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Psychedelics: a window into perceptual processing

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5.1 Introduction

In 1938, Swiss chemist Albert Hofmann was searching for a novel analeptic (a drug that stimulates the central nervous system) but ended up synthesizing the psychedelic compound known today as lysergic acid diethylamide (LSD).[1] An initial accidental ingestion of LSD led Hofmann to perform a planned self-experiment by ingesting what he thought was the lowest dose of the drug needed to elicit a psychedelic response (0.25 mg). He later discovered that psychedelic experiences can be elicited using significantly lower doses of LSD. In 'The discovery of LSD and subsequent investigations on naturally occurring hallucinogens', Hofmann (1970) describes his psychedelic episode as follows:

> Last Friday, April 16, 1943, I was forced to stop my work in the laboratory in the middle of the afternoon and to go home, as I was seized by a peculiar restlessness associated with a sensation of mild dizziness. On arriving home, I lay down and sank into a kind of drunkenness which was not unpleasant and which was characterized by extreme activity of imagination. As I lay in a dazed condition with my eyes closed (I experienced daylight as disagreeably bright) there surged upon me an uninterrupted stream of fantastic images of extraordinary plasticity and vividness and accompanied by an intense, kaleidoscope-like play of colors. This condition gradually passed off after about two hours. (p. 93)

[1] The label 'LSD' was chosen because of its structural similarity to the respiratory stimulant nikethamide, a drug that was used as a respiratory stimulant, but was discontinued because of its unacceptably high incidence of toxicity (which included headaches, agitation, muscle spasms, or convulsions) at doses effective for stimulating respiration.

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As Hofmann's description illustrates, ingesting psychedelic drugs can radically alter visual perception. A wide spectrum of psychedelic visual phenomena has since been observed, ranging from apparent amplifications of visual acuity and increased colour brightness and purity to progressively warped or melted objects or scenes that appear to be drifting or breathing (Díaz, 2010; Gouzoulis-Mayfrank et al., 2002; Jastrzębski & Bala, 2013; Schmid et al., 2015).

Although LSD was the first synthetic psychedelic drug, naturally occurring psychedelic substances have been used for centuries, mostly by indigenous peoples in the Americas. For example, indigenous peoples in Mexico used a type of mushroom, which they referred to as 'sacred mushrooms', for ceremonial purposes. Today, people colloquially refer to them as 'magic mushrooms' or 'shrooms'.

In the late 1950s, in an attempt to isolate the main active components of sacred mushrooms, Hofmann ingested 32 dried mushrooms imported from Mexico. He describes the peak of his six-hour psychedelic episode as follows:

> At the peak of the intoxication, about 1 1/2 hours after ingestion of the mushrooms, the rush of interior pictures, mostly abstract motifs rapidly changing in shape and color, reached such an alarming degree that I feared that I would be torn into this whirlpool of form and color and would dissolve. (Hoffman, 1970, p. 98)

Hofmann later discovered that the main active component of sacred mushrooms was psilocybin, although psilocin (also an alkaloid) was also present in small amounts. Scientists have since ascertained that the psychedelic effects of hallucinogens depend on which receptor system in the brain they activate (Halberstadt, 2015).

LSD and psilocybin belong to a group of psychedelic drugs known to function as partial or full serotonin (5-HT) agonists and thus bind to and activate the 5-HT receptor system.[2] Other drugs in this group include dimethyltryptamine (DMT) and mescaline (a naturally occurring alkaloid found in the peyote cactus). The visual distortions elicited by DMT and mescaline are very similar to those elicited by LSD and psilocybin (Halberstadt, 2015; see also Cott & Rock, 2008; Huxley, 1954). They typically involve seeing bright colours,

[2] Partial agonists lead to more moderate activation of the neurons they bind to compared to full agonists. The psychedelic effects of hallucinogens that function as partial or full serotonin agonists is distinguishable from the psychedelic effects produced by non-serotonergic hallucinogens, including dissociative anaesthetics (e.g. ketamine), entactogens (e.g. MDMA: 3,4-methylenedioxymethamphetamine), and phytocannabinoids (Halberstadt, 2015).

kaleidoscopic images, and fast-changing geometric shapes that give the appearance of breathing, melting, or bleeding objects (Aday et al., 2021; Dubois & VanRullen, 2011; Studerus et al., 2011). For example, Cott and Rock (2008) provide the following report of a subject under the influence of DMT:

> The room erupted in incredible neon colors, dissolving into the most elaborate incredibly detailed fractal patterns that I have ever seen. My visual field was consumed with disturbances, and they quickly escalated in intensity. There was all kinds of morphing, bending, rippling, and breathing of objects when my eyes were opened. The entire room was crawling with beautiful geometric hallucinations. (p. 363)

Studies indicate that psilocybin—one of the most studied psychedelic drugs—disrupts long-range signal transmission between the prefrontal cortex and other cortical regions of the brain (Carhart-Harris et al., 2012; Muthukumaraswamy et al., 2013). Large-scale prefrontal cortex networks, such as the default mode network, are critical for high-level cognition. Various high-level cognitive capacities, including attention, reasoning, and impulse control, are mediated by the large-scale prefrontal cortex networks (Wood & Grafman, 2003). Abnormal activity during daydreaming and mind-wandering further suggests that the altered high-level states of consciousness occurring during psilocybin intoxication may be related to a disruption of large-scale prefrontal networks (Carhart-Harris et al., 2012). Indeed, high doses of psilocybin commonly elicit dream-like experiences, which tend to be assigned mystical or transcendent meaning (Díaz, 2010; Preller & Vollenweider, 2018).

