

**Clarifying the Mechanisms by which Psychedelics Achieve Therapeutic Efficacy**

by

Andrew Jones

B.A., The University of British Columbia, 2015

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF  
THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF ARTS

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES  
(Philosophy)

THE UNIVERSITY OF BRITISH COLUMBIA  
(Vancouver)

August 2018

© Andrew Jones, 2018

The following individuals certify that they have read, and recommend to the Faculty of Graduate and Postdoctoral Studies for acceptance, a thesis/dissertation entitled:

Clarifying the Mechanisms by which Psychedelics Achieve Therapeutic Efficacy

submitted by Andrew Jones in partial fulfillment of the requirements for

the degree of Master of Arts

in Philosophy/ Science and Technology Studies

**Examining Committee:**

Alan Richardson

Supervisor

Robert Brain

Supervisory Committee Member

Supervisory Committee Member

Additional Examiner

**Additional Supervisory Committee Members:**

Supervisory Committee Member

Supervisory Committee Member

## **Abstract**

The potential psychotherapeutic value of psychedelic drugs has recently generated much scientific and public interest. Many comparative trials have suggested that these drugs can produce significant benefits for individuals suffering from various treatment-resistant psychological disorders. However, recent work in the philosophy of medicine has emphasized the importance of complementing evidence produced by comparative trials with “mechanistic evidence”. Mechanistic evidence is evidence that is produced by reasoning about the causal pathways (or mechanisms) by which treatments achieve their effects. It is important, therefore, to have a strong understanding of the mechanistic evidence for the therapeutic efficacy of psychedelics. This thesis seeks to strengthen the understanding of the mechanistic evidence for the therapeutic efficacy of psychedelics. By surveying past and contemporary proposals about how psychedelics produce benefit, I articulate two broad views that dominate contemporary understandings of the mechanistic evidence. According to “mind-manifesting” views, psychedelics are therapeutically useful because they facilitate access to unconscious content. On the other hand, according to “mind-modifying” views, psychedelics are therapeutically useful because they disrupt rigid thought patterns and increase psychological flexibility. I argue that these two views are sometimes conflated or not clearly distinguished by contemporary researchers, and that they need to be teased apart to generate a stronger understanding of exactly how psychedelics produce beneficial outcomes. I then explore the viability of using “psychedelic testimony” to help tease these views apart.

## **Lay Summary**

Recently, many studies have suggested that psychedelic drugs can be used to treat psychological disorders. When exploring the value of using a drug to treat disorders, it is important not only to understand *that* a drug produces a beneficial outcome, but to also clearly understand *how* that drug produces such an outcome. How exactly, then, do psychedelics produce beneficial outcomes? This thesis aims to clarify how psychedelics produce beneficial outcomes by surveying past and contemporary answers to this question. I claim that there are two broad views in current psychedelics research. According to “mind-manifesting” views, psychedelics are therapeutically valuable because they facilitate access to unconscious material. Alternatively, according to “mind-modifying” views, psychedelics produce benefit by disrupting rigid thought patterns and increasing psychological flexibility. However, these views are sometimes conflated in current research, and to generate a better understanding of how psychedelics produce benefit they need to be clearly distinguished.

## **Preface**

This thesis is wholly the original and unpublished work produced independently by the author,  
Andrew Jones.

## Table of Contents

<b>Abstract.....</b>	<b>iii</b>
<b>Lay Summary .....</b>	<b>iv</b>
<b>Preface.....</b>	<b>v</b>
<b>Table of Contents .....</b>	<b>vi</b>
<b>Acknowledgements .....</b>	<b>vii</b>
<b>Dedication .....</b>	<b>viii</b>
<b>Chapter 1: Introduction .....</b>	<b>1</b>
<b>Chapter 2: The Mind-Manifesting View.....</b>	<b>7</b>
<b>Chapter 3: The Mind-Modifying View .....</b>	<b>19</b>
3.1    Current Research on the Mechanisms of Psychedelic Drug Effects.....	20
3.2    Mind-Manifesting or Mind-Modifying? .....	33
<b>Chapter 4: Conclusion .....</b>	<b>40</b>
<b>Works Cited.....</b>	<b>43</b>

## **Acknowledgements**

This thesis would not have been possible without the encouragement and open-minded attitudes of many faculty members in UBC's philosophy and science and technology studies community. In particular, I would like to thank Suzie Anger, Adam Frank, and Carla Nappi for helping me realize that stigmatized topics can be studied academically and for their advice on how I might approach such topics. Also, I would like to thank Evan Thompson for discussions on early versions of this thesis, and Robert Brain for his helpful advice and contributions as a second reader. Finally, I would like to thank my supervisor, Alan Richardson, whose advice and support helped me turn many haphazard ideas about psychedelic science into a focused and coherent thesis.

I also owe a lot to my fellow graduate student colleagues who provided feedback on presentations of this project in both formal and informal settings. I would like to thank all the STS students who listened to my ramblings and gave me suggestions, in particular, Nathan TeBokkel, Sara Press, Claire Oliver and Katie Powell. Thanks is also owed to fellow philosophy graduate students who helped me work through this project, such as Kinley Gillette, Kyle Da Silva, Jakub Stach and Matthew Kinakin. Furthermore, I would like to thank graduate students in the philosophy department at the University of Waterloo who provided feedback on a presentation of a draft of this thesis.

Lastly, I would like to thank my parents for all their many ways of supporting me.

## **Dedication**

*To my parents.*

## Chapter 1: Introduction

In April of 1956, a British psychiatrist by the name of Humphrey Osmond gave a talk entitled “A Review of the Clinical Effects of Psychotomimetic Agents” at a conference hosted by the New York Academy of Sciences. Since the beginning of the decade, Osmond had been studying the biochemical and psychotherapeutic properties of LSD and mescaline, which were commonly referred to as “psychotomimetic” (psychosis-mimicking) agents. The term ‘psychotomimetic’ was reflective of the “model-psychosis” research paradigm that most of Osmond’s early work took place within. According to this paradigm, the cognitive and perceptual distortions produced by these drugs were similar to the symptoms of schizophrenia and psychosis, and thus the study of psychotomimetic agents could shed light on the biochemical basis of these disorders (Dyck, 32).

The talk, which possessed the thoughtful conviction generated by years of research, focused primarily on the aptness of the terms that researchers used to refer to substances like LSD and mescaline. Besides ‘psychotomimetic’, other terms were used that also reflected the model-psychosis paradigm, such as hallucinogen (hallucination-producing), schizotoxin (schizophrenia-causing), psychotoxin (psychosis-causing), and phantasticant (fantasy-stimulating) (Strassman, 30). But, as Osmond argued, although such terms may describe some aspects of these drugs, they do not capture their therapeutic and philosophical potential. Throughout his research, Osmond became convinced that these agents have beneficial therapeutic applications (Dyck, 69). After some deliberation about a more suitable term, Osmond settled on ‘psychedelic’, which literally means “mind-manifesting”. He thought this to be a term that more accurately represents the effects of these drugs since it included “the concepts of enriching the mind and enlarging the vision” (Osmond, 428).

The notion of “psychedelic” or “mind-manifesting” captured views held by psychiatrists who explored the psychotherapeutic potential of LSD in the 1950s and early 60s. Most of these psychoanalytically-oriented researchers held that LSD could complement psychotherapy by facilitating access to a patient’s unconscious mind. LSD was thought to produce radical alterations to the dynamics of the ego, allowing psychological content that would otherwise be inaccessible to “manifest” into conscious awareness.

Today, roughly 60 years later, the term ‘psychedelic’ has prevailed as the dominant way to refer to drugs such as LSD, mescaline, DMT, and psilocybin. Currently, research into the therapeutic value of psychedelics is generating a substantial amount of popular and scientific interest. For instance, in April of 2017, the largest ever “Psychedelic Science” conference was held in Oakland, California, where roughly 2500 researchers, therapists, writers and students from all over the globe gathered to discuss and hear about the newest research surrounding psychedelic drugs (Doblin, *From the Desk of Rick Doblin*). Also, the potential therapeutic value of psychedelics has caught the attention of many mainstream media sources and scientific journals<sup>1</sup>, and the popularity of journalist Michael Pollan’s recent book, *How to Change Your Mind*, is indicative of the burgeoning interest in psychedelics in popular culture. Much of the current research has focused on the value of psychedelics for treating depression (Sanches et al) and addiction (Kerbs and Johansen; Bogenschutz et al.; Johnson et al.; Thomas et al.; Brown; Schenberg et al.), but studies have also examined their ability to treat post-traumatic stress disorder (Mithoefer et al.), anxiety and depression associated with terminal illness (Grob et al.;

---

<sup>1</sup> In 2017, for example, hundreds of articles about the therapeutic benefits of psychedelics have appeared in various journals such as *Psychopharmacology*, *Biological Psychiatry*, *The New England Journal of Medicine*, *Forbes*, *Scientific American*, *The New York Times*, *The American Psychiatric Association*, *The Boston Globe*, and *The Wall Street Journal* (Maps in the Media).

Gasser et al.), obsessive compulsive disorder (Moreno et al.), and even migraine headaches (Sewell et al.)<sup>2</sup>. Further, the legal medical use of psychedelics and the establishment of psychedelic treatment centers may become a reality in the next few years in the U.S.<sup>3</sup>.

As is well known, though, the path from Osmond's coining of the term psychedelic to today's explosion of interest has not followed a linear increase in enthusiasm. While scientific exploration of psychedelics proliferated in the 50s and early 60s, psychedelics eventually became associated with an emerging counterculture and were criminalized, resulting in the shutdown of psychedelic research<sup>4</sup>. Only in the last two and a half decades have researchers began again to explore these substances.

Much of the STS-oriented literature on the topic of psychedelic science has focused on efforts made by researchers and organizations to destigmatize psychedelics and bring psychedelic research back into mainstream science (Corbin; Langlitz). For instance, Michelle Corbin has argued that psychedelics researchers use "tactics of legitimization" to justify the study of these controversial substances (1413).

The purpose of this thesis is not to engage with this literature on the legitimization of psychedelic research. Instead, this thesis seeks to examine how current researchers understand the mechanistic evidence which suggests that psychedelics have psychotherapeutic applications. Mechanistic evidence is evidence produced by reasoning about the causal pathways by which

---

<sup>2</sup> Studies have also shown that the use of psychedelics can reduce suicidality (Hendricks et al.) and recidivism (Hendricks et al., "Hallucinogen Use Predicts Reduced Recidivism").

<sup>3</sup> Certain forms of psychedelic therapy have recently been granted 'breakthrough therapy' by the FDA and are currently going through phase 3 clinical trials (Doblin, "Latest Developments in Psychedelic Science from MAPS").

