

PSYCHEDELIC EXPERIENCES WITH HETEROGENEOUS INTERPRETATIONS BETWEEN RELIGIOUS, AESTHETIC AND THERAPEUTIC PRACTICES

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ABSTRACT: This paper explores the heterogeneous interpretations and uses of psychedelic substances across religious, aesthetic and therapeutic practices. It traces the historical use of natural psychedelics in Mesoamerican cultures and their subsequent condemnation during western colonization, with a semiotic approach aimed at demonstrating how the interpretations of drug effects are shaped by different cultural and encyclopedic frameworks. It discusses the intercultural translation challenges that arose when European colonizers first encountered indigenous psychedelic practices, leading to misinterpretations and prohibitions. It highlights the contrast between indigenous perspectives, which view these substances as sacred and therapeutic, and initial western interpretations that associated them with demonic influence. Then, the paper explores the evolution of scientific and artistic perspectives on psychedelics, starting from chemical discoveries to the emergence of a psychedelic culture, highlighting how these substances transitioned from being an object of scientific study to a catalyst for aesthetic and cultural experiences. The study concludes by addressing the recent “psychedelic renaissance” in scientific research, which has demonstrated potential therapeutic benefits of these substances in treating mental health disorders. It underscores the semiotic mechanism by which the qualities attributed to psychedelic experiences are shaped by prior knowledge, interpretative habits, and cultural discourses.

Il presente articolo esplora l'eterogeneità delle interpretazioni e degli usi delle sostanze psichedeliche, all'interno di contesti religiosi, scientifici, estetici e terapeutici. Attraverso un approccio semiotico, si ricostruisce brevemente la storia delle sostanze psichedeliche naturali nelle culture mesoamericane e la loro successiva condanna nel periodo della colonizzazione occidentale, con l'obiettivo di mostrare come l'interpretazione degli effetti delle droghe sia stata profondamente modellata da differenti quadri culturali ed enciclopedici. L'articolo analizza le difficoltà di traduzione interculturale emerse nei primi incontri tra colonizzatori europei e pratiche psichedeliche indigene; viene messo in evidenza il contrasto tra le prospettive

indigene, che attribuiscono a tali sostanze valore sacri e terapeutici, e le prime interpretazioni occidentali, che le associavano invece alla pazzia e all'influenza demoniaca. Successivamente si esamina l'evoluzione delle prospettive interessate all'esplorazione degli effetti psichedelici, arrivando alla nascita di una cultura psichedelica, mostrando come queste sostanze siano passate da essere oggetto di studio scientifico a catalizzatori di esperienze estetiche e spirituali. L'articolo si conclude analizzando l'attuale "rinascimento psichedelico" in ambito scientifico, evidenziando i meccanismi neurocognitivi innescati dall'assunzione di queste sostanze, e i potenziali benefici terapeutici nel trattamento di alcuni disturbi mentali. Infine, si sottolinea come, al di là delle differenze tra i contesti d'uso, vi sia un meccanismo semiotico condiviso, tale per cui l'interpretazione dell'esperienza non emerge mai in modo neutro, ma a partire da conoscenze precedenti, aspettative soggettive e narrazioni culturali preesistenti.

KEYWORDS: Psychedelic, Drugs, Interpretations, Rituals, Therapies

PAROLE CHIAVE: Psichedelici, Droghe, Interpretazioni, Rituali, Terapie

1. Introduction

Natural psychedelics, such as psilocybin mushrooms, mescaline cacti peyote and ayahuasca, have been used for centuries or millennia by various populations within ritualistic and spiritual contexts, particularly in the Mesoamerican region. During the Western colonization of the Americas, the use of these substances was largely condemned by European catholic authorities, and subsequently forced into clandestinity. In later centuries, these drugs became a subject of scientific interest, through the chemical extraction of natural psychoactive substances, and their experimental use on subjects. Psychedelic drugs have subsequently begun to attract aesthetic interest in western cultures, inspiring explorations and representations of altered states of consciousness. In recent years, the expression "psychedelic renaissance" has been used to describe the resurgence of scholarly and scientific attention toward these substances across a wide range of disciplines, including neuroscience (Carhart-Harris 2018; Codignola 2018), philosophy (Letheby 2021), and cultural studies (Pollan 2018; Jay 2019). This renewed interest has been largely driven by scientific findings demonstrating the potential therapeutic benefits of psychedelics in treating mental health

conditions such as depression, PTSD, and addiction (Griffiths *et al.* 2006; Yehuda and Lehrner 2023). Groundbreaking clinical studies have shown that psychedelic substances, when consumed in safe and controlled environment, can foster psychological well-being by inducing altered states of consciousness that promote emotional processing, neuroplasticity, and a sense of interconnectedness.

