

BAYESIAN NEUROSCIENCE OF PSYCHEDELIC DRUGS

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“This is your Bayesian Brain on Drugs: Toward a Predictive Processing Framework for Psychedelic Neuroscience and Phenomenology”

(Forthcoming, 2017)

Luke McGowan, Link Swanson, Katrin Preller, Karl Friston, Franz Vollenweider, Michael Kometer, Matthew Baggott, Christopher Letheby, George Mashour, Philip Corlett, Robin Carhart-Harris, Anil Seth, Timo Schmidt

University of Zurich • Yale University • University of Minnesota • University College London • Imperial College London • University of Sussex • University of Adelaide • University of Michigan, Ann Arbor • California State University, Fullerton

ABSTRACT OF THE PAPER

“We argue that a Bayesian predictive processing account of brain function is a useful framework for developing an integrated, multi-level neuroscience of psychedelic drugs, spanning receptor pharmacology, neuroanatomy, computation, cognition, and phenomenology. The paper extends Bayesian interpretations of drug models of clinical psychosis (delusions and hallucinations) to psychedelic neuroscience. Paradigm perceptual and cognitive effects of serotonergic psychedelics (LSD, psilocybin, DMT) are interpreted within the predictive processing framework. Future research and methodological issues inspired by the framework are considered.”

OUR PLAN FOR THIS TALK

1. -> PSYCHEDELIC RESEARCH IN THE 21ST CENTURY
2. BAYESIAN MODELS IN NEUROSCIENCE
3. BAYESIAN MODELS OF PSYCHEDELIC EFFECTS
4. CONCLUSION & FUTURE DIRECTIONS

PSYCHEDELIC RESEARCH IN THE 21ST CENTURY

PSYCHEDELIC SCIENCE 2017

[About](#) [Conference](#) [Workshops](#) [Cruise & Banquet](#) [Marketplace](#) [Tickets](#) 

April 19-24, 2017 — Oakland, California

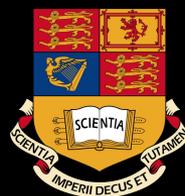
At Psychedelic Science 2017, the international scientific community is coming together at the Oakland Marriott City Center in Oakland, Calif., to explore new research into the benefits and risks of MDMA, LSD, psilocybin, ayahuasca, ketamine, ibogaine, medical marijuana, and more.

CONFERENCE SOLD OUT

[WATCH LIVE](#)

[FULL SCHEDULE](#)

RECENT RESURGENCE OF PSYCHEDELIC DRUG RESEARCH



Imperial College
London



JOHNS HOPKINS
UNIVERSITY



THE UNIVERSITY
of
WISCONSIN
MADISON

CLINICAL STUDIES USING PSYCHEDELIC DRUGS

Psychedelic therapy in recent clinical applications for treating:

- PTSD
- Anxiety
- Depression
- OCD
- Addiction



Rapid and sustained symptom reduction following psilocybin treatment for anxiety and depression in patients with life-threatening cancer: a randomized controlled trial

Stephen Ross^{1,2,3,4,5,6}, Anthony Bossis^{1,2,4}, Jeffrey Guss^{1,2,4}, Gabrielle Agin-Liebes¹⁰, Tara Malone¹, Barry Cohen⁷, Sarah E Mennenga¹, Alexander Belser⁸, Krystallia Kalliontzi², James Babb⁹, Zhe Su³, Patricia Corby² and Brian L Schmidt²



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PSYCHEDELICS AS INVESTIGATIVE TOOLS IN NEUROSCIENCE

Psychedelics are used as probes to investigate the mechanisms of normal perception and cognition:

- Brain imaging
- Receptor pharmacology
- Computational models
- Psychophysics

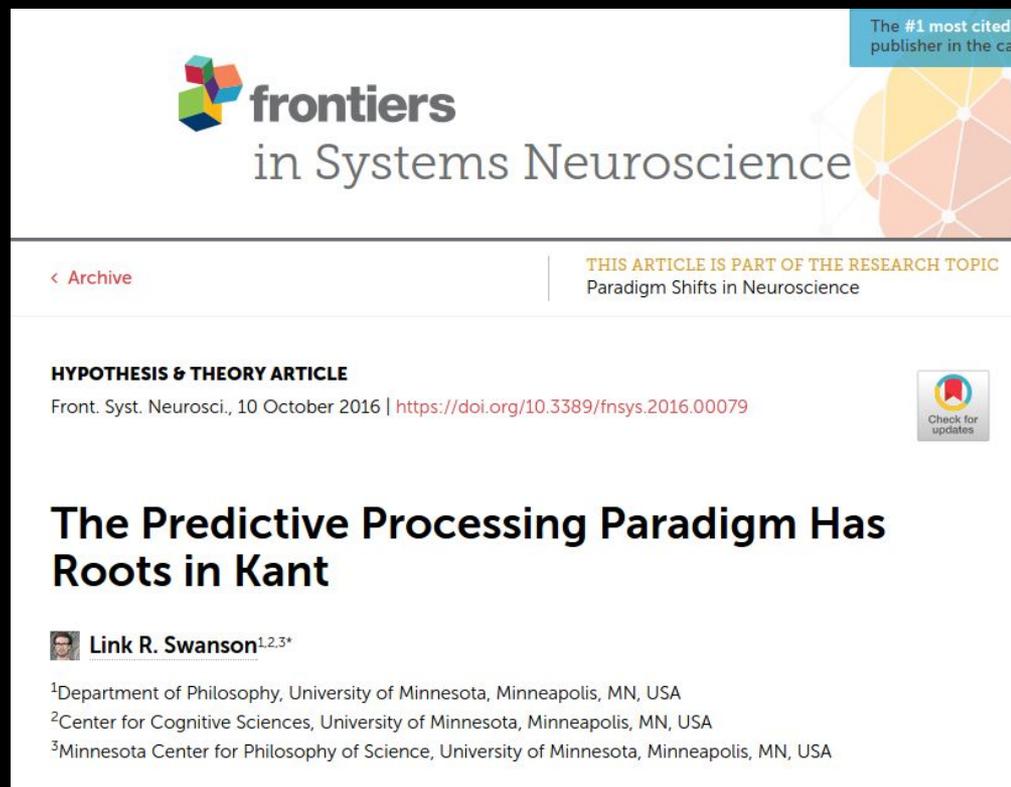


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BAYESIAN BRAIN: OLD IDEAS IN NEUROCOMPUTATIONAL DISGUISE?

- Directly inspired by Helmholtz (1821 - 1894)
- Indirectly influenced by Kant (1781) (see Swanson, 2016)
- ‘unconscious inference’ (Barlow, 1961; Gregory, 1970)
- ‘analysis by synthesis’ (Neisser, 1967)



The #1 most cited publisher in the category

 **frontiers**
in Systems Neuroscience

[< Archive](#) | THIS ARTICLE IS PART OF THE RESEARCH TOPIC
Paradigm Shifts in Neuroscience

HYPOTHESIS & THEORY ARTICLE
Front. Syst. Neurosci., 10 October 2016 | <https://doi.org/10.3389/fnsys.2016.00079> 

The Predictive Processing Paradigm Has Roots in Kant

 **Link R. Swanson**^{1,2,3*}

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³Minnesota Center for Philosophy of Science, University of Minnesota, Minneapolis, MN, USA

BAYESIAN PREDICTIVE PROCESSING



“Brains ... are bundles of cells that support perception and action by constantly attempting to match incoming sensory inputs with top-down expectations or predictions.”

Clark (2013) p.181

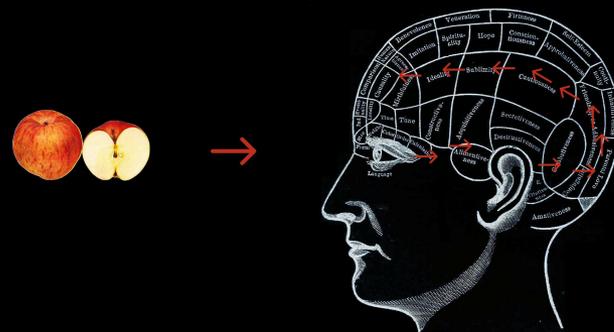
“Neuronal activity encodes expectations about the causes of sensory input, where these expectations minimize prediction error.”

(Kanai et al, 2015)

PERCEIVING THE WORLD:

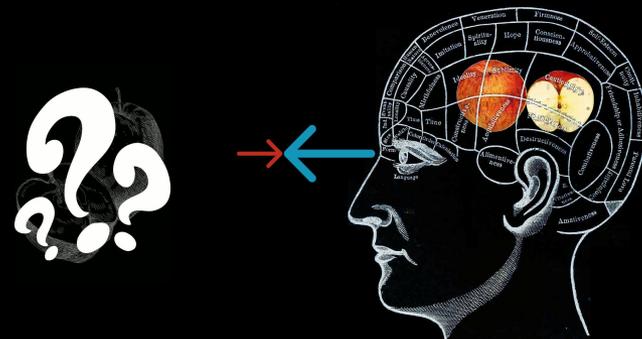
How we usually think of perception:

Sense organs 'detect' external objects and transfer perceptions to the brain

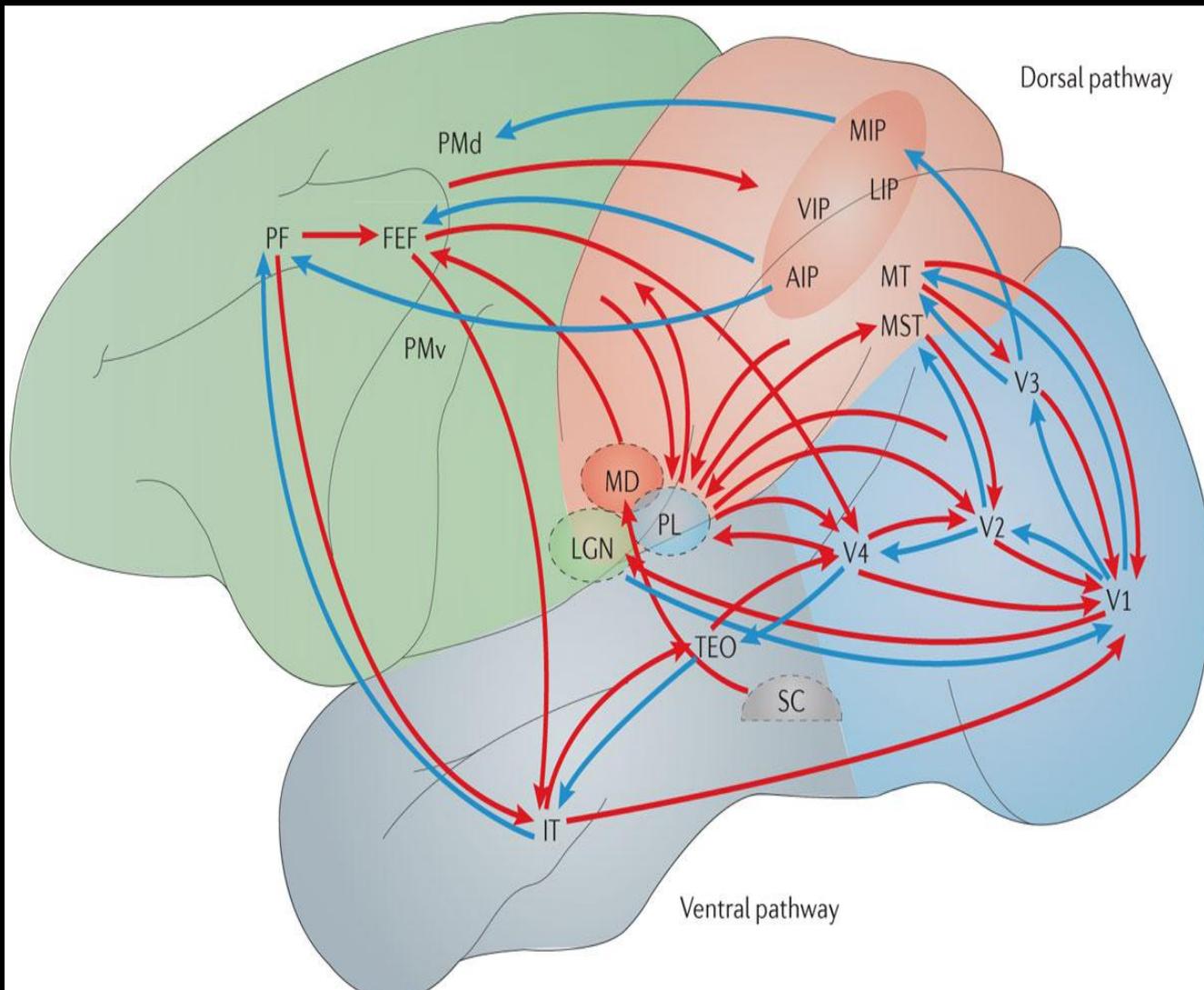


Predictive Processing account of perception:

Brain generates perceptions of the most likely external causes using prior experience/learning



CORTICAL HIERARCHY



IMAGINATION NECESSARY FOR PERCEPTION



“Perceiving and imagining, (if these models are on the right track) are simultaneous effects of a single underlying neural strategy.”

(Clark, 2015a, p. 39)

PERCEPTION AS 'CONTROLLED HALLUCINATION'

- Brains endogenously generate perceptual experience (dreams, hallucinations, perceptual illusions, imagination, mental imagery)
- This same system is used to perceive the external world!



PERCEPTION AS 'CONTROLLED HALLUCINATION'