<sup>4</sup> For detailed accounts of the countercultural association see Shalin & Lee and Lattin. For an account of how this association led to the termination of psychedelic research see Doblin, *Regulation of the Medical Use of Psychedelics and Marijuana*.

treatments achieve their effects. For instance, Jeremy Howick claims that mechanistic reasoning “involves an inference from mechanisms to claims that an intervention produces a patient relevant outcome. Such reasoning will involve an inferential chain linking the intervention...with a clinical outcome” (128). Recent work in the philosophy of medicine has emphasized the importance of mechanistic evidence and its need to be integrated with evidence produced by comparative trials (Russo and Williamson; Clarke et al.). However, it is important to distinguish “just-so” causal stories about how a treatment works from high quality mechanistic reasoning. In other words, mechanistic evidence needs to be of a certain quality for it to adequately contribute to the question of whether interventions are justified. While it is not my intention here to enter into the debate about what constitutes high quality mechanistic evidence, one plausible proposal is that specificity and detail is a virtue of mechanistic evidence. That is, better mechanistic evidence articulates more features of the causal pathways that link an intervention with an outcome (Clarke et al, 357). In the context of the controversial and emerging field of psychedelic medicine, having high quality mechanistic evidence is crucial to determining whether these drugs should become a widespread form of medicine. The goal of this thesis, therefore, is to gain some clarity about how researchers understand the mechanistic evidence which suggests that psychedelics are beneficial for disorders such as depression, addiction and obsessive-compulsive disorder (OCD).

To accomplish this goal, I ask: While the term ‘psychedelic’ continues to be used, does the meaning of this term (“mind-manifesting”) continue to capture how researchers understand the therapeutic value of these drugs? In other words, do contemporary researchers still see the therapeutic value of these substances as lying within their ability facilitate access to unconscious content, or do current views, aided by new perspectives on the brain and new neuroimaging

technology, suggest a different mechanism by which psychedelics achieve therapeutic benefit? Providing an answer to this question can help elucidate how current researchers understand certain features of the mechanistic evidence for the therapeutic efficacy of psychedelics.

Link Swanson has attempted to take steps towards generating a “unifying theory of psychedelic drug effects” by comparing past and current accounts of psychedelic drug effects (2). With this goal in mind, Swanson seeks to identify fundamental features of past accounts that persist in contemporary accounts, which could potentially serve as prototypical “unifying principles” (2). According to Swanson, past and contemporary researchers both hold that psychedelics “perturb adaptive mechanisms which normally constrain perception, emotion, cognition, and self-reference” and are “therapeutically useful precisely because they offer a way to temporarily inhibit these adaptive constraints” (16).

While I agree with Swanson that past and current accounts both contain these fundamental features, the identification of these general features does not speak to the question of whether current views can still be seen as “mind-manifesting”. To answer this question, I take a more specific look at current research. I claim that most current research implies a “mind-modifying” view of the mechanisms by which psychedelics achieve therapeutic efficacy, according to which psychedelics are therapeutically useful not because they facilitate access to unconscious content, but because they restructure and alter rigid neurological and cognitive patterns. While “mind-modifying” and “mind-manifesting” views are not necessarily mutually exclusive, they are different. Mind-manifesting views imply that the subjective content that one encounters during the psychedelic experience is directly relevant to the therapeutic value of psychedelic drugs. Mind-modifying views, however, imply that the subjective content that one encounters is

irrelevant to the therapeutic value of psychedelics, since the therapeutic value of psychedelics lies in their ability to dismantle rigid neural patterns and increase cognitive flexibility. However, it is not clear whether current researchers see the subjective content as being relevant to therapeutic outcome. While much current research implies a mind-modifying view, some proposals still acknowledge the therapeutic importance of subjective content, which leads to a conflation of mind-manifesting and mind-modifying views in the current understanding of the reason why psychedelics are therapeutically efficacious.

In the following chapter I examine the claims of psychedelic psychotherapists from the 1950s and early 60s to provide a detailed picture of the “mind-manifesting” view of the therapeutic efficacy of psychedelics. In chapter 3, I examine current proposals about how psychedelics work therapeutically and articulate the “mind-modifying” view. I then describe how these views are sometimes conflated in current research. Finally, I consider a potential way of determining which view best captures the way in which psychedelics work therapeutically and explore potential problems with this approach.

## Chapter 2: The Mind-Manifesting View

During his 1956 conference talk, Osmond provided an analogy to illustrate his view of the effects of psychedelic drugs:

Psychoanalysis resembles Galileo's telescope, which lets one see a somewhat magnified image of an object the wrong way round and upside down. The telescope changed our whole idea of the solar system and revolutionized navigation.

[Psychedelics] are more like the radar telescopes now being built to scan the deeps of outer, invisible space. They are not convenient. One cannot go bird watching with them. They explore a tiny portion of an enormous void...Our newer instruments, employed with skill and reverence, allow us to explore a greater range of experience more intensively. (428-429)

As the comparison between Galileo's telescope and modern radar telescopes reveals, Osmond held that psychedelics were able to reveal layers of the mind that are normally invisible or inaccessible.

By examining the claims of past researchers, this chapter aims to articulate what I refer to as the "mind-manifesting" view of the therapeutic efficacy of psychedelics. This view holds that psychedelics achieve their therapeutic benefit by facilitating access to unconscious content. The mind-manifesting view was popular among psychiatrists who studied LSD in the 1950s and 60s, most of whom were working within Freudian schools of thought. To present a clearer picture of this view, then, it is necessary to first describe Freud's concepts of primary and secondary processes, which were central to his conception of psychodynamics.

Freud used the term ‘primary process’ to refer to states of consciousness that are relatively unstructured and disorganized, such as in psychosis or dreaming. In these states, according to Freud, cognition is easily influenced by wishful and primitive modes of thinking, and “psychical” or “nervous” energy is unbound and “freely mobile” (Freud, qtd. in Carhart-Harris and Friston, 1266-1267). The secondary process is a function of the ego that organizes and structures cognition and converts the unbound nervous energy into bound energy. Rational thinking and other forms of non-altered states of consciousness are the result of the function of the secondary process. Thus, for Freud, the relation between the primary and secondary processes is one of constraint: the secondary process constrains the primary process to produce a stable and coherent state of consciousness (Carhart-Harris and Friston, 1266-1267).

Some recent work has been done on examining the way in which past researchers understood the therapeutic value of psychedelics (Jacobs, 433; Carhart-Harris et al., 3; Swanson, 9-10). As Swanson has pointed out, past researchers held that psychedelics are therapeutically useful because they disrupt this constraining relation between the primary and secondary process: past researchers working within the psychoanalytic paradigm held that “psychedelic drugs interfere with the structural integrity of the ego and thereby reduce its ability to suppress the primary process and support the secondary process... This ‘frees’ the primary process which then spills into conscious awareness, resulting in perceptual instability, wildly vivid imagination, emotional intensity, conceptual paradox, and loss of usual self-boundaries” (9). Although I do not disagree with this claim, to clearly and comprehensively articulate the mind-manifesting view, it will be useful to revisit the primary sources on which this claim is based.

While the term ‘psychedelic’ was not coined until 1956, acknowledgement of the potential therapeutic value of psychedelics developed alongside of investigations into their

psychotomimetic properties. LSD's therapeutic potential was acknowledged as early as 1950 in an article entitled "LSD 25 as an Aid in Psychotherapy" published by Busch and Johnson. These authors noted that during states of delirium induced by a toxic chemical, patients suffering from psychological disorders were often able to "verbalize repressed conflicts" (Busch and Johnson, 2). This observation led them to search for drugs that could generate a temporary delirious state. At this time, Sandoz lab in Switzerland had been distributing LSD to various psychiatric departments, and they suggested that Busch and Johnson use LSD. Many of the 29 patients that Busch and Johnson gave LSD to were diagnosed with some form of psychosis and hospitalized. After taking LSD, it was easier for a handful of patients to recollect early memories. For example, describing the effects of LSD on the patients, Busch and Johnson reported that patients "recall[ed]...childhood more vividly", "showed more feeling", were "better able to talk about...early life [and] showed some regressive behavior and seemed to re-live childhood experiences" and "Relived traumatic episodes of...childhood" (3).

Eight patients made considerable progress with the use of LSD. To explain these results, Busch and Johnson claimed that the "effect was in the nature of a transitory toxic state, which disturbed the barrier of repression and permitted a re-examination of significant experiences of the past, which sometimes were relived with frightening realism. With this, some of the patients were then able to re-evaluate the emotional meaning of some of their symptoms and improved" (4). The conclusion was that LSD permits the "recall of the provoking experiences" and that it could therefore allow effective psychotherapy to happen within a shorter period (4).

This study ushered in a wave of enthusiasm for psychoanalytical therapists who saw LSD as a therapeutically valuable drug since it provides access to unconscious material. For example, R.A. Sandison suggested that in "so many cases the rigid conscious barriers and resistances

offered by the patient are too great to be overcome. LSD gives these people some real and tangible experience of their own unconscious” and “produces an upsurge of unconscious material into consciousness” (519). In 1958, Feld et al. claimed that “LSD-25 has the astonishing quality of bringing into focus the patient’s repressed emotional attitudes, conflicts, etc. and permits their reactivation” (182). Ball and Armstrong claimed that LSD is useful for therapy because it enables “the patient to have heightened recall of previous events, facilitates the appearance of unconscious material and aids the development of increased clarity of insight and awareness of self” (231). Eisner and Cohen claimed that “LSD is extraordinary if only because of the rich view of the unconscious which it permits” and it acts as “a facilitator of recall and as an aid in the abreaction of traumatic events, whether suppressed or repressed” (537). Ling and Buckman compared the action of LSD to what a surgeon does: “It is suggested that deep treatment of this type should be considered in the same light as a careful surgeon approaches operating on the abdomen. LSD provides the means of opening the unconscious and exposing it primarily to the patient in co-operation with the psychiatrist; the surgeon has the ability of opening the abdomen and then making changes or removing organs while the patient is unconscious” (2).

As pointed out by Swanson, the way in which LSD was thought to achieve this increased access to the unconscious was by producing some kind of alteration or disruption to the ego’s ability to constrain the unconscious. For instance, Ling and Buckman claimed that “the rationale of this treatment is that the false ego which has held the patient from his neurosis, crumbles under treatment, giving him access to unconscious contents towards which he has to form a new attitude” (27). Klee noted that while many authors report that LSD disintegrates or disturbs the ego, these claims are speculative and anecdotal, and so a more precise statement of LSD effects on the ego needs to be developed. To accomplish this, Klee references Freud’s claim that the ego

is a “body ego” that is constantly maintained and shaped in relation to perception. Since LSD disrupts perceptual processing, it disrupts an individual’s sense of self (60). Eisner and Cohen claimed that “[d]rugs like LSD may temporarily check the manifold restraints which must occupy most of the work of the mind” (533). In more physiological terms, they stated that LSD causes the “inhibition of inhibiting neurophysiological systems which in turn facilitates reappearance of forgotten memories, the recovery of repressed events, and the access to deeper, more symbolic material in the unconscious” (538).

While researchers often acknowledged that the ego “crumbles” or that its constraint over primary processes is inhibited during the LSD state, some also noted that the ego’s ability to defend against the emergence of unconscious material is not completely absent. For instance, Chandler and Hartman claimed that “[t]he increase in the scope of awareness produced by the drug includes a sharpening in the awareness of the ego structure itself and the various ego defensive mechanisms. The patient can literally “see” himself resisting, rationalizing, denying, isolating, etc” (74). The idea here is that not only does unconscious content become more visible during LSD therapy, but that the strategies that the ego ordinarily uses to repress this content also become more visible: “The defensive systems of the patient show up more clearly under the drug” (69). Furthermore, the ego still retains some ability to repress unconscious contents. Chandler and Hartman explain that “the “primary process” is much more in evidence during the sessions. The emotions are more intensely felt, and primitive impulses are raised to conscious awareness. However, because the basic ego functions are retained, these impulses are expressed through imagery and fantasy, or just as simple awareness, rather than acted out in physical reality” (69). Furthermore, Klee noted that during the LSD session, as the content from the unconscious manifests into awareness, there is often a reactionary “mobilization of repressive

efforts” (466-67). While certain defense mechanisms such as repression may be diminished by LSD, other defenses, such as “regression denial, introjection, and projection” remain intact (471).

