018). In these users the outcomes in well-being might be related to the expectation build around psychedelic use in the psychedelic culture and literature. Furthermore the pharmacological mechanism of psychedelics might be different in these users due to greater exposure to this class of drugs. To improve translational relevance, future

studies should use the EBI in clinical populations to assess its ability to predict changes in clinically recognised phenomena, such as depressive symptoms and anxiety. The prediction model of changes in well-being predicted only 20% of the variance. However, we do expect this model to perform better in a clinical trial and in a controlled environment. Second, the study has relied on self-reports of drugs, doses and timing, which are not as accurate as in laboratory studies. Psychedelics that are sold in the market are unreliable in many cases and one cannot be sure which drug and what dose was used. Third, there was limited analysis of convergent validity. Although there is clearly some overlap with the MEQ, we are not aware of any other questionnaires that measure a construct closely related to EBI. One way to address this in the future might be to compare EBI scores with quantitative outcomes from qualitative interviews, to assess whether there is some correspondence. A better demonstration of the convergent validity of the EBI will serve to further strengthen its construct validity (Campbell and Fiske, 1959).

In conclusion, EB is an essential component of psychedelicassisted therapy, and therefore should be measured in future experimental medicine studies and clinical trials with psychedelics, alongside measures of peak and challenging experiences. Quantifying the psychological mechanism of psychedelicassisted therapy is essential as psychedelic-assisted therapy is rightly both a pharmacological and psychological intervention. The predictive value of peak experiences is well-established within this context, and now the importance of EBs can be better researched and potentially supported as well. Furthermore, based on qualitative studies (Belser et al., 2017; Gasser et al., 2014; Watts et al., 2017) and a broader awareness of the phenomenology of the psychedelic experience, we believe there is scope for additional quantitative measures (e.g. of psychological insight) to be developed, so that a fuller understanding of the psychological and neurobiological mechanism of psychedelic (mind-revealing) therapy can be appreciated and utilised for positive ends.

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References

Abramson HA (1960) The Use of LSD in Psychotherapy: Transactions. New York: Josiah Macy, Jr. Foundation.