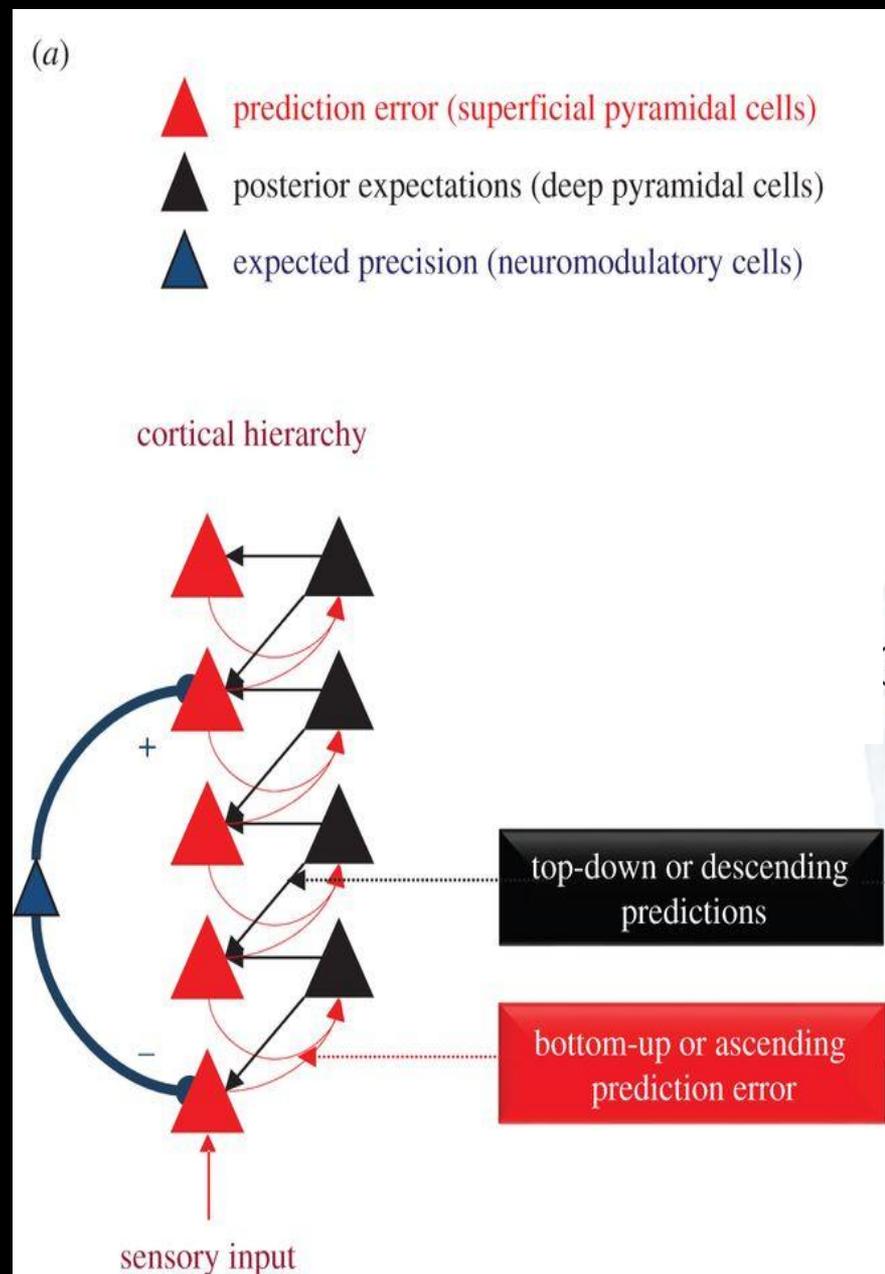
“The [neural] system is trying to generate (at multiple spatial and temporal scales) the incoming sensory signal for itself. When this succeeds, and a match is established, we experience a structured visual scene.”

(Clark, 2015a, p. 14)

PREDICTIVE CODING

“The available evidence suggests that superficial pyramidal cells (red triangles) compare the expectations (at each level) with top-down predictions from deep pyramidal cells (black triangles) of higher levels.”

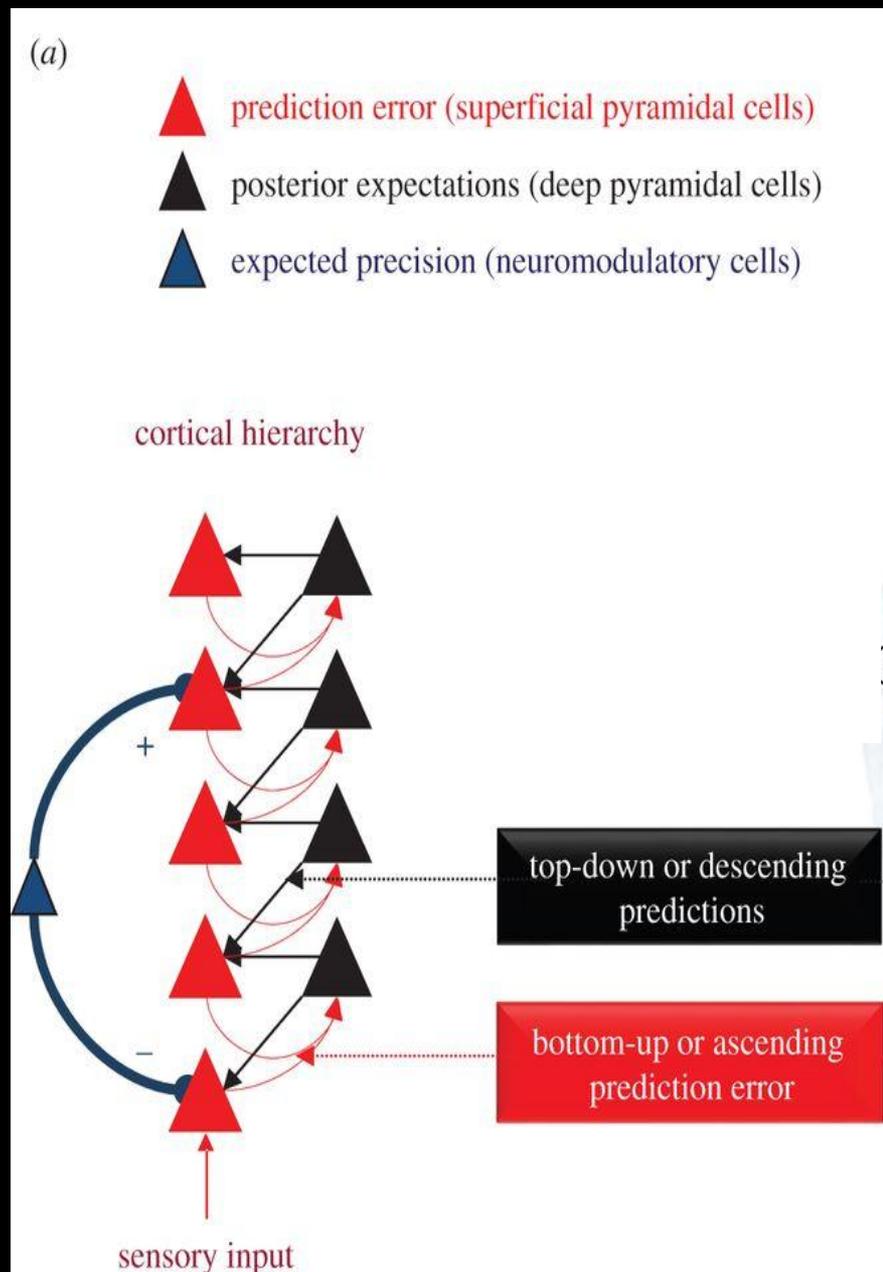
(Kanai et al, 2015)