The unconscious content that was made accessible by LSD came in various forms. Patients often reported having vivid recall of or reliving of emotionally-charged childhood or traumatic memories, experiencing dream-like visual imagery or hallucinations, and experiencing primal impulses and archetypal patterns. Many studies reported instances of accessing early childhood memories and memories of traumatic events. Sandison noted that “[o]ne of the striking things about LSD treatment is the way in which the majority of the patients regress into childhood and appear to remember things which were apparently forgotten” (498). Also, Chandler and Hartman emphasized the clarity of the recall of past events even go as far to say that “the term "reliving" describes the more intense experiences better than the term “recall”” (71). Feld et al. mentioned a patient who relived a traumatic truck accident (179), and Sandison even noted that people sometimes report remembering details about their own experience of being born (498).

The visual hallucinations and internal imagery that patients reported during the LSD experience were analyzed in the same way that other primary process content would be within the psychoanalytic paradigm, such as dreams. In 1952, for example, Savage noted that the hallucinations LSD produces are similar to dreams and they can therefore be valuable for personality analysis and free association: LSD “is of potential use in personality exploration by the analysis of the hallucinations that it produces” (899). Savage mentioned a study of LSD’s effects on depression, where one patient reported “distortions of vision, noting that other people appeared squat and shorter than himself” (899). Through free association, these images were interpreted as revealing an inferiority complex. Another patient experienced “a colourful

mediaeval pageant” and drew a picture representing the experience (900). A character in the pageant had a large, open mouth and only one eye open. After the session, free association led the patient to interpret these experiences as representing a conflict with the therapist: “This psychiatrist talked too much and saw only half of the patient’s difficulties” (900). According to Savage these hallucinations revealed unconscious conflicts that would have otherwise not been recognized, and he therefore concluded that “LSD affords therapeutically valuable insights into unconscious processes by the medium of the hallucinations it produces” (900).

Similarly, Sandison described a case of a patient who during LSD therapy consistently experienced images of snakes: “I then began to see serpents' faces all over the walls. Then I saw myself as a fat, pot bellied snake slithering gaily away to destruction...Then I felt a snake biting my tail - then I realized I was biting my own tail and eating myself up” (510). Sandison, working within a Jungian framework, interpreted the image in archetypal terms. The snake eating its own tail was thought to reference the Uroboros archetype, which Jung regarded as symbol of the alchemical process of self-transformation (510).

Perhaps the most comprehensive theoretical exploration of the types of content encountered during LSD psychotherapy comes from Stanislav Grof. While many psychoanalytically oriented researchers remained within the bounds of Freudian psychology and held that psychedelics facilitate access to unconscious content, Grof felt that LSD psychotherapy revealed and provided access to deeper layers of the unconscious that were unrecognized by Freudian theory. In *Realms of the Human Unconscious*, Grof outlined a cartography of the unconscious mind based on his observations from over 17 years of conducting LSD psychotherapy. These observations led Grof to integrate Freudian, Rankian and Jungian psychoanalytical concepts into a unified theory of the levels of the unconscious. According to

Grof, the unconscious is structured according to three levels: the psychodynamic, the perinatal, and the transpersonal.

The psychodynamic level is essentially the Freudian level of the unconscious, in which an individual's early childhood memories or trauma are repressed and exert an effect on personality or behaviour. Grof noted that these repressed memories typically come in thematic clusters and during LSD psychotherapy a particular cluster of memories might emerge into conscious awareness. Grof referred to these clusters of memories as "Systems of Condensed Experience" (COEX System). For Grof, a COEX System "can be defined as a specific constellation of memories consisting of condensed experiences...from different life periods of the individual. The memories belonging to a particular COEX system have a similar basic theme or contain similar elements and are associated with a strong emotional charge of the same quality" (46). Grof held that each COEX System has a core traumatic event that generates an emotional charge, which each thematically related subsequent experience clusters around: "The excessive emotional charge which is attached to COEX systems (as indicated by the often powerful abreaction accompanying the unfolding of these systems in LSD sessions) seems to be a summation of the emotions belonging to all the constituent memories of a particular kind" (47). Memories are organized into COEX systems through the psychodynamic relationship between primary and secondary processes. That is, the constraining dynamic properties of secondary processes organize and integrate the separate, related memories into a "distinct functional unit" (47). According to Grof, "individual COEX systems have fixed relations to certain defense mechanisms and are connected with specific clinical symptoms" and they become integrated into personality structure (47).

For Grof, psychedelics are therapeutically useful because they allow the core experiences of COEX systems to emerge into conscious awareness. This emergence is accompanied by a strong abreaction as the emotional charge associated with the emerging COEX system is released. By focusing on abreaction, Grof is in line with the other psychoanalytically oriented psychiatrists of his time. For instance, Sandison claimed that it is “the living out and acceptance of the whole emotional complex which is the healing process” and that the re-living of unconscious content is “normally accompanied by emotional release and is a true abreaction of great benefit to the patient” (“The Role of Psychotropic Drugs in Individual Therapy”, 497-498). The emotional release that is associated with the reliving of the childhood or traumatic memories was thought to be a major step in the therapeutic process and since LSD facilitated the reliving of past events, it made abreaction more likely to occur: “The abreaction to a single traumatic event in the patient's...life produces the most rapid, effective, dramatic and long-lasting cures among the good results which are claimed for the use of the drug in psychotherapy” (499). Researchers observed that patients feel a great deal of relief after abreaction in LSD therapy. For example, Eisner and Cohen claimed that “[t]he word most commonly used by a patient after an experience of this sort is that he feels “purged” (530-533).

Grof outlines a number of indications of the abreaction that accompanies the emergence of a COEX system into conscious awareness: “unexplainable mood qualities of great intensity...panic anxiety, severe depression..intense disgust...irrational guilt or inferiority feelings...general aggressive tension... all such initially incomprehensible emotions can be later identified as logical and integral parts of the pertinent COEX systems” (79). Perhaps most notable are the physical indications: “nausea and vomiting, breathing difficulties, various cardiovascular complaints, profuse salivation or sweating...sensations of pain in different parts

of the body...muscle tension, tremors, jerks, shaking and twitches, complicated twisting movements and catatoniform excitement or stupor...repetitive and stereotypical movements and verbal manifestations” (79-80).

For Grof, the core experiences of COEX systems reside in layers of the unconscious that the methods of traditional psychoanalysis are unable to access. Grof observed that the experiences described by patients during LSD psychotherapy typically go beyond the individual psychodynamic level, and he therefore suggested other levels of the unconscious. The perinatal level in Grof’s cartography is associated with experiences and reflections about biological birth. Grof mentions that during LSD therapy patients often report re-living their “birth trauma” (80). The trauma of birth is thought by Grof to provide a core experience of the COEX system, and its manifestation into conscious awareness is accompanied by abreaction and relief.

The following level in Grof’s cartography of the unconscious is the transpersonal realm, where individuals have experiences that seem to be independent of their individual identity. For example, patients may describe Jungian phenomena such as experiences of the collective unconscious and identifying with archetypes (Grof, 154).

Although LSD was seen as a valuable therapeutic tool, past researchers continually emphasized that its ability to disrupt ego structures and facilitate emergence of unconscious material is by itself not sufficient for psychological healing. It was by analyzing and working with this content that beneficial therapeutic outcomes were thought to be produced. LSD simply made it easier for therapists to analyze the unconscious content, like how telescopes help astronomers analyze astral bodies. Aside from Osmond’s initial comparison of psychedelics and telescopes, the “telescope analogy” was used to illustrate how LSD is valuable to psychotherapy: “It does not seem to be an exaggeration to say that psychedelics, used responsibly and with

proper caution, would be for psychiatry what the microscope is for biology and medicine or the telescope is for astronomy. These tools make it possible to study important processes that under normal circumstances are not available for direct observation” (Grof, *LSD Psychotherapy*).

While LSD was thought to help researchers see the unconscious content, the content needed to be worked with, interpreted, and integrated in a healthy way into the patient’s personality structure. For example, Chandler and Hartman claimed that “[n]o matter how effective a drug is in "making the unconscious conscious," it still requires much time and many sessions to work through the transference and to integrate the insights gained into the person's everyday living” (75). Similarly, Eisner and Cohen noted that the drug itself is inadequate on its own to achieve treatment. Subsequent therapeutic sessions are required to integrate the uncovered material: “For therapeutic gains to continue, the advances made during psychotherapy must be acted upon...[c]ontinuing psychotherapy here is valuable in restructuring of habit patterns” (533). Also, Abramson mentioned that the presence of a therapist is vital to achieving the therapeutic effects of LSD (153).

After viewing these claims of past psychedelics researchers, we are now in a position to articulate what I refer to as the “mind-manifesting view” of how psychedelics achieve their therapeutic effects. The mind-manifesting view is a perspective on how psychedelics produce beneficial outcomes. It can therefore be considered to be a form of mechanistic evidence for the therapeutic efficacy of psychedelics. That is, it is evidence for the therapeutic efficacy of psychedelic therapy that is generated by reasoning about the causal pathways by which psychedelics achieve their therapeutic effects. The mind-manifesting view traces the causal pathways leading from intervention to outcome as follows: 1) psychedelics disrupt the ego’s ability to constrain unconscious or primary processes; 2) this allows the content of the

unconscious to emerge (or “manifest”) into conscious awareness, which is often accompanied by some form of abreaction; 3) this unconscious content is then analyzed by the therapist to arrive at conclusions about a patient’s psychological conflicts which can then be worked through over a subsequent period of time.

Crucially, according to the mind-manifesting view, the unconscious content (memories, traumatic episodes, imagery etc) that emerges during psychedelic therapy plays a direct role in the occurrence of the final therapeutic outcome. On this view, it is this content that makes psychedelics therapeutically useful, since the job of psychedelics is to help bring it into awareness. The importance of content is seen in the value that researchers place on abreaction during psychedelic therapy. Abreaction results in relief for the patient necessarily because some type of content has emerged into consciousness, which allows for its healthy integration into personality structure.

Now that we have articulated the mind-manifesting view, we can ask: do contemporary psychedelics researchers also hold a mind-manifesting view?

### Chapter 3: The Mind-Modifying View

Much has changed in psychology and neuroscience since the early days of psychedelic research. Sociologist Nikolas Rose, for example, notes that in the 1990s a biological and neurochemical view of the mind and brain came to overshadow Freudian views of the unconscious and the psychoanalytic view of therapy (188-192). Also, considerable developments have occurred in neuroimaging and new accounts of cognitive architecture and the relation between the conscious and unconscious have come to dominate philosophical debates about the mind (Fodor). Given these changes, then, do current psychedelics researchers subscribe to the mind-manifesting view?

As mentioned in chapter 1, Swanson has claimed that certain fundamental features of past accounts of psychedelic drug effects have persisted in contemporary accounts: past and current researchers both hold that psychedelics inhibit mechanisms that serve to constrain perception and cognition, and that this inhibition is crucial to the therapeutic value of psychedelics (16). This convergence of views is perhaps not surprising since, as we will see, contemporary psychedelics researchers have attempted to reinstate Freud's concepts of primary and secondary processes in contemporary terms<sup>5</sup>. However, even though current researchers are employing this distinction, this does not necessarily mean that they subscribe to a mind-manifesting view of the therapeutic value of psychedelics.

