‘Bayesian’ theories: Application to mental disorders

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1

A New Model for Mental Illness

Mental illness is the result of an impairment in prediction, due to having a distorted internal model of the world, possibly due to an impairment in learning.

Bayesian approach in Computational Psychiatry

Mental illness could be due to differences in the models of the world that people's brains are working with:

- e.g. different priors

(e.g. pessimistic priors in depression, or priors on controllability, priors on mistrust in borderline).

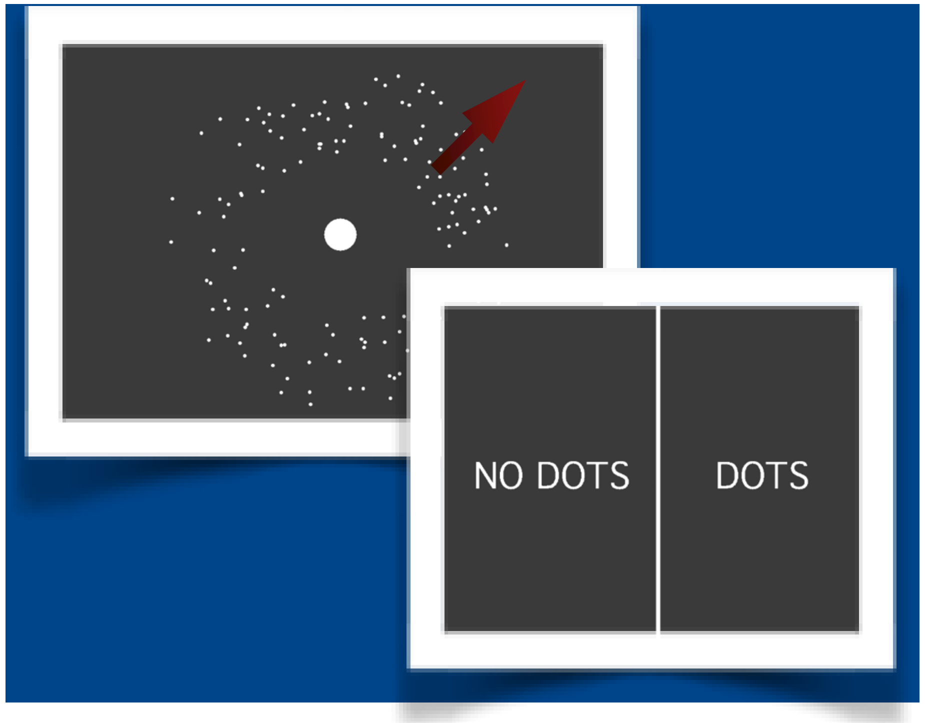
- or deficits / imbalance in incorporating priors with evidence (e.g. schizophrenia, autism)

- > a new area of research.

Example Application

- Bayesian models of Autism

- Example Study : Testing the models with the "moving dots" statistical learning task (Karvelis et al, eLife, 2018, Valton et al, Brain 2019)



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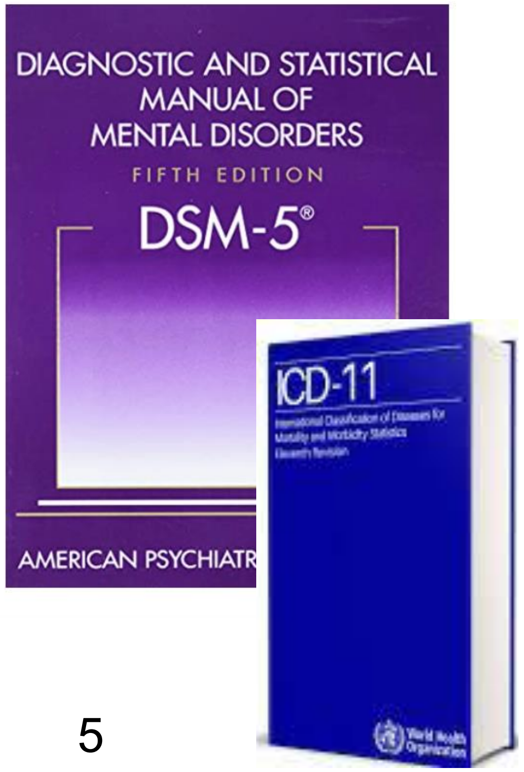
Autism Spectrum Disorder (ASD)

- Autism is a neurodevelopmental disorder of unknown aetiology characterized by:
  impaired social interaction,
  impaired verbal and non-verbal communication,
  restricted and repetitive behavior.

- Heterogeneous and a wide spectrum

- 1.1% of population in the UK - increasing

- Commonly thought to be biologically determined but diagnosis based on symptoms, no biomarker



Theories of ASD

- Theories have either focused on the social symptoms [e.g., deficit of theory of mind, reduced social salience, lack of social motivation]

- or on peculiarities of autistic perception [e.g., "weak central coherence", focus on detail, hyper/hyposensitivities], with DSM-V now including sensory sensitivities as core diagnostic feature

- Sensory first? cascading effects on development in a number of domains?

When a person with Autism walks into a room
The first thing they see is:

A pillow with a coffee stain shaped like Africa
A train ticket sticking out of a magazine,
25 floorboards, a remote control,
a paperclip on the mantelpiece,
a marble under the chair,
a crack in the ceiling,
12 grapes in a bowl,
a piece of gum,
a book of stamps
sticking out
from behind a
silver picture
Frame.

so It’s not surprising they ignore you completely.

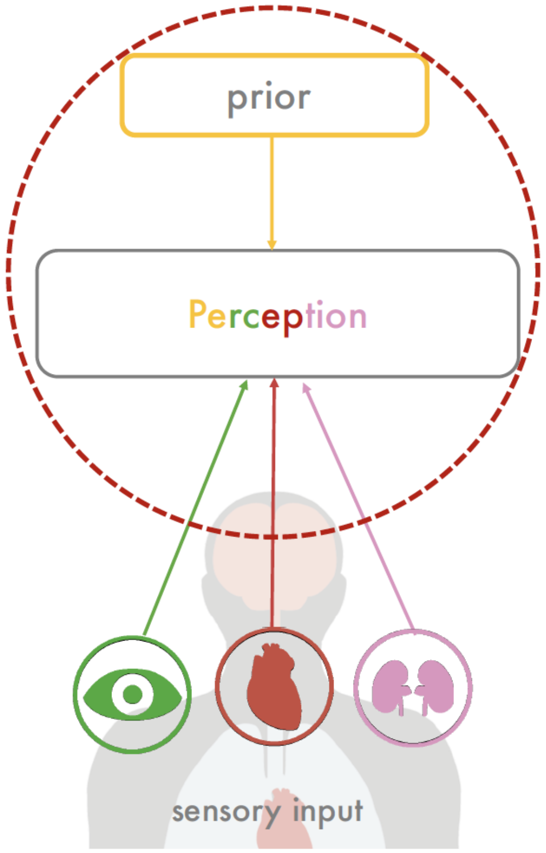
The National Autistic Society

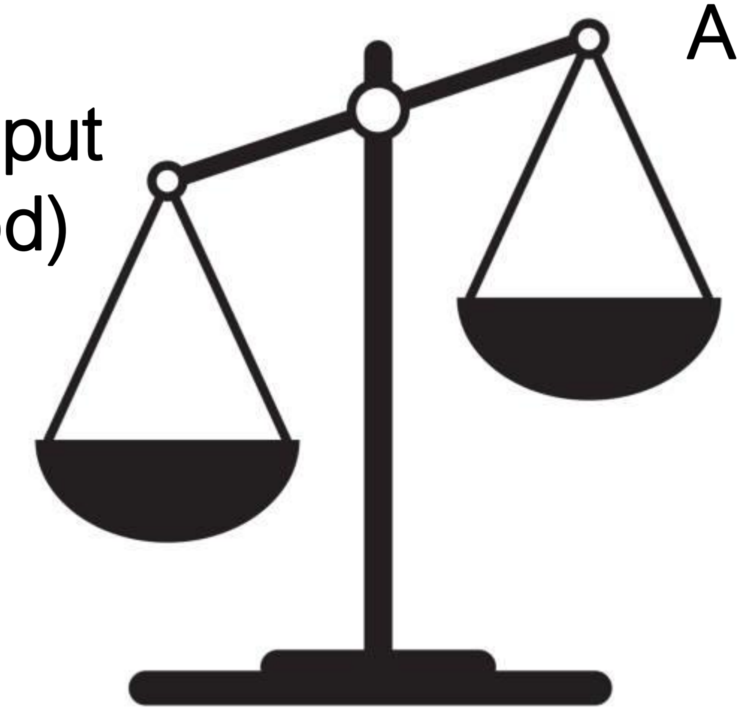
2

Autism as a Disorder of Prediction or Inference

- A general framework/ unifying theory/ canonical computation?
- 10 years - A flourishing field of research: ~86 articles in 2012-21 about Autism & Bayesian or Predictive coding (in title, abstract or keywords)

Relatively weaker priors in autism?





