IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	LIECHTI; Matthias Emanuel	Confirmation No.: 8795
Serial No.:	17/238,088	Group No.:
Filing or 371(c) Date:	April 22, 2021	Examiner:

Entitled: MDMA TREATMENT TO ENHANCE ACUTE EMOTIONAL EFFECTS PROFILE OF LSD, PSILOCYBIN, OR OTHER PSYCHEDELICS

THIRD-PARTY PRE-ISSUANCE SUBMISSION

Examiner:

The following documents, which are also identified in the Form PTO/SB/429 filed herewith, are submitted for your consideration as being of potential relevance to the examination of the present application:

1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8.
2. Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021)
3. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363.
4. SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134.
5. LIECHTI (2001) "Gender differences in the subjective effects of MDMA" Psychopharmacology. 154, 161–168.
6. WHITE (1996) "THE EFFECTS OF METHYLENEDIOXYMETHAMPHETAMINE (MDMA, "ECSTASY") ON MONOAMINERGIC NEUROTRANSMISSION IN THE CENTRAL NERVOUS SYSTEM" Progress in Neurobiology. 49, 455-479.

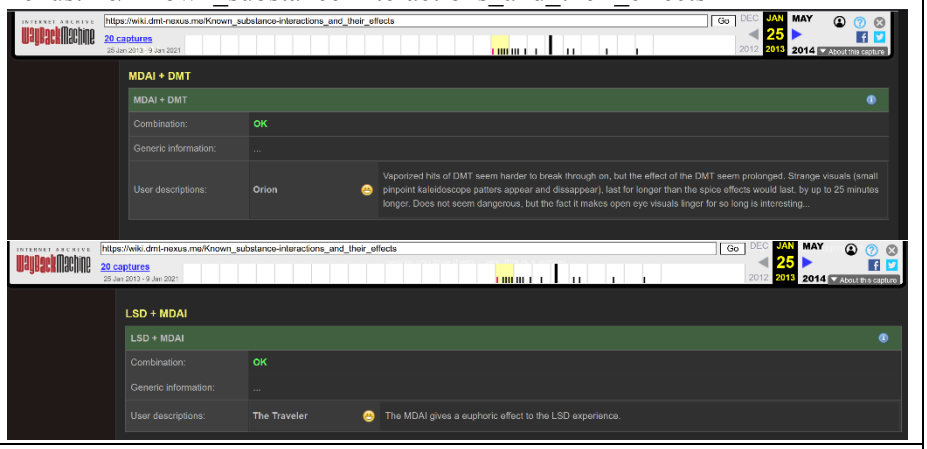
7. SANTOS-LONGHURST (2020) “LSD and MDMA: What to Know About Candyflipping” Healthline. Retrieved February 11 2020. https://web.archive.org/web/20200211232126/https://www.healthline.com/health/lsd-and-mdma
8. BOYS (2001) “Understanding reasons for drug use amongst young people a functional perspective” Health Education Research. 16(4):457-469.
9. HOLZE (2019) “Distinct acute effects of LSD, MDMA, and d-amphetamine in healthy subjects” Neuropsychopharmacology. 45:462–471.
10. OLSON (2020) “Tripping on nothing: placebo psychedelics and contextual factors” Psychopharmacology. 237:1371–1382.
11. SMIGIELSKI (2019) “Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat” Scientific Reports. 9:1-13.
12. Int’l Pat. App. No. WO/2020/157569 “METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS” (Published August 6th, 2020)
13. VAN WELL (2012) “Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors” PLoS One. 7(7)1-8.
14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2
15. Int’l Pat. App. Pub. No. WO/2016/199135 “AN IMPROVED CAPSULE FOR DELIVERING FLOWABLE SUBSTANCE” (Published December 15th, 2016)
16. CHARY (2018) “Candyflipping and Other Combinations: Identifying Drug–Drug Combinations from an Online Forum” Frontiers Psychiatry. 9:1-9.
17. DMT-NEXUS (2013) “Known substance-interactions and their effects” DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects
18. B-E-H, INC. (2012) “Searching for Samadhi in West Philadelphia LSD, MDMA (Ecstacy) & Alcohol” Erowid. Retrieved January 20, 2012 https://web.archive.org/web/20120120044616/https://erowid.org/experiences/exp.php?ID=79281
19. Kryptonite (2009) “A Glorious New Year LSD & MDMA (Ecstasy)” Erowid. Retrieved July 4th, 2010. https://web.archive.org/web/20100704210848/https://www.erowid.org/experiences/exp.php?ID=58609
20. DANFORTH (2016) “MDMA-assisted therapy: A new treatment model for social anxiety in autistic adults” Progress in Neuro-Psychopharmacology and Biological Psychiatry. 64:237-249.

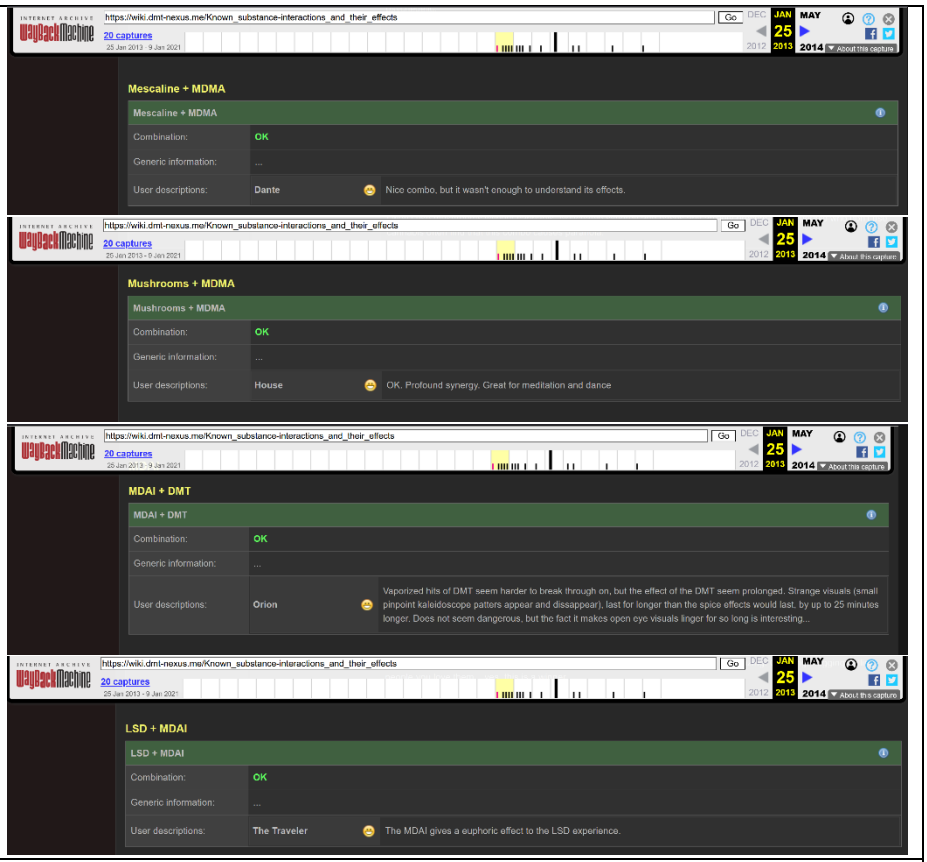
21. LIECHTI (2017) “Alterations of consciousness and mystical-type experiences after acute LSD in humans” Psychopharmacology. 234:1499–1510.

Attached hereto is a claim chart providing a concise description of the relevance of each reference in the document list to the elements of the presently pending claims.

U.S.S.N. 17/238,088 Pending Claims	References
1. A method of enhancing positive therapeutic effects of a psychedelic, including the steps of: inducing a positive psychological state in an individual with an empathogen/entactogen; administering a psychedelic to the individual; and enhancing a positive response to the psychedelic.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions began with **MDMA, then LSD or 2-CB** were added mid-way. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." 3. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other** (n = 11), hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7)."
2. The method of claim 1, wherein the empathogen/entactogen are administered in the same dosage form or in separate dosage forms as the psychedelic.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA, then LSD or 2-CB were added mid-way.** Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." 4. SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134. From **page 132** "Interspersed between test/training maintenance with 1.5 mg/kg MDMA or saline sessions were test sessions in which the animal received either a low dose of **MDMA** (0.15 mg/kg) or a low dose of **LSD** (0.04 mg/kg) or **both drugs administered at the same time**."
3. The method of claim 2, wherein the empathogen/entactogen and psychedelic are in the same dosage form and have different release profiles.	12. Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising

	administering to the subject a **pharmaceutical composition comprising: a) a therapeutically effective amount of one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component** and an **immediate release component**." 13. VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (**LSD binds to most 5-HT receptor sub-types** as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals."
4. The method of claim 1, wherein the empathogen/entactogen is chosen from the group consisting of 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylendioxyamphetamine (MDA), 3,4,-methylenedioxyethylamphetamine (MDEA), 5,6-methylenedioxy-2-aminoindane (MDAI), mephedrone, methylone, 3-MMC, homologues thereof,	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." 16. CHARY (2018) "Candyflipping and Other Combinations: Identifying Drug–Drug Combinations from an Online Forum" Frontiers Psychiatry. 9:1-9. From **page 5** "In the synthetic hallucinogen, LSD is a hub that bridges two subislands. The left subisland of the hallucinogen island contains substances canonically thought to be anticholinergic. Hyoscine and hyoscyamine are tropane alkaloids found in jimson weed. The right subisland contains amphetamine derivatives, such as **MDMA** and the **MDMA derivatives**

analogues thereof, and prodrugs thereof.	(bath salts), bk-MDMA (β-keto MDMA; **methylone**) and **bk-MDEA** (ethylone)." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 
5. The method of claim 4, wherein the empathogen/entactogen is MDMA and is administered in a dose of 20-200 mg.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions • **MDMA: 80–130 mg** • LSD: 50–200µg"
6. The method of claim 1, wherein the psychedelic is chosen from the group consisting of psilocybin, psilocin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), phenethylamine or tryptamine psychedelics, salts thereof, analogs thereof, prodrugs	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects

