Overview of Psychedelics: Nomenclature, Effects and Mechanisms of Action

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What Are Psychedelic Substances?

Definition and Nomenclature

psychedelic

/ˌsīkəˈdelik/ /ˌsaɪkəˈdɛlɪk/

The term *psychedelic* was originally coined by Humphry Osmond, a psychiatrist who pioneered research in psychedelics in the 1950s, 1960s and beyond. In a correspondence with the noted author and philosopher Aldous Huxley, Osmond crafted the term *psychedelic* as a combination of the Greek words *psyche* (for mind or soul) and *deluon* (meaning to make visible, or reveal).[1] As for a formal definition of psychedelic substances, none is commonly agreed upon. Longtime psychoactive drug pioneer, David Nichols defines the substances as follows:[2]

> Psychedelics (serotonergic hallucinogens) are powerful psychoactive substances that alter perception and mood and affect numerous cognitive processes.

Nichols goes on to distinguish some of the nuances surrounding different drugs that are often referred to as being psychedelic:[3]

> When I began my graduate studies in 1969, it was politically correct in scientific circles to refer to these substances only as *psychotomimetics*, a negative term suggesting that they fostered a mental state resembling psychosis. Later, as it was realized that these compounds did not provide very realistic models of psychosis or mental illness, it became more correct to refer to them as *hallucinogens*, again a pejorative term suggesting that they principally produce hallucinations. Yet that is not what they do in most users at ordinary doses, so this term likewise is not particularly descriptive or useful, although it is still widely used and seems to remain the preferred name for these substances in most scientific writing. In addition, the term *hallucinogen* is often used as a rather broad category to include all kinds of psychoactive molecules, including cannabinoids, “ecstasy,” dissociative agents, and others.

There are several similar descriptors that are used in reference to various substances that generate similar cognitive effects, including *psychoactive*, *psychotropic*, *hallucinogenic* and *psychedelic*. While some claim the terms are synonymous, others, such as Nichols, make distinctions. Among those who do differentiate, most generally agree that psychedelics are a subclass of the larger category of psychoactive substances.

The medical dictionary defines a *psychoactive* substance as one that "possesses the ability to alter mood, anxiety, behavior, cognitive processes, or mental tension."[4] While there is disagreement as to the number of categories of psychoactive substances, many sources tend to refer to four distinct subgroups: stimulants, depressants, opiates, and hallucinogens. This subcategorization scheme would then classify psychedelics as hallucinogens.

A final term that I'll mention that's often used instead of *psychedelics* is *entheogens*, which alludes to the spiritual or sacred aspect of using psychedelics.[5]

Notably, in contrast to true narcotics (i.e., substances derived from opium), psychedelic substances are not addictive. More specifically, psychedelics do not induce tolerance (reduced effects after repeated use), sensitization (increased effects after repeated use), or dependence (withdrawal symptoms upon cessation of drug use).[6]

Psychedelic Substances

Different categories of psychoactive substances that people refer to as being psychedelic include: classic psychedelics, dissociatives, deliriants, enactogens and empathogens, and oneirogens.

Classic Psychedelics

"Classic" Psychedelics generally include those substances that act on serotonin receptors[7] and "change the way we perceive the world around us":[8]

- **LSD** (Lysergic Acid Diethylamide): Synthetically produced substance first synthesized by Albert Hoffman in 1938. Typical dose is 50 – 150 μg.[9]
- **Psilocybin**: Naturally occurring substance found in certain mushrooms. Typical dose is 20 – 30 mg /70 kg body mass, or about 3 – 5 g mushrooms according to one source;[10] another source suggests a typical dose is 1 – 2.5 g.[11]
- **Ayahuasca**: Naturally occurring substance found in certain plants
- **DMT** (N,N-Dimethyltryptamine): Naturally occurring substance found in certain plants and animals. Typical dose is 20 – 40 mg smoked, 0.2 – 0.4 mg/kg body mass infused.[12]

Dissociatives

Dissociatives create feeling of detachment or disconnection from reality. While high doses of DMT, ayahuasca, salvia, and ibogaine can induce dissociative experiences, the classic dissociatives include:[13]

- **Ketamine**: Synthetically produced substance first synthesized in 1962, used medically as an anesthetic and an antidepressant.

