‘Bayesian’ theories: Application to Computational Psychiatry (CCN Lecture 15)

Peggy Seriès,
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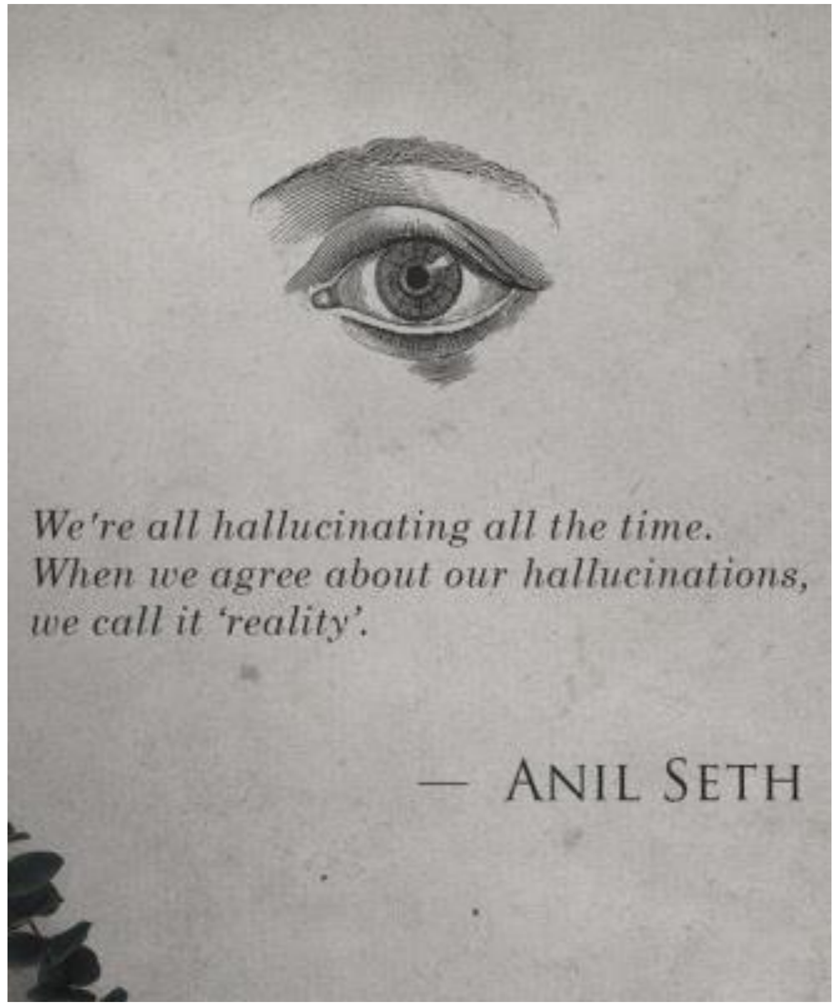
Bayesian Brain - Summary

- Behavioural studies suggest that human observers behave in ways compatible with Bayesian inference
- Bayesian modelling offers a way to "reverse engineer" the internal models.
- Perception is a reconstruction or even a "controlled hallucination", based on the internal model of the brain
- The same tools can be applied for cognition more generally.
- A possible tool for understanding mental illness? A case where the internal models would be maladaptive?



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 different exposure (trauma) or 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