thereof, and homologues thereof.	
7. The method of claim 6, wherein the psychedelic is LSD and is administered in a dose of 0.05-0.3 mg.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions • MDMA: 80–130 mg • **LSD: 50–200µg**"
8. The method of claim 1, wherein the empathogen/entactogen is administered at a time chosen from the group consisting of before administering the psychedelic, at the same time as administering the psychedelic, after administering the psychedelic, and before and after administering the psychedelic.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions b**egan with 2-CB or with LSD** or on rare occasions other substances such as **ayahuasca or psilocybin** were used." 4. SCHECHTER (1998) "`Candyflipping': Synergistic discriminative effect of LSD and MDMA" European Journal of Pharmacology. 341(2-3)131-134. From **page 132** "Interspersed between test/training maintenance with 1.5 mg/kg MDMA or saline sessions were test sessions in which the animal

	received either a low dose of **MDMA** (0.15 mg/kg) or a low dose of **LSD** (0.04 mg/kg) or **both drugs administered at the same time**." 18. B-E-H, INC. (2012) "Searching for Samadhi in West Philadelphia LSD, MDMA (Ecstasy) & Alcohol" Erowid. Retrieved January 20, 2012. https://web.archive.org/web/20120120044616/https://erowid.org/experiences/exp.php?ID=79281 "Each person is to take 2 hits of **LSD** followed by 1 pill of **MDMA** approximately **3.5 hrs thereafter**." 19. Kryptonite (2009) "A Glorious New Year LSD & MDMA (Ecstasy)" Erowid. Retrieved July 4th, 2010. https://web.archive.org/web/20100704210848/https://www.erowid.org/experiences/exp.php?ID=58609 
9. The method of claim 1, wherein the psychedelic is a short-acting psychedelic, and the empathogen/entactogen is administered 1-2 hours before the short-acting psychedelic.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA**, then **LSD** or 2-CB **were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used." 19. Kryptonite (2009) "A Glorious New Year LSD & MDMA (Ecstasy)" Erowid. Retrieved July 4th, 2010. https://web.archive.org/web/20100704210848/https://www.erowid.org/experiences/exp.php?ID=58609 "I took a bottle of **liquid acid** to a friend's new year's eve party. I usually take **MDMA** with hallucinogens as it can help to reduce anxiety if things go pear-shaped. I was very fortunate in that I had managed to procure eight very clean* pills and took five of these at roughly two-hour intervals starting **two hours before the first dose of acid**."

10. The method of claim 1, wherein the individual has a psychiatric disorder chosen from the group consisting of depression, anxiety, anxiety related to life-threatening disease, obsessive-compulsive disorder, personality disorder, and addiction.	2. Int'l Pat. App. Pub. No. WO/2021/202730 "MOLECULARLY-INITIATED, EXPERIENTIALLY-DELIVERED TREATMENTS AND SYSTEMS FOR PRACTICING SAME" (Published October 7, 2021) From **claim 3** "The method of claim 2, wherein the psychedelic agent is selected from the group consisting of: psilocybin, **3,4-Methylenedioxymethamphetamine (MDMA), lysergic acid diethylamide (LSD)**, N,N-Dimethyltryptamine (DMT), mescaline, peyote, 2,5-dimethoxy-4-bromophenethylamine (2C-B), 2,5-Dimethoxy-4-methylamphetamine (DOM), NBOMes (N-methoxybenzyl), **and any combination thereof**." From **claim 14** "The method according to any one of claims 1 to 13, wherein the individual is suffering from a mental health condition selected from the group consisting of: **depression, anxiety**, post-traumatic stress disorder (PTSD), **addiction**, and any combination thereof." 12. Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 43** "The method of any one of claims 1-38, wherein the neurological condition is **depression**, bipolar disorder, anxiety, social **anxiety**, post-traumatic stress disorder (PTSD), panic disorder, phobia, schizophrenia, psychopathy, or **antisocial personality disorder**." From **claim 47** "The method of claim 46, wherein the compulsive disorder is **obsessive compulsive disorder (OCD)**, gambling, or aberrant sexual behavior." 13. VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity

	during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals"
11. The method of claim 1, wherein said enhancing step further includes the step of reducing bad drug effects chosen from the group consisting of anxiety, fear, fear of loss of body control, anxious-ego dissolution, disembodiment, fear of impaired thought control, paranoia, panic, negative thoughts, grooming, nadir effects, and combinations thereof.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were **no serious adverse reactions** to the substances, **no psychoses**, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe improvements in their relationships and well-being at home and work." 11. Smigielski (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13. From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances, fear of losing control, anxiety, or panic**." From **page 3** "5D-ASC is designed to quantify positive and **negative forms of self/ego-dissolution**, including perceptual alterations." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 227**

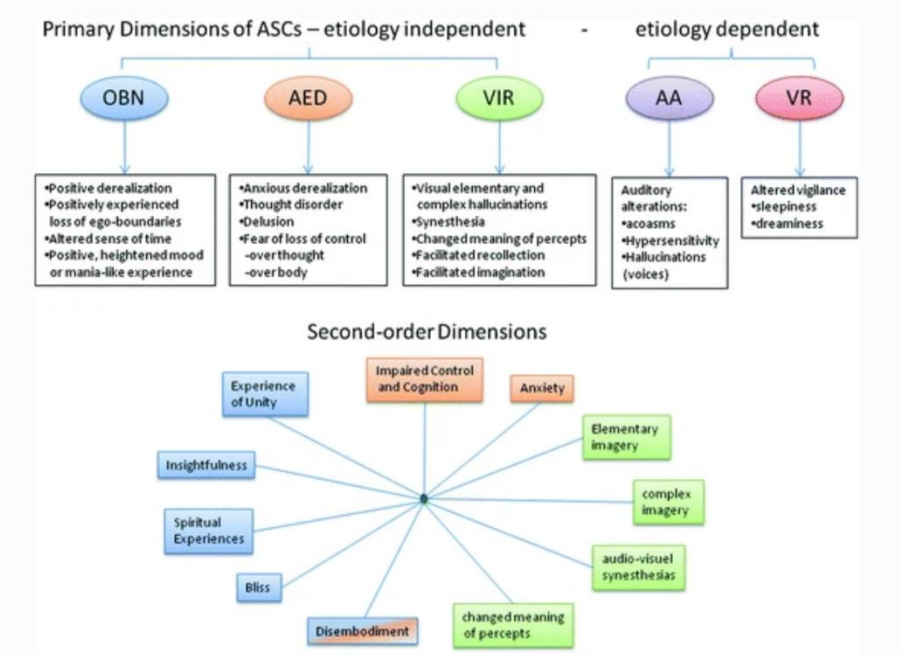
	
12. The method of claim 1, wherein said enhancing step further includes the step of improving good drug effects chosen from the group consisting of drug linking, oceanic boundlessness, experience of unity, spiritual experience, blissful state, insightfulness, connectedness, mystical experiences, mystical-type effects, positive mood, transcendence of time/space, ineffability, well-being, trust, feelings of love, feeling open, peak experience, and combinations thereof.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 4** "**Spiritual insights** provide an awareness of being part of a greater whole, something bigger than oneself. Clients often state that underlying all experience is the concept of love; **binding together all other aspects of life**. This is very powerful for clients who have up till now never enjoyed any significant experience of love. **Feeling love** is a fundamental characteristic of psychedelic substances and particularly MDMA. The substance gives the clients an opportunity to see themselves as loving and, crucially, lovable individuals, which offers immense healing potential for clients with traumatic histories." From **page 4** "But of the 97 clients who underwent psycholytic psychotherapy, the qualitative outcomes were overwhelmingly positive. There were no serious adverse reactions to the substances, no psychoses, no hospitalisations and no suicides of any clients who were actively undergoing psycholytic therapy. Almost all of the clients describe **improvements in their relationships** and **well-being** at home and work." 8. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From **page 465**

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

9. HOLZE (2019) “Distinct acute effects of LSD, MDMA, and d-amphetamine in healthy subjects” Neuropsychopharmacology. 45:462–471.

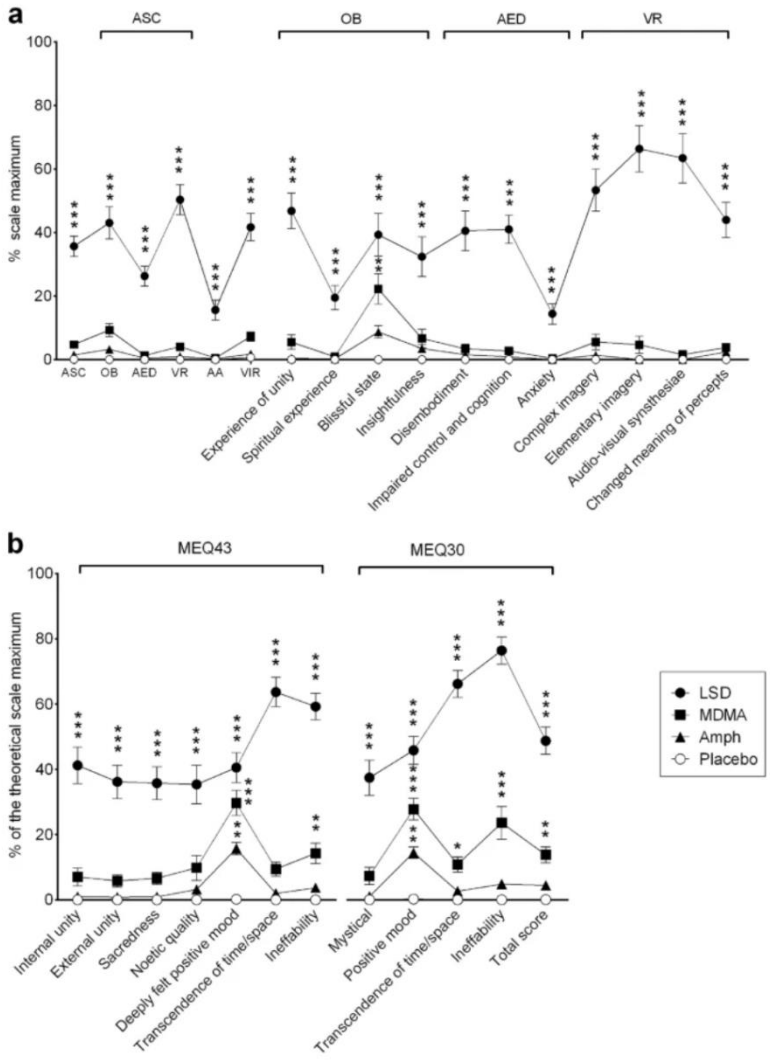
From **page 462** “MDMA produced greater ratings of **good drug effects, liking**, high, and ego dissolution compared with d-amphetamine. d-Amphetamine increased ratings of activity and concentration compared with LSD.”