PRECISION WEIGHTING

“Neuromodulatory gating or gain control (blue) of superficial pyramidal cells that determines their relative influence on deep pyramidal cells encoding expectations.”

(Kanai et al, 2015)



PRECISION WEIGHTING IN PREDICTIVE CODING

- Neuromodulatory gating adjusts the 'gain' (volume) on the prediction errors. This determines the extent to which the errors can trigger new predictions and update prior knowledge (aka, learning).
- Adjusting the gain is also known as 'precision weighting'



prediction error (superficial pyramidal cells)



posterior expectations (deep pyramidal cells)



expected precision (neuromodulatory cells)

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PREDICTIVE PROCESSING AND PSYCHEDELIC EFFECTS

PSYCHEDELIC EFFECTS IN THE PREDICTIVE BRAIN

HYPOTHESIS:

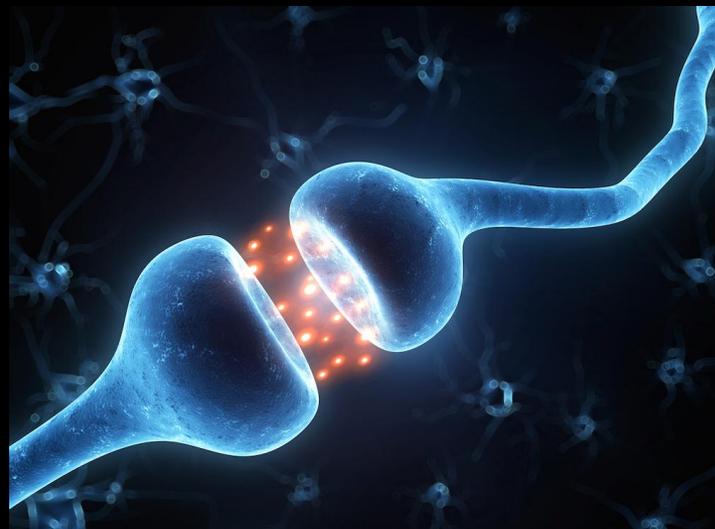
Psychedelic molecules alter neuromodulatory 'gain control' and 'precision weighting' mechanisms that balance predictions/priors with prediction errors in neural systems