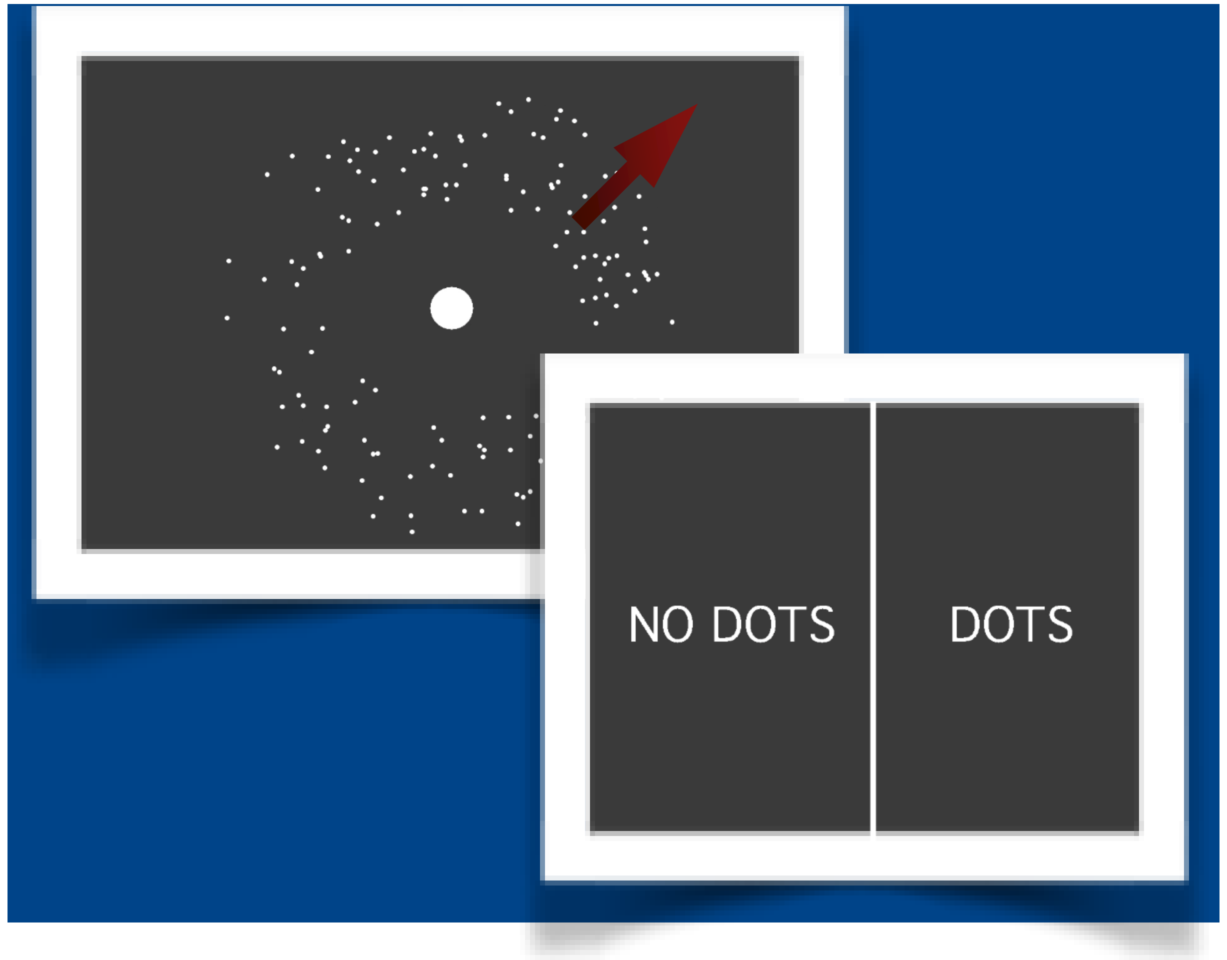
(e.g. pessimistic priors in depression, or priors on controllability, priors on mistrust in borderline).

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

- > a new area of research.