In this chapter, I examine current research on the mechanisms through which psychedelics produce therapeutic effects. I will first explain Entropic Brain Theory (EBT), which is perhaps

---

<sup>5</sup> Given the attempts of psychedelics researchers to legitimate psychedelic research and bring it into mainstream science, it seems odd that they would attempt to reinstate Freudian notions which are no longer popular. However, Carhart-Harris and Friston point out that Freud's distinction between primary and secondary processes was based on his observation of altered or aberrant forms of consciousness, and therefore psychedelic research, which is also based on such observations, is leading to similar conclusions (1266).

the most developed contemporary account of psychedelic drug effects. I will also point to less theoretically developed proposals about the therapeutic mechanisms of psychedelics that are based on recent empirical evidence. I will then argue that these accounts imply a “mind-modifying” view of the therapeutic value of psychedelics, in contrast to a mind-manifesting view. I will then explain how, despite this implication of current accounts, mind-manifesting and mind-modifying views are conflated in contemporary views. Finally, I will explore the possibility of using subjective descriptions of psychedelic experience to disentangle these views and determine which of them best captures the therapeutic effects of psychedelics.

### **3.1 Current Research on the Mechanisms of Psychedelic Drug Effects**

The most developed contemporary theory that provides a mechanistic account of the therapeutic and non-therapeutic effects of psychedelic drugs is perhaps Entropic Brain Theory (EBT), which was proposed by Carhart-Harris et al. in a paper titled “The Entropic Brain: A Theory of Conscious States Informed by Neuroimaging with Psychedelic Drugs”. Essentially, EBT proposes that degrees of disorder (i.e. entropy) can be used to characterize conscious states. The theory builds on earlier work done by Carhart-Harris and Friston that attempts to articulate the neural substrates of Freud’s primary and secondary process.

Carhart-Harris and Friston’s work is done within the context provided a predictive processing model, which holds that the brain is a hierarchically structured inference machine<sup>6</sup>.

According to this model, the brain optimizes its representation of the external world by

---

<sup>6</sup> Predictive processing models have become popular in theoretical neuroscience. According to Carhart-Harris and Friston, the view that the brain is an inference machine is now a “fundamental premise in neurobiology” (1267). See also Dayan et al. who locate the origins of this view in the work of Herman von Helmholtz.

deploying top-down predictions about the information generated by lower level functions such as perceptual processing. These top-down predictions are deployed by “higher-order cortical structures” that strive to adequately represent or “explain” the information presented by neural activity in systems that are lower in the inferential hierarchy (Swanson, 14-16). Neural activity at lower levels does not cease until higher systems have conveyed the fact that they have produced an adequate prediction via a feedback signal: “lower levels will not ‘shut up’ until they receive top-down feedback (inference) signals that adequately fit (explain) the bottom-up (evidence) signals” (14). However, if the prediction or explanation produced by higher levels does not match the information provided by signals in lower levels, “prediction error signals” occur that communicate the mismatch to other relevant areas (14). The job of higher level cortical structures, then, is to attempt to minimize the amount of prediction error signals. Carhart-Harris and Friston use the concept of “free energy” to describe the amount of prediction error in the brain: “free-energy is a measure of surprise and is essentially the amount of prediction-error. It is an information theory quantity that, mathematically, plays the same role as free-energy in statistical thermodynamics. Free-energy is not an abstract concept; it can be quantified easily and is used routinely in modelling empirical data” (1267).

According to Carhart-Harris and Friston, the dynamic relationship between higher and lower level systems maps onto Freud’s primary and secondary processes. As described in the previous chapter, Freud held that secondary processes are a function of the ego that work to constrain and organize the unstructured nervous activity or energy of the primary process. Likewise, by working to reduce the amount of prediction error or free-energy, higher level cortical networks attempt to constrain and organize conscious experience: “The hierarchical architecture may also accommodate the distinction between the Freudian primary and secondary

processes, where the secondary process provides top-down predictions to reduce free-energy associated with the primary process (cf. converting free energy into bound energy)” (1267).

Carhart-Harris and Friston point to a particular higher-order cortical network which they claim is the neural substrate of Freud’s ego. This large-scale network is the Default Mode Network (DMN), which consists of strongly connected brain regions that are more active during resting state metacognitive functions and that are associated with ego-related functions, such as “self-referential processing, autobiographical recollection, mind-wandering and theory-of-mind” (1268)<sup>7</sup>. The connectivity between these regions strengthens through ontogenetical development, and certain connections between regions of the DMN that exist in adult brains adults do not occur in infant brains, suggesting that the DMN develops alongside of the development of ego (1268).

EBT was stimulated by the results of a series of neuroimaging studies conducted on participants under the influence of psilocybin. An initial fMRI study found a decrease in cerebral blood flow in high-level association regions of the cortex during psilocybin intoxication, specifically in regions of the DMN. The same study also found decreases in large scale network connectivity during psilocybin intoxication (Carhart-Harris et al., “Neural Correlates of the Psychedelic State as Determined by fMRI Studies with Psilocybin”). Furthermore, these results were corroborated by an MEG study done by Muthukumaraswamy et al. which found “broadband cortical desynchronization” in the psychedelic state. Together, these studies imply that under the influence of psilocybin, the DMN becomes less metabolically active, less

---

<sup>7</sup> The brain areas that make up the DMN “include the medial prefrontal cortex, the posterior cingulate cortex, the inferior parietal lobule, the lateral and inferior temporal cortex and the medial temporal lobes” (Carhart-Harris and Friston, 1267).

integrated, and desynchronized (Carhart-Harris et al., “The Entropic Brain”, 6).

As described above, the DMN is hypothesized by Carhart-Harris and Friston to be a higher-level network that works to reduce prediction error or free energy. Since psilocybin disorganizes this network, a resulting increase in free energy or prediction error is thought to occur in the psychedelic state. EBT uses the notion of entropy to capture this increase in free energy. In this context, entropy refers to uncertainty about the state of the system which increases as disorder and randomness within the system increases (Carhart-Harris et al., “The Entropic Brain”, 1)<sup>8</sup>. As prediction error increases, disorder and uncertainty increase within the brain. The authors therefore propose that the neurophysiology and the subjective experience of the psychedelic state can be described as a state of increased entropy<sup>9,10</sup>.

EBT also employs the notion of “self-organized criticality” to describe the neural dynamics that underlie the primary and secondary processes. Self-organized criticality refers to how a complex, self-organized system strives to remain balanced at a certain point on a spectrum between maximum intensities of order and disorder (Carhart-Harris et al., “The Entropic Brain”, 2). As a system leans towards one end of the spectrum, its behavior and stability reflect the

---

<sup>8</sup> “Entropy in its purest information theoretical sense is a dimensionless quantity that is used for measuring uncertainty or ignorance about the state of a system. By implication, entropy/uncertainty is greater the more random a system is. Thus, entropy is most strictly a measure of uncertainty but it also reflects the degree of randomness or disorder in a system” (Carhart-Harris et al., “The Entropic Brain”, 1).

<sup>9</sup> It is not my intention to defend the use of these concepts or EBT. My aim is to explain how current researchers understand what psychedelics do to the brain. The authors provide the following rationale for the use of entropy: “Entropy is a powerful explanatory tool for cognitive neuroscience since it provides a quantitative index of a dynamic system’s randomness or disorder while simultaneously describing its informational character, i.e., our uncertainty about the system’s state if we were to sample it at any given time-point. When applied in the context of the brain, this allows us to make a translation between mechanistic and qualitative properties. Thus, according to this principle, increased subjective uncertainty or “puzzlement” accompanies states of increased system entropy” (Carhart-Harris et al., “The Entropic Brain”, 1).

<sup>10</sup> For those interested, Carhart-Harris et al. provide an explanation of how entropy in the brain is measured (“The Entropic Brain”, 10).

increase or decrease in order: “A system with high order (low entropy) exhibits dynamics that resemble ‘petrification’ and are relatively inflexible but more stable, while a system with low order (high entropy) exhibits dynamics that resemble ‘formlessness’ and are more flexible but less stable” (Swanson, 12). Criticality refers to a “transition zone” on the spectrum in which the system remains balanced between different states of order and disorder, or between different phases (12).

According to EBT, normal waking consciousness takes place within a “sub-critical” state (Carhart-Harris et al., “The Entropic Brain”, 7). This is because certain high-level brain networks, such as the DMN, normally suppress the amount of disorder or entropy in the brain by reducing prediction error signals. Since psychedelics interfere with the ability of the DMN to perform this entropy-suppression function, however, they cause the brain to move towards a critical state. EBT maintains that primary states (i.e. Freud’s primary process) are conscious states that are characterized by increased entropy. Or, in other words, primary conscious states occur when the brain enters criticality. Secondary states are those forms of consciousness that are produced by the constraining efforts of secondary processes, such as the form of consciousness characteristic of the typical adult ego. Secondary states thus occur in a sub-critical state because of the entropy suppression function of high-level networks.

In sum, EBT holds that the switch from secondary to primary conscious states reflects an increase in entropy that brings the brain into a critical state. By interfering with entropy suppression mechanisms, psychedelic drugs cause the brain to make this switch and operate in a critical state.

What does EBT imply about the mechanisms through which psychedelics achieve therapeutic efficacy? According to EBT, psychedelics are valuable for treating disorders such as

OCD, addiction and depression because they break down rigid thought patterns and produce more flexible forms of cognition: “Specifically, it is proposed that psychedelics work by dismantling reinforced patterns of negative thought and behavior by breaking down the stable spatiotemporal patterns of brain activity upon which they rest” (Carhart-Harris et al., “The Entropic Brain”, 14). This proposal is in line with evidence which suggests that depressed patients have hyper-connectivity between certain regions in the DMN and that the extent of this hyper-connectivity correlates with the amount of depressive rumination (Berman et al.). By decreasing connectivity in the DMN, psychedelics such as psilocybin reduce the hyper-connectivity that underlies pathological ruminations, resulting in a relief from depressive symptoms. However, EBT places this proposal within its larger theoretical framework that employs the notions of entropy and self-criticality. As we have seen, EBT places conscious states on a spectrum between maximum intensities of order and disorder. At the order end of the spectrum, conscious states are characterized by low disorder, low entropy and rigidity. Examples of these states, according to EBT, include OCD, depression, seizure, rigid and narrow thinking/inflexible cognition, and addiction. At the disorder end of the spectrum, conscious states are characterized by high disorder, high entropy, and flexibility. Examples of these states include infant consciousness, the psychedelic state, magical thinking, early psychosis and creative or divergent thinking (Carhart-Harris et al., “The Entropic Brain”, 13). EBT therefore holds that disorders such as OCD, depression and addiction are the result of too much constraint by high-level networks. Since psychedelics reduce this constraint and bring the brain into a critical state where entropy is increased, they are thought to increase cognitive flexibility and provide relief

from overly rigid thought patterns<sup>11</sup>.