- **PCP** (Phenylcyclohexyl Piperidine): Synthetically produced substance first synthesized in 1926, originally used as an anesthetic, but subsequently discontinued.

Deliriants

Deliriants, which generally include substances that inhibit the neurotransmitter acetylcholine, create "visions and hallucinations that are untethered from reality."[14] Common deliriants include plant-derived substances from **Datura, Brugmansia** and **Borrachero Tree**, as well as high doses of synthetically-produced **DPH** (Diphenhydramine, Benadryl) and DXM (Dextromethorphan).

Entactogens and Empathogens

Entactogens & Empathogens "increase feelings of oneness or emotional openness." The classic entactogen is **MDMA** (3,4-Methylenedioxymethamphetamine, Ecstasy).[15]

Oneirogens

Oneirogens induce vivid dreaming. One of the more well-known plant-derived oneirogens is **Salvia divinoum**.

What Effects Do Psychedelic Substances Generate?

What generally comes to mind when people think of psychedelic experiences is the phenomenological effects – the "trips" – they produce in users. Yet, there are additional types of effects generated by psychedelic substances, namely acute and/or long-term cognitive and psychological effects, which have generally been reported to be life-enhancing. Let's take a closer look at these different types of effects.

Psychedelic Drug-Induced Phenomenological Effects

Altered States of Consciousness

Many sources define psychedelic substances as those that induce *altered states of consciousness*. There is no consensus as to the definition of an altered state of consciousness, since such a definition would require determining what constitutes normal consciousness, which is highly debatable. Further complicating the matter is the fact that attempted definitions of altered states of consciousness are found within the realms of philosophy, psychology, and neuroscience,[16] each of which brings its own perspective to the subject.

Here are a few examples of different characterizations of altered states of consciousness that I found to be helpful:

- Psychologist Charles Tart describes an altered state of consciousness as a profound change in the "overall pattern of subjective experiences."[17]
- Psychologist Christa Smith indicates that “Altered states … allow us to see our lives and ourselves with a broader lens and from different angles of perception than the ordinary mind.”[18]
- Several sources relate consciousness to our level of awareness. For example, an open-source introduction to psychology course claims that “Consciousness describes our awareness of internal and external stimuli.”[19]

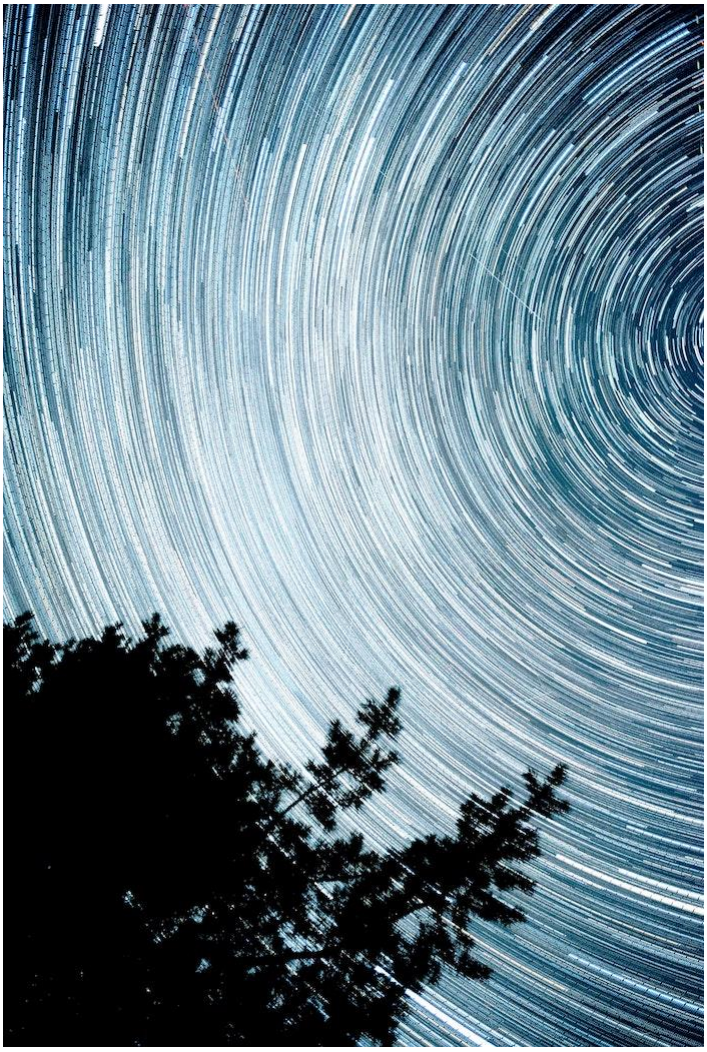
Examples and sources of alternative states of consciousness include:[20]