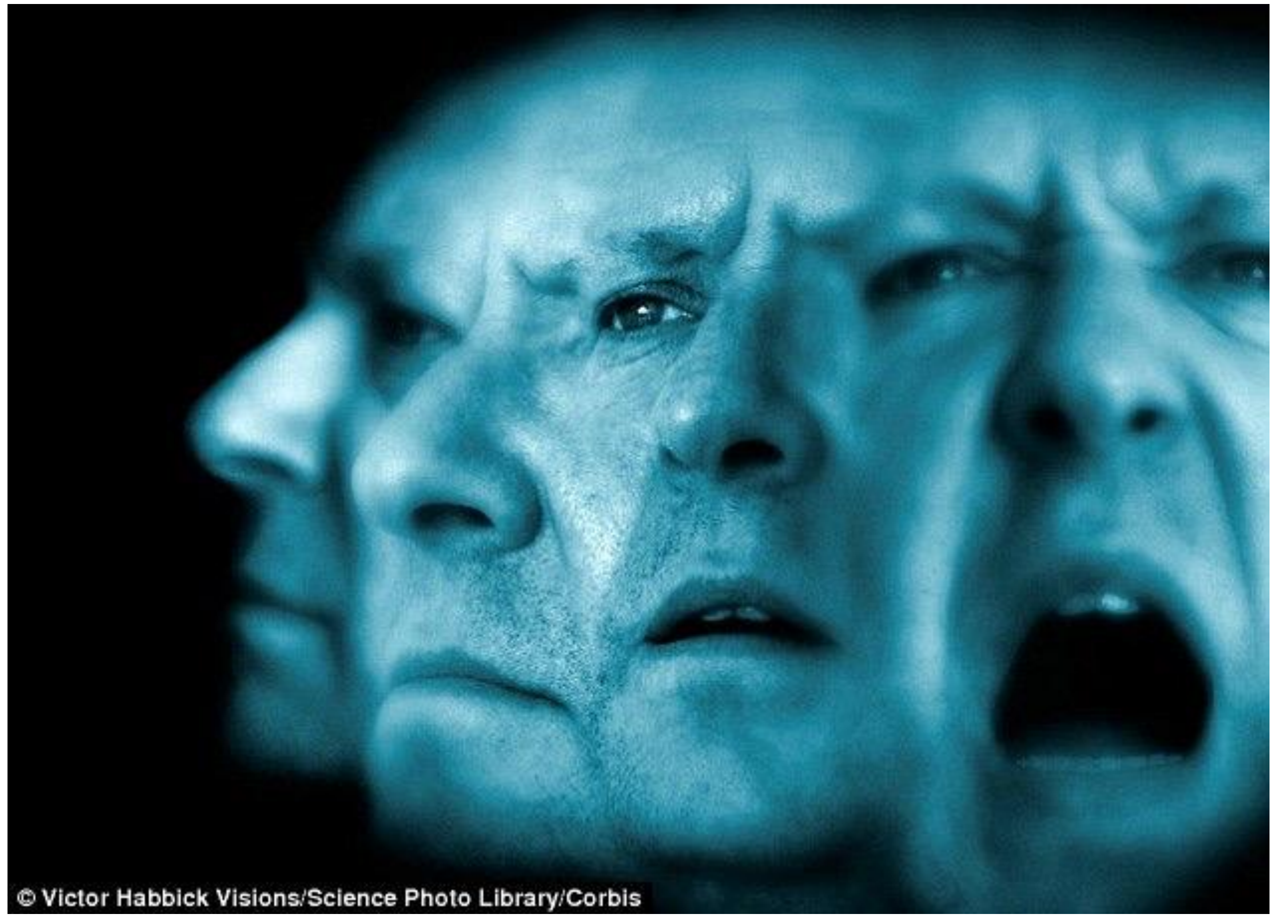
Today's Lecture

- Bayesian models of Schizophrenia
- 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)
- Discussion: Status of the field and Methodological challenges



Schizophrenia affects the way you think

- about 1/100 people.
- usually starts during early adulthood.
- **Positive symptoms** experiencing things that are not real (hallucinations) and having unusual beliefs (delusions)
- **Negative symptoms** include lack of motivation and becoming withdrawn.
- **Cognitive symptoms** including social deficits.



https://www.youtube.com/watch?v=SN1GCoVzxGg

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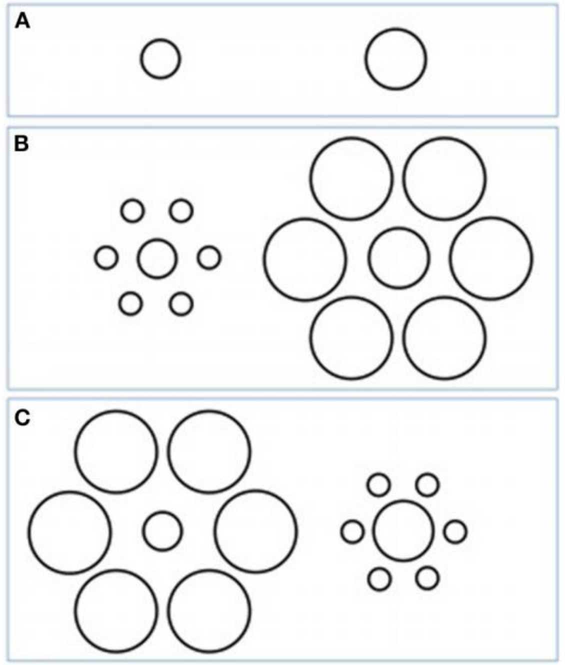
Schizophrenia affects the way you see

• Several authors defend that visual perception plays an important role in the psychopathology of schizophrenia, and constitutes a unique way to explore the underlying mechanisms of reality construction (Silverstein and Keane, 2011).

• Patients with schizophrenia are less susceptible to visual illusions



frontiers in INTEGRATIVE NEUROSCIENCE

REVIEW ARTICLE
published: 12 August 2014
doi: 10.3389/fnint.2014.00063

What visual illusions teach us about schizophrenia

Charles-Edouard Notredame[1,2]*, Delphine Pins[2], Sophie Deneve[3] and Renaud Jardri[1,2,3]