- Barrett FS, Bradstreet MP, Leoutsakos J-MS, et al. (2016) The Challenging Experience Questionnaire: Characterization of challenging experiences with psilocybin mushrooms. *J Psychopharmacol* 30: 1279–1295.
- Barrett FS, Preller KH and Kaelen M (2018) Psychedelics and music: Neuroscience and therapeutic implications. *Int Rev Psychiatry* 1–13.
- Baum D (2016) Legalize It All: How to win the war on drugs. Harper's Magazine. Available at: https://harpers.org/archive/2016/04/legalize-it-all/ (accessed 28 November 2018).
- Belser A (2016) Real, Relational, and Embodied: The First Qualitative Study of Patient Experiences of Psilocybin-Assisted Psychotherapy. In: *Interdisciplinary Conference on Psychedelics Research (ICPR)*, 6 June 2016. Amsterdam. Youtube–Available at: https://www.youtube.com/watch?v=DUYDjV8lQxo
- Belser AB, Agin-Liebes G, Swift TC, et al. (2017) Patient experiences of psilocybin-assisted psychotherapy: An interpretative phenomenological analysis. *J Humanist Psychol* 57: 354–388.
- Bogenschutz MP, Forcehimes AA, Pommy JA, et al. (2015) Psilocybinassisted treatment for alcohol dependence: A proof-of-concept study. *J Psychopharmacol* 29: 289–299.
- Bonny HL and Pahnke WN (1972) The use of music in psychedelic (LSD) psychotherapy. *J Music Ther* 9: 64–87.
- Breuer J and Freud S (1895) Studies on Hysteria. London: Hachette UK. Budaev SV (2010) Using principal components and factor analysis in animal behaviour research: Caveats and guidelines. Ethology 116: 472–480.
- Campbell DT and Fiske DW (1959) Convergent and discriminant validation by the multitrait-multimethod matrix. *Psychol Bull* 56: 81.
- Carbonaro TM, Bradstreet MP, Barrett FS, et al. (2016) Survey study of challenging experiences after ingesting psilocybin mushrooms: Acute and enduring positive and negative consequences. J Psychopharmacol 30: 1268–1278.
- Carhart-Harris R, Bolstridge M, Day C, et al. (2017a) Psilocybin with psychological support for treatment-resistant depression: Six-month follow-up. *Psychopharmacology* 235(2): 399–408.
- Carhart-Harris R, Roseman L, Haijen E, et al. (2017b) Psychedelics and the essential importance of context. *J Psychopharmacol* 32(7): 725–731.
- Carhart-Harris RL (2018) Serotonin, psychedelics and psychiatry. World Psychiatry 17: 358–359.
- Cattell RB (1966) The scree test for the number of factors. *Multivariate Behav Res* 1: 245–276.
- Cohen S (1959) The therapeutic potential of LSD-25. In: Featherstone RM and Simon A (eds) A Pharmacologic Approach to the Study of the Mind. Springfield, Ill.: Thomas, pp. 251–257.
- Controlled Substances Act (1970) Pub. L. No. 91-513, 84 Stat. 1236 (codified as amended at 21 U.S.C. § 812 (2012). HeinOnline.
- Crocket RW, Sandison RA and Walk A (1963) Hallucinogenic Drugs and Their Psychotherapeutic Use. London: HK Lewis.
- Cronbach LJ (1951) Coefficient alpha and the internal structure of tests. *Psychometrika* 16: 297–334.
- Dakwar E, Anerella C, Hart C, et al. (2014) Therapeutic infusions of ketamine: Do the psychoactive effects matter? *Drug Alcohol Depend* 136: 153–157.
- Dimascio A and Klerman GL (1960) Experimental human psychopharmacology: The role of non-drug factors. In: Sarwer-Foner GJ (ed.) *The Dynamics of Psychiatric Drug Therapy*. Springfield, Ill.: Thomas, pp. 56–84.
- Dishotsky NI, Loughman WD, Mogar RE, et al. (1971) LSD and genetic damage. *Science* 172: 431–440.
- Dittrich A (1975) Zusammenstellung eines Fragebogens (APZ) zur Erfassung abnormer psychischer Zustände [Construction of a questionnaire (APZ) for assessing abnormal mental states]. Z Klin Psychol Psychiatr Psychother 23: 12–20.
- Dittrich A (1998) The standardized psychometric assessment of altered states of consciousness (ASCs) in humans. *Pharmacopsychiatry* 31: 80–84.