The destabilization of large-scale prefrontal networks is thought to be mediated by psychedelics causing hyperexcitability in cortical neurons both directly and as a result of a disruption of attentional gating in the thalamus (Muthukumaraswamy et al., 2013; Vollenweider & Smallridge, 2022). As we shall see, the thalamus plays a critical role in gating information inflow to cortical areas and is thus central to attention. Disruptions of the attentional gating mechanism in the thalamus have been found to lead to a sensory overload in both the prefrontal and visual cortices (Vollenweider & Smallridge, 2022). Direct cortical excitability, attentional gating, and large-scale prefrontal networks have all been found to play a key role in mediating attention. Given the evidence that psilocybin disrupts long-range signal transmission between the prefrontal cortex and other cortical regions of the brain, it is possible that the mechanisms underlying its psychedelic effects are linked to a distortion of key attentional mechanisms in the brain.

Although the visual experiences elicited by psychedelic drugs are atypical, the scientific community has long recognized that aberrant cases often provide a window into the nature of scientific phenomena. As Block (2015) notes, the famous double-slit experiment was crucial in demonstrating the wave–particle duality of light. Scientists observed that when a light source such as a laser beam went through two slits, it produced bright and dark bands on the screen, a result which would not have occurred if light consisted only of particles. Neuroscientists have also recognized that atypical cases offer a window into the nature of visual perception. A new cell type in the mouse retina was recently discovered when researchers noticed that whereas it looked monopolar (i.e. did not receive direct photoreceptor input), it had none of the markers of inhibitory retinal cells, which was puzzling since monopolar cells provide inhibition in order to regulate nerve cell signalling (Santina et al., 2016). What such cases illustrate is that atypical phenomena can further our understanding of ordinary phenomena. The phenomenon of psychedelic visual distortions thus offers an opportunity to further our understanding of the mechanisms underlying ordinary visual perception.

An increasingly common way to account for ordinary visual perception is to appeal to predictive processing (Clark, 2013, 2016; Friston, 2005, 2009, 2010; Hohwy, 2012, 2013). Advocates of the Predictive Processing (PP) framework have recently suggested that this framework can be extended to account for psychedelic experiences caused by classical hallucinogens such as LSD, psilocybin, and mescaline (Carhart-Harris & Friston, 2019; Pink-Hashkes, 2017; Swanson, 2018). This chapter presents findings indicating that psilocybin-induced visual distortions and impaired executive functioning originate in temporary disruptions of attentional mechanisms; it is then argued on the basis of these findings that the PP framework is unable to support a unified account of psychedelic experiences. Lastly, an alternative theory of perceptual processing is proposed—the Gist Theory of Perception (GTP)—that can explain how these psilocybin-induced disruptions of attentional mechanisms may elicit psychedelic experiences.

5.2 Psychedelic effects on attention

The similarities among the psychedelic experiences elicited by hallucinogens such as LSD, psilocybin, mescaline, and DMT, suggest that they may share underlying mechanisms (Carter et al., 2005; Gouzoulis-Mayfrank et al., 2002; Hollister & Hartman, 1962; Jastrzębski & Bala, 2013; Kometer et al., 2012;

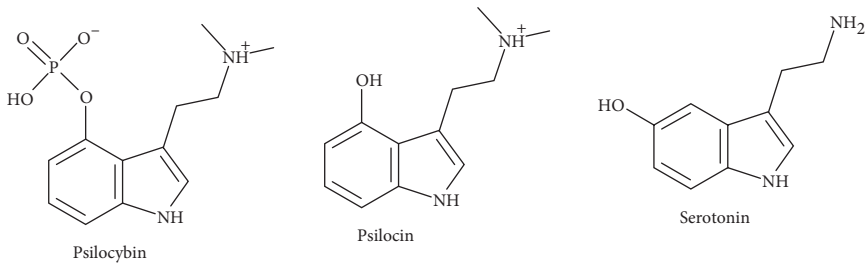

Figure 5.1 Similarities in the chemical structures of psilocybin (left), psilocin (centre), serotonin (right).

Redrawn from https://psychedelicreview.com/the-state-of-the-art-of-psilacetin-4-aco-dmt/ (open source).

Kraehenmann et al., 2015; Schmid et al., 2015). One of the most studied psychedelics today is psilocybin, the active ingredient in *psilocybe* mushrooms. When ingested, psilocybin is metabolized to the metabolic product psilocin, which shares its core chemical structure with 5-HT (Figure 5.1).

Psilocin functions almost exclusively as a 5-HT agonist, which means that it binds to 5-HT receptors and simulates the activity typically produced by 5-HT (see e.g. Stenbæk et al., 2021). The psychedelic effects of psilocybin are directly correlated with the binding of psilocin to 5-HT_{2A} receptors (Glennon, 1990; Madsen et al., 2019; Nichols, 2004, 2016; Presti & Nichols, 2004; Vollenweider et al., 1998). These receptors are located on layer 5 pyramidal neurons (shown as Roman numeral V in Figure 5.2) in the primary visual cortex (V1).

Psilocin has some affinity for all the 5-HT_1 and 5-HT_2 receptor subtypes, with the greatest affinity for the 5-HT_{2A} receptors in the raphe nuclei in the brain stem (Figure 5.3), which is the primary location in the brain for the production of 5-HT (see, for example, Hornung, 2003; Madsen et al., 2019; Stenbæk et al., 2021). After synthesis, 5-HT is normally released throughout the brain and the rest of the central nervous system (Figure 5.3). But psilocin occupancy of 5-HT_{2A} receptors in the raphe nuclei inhibits the release of 5-HT, resulting in a systemic decrease of the brain's 5-HT levels (Carter et al., 2005).

Whereas the underlying mechanisms of psilocybin-induced visual distortions are not fully known,[3] this chapter argues that the current evidence

[3] Though serotonin plays a crucial role in the understanding of psychedelic mechanisms, a study on 35 psychedelic drugs, including psilocybin, found that not all serotonergic agonists lead to psychedelic effects, just as not all psychedelic drugs are serotonergic agonists (Ray, 2010). These results indicate that serotonin may not be the only factor in the psychedelic mechanisms but may be one of the factors (Brogaard & Gatzia, 2015).