This study, which adopts a semiotic approach, focuses on the heterogeneity of uses and interpretations of hallucinogenic substances and their effects, whose history is briefly reconstructed. Our objective is to demonstrate how the interpretation of drugs-induced experience is always influenced by the encyclopedic frameworks (Eco 1975; Paolucci 2020) that underlie subjective experiences — that is, the contexts, discourses, and interpretative habits circulating within cultures, which shape both individual experience and collective knowledge. The paper also addresses the differences and similarities between religious and therapeutic drugs' uses, focusing on the relation between the subjective phenomenal experience, the materiality of the drug, and the discourses surrounding it.

2. Psychedelic experiences and intercultural translation

Psychedelic naturally occurring substances, such as mescaline cacti, psilocybin mushrooms, and ayahuasca⁽¹⁾, have been used for centuries within ritualistic and spiritual contexts by Mesoamerican native populations, who have orally transmitted practices and narratives emphasizing the divine origin and profound spiritual effects of these psychoactive substances. In these contexts, drugs are used as medicines for curing spiritual, psychological and physical issues, effectively bridging therapeutic and religious ritual practices. In the absence of written texts, these substances have often been visually represented as sacred objects, as divine gifts, thus serving a crucial role in maintaining the well-being of their respective communities (Schultes *et al.* 1979).

(1) Psychedelic substances share similar chemical structures and pharmacological effects, primarily acting as serotonin receptor agonists, particularly at the 5-HT_{2A} receptor, triggering profound alterations in perception and consciousness. However, the term “psychedelic” was only coined in the second half of the twentieth century.

For instance, in Guatemala, “mushroom stones” dating back to the Maya and Olmec civilizations depict human or divine figures emerging from mushroom caps, symbolizing the sacred relation with these fungi (Heim and Wasson 1958). In this case, the substance is represented in its physical sacralized form; however, there are also instances where the effects of these substances are depicted, that is, visual representations of the subjective experience and the perceptual alteration induced by their consumption. This kind of representation, which functions as an inter-semiotic translation of embodied perceptual features into visual texts, is a longstanding practice that continues today, often carrying social and political significance. Thus, the use and representation of psychedelics in traditional cultures also serve to preserve social cohesion and cultural identity, both of which have been threatened by colonialism.

With the arrival of European colonizers in the sixteenth century, indigenous perspectives about psychedelic substances were first confronted by an external gaze that failed to comprehend their cultural and spiritual importance. The earliest written accounts of the use of psychedelic drugs, produced during the Spanish conquest of Central and South America, are shaped by the phenomenon of “coherent distortion” (Lorusso 2010) inherent in intercultural translations, as they were produced by European individuals unfamiliar with the encyclopedic frameworks of the indigenous populations. Lorusso explains that cultures “imprint a sort of ‘coherent distortion’ on everything that enters their space” (Lorusso 2010, p. 70), meaning that semiotic phenomena are transformed according to the interpretative habits of the semiosphere and the encyclopedic framework of reference. A striking example is found in sixteenth-century accounts of the San Pedro cactus (originally called *achuma*), used by Indigenous groups for both religious and therapeutic rituals. A Jesuit missionary described *achuma* as “the plant with which the devil deceived the Indians of Peru in their paganism, which they used for their lies and superstitions” and claimed that, under its effects, the indigenous people “imagined thousands of absurdities, convincing themselves that they were true” (Cobo V, VII; Jay 2019, p. 32). Similarly, the Franciscan André Thévet, in his *Histoire Mexique*, describes a Mexican indigenous group, the Otomí, as being deceived by the devil into consuming *nauacatl*, an herb that “drove

them mad and caused them to have many visions” (Thévet 1905; Heim and Wasson 1958, p. 133). In fact, this was not an herb but a mushroom containing psilocybin, known in the Nahuatl language as *teonanácatl*, which literally means “flesh of the gods”, (Heim and Wasson 1958)⁽²⁾.

