

# BAYESIAN NEUROSCIENCE OF PSYCHEDELIC DRUGS

Link Swanson

PhD Candidate in Cognitive Science

University of Minnesota

April 25, 2017 | CCS Spring Research Day

# **“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 SCIENCE2017

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



# 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<sup>1,2,3,4,5,6</sup>, Anthony Bossis<sup>1,2,4</sup>, Jeffrey Guss<sup>1,2,4</sup>,  
Gabrielle Agin-Liebes<sup>10</sup>, Tara Malone<sup>1</sup>, Barry Cohen<sup>7</sup>,  
Sarah E Mennenga<sup>1</sup>, Alexander Belser<sup>8</sup>, Krystallia Kallontzi<sup>2</sup>,  
James Babb<sup>9</sup>, Zhe Su<sup>3</sup>, Patricia Corby<sup>2</sup> and Brian L Schmidt<sup>2</sup>



*Journal of Psychopharmacology*  
2016, Vol. 30(12) 1165–1180  
© The Author(s) 2016



Reprints and permissions:  
[sagepub.co.uk/journalsPermissions.nav](http://sagepub.co.uk/journalsPermissions.nav)  
DOI: 10.1177/0269881116675512  
[jop.sagepub.com](http://jop.sagepub.com)



# 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



# 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

# 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 screenshot shows a research article from the journal "frontiers in Systems Neuroscience". The top right corner features a blue banner with the text "The #1 most cited publisher in the category". The article title is "The Predictive Processing Paradigm Has Roots in Kant". The author's name is Link R. Swanson, with superscripts 1, 2, and 3 indicating affiliations. The article is categorized as a "HYPOTHESIS & THEORY ARTICLE" and is dated 10 October 2016. It includes a DOI link: <https://doi.org/10.3389/fnsys.2016.00079>. There are also links for "Archive" and "Check for updates".

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>

Check for updates

**The Predictive Processing Paradigm Has Roots in Kant**

Link R. Swanson<sup>1,2,3\*</sup>

<sup>1</sup>Department of Philosophy, University of Minnesota, Minneapolis, MN, USA  
<sup>2</sup>Center for Cognitive Sciences, University of Minnesota, Minneapolis, MN, USA  
<sup>3</sup>Minnesota 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.”

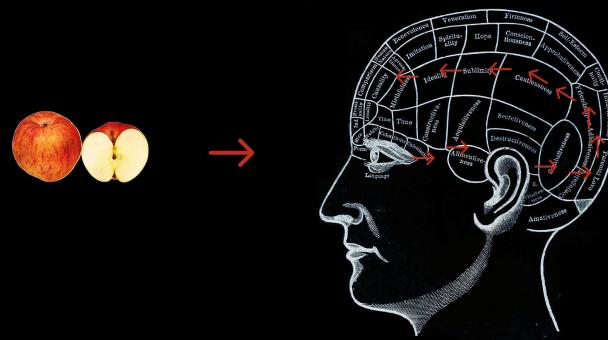
Clark (2013) p.181

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

(Kanai et al, 2015)

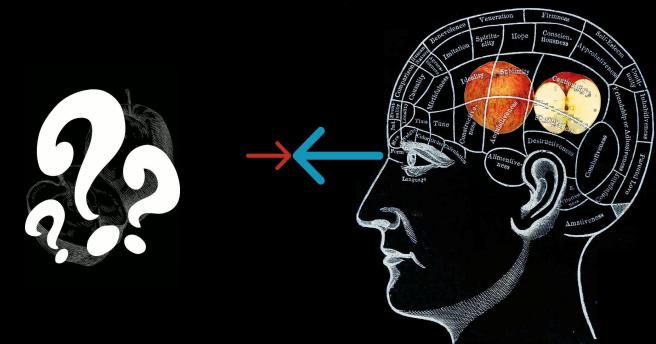
# PERCEIVING THE WORLD:

## How we usually think of perception:



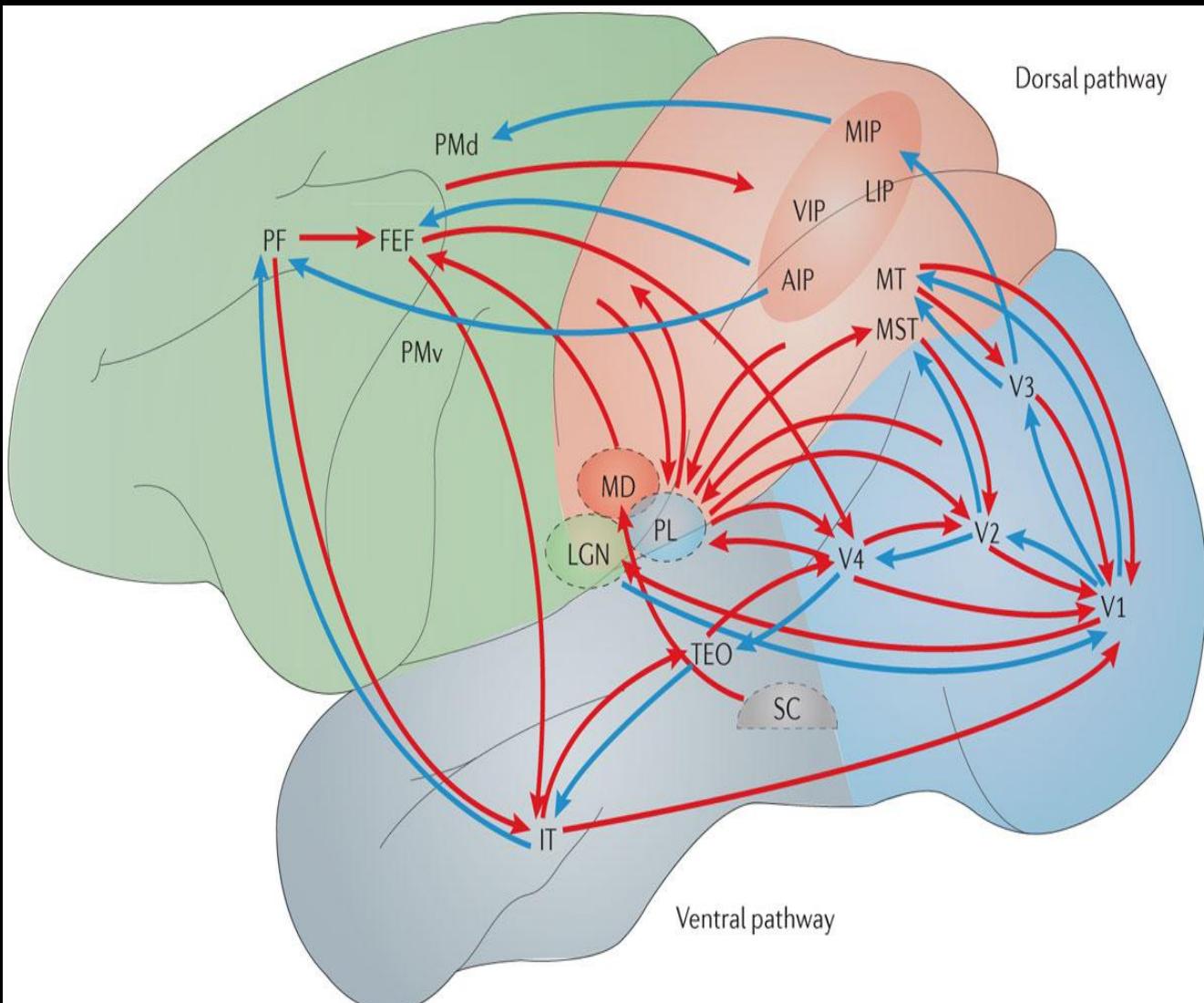
Sense organs ‘detect’ external objects and transfer perceptions to the brain