Explain:

- **hypersensitivities, sensory overload**
- **reduced sensitivity to illusions**
- **reduced global processing, « weak central coherence »**
- **repetitive behaviour**
- **social impairments ("theory of mind")**

[Pellicano & Burr 2012; Skewes et al 2014, Powell et al 2016]

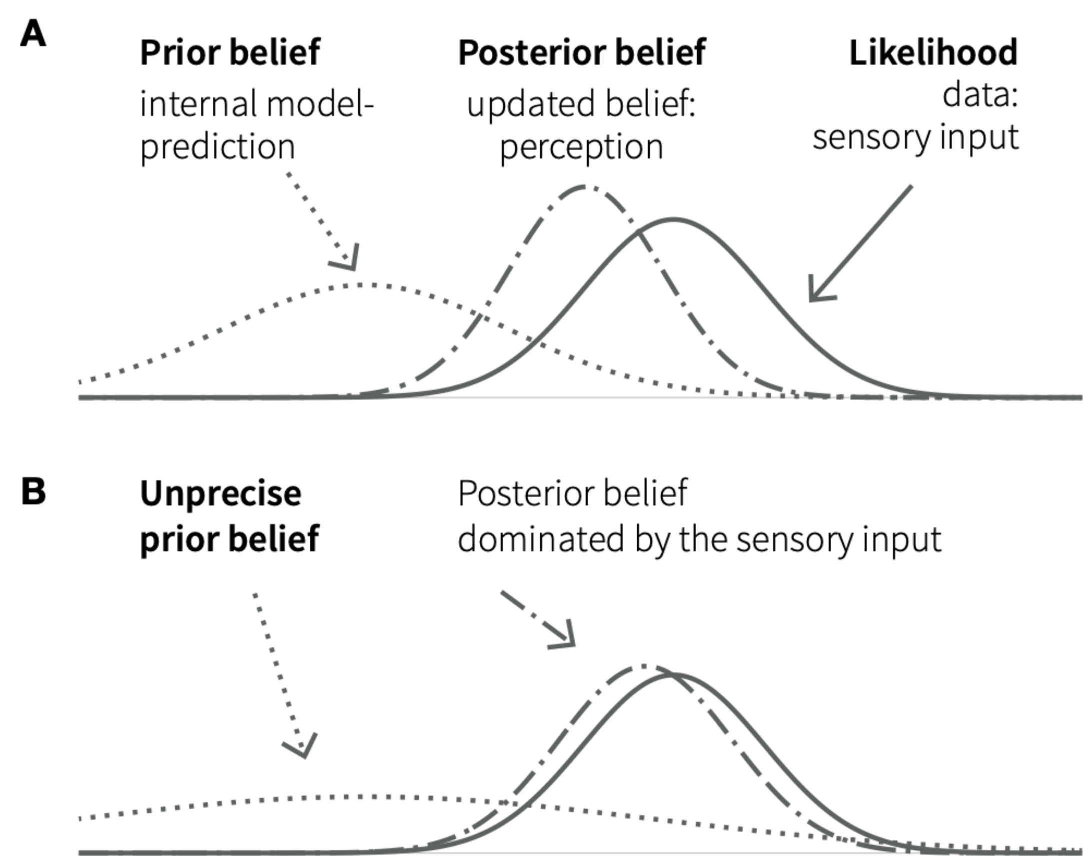
Relatively weaker priors in autism?

Sensory input unaffected

Hypothesis 1
Weaker / flatter Priors

Lower precision

π_{prior}



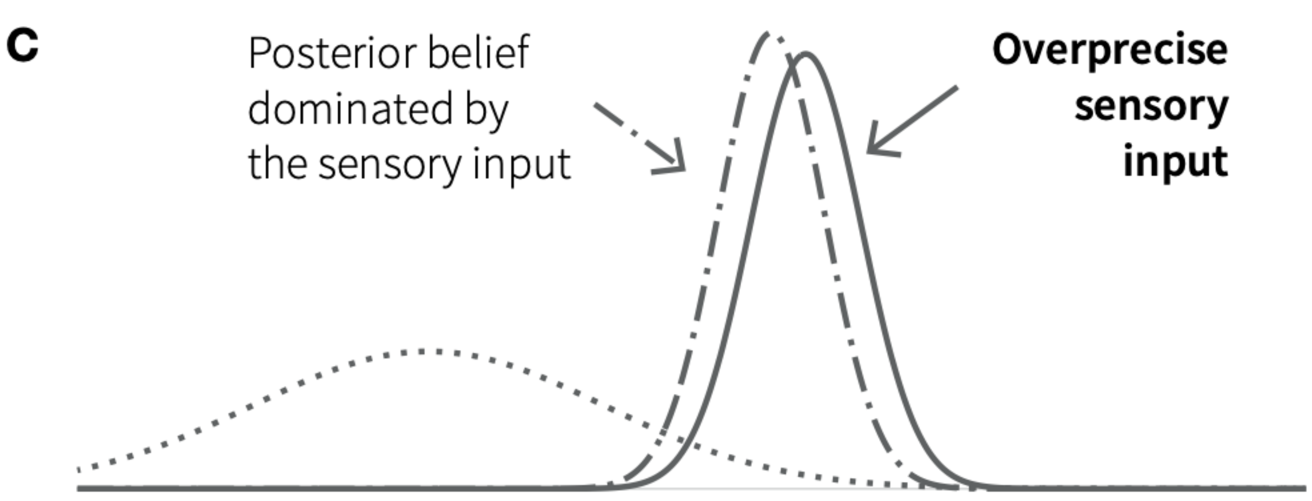
Relatively weaker priors in autism?

<u>Hypothesis 2</u>
Sensory information more precise

Higher precision

$\pi_{likelihood}$

prior expectations unaffected



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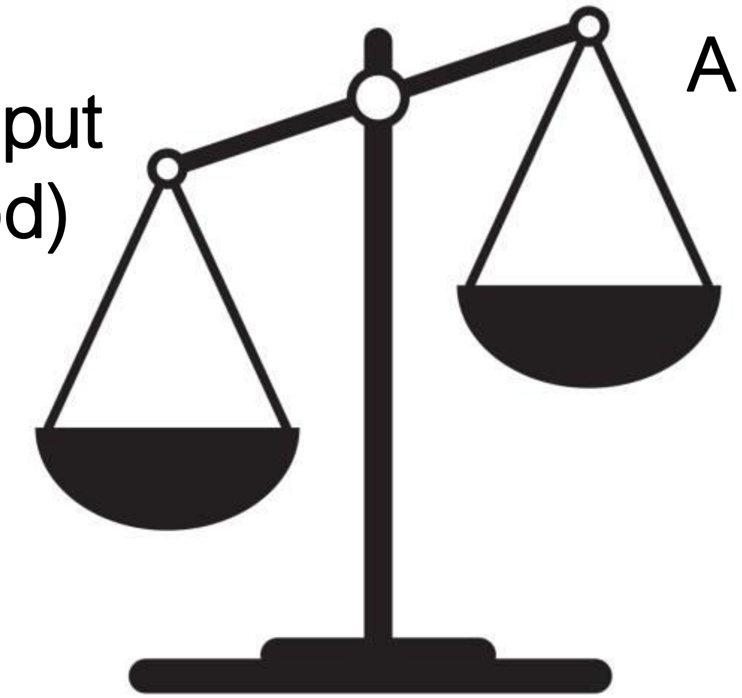
Predictive Coding: Increased weight on prediction error

Sensory Input (Likelihood)



A priori expectations

Relatively lower precision

π_{prior}

Relatively higher precision

$\pi_{likelihood}$

Weight on PE
Learning rate

Prediction error

$$\mu_{posterior} = \mu_{prior} + \frac{\pi_{likelihood}}{\pi_{posterior}}(x - \mu_{prior}) \quad (1)$$

where

$$\pi_{posterior} = \pi_{prior} + \pi_{likelihood} \quad (2)$$

2

Or a problem of inflexibility?

- **<u>Hypothesis 3:</u>** Inflexibility – Priors are more rigid or High and Inflexible Precision of Prediction Errors (HIPPEA) [Van de Cruys et al. 2014]
- In dynamic contexts: Overestimation of environmental volatility [Lawson et al 2016];

"The world is moving too fast"

Original Article

autism

Autism
1–12

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The world is nuanced but pixelated: Autistic individuals' perspective on HIPPEA

Greta Krasimirova Todorova, Rosalind Elizabeth Mcbean Hatton, Sarveen Sadique and Frank Earl Pollick

Abstract
Little attention has been given to the voice of autistic individuals during the development of theories that are trying to explain the condition. This can often make individuals feel that they have to fit into the theory's definition, rather than it fitting into their experience. We aimed to understand to what extent the HIPPEA (High, Inflexible Precision of Prediction Errors in Autism) theory resonates with the lived experiences of autistic individuals. We conducted 21 questionnaires and 8 follow-up interviews and used a hybrid (deductive and inductive) approach to analyse the data. Based on the participants' views, HIPPEA provides an explanation for many of the lived experiences of autistic individuals. However, refinement is needed with respect to interpersonal interactions, emotional processing and individuals' motivation to engage with their environment despite challenges with the way the world is organised. Furthermore, more details are needed for the theory to accurately allow us to understand autism.