- Sleep/Dreams
- Hallucinations
- Hypnotic states
- Meditative states
- Drug-induced states

- Trauma-induced states
- Epileptic Seizures
- Sensory Deprivation
- Mania/Hysteria

Taken collectively, my sense is that perhaps an apt descriptor of psychedelic-induced altered states of consciousness is that within these states, people process information differently than they normally might. Specifically, their altered states lead them to change the nature of which information they focus on (deem important) and how they interpret it.

Mystical Experiences



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Perhaps the most alluring aspect of psychedelic substances is their ability to induce mystical experiences in users. A mystical experience is a form of altered state of consciousness. As with consciousness, and also with altered states of consciousness, it's difficult to pin down a

definition of a mystical experience. The Stanford Encyclopedia of Philosophy provides a definition of *mystical experience* that's as good as any:[21]

> A (purportedly) super sense-perceptual or sub sense-perceptual unitive experience granting acquaintance of realities or states of affairs that are of a kind not accessible by way of sense-perception, somatosensory modalities, or standard introspection.

Many psychedelics researchers, including pioneer Walter Pahnke, define mystical experiences in terms of the phenomena they entail. Pahnke provides nine interrelated categories of phenomena that characterize mystical experiences:[22]

1. **Unity**: a feeling of oneness with all
2. **Objectivity and reality**: insightful knowledge
3. **Transcendence of space and time**
4. **Sense of sacredness**
5. **Deeply-felt positive mood**
6. **Paradoxicality**: many aspects of the experience are felt to be true, despite the fact that they defy logic
7. **Alleged ineffability**: an inability for the experiencer to describe the experience
8. **Transiency of the forms of conscious experienced**
9. P**ositive changes in attitude and/or behavior** of the experiencer toward: themselves, others, life, and mystical consciousness itself.

Mystical experiences are not new phenomena. They've been reported throughout history as transcendent experiences, often by people who have gained insight into some truth, in particular, one communicated by God or some sacred being. However, mystical experiences have generally been rare phenomena that have appeared either spontaneously to select individuals, or after earnest preparation by religious or spiritual seekers.

In his 1960s research, Pahnke sought to establish that mystical experiences induced by psychedelics were phenomenologically equivalent to religiously-induced mystical experiences. Pahnke's studies established this to be the case, with the implication that the same type of experience that has historically been so elusive could now be reproduced on-demand by any person seeking such an experience, simply by using psychedelics. In particular, mystical experiences could be reliably induced and "studied scientifically under laboratory conditions."[23]

During the late 1960s research into psychedelics was banned, leading to a decades-long hiatus in research. Since the early 1990s, however, there's been a revival in psychedelics research,[24] and in 2006, Rolland Griffiths, a psychiatrist and neuroscientist at Johns Hopkins University, replicated Pahnke's studies and continues to uncover new insights into the experiences these mysterious substances generate.[25]

The greater significance of being able to reliably induce mystical experiences is that they are being shown to be primary predictors of therapeutic outcomes in large portions of patients.[26] For example, one researcher reports that "Such experiences are reported as profoundly meaningful, spiritual and transformative peak life events, and are associated with adaptive outcomes across a range of psychological domains."[27]