## Predictive Processing account of perception:

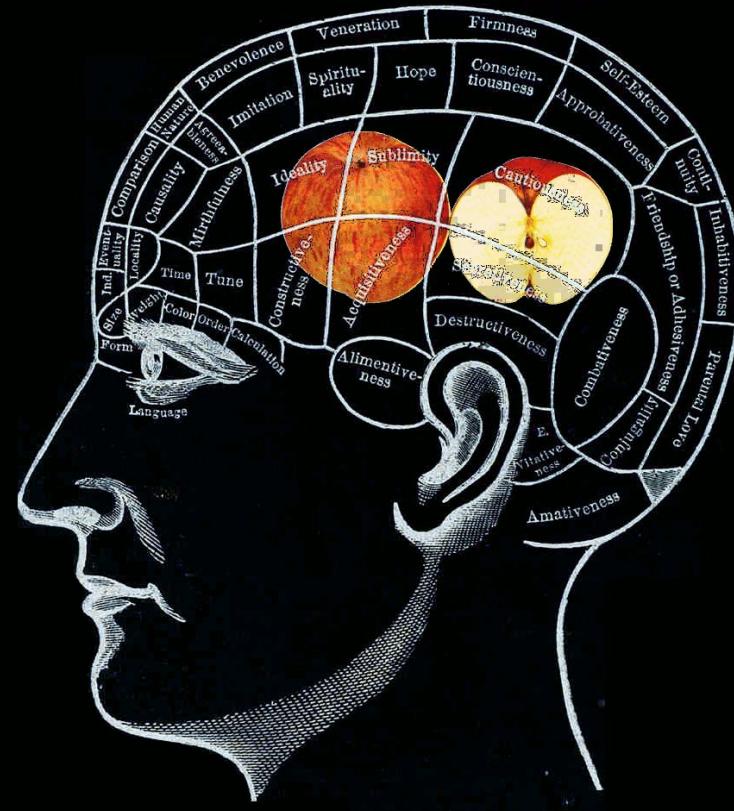


Brain generates perceptions of the most likely external causes using prior experience/learning

# CORTICAL HIERARCHY



# CORTICAL HIERARCHY OF NEURAL PREDICTIONS AND ERRORS



# 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’



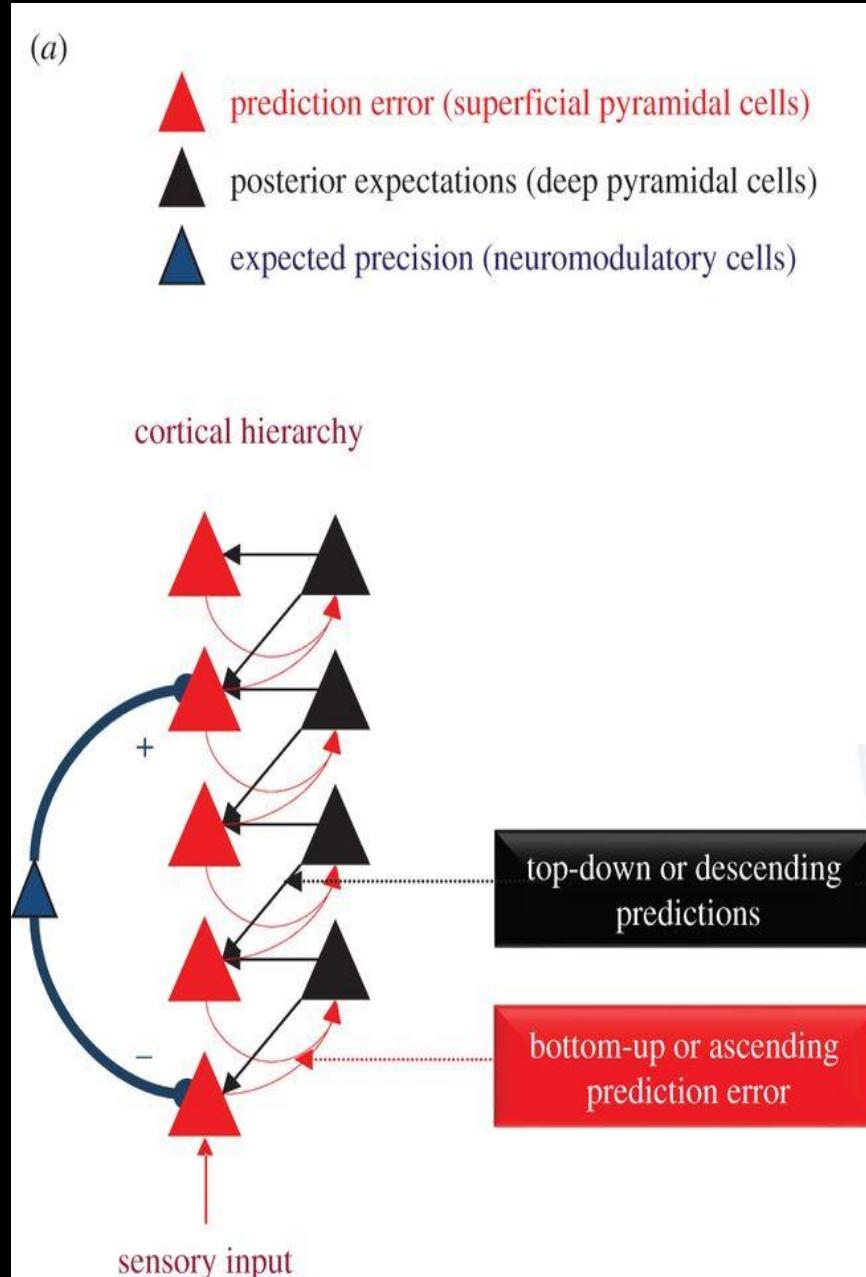
“The [neural] system is trying to generate (at multiple spatial and temporal scales) the incoming sensory signal for itself. When this succeeds, and a match is established, we experience a structured visual scene.”