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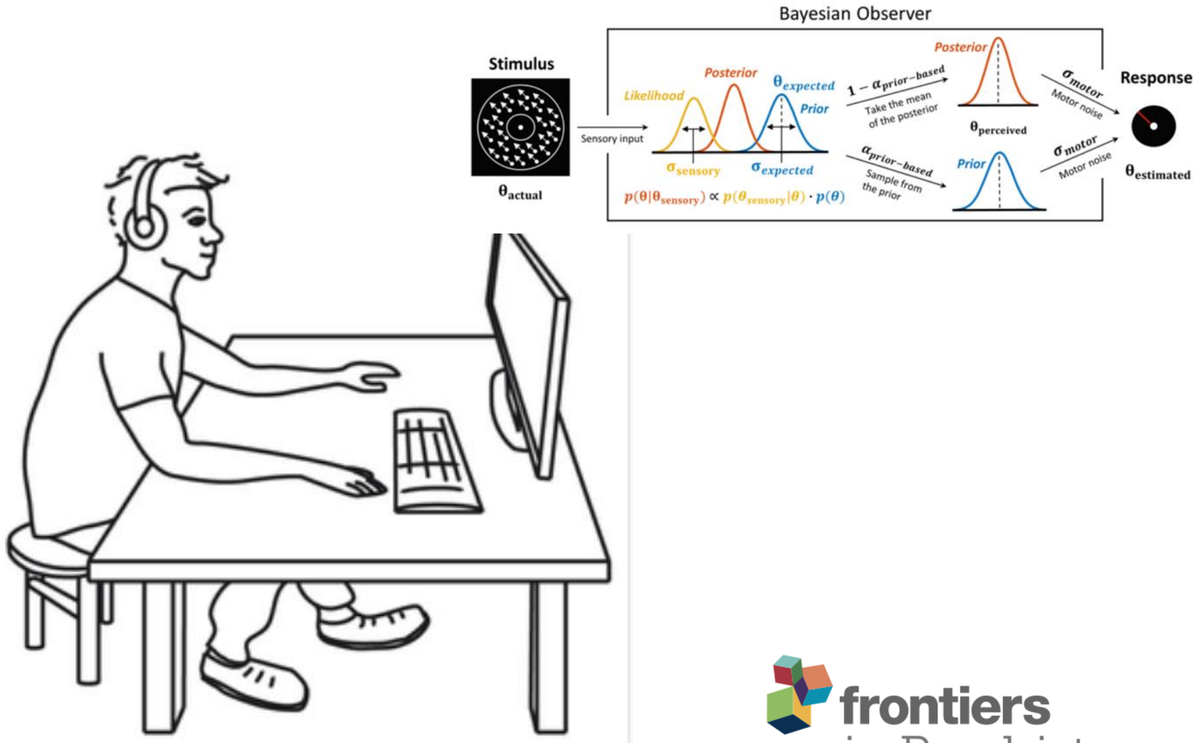
Clinical interest: providing quantitative tests

If these theories are validated, we will be able to..

- Provide objective and quantitative, behavioral tests facilitating diagnosis that could be conducted by non-specialists.
- Combination with modelling: quantifying parameters at the individual level
- Understanding comorbidities (e.g. trauma, anxiety, depression, psychosis) and similarities/differences other disorders (ASD vs schizophrenia).
- Precisely define the learning conditions in which patients can benefit from learning-based therapies.
- fMRI - Neurobiological substrate



frontiers in Psychiatry

2016

Can Bayesian Theories of Autism Spectrum Disorder Help Improve Clinical Practice?

Helene Haker[1], Maya Schneebeli[1] and Klaas Enno Stephan[1,2,3]*

[1] Translational Neuromodeling Unit (TNU), Institute for Biomedical Engineering, University of Zurich and ETH Zurich, Zurich, Switzerland, [2] Wellcome Trust Centre for Neuroimaging, University College London, London, UK, [3] Max Planck Institute for Metabolism Research, Cologne, Germany

Diagnosis and individualized treatment of autism spectrum disorder (ASD) represent major problems for contemporary psychiatry. Tackling these problems requires guidance by a pathophysiological theory. In this paper, we consider recent theories that re-conceptualize ASD from a "Bayesian brain" perspective, which posit that the core abnormality of ASD resides in perceptual aberrations due to a disbalance in the precision of prediction errors (sensory noise) relative to the precision of predictions (prior beliefs). This results in percepts that are dominated by sensory inputs and less guided by top-down regularization and shifts the perceptual focus to detailed aspects of the

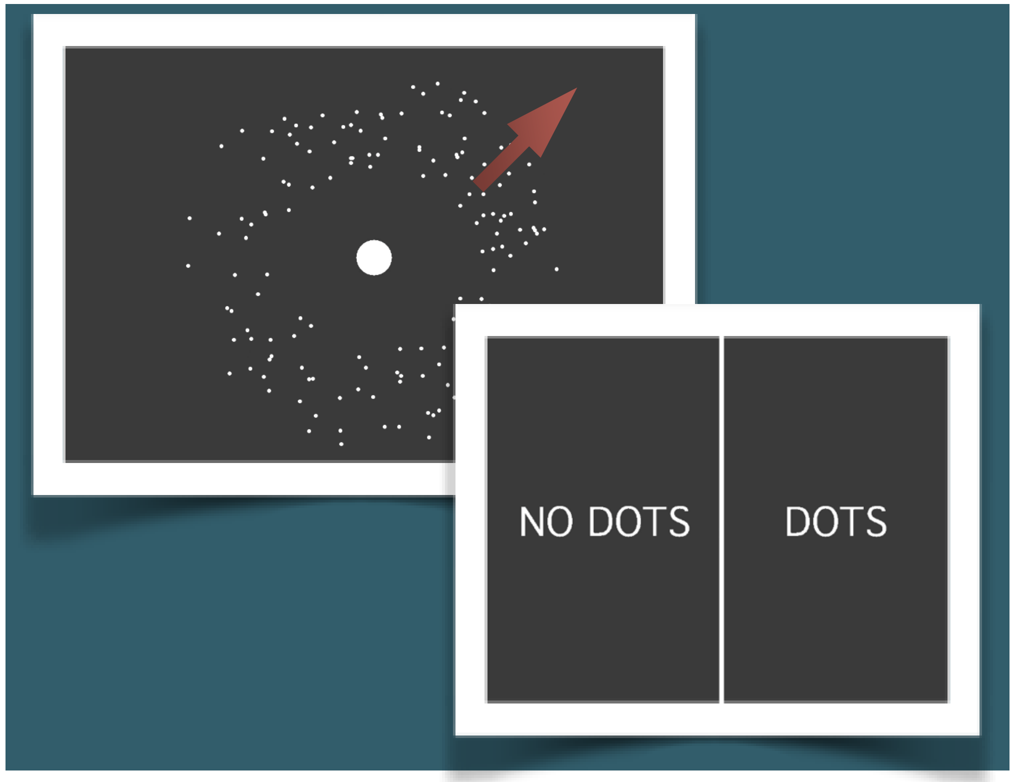
Can we quantitatively test & refine current theories & make them clinically relevant?

- Can we measure priors and likelihoods in individual participants?
- How come theories of SCZ and ASD are so similar?
- Are priors learned in the same way in SCZ and ASD as in controls?
- Are priors combined with likelihoods in the same way?

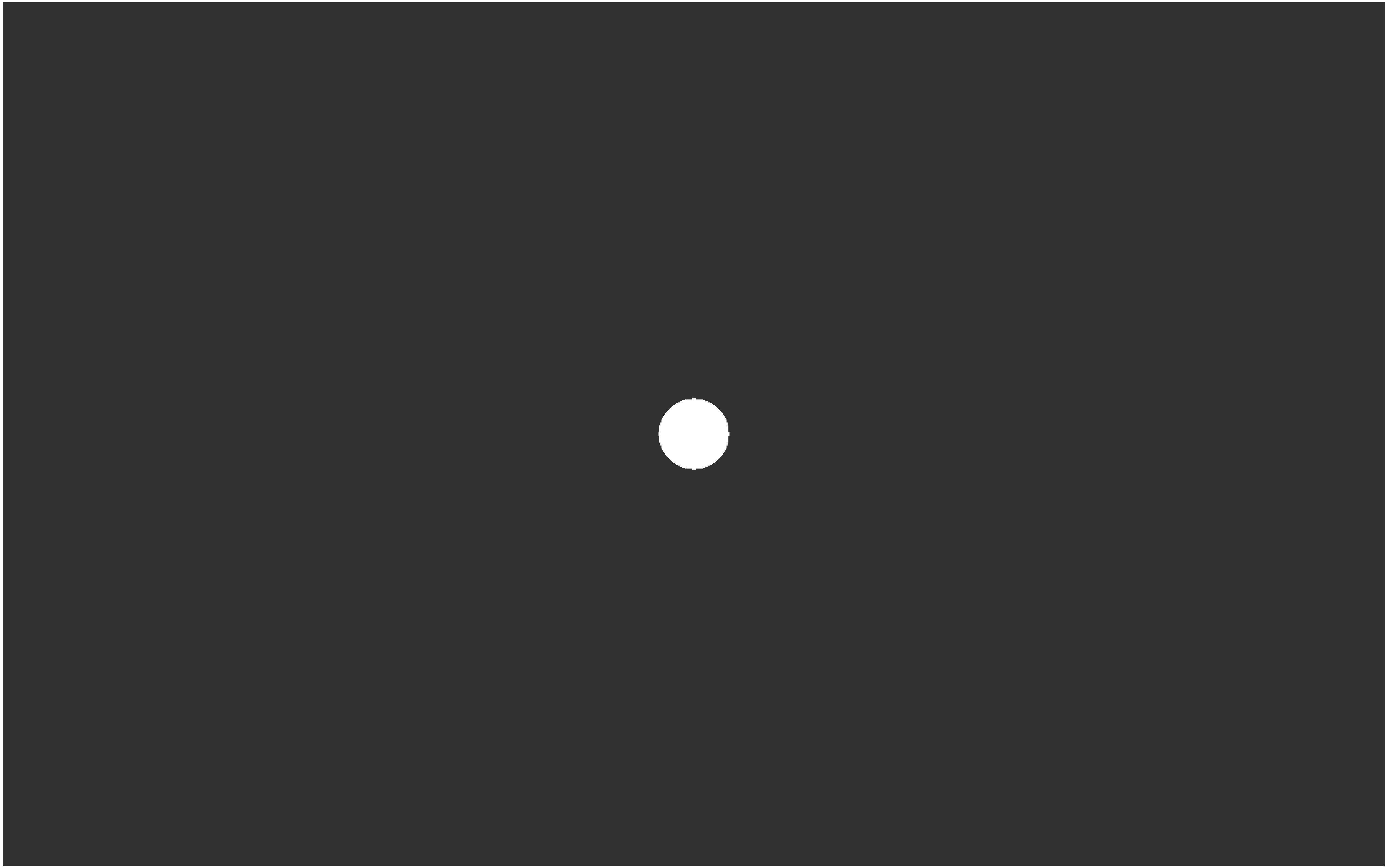
Testing the models with a statistical learning task:

How do humans learn and use the statistics of the visual environment?