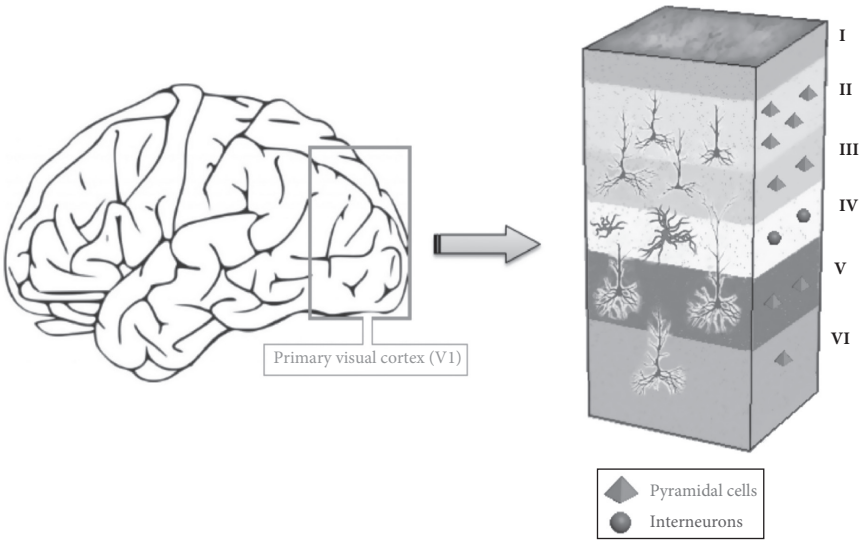

Figure 5.2 The grey matter in V1 is divided into six layers, depicted on the right as layers I, II, III, IV, V, VI, each comprising different types of neurons. Pyramidal cells, shown as green triangles, and interneurons, shown as red spheres, are two types of neurons and are physiologically separated. Pyramidal cells are also found in the prefrontal cortex.
Image adopted from Bachatene et al. (2012).

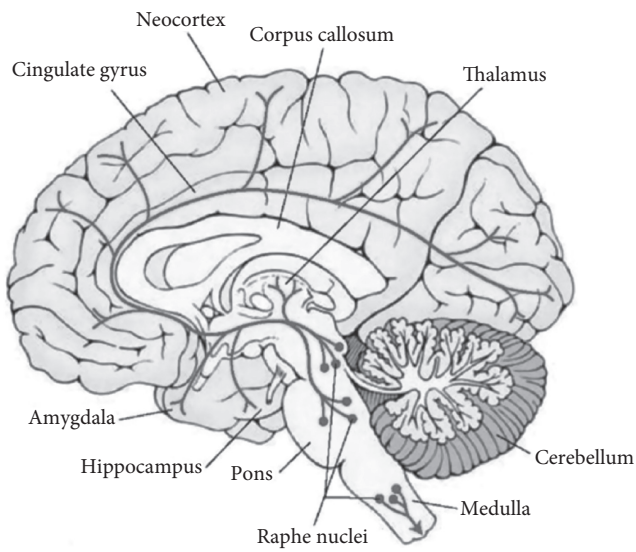

Figure 5.3 Major serotonin-containing neurons and their projections. Raphe nuclei are positioned midline in the brainstem throughout the midbrain, pons, and medulla.
Source: Wikimedia Commons.

supports the hypothesis that these effects occur primarily as a result of a modulation of the brain's attentional mechanisms.

In the neurotypical brain, attention can alter neural activity by modulating signal transmission, local cortical excitability, or attentional gating. Enhanced signal transmission involves a large-scale selective synchronization of neural activity between task-relevant areas, leading to large-scale tuning for (or selection of) attended stimuli (D'Andrea et al., 2019; Westerberg et al., 2021). For example, selective feature attention to red dots surrounded by grey distractors has been found to establish selective synchronization of neural activity between the prefrontal cortex and V4 (Bosman et al., 2012; Grothe et al., 2018). Increased local cortical excitability raises the levels of excitatory neurotransmitters and neural firing rates, thereby shrinking and orienting the neurons' receptive fields toward attended stimuli (Okazaki et al., 2020). Attentional gating involves the inhibition of neural activity in the central thalamus, which can be thought of as the switchboard of the brain (shown in Figure 5.3). Visual signals are projected back to the thalamus via inhibitory interneurons (depicted in Figure 5.2 as red dots) that signal to the thalamus to attenuate random noise and neural activity elicited by unattended (irrelevant) stimuli (Fischer & Whitney, 2012; Okazaki et al., 2020; Saalmann et al., 2012; Zhou et al., 2016). This attentional gating mechanism in the thalamus regulates the allocation of attentional resources by filtering out irrelevant and random activity from the visual signals that the thalamus sends back to the visual cortex for further processing.

The current evidence suggests that psilocybin destabilizes large-scale resting-state functional connectivity, signal transmission, and attentional gating mechanisms while enhancing local cortical excitation (see, for example, Barnett et al., 2020; Brogaard, 2013; Brogaard & Gatzia, 2015; Pallavicini et al., 2019; Vollenweider & Smallridge, 2022). Psilocin binding in the primary visual cortex disrupts exogenous attentional mechanisms, whereas its binding in the prefrontal cortex disrupts endogenous attentional mechanisms (Vollenweider & Smallridge, 2022). *Endogenous attention*—also known as top-down attention—refers to subject-controlled selective or distributed attention to spatial locations, objects, or features (Dugué et al., 2020). For example, when you turn your head to look at your alarm clock, you selectively orient your attention to an object. When your cat attempts to catch the red laser spotlight that you teasingly move around on the floor, he relies on sustained, selective feature attention to track it. *Exogenous attention*—also known as bottom-up attention—refers to automatic attentional orienting to salient stimuli or exogenous cues (Cascasco, 2011, 2014; Carrasco et al., 2004; Chica

et al., 2013; Fuller & Carrasco, 2006). Threatening stimuli typically capture exogenous attention (Van Steenbergen et al., 2011). For example, if you were to hear the loud caterwauling of a bobcat (an exogenous cue) in your garden while enjoying a late after-dinner drink with your friends, your attention will undoubtedly be automatically oriented towards the location from where the sounds emanated. The same effect occurs when someone calls your name in a crowded restaurant. Despite the loud noises surrounding you, you can't help but notice that someone called your name.

