Perception is in the Details: A Predictive Coding Account of the Psychedelic Phenomenon

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Abstract

Psychedelic substances are used for clinical applications (e.g., treatment of addictions, anxiety and depression) as well as an investigative tool in neuroscientific research. Recently it has been proposed that the psychedelic phenomenon stems from the brain reaching an increased entropic state. In this paper, we use the predictive coding framework to formalize the idea of an entropic brain. We propose that the increased entropic state is created when top-down predictions in affected brain areas break up and decompose into many more overly detailed predictions due to hyper activation of 5-HT_{2A} receptors in layer V pyramidal neurons. We demonstrate that this novel, unified theoretical account can explain the various and sometimes contradictory effects of psychedelics such as hallucination, heightened sensory input, synesthesia, increased trait of openness, 'ego death' and time dilation by up-regulation of a variety of mechanisms the brain can use to minimize prediction under the constraint of decomposed prediction.

Keywords: predictive coding; psychedelics; level of detail; Bayesian networks, Lysergic acid diethylamide, Psilocybin.

Introduction

A recent review paper (Nichols, 2016) examines both the current scientific knowledge regarding psychedelics as well as the many positive results in clinical experiments using psychedelics to treat depression and addiction. The brain, under the influence of psychedelics, has been described as 'being in more states than usual' (Carhart-Harris et al., 2014), based on an increased activity in a number of specific brain networks such as the default mode network. They suggested that this higher variance of activity allows for enhancement of the repertoire of possible states over time, and introduced the term *Entropic Brain* to describe this higher entropic state. On a more implementational level, the current consensus is that psychedelics cause their effects by being (partial) agonists of serotonin, i.e., 5-hydroxytryptamine 2A (5-HT_{2A}) receptors, with particular importance to those expressed on apical dendrites of neocortical pyramidal cells in layer V. The 5-HT_{2A} receptors are excitatory receptors, making the neurons more likely to fire.

In this paper, we combine both these computational-level and implementational-level insights into a predictive coding account of the effect of psychedelics. We unify notions proposed by Kwisthout, Bekkering, & van Rooij (2017) regarding the importance of the amount of details or granularity of predictions, and Bastos et al.'s (2012) canonical microcircuits for predictive coding. We propose that the increased entropic state is created when top-down predictions in affected brain areas break up and decompose into many more overly detailed predictions due to hyper activation of 5-HT_{2A} receptors in layer V pyramidal neurons. We demonstrate that this novel, unified theoretical account can explain the various and sometimes contradictory cognitive effects of psychedelics such as hallucination, heightened sensory input, synesthesia, increased trait of openness, 'ego death' and time dilation by up-regulation of a variety of mechanisms the brain can use to minimize prediction under the constraint of decomposed predictions.

In the next section we will introduce the main ideas of the predictive coding account. We will then formulize the Entropic Brain hypothesis into a predictive coding account of the psychedelic phenomenon. In the second part of this paper we will show how this formalization can explain the various and sometimes contradictory cognitive effects of psychedelics.

A Predictive Coding Primer

In his book "The Doors of Perception" (1954), Aldous Huxley described some of his psychedelic experiences, which led him to propose the idea that perception is a door between things that are known and things that are unknown. This idea turned out prescient of the contemporary predictive coding account of brain processing. According to predictive coding, perception is a continuous process of combining the brain's previous knowledge with new incoming data by using Bayesian updating, so as to best represent the environmental causes of its sensory input. This enables the brain to predict its sensory inputs. Furthermore, the brain is thought to create a hierarchically ordered model (Friston, 2008). For any

pair of levels, the higher-level will have context-dependent hypotheses predicting the bottom-up signals from lower-levels. The hypothesis that generates the best predictions will determine perception. Calculating which hypothesis generates the best predictions is done by calculating the posterior probability of the hypothesis. The posterior probability combines both the likelihood of the bottom-up input and the prior probability of the hypothesis before receiving the input. This can be seen as an advantageous tactic especially under conditions of noisy unreliable bottom-up data, since previous knowledge can be used to come up with the best hypothesis. The predictions stemming from the best hypothesis inhibit the bottom up incoming data 'explaining it away' (Clark, 2016).