In these European accounts, the altered states induced by hallucinogenic plants are often compared to the drunkenness caused by alcohol (Heim and Wasson 1958, p. 223), thus reframed through pre-existing Western categories. Moreover, such accounts are based solely on external observation, without firsthand experiential engagement, they are situated outside both the individual drugged body and the social body within which the drug is consumed. This detachment leads to what Eco (1975) calls “aberrant decoding,” whereby the specific meanings and effects of the practices are misinterpreted.

In indigenous cultures psychoactive plants hold a sacred role, and their effects are experienced euphorically within well-defined ritual contexts; however, from the western perspective, these substances appear sacrilegious, as they sharply contrast with catholic rituals, which prioritize structured ceremonies, hierarchical mediation, and doctrinal control over spiritual experiences. While both cultures recognize the opposition between ordinary perception and the altered states induced by hallucinogenic substances, they interpret this contrast through different value systems: for indigenous cultures, perceptual alteration is a visionary experience, a moment of spiritual awareness characterised by its *noetic* quality; for Westerners, by contrast, it is interpreted as mere hallucination, a symptom of madness, and thus as a threat to society. Furthermore, in indigenous practices, psychedelics are never used in isolation, but they are always holistically embedded within a discursive network, a web of beliefs and practices in which the drug functions as an artifact, a mediating tool that facilitates both individual and collective religious experiences while simultaneously serving as a therapeutic agent. However, the power of psychoactive substances does not operate in direct or immediate way; rather, it must always be channeled,

(2) Interestingly, in all these traditional cultures, psychedelic substances always bear names that reference the spiritual and transcendental realm. For this reason, they have been termed *entheogenic* substances in the field of ethnobotany and anthropology (Heim and Wasson 1958).

thus requiring the development of specific skills, specific competences for their proper use. In this context, the figures of the shaman and the healer emerge as bearers of interpretative competence, necessary for enabling the correct use of psychedelics and the proper interpretation of both their own and others' experiences, thus assuming also the role of helpers for other subjects. Additionally, ritual practices place significant emphasis on the characteristics of the context — elements that are not themselves psychoactive, but play a crucial role in shaping the meaning of the psychedelic experience (Williams *et al.* 2022). For instance, traditional songs such as the *ikaros* play a fundamental function in structuring the ritual and the psychedelic experience (Dolmatoff 1975).

The reductive western interpretation of these practices stems, in part, from a failure to recognize the importance of contextual elements that, in their original cultural settings, are considered essential in shaping the psychedelic experience. This interpretative approach has led to a long-standing neglect and, to some extent, the oblivion of the potential of psychedelic substances within the European encyclopedic framework. Meanwhile, Mesoamerican populations have continued — and still continue — to perform their rituals. Psychedelics use retains still today a therapeutic value for Mesoamerican populations, as a form of collective resilience, providing a space for processing colonial trauma, maintaining social cohesion, and preserving cultural identity, with psychedelic substances constituting a fundamental part of the indigenous knowledge system. In this sense, the use of psychedelics is also serving a political and cultural function, aimed at preserving and revitalizing traditions that colonialism sought to suppress. In fact, since the beginning of colonialism, indigenous rituals have undergone a process of transformation, leading primarily to the hybridization of traditional religious imagery with Catholic religious imagery — a process in which the use of psychedelic substances has been integrated into Catholic ceremonies. Notable examples include *Santo Daime* in Brazil — centered around Catholic-inspired ceremonies involving ayahuasca — and the Native American Church in the United States, which formed around the ritual use of peyote. More recently, psychedelic rituals — particularly those involving ayahuasca — have been exported globally, giving rise to what has been described as “urban neo-shamanism,”. Here,

it is crucial to distinguish between the different operational contexts in which these substances are consumed. Although a thorough analysis of this phenomenon exceeds the scope of this discussion, it is evident from a semiotic perspective that the shift from traditional to urban contexts profoundly alters the meaning of the psychedelic–ritual experience, rendering it significantly different from Indigenous practices. In this process, a form of cultural appropriation, rooted in colonialism is evident and must be critically examined (De Mori 2021). What changes most radically is the belief in the efficacy of the psychedelic experience: in urban contexts, attention appears to be primarily focused on the drug, whereas in traditional contexts “efficacy is not dependent on the drug, but on the correct communication between the healer (or sorcerer) and the non–human powers” (De Mori 2021). This occurs because efficacy is socially, culturally and semiotically constructed, meaning that: “different forms of discourse shape differing opinions about the item and thus inform different certainties about its qualities. [...] ayahuasca as a substance is constituted by basically the same, or similar, human pharmacology, but the qualities that are attributed to this substance show significant variation.” (De Mori 2021)