The characteristic visual distortions (e.g. increased colour brightness and purity) elicited by high doses of psilocybin result primarily from the binding of psilocin to 5-HT_{2A} receptors in layer 5 of pyramidal neurons in V1 (see, for example, Madsen et al., 2019). Activation of the 5-HT_{2A} receptor elicits both excitation and inhibition. 5-HT_{2A} receptor activation increases local levels of glutamate (the brain's main excitatory neurotransmitter), resulting in hyperexcitation of local cortical neurons in V1 (Ceglia et al., 2004; Ciranna, 2006; Torres-Escalante et al., 2004).

Psilocin binding to 5-HT_{2A} receptors in V1 thus imitates local cortical excitation mediated by exogenous attention.[4] This hyperexcitation in V1 may explain why subjects on psilocybin commonly report colours becoming phosphorescent in intensity (Cott & Rock, 2008, p. 363; Hartman & Hollister, 1963), which is consistent with findings indicating that psilocybin increases signal amplitudes (the physical correlates of intensity) in V1 during visual imagery (Nichols, 2016).

Elevated levels of glutamate in V1 also activate interneurons that connect V1 with the thalamus (Kim et al., 2020). There is also evidence to suggest that psilocin can activate these interneurons directly (Markram et al., 2004). Activation of these interneurons leads to an increased release of gamma-aminobutyric acid (GABA) (the brain's main inhibitory neurotransmitter) into the thalamus, which in turn disrupts the attentional gating mechanisms in the thalamus. Disruption of the gating mechanisms reduces the thalamus's ability to detect and filter out irrelevant or random noise from the visual signal (e.g. unattended stimuli or internally generated neural activity) before forwarding it to the visual cortex for further processing (Kim & McCormick, 1998; Markram et al., 2004; Vollenweider & Smallridge, 2022). In the presence of psilocin, incoming visual signals contain a great deal of noise. The brain's

[4] There is also evidence to suggest that psilocin binding to 5-HT_{2A} receptors in layer 5 pyramidal neurons causes the formation of additional dendrites (receiving ends) of these neurons, which improves neural transmission and may be a reason for the persistent positive effect on mood disorders (DiBerto & Roth, 2021).

visual system treats the noisy signals as it would ordinarily treat high-precision signals, meaning that the brain attempts to make sense of highly noisy, or low-precision, signals.

Psilocin also binds to 5-HT_{2A} receptors in layer 5 pyramidal cells in the brain's prefrontal cortex, which is even more densely populated with this receptor subtype. Direct binding of psilocin to interneurons linking the prefrontal cortex with the thalamus coupled with excessive glutamate levels in the prefrontal cortex increases the release of GABA into the thalamus. GABA subsequently inhibits activity in the thalamus, which increases the inflow of information to the prefrontal cortex.

The hypothesis that psilocin binding in the prefrontal cortex has an inhibitory effect on the thalamus has received additional support from functional magnetic resonance imaging (fMRI) studies indicating decreases in the cerebral blood flow and the blood-oxygenation-level-dependent (BOLD) imaging signal in the thalamus (Carhart-Harris et al., 2012; Lee & Roth, 2012; Tagliazucchi et al., 2014). The detection of decreased blood flow and deoxygenated blood in the thalamus demonstrates that psilocin inhibits the thalamus' ability to tune for attended stimuli.

Moreover, fMRI and MEG studies have linked psilocin binding at the 5-HT_{2A} receptor in the prefrontal cortex to desynchronous default cortical activity and network disintegration (Carhart-Harris et al., 2012; Muthukumaraswamy et al., 2013; Wood et al., 2012). As in the case of the visual cortex, psilocin activity in the prefrontal cortex also increases the release of glutamate, causing transient local hyperexcitation. Desynchronous default cortical activity, local hyperexcitation, and an increased inflow of sensory information from the thalamus compromise this hub's capacity to constrain thought processes and prevent an overly explorative or 'unconstrained' mode of thinking.[5] Indeed, this is the main reason psychedelic experiences are often described as mystical or transcendent (see, for example, Stenbæk et al., 2021). The temporary lifting of the normal constraints on thinking can trigger non-linear thought processes and increased or more distant associations (Bayne & Carter, 2018; Deshon et al., 1952, p. 47; Swanson, 2018).[6]

[5] Doss et al. (2022) argue that psilocin binding at 5-HT_{2A} receptors in the claustrum—which connects to cortical (e.g. the prefrontal cortex) and subcortical brain regions (e.g. the thalamus)—may result in a decoupling of connections between the claustrum and the prefrontal cortex. This, in turn, may account for impaired executive cognitive functioning.

[6] The classification of associative responses into immediate, intermediate, and distant responses reflects how predictable the connection is between a cue and the associative response. For example, if the cue is 'husband', then 'wife' is an immediate response, 'man' is intermediate, and 'stupid' is distant.