Researchers have reliably established the ability to produce mystical experiences in a majority of study participants. Not all study participants who have experienced mystical phenomena have realized long term therapeutic benefits, such as abstention from tobacco or alcohol use. At the same time, not all participants who have realized long term benefits have experienced complete mystical phenomena. Yet, overall, the association between study participants who experience mystical phenomena and those who achieve long-term benefits is high.[28]

Other Characterizations of Psychedelic Phenomena

An additional notable aspect of psychedelic experiences is their multi-faceted nature. Indeed, Pahnke suggests that the distinguishing factor of psychedelics is the variety of psychological phenomena they facilitate. He describes five major classes of potential psychedelic drug experiences:[29]

1. **Psychotic Psychedelic Experiences** involve intense, negative experiences of fear, to the point of panic, paranoid delusions of suspicion or grandeur, toxic confusion, impairment of abstract reasoning, remorse, depression, and isolation or somatic discomfort or both.
2. **Cognitive Psychedelic Experiences** involve astonishingly lucid thought, where problems are seen from a novel perspective.
3. **Aesthetic Psychedelic Experience**s involve changes and intensification of all sensory modalities.
4. **Psychodynamic Psychedelic Experience**s involve the dramatic emergence into consciousness of material that was previously unconscious or preconscious.
5. **Psychedelic Peak, Cosmic, Transcendental, or Mystical** involve six psychological experiences: (i) a sense of unity or oneness, (ii) transcendence of time and space, (iii) deeply felt positive mood, (iv) sense of awesomeness, reverence, and wonder, (v) meaningfulness of psychological or philosophical insight or both; and (vi) ineffability.

Psychedelic research pioneer Stanislov Grof further describes four "levels" of experiences associated with psychedelics:[30]

1. **Abstract and Aesthetic Experiences** involve an appreciation of changing colors and kaleidoscopic movements of shapes and forms.
2. **Psychodynamic Experiences** involve reliving or fantasizing about emotionally relevant situations from a person's life.

3. **Perinatal Experiences** involve a death and rebirth experience, which can catalyze dramatic changes in personality and behavior.
4. **Transpersonal Experiences** involve consciousness-expansion beyond normal ego-boundaries and may encompass different times, places, or creatures.

Given the variety and complexity of psychedelic phenomena, it's no surprise that "psychedelic 'trips' are remarkably subjective experiences. No two people report the same experience on these drugs—nor do single individuals say they have had the same experience during two different exposures."[31]

Psychedelic Drug-Induced Therapeutic Effects

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Scientific research during the 1950s and 1960s suggested that psychedelic substances have the potential to create long-lasting therapeutic benefits for individuals suffering from many psychological and cognitive disorders, including psychosis, depression/anxiety, and substance use disorders. More recent scientific research that started reemerging in the 1990s is revealing a greater potential for therapeutic benefits facilitated by psychedelic substances, not only to address disease and dysfunction in ailing individuals, but also to enhance well-being in healthy people.

Short-Term Effects

Microdosing

Sub-threshold doses of psychedelic substances – *microdoses* – are doses that are too low to generate hallucinogenic experiences, but high enough to potentially generate acute and long-term cognitive and psychological benefits. Microdosing is increasingly being used by healthy individuals to enhance wellbeing by generating such benefits as "increases in vitality, creativity, productivity, social ability, focus, analytic thinking, positive mood, memory, mindfulness and

general wellbeing."[32] Typical doses for microdosing range from about 5% to 10% of macrodoses.[33]

The evidence supporting the efficacy of microdosing is currently all anecdotal. Scientific studies on the efficacy of microdosing psychedelics has been difficult to establish for two reasons. The first is that it's difficult to isolate effects actually attributable to the substances themselves from effects due to expectancy (i.e., the placebo effect). The second difficulty associated with establishing efficacy is that effects vary across individuals, which makes it difficult to isolate actual effects due to the substances from baseline differences across individuals.[34]

Macrodosing

As with those who microdose, people who take full doses of psychedelic substances report the same types of feelings of enhanced well-being for weeks, if not months or longer, after their experience.[35]