It should be evident that this proposal about the therapeutic value of psychedelics is not mind-manifesting. As we have seen, the mind-manifesting view holds that psychedelics are therapeutically valuable because they facilitate access to unconscious content. The view implied by EBT, however, does not seem to suggest that the content of the unconscious plays a role in the final therapeutic outcome. Instead, EBT implies that psychedelics are therapeutically valuable because they modify the mind by breaking down rigid thought patterns and generating more flexible forms of cognition. I refer to this as a “mind-modifying view” of the therapeutic efficacy of psychedelics. While this mind-modifying view shares features with the mind-manifesting view, they are distinct in an important way. Both views involve the disinhibition of structures that constrain consciousness (the ego and high-level networks). Both views also involve an experience of the primary process: on the mind-manifesting view, the disinhibition of the ego’s constraint causes the primary process to emerge into awareness, and on the mind-modifying view, the disinhibition of entropy suppression by high-level networks causes the brain to enter a critical state. Yet according to the mind-modifying view, the therapeutic value of psychedelics resides in their ability to dismantle rigid patterns and increase flexibility, not in their ability to facilitate access to the content (memories, trauma etc.) of the unconscious. In other words, the mind-modifying view holds that psychedelics are valuable because they allow for the brain to *enter into* a critical state (i.e. primary consciousness). The act of entering into the critical state by itself is therapeutically valuable because it generates increased cognitive

---

<sup>11</sup> “Psychedelics maybe therapeutic because they work to normalize pathologically sub critical styles of thought (such as is seen in depression, OCD or addiction/craving for example) thereby returning the brain to a more critical mode of operating” (Carhart-Harris et al., “The Entropic Brain”, 12).

flexibility, regardless of the specific content that is encountered during the experience. On the mind-modifying view, then, in contrast to the mind-manifesting view, the specific content that is encountered during the psychedelic experience seems to be irrelevant to the therapeutic outcome.

EBT is a theoretically elaborate, ambitious and controversial framework which implies a mind-modifying view of the therapeutic value of psychedelics. However, other studies that are not embedded within such a grand theoretical framework also imply a mind-modifying view of the therapeutic value of psychedelics. For instance, Vollenweider and Kometer propose that psychedelics are therapeutically valuable because they increase neuroplasticity by raising levels of brain derived neurotrophic factor (BDNF), a brain hormone associated with neuroplasticity. Since, according to these authors, many mood disorders involve dysfunctions in the mechanisms related to neuroplasticity, psychedelics would be useful for treating such disorders (642). Further, Catlow et al. found that at appropriately low doses, psilocybin increased neurogenesis in mice. And recently, Ly et al. found that certain psychedelics increase a number of neural properties that have to do with neuroplasticity, such as neuritogenesis, spinogenesis, and synaptogenesis. These studies are all suggestive of a mind-modifying view, since they propose that psychedelics are therapeutically valuable because they induce structural and functional changes in the brain that change thinking patterns and increase cognitive flexibility. The mind-modifying view can therefore be taken to refer to a class of views which suggest that psychedelics alter or restructure cognitive processes and their underlying neural substrates.

It should now be clear that the mind-manifesting and mind-modifying views have significant differences with regards to their proposals about exactly why psychedelics are therapeutically valuable. However, although much current psychedelic research implies a mind-modifying view, it is not entirely clear whether contemporary psychedelics researchers subscribe

to a mind-modifying view or a mind-manifesting view, or even explicitly acknowledge that these views are different. For example, even though EBT implies a mind-modifying view, Carhart-Harris et al. end “The Entropic Brain” paper by claiming that:

Research with psychedelics could herald the beginning of a new scientifically informed-psychoanalysis that has the potential to influence modern psychology and psychiatry. The unique scientific value of psychedelics rests in their capacity to make consciously accessible that which is latent in the mind...mainstream psychology and psychiatry have under appreciated the depth of the human mind by neglecting schools of thought that posit the existence of an unconscious mind. Indeed, psychedelics’ greatest value may be as a remedy for ignorance of the unconscious mind. (18)

By suggesting that psychedelics have the “capacity to make consciously accessible that which is latent in the mind” (18), this passage seems suggestive of the mind-manifesting view where unconscious content plays a crucial role in therapeutic outcome. Furthermore, it is not specified what relationship EBT has to psychoanalysis, since a major tenet of psychoanalysis is that the integration of problematic unconscious content into awareness is crucial for healing.

The difficulty of specifying the relationship between contemporary views on psychedelic drug effects and psychoanalysis becomes apparent when examining how contemporary views account for the subjective content that is typically encountered during the psychedelic experience. For example, researchers using predictive processing models explain aspects of the psychedelic experience as resulting from a hyper-deployment of internal representations. Recent studies have established that psychedelics are agonists of 5HT<sub>2a</sub> receptors, a class of serotonin

receptors that are densely expressed on 5th cortical layer cells (Carhart-Harris). Predictive processing models claim that inferential hierarchies map onto the laminar organization of the cortex (Carhart-Harris). That is, higher-level networks occupy higher layers of the cortex and deploy schemas or templates that predict the basic sensory information presented by activity in lower cortical layers. By increasing the firing rate of neurons in higher cortical layers, psychedelics are thought to cause the hyper-deployment of templates that are used to predict lower level information. This would explain why, for instance, one might be more likely to perceive an object or a face in the clouds after taking a psychedelic (Carhart-Harris). This hyper-deployment of representational templates is interpreted by Carhart-Harris as latent content that is becoming manifest: “What is perceived as visual hallucinations are the brain’s own activity: internal representations which are usually latent which are now becoming manifest under the drug” (Carhart-Harris). The notion of “mind-manifesting” here is taken out of the psychoanalytical context and placed within a predictive processing context. On this predictive processing view, though, it is not clear how the content that one encounters during the psychedelic experience is relevant to psychoanalysis or psychological healing. Instead of being related to unconscious conflicts, the content seems to be the result of the brain’s processing gone awry.

Yet perhaps this predictive processing proposal only intends to account for the famous visual or auditory hallucinations that are often reported during the psychedelic experience. Despite the claims of past psychoanalytically oriented researchers, such as Savage and Grof, the hallucinations produced by psychedelics may not be implicated in their therapeutic outcome. Contemporary researchers might hold, though, that the *cognitive* content that is encountered during the experience does have implications for therapy. Recently, Carhart-Harris et al.

explored the fact that participants in studies who are administered psychedelics tend to report a feeling of “connectedness” to the world, to others and to their emotions (“Psychedelics and Connectedness”, 548). The authors propose that this feeling might be relevant to the therapeutic value of psychedelics (549). The rationale for this proposal builds on a study done by Tagliazucchi et al. in which increased “between-module” communication was observed in the brain after the administration of LSD (1046). In other words, the study suggests that in the psychedelic state, areas of the brain that are normally isolated from each other begin to share information. By disrupting the integrity and orchestrating function of individual networks such as the DMN, psychedelics allow normally disconnected networks to temporarily make contact. Carhart-Harris et al. suggest that this finding provides a plausible neural substrate for the “unitive experience” which is often reported during the psychedelic experience (“Psychedelics and Connectedness”, 549). “Unitive experience” refers to the experience of “oneness” that is often concomitant with the experience of ego dissolution. As the function of the DMN (or ego) becomes disintegrated, the boundaries between the self, others and the external environment began to diminish.

While the experience of connectivity can increase the sense of connection that individuals feel towards others and to the external world, the therapeutic significance of increased between-module communication may lie most in the personal insights that are often reported during the psychedelic state. Subjects tend to report connecting the dots between their past experiences, emotions, and current behaviors, which could result from the fact that regions in the brain that are normally isolated are now starting to share information. For instance, in a study by Watts et al. that examines the therapeutic value of experiences of connectedness during the psychedelic

state, one participant reported that:

It was different, separate fragments of that experience that all came together, colours, sounds, smells, and afterwards when I was talking, I started to see how they were all connected, all aspects of that experience when I was younger, it became clear that was where the problems I've had all stemmed from. (Watts et al., 539)

The idea that increased between module communication might help generate personal insights represents another way in which “mind-manifesting” might be interpreted in the contemporary context. The cognitive insights into past experiences and personality structure could be seen as a form of latent content that becomes available during the psychedelic state. Whether these insights represent a manifesting of the “unconscious” is not obvious, however, as Freudian concepts may not map onto increased between module communication. Yet the cognitive insights into the self could still in some sense be viewed as a form of latent content that becomes manifest during the experience.

Overall, then, it is not entirely clear whether contemporary researchers hold a mind-manifesting view (i.e. consider the subjective content experienced to be relevant to healing). While some subjective content does not seem relevant to healing on contemporary accounts (hallucinations), other views may leave room for the value of content (connectedness). What is perhaps clearer, though, is that contemporary practitioners of psychedelic therapy do hold a mind-manifesting view. For instance, Rick Doblin claims that psychedelics “catalyze a process of emerging material from the unconscious to the conscious mind” and that people who decide to use these substances in recreational contexts need to be prepared for this process and ready for

the integration of this material (Doblin, “Rick Doblin, Founder of MAPS, on the Integration Process”). Furthermore, Michael Mithoefer uses a metaphor to describe psychedelic therapy that is similar to the surgeon metaphor used by Ling and Buckman described in chapter 2. Mithoefer states that “if someone goes to the emergency room with a laceration, a doctor can remove obstacles to healing (e.g. remove foreign bodies, infection, etc.) and can help create favorable conditions for healing (e.g. sew the edges of the wound close together)” (Mithoefer, “A Manual for MDMA-Assisted Psychotherapy in the Treatment of Post- traumatic Stress Disorder”). The idea here is that the job of the therapist during psychedelic sessions is to remove repressed content that is disruptive to psychological well-being. Furthermore, Gabor Maté, an addictions researcher who has recently become interested in the medical use of psychedelics, sees their therapeutic value in their ability to help people deal with repressed trauma (Maté). These practitioners of psychedelic therapy adhere to the view that paying attention to the specific content that emerges from the unconscious during psychedelic therapy is crucial to the therapeutic value of psychedelics.

This examination of contemporary psychedelics researchers has revealed that researchers do not have a unanimous perspective on exactly why psychedelics are therapeutically valuable. Whether psychedelics are thought to be therapeutically valuable because they are mind-manifesting or because they are mind-modifying is not clear. It could be the case that there are a variety of ways in which psychedelics are therapeutically valuable. Psychedelics could be both mind-manifesting and mind-modifying. The experience of latent content could be relevant to healing some disorders, while the alteration of stubborn thought patterns could be useful for treating other disorders. If this is the case, though, the separate ways in which psychedelics achieve therapeutic efficacy need to be teased apart and clearly specified since this has important

implications for the design of study and therapy protocols and for the generation of high-quality mechanistic evidence. For example, if the mind-modifying aspects of psychedelics are hypothesized to be useful for treating OCD, then a protocol for treating OCD with psychedelics should work to augment their mind-modifying properties and place less significance on subjective content.

How can we determine which mechanisms produce the most therapeutic efficacy? Or if psychedelics work in a variety of ways, how can the diverse mechanisms be teased apart? In the next section, I will explore the viability of using “psychedelic testimony” as a means of teasing apart these proposals about mechanisms.

### **3.2 Mind-Manifesting or Mind-Modifying?**

The question of whether the therapeutic value of psychedelics lies in their mind-manifesting or mind-modifying properties can be rephrased as the question of whether the content of the subjective experience that one has during psychedelic therapy is responsible for positive therapeutic outcomes. As we have seen, according to the mind-manifesting view, the subjective content that arises during psychedelic therapy (such as memories, reliving of trauma, cognitive insights etc.) is crucial for therapeutic efficacy. According to the mind-modifying view, however, the content of the experience is less important or perhaps irrelevant since the therapeutic value of psychedelics lies in their ability to disrupt rigid thought patterns. How can we determine whether the content is relevant to the therapeutic outcome?