Psilocin has been found to affect executive cognitive capacities differently, with a greater impact on top-down attention (e.g. attentional tracking) than visual working memory (e.g. working memory for sequences of events). To measure attentional tracking, Olivia Carter et al. (2005) presented participants with 20 moving dots on a grey background; two (of a total of eight) dots were cued as targets by a change in colour (Figure 5.4A). To begin the trial, participants clicked the right mouse key, which made the cued dots change back to their original colour, thereby becoming visually indistinguishable from non-targets. After 3 s, the dots would stop moving, and one of the original targets

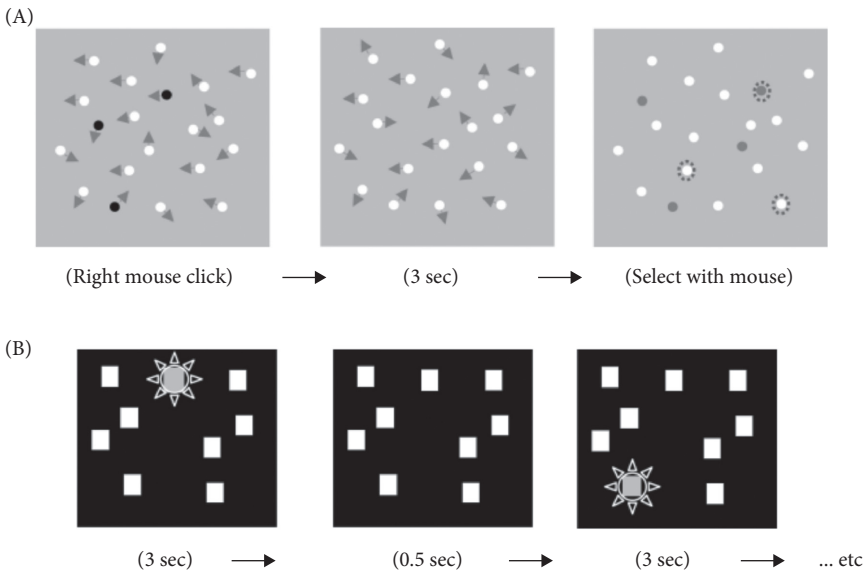

Figure 5.4 (A) The 20 moving dots on a grey background, two to eight of which were cued as targets (three cued targets are shown in black in the first image on the left). To begin the trial, the participants clicked the mouse key, after which all the dots became visually indistinguishable. After a 3 s delay, the dots came to a halt, and one of the original targets and three non-targets changed colour to orange (shown with a dotted outline for the target and grey for non-targets in the last image on the right). Participants were then asked to select the original target among the orange dots. (B) The visual working memory stimuli consisting of nine white boxes randomly placed on a black background. Two to nine of these boxes were subsequently highlighted one at a time by a change in colour (shown in grey in the first and last images). Participants were then asked to recall the sequence of highlighted boxes from memory by clicking on them in the right order.
Image adopted from Carter et al. (2005).

and three non-targets would change their colour to orange. At the end of the trial, participants were asked to identify which of the orange dots was the original target.

To measure visual working memory, the experimenters presented participants on psilocybin with nine white boxes randomly placed on a black background (Figure 5.4B). Of the nine white boxes, two were subsequently highlighted, one at a time, by a brief change in colour. At the end of the trial, participants were asked to recall the sequence of highlighted boxes from memory by clicking on them in the right order.

The results revealed only a negligible effect of psilocybin on the visual working memory task (Figure 5.4B) but there was a substantial effect on the attentional tracking task (Figure 5.4A). Previous studies found that 5-HT_{2A} antagonists can prevent perceptual effects of subsequent psilocybin intake by obstructing psilocin binding to the 5-HT_{2A} receptors (Kometer et al., 2012; Vollenweider et al., 1998). However, the administration of a 5-HT_{2A} antagonist to select participants did not reduce attentional impairments. The attentional impairments seem instead to have resulted from psilocin's inhibition of 5-HT released from raphe neurons, suggesting that 5-HT plays a critical role in the normal function of endogenous (top-down) attention. The totality of this evidence supports the hypothesis that the psychedelic effects of psilocybin occur primarily as a result of a modulation of the brain's attentional mechanisms.

5.3 Psychedelic experiences and Predictive Processing

An increasingly common way to account for ordinary visual perception is to appeal to predictive processing. Researchers have recently suggested that the PP framework can provide a model of the brain mechanisms accounting for altered visual experiences caused by psychedelic drugs, including psilocybin (Carhart-Harris & Friston, 2019). The following paragraphs show that the PP model of visual perception lacks the resources to account for the mechanism underlying psychedelic experiences.

In recent years, advocates of PP accounts of cognitive and neural processing have argued that the PP framework can offer a unified account of the psychedelic effects of classic hallucinogens, such as LSD, psilocybin, and mescaline (Carhart-Harris & Friston, 2019; Pink-Hashkes et al., 2017; Swanson, 2018). We are highly sceptical of this claim, and address one of the specific PP proposals below. But first we provide a general explanation of why we think the PP

framework is ill equipped to explain the mechanisms underlying psychedelic experiences.

The crux of the PP framework can be articulated as follows (see, e.g. Clark, 2016; Friston, 2009, 2010; Hohwy, 2013). Generative models at different levels of perceptual processing yield predictions (or perceptual hypotheses—see Hohwy, 2013) about the distal cause of the sensory signals that are assigned different Bayesian probabilities in accordance with Bayes' Theorem, which can be mathematically formulated as follows:

$$P(H \mid E) = \frac{P(H) \cdot P(E \mid H)}{P(E)}$$

where *E* is the incoming visual signal, and *H* is a hypothesis, or prediction, about the distal object. *P(H)* is the prior probability of *H* before the system receives signal *E*. *P(E|H)* is the likelihood, that is the probability of receiving signal *E*, given hypothesis *H*. *P(H|E)* is the posterior, that is the probability of *H* given E, and *P(E)* is a normalizing constant.

The model-generated predictions are sent down the perceptual hierarchy, where they are compared to incoming sensory signals, yielding a prediction error signal. Because predictions suppress congruent incoming sensory signals, the prediction error signals only convey information about the unexplained components of the sensory signal, which is then used to generate better predictions. This process continues until the system converges on a coherent or 'good enough' perceptual representation of the distal cause of the sensory signal. Perception, within the PP framework, is thus the process of arriving at a coherent or good enough representation of the distal cause by minimizing prediction error (Clark, 2016; Friston, 2009, 2010; Hohwy, 2013).