- Dyck E (2006) 'Hitting highs at rock bottom': LSD treatment for alcoholism, 1950–1970. Soc Hist Med 19: 313–329.
- Eisner BG and Cohen S (1958) Psychotherapy with lysergic acid diethylamide. J Nery Ment Dis 127: 528–539.
- Erritzoe D, Roseman L, Nour M, et al. (2018) Effects of psilocybin therapy on personality structure. *Acta Psychiatr Scand* 138: 368–378.
- Fisher FM (2015) Therapy with Substance: Psycholytic Psychotherapy in the Twenty First Century. London: Muswell Hill Press.
- Frederking W (1955) Intoxicant drugs (mescaline and lysergic acid diethylamide) in psychotherapy. *J Nerv Ment Dis* 121: 262–266.
- Garcia-Romeu AP, Johnson MW and Griffiths RR (2014) Examining the psychological mechanisms of psilocybin-assisted smoking cessation treatment: A pilot study. *Drug Alcohol Depend* 140: e66.
- Gasser P, Kirchner K and Passie T (2014) LSD-assisted psychotherapy for anxiety associated with a life-threatening disease: A qualitative study of acute and sustained subjective effects. *J Psychopharmacol* 29: 57–68.
- Griffiths RR, Johnson MW, Carducci MA, et al. (2016) Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J Psychopharmacol* 30: 1181–1197.
- Griffiths RR, Richards WA, McCann U, et al. (2006) Psilocybin can occasion mystical-type experiences having substantial and sustained personal meaning and spiritual significance. *Psychopharmacology* 187: 268–283.
- Grinspoon L and Bakalar JB (1979) *Psychedelic Drugs Reconsidered*. New York: Basic Books.
- Grof S (1975) Realms of the Human Unconscious: Observations from LSD Research. London: Souvenir Press Ltd; 2016 Edition.
- Grof S, Hofmann A and Weil A (1980) LSD Psychotherapy (The healing potential of psychedelic medicine). Ben Lomond, CA: Multidisciplinary Association for Psychedelic Studies; 2008 Edition.
- Haijen ECHM, Kaelen M, Roseman L, et al. (2018) Predicting responses to psychedelics: A prospective study. *Front Pharmacol* 9: 897.
- Hartogsohn I (2016) Set and setting, psychedelics and the placebo response: An extra-pharmacological perspective on psychopharmacology. J Psychopharmacol 30: 1259–1267.
- Hartogsohn I (2017) Constructing drug effects: A history of set and setting. *Drug Sci Policy Law* 3: 2050324516683325.
- Hintze JL and Nelson RD (1998) Violin plots: A box plot-density trace synergism. *Am Stat* 52: 181–184.
- Huxley A (1945) *The Perennial Philosophy*. Toronto: New Canadian Library.
- Hyde RW (1960) Psychological and social determinants of drug action.
 In: GJ Sarwer-Foner (ed.) *Dynamics of Psychiatric Drug Therapy*.
 Springfield: Thomas, pp. 297–315.
- Jackson SW (1994) Catharsis and abreaction in the history of psychological healing. Psychiatr Clin North Am 17: 471–491.
- Jensen S (1963) Treatment of chronic alcoholism with lysergic acid diethylamide. *Can Psychiatr Assoc J* 8: 182–188.
- Johnson FG (1969) LSD in the treatment of alcoholism. American Journal of Psychiatry 126: 481–487.
- Johnson MW, Garcia-Romeu A and Griffiths RR (2016) Long-term follow-up of psilocybin-facilitated smoking cessation. Am J Drug Alcohol Abuse 1–6.
- Kaelen M, Giribaldi B, Raine J, et al. (2017) The hidden therapist: Evidence for a central role of music in psychedelic therapy. *Psychopharmacology* 235: 505–519.
- Katzenelbogen S and Fang AD (1953) Narcosynthesis effects of sodium amytal, methedrine and LSD-25. Dis Nerv Syst 14: 85–88.
- Klavetter RE and Mogar RE (1967) Peak experiences: Investigation of their relationship to psychedelic therapy and self-actualization. J Humanist Psychol 7: 171–177.
- Kurland AA, Grof S, Pahnke WN, et al. (1972) Psychedelic drug assisted psychotherapy in patients with terminal cancer. J Thanatol 2(1–2): 644–691