This is fundamentally a semiotic and interpretative mechanism, in which the qualities of a given object or experience do not emerge from a pure encounter between subject and object. Rather, they are always partly determined by prior knowledge, interpretative habits, and discourses circulating within the encyclopedia, which render certain aspects of the object (or experience) relevant at the expense of others. As Paolucci writes in his *Cognitive Semiotics*: “our knowledge of the world is formed from elements deriving from objects and from elements deriving from previous knowledge circulating in the community.” (Paolucci 2021, p.66). Naturally, knowledge of a phenomenon also arises from direct experience with the object itself, not only from pre-existing frameworks (Paolucci 2021, pp. 70–72). However, in the case of early Western accounts, there was no direct bodily engagement with the substances in question. Consequently, interpretation was shaped entirely by prior knowledge — that is, by the value system embedded in the Catholic–Western encyclopedia. Only in the nineteenth century, when Westerners began to experiment bodily with psychedelic

substances, did the interpretive framework begin to shift. Yet even then, expectations, beliefs, and cognitive habits played a crucial role in shaping the discourses surrounding psychedelic experiences. In what follows, we will examine this mechanism at work in both scientific and aesthetic experimental practices, to illustrate how two opposing interpretive paradigms emerged concerning the effects and meanings of psychedelic experiences.

3. Scientific and aesthetic perspectives: from chemistry to psychedelic culture

The first transformation brought about by a scientific approach to natural psychoactive substances was the process of isolating their active compounds. This process of chemical isolation constitutes a material transformation — what Simondon would call *transduction* (Simondon 1964) — whereby a natural compound undergoes a transition that results in the emergence of a new entity. Transduction is a dynamic and structuring process that, beginning from an initial metastable state in which the substance exists in its natural form, initiates a propagation of separation throughout the system, ultimately producing the isolated molecule as a distinct entity. This process of material transduction also functions in way akin to an *intersemiotic translation*, as it is based on the search for an equivalence of effects between two materially different objects. In other words, it involves a comparison between the sensations elicited by the natural version of the substance and those produced by its chemically isolated counterpart. This comparative analysis is mediated by cultural knowledge, narratives, and discourses surrounding psychedelic experiences, which ultimately influence the interpretation of the drug's effects. In 1897, the German chemist Arthur Heffter identified the hallucinogenic properties of one of the alkaloids extracted from the Peyote cactus. Through self-experimentation with various chemical compounds derived from the plant he described experiencing a sensation of “nausea, occipital headache, intense dizziness, and clumsiness in moving” followed by visions of “tapestry patterns and mosaics” and “winding colored ribbons moving with the rapidity of

lightning.” (Heffter 1898, pp. 420–421; Perrine 2001, p. 43). Here the experience is primarily described in relation to visual perception, encompassing geometric and chromatic hallucinations which are typical of traditional indigenous art, and which will represent recurrent motifs within the textual production of psychedelic culture. Notably, there is a conspicuous absence of discourse pertaining to alterations in consciousness, which ostensibly remains lucid throughout the experience.

While Heffter perceives the hallucinogenic effects and may recognize a resemblance between the visions experienced firsthand and Peyote inspired art (Jay 2019), he does not mention religious or spiritual feelings, which are typical of traditional rituals. In fact, this and other experimental practices are always characterized by an exploratory approach that removes the ritual and collective configuration typical of traditional psychedelic uses, instead framing experimentation as a process aimed at identifying the specific pharmacological mechanism responsible for individual, phenomenal hallucinogenic effects. It is interesting to note that within a scientific context, individual experience is interpreted and verbally expressed in very different way compared to ritual use contexts. The material shift from the natural substance to the chemical one thus affects not only the physiological dimension, but also brings about changes in the sense-making practices employed by individuals before, during, and after the drug’s assumption.