(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.”

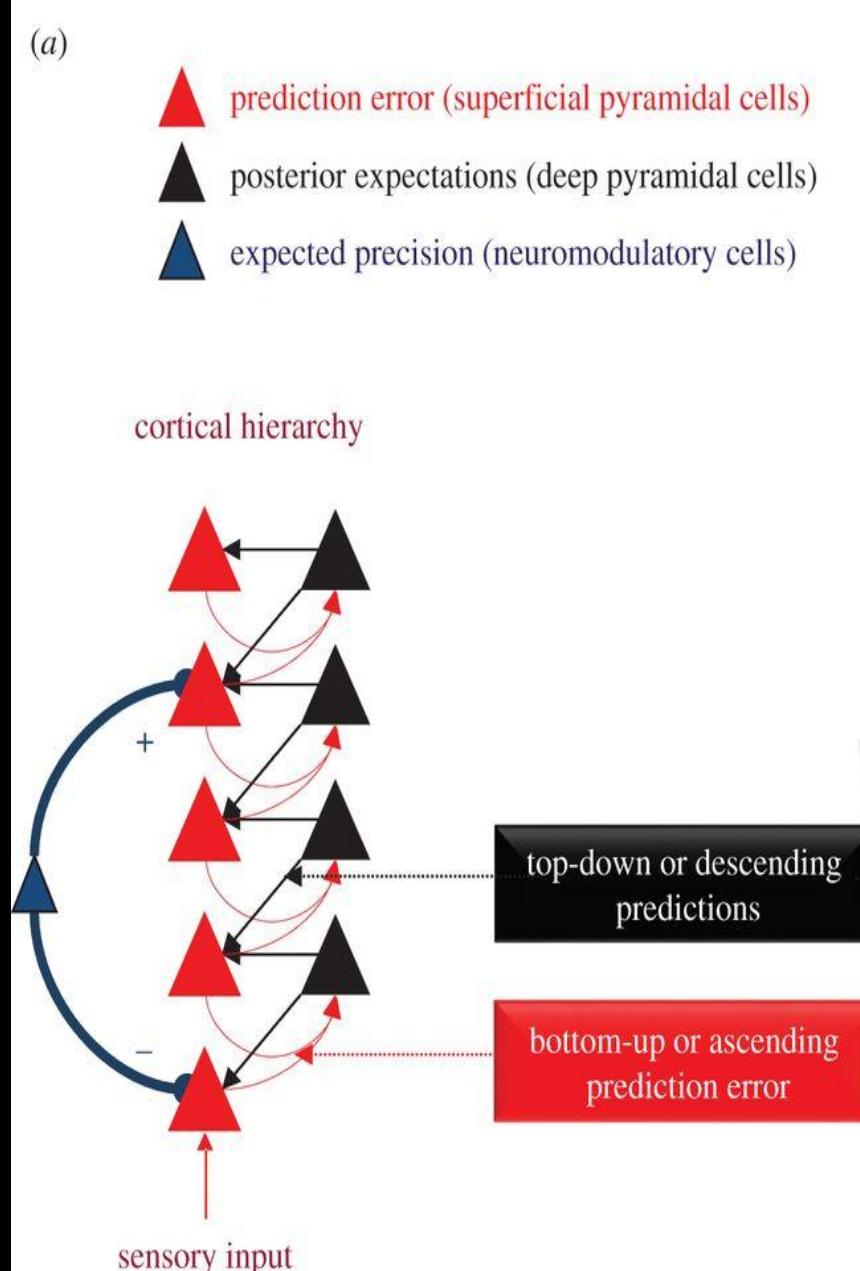
(Kanai et al, 2015)



# PRECISION WEIGHTING

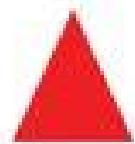
“Neuromodulatory gating or gain control (blue) of superficial pyramidal cells that determines their relative influence on deep pyramidal cells encoding expectations.”