YOU GUESSED IT:
PSYCHEDELICS TWEAK YOUR PRIOR PROBABILITIES



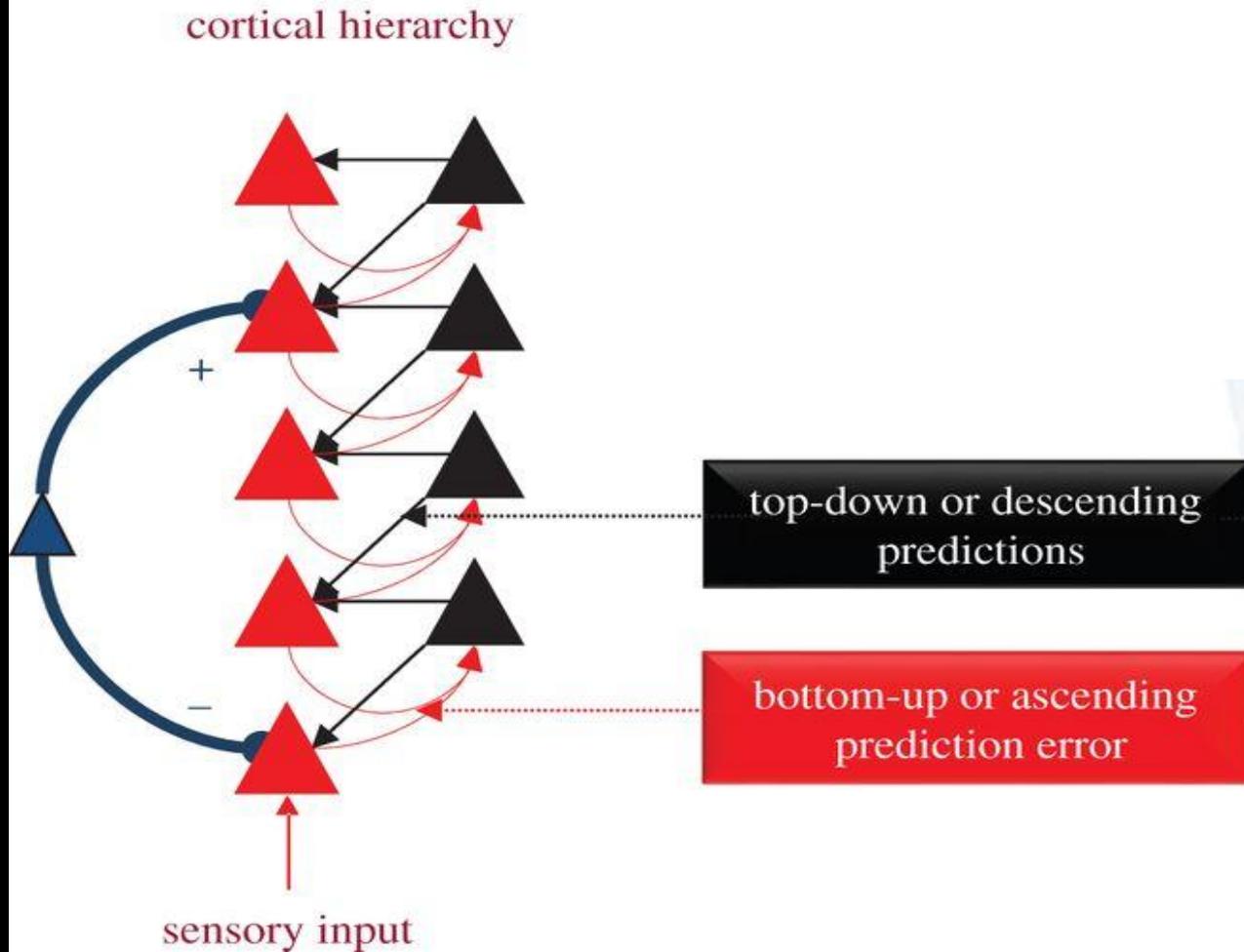
THE BASIC PP NEURAL MECHANISM OF PSYCHEDELICS

- Predictive processing hypothesizes that deep pyramidal cells in layer V are central to top-down predictions
- Psychedelics modulate the 5-HT_{2A} receptors on pyramidal cells in layer V
- Priors can be amplified or dampened
- Priors can be applied in unusual ways
- Prediction errors have less (or more) impact (precision weighting)
- Ordinary constraints are suspended



(a)

-  prediction error (superficial pyramidal cells)
-  posterior expectations (deep pyramidal cells)
-  expected precision (neuromodulatory cells)



PERCEPTUAL EFFECTS OF PSYCHEDELICS

“Visual alterations ranging from illusions to pseudo-hallucinations, and hallucinations ... the perception of more intense colors and textures, geometric shapes, rhythmic movements of objects, micropsia and macropsia, after images of objects in movement, and objects, animals, or subjects which are not present.”

(Preller & Vollenweider, 2016)

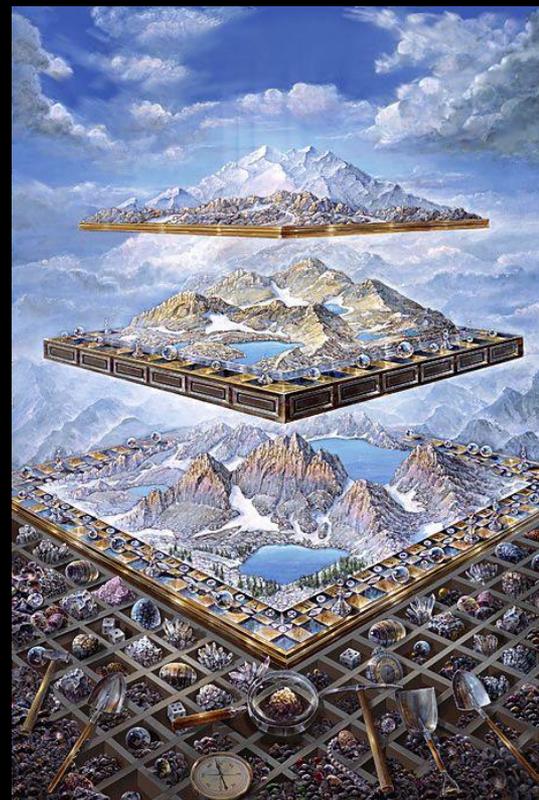




THE DYNAMIC UNFOLDING OF PSYCHEDELIC SESSIONS

“In fact many of the subjects under the influence of a psychedelic drug appear to progress through different stages over time and levels of changes along a perception-hallucination continuum of increasing arousal and ego dissolution.”

(Preller & Vollenweider, 2016)



EGO DISSOLUTION

“At the core of this process is the loosening of self boundaries and the diminishing of the ordinary ego functions which unfolds along a perception-hallucination continuum with increasing arousal to culminate in ego dissolution and a state of oneness with the external world.”