From **page 462** “MDMA acutely induces feelings of **well-being, love, empathy**, and prosociality”

From **page 462** “On the other hand, LSD was found to exhibit MDMA-like empathogenic mood effects such as increased **closeness, openness, and trust**”

From **page 468**

Fig. 3



10. OLSON (2020) "Tripping on nothing: placebo psychedelics and contextual factors" Psychopharmacology. 237:1371–1382.

From **page 1375** "The 5D-ASC measures changes in subjective experience (Dittrich 1998) and is commonly used in psychedelic studies. Each item uses a visual analogue scale ranging from "No, not more than usually" (0) to "Yes, much more than usually" (100). The measure has 11 subscales (Studerus et al. 2010a):

- **anxiety** (e.g. "I was scared without knowing exactly why"),
- spiritual experience ("My experience had religious aspects to it"),
- **insightfulness** ("I felt very profound"),
- **impaired control and cognition** ("I felt incapable of making even the smallest decision"),
- **disembodiment** ("I felt as if I no longer had a body"),
- experience of unity ("Everything seemed to unify into a oneness"),

- **blissful state** ("I experienced boundless pleasure"),
- changed meaning of percepts ("Some everyday things acquired special meaning"),
- complex imagery ("I saw whole scenes roll by with closed eyes or in complete darkness"),
- audio-visual synaesthesia ("The colours of things seemed to be altered by sounds or noises"), and
- elementary imagery ("I saw colours with closed eyes or in complete darkness")."

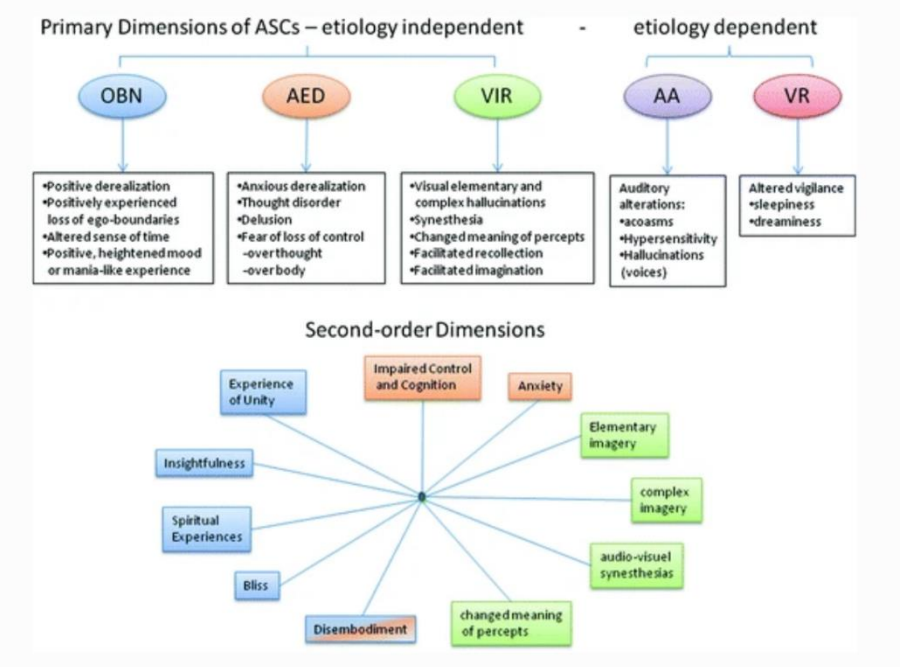
11. Smigielski (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13.

From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances, fear of losing control, anxiety, or panic**."

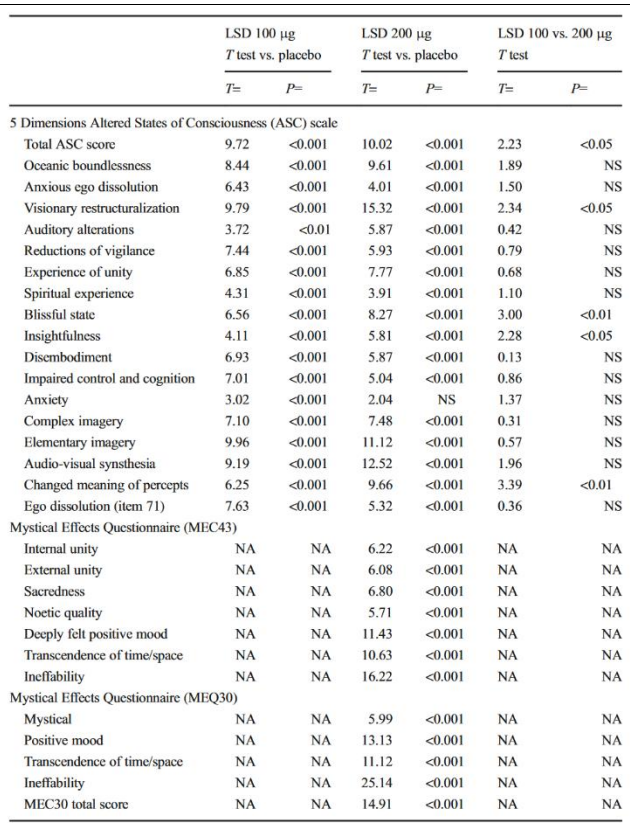
From **page 3** "5D-ASC is designed to quantify positive and **negative forms of self/ego-dissolution**, including perceptual alterations."

14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2

From **page 227**



	21. LIECHTI (2017) "Alterations of consciousness and mystical-type experiences after acute LSD in humans" Psychopharmacology. 234:1499–1510. From **page 1501** "The 5D-ASC dimension "**Oceanic Boundlessness**" (27 items) measures derealization and depersonalization associated with positive emotional states, ranging from heightened mood to euphoric exaltation. The corresponding lower-order scales include "**experience of unity,**" "s**piritual experience**," "**blissful state**," and "**insightfulness**." The dimension "**Anxious Ego Dissolution**" (21 items) summarizes ego disintegration and **loss of self-control** phenomena associated with **anxiety**. The corresponding lower-order scales include "**disembodiment**," "**impaired control of cognition**," and "**anxiety.**" The dimension "Visionary Restructuralization" (18 items) consists of the lower-order scales "complex imagery," "elementary imagery," "audio-visual synesthesia," and "changed meaning of percepts." Two additional dimensions describe "Auditory Alterations" (15 items) and "Reduction of Vigilance" (12 items). The scale is well-validated and widely used to characterize the subjective effects of various psychedelic drugs (Carhart-Harris et al. 2016b; Hasler et al. 2004; Hysek et al. 2011; Schmid et al. 2015; Vollenweider et al. 2007; Vollenweider and Kometer 2010)." From **page 1501** "We also derived the four scale scores of the newly validated revised 30-item MEQ: **mystical,** positive mood, **transcendence of time and space,** and **ineffability** (Barrett et al. 2015)." From **page 1504**

	Table 1 Statistics for the effects of LSD in the 5D-ASC and MEQ 

	LSD 100 µg *T* test vs. placebo		LSD 200 µg *T* test vs. placebo		LSD 100 vs. 200 µg *T* test	
	T=	*P*=	*T*=	*P*=	*T*=	*P*=
5 Dimensions Altered States of Consciousness (ASC) scale						
Total ASC score	9.72	<0.001	10.02	<0.001	2.23	<0.05
Oceanic boundlessness	8.44	<0.001	9.61	<0.001	1.89	NS
Anxious ego dissolution	6.43	<0.001	4.01	<0.001	1.50	NS
Visionary restructuralization	9.79	<0.001	15.32	<0.001	2.34	<0.05
Auditory alterations	3.72	<0.01	5.87	<0.001	0.42	NS
Reductions of vigilance	7.44	<0.001	5.93	<0.001	0.79	NS
Experience of unity	6.85	<0.001	7.77	<0.001	0.68	NS
Spiritual experience	4.31	<0.001	3.91	<0.001	1.10	NS
Blissful state	6.56	<0.001	8.27	<0.001	3.00	<0.01
Insightfulness	4.11	<0.001	5.81	<0.001	2.28	<0.05
Disembodiment	6.93	<0.001	5.87	<0.001	0.13	NS
Impaired control and cognition	7.01	<0.001	5.04	<0.001	0.86	NS
Anxiety	3.02	<0.001	2.04	NS	1.37	NS
Complex imagery	7.10	<0.001	7.48	<0.001	0.31	NS
Elementary imagery	9.96	<0.001	11.12	<0.001	0.57	NS
Audio-visual synsthesia	9.19	<0.001	12.52	<0.001	1.96	NS
Changed meaning of percepts	6.25	<0.001	9.66	<0.001	3.39	<0.01
Ego dissolution (item 71)	7.63	<0.001	5.32	<0.001	0.36	NS
Mystical Effects Questionnaire (MEC43)						
Internal unity	NA	NA	6.22	<0.001	NA	NA
External unity	NA	NA	6.08	<0.001	NA	NA
Sacredness	NA	NA	6.80	<0.001	NA	NA
Noetic quality	NA	NA	5.71	<0.001	NA	NA
Deeply felt positive mood	NA	NA	11.43	<0.001	NA	NA
Transcendence of time/space	NA	NA	10.63	<0.001	NA	NA
Ineffability	NA	NA	16.22	<0.001	NA	NA
Mystical Effects Questionnaire (MEQ30)						
Mystical	NA	NA	5.99	<0.001	NA	NA
Positive mood	NA	NA	13.13	<0.001	NA	NA
Transcendence of time/space	NA	NA	11.12	<0.001	NA	NA
Ineffability	NA	NA	25.14	<0.001	NA	NA
MEC30 total score	NA	NA	14.91	<0.001	NA	NA

Sixteen subjects participated in the high-dose study (200 µg) and 24 subjects in the moderate-dose study (100 µg). Dependent *T* tests were performed to assess differences from placebo, and independent *T* tests were performed to assess differences between doses of LSD