- On each trial, participants were presented with either a low contrast random dot motion stimulus (100% coherence) or a blank screen.
- Participants reported direction of motion (estimation), before reporting whether a stimulus was present (detection).



[Chalk, Seitz, Seriès, JOV 2010]



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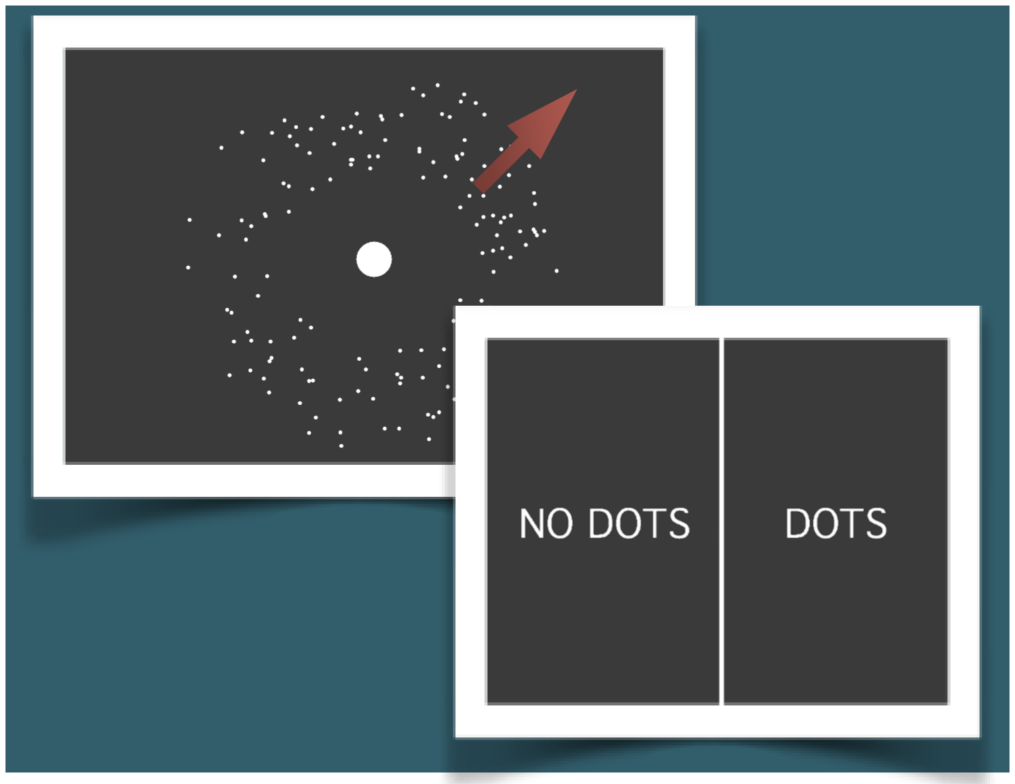
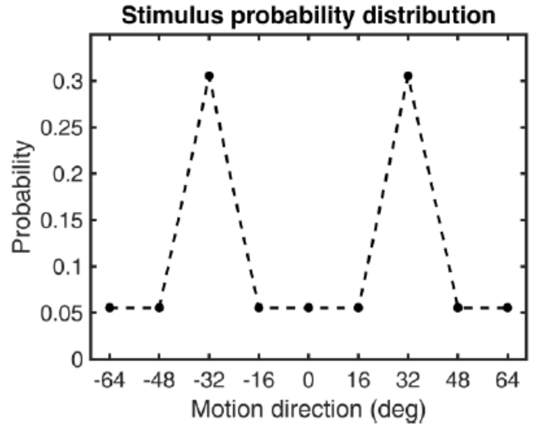


- On each trial, participants were presented with either a low contrast random dot motion stimulus (100% coherence) or a blank screen.
- Participants reported direction of motion (estimation), before reporting whether a stimulus was present (detection).

- Two directions of motion are more frequently presented. Are participants going to learn about this? implicitly? how will this change their perception?



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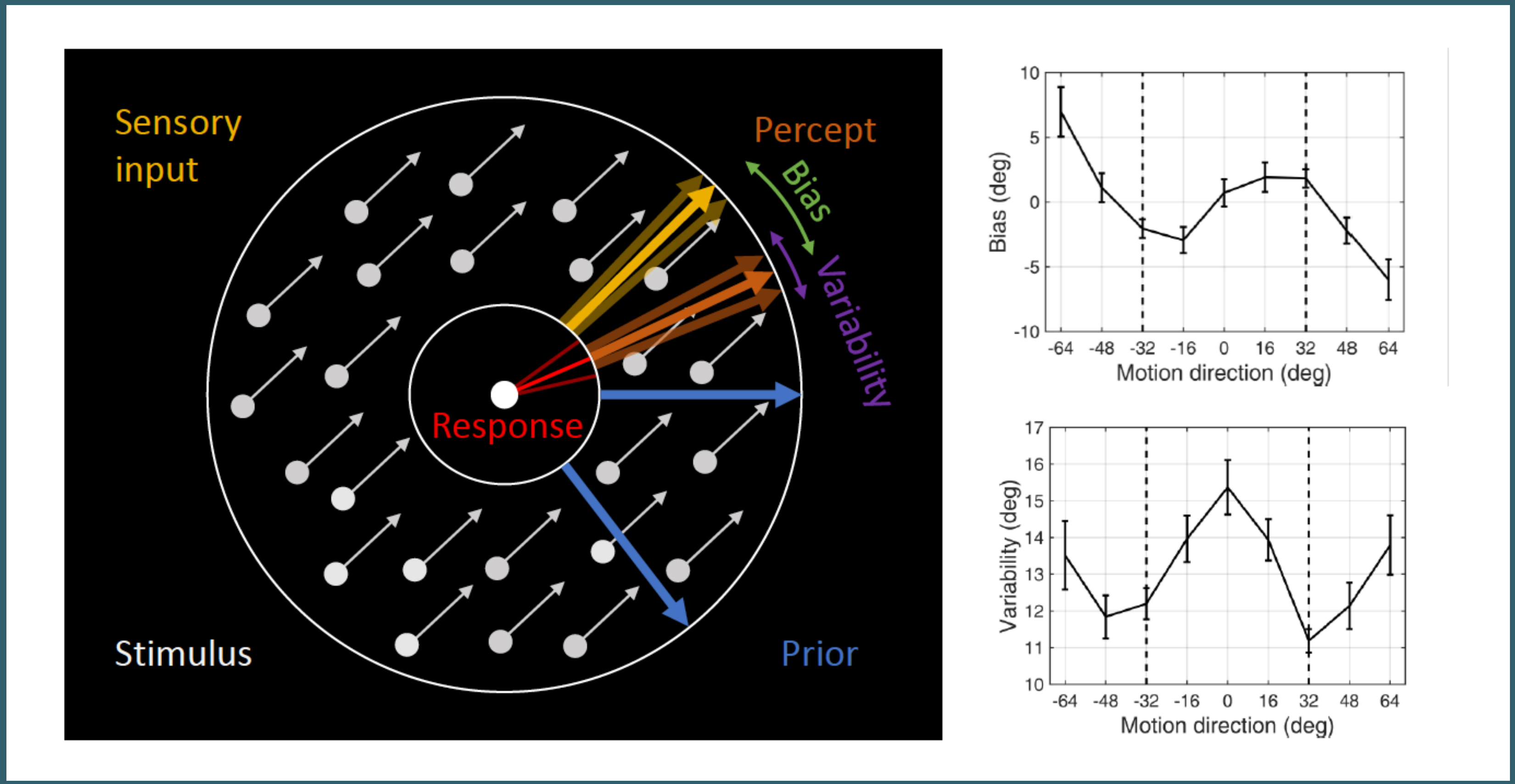
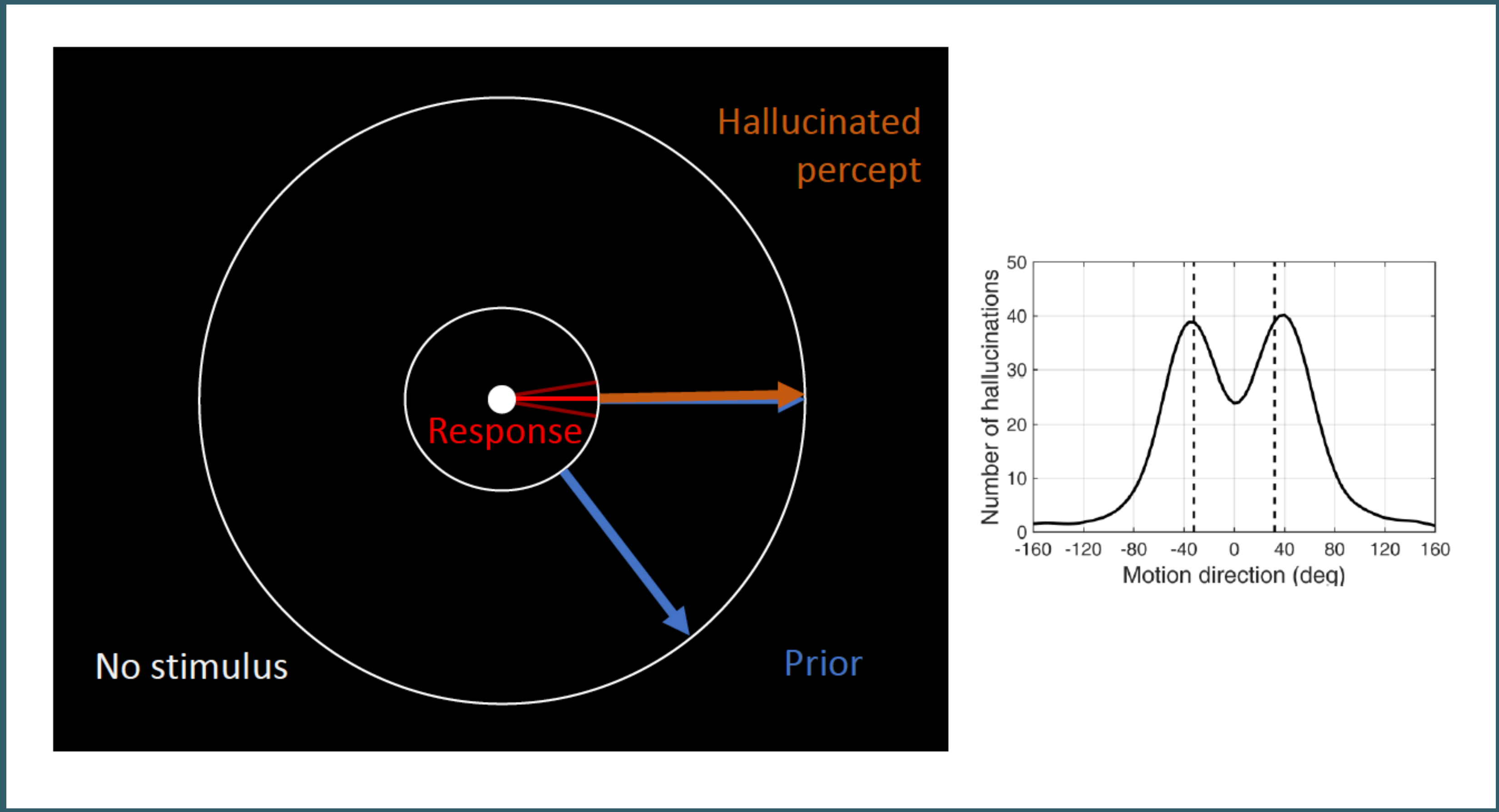
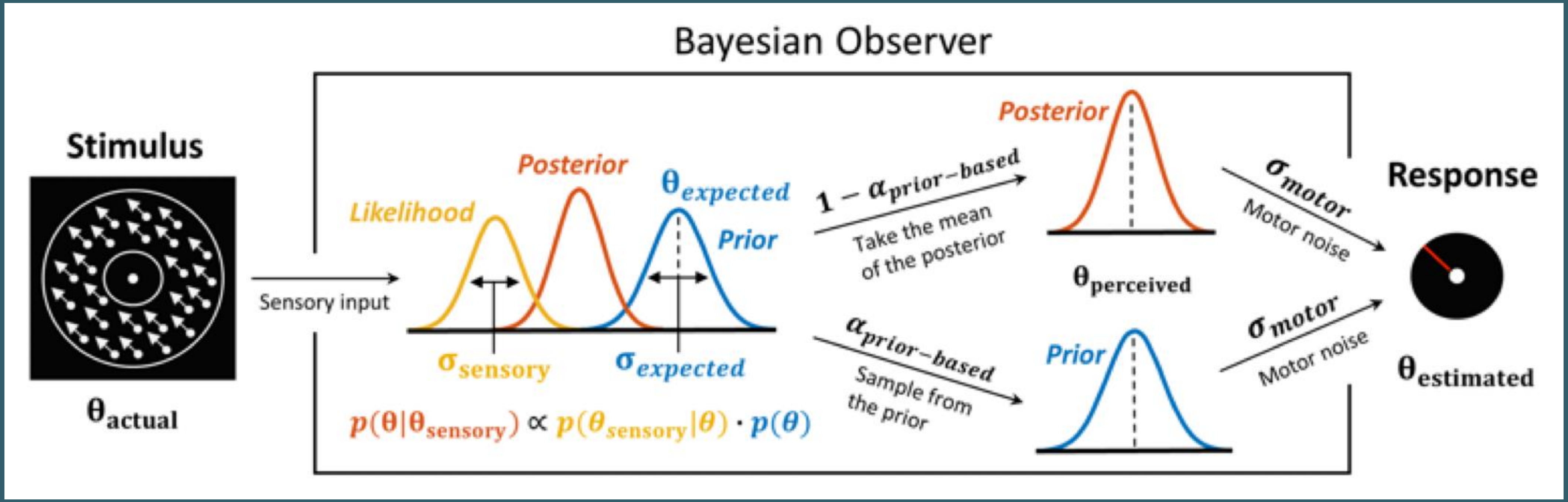