3.1. *Psychotomimetic and psychedelic paradigms*

Following its chemical identification, mescaline became, in the 1930s, the first psychedelic substance extracted from a plant with a history of ritual use to be studied in psychiatric research. This first wave of investigations was based on the hypothesis that mescaline could induce temporary psychotic states, as researchers observed parallels between its effects and clinical descriptions of mental disorders. For instance, altered perception, and particularly hallucinations, were reminiscent of symptoms reported by patients with schizophrenia⁽³⁾. According to the psychotomimetic hypothesis (Pollan 2018), inducing a temporary,

(3) The psychotomimetic hypothesis was also supported by the chemical similarity between mescaline and dopamine, an endogenous substance associated with schizophrenia (Pollan 2018).

controlled “psychotic state” in healthy individuals was thought to provide a more direct way to study the pathophysiology of psychosis, ultimately improving the understanding of these mental disorders. However, this aim was based on an incomplete understanding of both the mechanisms underlying psychedelic states and those of psychiatric conditions. In this initial experimental phase, no attention is paid to the environmental and contextual factors surrounding drug administration, elements we now know deeply influence the phenomenology of the experience. Similarly, the preparation of the subjects involved in the experiment is not considered worthy of attention, despite current understanding that an individual’s expectations play a crucial role in shaping the nature and quality of the psychedelic experience. In some ways, it is precisely the psychiatric context that constructs the cases that confirm the psychotomimetic interpretation; this is determined by an experimental configuration that drastically conditions the research results, which were already directed towards studying psychopathological mechanisms rather than the experience itself, thus confirming the initial theoretical assumptions. Most importantly, the psychotomimetic interpretative paradigm is not articulated by the individuals undergoing the psychedelic experience, but rather by external observers who interpret the first-person reports of those experiences through the lens of psychopathology.

To understand the transition from the psychotomimetic paradigm to the psychedelic one, it is necessary to step outside the psychiatric field and venture into the aesthetic-literary domain. A crucial reference in this shift is *The Doors of Perception* by Aldous Huxley, a 1954 text, in which the author narrates and analyzes his experience with mescaline. The British writer became interested in mescaline through the psychiatric studies of Humphry Osmond, and after undergoing what he described as a “revelatory” experience, he began a correspondence with the psychiatrist, which led to the creation of the neologism *psychedelic*, a term that would gain widespread recognition from that point onward. In his book, Huxley begins by describing alterations in visual perception with open eyes, noting a qualitative and affective transformation of space, time (which appears expanded), and objects. He emphasizes the sense of wonder experienced when contemplating everyday

objects — such as flannel trousers or a letter opener — along with visual details that are typically irrelevant in standard perception. He compares ordinary perception to a filter that reduces the complexity and the beauty of experience, whereas the mescaline-induced state of consciousness represents a “return to truth.” He later describes closed-eye visions characterized by moving lights and geometric patterns, accompanied by a profound sense of totality and a feeling of “participation in the manifest glory of things” (Huxley 1954, p. 18). Huxley’s account appears to depict an ecstatic, mystical experience (Leone 2014), marked by the feeling of fusion between subject and environment, the feeling of a noetic quality of what is experienced, and by a sense of ineffability (Ponzo 2022), the difficulty of translating the experience into words, which, however, does not result in absolute incommunicability. Although Huxley repeatedly laments the inadequacy of verbal language in conveying the meaning of the psychedelic experience, this very limitation becomes part of the process of verbal translation, which is always partial and negotiated⁽⁴⁾.

It is clear that the experience described by Huxley differs from the psychotic states outlined in psychiatric manuals. However, it is equally evident that Huxley’s interpretation, like any other interpretation, is shaped by his encyclopedic framework, his interest in eastern philosophies, his explicit quotation of William Blake’s visionary poems, and his implicit yet evident appreciation of William James’s *The Varieties of Religious Experience* (1900). Nevertheless, it is precisely through this interpretative trajectory that the altered state induced by a hallucinogenic substance comes to be experienced and understood as a revelatory, spiritually profound event, thereby showing parallels with traditional interpretations in ritual contexts. Huxley’s experience is crucial to the emergence of the psychedelic paradigm: he perceives that his experience lacks a psychotomimetic quality, yet he does not have a pre-defined linguistic term for translating his sensations. As a result, he invents the term *psychedelic*, drawing from another semiotic-linguistic system, Ancient Greek, available within his encyclopedic framework. This instance of linguistic invention functions as an act of intersemiotic

(4) The idea of negotiation in translation is central to Eco’s semiotics of translation (Eco 2003).

translation, in which the verbal sign *psychedelic*, derived from *psychè* and *delein*, meaning “to reveal the mind/consciousness”, encapsulates within its meaning a series of sensations corporeally experienced. This process of translation originates from what has been named a “syntax of the sensible” (Paolucci 2020, pp. 191–192), in which bodily sensations serve as the material formants used for translation, constructing an expressive plane oriented toward a desired content.