Recently, Kwisthout and colleagues proposed a computational-level distinction between the *precision* of a prediction and the amount of details or *granularity* of predictions (Kwisthout & van Rooij, 2015, Kwisthout et al., 2017). This work has shown that more detailed predictions cause higher prediction errors. This work is based on the idea that higher cognitive functions are better described by categorical probability distributions rather than the traditional Gaussian densities (Friston et al., 2015). An important distinction between Gaussian densities and categorical probability distributions is that in the latter the state space granularity (how detailed are the generative models and the predictions that follow from them) is crucial. Whereas the amount of uncertainty (or precision) in a Gaussian density can be adequately described by its variance, a categorical distribution needs both the state space granularity and the entropy of the distribution to describe its precision (Kwisthout & van Rooij, 2015).

Bastos et al. (2012) have suggested a '*canonical microcircuit*' that provides an implementational-level account of the predictive coding in the brain. The idea of such a canonical microcircuit is that a cortical column contains the circuitry necessary to implements a form of approximate Bayesian inference and that these circuits are replicated with minor variations throughout the cortex. This Microcircuit model is based on evidence showing that superficial pyramidal cells have forward connections to higher areas in the brain hierarchy while deep layers, including pyramidal cells in layer V of the cortex, send back propagating signals to lower areas. Bastos et al. present evidence showing that these backwards connections are inhibitory and can plausibly be seen as implementing the top-down 'predictions' as suggested by the predictive coding framework, while forward connections are plausible realizations of the signals representing 'prediction error'. They further suggest that superficial layers of cortex show neuronal synchronization and spike-field coherence predominantly in the gamma frequencies, while deep layers prefer lower (alpha or beta) frequencies. In essence, they claim that the top down predictions are communicated by lower alpha or beta frequencies while prediction error is communicated by faster gamma frequencies.

Muthukumaraswamy et al. (2013) found, following administration of Psilocybin, a desynchronization of neural activity especially in the slower alpha and beta rhythms, meaning neurons were acting in a more disjoint and separate way, suggesting that the brain was at a higher entropic state. Using dynamic causal modelling they found that this desynchronization is "likely triggered by 5-HT_{2A} receptor-mediated excitation of deep pyramidal cells" (Muthukumaraswamy et al., 2013, p. 15171). While synchronization of post synaptic neuronal groups creating brain wave oscillations are thought to be needed for communication between brain areas and passing of information, the actual information is thought to be found in the a sparse coding of neuron spiking as very specific timings compared to the oscillations (Fries, 2015).

A Predictive Coding Account of the Psychedelic State

As we have seen, the effects of psychedelics stem from the 5-HT_{2A} receptors on pyramidal cells in layer V being activated, lowering the threshold of individual neuronal firing and thus desynchronizing the activity of the neuronal population. We discussed above Bastos et al.'s (2012) view that the information communicated by the synchronous activity of these specific cells is likely to represent the brain's top-down predictions. It is known that within the neocortex, 5-HT_{2A} receptors are not distributed equally and different areas have different binding potentials. Higher binding potentials can be found in prefrontal and visual areas while the motor cortex has lower binding potentials (Forutan et al., 2002). Our theory focuses on the dense band of 5-HT_{2A} receptors in layer V pyramidal cells.