This is a difficult question to answer as it involves analyzing the subjective experience of individuals in altered states of consciousness. One obvious way to approach this question, then,

is by examining the descriptions or reports that study participants provide about their experiences while under the influence of psychedelics. I refer to these descriptions or reports as “psychedelic testimony”. Can psychedelic testimony be used to determine whether it is mind-manifesting or mind-modifying views that best explain the therapeutic efficacy of psychedelics?

A study by Garcia-Romeu et al. has suggested that “psilocybin-occasioned mystical experiences” correlate with long-term beneficial outcomes for the treatment of addiction (157). In other words, these results suggest that those who have mystical experiences during psychedelic therapy tend to have persistent health benefits. This study implies that the subjective content of the experience, that is, having a mystical experience, was relevant to treatment outcomes<sup>12</sup>. “Mystical experiences” were defined by the results of the “Mystical Scale”, a questionnaire designed to measure the occurrence of mystical experiences<sup>13</sup>. Focusing on mystical experiences, though, does not settle the tension between mind-manifesting and mind-changing views. However, it does provide a useful framework for correlating the character of psychedelic experience with healing outcome and therefore for exploring the question of whether mind-manifesting experiences are more efficacious than mind-modifying experiences.

In order to correlate mind-manifesting experiences with therapeutic outcome there needs to be a way to clearly define which experiences count as mind-manifesting and mind-modifying. As in the case of defining mystical experience, a questionnaire could be used that is designed to determine the extent to which a particular experience is mind-manifesting or mind-modifying. For example, such a “mind-manifesting scale” might include questions such as: “did you

---

<sup>12</sup> A recent study by Nichols et al. has suggested that this is not the case.

<sup>13</sup> See Hood for a detailed account of the Mystical Scale.

experience emotionally charged memories? Did you uncover forgotten memories? Did you gain personal insights that you otherwise would not have?” If a sufficient number of questions are answered positively, then an experience could be deemed “mind-manifesting”. A similar questionnaire used to define a mind-modifying experience might include questions such as: did you experience changes in perspective, without the experience of memories?

Once these categories of experience are sufficiently defined, they can be correlated with therapeutic outcome to determine which mechanism is most efficacious, or whether both are. Such a study would, of course, contain limitations that are common to any other correlational or qualitative study. But if conducted with sufficient quality, it would provide some evidence to help tease apart these mechanisms.

A larger problem, however, relates to the epistemological validity of psychedelic testimony and therefore extends to much psychedelic research that makes use of self-reports. While testimony is widely acknowledged as being a problematic methodology in psychology and neuroscience and thus used with great care, psychedelic testimony is especially problematic as the experiences are notoriously difficult to describe and interpret<sup>14</sup>. Despite these challenges, participants still find ways to provide psychedelic testimony during or after their experiences. This raises the question: how do participants learn to interpret their psychedelic experiences? In other words, where do participants get the scripts that they use to explain or describe their experiences? Preconceptions about the psychedelic experience could be generated by various forms of media, cultural background and word of mouth. Factors internal to study design could

---

<sup>14</sup> “Interpretations of the experience varied from participant to participant. Common words used to describe it were ‘intense’ and ‘weird’. Nine participants reported that it was difficult to describe aspects of the experience, with one using the word ‘ineffable’: “[It’s difficult] trying to find words to describe it... You really need to be a poet!” “It’s kind of weird to describe” (Turton et al., 30).

also significantly impact an individual's interpretation of the experience. Before psychedelic drugs are administered in experiments, participants are briefed about what to expect in order to provide informed consent. Such discussions and consent forms must provide information about the subjective effects that could occur (Doblin, *Regulation of the Medical Use of Psychedelics and Marijuana*, 227). Furthermore, "set" and "setting" are widely recognized by psychedelics researchers to have an enormous influence on the character of the experience (Winkelman, 3). Also, the kinds of questions asked by therapists and the discussions that occur between the therapist and participant during psychedelic therapy could easily influence the participant's interpretation of the experience, as studies have shown that psychedelics can increase suggestibility (Carhart-Harris et al., "LSD Enhances Suggestibility in Healthy Volunteers", 785). Any of these influences could provide frameworks for interpreting an experience that is already seen as difficult to interpret.

This is an important issue for psychedelic research as psychedelic testimony is often used to support neurobiological theories of drug effects. For instance, within the context of EBT, the identification of neural substrates for the ego and the primary process is supported by psychedelic testimony. As we have seen, neuroimaging studies with psilocybin have suggested that the DMN becomes desynchronized during the psychedelic experience. One piece of evidence that supports the identification of the DMN with the ego is the fact that participants often report experiences of ego disintegration:

[That was] real ego death stuff, [a] total dissolving of the ego-boundaries... I only existed as a concept... as an idea. (Turton, 21)

[It was] certainly quite difficult at times to know where I ended and where I melted into everything around me. (Turton, 17)

Similarly, the notion that the psychedelic experience brings the brain into a state of criticality is supported by the similarity between features of systems in critical states and the phenomenology of the psychedelic experience. As Swanson explains:

Physical systems at criticality exhibit increased transient ‘metastable’ states, increased sensitivity to perturbation, and increased propensity for cascading ‘avalanches’ of metastable activity. Importantly, EBT points out that these characteristics are consistent with psychedelic phenomenology, e.g., hypersensitivity to external stimuli, broadened range of experiences, or rapidly shifting perceptual and mental contents. (12)

Outside of EBT, psychedelic testimony about the experience of connectedness is often discussed in relation to the neurobiological finding of increased between module communication (Carhart-Harris et al., “Psychedelics and Connectedness”, 549).

The use of psychedelic testimony as evidence for neurobiological theories about psychedelic drug effects represents a kind of “psychedelic neurophenomenology”. Neurophenomenology is a methodological approach within neuroscience that emphasizes the theoretical value of using accounts of first-person experience to constrain theories about neurobiology and vice versa (Varela, 343). In other words, it holds that subjective experience can inform us about neurobiology and also neurobiology can inform us about subjective experience. Some authors have recently applied the methodology of neurophenomenology to psychedelic research (Winkelman; Kraehenmann). Yet these authors do not highlight a challenge that

psychedelic research presents for this methodology. Neurophenomenology requires “a disciplined examination of experience” (Varela, 338). In other words, useful first-person accounts are given by subjects who are trained to “bracket” their interpretations of and assumptions about the experience (338). Subjects must also “gain intimacy with the domain of investigation by reflectively focusing on how they are experiencing the stimulus” (Bockleman, 2). For neurophenomenology to ease the concerns about the evidential value of psychedelic testimony, then, subjects must be trained in this methodology and intimate with the psychedelic experience.

Can subjects be trained to perform a disciplined phenomenological examination of the psychedelic experience? Such training would likely require familiarity with the psychedelic experience, which would require receiving multiple doses of a psychedelic drug over time. Putting ethical issues aside, the unpredictable and variant nature of the psychedelic experience may make it difficult to become familiar with. Even if a determined subject could achieve this, however, it is not clear that such training would allow for insight into the *therapeutic* mechanisms of psychedelics. While such a subject could learn how to perform a disciplined phenomenological investigation of the subjective effects of psychedelics, the therapeutic value of psychedelics may diminish after repeated exposures. For example, if psychedelics work by facilitating access to unconscious content, then in a proper therapeutic setting this content would likely emerge within the first few initial experiences. Once the problematic content is experienced, the integration process would begin and there would be less value in repeated

psychedelic experiences<sup>15</sup>. If a subject requires multiple psychedelic experiences to become intimate with the psychedelic experience, then such a subject might have already reaped the therapeutic value of the experience by dealing with problematic unconscious content in initial exposures. In other words, by the time the subject is sufficiently trained to provide a phenomenologically disciplined first-person account of the therapeutic value of psychedelics, there might no longer be any therapeutic value to report. Therefore, while subjects could potentially be trained to provide disciplined descriptions of the phenomenology of the psychedelic experience, such descriptions might not include much about the therapeutic value of psychedelics.

---

<sup>15</sup> Psychedelic therapy would not involve more than 2 or 3 sessions where drugs are administered (Doblin, “Latest Developments in Psychedelic Science From MAPS”)

## Chapter 4: Conclusion

While many proposals have recently been made about how psychedelics achieve therapeutic effects, they are still in their infancy. Griffiths acknowledges that proposals about these mechanisms are still speculative (1195), and some researchers note that it is not clear whether it is the subjective effects or the neurological effects of psychedelics that contribute most to their efficacy. For instance, Swanson claims that: “there is a gap in our clinical understanding of the process by which psychedelic-assisted therapies improve mental health...Which psychedelic drug effects (in the brain or in subjective experience) enable clinical improvement? How?” (2).

By examining whether current researchers continue to hold a mind-manifesting view (that is, whether current researchers see the experienced content as relevant to therapeutic outcome), I have explored these questions. After a survey of current views, I have argued that it is not clear whether current researchers see the subjective content as being relevant to therapeutic outcome. Some proposals seem to imply a mind-modifying view which removes emphasis from the importance of content and posits that psychedelics work by restructuring thought patterns. Further, even when the importance of manifesting latent content is acknowledged, it is not clear how this content would relate to therapeutic outcomes within the context of contemporary views. On predictive processing accounts of manifested content, the relevance of content to therapeutic outcome is not clear. Other proposals though, such as those that focus on the therapeutic importance of connectedness, seem to reinstate a role for the experience of cognitive content in generating therapeutic outcome. However, it is not obvious whether this cognitive content is “manifested” in the sense in which the term was used by past researchers working within a Freudian framework.

This thesis has also explored a potential way in which researchers could clarify whether

the subjective content of the psychedelic experience is relevant to therapeutic outcome. By defining what constitutes a “mind-manifesting” experience, psychedelic testimony could be used to generate evidence about whether a mind-manifesting or mind changing view would best capture the way in which psychedelics work therapeutically. However, more work needs to be done on the evidential value of psychedelic testimony. Can phenomenologically-trained subjects help deepen the understanding of the therapeutic value of psychedelics?

This project has also begun to bridge a gap between debates in the philosophy of medicine and psychedelic research. As mentioned in the introduction, recent work in the philosophy of medicine has acknowledged the importance of developing quality appraisal tools for mechanistic evidence. Yet these debates are abstracted away from discussions of particular mechanisms. This is significant because quality appraisal tools for mechanistic evidence may need to be tailored to certain types of mechanisms. For example, evidential standards applied to mechanistic evidence about a well understood biological mechanism such as the heart may need to be different from evidential standards applied to a less understood and more complex mechanism such as the brain. Those who make proposals about the therapeutic mechanisms of psychedelics have not yet attempted to explicitly and systematically evaluate the quality of this mechanistic evidence. By bringing the debate about the quality of mechanistic evidence into contact with discussions of mechanistic evidence for psychedelic therapy, I have attempted to bridge this gap and begin a discussion about what should constitute high quality mechanistic evidence for psychotherapeutic interventions.