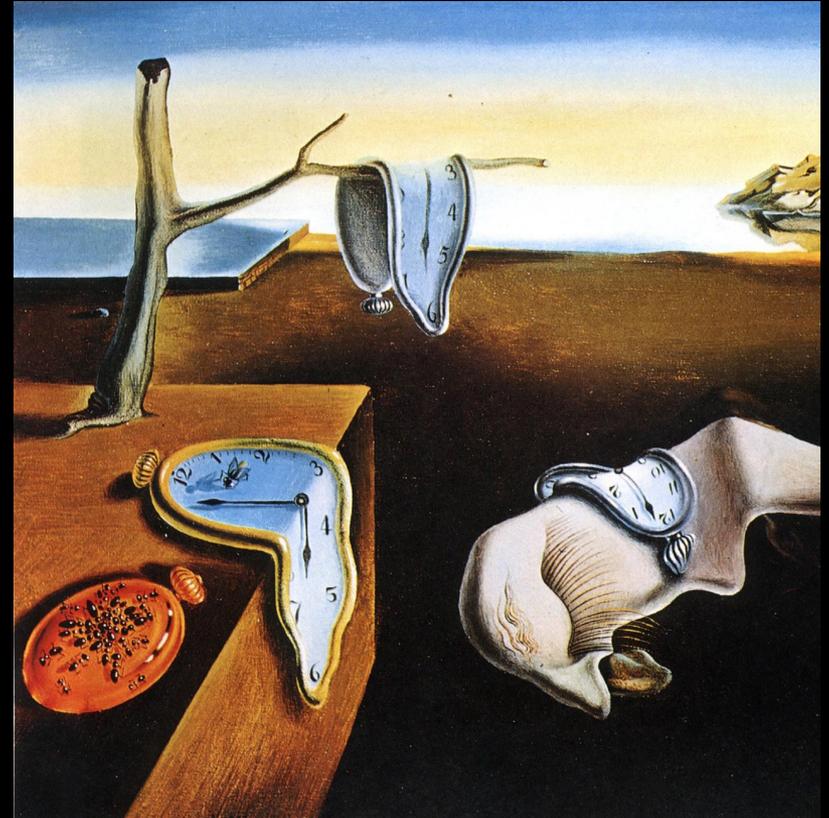
(Preller & Vollenweider, 2016)



TIME PERCEPTION

“Participants reported a feeling of speeding up or slowing down the passage of time, or even a feeling of timelessness, often associated with visual perceptual changes and alterations in self experience.”

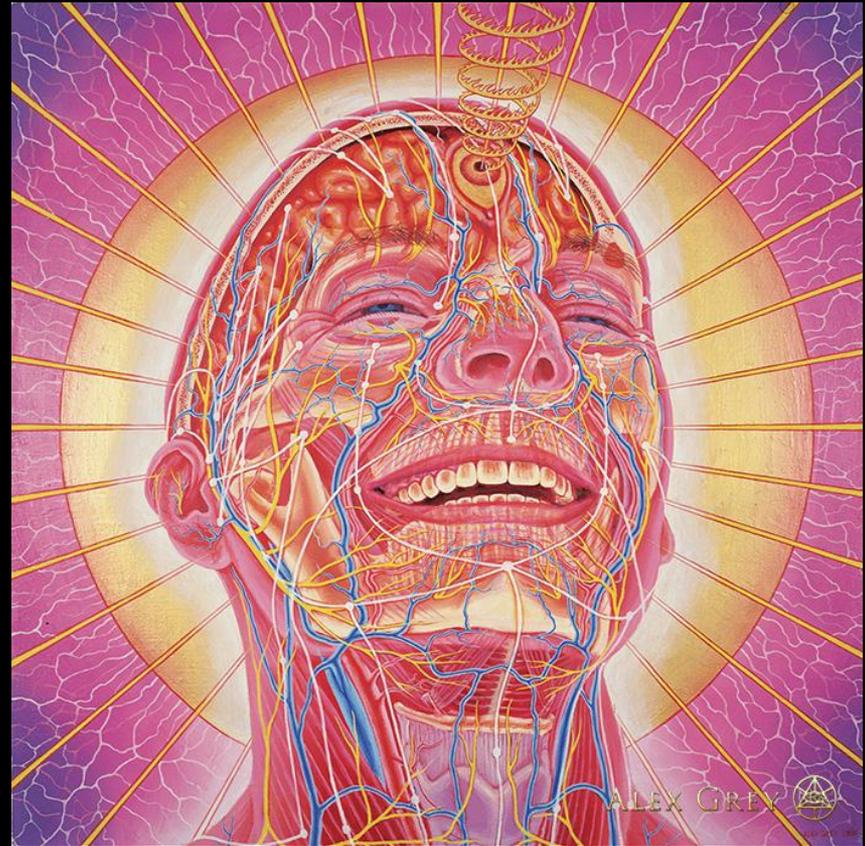
(Preller & Vollenweider, 2016)



EMOTIONAL EFFECTS

“Can intensify all forms of affective responses and may activate vivid memory traces with pronounced emotional undertones. ... a state of euphoria which can take different forms such as exhilarated elation with unmotivated laughter, deep feelings of peace, exuberant joy, and hedonistic pleasure.”

(Preller & Vollenweider, 2016)



COGNITION AND CREATIVITY

“Impaired attentional and disturbed cognitive functioning ... [yet, psychedelics] can induce creativity-enhancing experiences related to reduced inhibition, increased fluency and flexibility of ideas, increased visual imagery, empathy, and capacity to restructure problems.”