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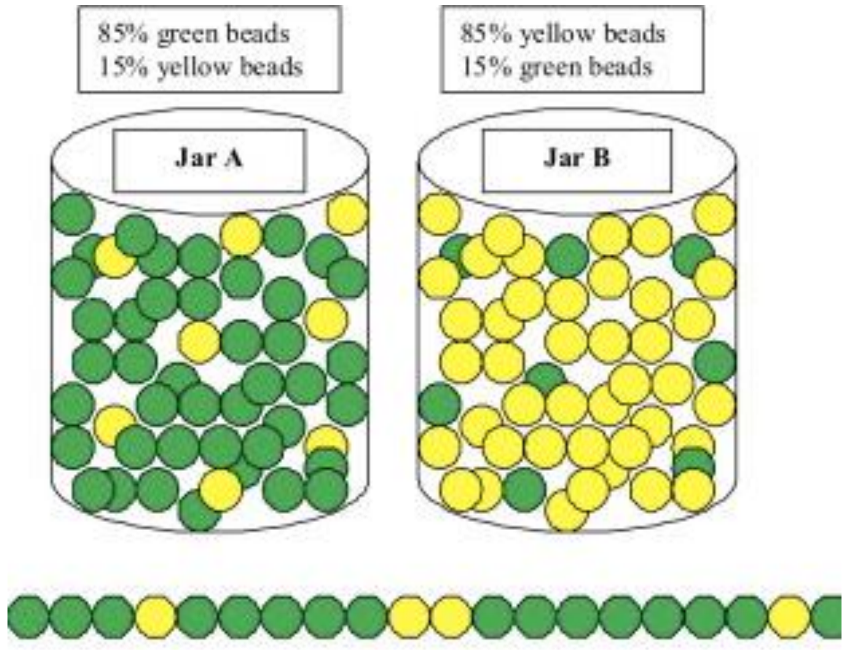
Illusion, namely a mismatch between the objective and perceived properties of an object present in the environment, is a common feature of visual perception, both in normal and pathological conditions. This makes illusion a valuable tool with which to explore normal perception and its impairments. Although still debated, the hypothesis of a modified, and typically diminished, susceptibility to illusions in schizophrenia patients is supported by a growing number of studies. The current paper aimed to review how illusions have been used to explore and reveal the core features of visual perception in schizophrenia from a psychophysical, neurophysiological and functional point of view. We propose an integration of these findings into a common hierarchical Bayesian inference framework. The Bayesian formalism considers perception as the optimal combination between sensory evidence

1

Schizophrenia affects how you make decisions

- Patients with schizophrenia have a tendency to "jump to conclusions"
- nonaffective psychosis is characterized by a hasty decision-making style (less information to make decisions on average, greater odds of extreme responding (less than 2 beads)), which is linked to an increased probability of delusions.



"Beads task": Which jar am I drawing from ?
When can you commit to a decision?

Schizophrenia Bulletin vol. 42 no. 3 pp. 652–665, 2016
doi:10.1093/schbul/sbv150
Advance Access publication October 31, 2015

Psychosis, Delusions and the "Jumping to Conclusions" Reasoning Bias: A Systematic Review and Meta-analysis

Robert Dudley*[,1,2], Peter Taylor[3], Sophie Wickham[3], and Paul Hutton[4]

[1]School of Psychology, Newcastle University, Newcastle Upon Tyne, UK; [2]Early Intervention in Psychosis Service, Northumberland, Tyne and Wear NHS Foundation Trust, Gateshead, UK; [3]Institute of Psychology, Health and Society, University of Liverpool, Liverpool, UK; [4]School of Health in Social Science, University of Edinburgh, Edinburgh, UK

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We did a systematic review and meta-analysis to investigate the magnitude and specificity of the "jumping to conclusions" (JTC) bias in psychosis and delusions. We examined the

paranoia are common themes[1] and such beliefs are a hallmark feature of diagnoses like schizophrenia and delusional disorder. Delusions are often preoccupying,

Towards A Bayesian approach

Nature Reviews Neuroscience | AOP, published online 3 December 2008;

Perceiving is believing: a Bayesian approach to explaining the positive symptoms of schizophrenia

Paul C. Fletcher and Chris D. Frith‡§*

Abstract | Advances in cognitive neuroscience offer us new ways to understand the symptoms of mental illness by uniting basic neurochemical and neurophysiological observations with the conscious experiences that characterize these symptoms. Cognitive theories about the positive symptoms of schizophrenia — hallucinations and delusions —

- Positive symptoms of schizophrenia are caused by abnormality in brains' prediction or inferencing mechanisms: new inputs are not properly integrated to previous knowledge, leading to false prediction errors.
- lead to false or strange perception, e.g. inability to discount one's own actions —> attributing self-generated actions (e.g. thoughts) to others (e.g. voices), and readiness to accept innocuous events as salient and important.
- Strange beliefs will develop to account for the strange perception.

Weaker Priors or Stronger Priors?

Some studies point to the idea of priors being weaker in schizophrenia (weaker predictions), some studies report the opposite:

RESEARCH

NEUROSCIENCE

Pavlovian conditioning-induced hallucinations result from overweighting of perceptual priors

A. R. Powers,[1] C. Mathys,[2,3,4] P. R. Corlett[1]*

Some people hear voices that others do not, but only some of those people seek treatment. Using a Pavlovian learning task, we induced conditioned hallucinations in four groups of people who differed orthogonally in their voice-hearing and treatment-seeking statuses. People who hear voices were significantly more susceptible to the effect. Using functional neuroimaging and computational modeling of perception, we identified processes that differentiated voice-hearers from non–voice-hearers and treatment-seekers from non–treatment-seekers and characterized a brain circuit that mediated the conditioned hallucinations. These data demonstrate the profound and sometimes pathological impact of top-down cognitive processes on perception and may represent an objective means to discern people with a need for treatment from those without.