Finally, this project leads to the question of whether psychedelics work primarily through one mechanism or whether there are multiple ways in which psychedelics are therapeutic. Studies have explored the potential of psychedelics for treating a wide variety of disorders, from

treatment-resistant OCD to migraine headaches and end of life anxiety. Is there one underlying mechanism through which psychedelics benefit all of these disorders, or do psychedelics possess multiple mechanism that can each be tailored to certain disorders? To enhance the quality of mechanistic evidence for psychedelics these questions will need to be explored and answered.

## Works Cited

- Abramson, Harold A. "Lysergic Acid Diethylamide (LSD-25): As an Adjunct to Psychotherapy with Elimination of Fear of Homosexuality." *The Journal of Psychology*, vol. 39, 1955, pp. 127-155. <https://doi.org/10.1080/00223980.1955.9916165>
- Ball, J.R. and Jean J. Armstrong. "The Use of L.S.D. 25 (D-Lysergic Acid Diethylamide) in the Treatment of the Sexual Perversions." *Canadian Psychiatric Association Journal*, vol. 6, no. 4, August 1961, pp. 231-235. <https://doi.org/10.1177/070674376100600407>
- Berman, M.G., S. Peltier, D.E. Nee, E. Kross. P.J. Deldin and J. Jonides. "Depression, Rumination and the Default Network." *Soc. Cogn. Affect. Neurosci.*, vol. 6, no. 5, Oct. 2011, pp. 548–555. doi:10.1093/scan/nsq080
- Bockelman, Patricia, Lauren Reinerman-Jones and Shaun Gallagher. "Methodological Lessons in Neurophenomenology: Review of a Baseline Study and Recommendations for Research Approaches." *Front Hum Neurosci.*, vol. 7, no. 608, 2013, pp. 1-9. doi: 10.3389/fnhum.2013.00608
- Bogenschutz, M. P., A. A. Forcehimes, J. A. Pommy, C.E. Wilcox, P. Barbosa, and R. J. Strassman. "Psilocybin-Assisted Treatment for Alcohol Dependence: A proof-of- Concept Study." *Journal of Psychopharmacology*, vol. 29, no. 3, 2015, pp. 289–99. doi:10.1177/0269881114565144
- Brown, T. K. "Ibogaine in the Treatment of Substance Dependence." *Current Drug Abuse Review*, vol. 6, no. 1, 2013, pp. 3–16. doi:10.2174/15672050113109990001.
- Busch, K. Anthony and Warren C. Johnson. "L.S.D. 25 As an Aid in Psychotherapy." *Diseases of the Nervous System* vol. 11, no.8, August 1950, pp. 1-4. <https://www.ncbi.nlm.nih.gov/pubmed/14793387>
- Carhart-Harris, Robin. "Brain Imaging Studies with Psilocybin and MDMA." *YouYube*, Aug. 2013, <https://www.youtube.com/watch?v=CNR4o5JZEi0&t=890s>
- Carhart-Harris, R. L., R. Leech, P.J. Hellyer, M. Shanahan, A. Feilding, and E. Tagliazucchi. "The Entropic Brain: A Theory of Conscious States Informed by Neuroimaging Research with Psychedelic Drugs." *Front. Hum. Neurosci.*, vol. 8, issue. 20, 2014, pp. 1-22. doi: 10.3389/fnhum.2014.00020
- Carhart-Harris, Robin, David Erritzoe, Tim Williams, James M. Stone, Laurence J. Reed, Alessandro Colasanti, Robin J. Tyacke, Robert Leech, Andrea L. Malizia, Kevin Murphy, Peter Hobden, John Evans, Amanda Feilding, Richard G. Wise, and David J. Nutt. "Neural

- Correlates of the Psychedelic State as Determined by fMRI Studies with Psilocybin.” *PNAS*, vol. 109, no. 6, Feb. 2012, pp. 2138–2143. doi: 10.1073/pnas.1119598109
- Carhart-Harris, Robin and K.J Friston. “The Default-Mode, Ego-Functions and Free-Energy: A Neurobiological Account of Freudian Ideas”. *Brain*, no. 133, 2010, pp. 1265–1283. doi:10.1093/brain/awq010
- Carhart-Harris, Robin L., Leor Roseman, Mark Bolstridge, Lysia Demetriou, J Nienke Pannekoek, Matthew B Wall, Mark Tanner, Mendel Kaelen, John McGonigle, Kevin Murphy, Robert Leech, H Valerie Curran and David J Nutt. “Psilocybin for Treatment-Resistant Depression: fMRI-Measured Brain Mechanisms.” *Scientific Reports*, vol. 7, 13187. October 2017 doi:10.1038/s41598-017-13282-7
- Carhart-Harris, R.L., D. Erritzoe<sup>1</sup>, E. Haijen, M. Kaelen and R. Watts. “Psychedelics and Connectedness.” *Psychopharmacology*, vol. 235, no. 2, Feb. 2018, pp. 547–550. doi 10.1007/s00213-017-4701-y
- Carhart-Harris, R.L., M. Kaelen, M. G. Whalley, M. Bolstridge, A. Feilding & D. J. Nutt. “LSD Enhances Suggestibility in Healthy Volunteers.” *Psychopharmacology*, vol. 232, no. 4, Feb. 2015, pp. 785–794. doi 10.1007/s00213-014-3714-z
- Catlow, Briony J., Shijie Song, Daniel A. Paredes, Cheryl L. Kirstein and Juan Sanchez-Ramos. “Effects of Psilocybin on Hippocampal Neurogenesis and Extinction of Trace Fear Conditioning.” *Exp Brain Res.*, vol. 228, no. 4, June 2013, pp. 481–491. doi 10.1007/s00221-013-3579-0
- Chandler, Arthur L. and Mortimer A. Hartman. “Lysergic Acid Diethylamide (LSD-25) as a Facilitating Agent in Psychotherapy” *Ama Arc Gen Psychiatry*, vol. 2, no. 3, Mar 1960, pp. 64-77. doi:10.1001/archpsyc.1960.03590090042008
- Clarke, B., D. Gilles, P. Illari, F. Russo, J. Williamson. “Mechanisms and the Evidence Hierarchy.” *Topoi*, vol. 33, no. 2, 2014, pp. 339-360. doi.org/10.1007/s11245-013-9220-9
- Corbin, Michelle. “Tactics of Legitimation in the Psychedelic Sciences: Lessons for Feminist Sociology of Knowledge.” *American Behavioural Scientist*, vol. 56, no. 10, 2012, pp. 1413–1433. doi: 10.1177/0002764212454422
- Dayan P, G.E. Hinton and R.M. Neal. “The Helmholtz Machine.” *Neural Computation*, vol. 7, no. 5, Sept. 1995, pp. 889–904. <https://www.ncbi.nlm.nih.gov/pubmed/7584891>

- Doblin, Rick. "From the Desk of Rick Doblin, Ph.D." *MAPS Bulletin Spring 2017: Vol 27, No. 1 Special Edition: Psychedelic Science*, <http://www.maps.org/news/bulletin/articles/6607-spring-2017>
- Doblin, Rick. "Latest Developments in Psychedelic Science From MAPS." *YouTube*, Aug. 2017, <https://www.youtube.com/watch?v=2q4VZUOGk2I&t=619s>
- Doblin, Rick. *Regulation of the Medical Use of Psychedelics and Marijuana*. 2000. John F. Kennedy School of Government, PhD Dissertation, *HOLLIS*, <http://id.lib.harvard.edu/alma/990087435610203941/catalog>
- Doblin, Rick. "Rick Doblin, Founder of MAPS, on the Integration Process." *YouTube*, April 2017, <https://www.youtube.com/watch?v=qwEmZW7H05g&t=147s>
- Dyck, Erika. *Psychedelic Psychiatry: LSD on the Canadian Prairies*. U of Manitoba P, 2012.
- Eisner, B. G., and S. Cohen. "Psychotherapy with Lysergic Acid Diethylamide." *J. Nerv. Ment. Dis.* Vol. 127, no. 6, Dec 1958, pp. 528–539. <https://www.ncbi.nlm.nih.gov/pubmed/13621221>
- Feld, Myron, Joseph R. Goodman and John A Guido. "Clinical and Laboratory Observations on LSD-25." *J. Nerv. Ment. Dis.*, vol. 126, no. 2, February 1958, pp. 176-183. [https://journals.lww.com/jonmd/Citation/1958/02000/Clinical\\_and\\_Laboratory\\_Observations\\_on\\_Lsd\\_25.6.aspx](https://journals.lww.com/jonmd/Citation/1958/02000/Clinical_and_Laboratory_Observations_on_Lsd_25.6.aspx)
- Fodor, J. A. *The Modularity of Mind*, MIT Press, 1983.
- Freud, Sigmund. *An Outline of Psychoanalysis*. Standard edn., Vol. 23, Vintage, 1940.
- Garcia-Romeu, Albert, Roland R. Griffiths and Matthew W. Johnson. "Psilocybin-occasioned Mystical Experiences in the Treatment of Tobacco Addiction." *Curr Drug Abuse Rev.*, vol. 7, no. 3, 2015, pp. 157–164. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4342293/>
- Gasser, Peter., Katharina Krichner, and Torsten Passie. "LSD-Assisted Psychotherapy for Anxiety Associated with a Life-Threatening Disease: A Qualitative Study of Acute and Sustained Subjective Effects". *Journal of Psychopharmacology*, vol. 29, no. 1, Nov. 2014, pp. 1-12. [doi.org/10.1177/0269881114555249](https://doi.org/10.1177/0269881114555249)
- Griffiths, Roland R., Matthew W. Johnson, Michael A. Carducci, Annie Umbricht, William A.

- Richards, Brian D. Richards, Mary P. Cosimano and Margaret A. Klinedinst. "Psilocybin Produces Substantial and Sustained Decreases in Depression and Anxiety in Patients with Life-Threatening Cancer: A Randomized Double-blind Trial." *Journal of Psychopharmacology*, vol. 30, no. 12, 2016, pp. 1181-1197. doi: 10.1177/0269881116675513
- Grob, C. S., A. L. Danforth, G. S. Chopra, M. Hagerty, C. R. McKay, A. L. Halberstadt, and G. R. Greer. 2011. "Pilot Study of Psilocybin Treatment for Anxiety in Patients with Advanced-Stage Cancer". *Arch Gen Psychiatry*, vol. 68, no.1, Jan. 2011, pp. 71-78. doi:10.1001/archgenpsychiatry.2010.116
- Grof, Stanislav. *Realms of the Human Unconscious: Observations from LSD Research*. Viking Press, 1975.
- Grof, Stanislav. *LSD Psychotherapy*, HunterHouse, 1994. *The Psychedelic Library*, <http://www.psychedelic-library.org/grofpref.htm>
- Hendricks, P. S., C. B. Clark, M. W. Johnson, K. R. Fontaine, and K. L. Cropsey. "Hallucinogen Use Predicts Reduced Recidivism among Substance-Involved Offenders under Community Corrections Supervision." *Journal of Psychopharmacology*, vol. 28, no. 1, 2014, pp. 62–66. doi:10.1177/0269881113513851
- Hendricks, P. S., C. B. Thorne, C. B. Clark, D. W. Coombs, and M. W. Johnson. "Classic Psychedelic Use is Associated with Reduced Psychological Distress and Suicidality in the United States Adult Population." *Journal of Psychopharmacology*, vol. 29, no. 3, 2015, pp. 280–88. doi:10.1177/0269881114565653
- Hood, R.W. "The Construction and Preliminary Validation of a Measure of Reported Mystical Experience." *J Sci Study Relig.*, vol. 14, no. 1, 1975, pp. 29–41. <http://datadump.thelightningpath.com/readings/hood-mystical.pdf>
- Howick, Jeremy. *The Philosophy of Evidence-Based Medicine*, Wiley-Blackwell, 2011.
- Jacobs, Adam. "Acid Redux: Revisiting LSD Use in Therapy." *Contemporary Justice Review*, vol. 11, no. 4, 2008, pp. 427-439. doi: 10.1080/10282580802482652
- Johnson, M. W., A. Garcia-Romeu, M. P. Cosimano, and R. R. Griffiths. "Pilot Study of the 5-HT<sub>2A</sub>R Agonist Psilocybin in the Treatment of Tobacco Addiction." *Journal of Psychopharmacology*, vol. 28, no. 11, pp. 983–92. 2014. doi:10.1177/0269881114548296.