Notably, there is a risk that individuals who use psychedelic substances, especially those who take larger doses, may experience a "bad trip." Bad trips generally involve feelings of anxiety, panic, and paranoia,[36] and in rarer instances may also include "individuals putting themselves at risk for physical harm, seeking medical help, and enduring negative psychological or psychiatric problems."[37] Yet, this risk of drug-related harm is low. Critically, in a study conducted by researchers at Johns Hopkins, 76% of people who specifically reported having had a "challenging experience" after using psychedelic substances generally indicated that the session "led to increases in current well-being and life satisfaction." In fact, "A substantial majority of participants (84%) rated that they benefited from the challenging portions of their sessions."[38]

Long-Term Effects

"In early trials of hallucinogens administered under supportive conditions, 50 - 80% of participants claimed lasting beneficial changes in personality, values, attitudes and behavior."[39] Incredibly, a significant portion of individuals who use psychedelic substances report that the experience was one of the most, if not *the* most, meaningful and/or spiritually significant experiences of their life.[40]

In a 2017 study,[41] UK researchers report,

> [S]tudies have shown that naturalistic psychedelic use is associated with:
>
> - Reduced rates of suicidality and psychological distress in the general population
> - Higher scores in assessments of confidence and optimism
> - Increased value placed on spiritual/mystical beliefs as well as concern for others and nature/the environment … [where] Nature relatedness, in particular, may be associated with reduced anxiety and increased personal well-being, and exposure to awe-inspiring nature has been shown to increase pro-social attitudes and behavior.

Moreover, the UK researchers note that there is evidence that even one dose of a psychedelic substance may cause: increases in the personality trait of openness; increases in trust, optimism, and subjective well-being; and improvements in symptoms of anxiety, depression, and addiction.

What's Responsible for the Therapeutic Benefits of Psychedelic Substances?

Psychedelics are chemical substances that act on the brain, creating both pharmacological and phenomenological effects. Furthermore, incorporating psychedelic drug sessions into a broader course of psychotherapy facilitates psychotherapeutic effects. Taken together, we can thus ask: are the therapeutic benefits associated with psychedelic drugs attributable to:

(i) The pharmacological effects of the drugs,
(ii) The phenomenological experiences induced by the drugs, or
(iii) The psychotherapeutic effects resulting from mystical experiences and/or drug therapy sessions?

During the 1950s and 1960s, researchers of the latter two questions discovered that psychedelics used in conjunction with psychotherapy was having dramatic effects for treating alcoholism. Researchers figured that the mystical experiences played a fundamental role in the positive effects being achieved. This hypothesis spurred a large body of research in several complementary areas:

(i) Reliably generating mystical experiences in patients,
(ii) Reliably characterizing mystical experiences produced by psychedelic substances, and
(iii) Understanding which aspects of psychedelic drug-induced mystical experiences were responsible for generating therapeutic benefits.

Subsequently, as imaging technologies (PET scans and fMRI scans) started becoming available in the 1990s, researchers also began examining the pharmacological and neurological underpinnings of psychedelic experiences. Researchers have been examining both psychedelic experiences in general, as well as mystical experiences in particular, with an eye toward understanding how they generate therapeutic effects.

Let's take a closer look at the psychological and pharmacological underpinnings of mystical experiences and the therapeutic benefits they facilitate.

Mystical Experiences Are Predictive of Therapeutic Benefits

As previously mentioned, mystical experiences induced through the use of psychedelic substances are being shown to be primary predictors of therapeutic outcomes in large portions of patients.[42] As this relationship became accepted, researchers sought to better characterize mystical experiences, so as to establish more precisely which aspects were responsible for increases in wellbeing. Researchers also sought to better understand how to use psychedelics and associated mystical experiences to reliably generate therapeutic benefits in patients.