- Lasagna L (1963) The relation of drug induced changes to personality. In: M. Rinkel (ed.) Specific and Non-specific Factors in Psychopharmacology. New York: Philosophical Library, pp. 114–129.
- Leary T, Litwin GH and Metzner R (1963) Reactions to psilocybin administered in a supportive environment. *J Nerv Ment Dis* 137: 561–573.
- Lebedev AV, Kaelen M, Lovden M, et al. (2016) LSD-induced entropic brain activity predicts subsequent personality change. *Hum Brain Mapp* 37: 3203–3213.
- Leuner H (1961) Psychotherapy with hallucinogens. *Hallucinogenic Drugs* 67: 67–73.
- Loizaga-Velder A (2013) A psychotherapeutic view on therapeutic effects of ritual ayahuasca use in the treatment of addiction. MAPS Bull 23: 36–40.
- Ludwig AM (1985) Cognitive processes associated with 'spontaneous' recovery from alcoholism. J Stud Alcohol 46: 53–58.
- MacLean JR, MacDonald DC, Byrne UP, et al. (1961) *The use of LSD-25 in the treatment of alcoholism and other psychiatric problems*. New Haven: Laboratory of applied Biodynamics, Yale University.
- MacLean KA, Johnson MW and Griffiths RR (2011) Mystical experiences occasioned by the hallucinogen psilocybin lead to increases in the personality domain of openness. *J Psychopharmacol* 25: 1453–1461.
- MacLean KA, Leoutsakos JMS, Johnson MW, et al. (2012) Factor analysis of the mystical experience questionnaire: A study of experiences occasioned by the hallucinogen psilocybin. J Sci Study Relig 51: 721–737.
- Martin AJ (1957) LSD (lysergic acid diethylamide) treatment of chronic psychoneurotic patients under day-hospital conditions. *Int J Soc Psychiatry* 3: 188–195.
- Maslow AH (1959) Cognition of being in the peak experiences. *J Genet Psychol* 94: 43–66.
- Maslow AH (1964) Religions, Values, and Peak-Experiences. Columbus: Ohio State University Press.
- Nour MM, Evans L, Nutt D, et al. (2016) Ego-dissolution and psychedelics: Validation of the ego-dissolution inventory (EDI). *Front Hum Neurosci* 10: 269.
- O'Reilly P and Funk A (1964) LSD in chronic alcoholism. *Can Psychiatr Assoc J* 9: 258–261.
- Oram M (2012) Efficacy and enlightenment: LSD psychotherapy and the drug amendments of 1962. *J Hist Med Allied Sci*. Epub ahead of print 16 August 2012. DOI: 10.1093/jhmas/jrs050.
- Oram M (2014) The trials of psychedelic medicine: LSD psychotherapy, clinical science, and pharmaceutical regulation in the United States, 1949–1976. PhD Doctorate. University of Sydney, School of Philosophical and Historical Inquiry, Department of History.
- Osmond H (1957) A review of the clinical effects of psychotomimetic agents. *Ann N Y Acad Sci* 66: 418–434.
- Pahnke WN and Richards WA (1966) Implications of LSD and experimental mysticism. J Religion Health 5: 175–208.
- Pahnke WN, Kurland AA, Goodman LE, et al. (1969) LSD-assisted psychotherapy with terminal cancer patients. *Curr Psychiatr Ther* 9: 144–152.
- Pahnke WN, Kurland AA, Unger S, et al. (1970) The experimental use of psychedelic (LSD) psychotherapy. *JAMA* 212: 1856–1863.
- Richards WA (2015) Sacred Knowledge: Psychedelics and Religious Experiences. New York: Columbia University Press.
- Richards WA, Rhead JC, DiLeo FB, et al. (1977) The peak experience variable in DPT-assisted psychotherapy with cancer patients. J Psychedelic Drugs 9: 1–10.
- Roseman L, Nutt DJ and Carhart-Harris RL (2017) Quality of acute psychedelic experience predicts therapeutic efficacy of psilocybin for treatment-resistant depression. Front Pharmacol 8: 974.
- Ross S, Bossis A, Guss J, 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. *J Psychopharmacol* 30: 1165–1180.

- Sandison R (1955) LSD treatment for psychoneurosis: Lysergic acid diethylamide for release of depression. *Nurs Mirror* 100: 1529–1530.
- Schenberg EES (2018) Psychedelic-assisted psychotherapy: A paradigm shift in psychiatric research and development. *Front Pharmacol* 9: 733.
- Stace WT (1960) Mysticism and philosophy. London: Macmillan Publishers.
- Strassman RJ, Qualls CR, Uhlenhuth EH, et al. (1994) Dose-response study of N, N-dimethyltryptamine in humans: II. Subjective effects and preliminary results of a new rating scale. *Arch Gen Psychiatry* 51: 98–108.
- Studerus E, Gamma A and Vollenweider FX (2010) Psychometric evaluation of the altered states of consciousness rating scale (OAV). *PloS One* 5: e12412.
- Studerus E, Gamma A, Kometer M, et al. (2012) Prediction of psilocybin response in healthy volunteers. *PloS One* 7: e30800.
- Taggart F, Stewart-Brown S and Parkinson J (2015) Warwick-Edinburgh Mental Well-being Scale (WEMWBS) User Guide, Version 2. NHS Health Scotland.
- Tennant R, Hiller L, Fishwick R, et al. (2007) The Warwick-Edinburgh mental well-being scale (WEMWBS): Development and UK validation. *Health Qual Life Outcomes* 5: 63.
- Watts R, Day C, Krzanowski J, et al. (2017) Patients' accounts of increased 'Connectedness' and 'Acceptance' after psilocybin for treatment-resistant depression. *J Humanist Psychol* 57: 520–564.