Biases:
participants perceive motion direction as being more similar to frequent directions than really is



“Hallucinations”:
participants sometimes perceive frequent motion direction even when it’s not there

[Chalk, Seitz, Seriès, 2010]



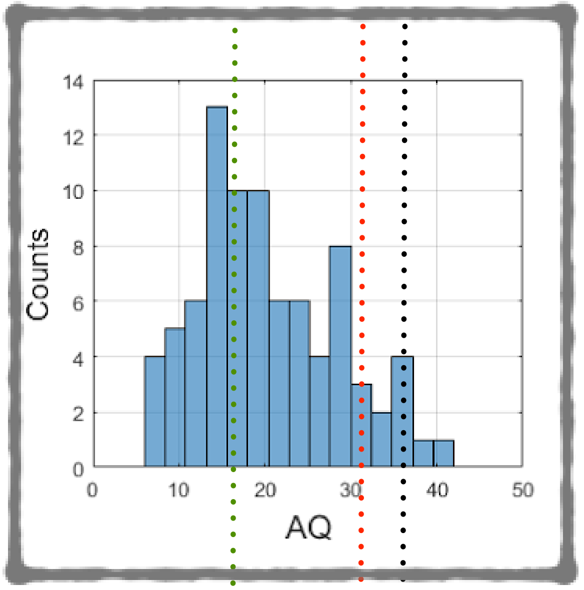
- **Behaviour is consistent with Bayesian model:**
  Participants combine a noisy estimate of the motion direction with a prior belief which represents an estimate of the stimulus distribution
- **We can recover the shape of likelihood and priors for each participant**

Fast, implicit learning of stimulus statistics modulates perception -- compatible with the construction of Bayesian priors and Bayesian inference.

Q: How would participants with autism (or autistic traits) behave in this task?

Autistic traits: weaker impact of the prior

- 83 healthy participants scored for schizotypy (RISC & SPQ) and autistic traits (AQ)

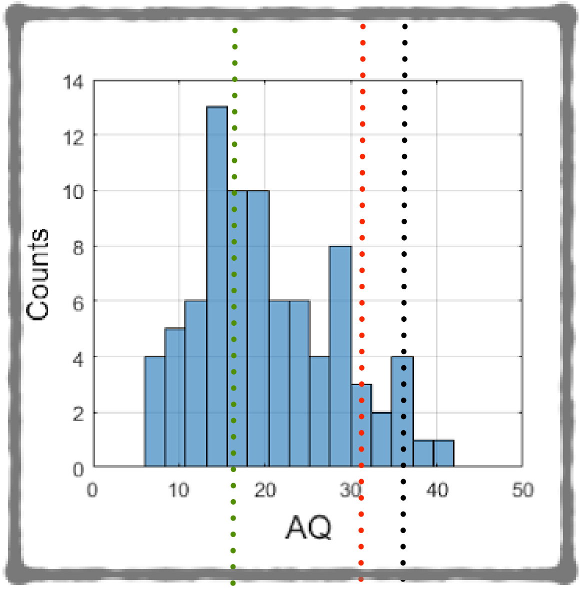


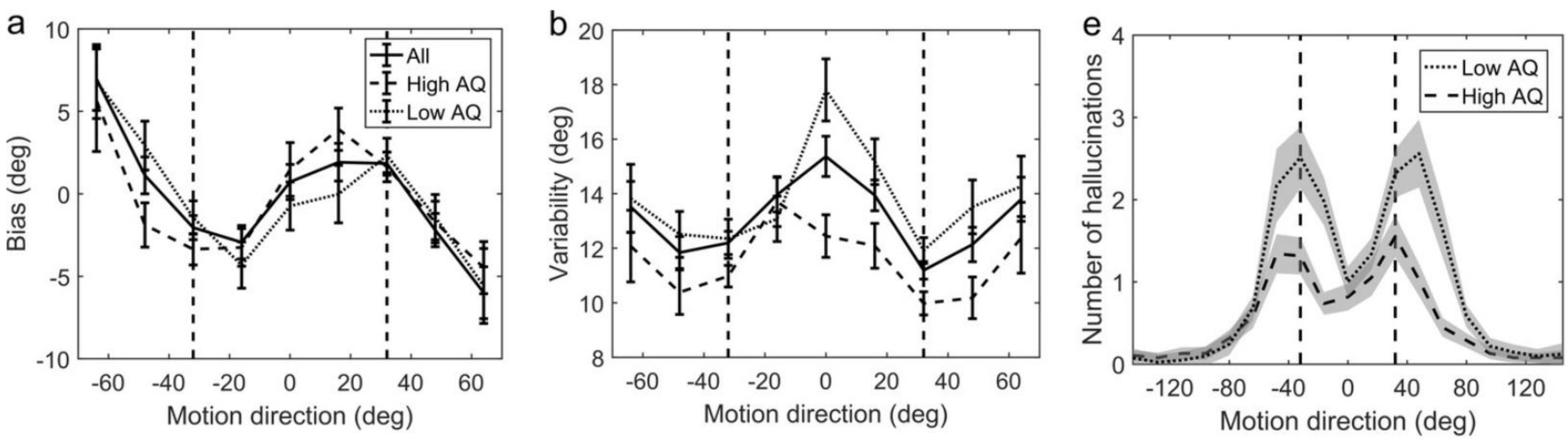
eLife [Karvelis, Seitz, Lawrie and Seriès, 2018]

Autistic traits: weaker impact of the prior

- 83 healthy participants scored for schizotypy (RISC & SPQ) and autistic traits (AQ)
- High AQ participants show less bias, are more precise in their estimations, and have fewer hallucinations. Correlations between AQ and those measures were stat. significant.