Characterizing Mystical Experiences

Common Core Thesis

The Common Core Thesis states that, whether experienced by lamas in Tibet or by laymen in Tipperary, all mystical experiences share a common set of qualities. Psychedelics guru Aaron Nesmith-Beck provides a concise account of the origin of Common Core Thesis:[43]

> In his 1902 book *The Varieties of Religious Experience*, the American philosopher William James popularized the term "religious experience", which is synonymous with mystical experience (and "visionary experience"). James suggested there was a common core to these experiences, regardless of difference in existing belief structure…
>
> In 1960, a British philosopher named Walter Stace published *Mysticism and philosophy*, in which he analyzed firsthand accounts of mystical experience from a wide range of religious texts. Stace, like James, concluded that there was in fact a common set of qualities that defined the mystical experience, independent of culture or origin. Modern research has confirmed this theory, now known as the "common core thesis."

Features of Mystical Experiences

Building on his Common Core Thesis, Stace established an organizational framework for characterizing mystical experiences that contained nine factors:[44]

(1) **Internal unity**: undifferentiated awareness

(2) **External unity**: unity with the surrounding environment

(3) **Nontemporal and Nonspatial Quality**: feelings of infinite time & limitless space

(4) **Inner Subjectivity**: a sense of life or living presence in all things

(5) **Objectivity and Reality**: noetic quality, a sense that the experience was a source of objective truth

(6) **Sacredness**: worthy of reverence, divine, or holy

(7) **Deeply Felt Peace and Joy**

(8) **Paradoxicality**: needing to use illogical or contradictory statements to describe the experience

(9) **Ineffability**: difficulty of communicating or describing the experience to others

Stace's nine-factor framework was subsequently used as a basis, first, by Pahnke to create the Mystical Experience Questionnaire (MEQ)[45] and, then, by Ralph Hood to create Hood's Mysticism Scale.[46] Two decades later, in 1998, Adolf Dittrich established an alternative framework for characterizing Abnormal Mental States (APZ) based upon three primary dimensions:[47]

(1) ''**Oceanic Boundlessness**'' (OBN): positively experienced depersonalization and derealization, deeply-felt positive mood, and experiences of unity.

(2) ''**Dread of Ego Dissolution**'' (DED): negatively experienced derealization and depersonalization, cognitive disturbances, catatonic symptoms, paranoia, and loss of thought and body control

(3) ''**Visionary Restructuralization**'' (VRS): visual (pseudo)-hallucinations, illusions, auditory-visual synesthesiae, and changes in the meaning of percepts.

Thereafter, Dittrich's framework was used as the basis for alternative assessments, including OAV (which stands for the German names of the three dimensions OBN, DED, and VRS), as well as its extended version, 5D-ASC ("five dimensions of ASC questionnaire").[48]

These are among the most well-know of the mystical experience assessments. There is a rich literature supporting the development and validation of these and other similar such characterizations of mystical experiences.

Reliably Generating Therapeutic Benefits

There is general consensus about certain aspects of the process involving the use of psychedelics for generating therapeutic benefits for patients. A brief summary of each is presented below.

Unresolved Issues Create Dysfunction

It is often the suppression of underlying, unresolved issues by patients – due to patients' inability to face their problems head-on – that leads to the chronic addictions or other dysfunctions from which individuals suffer.[49]

Importance of Set

Pre-psychedelic therapy sessions should be used to prepare patients for psychedelic experiences, by helping patients decrease anxieties about and establish proper expectations of the psychedelic experience.[50]

Importance of Setting

Therapists should provide comfortable, non-threatening environments in which patients are guided by therapists while experiencing trips.[51] Notably, bad outcomes may be significantly reduced by establishing proper set and setting:

> A survey of 1,993 people, conducted by Roland Griffiths' group, showed that 7.6% of recreational users had a difficult psychedelic experience and subsequently sought treatment for psychological symptoms; whereas, in carefully screened, well- prepared and closely monitored volunteers the rate was only 0.9%.[52]

Mystical Experiences Enable Resolution

Psychedelic substances produce mystical experiences, during which time individuals are better able to resurrect traumatic experiences and view them from new, less-threatening perspectives. By enabling patients to detach, in a sense, from previously traumatic situations, they are now able to process, resolve, and/or accept the situations.[53]