(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)**

# OUR PLAN FOR THIS TALK

1. ~~PSYCHEDELIC RESEARCH IN THE 21ST CENTURY~~
2. ~~BAYESIAN MODELS IN NEUROSCIENCE~~
3. -> PREDICTIVE PROCESSING & PSYCHEDELICS
4. CONCLUSION & FUTURE DIRECTIONS

# PREDICTIVE PROCESSING AND PSYCHEDELIC EFFECTS

# PSYCHEDELIC EFFECTS IN THE PREDICTIVE BRAIN

## HYPOTHESIS:

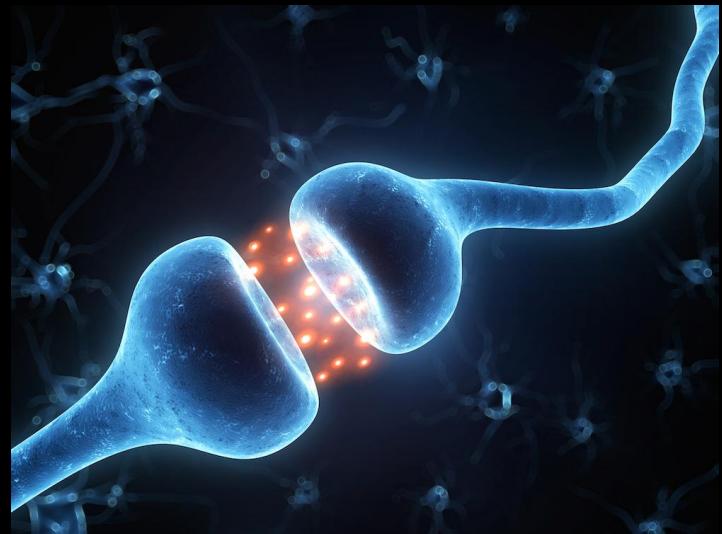
Psychedelic molecules alter neuromodulatory ‘gain control’ and ‘precision weighting’ mechanisms that balance predictions/priors with prediction errors in neural systems

# YOU GUESSED IT: PSYCHEDELICS TWEAK YOUR PRIOR PROBABILITIES



# THE BASIC PP NEURAL MECHANISM OF PSYCHEDELICS

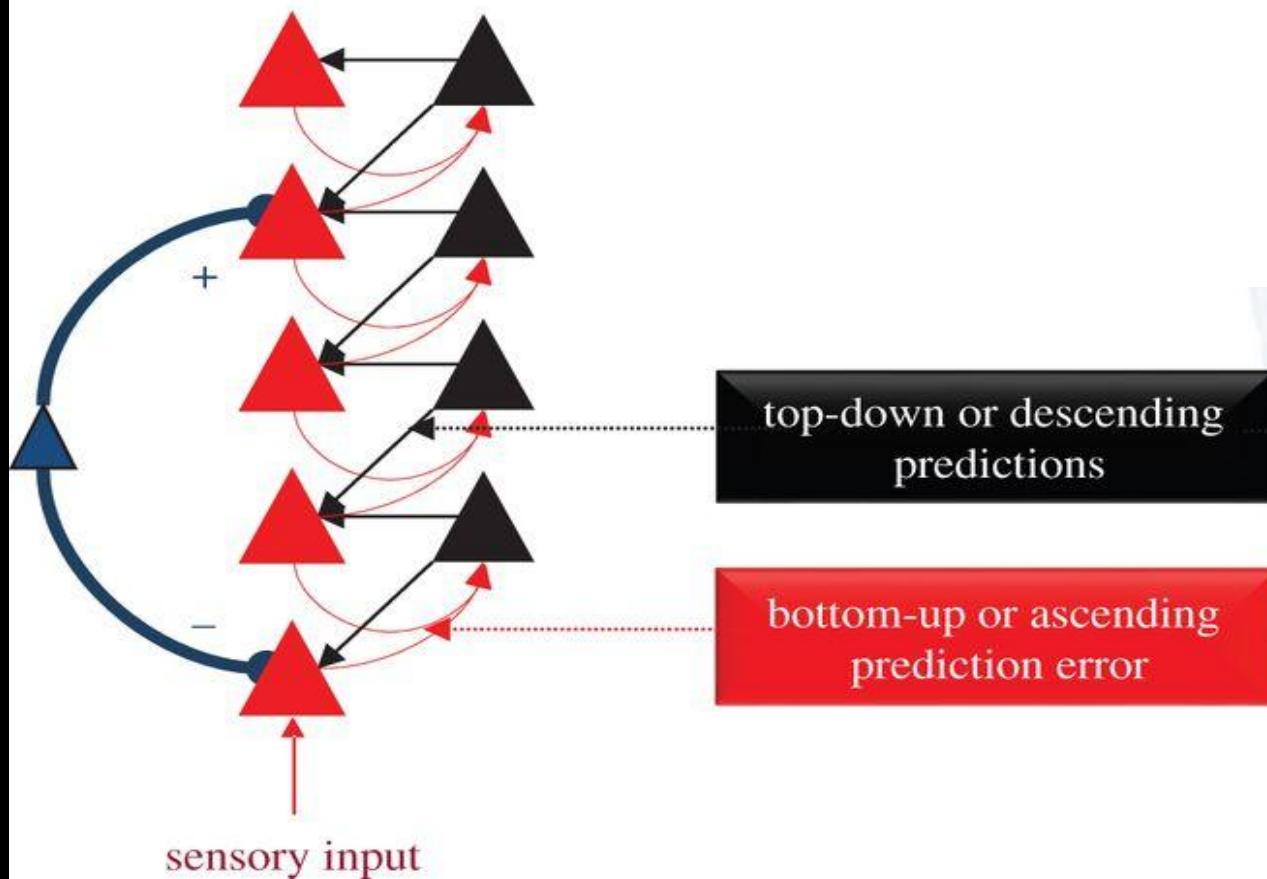
- Predictive processing hypothesizes that deep pyramidal cells in layer V are central to top-down predictions
- Psychedelics modulate the 5-HT2A receptors on pyramidal cells in layer V
- Priors can be amplified or dampened
- Priors can be applied in unusual ways
- Prediction errors have less (or more) impact (precision weighting)
- Ordinary constraints are suspended