▶ compatible with the idea of them relying less on expectations

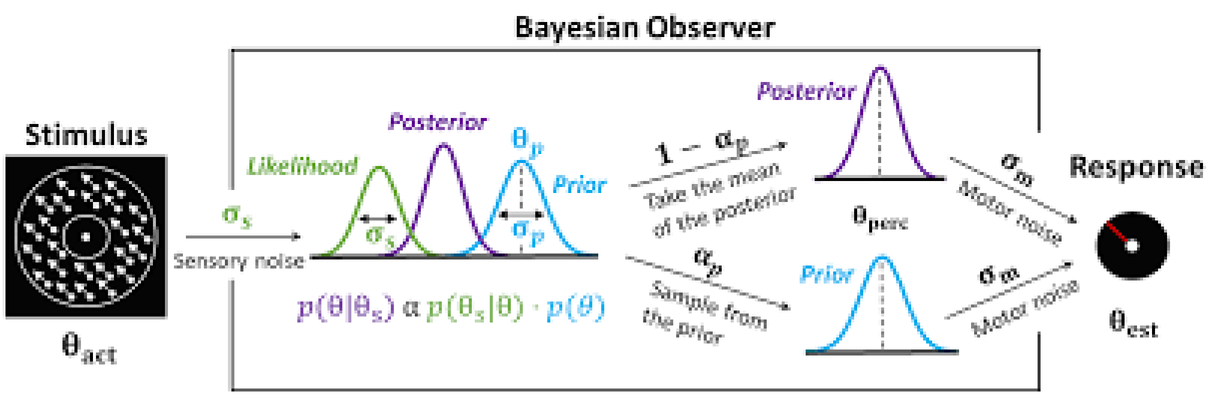


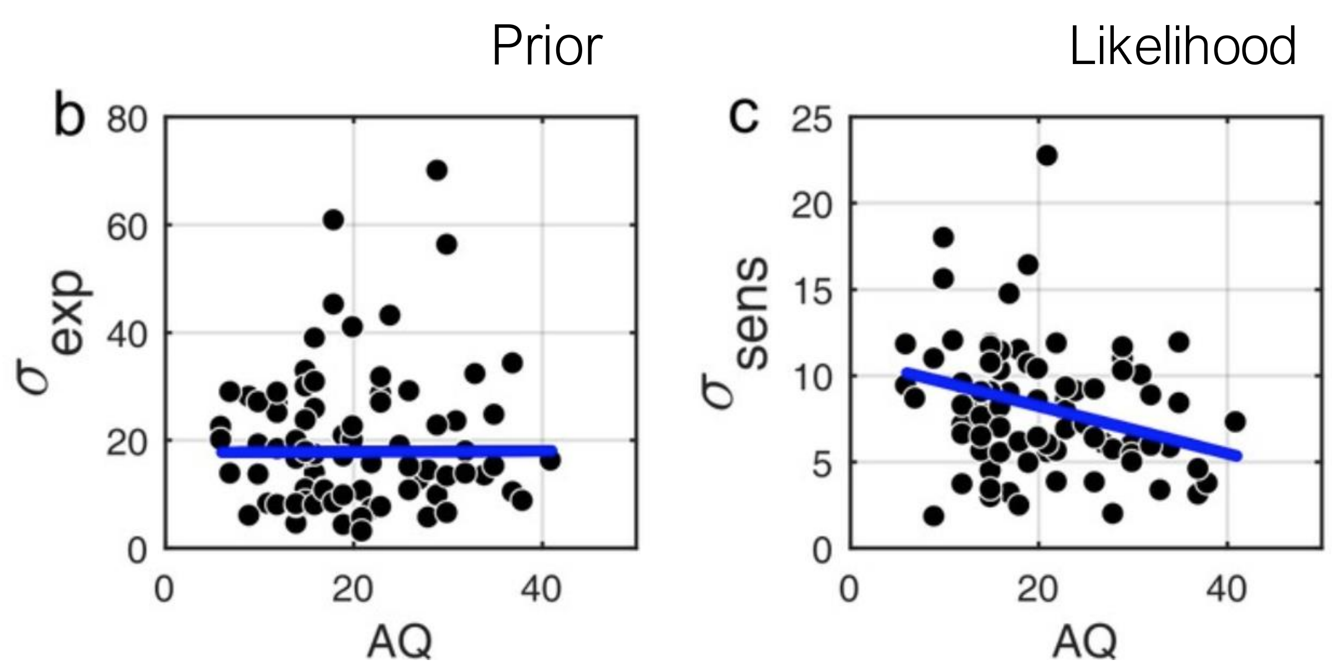


eLife [Karvelis, Seitz, Lawrie and Seriès, 2018]

Autistic traits: weaker impact of the prior

- Modelling can be used to quantitatively measure the relative and absolute impact of the likelihood and the prior on perception: a difference in likelihood more than in the prior.
- Results surprisingly support the (controversial) “enhanced sensory precision model”.
- To be tested in a patients group.





[Karvelis, Seitz, Lawrie and Seriès, 2018]

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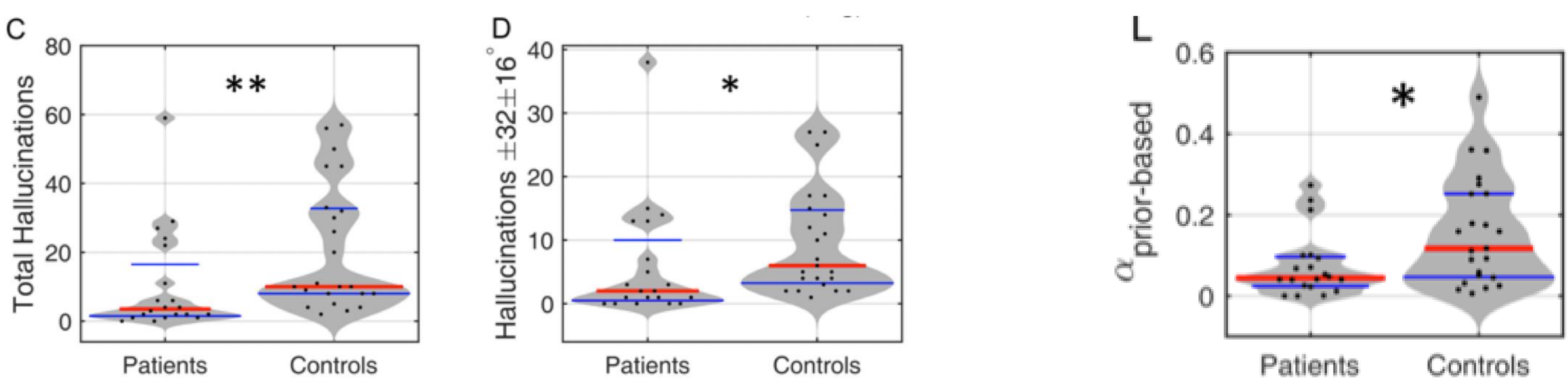
SCZ: intact stat. learning but fewer “hallucinations”

- 25 individuals with psychosis (DSM-IV schizophrenia, *n* = 21; or schizoaffective disorder, *n* = 4) recruited across NHS Lothian — 23 controls
- All patients medicated (85% 2nd gen anti-psychotics, 50% also mood stabilisers).
- Intact statistical learning in patients, no differences in width of prior or likelihood, but slower reaction times and less influence of priors when stimulus is absent or weak (consistent with current theories, except Powers et al 2017);
- Medication and patients’ wellbeing might explain absence of stronger differences



BRAIN A JOURNAL OF NEUROLOGY

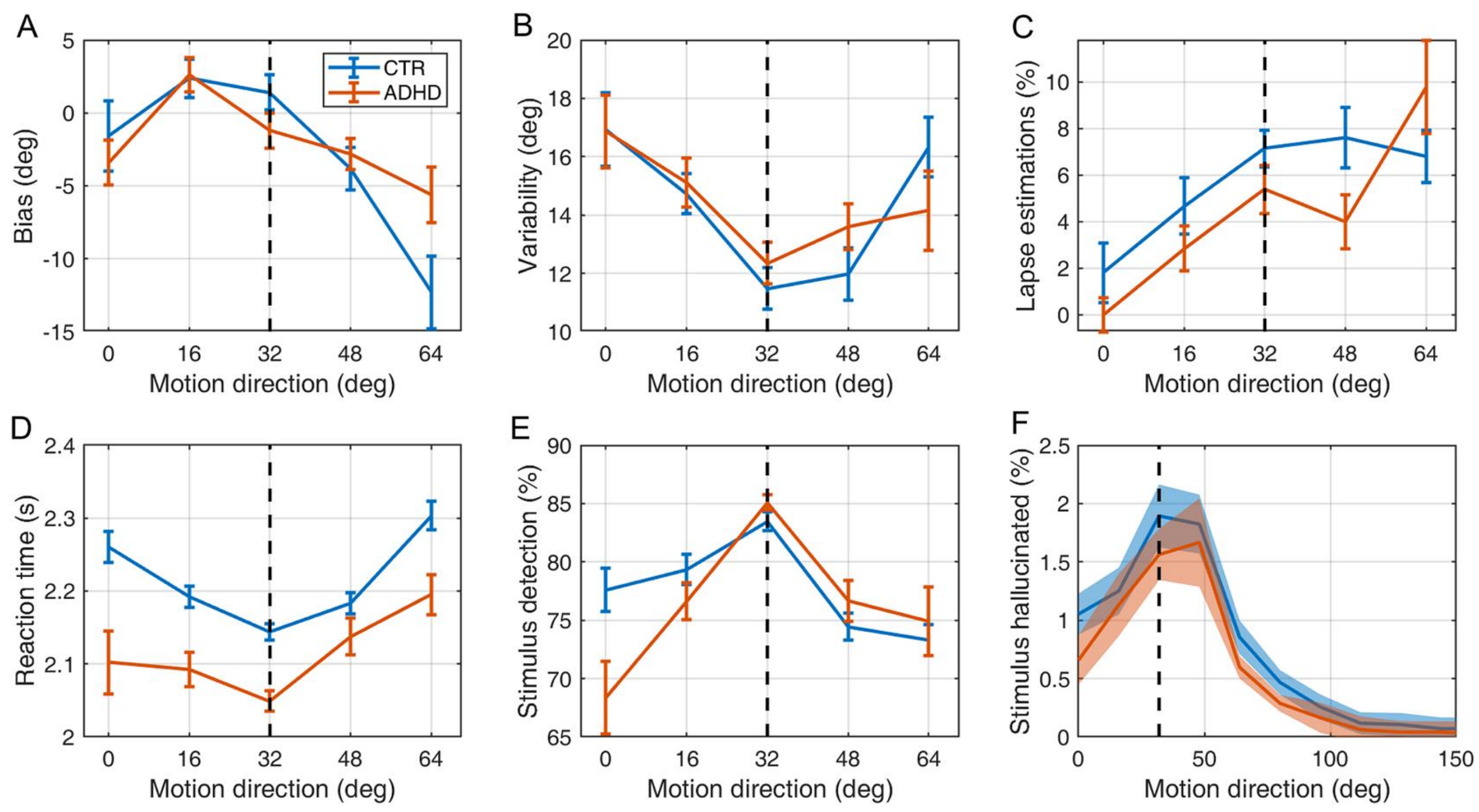
[Valton, Karvelis, Richards, Seitz, Lawrie and Seriès, 2019]