Based on Kwisthout et al.'s (2017) notion of state space granularity in predictions, we suggest that hyper-activation of the cells in layer V decomposes the broad categorical prediction that is usually calculated by this neuronal population into sub categories, creating a set of higher detailed predictions. These decomposed predictions stemming from prefrontal, parietal and somatosensory cortex are sent backwards to lower layers of the cortical hierarchy. The decomposed higher detailed prediction that has the highest posterior probability now dominates perception. However, under most conditions, no matter which of the higher detailed decomposed predictions best fits the data, it will still fit less data than the 'usual' broad prediction. This will cause a higher level of bottom up prediction error. As we shall see in the second part of the paper, the compensatory mechanisms called to deal with this higher level of prediction error can explain the wide variety of psychedelic effects.

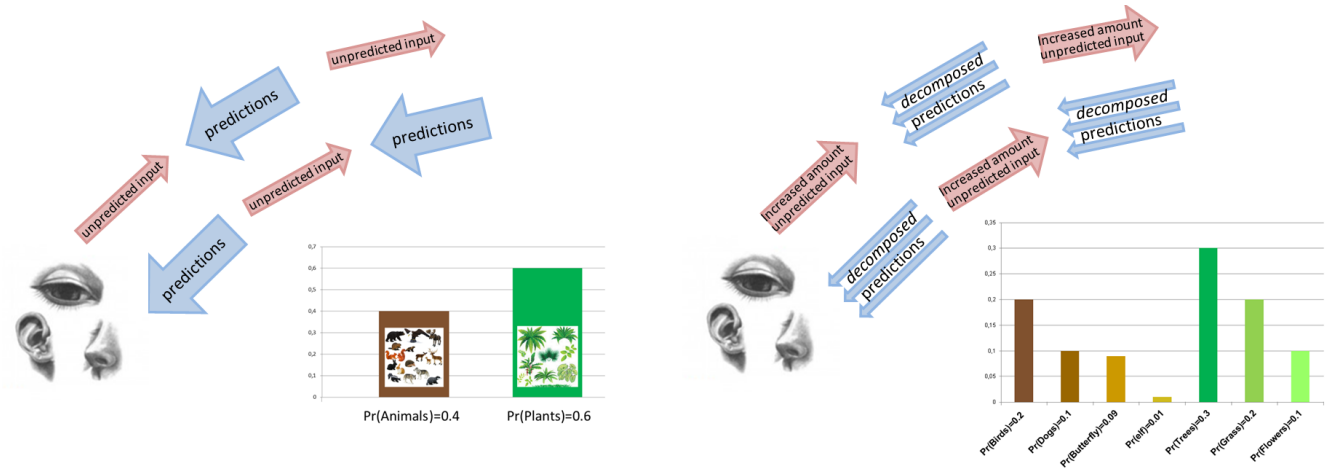

Figure 1. The predictive coding account assumes that the brain generates predictions using a cascading hierarchy of generative models, processing only that part of the inputs that was unpredicted. Under normal circumstances one might predict to observe animals or plants, and interpret the inputs in a likewise manner (left panel). We suggest that after administration of psychedelics these predictions become more decomposed, leading to more fine-grained, very specific predictions, each of which has a fairly low probability. This will in general lead to a higher prediction error and unstable predictions (right panel). Figure adapted from Clark (2016).

To clarify further what a decomposed set of predictions means, imagine a person walking in the forest receiving some sensory input (Figure 1). Under regular conditions the set of her predictions might be P(Animals) = 0.4, P(Plants) = 0.6. The relatively low entropy of these predictions can be computed to be $H = -\sum p_i \log_2(1/p_i)$ = 0.97 bits. This means there is relatively little uncertainty regarding these possible predictions. Now let us imagine this person is under influence of psychedelics. Under this condition her set of predictions will be decomposed, for instance: P(Birds) = 0.2, P(Dogs) = 0.1, P(Butterfly) = 0.09, P(Elf) = 0.01, P(Trees) = 0.3, P(Grass) = 0.6, P(Flowers) = 0.1. As we can see, the main categorical predictions of 'Animals' and 'Plants' break up, each into more detailed sub categories. These decomposed predictions bring about a higher entropic state, $H = -\sum p_i \log_2(1/p_i)$ = 2.49 bit. In most cases this will result in higher prediction error from lower layers as these decomposed predictions 'explain away' less of the prediction error from lower layers than normal. The 'extra' predictions being activated are likely to be dependent on a subject's personal experiences and history. In general we should expect a flattening of the prediction distribution, and well-established prediction categories that contain many subcategories will be affected more than predictions with fewer subcategories.