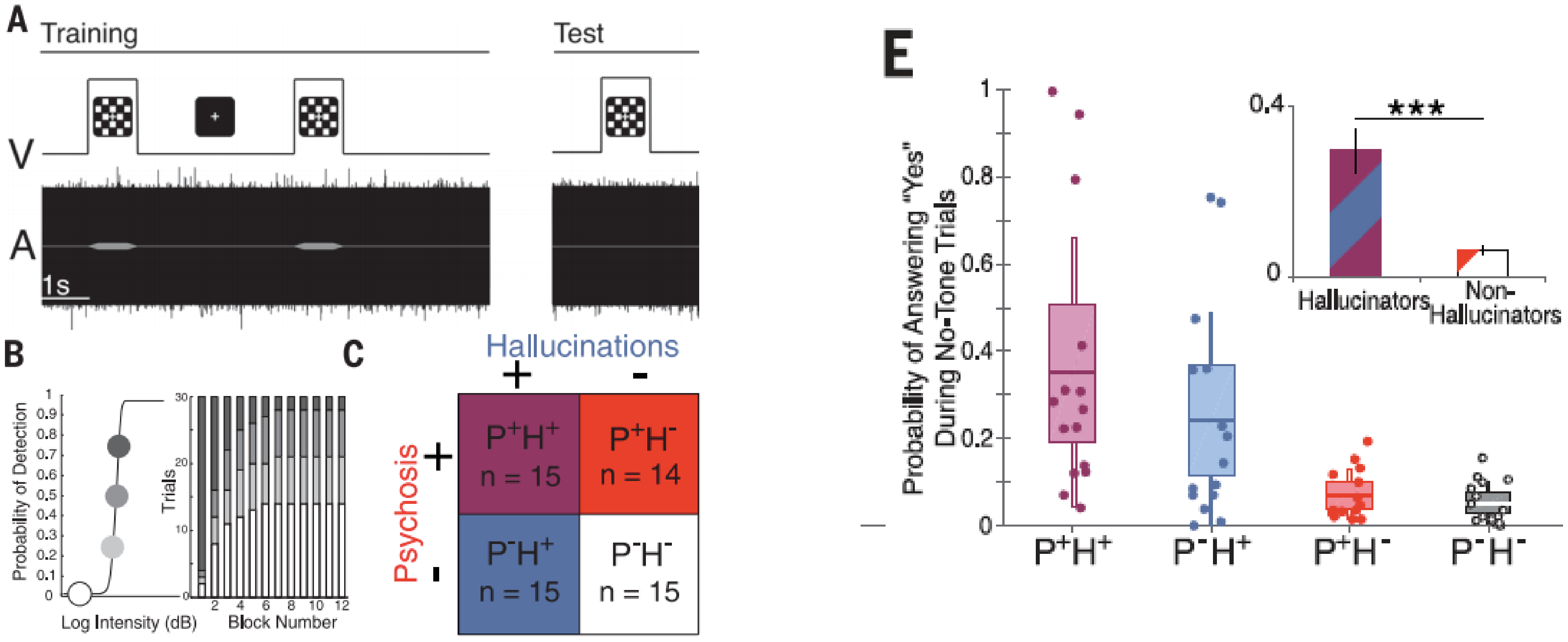
Powers *et al.*, *Science* **357**, 596–600 (2017)

- Participants had to **detect a 1-kHz tone occurring concurrently with checkerboard** visual stimulus

- **4 groups:**
  1) psychotic illness who heard voices (P+H+, n = 15);
  2) psychotic illness but no voices (P+H–, n = 14);
  3) control group who heard daily voices, but had no diagnosed illness (P–H+, n = 15)—they attributed their experiences metaphysically;
  4) controls without diagnosis or voices (P–H–, n = 15)

Stronger Priors in People who Hear Voices

Hallucinators, independently of diagnosis, had more conditioned hallucinations (i.e thought they heard the tone when it was not there but the visual stimulus was present).



Powers *et al.*, *Science* **357**, 596–600 (2017)

Impaired Predictions in Schizophrenia: Consensus?

- Sensory priors are too broad/ weak and fail to attenuate sensory inputs.

▶ a changing and unstable world, aberrant salience.