NA not assessed

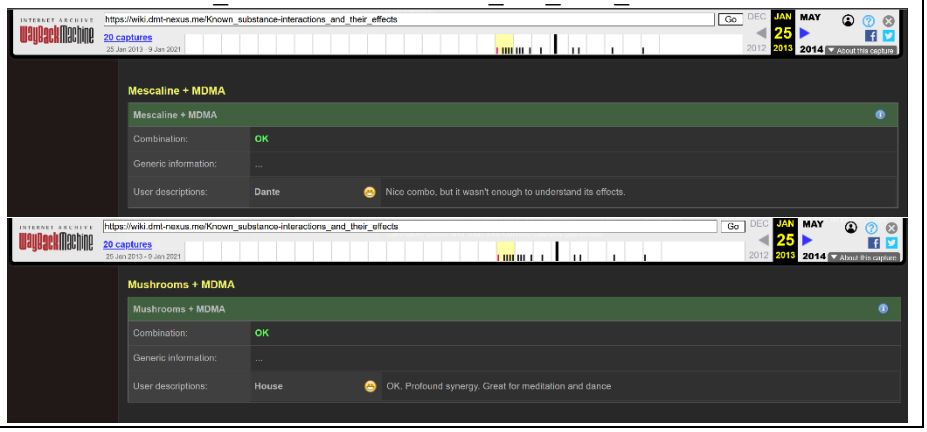
13. The method of claim 1, wherein the empathogen/entactogen reduces anxiety up to 6 hours after administration.	5. LIECHTI (2001) "Gender differences in the subjective effects of MDMA" Psychopharmacology. 154, 161–168. From **page 163** "F and P values for significant main effects and interactions are presented in Table 1. **Subjective effects of MDMA began 30–60 min after MDMA administration, peaked at 75–120 min, and lasted for a mean duration of 3.5h**." 7. SANTOS-LONGHURST (2020) "LSD and MDMA: What to Know About Candyflipping" Healthline. Retrieved February 11 2020. https://web.archive.org/web/20200211232126/https://www.healthline.com/health/lsd-and-mdma "**MDMA**, which is usually taken several hours after LSD, typically kicks in within 20 to 70 minutes and lasts from **3 to 6 hours**." 21. DANFORTH (2016) "MDMA-assisted therapy: A new treatment model for social anxiety in autistic adults" Progress in Neuro-Psychopharmacology and Biological Psychiatry. 64:237-249.

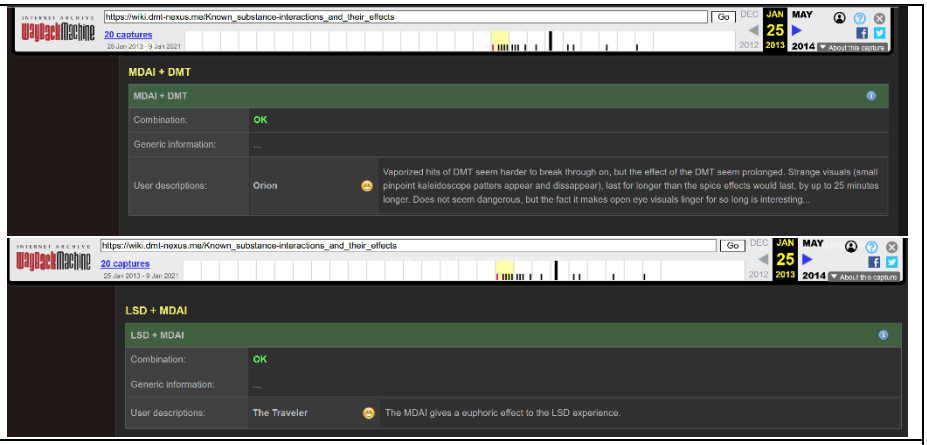
	From **page 237** "**MDMA-assisted therapy could reduce social anxiety** symptoms and increase social adaptability."
14. A composition comprising an empathogen/entactogen and a psychedelic in the same dosage form.	12. Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component** and an **immediate release component**." 13. VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals"
15. The composition of claim 14, wherein said empathogen/entactogen and said psychedelic have different release profiles.	12. Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020)

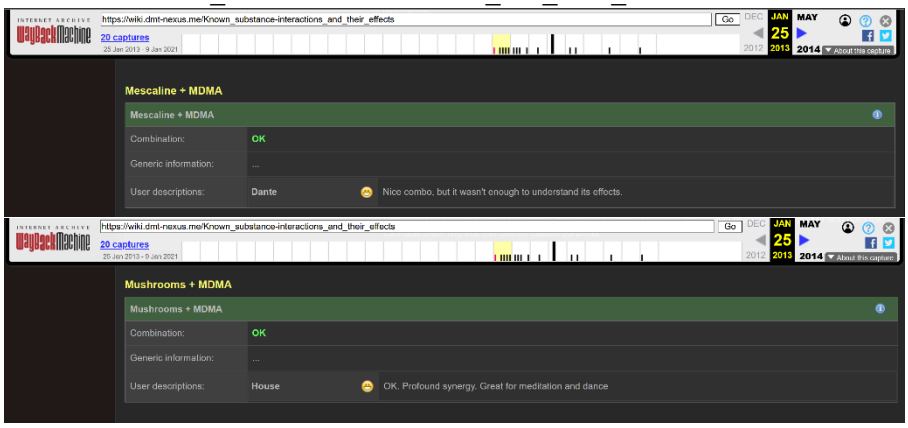
	From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component** and an **immediate release component**." 13. VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals"
16. The composition of claim 14, wherein said empathogen/entactogen is chosen from the group consisting of 3,4-methylenedioxymethamphetamine (MDMA), 3,4-methylendioxyamphetamine (MDA), 3,4,-methylenedioxyethylamphetamine (MDEA), 5,6-methylenedioxy-2-aminoindane (MDAI), mephedrone, methylone, 3-MMC,	12. Int'l Pat. App. No. WO/2020/157569 "METHODS AND COMPOSITIONS COMPRISING A 5HT RECEPTOR AGONIST FOR THE TREATMENT OF PSYCHOLOGICAL, COGNITIVE, BEHAVIORAL, AND/OR MOOD DISORDERS" (Published August 6th, 2020) From **claim 1** "A method of managing a neurological condition or one or more symptoms thereof in a subject in need thereof, comprising administering to the subject a pharmaceutical composition comprising: a) a therapeutically effective amount of **one or more 5HT receptor agonist** or a pharmaceutically acceptable salt, solvate, metabolite, derivative, or prodrug thereof." From **claim 8** "The method of any one of the preceding claims, wherein the pharmaceutical composition comprises a **controlled release component** and an **immediate release component**."

homologues thereof, analogues thereof, and prodrugs thereof.	13. VAN WELL (2012) "Effects of Acute MDMA Intoxication on Mood and Impulsivity: Role of the 5-HT2 and 5-HT1 Receptors" PLoS One. 7(7):1-8. From **page 1** "3,4-Methylenedioxymethamphetamine **(MDMA) is a serotonin (5-HT) agonist** and a reuptake inhibitor of serotonin and dopamine (DA) that has been shown to affect mood [1] and impulsivity during intoxication [2], [3], [4] and abstinence [5], [6]. Mood has been shown to be affected by fluctuations in 5-HT levels." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 50** "Although **hallucinogens** do not bind exclusively to 5-HT2A receptors (LSD binds to most **5-HT** receptor sub-types as well as to dopaminergic and adrenergic receptors), it has been evidenced in both humans and experimental animals that the activation of 5-HT2A receptors is necessary to generate hallucinogenesis and a related behavioral response in animals" 15. Int'l Pat. App. Pub. No. WO/2016/199135 "AN IMPROVED CAPSULE FOR DELIVERING FLOWABLE SUBSTANCE" (Published December 15th, 2016) From **claim 49** "The device of claim 40, wherein said at least one flowable substance comprises a medicament selected from a group consisting of saline, natural substances, medicaments for treatments for allergic rhinitis, medicaments for treatments for osteoporosis, vaccinations and immunizations, sexual dysfunction drugs, medicaments for treatments for B12 deficiency, medicaments for smoking cessation, medicaments for treatment of gynecological problems, medicaments for treatment of other women's health issues, medicaments for general anesthetics, local anesthetics, opioid analgesics, agonist-antagonists and antagonists, antitussives, medicaments for treatment of motor disorders, antiepileptics, antipsychotics (neuroleptics), sedative-hypnotics, anxiolytics, and centrally acting muscle relaxants, medicaments for treatments for anxiety disorders, skeletal muscle relaxants, medicaments for treatments for Parkinson's disease, medicaments for treatments for Alzheimer's disease, medicaments for treatment of allergic rhinitis, steroids, corticosteroids, Flonase, Patanase, Beconase, antihistamines, Astelin, Otrivin, Livostin, Theramax, Avamys, Lufeel, Sinofresh, Nasonex, Nasocort, Veramyst, medicaments for treatment of osteoporosis, Miacalcin, Fortical and Stadol, medicaments for vaccinations and immunizations, LAVIN, and influenza vaccines including FluMist, NasalFent. Calcitonin, parathyroid hormone, Neurotransmitters and neuromodulators, acetylcholine (ACH), Anticholinergic drugs, adenosine triphosphate (ATP), aspartate (Asp), beta-amyloid, beta-endorphin,