3.2. *Rise and decline of psychedelic culture*

The success of Huxley’s text (from which the psychedelic rock band *The Doors* took its name) contributed to the formation of a psychedelic (sub)culture, during the 1960s, especially in USA, where the use of drugs intersected with aesthetic production and political discourse. The central drug of psychedelic culture was not mescaline but the newly synthesized LSD — an extremely potent hallucinogenic substance (in terms of dose-to-psychoactive effect ratio), which was accidentally discovered by the Swiss chemist Albert Hofmann (1979). Nonetheless, the experiential configuration described by Huxley in relation to mescaline’s effects can also be found in accounts of LSD experiences, because of their similar chemical composition and pharmacological mechanisms.

The psychedelic culture of the 1960s is characterized by the desire “to modify social and aesthetic human relations through a controlled and conscious use of predominantly hallucinogenic drugs” (Spaziant 2005, p. 21). In this cultural context the drug is valued as a tool for both individual and collective transformation, political opposition to the establishment, and identity affirmation; thus, it also recovers a collective dimension and social cohesion, typical of traditional uses. This collective interest was reflected in the textual representation of the psychedelic experience, giving rise to a kind of *psychedelic discourse*, in which the experiential configurations of psychedelia (such as perceptual and consciousness alteration) were represented, transposed, and translated into other discursive configurations — literary, musical, visual, and audiovisual. For instance, in the musical domain, as Spaziant highlights (2005, p. 24), psychedelic music is particularly concerned with

the exploration of sonic effects, alterations in timbre and tonalities, realised through the use of techniques such as distortion, phasing, delay, and reverb. These techniques transform and modulate the sonic substance following a “logic of effects” that mirrors the altering, hallucinogenic, and transformative properties of psychedelic drugs. Moreover, the relationship between the psychedelic experience and musical experience emerges on another level: music which is itself shaped through a form of translation of the psychedelic experience, in turn becomes an integral part of that very experience. This musical translation does not aim to explain or represent the psychedelic experience in descriptive or analytical way, but rather to generate an autonomous experiential dimension, one which resonates with the effects induced by the drug. In this sense, it also reclaims a traditional configuration akin, in some respects, to the role of music as an accompaniment in ceremonial practices⁽⁵⁾.

In psychedelic culture, the altered state of consciousness is often described through the metaphor of an inner journey — the *trip* — which, at its peak, can lead to a sensation *ego dissolution*, a kind of merging of the subject with the surrounding environment, where the subject can lose the ordinary self-consciousness, which in some respects resembles the sense of fusion and totality described in mystical narratives. The trip, and especially the experience of identity loss, can be either euphoric or dysphoric, depending on the psychophysical state of the individual and the context in which the experience takes place. The experience induced by the consumption of a hallucinogenic drug can thus manifest diverse phenomenological features, and not always is the experience, in its entirety, perceived as revelatory and thus properly *psychedelic*. The inner journey can turn into a *bad trip*, leading to sensations of anxiety, fear, and obsessive thoughts, which, in predisposed individuals, may even trigger psychotic episodes. This potential for the

(5) We do not have the space to discuss all the different enunciative strategies used to translate the psychedelic experience. One particularly interesting case, which we plan to address in future work, is the audiovisual representation of the psychedelic experience. In some ways, the audiovisual medium is particularly suited to translating altered perceptions due to its syncretic nature and its prosthetic status (Paolucci 2020), being able to offer the human eye perceptions that are impossible in ordinary experience, analogous to the altered perceptions induced by psychedelic drugs.

psychedelic experience to take on a quasi-psychotic dimension could suggest a reconsideration of the psychotomimetic paradigm. However, contemporary research has demonstrated that under controlled conditions — and with the guidance of a sober facilitator who accompanies the participant — the drug-induced experience is more euphoric and often accompanied by a positive sense of self-renewal. This attention to the phenomenological and contextual variability of drug effects in 1960s psychedelic culture led to the formalization of the concepts of “set” and “setting”: the former refers to the psychological background and mental state of the subject of experience, including thoughts, mood, and expectations; the latter encompasses the physical and social environment in which the experience takes place.