- Klee, G. D. "Lysergic Acid Diethylamide (LSD-25) and Ego Functions." *Arch. Gen. Psychiatry*, vol. 8, no. 5, May 1963, pp. 461–474. doi: 10.1001/archpsyc.1963.01720110037005
- Kraehenmann, Rainer. "Dreams and Psychedelics: Neurophenomenological Comparison and Therapeutic Implications." *Curr Neuropsychopharmacol.*, vol. 15, no. 7, 2017, pp. 1032-1042. doi: 10.2174/1573413713666170619092629
- Krebs, T. S., and P. O. Johansen. "Psychedelics and Mental Health: A Population Study." *PLoS One*, vol. 8, no. 8, August 2013. doi:10.1371/journal.pone.0063972
- Langlitz, Nicholas. *Neuropsychedelica: The Revival of Hallucinogen Research since the Decade of the Brain*, U of California P, 2013.
- Lattin, Don. *The Harvard Psychedelics Club*. Harper One, 2011
- Lee, M.A., and B. Schlain. *Acid Dreams: The Complete Social History of LSD: The CIA, the Sixties, and Beyond*. Pan Books, 1985.
- Ling, T., and J. Buckman. *Lysergic Acid (LSD 25) and Ritalin in the Treatment of Neurosis*, Lambarde Press, 1963.
- Ly, Calvin, Alexandra C. Greb, Lindsay P. Cameron, Cassandra M. Ori-McKenney, John A. Gray and David E. Olson. "Psychedelics Promote Structural and Functional Neural Plasticity." *Cell Reports*, vol. 23, no. 11, June 2018, pp. 3170-3182. <https://doi.org/10.1016/j.celrep.2018.05.022>
- "MAPS in the Media". *Maps.org*, Multidisciplinary Association for Psychedelic Studies. <http://www.maps.org/news/media>. Accessed 24 July 2018.
- Maté, Gabor. "Manifesting the Mind: Inside the Psychedelic Experience." *YouTube*, Aug. 2016, <https://www.youtube.com/watch?v=ZdO-Nyk4-jU&t=4s>
- Mithoefer, Michael C. "A Manual for MDMA-Assisted Psychotherapy in the Treatment of Post-traumatic Stress Disorder", *Multidisciplinary Association for Psychedelic Studies*, Jan. 2013. [https://www.maps.org/research-archive/mdma/MDMA-Assisted\\_Psychotherapy\\_Treatment\\_Manual\\_Version\\_6\\_FINAL.pdf](https://www.maps.org/research-archive/mdma/MDMA-Assisted_Psychotherapy_Treatment_Manual_Version_6_FINAL.pdf)
- Mithoefer, M. C., M. T. Wagner, A. T. Mithoefer, L. Jerome, and R. Doblin. "The Safety and Efficacy of 3,4-Methylenedioxymethamphetamine-Assisted Psychotherapy in Subjects with Chronic, Treatment-Resistant Posttraumatic Stress Disorder: The First Randomized Controlled Pilot Study." *Journal of Psychopharmacology*, vol. 25, no. 4, 2010, pp. 439–52. doi:10.1177/0269881110378371.

- Mithoefer, M. C., M. T. Wagner, A. T. Mithoefer, L. Jerome, S. F. Martin, B. Yazar-Klosinski, Y. Michel, T. D. Brewerton, and R. Doblin. “Durability of Improvement in Post-Traumatic Stress Disorder Symptoms and Absence of Harmful Effects or Drug Dependency After 3,4-Methylenedioxymethamphetamine-Assisted Psychotherapy: A Prospective Long-Term Follow-Up Study.” *Journal of Psychopharmacology*, vol. 27, no. 1, 2013, pp. 28–39. doi:10.1177/0269881112456611.
- Moreno, F. A., C. B. Wiegand, E. K. Taitano, and P. L. Delgado. “Safety, Tolerability, and Efficacy of Psilocybin in 9 Patients with Obsessive-Compulsive Disorder.” *The Journal of Clinical Psychiatry*, vol. 67, no. 11, 2006, pp. 1735–40. doi:10.4088/JCP.v67n1110.
- Muthukumaraswamy, S., R.L. Carhart-Harris, R.J. Moran, M.J. Brookes, T.M. Williams, and D. Ertizoe. “Broadband Cortical Desynchronization Underlies the Human Psychedelic State.” *J. Neurosci*, vol. 33, no. 38, Sept. 2013, pp. 15171–15183. doi: 10.1523/jneurosci.2063-13.2013
- Nicholas, Christopher R., Kelsey M. Henriquez, Michele C. Gassman, Karen M. Cooper, Daniel Muller, Scott Hetzel, Randall T. Brown, Nicholas V. Cozzi, Chantelle Thomas and Paul R. Hutson. “High Dose Psilocybin is Associated with Positive Subjective Effects in Healthy Volunteers.” *J Psychopharmacol.*, vol. 32, no. 7, July 2018, pp. 770-778. doi:10.1177/0269881118780713
- Osmond, Humphrey. “A Review of the Clinical Effects of Psychotomimetic Agents.” *Annals of the New York Academy of Sciences*, vol. 66, no. 3, March 1957, p. 418-434. *Wiley Online Library*, doi:10.1111/j.1749-6632.1957.tb40738.x
- “A Phase 3 Program of MDMA-Assisted Psychotherapy for the Treatment of Severe Posttraumatic Stress Disorder (PTSD)”. *Maps.org*, Multidisciplinary Association for Psychedelic Studies. <http://www.maps.org/research/mdma/ptsd/phase3>. Accessed 3 August 2018
- Pollan, Michael. *How to Change Your Mind*, Penguin Press, 2018
- Rose, Nikolas. *The Politics of Life Itself: Biomedicine, Power, and Subjectivity in the Twenty First Century*, Princeton University Press, 2007.
- Russo, F., J. Williamson. “Interpreting Causality in the Health Sciences.” *Int Stud Philos Sci*, vol. 21, no. 2, 2007, pp. 157-170. doi.org/10.1080/02698590701498084
- Sanches, R. F., F. D. L. Osório, R. G. Dos Santos, L. R. H. Macedo, J. P. Maia-de-Oliveira, L. Wichert-Ana, D. B. de Araujo, J. Riba, J. A. S. Crippa, and J. E. C. Hallak. “Antidepressant Effects of a Single Dose of Ayahuasca in Patients with Recurrent Depression.” *Journal of*

*Clinical Psychopharmacology*, vol. 36, no. 1, pp. 77-81. 2016  
doi:10.1097/JCP.0000000000000436.

Sandison, R. A. “Psychological Aspects of the LSD Treatment of the Neuroses.” *J. Ment. Sci.*, vol. 100, no. 419, April 1954, pp. 508–515. doi: 10.1192/bjp.100.419.508

Sandison, R.A. “The Role of Psychotropic Drugs in Individual Therapy.” *Bull World Health Organ*, vol. 21, no. 4-5, 1959, pp. 495–503.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2537985/>

Savage, Charles. “Lysergic Acid Diethylamide (LSD-25): A Clinical Psychological Study.” *Journal of the American Psychological Association*, vol. 108, no. 12, June 1952, pp. 896-900.  
<https://doi.org/10.1176/ajp.108.12.896>

Schenberg, E. E., M. A. de Castro Comis, B. R.Chaves, and D. X. Da Silveira. “Treating Drug Dependence with the Aid of Ibogaine: A Retrospective Study.” *Journal of Psychopharmacology*, vol. 28, no. 11, pp. 993–1000. 2014 doi:10.1177/0269881114552713

Sewell, R. A., J. H. Halpern, and H. G. Pope Jr. “Response of Cluster Headache to Psilocybin and LSD”. *Neurology*, vol. 66, no. 12, 2006, pp. 1920–22.  
doi:10.1212/01.wnl.0000219761.05466.43.

Strassman, Rick. *DMT The Spirit Molecule: A Doctor’s Revolutionary Research into the Biology of Near-Death and Mystical Experiences*. Park Street P, 2001

Swanson, Link R. “Unifying Theories of Psychedelic Drug Effects.” *Front. Pharmacol*, vol. 9, no. 172, March 2018, pp. 1-23. doi: 10.3389/fphar.2018.00172

Tagliazucchi, E., L. Roseman, M. Kaelen, C. Orban, S. Muthukumaraswamy, S and K. Murphy. “Increased Global Functional Connectivity Correlates with LSD-Induced Ego Dissolution.” *Curr Biol.*, vol. 26, no. 8, April 2016, pp. 1043–1050. doi: 10.1016/j.cub.2016.02.010

Thomas, G., P. Lucas, N. R. Capler, K. W. Tupper, and G. Martin. “Ayahuasca-Assisted Therapy for Addiction: Results from a Preliminary Observational Study in Canada.” *Current Drug Abuse Review*, vol. 6, no. 1, pp. 30–42. 2013 doi:10.2174/15733998113099990003

Turton, S., D. J. Nutt and R. L. Carhart-Harris. “A Qualitative Report on the Subjective Experience of Intravenous Psilocybin Administered in an fMRI Environment.” *Curr Drug Abuse Rev*, vol. 7, no. 2, 2014, pp. 117-127.  
<https://doi.org/10.2174/1874473708666150107120930>

Varela, F. J. “Neurophenomenology: A Methodological Remedy for the Hard Problem.” *J of*

*Consciousness Studies*, vol. 3, no. 4, April 1996, pp. 330-349.  
<https://www.ingentaconnect.com/content/imp/jcs/1996/00000003/00000004/718>

Vollenweider, F. and M. Kometer. “The Neurobiology of Psychedelic Drugs: Implications for the Treatment of Mood Disorders.” *Nat Rev Neurosci.*, vol. 11, no. 9, Sept. 2010, pp. 642-651  
doi:10.1038/nrn2884

Watts, Rosalind, Camilla Day, Jacob Krzanowski, David Nutt and Robin Carhart-Harris.  
“Patients’ Accounts of Increased “Connectedness” and “Acceptance” After Psilocybin for Treatment-Resistant Depression.” *Journal of Humanistic Psychology*, vol. 57, no. 5, 2017, pp. 520–564. <https://doi.org/10.1177/0022167817709585>

Winkelman, Michael J. “The Mechanisms of Psychedelic Visionary Experiences: Hypotheses from Evolutionary Psychology.” *Front. Neurosci.*, vol. 11, no. 539, Sept. 2017, pp. 1-17. doi: 10.3389/fnins.2017.00539