In the PP framework, not all prediction errors are given the same weight in the revision of predictions (or the models that generate them). How much weight is assigned to a prediction error signal depends on how precise the signal is predicted to be. High-precision signals tend to be far more reliable than low-precision signals. So, if a prediction error signal is predicted to be highly precise, the prediction error encoded by the signal contributes significantly to the revision of the prediction. If, by contrast, the signal is predicted to have low precision, then the signal is attenuated, and the encoded prediction error does not lead to a revision of the prediction (Hohwy, 2013).

The upshot is this: on the PP framework, the perceptual system does not just try to predict the hidden causes of sensory signals, it also tries to predict the

precision of these signals. Like expected causes, expected precisions are based on statistical regularities extracted from past experiences. For example, the brain takes foggy viewing conditions to be statistically correlated with imprecise, or noisy, visual signals. So, in foggy viewing conditions, prediction error signals are attenuated, and existing predictions guide the brain's expectations about its environment.

Though the PP framework may seem innocuous at first glance, it makes two controversial claims (Clark, 2016; Friston, 2010; Hohwy, 2013). The first is that prediction error minimization is the only fundamental cognitive kind needed to explain all mental processes. The second is that all bottom-up processes are prediction error signals. In what follows, we argue that psychedelic experiences present a problem case for both of these core claims.

Recall that within the PP framework, the perceptual system deals with the expected precision of an incoming signal by attributing gain to the signal in accordance with its expected precision (Clark, 2016, pp. 53–59; Hohwy, 2013, pp. 64–66). The greater the expected precision of a signal, the greater the gain of the signal. So, signals expected to be low in precision do not play any significant role in the revision of predictions or models. Instead, the perceptual system relies almost entirely on its previously acquired information. When the sensory signal is predicted to have a high precision, the gain is high, and the signal plays a significant role in the revision of the hypothesis and model.

Ordinarily, the perceptual system is able to predict with fairly high reliability that a noisy signal has low precision. This, in turn, attenuates the signal's effect on hypothesis generation and revision. However, psilocybin impairs the perceptual system's ability to reliably estimate the precision of incoming signals. As the perceptual system is unable to reliably gauge the precision of incoming signals, it does not attenuate low-precision signals, as posited by PP (e.g. as it is developed by Hohwy, 2013). Psychedelic experiences thus present a counterexample to PP.

The signals that enter the sensory cortices as a result of the destabilization of the attentional gating mechanisms in the thalamus are low-precision (noisy) signals, but the perceptual system fails to predict their low precision and therefore does not attenuate them. Despite not being attenuated, the randomly generated predictions are not updated in light of their failure to match the low-precision signals. So, the low-precision signals do not encode prediction errors, which runs counter to the two aforementioned central premises of PP, namely that all the perceptual system does is minimize prediction errors and all bottom-up signalling is prediction error signalling.

Before dismissing the claim that the PP framework can accommodate psychedelic experiences, let's briefly look at a proposal set forth by Carhart-Harris and Friston (2019). They argue that the PP framework is well equipped to provide a unified model of the brain mechanisms underpinning psychedelic experiences caused by classic hallucinogens such as LSD, psilocybin, and mescaline. The principle of action of classic psychedelics, they argue, is to relax the overall state of the brain, which occurs when the psychedelic binds to the 5-HT_{2A} receptors primarily in the highest levels of the cortex and to a lesser extent in lower levels of the cortex (e.g. the visual cortex). The relaxing of the overall state of the brain results in low precision being assigned to prior beliefs.

In the normally functioning brain, prior beliefs of high precision suppress prediction error signals, thereby preventing these signals from revising our prior beliefs. However, Carhart-Harris and Friston (2019) argue that, under the influence of psychedelics, the low precision assigned to our prior beliefs allows new information to revise those antecedent beliefs. To illustrate how the relaxing of the brain can distort visual perception, they invite us to consider a case where it appears that the walls of your living room are breathing. Normally, the prior belief that walls do not breathe is assigned such a high probability that it effectively suppresses or constrains all prediction error signals suggesting otherwise. But under the influence of psychedelics, this prior belief is assigned very low precision, which means that it will no longer suppress and constrain signals carrying the information that your walls are breathing. Your brain thus settles on a perceptual representation of walls as breathing.

The problem with this PP account of psychedelic experiences, however, is that when prior beliefs are assigned very low precision, they are essentially muted. But if that is the case, how are prediction error signals generated? The PP framework holds that prediction error signals originate in mismatches between high-precision predictions and incoming sensory signals. But if psychedelics lower the precision of prior beliefs about its surroundings (e.g. Hohwy, 2013), then there are no high-precision predictions to be matched to incoming sensory signals. As a result, no prediction error signals can be generated. Indeed, given that the PP framework insists that the only bottom-up processes are prediction error signals, the lack of suitable high-precision predictions seems to render the process by which psychedelic experiences are elicited mysterious. These considerations indicate that the PP framework is ill equipped as a model of psychedelic experience.

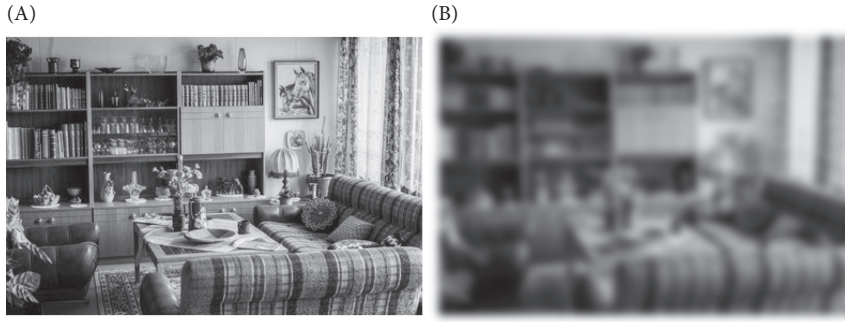

Figure 5.5 (A) *Left*: Original photo of a living room. (B) *Right*: Living room scene gist.