The importance of bottom-up data in this process

A known concept in the psychedelic community is "set and setting". The mind's *set* can be compared to the brain's predictions while *setting* considers the environmental data. When precise environmental data combines with decomposed higher detailed predictions the result will be a uniquely clear perception. This type of perception is commonly described by users and can be read in Aldus Huxley's (1954) description of the vividness of Red Hot Poker flowers he perceived while under the influence of psychedelics. However, due to environmental changes and noise, this clear perception is not likely to stay stable over time. The noisier the bottom-up signal, the more the top-down predictions influence perception (Seth, 2014). Under decomposed predictions, lowering precision of sensory data can result in misclassification of the data. The brain's best explanation for the imprecise 'noisy' data might be one of the sub-threshold predictions that got activated. This will result in a 'hallucination'. Psychedelics are known to both obscure and distort perceptual data as well as add clarity and give the sense of enhanced resolution. These two different sides of the psychedelic state are dependent on the precision of the bottom-up data, i.e., the noisiness of the setting. The more noisy the bottom-up data is, the more likely hallucinations will be.

Prediction error minimization and the psychedelic state

Under normal conditions the brain can decrease prediction error in several ways (Friston et al., 2012; Kwisthout et al., 2017). It could update predictions; lower prediction error by intervening in the world or it may update the causal model that generated the predictions. In this section, we explore how upregulating these mechanisms, in order to deal with the increased prediction error caused by decomposed predictions, can explain many of the documented psychedelic effects. We will investigate the effects of prediction updating, active inference, changing the weight of predictions, and long-term learning effects.

Updating the predictions

As we have explained, in the case of decomposed predictions, a smaller amount of sensory inputs will be explained by any specific prediction. This will cause

increased prediction errors. One mechanism the brain might use to minimize prediction error is to change the prediction distribution. However, as the predictions remain decomposed no prediction will be enough to explain away the prediction error for long and so once again the distribution will change and perhaps this time the probability of an otherwise unlikely input becomes the leading prediction and affects perception. This constant revising of the probability distribution will lead to a destabilization of perception. Objects, scenes and even abstract thoughts will 'morph' and change at a rapid speed; however, each percept reflects the best possible prediction at that moment. A room might look bigger or smaller or the prediction of the light condition might change causing colors to morph. This can be the cause of individuals reporting a tendency to see "multiple viewpoints" (Sessa, 2008).

Predictions from other layers of the brain hierarchy that were not affected by activation of the 5-HT_{2A} receptors can be upregulated by either increasing their relative strength or lowering their level of detail. This will cause the predictions from these layers to enforce their predictions on more of the incoming data. Google's deep neural network 'deep dream'[1] (originally created for identifying images) illustrates how this might happen. By allowing different layers of the network to strengthen their predictions these networks were able to produce hallucinatory effects. Strengthening predictions of lower layers (that identified lines) created images with amplified lines, while increasing predictions from higher level abstract layers (e.g., identifying buildings) created images with 'imaginary' buildings being imposed on the original picture. Further proof that this is actually happening in the brain can be seen in the work of Bressloff et al. (2001). Their simulated attenuated low-level predictions of the visual system (V1) and found remarkable resemblance with geometrical hallucinations drawn by people on LSD. This shows that increased predictions from V1 are likely to be behind the specific geometrical visual hallucination. Furthermore, Carhart-Harris et al. (2016) found that increased cerebral blood flow (CBF) in the visual cortex as well as a greatly expanded functional connectivity profile in V1 correlated strongly with subjects' ratings of visual hallucinations. It is impossible to know at the moment whether the increase in CBF is due to increased predictions errors, upregulating of predictions, or both.