(a)

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

cortical hierarchy



# 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)

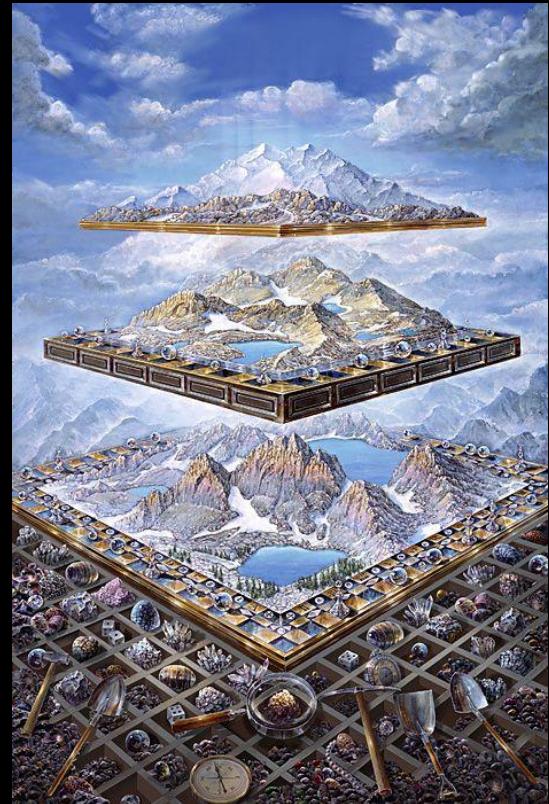




# THE DYNAMIC UNFOLDING OF PSYCHEDELIC SESSIONS

“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.”