(Preller & Vollenweider, 2016)



SET AND SETTING (AND INTENTIONS)

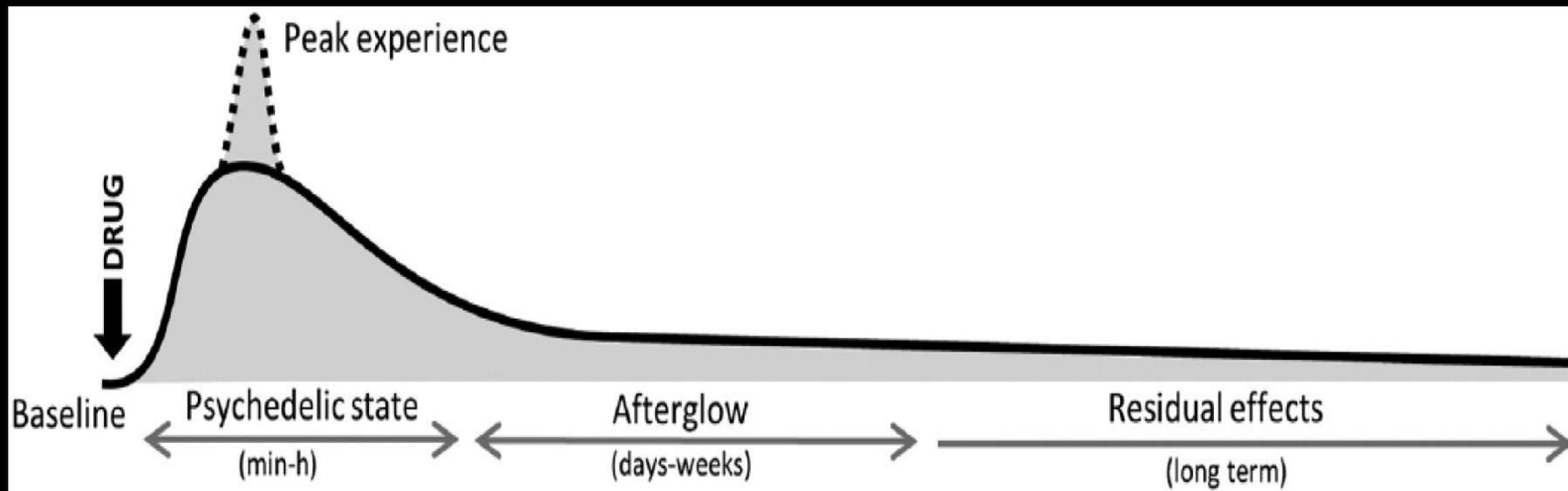
- Personality
- Mood
- Expectations
- Physical environment
- Cultural environment
- Peers
- (Priors)



PANIC AND ANXIETY ('BAD TRIPS')



AFTERGLOW AND INTEGRATION



- Disruption of constraints of prior learning
- “The world was as if newly created” - Hoffman (1943) (day after 1st LSD trip)
- Ordinary predictive patterns slowly take hold

PSYCHEDELIC THERAPY

- Anxiety
- Depression
- Post-Traumatic Stress Disorder (PTSD)
- Obsessive-Compulsive Disorder (OCD)
- Drug Abuse Cessation

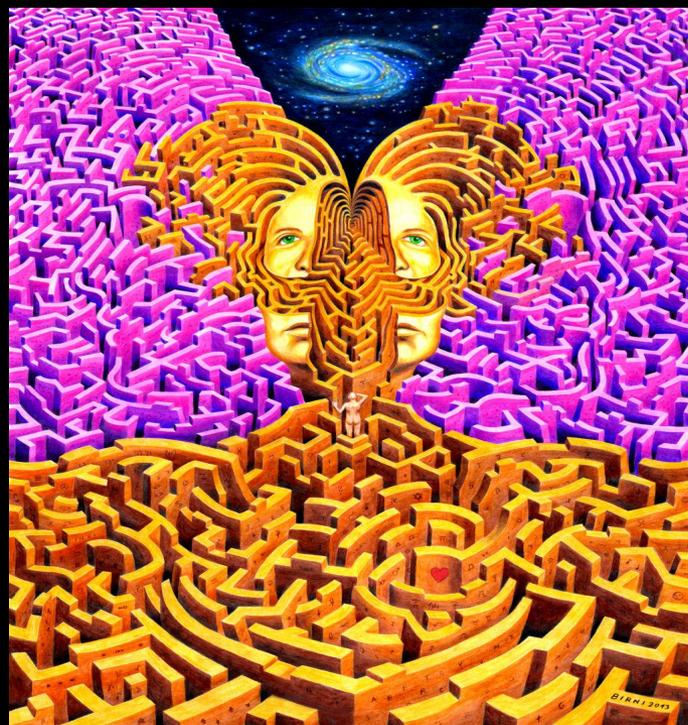


Disruption of constraints/prior habits & learning

PRIOR KNOWLEDGE BOTH CONSTRAINING AND ENABLING

“Prior learning makes certain other regularities harder (at times impossible) to spot. Prior knowledge is thus always both constraining and enabling.”

(Clark 2015, 288).



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