Acting on the Environment

Another mechanism of minimizing prediction error is intervening in the world (i.e., acting on the environment) (Brown, Friston, & Bestmann, 2011). This changes the actual inputs and sets some of the model's parameters and thus decreases uncertainty. Changing the brain's input can happen both in a passive way, for instance by moving one's eyes, or by actively moving objects in the environment. Since 5-HT_{2A} receptors are not as prevalent in the primary motor cortex, top-down prediction from that area wouldn't be as affected and this mechanism is likely to remain intact even under the influence of Psychedelics. This can explain why hallucinations seem to grow stronger while sitting still and can help influence harm reduction policies. By creating motor output, for instance while walking or dancing, the mechanism of active inference (in which motor output minimizes proprioceptive prediction error between the expected and actual position of one's limb, bringing the actual position closer to the expected position; see, e.g., Brown et al., 2011) might enable the brain to lower prediction errors stemming from other parts of the brain too.

Changing Weight of the Prediction Error

While chemical tolerance to Psychedelics drugs should not exist more than a few days after ingestion (Leshner, 2001) many experienced users will admit that the first few experiences feel stronger than later experiences and increased dosage is needed to reach the same state. This might happen as a result of the brain's attempt to minimize prediction error by lowering the weight of the prediction error or attributing this higher prediction error to 'inherent' noise that does not need to be explained. An example of inherent noise that the brain learns to ignore can be seen in a fair coin toss (Kwisthout et al., 2017). Even if you guess the coin will land on 'heads' and then it actually lands on 'tails' no surprise will follow. The brain has learnt that this type of stochastic noise is inherent to a fair coin toss. The same could happen under extended use of psychedelics. The brain could learn that this state is inherently noisier and lower the weight of the prediction error. We can only postulate that this might happen through affecting the dopamine system which has been implicated in precision weighting of prediction error (Friston et al., 2012).

Long Term Learning Effects

Within the predictive coding framework the model constructed by the brain is considered to be encoded in the network connectivity. Changes in this connectivity will lead to long term learning. While learning effects in humans after administration of 5-HT_{2A} agonists have not directly been studied in the last decades an interesting study in rabbits has found that agonists at the 5-HT_{2A} receptor including LSD enhanced associative learning at doses that produce cognitive effects in humans (Harvey, 2003). Using the predictive coding framework, depression, addiction and obsessive compulsive disorders have been suggested to stem from overly strong and narrow predictions from certain networks that get 'stuck' (Edwards et al., 2012) and aren't updated based on the bottom-up data. Momentarily decomposing these predictions by 5-HT_{2A} agonists, especially with a combination of supportive bottom-up information coming from a therapeutic setting, might lead to long term model updates. This could be the reason behind the success of

[1] https://deepdreamgenerator.com/

recent clinical trials that have used 5-HT_{2A} agonist to treat these disorders.

A long term model update that psychedelic are known to cause is increasing the trait of 'openness' (MacLean, Johnson, & Griffiths, 2011). The mechanism we suggest to explain this is as follows. A higher prediction error state caused by administration of 5-HT_{2A} agonists coupled with a positive rewarding setting, leads to surprise becoming a more sought after state. Interest in exploring the unknown and trying new things might grow and people might be 'motivated to enlarge their experience into novel territory' which is what defines the trait of openness (DeYoung et al., 2009).

Psychedelics research findings reinterpreted

In the following section we will re-interpret previous findings in psychedelics research in light of our theoretical account and see how our account can clarify and shed further light on these results.