	bradykinin, dopamine (DA), L-DOPA, Carbio-Dopa, epinephrine, dynorphins, endomorphins, enkephalins, 5-hydroxytryptamine (5-HT), Sumatriptan, Imitrex, Migranal, Zolmitriptan, Zomig, Gamma-aminobutyric acid (GABA), glutamate (glu), glycine, histamine, leptin, nerve growth factor and other growth factors), norepinephrine, nitric oxide, Substance P. alfentanil, desflurane, enflurane, etomidate, fentanyl, halothane, isoflurane, ketamine, methohexital, methoxyflurane, midazolam, morphine, nitrous oxide (N20), propofol, sevoflurane, Sufentanil, Sublimase, thiopental, benzocaine, bupivacaine, cocaine, lidocaine, prilocaine, procaine, ropivacaine, tetracaine, Opioid analgesics, agonist-antagonists, and antitussives, agonists, codeine, diphenoxylate, fentanyl, heroin and other opiods, cannabis and cannabinoids, hydrocodone, 1-alpha-acetyl-methadol, levomethadyl acetate, loperamide, meperidine, methadone, morphine, oxycodone, d-propoxyphene, combinations of opioids plus acetaminophen and asa, and tramadol, agonist/antagonists and antagonists, buprenorphine, butorphanol, nalbuphine, nalorphine, naloxone, naltrexone, nalmefene, pentazocine, codeine, dextromethorphan, and hydrocodone, medicaments for treatment of Parkinson's disease and motor disorders, amantadine, apomorphin, baclofen, benzodiazepines, benztropine, bromocriptine, carbidopa, cyclobenzaprine, dantrolene, dopamine, entacapone, haloperidol, L-DOPA, pergolide, pramiprexole, ropinerole, selegiline (deprenyl), trihexyphenidyl, rasagiline, azilect, selegiline, ladostigil, rotigotine, neupro, mono amine oxidase inhibitor, COMT inhibitor, antiepileptics, acetazolamide, carbamazepine, clonazepam, diazepam, ethosuximide, felbamate, gabapentin, Lamotrigine, lorazepam, phenobarbital, phenytoin, primidone, tiagabine, topiramate, valproic acid, Vigabatrin, Midazolam, antidepressants, amitriptyline, bupropion, citalopram, clomipramine, desipramine, fluoxetine, fluvoxamine, imipramine, nortriptyline, paroxetine, phenelzine, sertraline, trazodone, tranylcypromine, venlafaxine, antimanic drugs, carbamazepine, lithium carbonate valproic acid, antipsychotics (neuroleptics), chlorpromazine (CPZ), clozapine, fluphenazine, haloperidol, olanzapine, quetiapine, risperidone, sertindole, thioridazine, thiothixene, ziprasidone, sedative-hypnotics, anxiolytics, and centrally acting muscle relaxants, alprazolam, chloral hydrate, diphenhydramine, flumazenil, flurazepam, hydroxyzine, lorazepam, oxazepam, phenobarbital, temazepam, triazolam, zaleplon, Zolpidem, anxiety disorders and skeletal muscle relaxants, alprazolam, chlorazepate, chlordiazepoxide, diazepam, flumazenil (antagonist), lorazepam, oxazepam, amphetamine, caffeine, ephedrine, methamphetamine, methylphenidate, phentermine, sibutramine, disulfiram, ethanol, methanol, naltrexone, atropine, scopolamine, ketamine, **lysergic acid diethylamide (LSD)**, **MDMA** (methylene dioxy-methyl amphetamine), mescaline, phencyclidine (PCP), donabinol, marijuana/THC, organic solvents, nicotine, Pentobarbital, neuroprotective compounds, neuroprotective peptides, neuroprotective factors, davunetide, anti-schizophrenic drugs, anti-depression drugs, comtan, Entacopone, anti ADHD agents, and anti ADHD drugs as Methylphenidrate (ritalin), anti-autism and anti-autism symptoms drugs, medicaments for treatment of

	Alzheimer's disease, donepezil, galantamine, rivastigmine, Tacrine, insulin, Detemir, Novolin, Humulin, insulin-like hormone, dopamine agonist and dopamine antagonist and **any combination thereof**."
17. The composition of claim 16, wherein said empathogen/entactogen is MDMA and is present in a dose of 20-200 mg.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions **MDMA: 80–130 mg** LSD: 50–200µg"
18. The composition of claim 14, wherein said psychedelic is chosen from the group consisting of psilocybin, psilocin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), phenethylamine or tryptamine psychedelics, salts thereof, analogs thereof, prodrugs thereof, and homologues thereof.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions began with **MDMA**, then **LSD** or 2-CB were added mid-way. Sometimes sessions began with **2-CB** or with LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 

	
19. The composition of claim 18, wherein said psychedelic is LSD and is present in a dose of 0.05-0.3 mg.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "The choice and dosages of substances used for the sessions MDMA: 80–130 mg **LSD: 50–200µg**"
20. A method of enhancing positive therapeutic effects of a psychedelic, including the steps of: inducing the release of endogenous monoamines, and stimulating 5-HT.sub.2A receptors.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "MDMA exerts its effects at **5-HT2A** and 5-HT2B receptors, creating feelings of reduced anxiety and depression and a sense of euphoria and well-being (Brunner and Hen, 1997; Graeff et al., 1996)." 6. WHITE (1996) "THE EFFECTS OF METHYLENEDIOXYMETHAMPHETAMINE (MDMA, "ECSTASY") ON MONOAMINERGIC NEUROTRANSMISSION IN THE CENTRAL NERVOUS SYSTEM" Progress in Neurobiology. 49, 455-479. From **page 456** "It is now well established that administration of single doses of **MDMA** to laboratory animals **induces acute increases in extracellular levels of the monoamines** serotonin (5HT), dopamine (DA) and norepinephrine (NE) in several brain regions"
21. The method of claim 20, wherein said inducing step is accomplished by administering an empathogen/entactogen is chosen from the group consisting of 3,4-methylenedioxymetha	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "**MDMA exerts its effects at 5-HT2A** and 5-HT2B receptors, creating feelings of reduced anxiety and depression and a sense of euphoria and well-being (Brunner and Hen, 1997; Graeff et al., 1996)."

mphetamine (MDMA), 3,4-methylendioxyamphetamine (MDA), 3,4,-methylenedioxyethylamphetamine (MDEA), 5,6-methylenedioxy-2-aminoindane (MDAI), mephedrone, methylone, 3-MMC, homologues thereof, analogues thereof, and prodrugs thereof.	6. WHITE (1996) "THE EFFECTS OF METHYLENEDIOXYMETHAMPHETAMINE (MDMA, "ECSTASY") ON MONOAMINERGIC NEUROTRANSMISSION IN THE CENTRAL NERVOUS SYSTEM" Progress in Neurobiology. 49, 455-479. From **page 456** "It is now well established that administration of single doses of **MDMA** to laboratory animals **induces acute increases in extracellular levels of the monoamines** serotonin (5HT), dopamine (DA) and norepinephrine (NE) in several brain regions"
22. The method of claim 20, wherein said stimulating step is accomplished by administering a psychedelic chosen from the group consisting of psilocybin, psilocin, lysergic acid diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), phenethylamine or tryptamine psychedelics, salts thereof, analogs thereof, prodrugs thereof, and homologues thereof.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions began with MDMA, then **LSD** or 2-CB were added mid-way. Sometimes sessions began with **2-CB** or with LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 

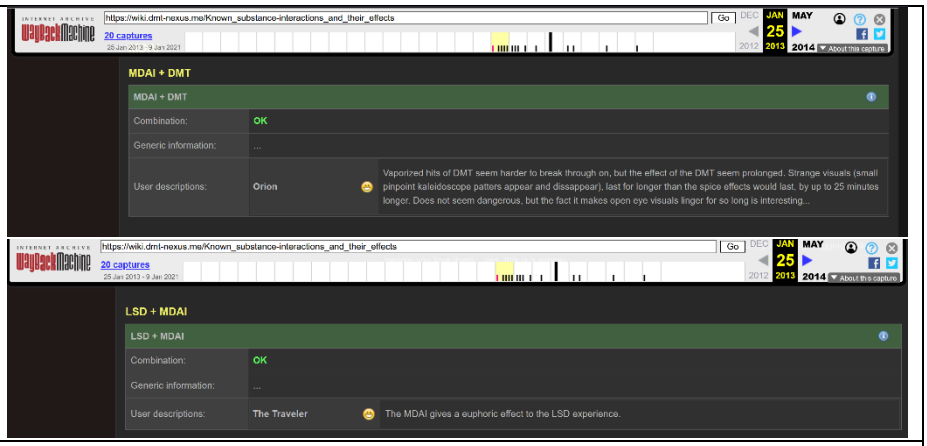
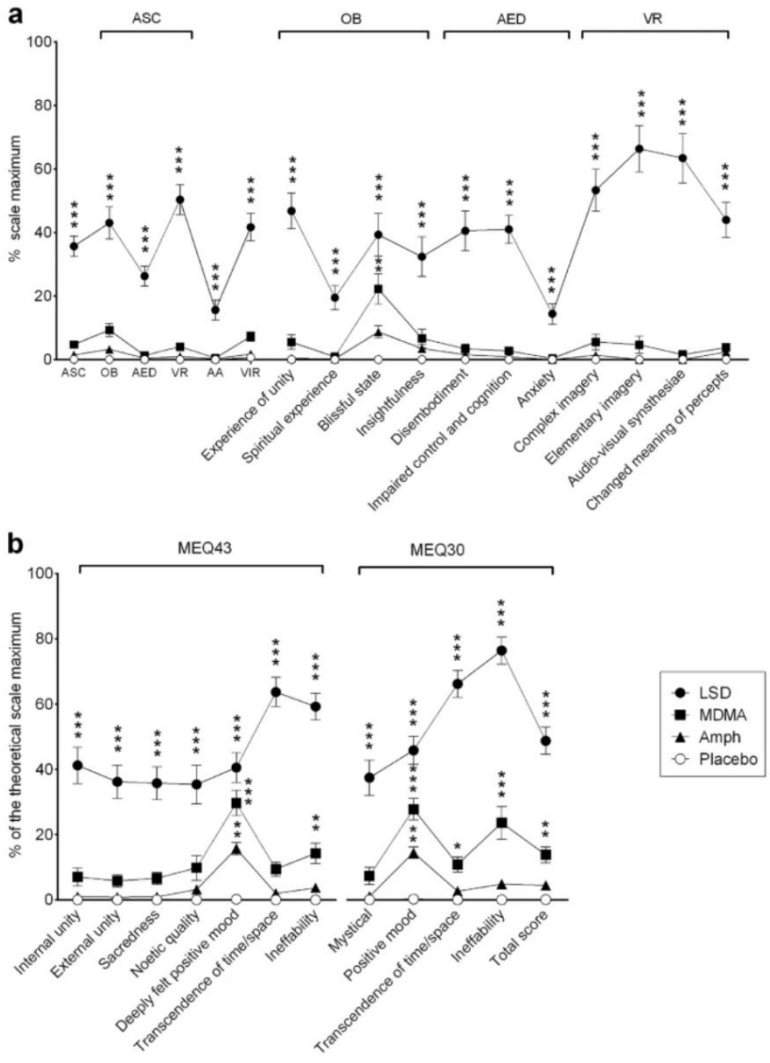
	
23. The method of claim 20, further including the step of improving good drug effects and reducing bad drug effects.	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "There followed another period of silence followed by music to bring the clients to the point where the MDMA and the LSD or 2-CB met. At the second peak, they would begin the intensive **psychotherapeutic work** again, which could last for another five to six hours." 3. LICHT (2012) "Simultaneous polysubstance use among Danish 3,4-methylenedioxymethamphetamine and hallucinogen users: combination patterns and proposed biological bases" Hum. Psychopharmacol. Clin. Exp. 27: 352–363. From **page 355** "The most prevalent observations were cannabis enhancing the effects of hallucinogens (n = 17) and MDMA (n = 7), **MDMA and hallucinogens enhancing each other (n = 11)**, hallucinogens enhancing each other (n = 6), amphetamines (n = 8) and cocaine (n = 6) counteracting hallucinogens, and cocaine counteracting the effects of MDMA (n = 7). 8. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From **page 465**