5.4 Gist perception and psychedelic experiences

On an alternative account of perceptual processing, namely GTP, visual perception begins with the brain extracting the gist of an object or scene (Brogaard & Sørensen, 2024, in press b). We have known for quite some time that the visual system extracts a great deal of information from a single glance (20–300 ms) at a scene (Biederman et al., 1974). Object and scene gists consist of spatial low-frequency information. The spatial low-frequency information contained in object gists includes information about the contour of the object and its surface pattern (Figure 5.5). The spatial low-frequency information contained in scene gists includes information about object contours, object surface patterns, global scene layout, and statistical scene regularities (e.g. toilets are frequently found in bathrooms) learned from past exposures to similar scenes (Figure 5.5B) (Auckland et al., 2007; Bar, 2004; Oliva & Torralba, 2007; Schyns & Oliva, 1994). Scene context can facilitate object recognition. Seeing a blurry image next to your nightstand in the dark of night, for example, can help identify the object in the scene as a lamp (Figure 5.6A).

Studies indicate that object and scene gists are rapidly projected from V1 to the orbitofrontal cortex (OFC) in the prefrontal cortex via a magnocellular pathway (Kveraga et al., 2007). Here, object and scene gists activate compatible, generic object or scene categories (e.g. the object category of table lamp or the scene category of living room). The spatial high-frequency information contained in the visual signal is also processed more slowly in a partial bottom-up fashion in the visual perceptual stream, starting in V1 and ending in the inferior temporal (IT) cortex (Bar et al., 2006; Torralba et al., 2006). The lower regions of the visual perceptual pathway make predictions about the low-level

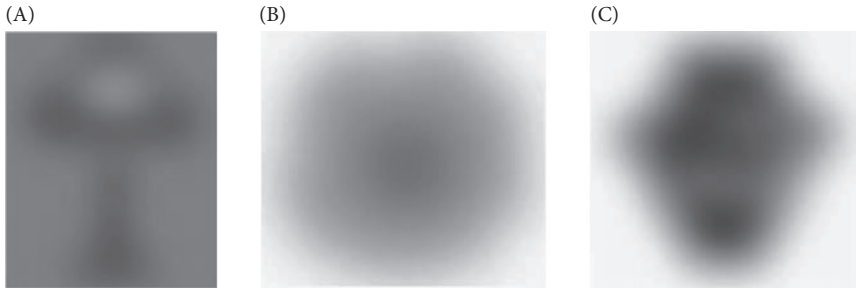

Figure 5.6 Photos (256 pixels) of familiar objects: a lamp (A), a flower (B), and a vase (C), respectively. Each is filtered to include only low spatial frequency information (0–4 cycles/picture). The photos represent object gists consisting of spatial low-frequency information extracted from visual signals in the primary visual cortex for rapid projection to the prefrontal cortex. Here, the object gists activate compatible object categories (e.g. the category of table lamp).
Images adopted from Bar (2003).

features of the distal object (e.g. luminance contrast, texture, and sharp edges) by using well-defined low-level visual processes, such as double-opponent processes, to process the spatial high-frequency information of the visual signal. The partially processed spatial high-frequency information is then matched with the activated object or scene categories in OFC, resulting in a categorization of the partially processed visual information. The categorized visual information is finally encoded as a perceptual representation in working memory.

Because psilocybin disrupts the attentional gating mechanism in the thalamus (see, for example, Brogaard, 2013), the influence of psilocybin results in V1 extracting object and scene gists from a noisy, or low-precision, visual signal and projecting them to the prefrontal cortex. The higher the dose of psilocybin, the more noise is reflected in the object and scene gists. In an attempt to make sense of the noise contained in the object and scene gists, the brain may miscategorize some of the incoming visual information. The miscategorizations of the noise contained in the gists can result in a perceptual representation of familiar shapes being superimposed on to the visual scene. A simulation of a psychedelic experience where familiar shapes of animals and body parts are superimposed on the natural scene can be seen in Figure 5.7B. Here, the vegetation, the rocks, and the water passing through are seen as eyes, birds, and animals.

A version of this phenomenon, where the brain turns an indeterminate stimulus into a familiar one, is fairly common in ordinary visual

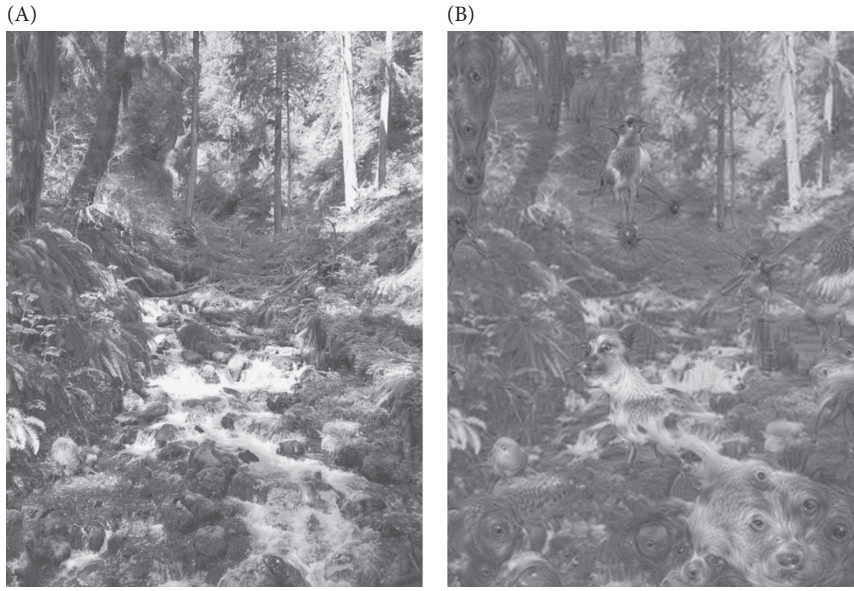

Figure 5.7 (A) An ordinary experience of a water stream. (B) A corresponding (simulated) psychedelic experience in which eyes and animal shapes are seen in a water stream.
Source: Wikimedia Commons.