Kometer et al. (2006) presented so-called *Kanizsa triangles* to subjects after administration of psilocybin. These shapes are perceived as complete triangles and circles rather than the complex shapes that they actually are, because of a top-down learnt prediction. Viewing this shape under normal conditions has been shown to evoke a unique change lowering of voltage as measured on the skull 170ms[2] after presentation of this stimulus. Following administration of Psilocybin, Kometer et al. found a decrease in strength of this ERP suggesting a lower strength of these predictions. This is in accordance with the model of decomposed predictions, since decomposed predictions will indeed cause each prediction to be weaker than normal. This same experiment also found desynchronization of alpha band activity which we have discussed previously.

In a behavioral experiment, Spitzer et al. (1996) found increased indirect semantic priming after administration of Psilocybin. They claim their data suggests that Psilocybin leads to an "increased availability of remote associations and thereby may bring cognitive contents to mind that under normal circumstances remain non-activated" (Spitzer et al., p. 1056). This would indeed be expected if broad categorical 'semantic' predictions are decomposed, activating many more detailed semantic predictions, and allowing for more remote associations to be activated.

Another well-documented effect is known as 'Time Dilation' in which subjective time seems to slow down. A few minutes can subjectively be perceived as taking much longer. Here we postulate that subjective sensation of time is dependent on the amount of prediction error and possibly prediction updates the brain makes in order to minimize prediction error. This idea is based on Ulrich (2006) who discovered that the extent to which a stimulus can be predicted affects time perception, with unexpected stimuli perceived as longer. Similarly, Tse et al. (2004) found that a stimulus which stands out as different from all the others in a series appears to last longer than the other stimuli. An increase of prediction updates might cause the subjective feeling that more time has passed. This is similar to the common feeling that the first day of a journey to another country seems longer because it is filled with so many new experiences and so many prediction updates must happen in that day.

The last phenomenon we would like to touch upon is the notion of 'Ego death' many psychedelic users report. Apps & Tsakiris (2013) describe a predictive coding account of the neural and computational basis of self-recognition. Here, one's body is recognized as the most likely "me". This probabilistic inference arises through the integration of information from hierarchically organized unimodal systems in higher-level multimodal areas. As we have seen, the brain's attempt to minimize increased prediction error induced by psychedelics breaks down this hierarchical structure which might lead to a total inability to distinguish between environment and self and the unique perception of 'oneness' described by many experiencing 'ego loss'. While Apps & Tsakiris' account deals with the 'minimal self', we postulate looking at the 'higher ego' as a collection of high-level relatively inflexible predictions regarding the future behaviour of the 'self-organism' in a variety of situations. Following administration of 5-HT_{2A} agonists these predictions will break up based on the subjective pieces of information compromising this category. This relaxation of otherwise rigid predictions about the self might explain positive results for treatment of depression and addiction after administration of psychedelics that have been reported (Nichols, 2016).

Conclusions

In this paper we presented a computational theory explaining the effects of psychedelics in terms of the predictive coding account of cortical processes. Our theory further explicates the *Entropic Brain* hypothesis (Carhart-Harris et al., 2014) in terms of predictive coding. We proposed that administration of psychedelics cause the brain to make *overly detailed* (i.e., decomposed) predictions of the inputs it receives, leading to an increased prediction error. Crucially, while dopamine is considered to modulate *precision weighting* of prediction errors (Friston et al., 2012), our theory suggests that serotonin might have a role in modulating the *granularity* ("level of detail") of predictions. Our theory explains how a simple lowering of the excitation threshold of the pyramidal neurons in layer V in prefrontal, parietal and somatosensory cortex (caused by administration of 5-HT_{2A} agonists) in fact *decomposes* predictions from those areas, causing increased prediction errors from lower levels in the brain hierarchy. The brain's attempts to minimize these increased prediction errors by active inference, prediction updating, modulation of the weights

[2] This is known as the *N170* event-related potential (ERP).

of prediction errors, or model revision can explain several (and sometimes contradictory) cognitive effects of psychedelics such as hallucination, heightened sensory input, synesthesia, increased trait of openness, 'ego death' and time dilation.

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