	Table IV. *Combined functional substance use reported by the sample over the past year* Used with [substance] to improve its effects cannabis – 16 18 8 14 93 amphetamines 37 – 20 7 3 29 ecstasy 55 39 – 11 19 45 LSD 24 10 9 – 3 6 cocaine 42 4 5 1 – 45 alcohol 110 38 23 4 29 – hallucinogenic mushrooms 2 0 0 1 0 1 Used to help ease after effects of [substance] cannabis – 5 2 0 4 18 amphetamines 83 – 6 1 1 47 ecstasy 114 7 – 3 10 59 LSD 29 0 5 – 0 13 cocaine 80 1 1 0 – 34 alcohol 70 18 7 0 14 –
24. The method of claim 23, wherein the good drug effects are chosen from the group consisting of drug linking, oceanic boundlessness, experience of unity, spiritual experience, blissful state, insightfulness, connectedness, mystical experiences, mystical-type effects, positive mood, transcendence of time/space, ineffability, well-being, trust, feelings of love, feeling open, peak experience, and combinations thereof, and the bad drug effects are chosen from the group consisting of anxiety, fear, fear of loss of body control, anxious-ego dissolution, disembodiment, fear of impaired thought control, paranoia, panic, negative thoughts, grooming,	9. HOLZE (2019) "Distinct acute effects of LSD, MDMA, and d-amphetamine in healthy subjects" Neuropsychopharmacology. 45:462–471. From **page 462** "MDMA acutely induces feelings of **well-being, love, empathy**, and prosociality" From **page 462** "On the other hand, LSD was found to exhibit MDMA-like empathogenic mood effects such as increased **closeness, openness, and trust**" From **page 468**

nadir effects, and combinations thereof.

Fig. 3



10. OLSON (2020) "Tripping on nothing: placebo psychedelics and contextual factors" Psychopharmacology. 237:1371–1382.

From **page 1375** "The 5D-ASC measures changes in subjective experience (Dittrich 1998) and is commonly used in psychedelic studies. Each item uses a visual analogue scale ranging from "No, not more than usually" (0) to "Yes, much more than usually" (100). The measure has 11 subscales (Studerus et al. 2010a):

- **anxiety** (e.g. "I was scared without knowing exactly why"),
- spiritual experience ("My experience had religious aspects to it"),
- **insightfulness** ("I felt very profound"),
- **impaired control and cognition** ("I felt incapable of making even the smallest decision"),
- **disembodiment** ("I felt as if I no longer had a body"),
- experience of unity ("Everything seemed to unify into a oneness"),

- **blissful state** ("I experienced boundless pleasure"),
- changed meaning of percepts ("Some everyday things acquired special meaning"),
- complex imagery ("I saw whole scenes roll by with closed eyes or in complete darkness"),
- audio-visual synaesthesia ("The colours of things seemed to be altered by sounds or noises"), and
- elementary imagery ("I saw colours with closed eyes or in complete darkness")."

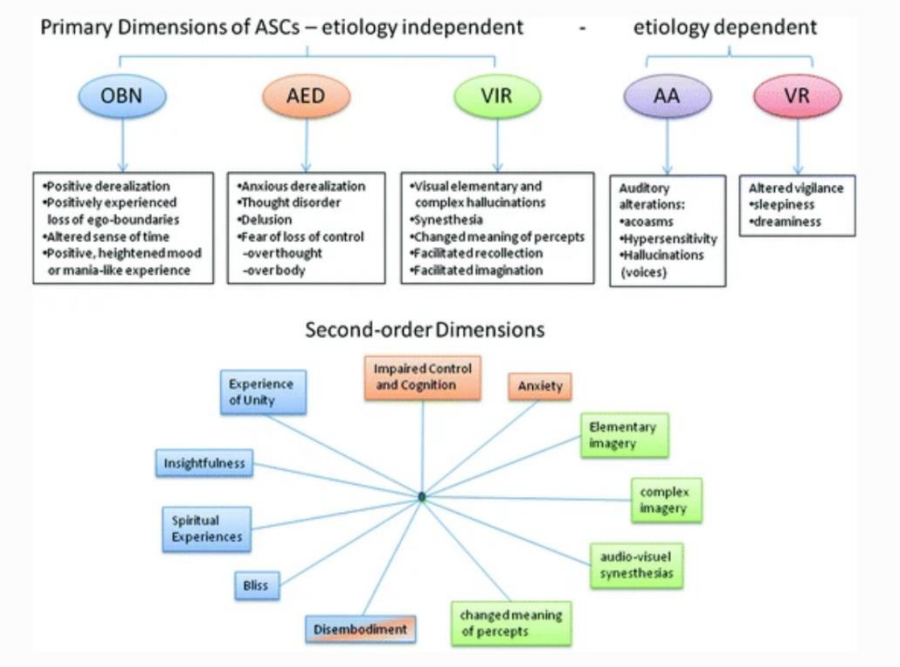
11. Smigielski (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13.

From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances, fear of losing control, anxiety, or panic**."

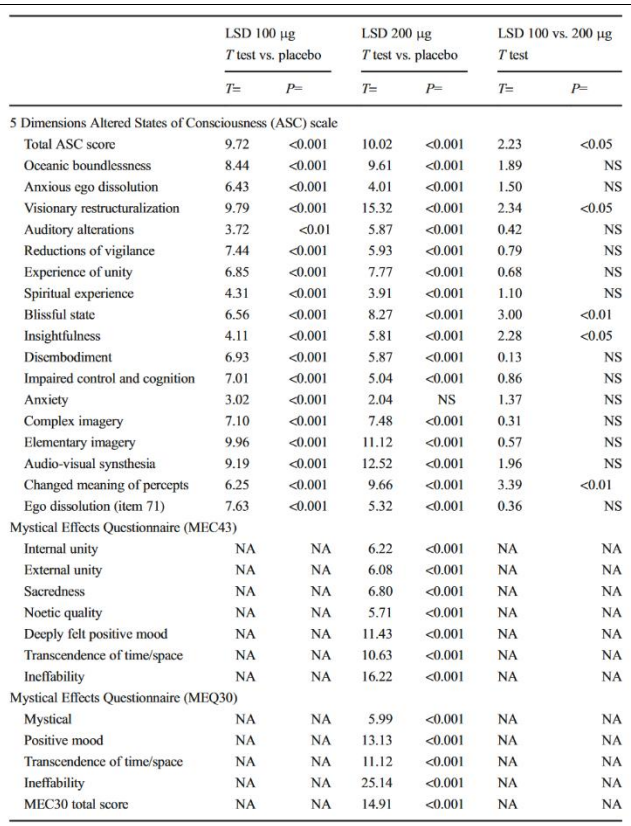
From **page 3** "5D-ASC is designed to quantify positive and **negative forms of self/ego-dissolution**, including perceptual alterations."

14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2

From **page 227**



	21. LIECHTI (2017) "Alterations of consciousness and mystical-type experiences after acute LSD in humans" Psychopharmacology. 234:1499–1510. From **page 1501** "The 5D-ASC dimension "**Oceanic Boundlessness**" (27 items) measures derealization and depersonalization associated with positive emotional states, ranging from heightened mood to euphoric exaltation. The corresponding lower-order scales include "**experience of unity,**" "s**piritual experience**," "**blissful state**," and "**insightfulness**." The dimension "**Anxious Ego Dissolution**" (21 items) summarizes ego disintegration and **loss of self-control** phenomena associated with **anxiety**. The corresponding lower-order scales include "**disembodiment**," "**impaired control of cognition**," and "**anxiety.**" The dimension "Visionary Restructuralization" (18 items) consists of the lower-order scales "complex imagery," "elementary imagery," "audio-visual synesthesia," and "changed meaning of percepts." Two additional dimensions describe "Auditory Alterations" (15 items) and "Reduction of Vigilance" (12 items). The scale is well-validated and widely used to characterize the subjective effects of various psychedelic drugs (Carhart-Harris et al. 2016b; Hasler et al. 2004; Hysek et al. 2011; Schmid et al. 2015; Vollenweider et al. 2007; Vollenweider and Kometer 2010)." From **page 1501** "We also derived the four scale scores of the newly validated revised 30-item MEQ: **mystical,** positive mood, **transcendence of time and space,** and **ineffability** (Barrett et al. 2015)." From **page 1504**

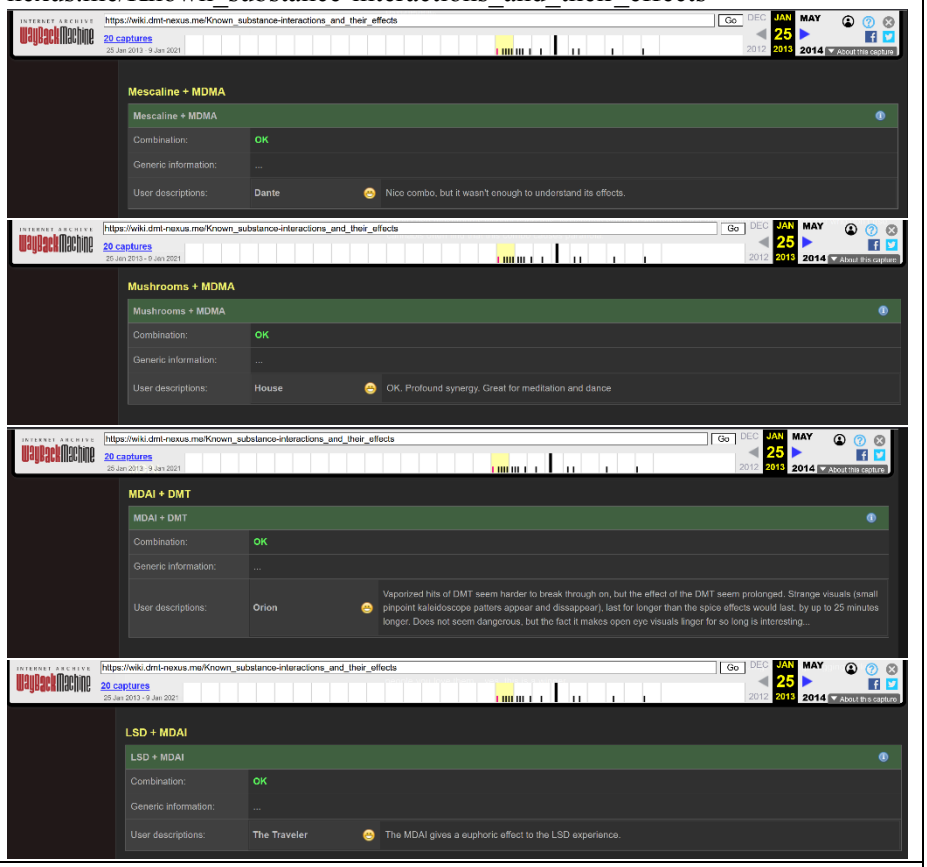
	Table 1 Statistics for the effects of LSD in the 5D-ASC and MEQ 