Importance of Integration

Post-psychedelic therapy sessions help patients interpret and integrate new-found perspectives into their daily lives. It is this integration that enables patients to achieve long-lasting therapeutic benefits. The greater is the ability to resolve and integrate such problems, the greater will be the long-lasting therapeutic benefits achieved.[54]

Neurological Activity

As previously mentioned, classic psychedelics generally include those substances that act on serotonin receptors generally,[55] and 2A receptors (5-HT2A) specifically.[56] Research on these effects has shown them to entail several interrelated phenomena, including decreases in activity at the default mode network, decreases in communication hub connectivity, and increases in neuroplasticity. Let's unpack this a bit.

Brain Networks

The advent of brain imaging technologies in the 1990s enabled researchers to directly examine — in real-time — patterns in brain activity. With the benefit of these technologies, researchers have discovered two distinct networks in the brain — the salience network and the default mode network — each of which is active during particular states of consciousness.

The ***salience network*** includes regions of the brain that are active during periods of *normal waking,* or *secondary, consciousness.* Also called the *task-positive* or *extrinsic network*, these regions of the brain are active during periods of *cognitive engagement* or *salient-sensory*

events. Simply put, the salience network is engaged whenever the brain is actively employed in completing tasks or otherwise solving problems that require attention to the job at hand.[57]

In contrast, the **default mode network (DMN)** includes regions in the brain that are active during states of consciousness known as *primary states* or *resting states*. Also called the *task-negative* or *intrinsic system*, these areas of the brain are engaged while in *stimulus-independent* or *task-unrelated* thoughts. When individuals are not focused on a specific job or problem requiring conscious attention, the mind wanders, and the DMN is activated. During this period, individuals engage in rumination, daydreaming, latent thought, and exploration. More specifically, when the DMN is active, individuals engage in thoughts about themselves; about their past, current, and expected future experiences; and about how they interact with and relate to the world.[58] The DMN "is responsible for, among other things, our sense of self in space and time, distinguishing between self and other, discursive thought (mind-wandering), remembering the past, and imagining the future. "[59] The DMN "becomes engaged when individuals reference information to themselves or reflect on personal preferences, beliefs, values, feelings, abilities, and physical attributes as well as engage in personal moral dilemmas."[60]

Effects of Psychedelics

As discussed earlier, psychedelics appear to have the potential to generate both:

(i) Acute pharmacological (e.g., hallucinations) and phenomenological (mystical states) effects, as well as
(ii) Longer lasting physiological (e.g., neuroplastic) and psychological (e.g., enhanced well-being) benefits.

The same types of brain imaging technologies that facilitated discovery of the salience and default mode networks have also enabled researchers to start to understand how psychedelics act on the brain to create their effects. It appears that there are two mechanisms responsible for the acute and longer lasting cognitive effects of psychedelics: psychedelics decrease activity in the DMN, and they decrease connectivity between different regions of the DMN.

Decrease Activity in DMN

Given the nature of people's reported experiences while using psychedelics, noted psychedelics researcher Robin Carhart-Harris and colleagues expected to find that brain activity increases when people use psychedelics. They were thus surprised to find just the opposite: a decrease in activity. The area of the brain that experienced a decrease in activity was the DMN.[61] In other words, psychedelics suppress users' tendency to engage in rumination. Furthermore, "the participants experiencing the most intense psychedelic effects also showed the strongest decreases of activity in those particular areas. In other words, the lesser the activity, the stronger the trip."[62]

Perhaps one of the most striking phenomena that occurs during psychedelic experiences is that known as *ego death*. Ego death is described as an experience of a dissolving of the boundaries between oneself and everything else and becoming one with the world. If, indeed, the DMN is responsible for people's sense of self, that is, their understanding of how they exist as distinct from the rest of the world, then it's easy to see how a potentially radical decrease in activity in the DMN can lead to a sensation like ego death. Several researchers eloquently express this thought:

From Eisenberg, S. (2020): "Considering the DMN's association with metacognition and self-relevant thought, it is not difficult to see the link between a drop-off in the DMN's activity and a phenomenon such as ego death."