Unfortunately, this promise for conscious and controlled use, with care to contextual and subjective preparation, soon gave way to abuse and uncontrolled consumption, a shift facilitated by the *Controlled Substances Act* of 1970, which classified psychedelic drugs (mescaline, psilocybin and LSD) as among the most harmful and dangerous substances in the world and, most notably, as “devoid of any medical potential” (Jay 2019, p. 251). This classification effectively halted scientific research, while simultaneously signaling the perceived threat of psychedelics to capitalist and consumerist Western society. Western political institutions had encountered psychedelic substances used in the ritual practices of Amerindian populations through a violent colonial process; they judged the hallucinogenic effects of these substances as merely illusory or as manifestations of *mental disorders* and, on multiple occasions, prohibited their use. Yet, precisely as psychedelic culture was being dismantled by Nixon’s “war against drugs”, LSD was being secretly tested in CIA laboratories. The secret agency sought to use the drug as a tool for psychological manipulation, information extraction, essentially as a truth serum, basically as a potential biochemical weapon. There is not enough space here to discuss in depth the political implications of this practice, which has fortunately been documented (Codignola 2018). However, the underlying ideology is evident: it reflects a desire to exert total control over individuals’ minds, a *psycho-power* in service of political hegemony, while at the same time open scientific debates were blocked.

4. Psychedelic renaissance, neurocognitive research, and therapeutic practices

For several decades, psychedelic substances remained out of the spotlight, only to resurface over the past twenty years in what has been increasingly described as a *psychedelic renaissance*, marked by renewed discoveries, publications, and growing discourse surrounding psychedelia (Belouin and Henningfield 2018; Letheby 2021). Throughout a long and turbulent history, the heterogeneity of uses and interpretations of these peculiar substances is undeniable. Could this heterogeneity be linked to the pharmacological complexity of psychedelics? Perhaps the phenomenological variability of psychedelic experiences calls for an expanded pharmacological framework — one in which the chemical substance acting at the neurocognitive level is not considered independent of contextual and subjective factors, instead it's deeply related to them; recent discoveries, suggesting potential therapeutic applications, seem to point in this direction.

In some countries, such as Canada, Switzerland and the United Kingdom, new regulations have enabled the resumption of scientific research on psychedelic substances (Pollan 2018). Thanks to advances in neuroimaging technologies, significant progress has been made in understanding the neuro-pharmacological mechanisms underlying psychedelic experiences. Robin Carhart-Harris (2018), a pioneer in the field, proposed the *entropic brain theory* to explain how psychedelics alter brain activity. According to Carhart-Harris (2019), psychedelics bind to 5-HT_{2A} receptors, triggering erratic glutamate release and weakening synchronized neural oscillations, particularly in low-frequency bands like the alpha rhythm. This results in three key neural signatures: 1) disintegration of resting-state networks; 2) desegregation between typically distinct systems, and 3) increased entropy, or unpredictability, in brain activity (Letheby 2021, p. 118). These findings align with recent models of *predictive processing*, which view the brain as a “prediction machine” that constructs top-down models (priors) to interpret sensory input. Carhart-Harris and Friston (2019) proposed the *REBUS* model (RElaxed Beliefs Under pSychedelics), suggesting that psychedelics reduce the precision of high-level priors — especially

those related to self-identity — allowing suppressed or novel information to enter consciousness. This “relaxation of beliefs” may explain why psychedelics are reported to facilitate *emotional breakthroughs*, *cognitive flexibility*, and a sense of *novel perspective*, elements that are proving increasingly relevant in therapeutic settings. Under this model, psychedelic therapy functions by loosening rigid or maladaptive belief structures, such as those seen in depression, anxiety, or addiction, and enabling a reorganization or “reset” of mental frameworks. The growing scientific interest in psychedelics has also reignited a discussion on the spiritual and existential dimensions of these experiences. According to the studies conducted by Griffiths *et al.* (2006; 2019), there is statistical evidence supporting the claim that psilocybin, the hallucinogenic compound found in Mexican mushrooms, has the potential to induce deeply spiritual and mystical experiences. Many participants reported a complete mystical experience, characterized by a profound sense of connection with themselves and the universe, difficulty in describing the experience in words (ineffability), and the perception of having encountered something sacred and deeply true, more true than the ordinary reality (noetic quality). A follow-up conducted fourteen months later revealed that the majority of participants continued to regard this experience as one of the most meaningful of their lives, and reported lasting positive changes in their attitudes, behaviors, and overall well-being.