ADHD: Intact statistical learning and prior integration

- 20 ADHD vs 30 controls,

  Diagnoses verified using the Diagnostic Interview for ADHD in adults (DIVA

- Intact Statistical learning and inference;
- No difference between groups

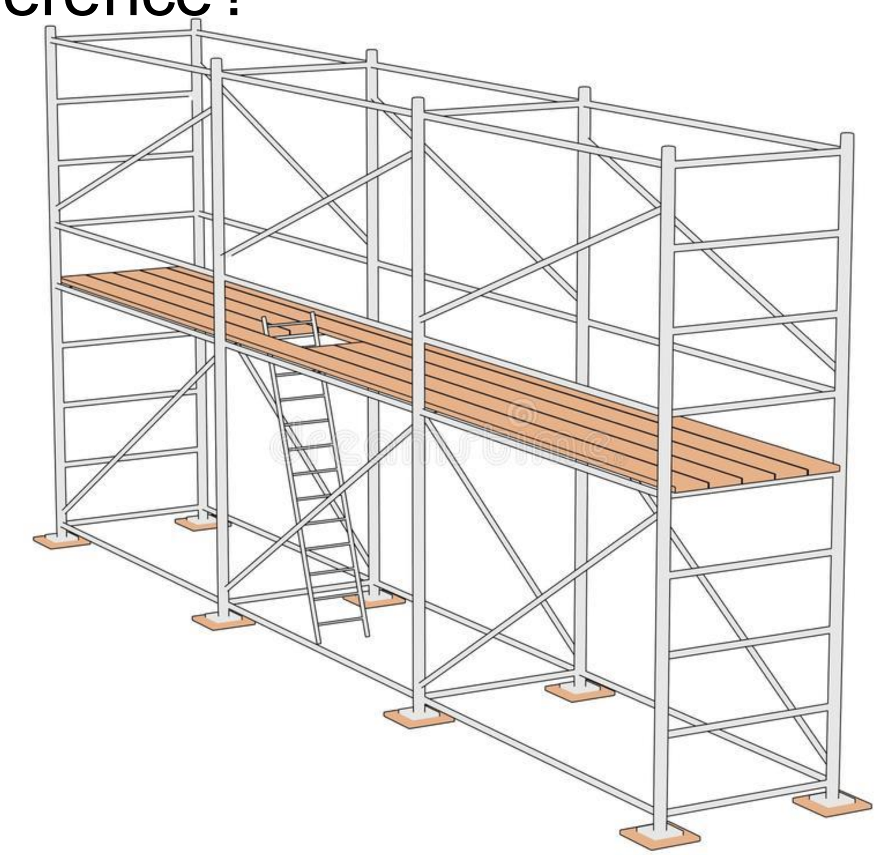


PLOS ONE [Richards, Karvelis, Lawrie & Seriès 2020]

Unifying data and theories

- Some (subtle) evidence for the current theories (weaker impact of prior, enhanced sensory precision in ASD), with contrasting features in ASD vs Schizophrenia;
- Many questions: Generalisation of the model to other tasks, modalities?
  Is it wise to think there is a unique machinery for Bayesian inference / predictive coding?
  Do impairments depend on how hierarchical the inference?
  Learning vs use of existing priors?
  volatility, context? social elements?

- Could we build a more sophisticated computational framework that would address these questions, account for algorithmic/implementation levels and the heterogeneity of findings?



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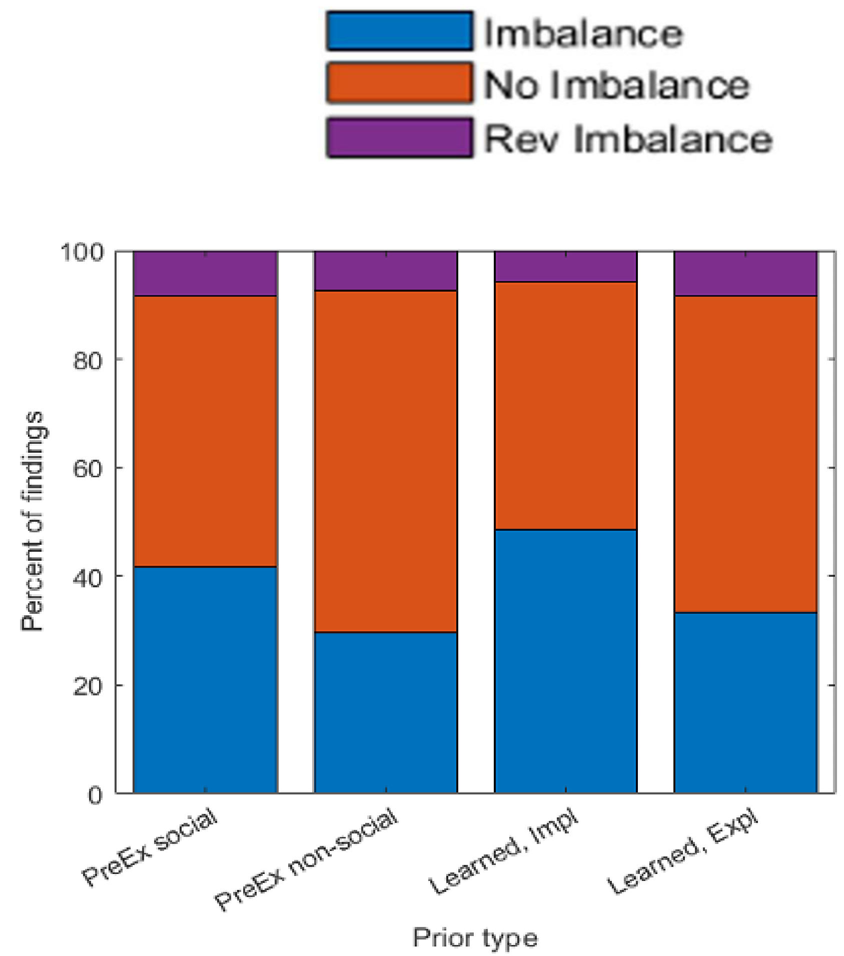
10 years of Bayesian theories of Autism

- Meta-analysis: 86 articles in [2012-2021] on autism and Bayesian or predictive coding (in title, abstract or keywords)
- Test the imbalance hypothesis (weaker relative influence of priors);
- Classified by: i) pre-existing/structural vs learned during task; (ii) implicit vs. explicit; (iii) social vs. non-social; iv) AQ vs. autistic patients



Neuroscience and Biobehavioral Reviews 145 (2023) 105022

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10 years of Bayesian theories of autism: A comprehensive review

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3

10 years of Bayesian theories of Autism

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10 years of Bayesian theories of autism: A comprehensive review

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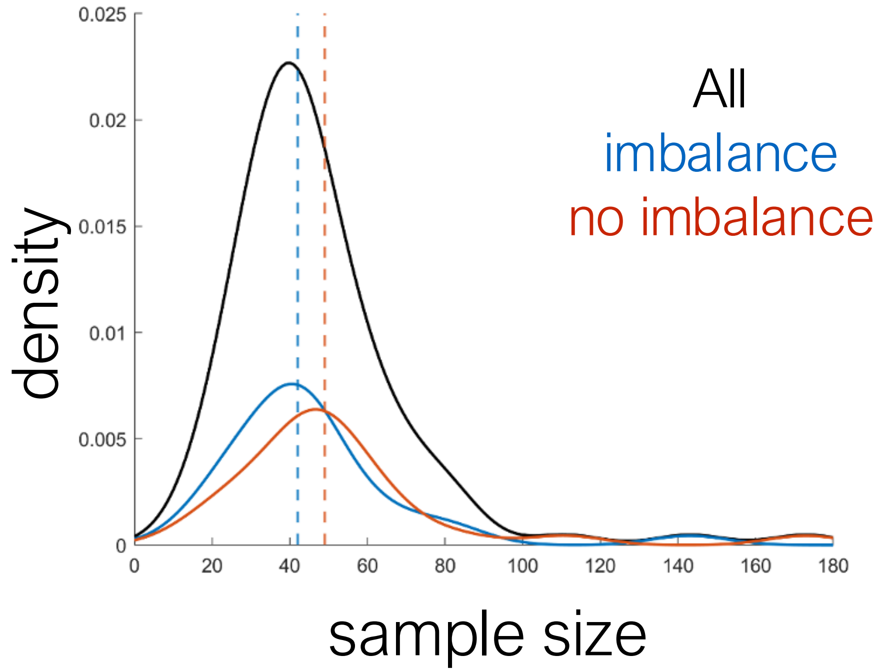
- Surprisingly, contrary to the popularity of theories, the experimental results do not clearly show a general imbalance between likelihood and priors.