From Aaron (2017): "The experience of unity that is central to mystical experiences involves a decrease in self-referential processing. There is compelling evidence for a network of brain areas (i.e., the nodes of the DMN) that are involved in self-referential processing and maintenance of a sense of the self in space and time. Decreased activity in these areas has been observed using multiple imaging modalities, both after administration of classic hallucinogens and during meditation practices."

Decrease Connectivity of Network Hubs

An important characteristic of the DMN is its high degree of connectivity in the brain: "[T]he default network is intrinsically organized into distinct subsystems that converge on core hubs." This structure appears to support the DMN in playing "a key integrative role" in coordinating communicating across the brain. That is, "These hubs may be critical for efficient information transfer in the brain by allowing communication between different regions via the fewest number of connections."[63]

Intriguingly, Carhart-Harris believes psychedelics facilitate a decoupling of the connector hubs, that is, a decrease in ordered communications across the brain.[64] This uncoupling of regions within the DMN associated with psychedelic use may have astounding implications for enabling some people, particularly those with cognitive dysfunction, to (i) experience new perspectives on past events and ideas, and (ii) reset their thought processes as per these new perspectives.

New Perspectives

Decreases in hub connectivity force information to pass along different routes – and routes much more random in nature – than the information normally would as it travels through the brain.[65] These more roundabout paths of information flows lead to novel inter-communications among areas of the brain that don't normally talk to one other.[66]

More disorganized network activity could very well explain the phenomenological experiences associated with using psychedelics. As described by psychedelics researcher David Nutt:[67]

> There's something about the 5-HT2A [serotonin receptor in the brain] that helps to structure brain activity—and psilocybin disrupts normal patterns of activity in brain networks … When we saw it, it all made perfect sense. We could explain hallucinations by a disruption in the coordination of the visual system. We could explain the out-of-body experiences by the disruption of the default mode network.

Random interactivity among areas of the brain that don't normally communicate with one another enables people to view and interpret information differently than they normally would. The ability to reassess information, experiences, and beliefs from new perspectives has the potential to deeply alter one's perspectives on oneself and on the world, which is, indeed, a common outcome associated with the use of psychedelics.[68]

Plasticity

We've seen that the use psychedelics causes a breakdown in the normal ways the brain processes information, particularly that information related to one's sense of self. Such disruptions enable individuals to gain new perspectives – and insights – about their view of the world. Yet, these disruptions in normal flows of information are temporary in nature, since DMN hubs re-couple once the pharmacological effects of the drugs wear off.

Yet, the experiences provided by the drugs – in particular, the new perspectives and insights gained – open the door to enabling users to make permanent changes to their approaches to life. When users couple their experiences with meditation or other forms of psychotherapy, they essentially rewire their brains to make their new thought processes more permanent.[69] As such, the use of psychedelics has the potential to ultimately generate life-changing therapeutic benefits.

Depression, Addiction, PTSD

As a final thought, understanding the neurological underpinnings of how psychedelics affect the brain helps explain the potential for psychedelics to facilitate tremendous therapeutic benefits for sufferers of such chronic diseases as depression, addiction, and PTSD. Specifically, we've discussed how the connectivity of the DMN is responsible for maintaining control over information flows and processing in the brain and how psychedelics interrupt those normal processes. We've also discussed how the DMN is responsible for rumination and latent thought and how psychedelics decrease activity in the DMN, thereby suppressing normal cycles of rumination.

It turns out that individuals who suffer from depression, addiction, and PTSD all tend to engage in endless cycles of rumination ("pathological brooding"), where the cycles involve thought processes that are "overstable," that is, fixed in "rigidly pessimistic modes."[70] Psychedelics offer users the potential to decrease their tendency to endlessly fixate on specific thoughts. At the same time, psychedelics also enable users to potentially escape their rigidly defined perspectives on situations and reimagine them from much different lights, especially with the help of psychotherapy. It's no wonder the use of psychedelics is resulting in mind-boggling

success rates for increasing well-being in people who suffer from depression, addiction, and PTSD.

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