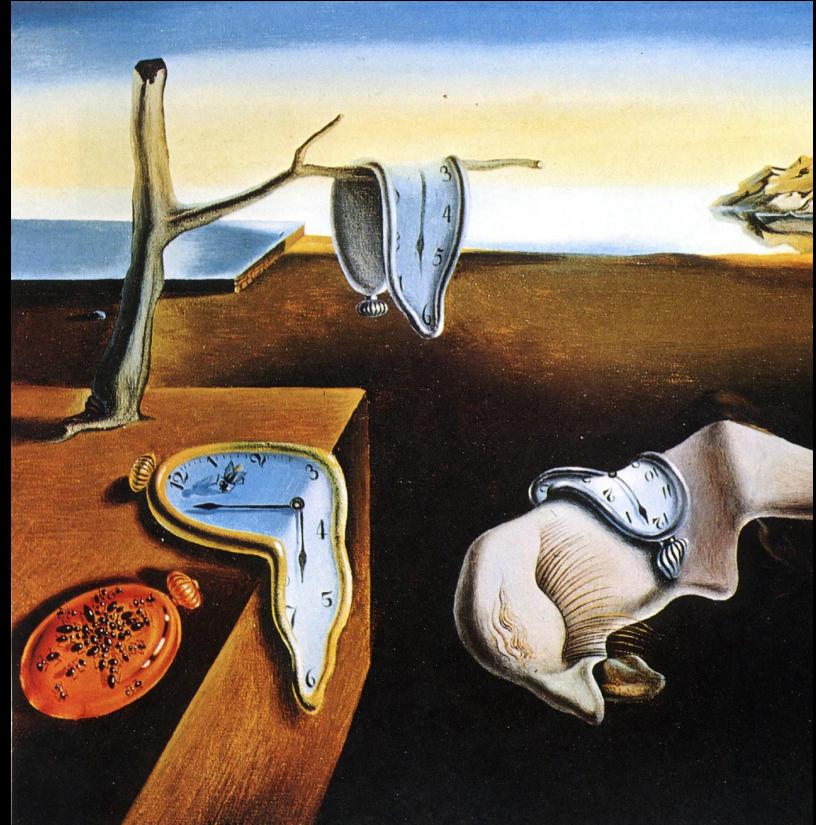
(Preller & Vollenweider, 2016)



# 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.”

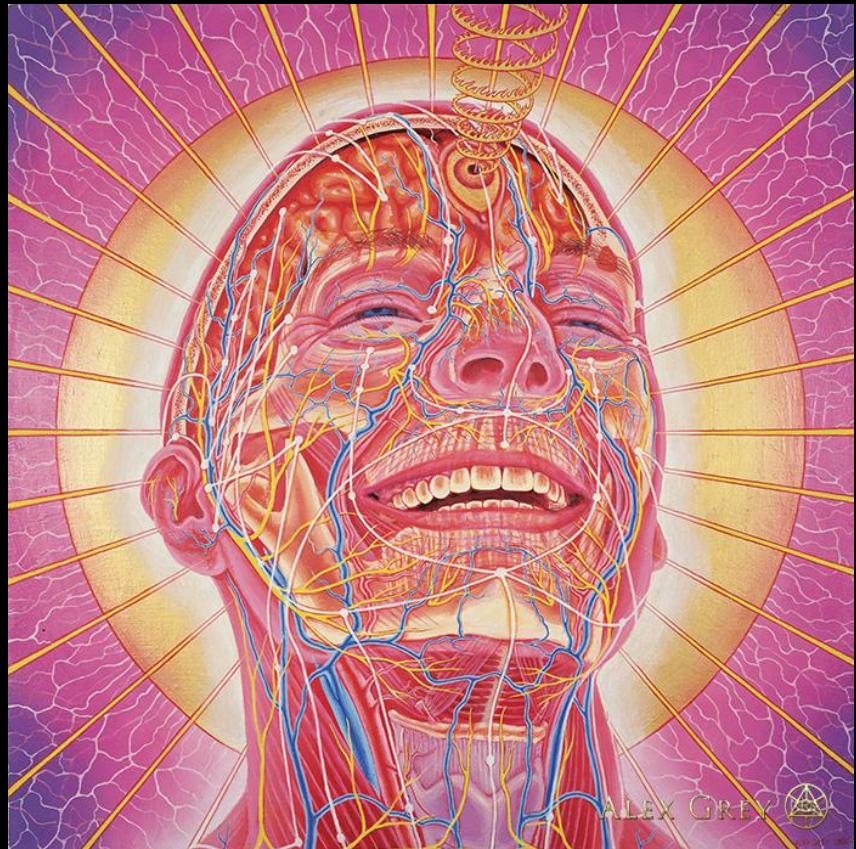
(Preller & Vollenweider, 2016)