Modern therapies supporting the use of psychedelic substances focuses precisely on this subjective, phenomenal experience, proposing a conception of the drug as a semiotic-material object, whose agency emerges from the relation between chemical and neuropharmacological aspects, subjective expectations, and contexts of use (Hendy 2022). The pharmacological action is not independent of subjective and contextual characteristics; the psychedelic experience depends on a specifically semiotic dimension of interpretation (sense-making) within the experience, a process in which difficulties or criticalities may arise, and which must therefore be experimented under controlled conditions. Chris Letheby (2021) has proposed to consider psychedelic therapy as a two-factor structure:

The first factor is the induction of plasticity at multiple levels: neural, cognitive, and phenomenological. Psychedelics induce molecular-level plasticity independently of their effects on cognition and consciousness (Ly *et al.* 2018), but also induce entropic brain activity by disintegrating cortical networks such as the DMN [...] This first factor alone — the induction of plasticity — may be sufficient for the shortterm ‘afterglow’ of several weeks, in which subjects report feeling lighter, freer, more energised and unburdened. [...] However, a second factor is required for truly durable change: the discovery of new forms of self-modelling during the experience and the consolidation of these during the subsequent period of integration. It’s not just the plasticity — it’s the way you use it. (Letheby 2021, pp. 147–148)

Therapeutic efficacy, as was understood in Indigenous knowledge systems, is no longer solely determined by the chemical–physical substance itself, but by the possibility (not necessarily realized) of altering the perception of the self through alternative interpretations and processes of sense-making, that is, through an alternative narrative of one’s identity. In this sense, Andy Clark, in his latest book (2023), talks about psychedelics as tools for “hacking” the cognitive–predictive system:

The idea here is that the drugs can help jolt the mind out of entrenched negative patterns, making it more flexible and open. In the cases of many affective disorders such as severe and chronic depression, the simple fact of temporarily experiencing the world very differently can be liberating. What had seemed like deep, immovable facts about how things are (and how you are) release their stranglehold, allowing other ways of seeing the world and “being you” to emerge. (Clark 2023, p.195).

This kind of use of psychedelic substances as medications within a psychotherapeutic framework can represent a significant innovation in the treatment of mental disorders. While classic antipsychotic medications involve continuous administration aimed at treating symptoms rather than resolving underlying causes, the therapeutic use of psychedelics is episodic, and the underlying goal is not merely the achievement

of a pharmacological effect but the facilitation of a profound psychological transformation in the subject (Yehuda and Lehrner 2023). In this light, the contemporary study and therapeutic use of psychedelic substances may help overcome a dualistic conception of reality, revealing an intrinsic interdependence between the material and cognitive dimensions. Such an expanded understanding of their role allows for a potential convergence between contemporary Western frameworks and traditional Indigenous perspectives (Williams *et al.* 2022). It's important to advocate for the integration of diverse perspectives and interpretative paradigms; the goal should be to seek a point of convergence between Western and Indigenous worldviews, between the therapeutic and the ritual, the individual and the collective, the scientific and the spiritual, because these dimensions are not necessarily contradictory. Acknowledging analogies and connections between different practices, tracing their histories, can help to avoid forms of postcolonial appropriation by recognizing the value and legitimacy of Indigenous knowledge systems and cultural frameworks. As we tried to show, it is only after a turbulent history of uses and interpretations that Westerner cultures started to notice the possibility of euphoric and therapeutic use of psychedelics, and more importantly understood their effects as not merely determined by physiological dynamics.

5. Conclusions

In this study, we aimed to highlight the heterogeneity of uses and interpretations of psychedelic substances, which, from a semiotic perspective, can be examined as semiotic–material substances whose agency is not solely determined by their (complex) chemical–physical properties but also by the (equally complex) practices of use and interpretations through which they are understood. For this reason, we sought to retrace key historical moments that have contributed to the development of diverse — and sometimes contradictory — interpretative paradigms, beginning with the clash between the indigenous cultures of the American continent and colonial Europe, moving through the chemical, psychiatric and aesthetic interest of the twentieth century,

and finally reaching contemporary neurocognitive and therapeutic perspectives.

Today, psychedelia is still placed at the intersection of religious–spiritual discourses and scientific–therapeutic ones, prompting reflection on the relationship between spiritual experience and psychological well-being. Although it may appear contradictory, the intertwining of therapeutic and spiritual dimensions was deeply rooted in the shamanic and ritual practices of Indigenous Mesoamerican populations, for whom the healing process — both individual and collective — is inseparable from religious and spiritual activity. In my view, we should not exclude the possibility that, in certain cases, the attainment of psychological well-being may occur through spiritual, mystical, or transcendent experiences, particularly within contemporary Western culture, which is profoundly shaped by processes of disenchantment and corresponding attempts at re-enchantment.

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