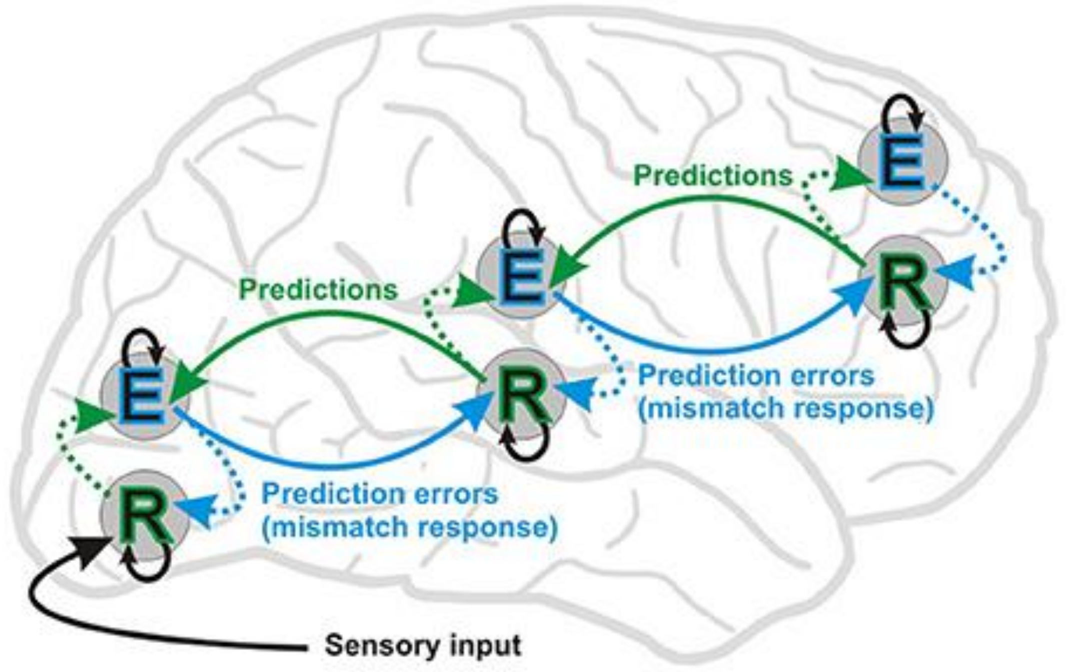
- Consistent with a variety of experimental results: resistance to illusions, Mismatch negativity, eye movements, force-matching experiments.

[Dakin et al., 2005; Dima et al., 2009; Sanders et al., 2012; Schmack et al., 2015; Schneider et al., 2002; Seymour et al., 2013; Uhlhaas et al., 2004]

- To compensate, more cognitive priors might become too strong

▶ psychosis (hallucinations, delusions)

[Schmack et al., 2015; 2017; Powers et al 2017]



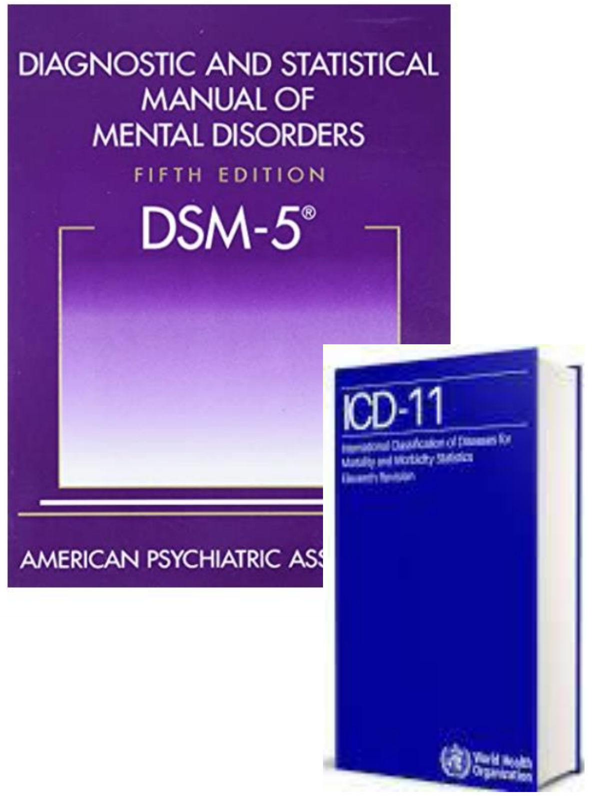
Autism Spectrum Disorder (ASD)

- 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

Autism as a Disorder of Prediction or Inference

TICS-1125; No. of Pages 7 ARTICLE IN PRESS

Opinion

When the world becomes 'too real': a Bayesian explanation of autistic perception

Elizabeth Pellicano[1,3] and David Burr[2,3]

[1] Centre for Research in Autism and Education (CRAE), Institute of Education, University of London, London, UK
[2] Department of Psychology, University of Florence, Florence, Italy

2012

frontiers in HUMAN NEUROSCIENCE — HYPOTHESIS AND THEORY ARTICLE — published: 14 May 2014 — doi: 10.3389/fnhum.2014.00302

An aberrant precision account of autism

Rebecca P. Lawson[1]*, Geraint Rees[1,2] and Karl J. Friston[1]

Autism as a disorder of prediction

Pawan Sinha[a,1], Margaret M. Kjelgaard[a,b], Tapan K. Gandhi[a,c], Kleovoulos Tsourides[a], Annie L. Cardinaux[a], Dimitrios Pantazis[a], Sidney P. Diamond[a], and Richard M. Held[a,1]