# 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)

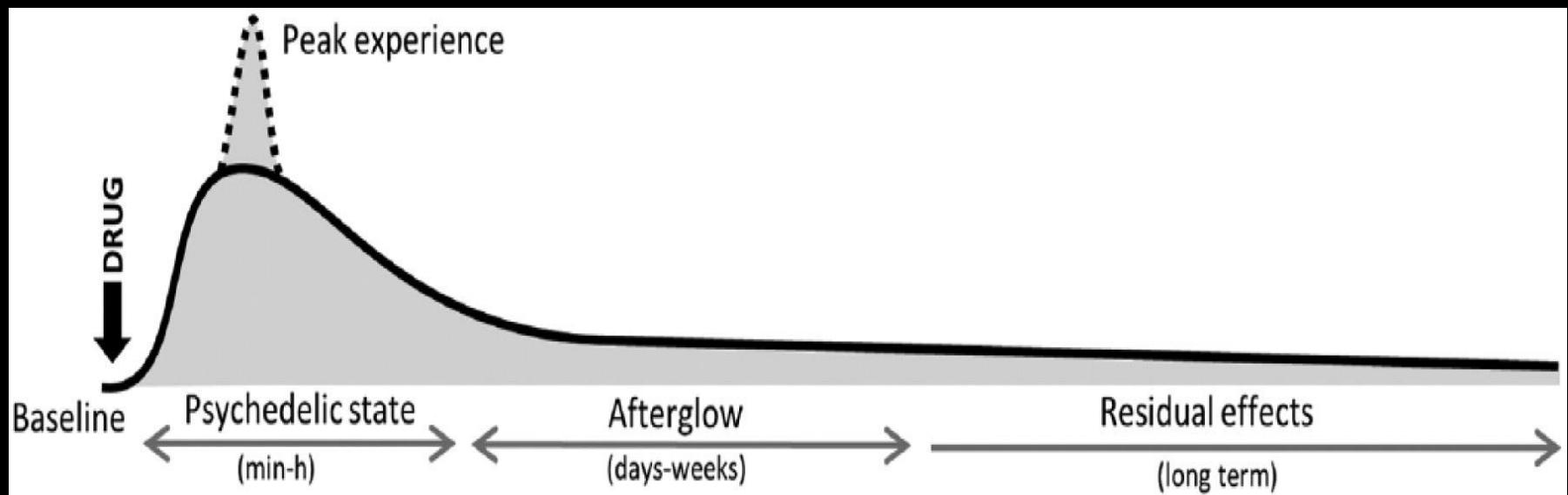
- Personality
- Mood
- Expectations
- Physical environment
- Cultural environment
- Peers
- (Priors)



# 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

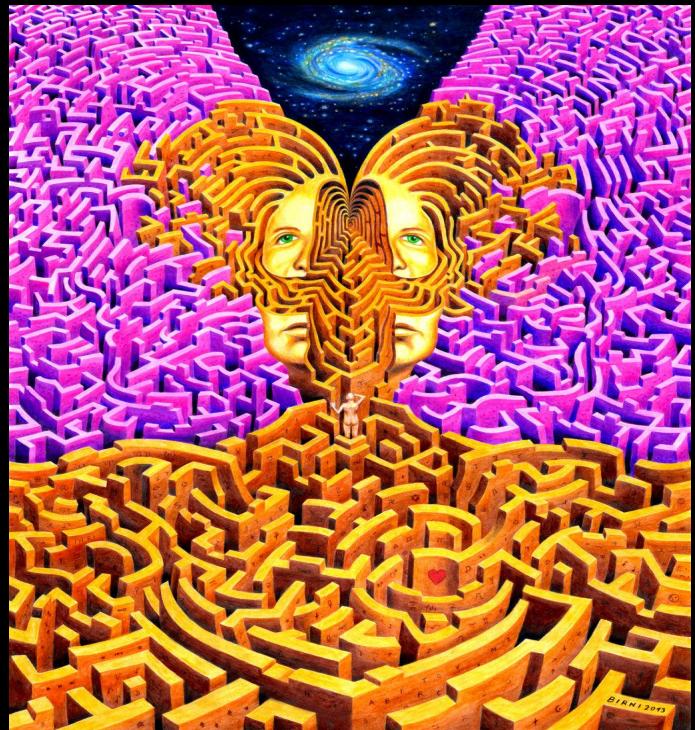


Disruption of constraints/prior habits & learning

# 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).



# OUR PLAN FOR THIS TALK

1. ~~PSYCHEDELIC RESEARCH IN THE 21ST CENTURY~~
2. ~~BAYESIAN MODELS IN NEUROSCIENCE~~
3. ~~PREDICTIVE PROCESSING & PSYCHEDELICS~~
4. -> CONCLUSION & FUTURE DIRECTIONS