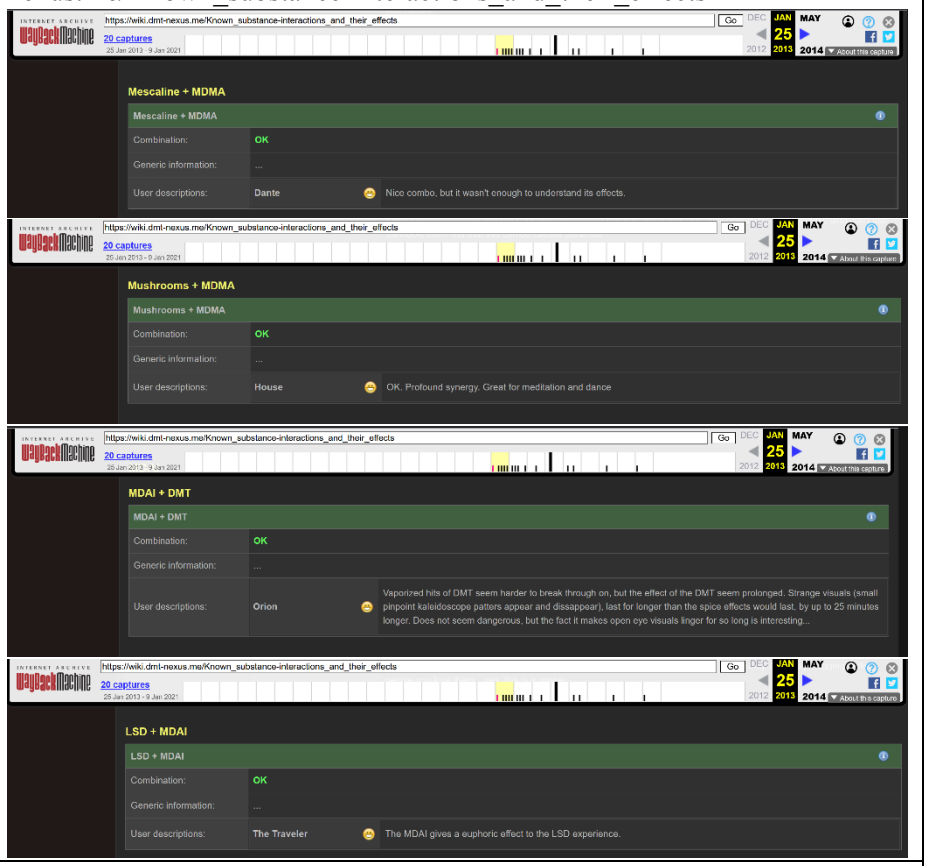
	LSD 100 µg *T* test vs. placebo		LSD 200 µg *T* test vs. placebo		LSD 100 vs. 200 µg *T* test	
	T=	*P*=	*T*=	*P*=	*T*=	*P*=
5 Dimensions Altered States of Consciousness (ASC) scale						
Total ASC score	9.72	<0.001	10.02	<0.001	2.23	<0.05
Oceanic boundlessness	8.44	<0.001	9.61	<0.001	1.89	NS
Anxious ego dissolution	6.43	<0.001	4.01	<0.001	1.50	NS
Visionary restructuralization	9.79	<0.001	15.32	<0.001	2.34	<0.05
Auditory alterations	3.72	<0.01	5.87	<0.001	0.42	NS
Reductions of vigilance	7.44	<0.001	5.93	<0.001	0.79	NS
Experience of unity	6.85	<0.001	7.77	<0.001	0.68	NS
Spiritual experience	4.31	<0.001	3.91	<0.001	1.10	NS
Blissful state	6.56	<0.001	8.27	<0.001	3.00	<0.01
Insightfulness	4.11	<0.001	5.81	<0.001	2.28	<0.05
Disembodiment	6.93	<0.001	5.87	<0.001	0.13	NS
Impaired control and cognition	7.01	<0.001	5.04	<0.001	0.86	NS
Anxiety	3.02	<0.001	2.04	NS	1.37	NS
Complex imagery	7.10	<0.001	7.48	<0.001	0.31	NS
Elementary imagery	9.96	<0.001	11.12	<0.001	0.57	NS
Audio-visual synsthesia	9.19	<0.001	12.52	<0.001	1.96	NS
Changed meaning of percepts	6.25	<0.001	9.66	<0.001	3.39	<0.01
Ego dissolution (item 71)	7.63	<0.001	5.32	<0.001	0.36	NS
Mystical Effects Questionnaire (MEC43)						
Internal unity	NA	NA	6.22	<0.001	NA	NA
External unity	NA	NA	6.08	<0.001	NA	NA
Sacredness	NA	NA	6.80	<0.001	NA	NA
Noetic quality	NA	NA	5.71	<0.001	NA	NA
Deeply felt positive mood	NA	NA	11.43	<0.001	NA	NA
Transcendence of time/space	NA	NA	10.63	<0.001	NA	NA
Ineffability	NA	NA	16.22	<0.001	NA	NA
Mystical Effects Questionnaire (MEQ30)						
Mystical	NA	NA	5.99	<0.001	NA	NA
Positive mood	NA	NA	13.13	<0.001	NA	NA
Transcendence of time/space	NA	NA	11.12	<0.001	NA	NA
Ineffability	NA	NA	25.14	<0.001	NA	NA
MEC30 total score	NA	NA	14.91	<0.001	NA	NA

Sixteen subjects participated in the high-dose study (200 µg) and 24 subjects in the moderate-dose study (100 µg). Dependent *T* tests were performed to assess differences from placebo, and independent *T* tests were performed to assess differences between doses of LSD

NA not assessed

25. A method of treating a patient including the step of: enhancing a mood of the patient prior to psychedelic treatment	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA, then LSD or 2-CB were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used."
26. The method of claim 25, wherein said enhancing step is further defined as administering an empathogen/entactogen ichosen from the group consisting of 3,4-methylenedioxymetha mphetamine (MDMA), 3,4-methylendioxyampheta	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA, then LSD or 2-CB were added mid-way**. Sometimes sessions began with 2-CB or with LSD or on rare occasions other substances such as ayahuasca or psilocybin were used."

mine (MDA), 3,4,-methylenedioxyethylamphetamine (MDEA), 5,6-methylenedioxy-2-aminoindane (MDAI), mephedrone, methylone, 3-MMC, homologues thereof, analogues thereof, and prodrugs thereof.	16. CHARY (2018) "Candyflipping and Other Combinations: Identifying Drug–Drug Combinations from an Online Forum" Frontiers Psychiatry. 9:1-9. From **page 5** "In the synthetic hallucinogen, LSD is a hub that bridges two subislands. The left subisland of the hallucinogen island contains substances canonically thought to be anticholinergic. Hyoscine and hyoscyamine are tropane alkaloids found in jimson weed. The right subisland contains amphetamine derivatives, such as **MDMA** and the **MDMA derivatives** (bath salts), bk-MDMA (β-keto MDMA; **methylone**) and **bk-MDEA** (ethylone)." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 
27. The method of claim 25, wherein the psychedelic is chosen from the group consisting of psilocybin, psilocin, lysergic acid	1. SESSA (2015) "Underground MDMA-, LSD- and 2-CB-assisted individual and group psychotherapy in Zurich: Outcomes, implications and commentary" Drug Science, Policy and Law. 2(0):1-8. From **page 3** "Most psycholytic sessions **began with MDMA, then LSD or 2-CB were added mid-way**. Sometimes sessions began with 2-CB or with

diethylamide (LSD), mescaline, dimethyltryptamine (DMT), 2,5-dimethoxy-4-iodoamphetamine (DOI), 2,5-dimethoxy-4-bromoamphetamie (DOB), phenethylamine or tryptamine psychedelics, salts thereof, analogs thereof, prodrugs thereof, and homologues thereof.	LSD or on rare occasions other substances such as **ayahuasca** or **psilocybin** were used." 17. DMT-NEXUS (2013) "Known substance-interactions and their effects" DMT-Nexus. Retrieved January 25, 2013. https://web.archive.org/web/20130125065447/https://wiki.dmt-nexus.me/Known_substance-interactions_and_their_effects 
28. The method of claim 25, wherein said enhancing a mood step is further defined as increasing positive acute effects chosen from the group consisting of good drug effect, drug liking, well-being, trust, feelings of love, openness, oceanic boundlessness, experience of unity, spiritual experience, blissful state,	8. BOYS (2001) "Understanding reasons for drug use amongst young people a functional perspective" Health Education Research. 16(4):457-469. From **page 465**

insightfulness, mystical-type experience, and positively experienced psychedelic effects, aspects of ego-dissolution, and combinations thereof, and decreasing negative acute effects chosen from the group consisting of bad drug effect, anxiety, fear, increased ratings of anxious ego-dissolution, descriptions of acute paranoia, states of panic and anxiety, and combinations thereof.

Table IV. *Combined functional substance use reported by the sample over the past year*

	Cannabis (n = 153)	Amphetamines (n = 60)	Ecstasy (n = 43)	LSD (n = 17)	Cocaine (n = 44)	Alcohol (n = 128)
Used with [substance] to improve its effects						
cannabis	–	16	18	8	14	93
amphetamines	37	–	20	7	3	29
ecstasy	55	39	–	11	19	45
LSD	24	10	9	–	3	6
cocaine	42	4	5	1	–	45
alcohol	110	38	23	4	29	–
hallucinogenic mushrooms	2	0	0	1	0	1
	Cannabis (n = 223)	Amphetamines (n = 19)	Ecstasy (n = 15)	LSD (n = 3)	Cocaine (n = 23)	Alcohol (n = 112)
Used to help ease after effects of [substance]						
cannabis	–	5	2	0	4	18
amphetamines	83	–	6	1	1	47
ecstasy	114	7	–	3	10	59
LSD	29	0	5	–	0	13
cocaine	80	1	1	0	–	34
alcohol	70	18	7	0	14	–

9. HOLZE (2019) “Distinct acute effects of LSD, MDMA, and d-amphetamine in healthy subjects” Neuropsychopharmacology. 45:462–471.