2025

Neuroscience and Biobehavioral Reviews 145 (2023) 105022

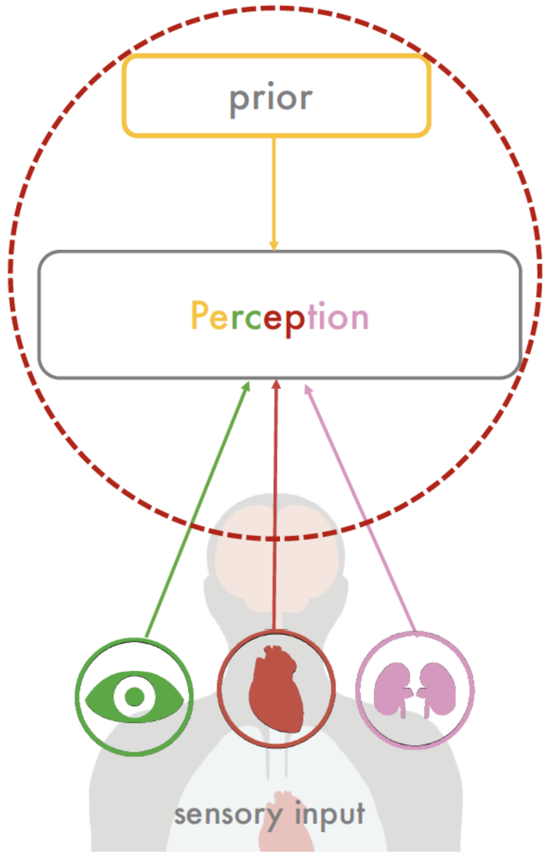
10 years of Bayesian theories of autism: A comprehensive review

Nikitas Angeletos Chrysaitis, Peggy Seriès

Institute for Adaptive and Neural Computation, University of Edinburgh, 10 Crichton Street, Edinburgh EH8 9AB, United Kingdom

- 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?



Could 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]

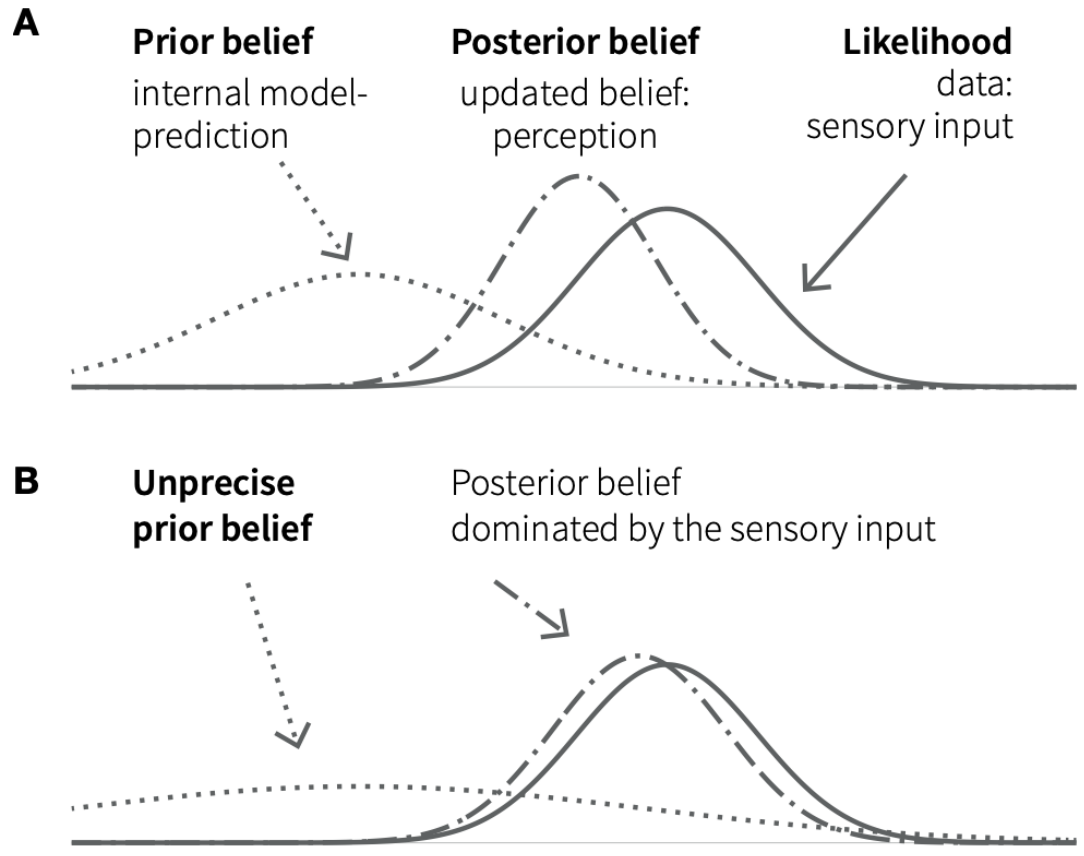
Relatively weaker priors in autism?

Sensory input unaffected

Hypothesis 1
Weaker / flatter Priors

Lower precision

π_{prior}



Relatively weaker priors in autism?