- A little more evidence for the learned priors and social conditions.

10 years of Bayesian theories of Autism



- no obvious patterns differentiating the positive results to the negative results
- **Sample size** similar for imbalance vs no imbalance, **effect size** similar between imbalance vs reverse imbalance. More imbalance evidence in **patients vs AQ**. **Neuroimaging vs behavioural**.
- Huge **heterogeneity** of tasks, methods;
  Lack of consistency in group definition
  No replication. Very low power (~40%).
- Only 12/86 studies had an **explicit modelling component**! methodology often sub-standard.. (Wilson & Collins 2019)

→ We need to improve our experimental standards to be more theory-driven and quantitative and refine our theories

We need to do better

Improve Methodology of Behavioural Research

1. Explain how priors/predictions and likelihoods/prediction errors are conceptualised. How an imbalance would manifest in the data. Contrast the different theories.
2. Fit Bayesian/predictive coding computational models
   Model comparison. Model and parameter recovery (Wilson & Collins, 2019).
3. Pre-register the study. Motivate sample size. Improve consistency / definition of groups.
4. Measure prior acquisition and flexibility as well as imbalance.

Fortunately, the standards are improving.

Towards more nuanced theories

Bayesian theories are/ will stay useful but a uniform imbalance between priors and likelihood will probably not easily provide a general explanation for the diversity and complexity of ASD.

Refine our theories

1. Static Bayesian/predictive Processes vs updating/Learning of internal models. Static vs dynamical modulation of precision.
2. Better framework for the hierarchy of priors in the brain & implementation.
3. Establish if/what flavor of predictive coding is implemented
   if starting from algorithmic/implementation level more helpful.
   Strengthen the link between E/I imbalance, (divisive normalization) and inference.

4. Explore whether similarities of current theories for different diagnostic classes can explain comorbidities (e.g. ASD and anxiety, cPTSD and SCZ).
5. Developmental approach?

Conclusions

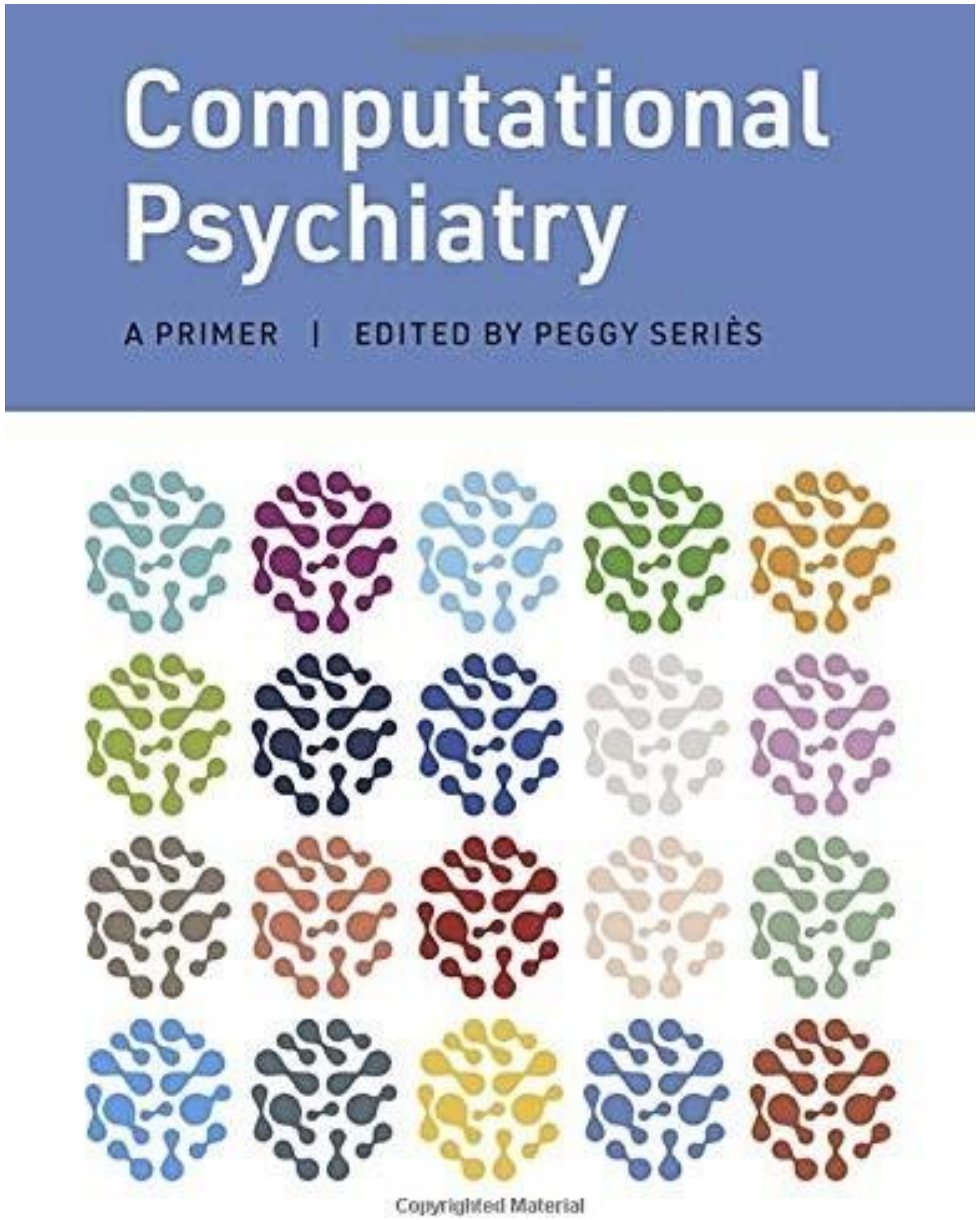
In schizophrenia and ASD (like in other disorders), CP shows great potential for:

1. identifying and quantifying behavioural differences (diagnosis)
2. understanding how/why the brain generates dysfunctional behaviours (bridge with neuroscience);
3. development new learning-based psychotherapies or drugs
4. Possibly revising the classification of disorders, addressing comorbidities and provide biomarkers

4 Conclusions

- but still at a mostly exploratory stage.. Need to refine the still crude theories, and improve the standards to validate them and make them useful for the clinic.

- A field in maturation at the same time as the dialogue between clinicians, experimentalists and theorists is being refined.



2020

Chapter 1: Introduction: Toward a Computational Approach to Psychiatry

Janine M. Simmons, Bruce Cuthbert, Joshua A. Gordon, & Michele Ferrante.

Chapter 2: Methods of Computational Psychiatry: A brief Survey

Peggy Seriès

Chapter 3: Biophysically Based Neural Circuit Modeling of Working Memory and Decision Making and Related Psychiatric Deficits

Xiao-Jing Wang and John D. Murray

Chapter 4: Computational Models of Cognitive Control: Past and Current Approaches

Debbie M. Yee and Todd S. Braver

Chapter 5: The Value of Almost Everything: Models of the Positive and Negative Valence Systems and their relevance to Psychiatry

Peter Dayan

Chapter 6: Psychosis and Schizophrenia from a Computational Perspective

Rick A Adams

Chapter 7: Depressive Disorders from a Computational Perspective

Samuel Rupprechter, Vincent Valton, Peggy Seriès

Chapter 8: Anxiety Disorders from a Computational Perspective

Erdem Pulcu and Michael Browning

Chapter 9: Addiction from a Computational Perspective

David Redish

Chapter 10: Tourette Syndrome from a Computational Perspective

Vasco A. Conceição and Tiago V. Maia

Chapter 11: Perspectives and Further Study in Computational Psychiatry

Peggy Seriès

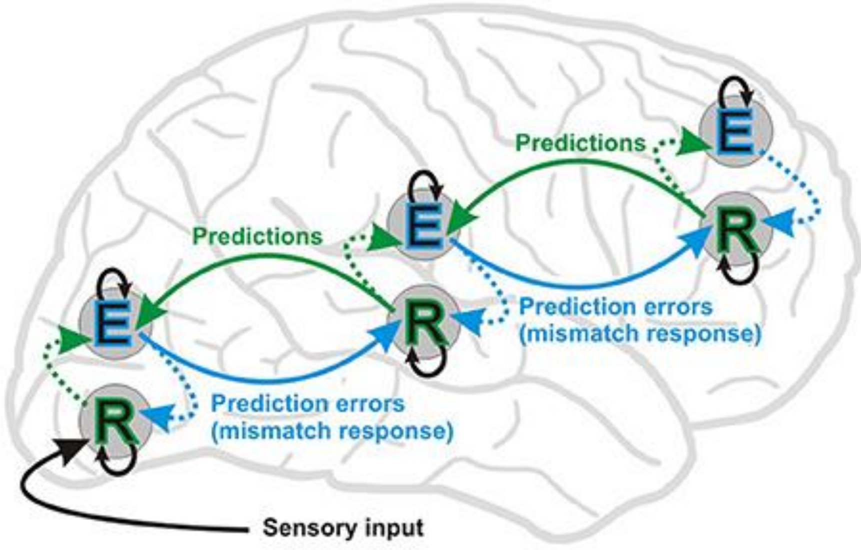
Additional slides and references

Impaired Inference in Psychosis/Schizophrenia

- Also framed in terms of imbalance between priors and likelihood.

Sensory priors are too broad/ weak and fail to attenuate sensory inputs.
▶ a changing and unstable world, aberrant salience.

To compensate, more **cognitive priors might become too strong**
▶ psychosis (hallucinations, delusions)
[Schmack et al., 2015; 2017; Powers et al 2017]



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