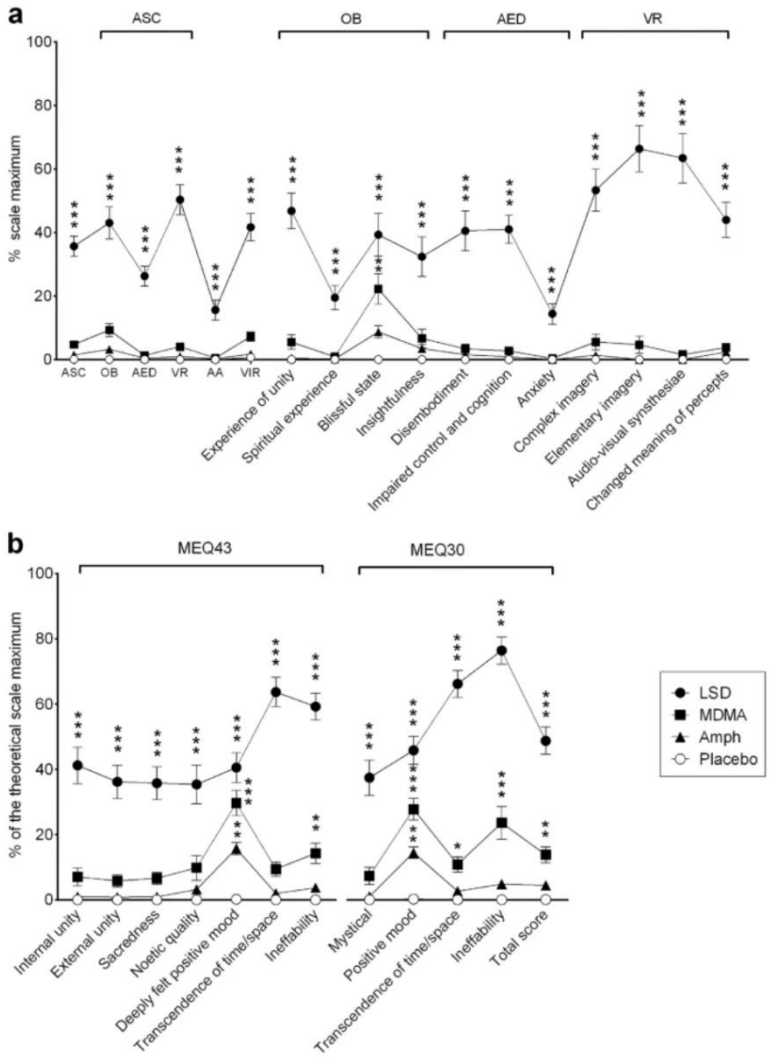
From **page 462** “MDMA produced greater ratings of **good drug effects, liking**, high, and ego dissolution compared with d-amphetamine. d-Amphetamine increased ratings of activity and concentration compared with LSD.”

From **page 462** “MDMA acutely induces feelings of **well-being, love, empathy**, and prosociality”

From **page 462** “On the other hand, LSD was found to exhibit MDMA-like empathogenic mood effects such as increased **closeness, openness, and trust**”

From **page 468**

Fig. 3

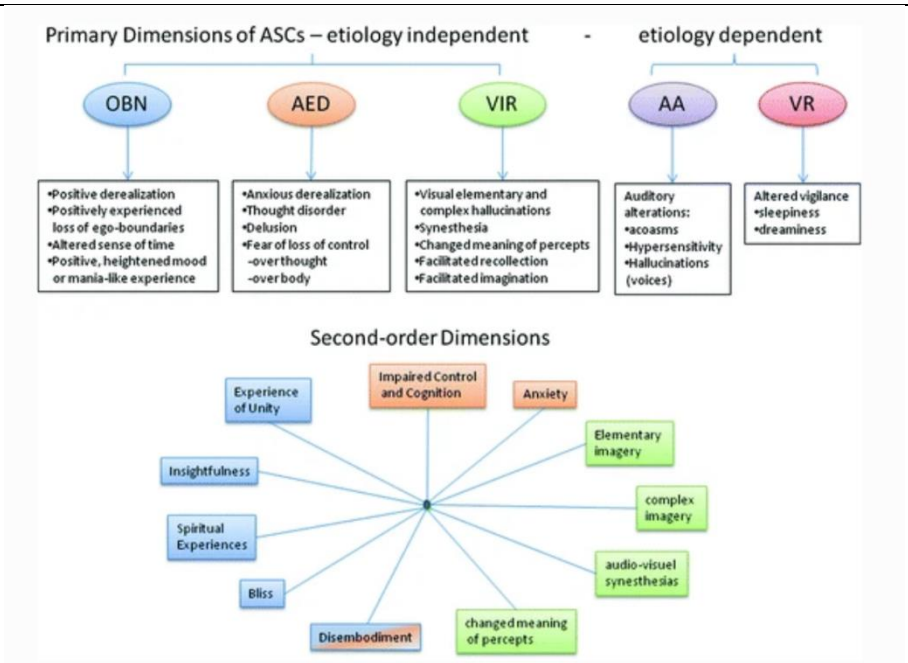


10. OLSON (2020) "Tripping on nothing: placebo psychedelics and contextual factors" Psychopharmacology. 237:1371–1382.

From **page 1375** "The 5D-ASC measures changes in subjective experience (Dittrich 1998) and is commonly used in psychedelic studies. Each item uses a visual analogue scale ranging from "No, not more than usually" (0) to "Yes, much more than usually" (100). The measure has 11 subscales (Studerus et al. 2010a):

- **anxiety** (e.g. "I was scared without knowing exactly why"),
- spiritual experience ("My experience had religious aspects to it"),
- **insightfulness** ("I felt very profound"),
- **impaired control and cognition** ("I felt incapable of making even the smallest decision"),
- **disembodiment** ("I felt as if I no longer had a body"),
- experience of unity ("Everything seemed to unify into a oneness"),

	• **blissful state** ("I experienced boundless pleasure"), • changed meaning of percepts ("Some everyday things acquired special meaning"), • complex imagery ("I saw whole scenes roll by with closed eyes or in complete darkness"), • audio-visual synaesthesia ("The colours of things seemed to be altered by sounds or noises"), and • elementary imagery ("I saw colours with closed eyes or in complete darkness")." 11. Smigielski (2019) "Characterization and prediction of acute and sustained response to psychedelic psilocybin in a mindfulness group retreat" Scientific Reports. 9:1-13. From **page 2** "Although the content and intensity of psychedelic experiences depend most critically on dosage, the same dose can induce a pleasurable state of self-dissolution or, under certain circumstances, a more distressing response associated with **thought disturbances, fear of losing control, anxiety, or panic**." From **page 3** "5D-ASC is designed to quantify positive and **negative forms of self/ego-dissolution**, including perceptual alterations." 14. HALBERSTADT (2018) Behavioral Neurobiology of Psychedelic Drugs. Springer ISBN: 978-3-662-55878-2 From **page 227**



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From **page 1504**

Table 1 Statistics for the effects of LSD in the 5D-ASC and MEQ

	LSD 100 µg *T* test vs. placebo		LSD 200 µg *T* test vs. placebo		LSD 100 vs. 200 µg *T* test	
	T=	*P*=	*T*=	*P*=	*T*=	*P*=
5 Dimensions Altered States of Consciousness (ASC) scale						
Total ASC score	9.72	<0.001	10.02	<0.001	2.23	<0.05
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Complex imagery	7.10	<0.001	7.48	<0.001	0.31	NS
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Mystical Effects Questionnaire (MEC43)						
Internal unity	NA	NA	6.22	<0.001	NA	NA
External unity	NA	NA	6.08	<0.001	NA	NA
Sacredness	NA	NA	6.80	<0.001	NA	NA
Noetic quality	NA	NA	5.71	<0.001	NA	NA
Deeply felt positive mood	NA	NA	11.43	<0.001	NA	NA
Transcendence of time/space	NA	NA	10.63	<0.001	NA	NA
Ineffability	NA	NA	16.22	<0.001	NA	NA
Mystical Effects Questionnaire (MEQ30)						
Mystical	NA	NA	5.99	<0.001	NA	NA
Positive mood	NA	NA	13.13	<0.001	NA	NA
Transcendence of time/space	NA	NA	11.12	<0.001	NA	NA
Ineffability	NA	NA	25.14	<0.001	NA	NA
MEC30 total score	NA	NA	14.91	<0.001	NA	NA

Sixteen subjects participated in the high-dose study (200 µg) and 24 subjects in the moderate-dose study (100 µg). Dependent *T* tests were performed to assess differences from placebo, and independent *T* tests were performed to assess differences between doses of LSD

NA not assessed

Electronic Acknowledgement Receipt

EFS ID:	45481254
Application Number:	17238088
International Application Number:	
Confirmation Number:	8795
Title of Invention:	MDMA TREATMENT TO ENHANCE ACUTE EMOTIONAL EFFECTS PROFILE OF LSD, PSILOCYBIN, OR OTHER PSYCHEDELICS
First Named Inventor/Applicant Name:	Matthias Emanuel LIECHTI
Customer Number:	48924
Filer:	Shahin Shams
Filer Authorized By:	
Attorney Docket Number:	0614.00040
Receipt Date:	14-APR-2022
Filing Date:	22-APR-2021
Time Stamp:	22:49:42
Application Type:	

Payment information:

Submitted with Payment	yes
Payment Type	CARD
Payment was successfully received in RAM	$90
RAM confirmation Number	E20224DM49382561
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Warnings:					
Information:					
2	Evidence of Publication	21-LIECHTI.pdf	836250 95e01161bae250968188ae2cca20795c77b26a56	no	12
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Warnings:					
Information:					

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If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

New International Application Filed with the USPTO as a Receiving Office

If a new international application is being filed and the international application includes the necessary components for an international filing date (see PCT Article 11 and MPEP 1810), a Notification of the International Application Number and of the International Filing Date (Form PCT/RO/105) will be issued in due course, subject to prescriptions concerning national security, and the date shown on this Acknowledgement Receipt will establish the international filing date of the application.