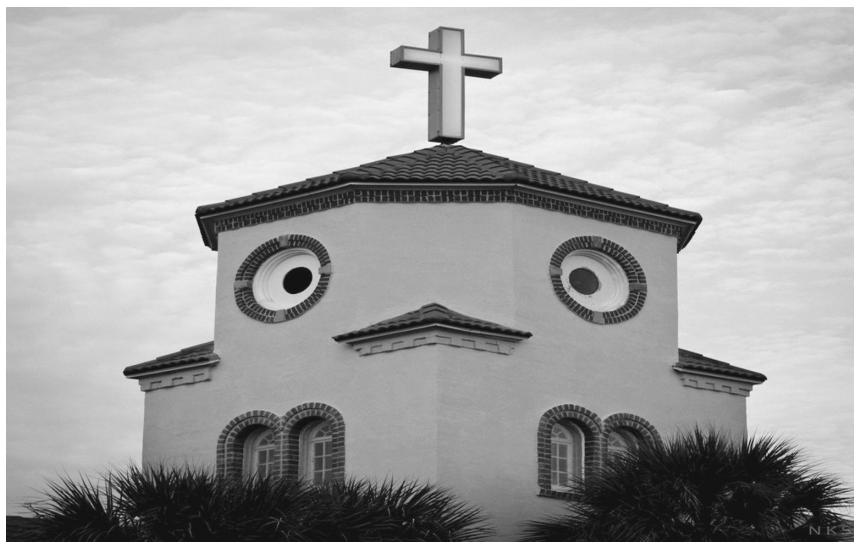

Figure 5.8 The psychological phenomenon known as 'pareidolia' causes us to see a chicken face in the church.
Source: Wikimedia Commons.

Figure 5.9 Still picture from high-dose psilocybin (mushrooms) trip simulation video.
Source: https://youtu.be/tFiNwrY-dSA

experience. This phenomenon is also known as 'pareidolia'. Common examples of pareidolia include seeing faces or animals in things such as clouds, rocks, or buildings. In Figure 5.8, for example, the spatial arrangement of the church, consisting of the two round windows and a tilted corner roof, elicits a pareidolic experience of a chicken's face.

The psychedelic experience shown in Figure 5.7B bears a striking similarity to the ordinary phenomenon of pareidolia.

At moderate doses of psilocybin, the lower levels of noise may not make any noticeable difference to the object and scene gists projected directly from V1 to the prefrontal cortex. But low-level visual processing is more meticulous and, therefore, more sensitive to noise. In the presence of noise, the calculations of the edges of objects are much less precise than in ordinary circumstances. Due to the lack of precision, each new incoming signal will result in somewhat different calculations of the edges of objects. As the edge of the object is determined to be in different locations at different times, the object looks like it is contracting and expanding over time, thereby giving rise to the appearance of breathing, as is evident in video simulations of psychedelic experiences.[7] As

[7] See, for example, this high-dose psilocybin trip simulation video: https://youtu.be/tFiNwrY-dSA (accessed 30 January 2022).

the psychedelic brain determines the edge of the object to be in different locations at different times, a still picture from a video simulation of a psychedelic experience of an object as 'breathing' is bound to make the object look blurry, or as if it is lacking precise boundaries (Figure 5.9).

Although psychedelics can result in blurry experiences (Hollister & Hartman, 1962), the blurriness of the still picture in Figure 5.9 of the simulated psychedelic experience is an artefact of the simulated psychedelic experience being artificially captured at a fixed time.

The gist account can also provide an explanation of the enhancing effects of psychedelics on the appearance of colours, causing them to look purer (or more saturated) and more intense than they would in ordinary visual experience. On the gist account, spatial high-frequency information from the incoming visual signal is processed in the lower areas of the visual perceptual stream in a partially bottom-up fashion. This lower visual processing results in the experience of colour intensity (or brightness), purity (or saturation), and hue. The perceived brightness of an external surface is not only determined by the luminance of the surface but also by the luminance of its surroundings (Kinoshita & Komatsu, 2001). Specifically, the perceived brightness of an external surface is the result of the pattern of activation of V1 neurons sensitive to the luminance of both the surface and its surround (Kinoshita & Komatsu, 2001; Morland et al., 1999). The experience of colour purity and hue as separate dimensions of colours, by contrast, occurs further upstream, presumably in the V4/V8 colour region (Heywood & Kentridge, 2003; Kentridge et al., 2004). However, there is evidence to suggest that the pattern of activation of V1 neurons in response to chromatic contrast (where 'chroma' contains information relating to both colour purity and hue) can affect the appearance of the purity of surface colours (Johnson et al., 2001, 2008). As we have seen, psilocin binding at layer 5 pyramidal neurons in V1 results in hyperexcitability of local V1 neurons. Given the dominance of luminance- and chroma-sensitive neurons in V1, psilocin is likely to cause hyperexcitability in the latter type of neurons. The appearance of enhanced brightness and colour purity of an external surface under psilocybin intoxication may thus be the result of hyperexcitability of luminance- and chroma-sensitive V1 neurons.

The gist account is also compatible with the findings that high doses of psilocybin impair endogenous attention, such as attentional tracking. As shown in Section 2, the available evidence suggests that psilocin distorts large-scale prefrontal networks, while simultaneously inhibiting the release of 5-HT from raphe neurons in the prefrontal cortex. As we have shown, the distortion of

large-scale prefrontal networks and the reduced release of 5-HT seem to contribute to the impairment of endogenous attention.

The above considerations indicate that GTP is better equipped than the PP approach to provide a unified model of the perceptual mechanisms underpinning psychedelic experiences caused by classic hallucinogens such as LSD, psilocybin, and mescaline.

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