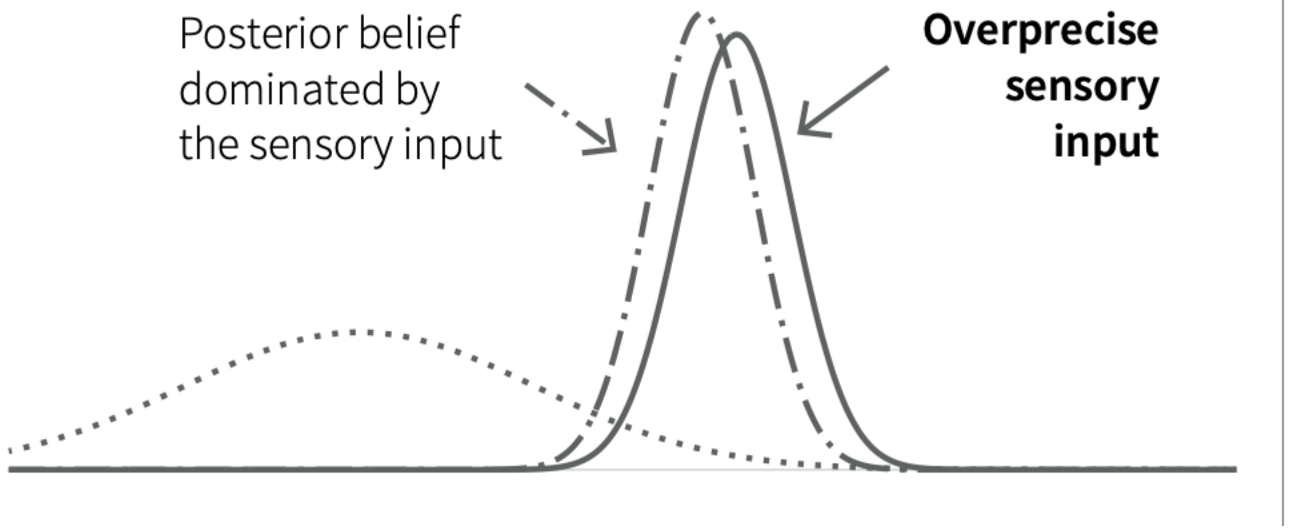
prior expectations unaffected

Hypothesis 2
Sensory information more precise

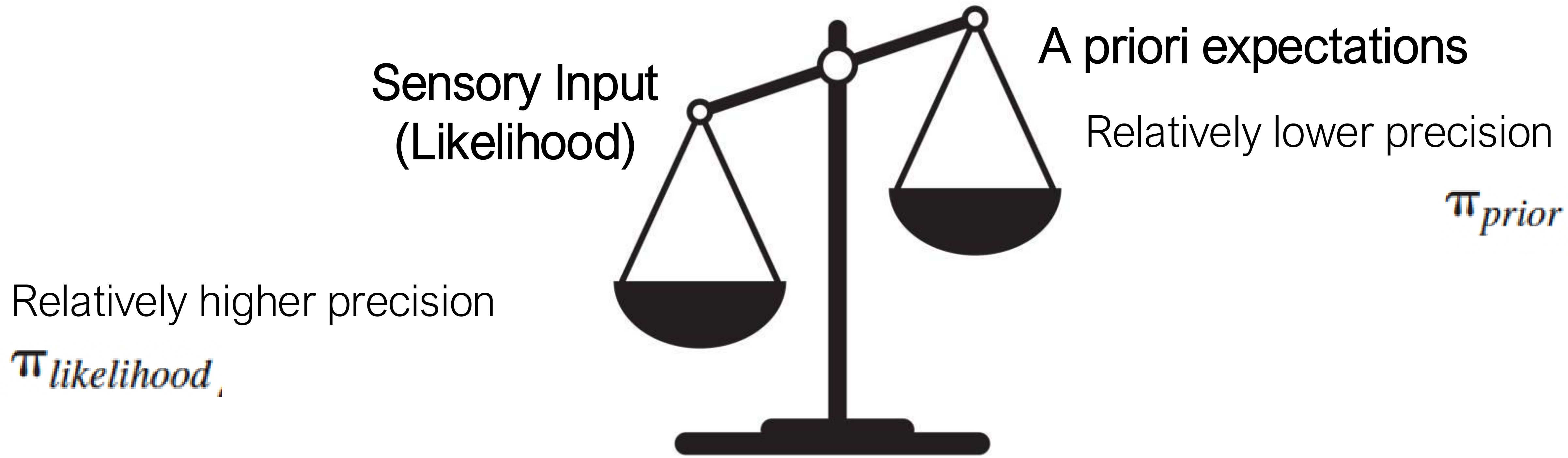
Higher precision

$\pi_{likelihood}$

C



Predictive Coding Reformulation: Increased weight on prediction error



Weight on PE
Learning rate

Prediction error

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

where

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

Or a problem of inflexibility?

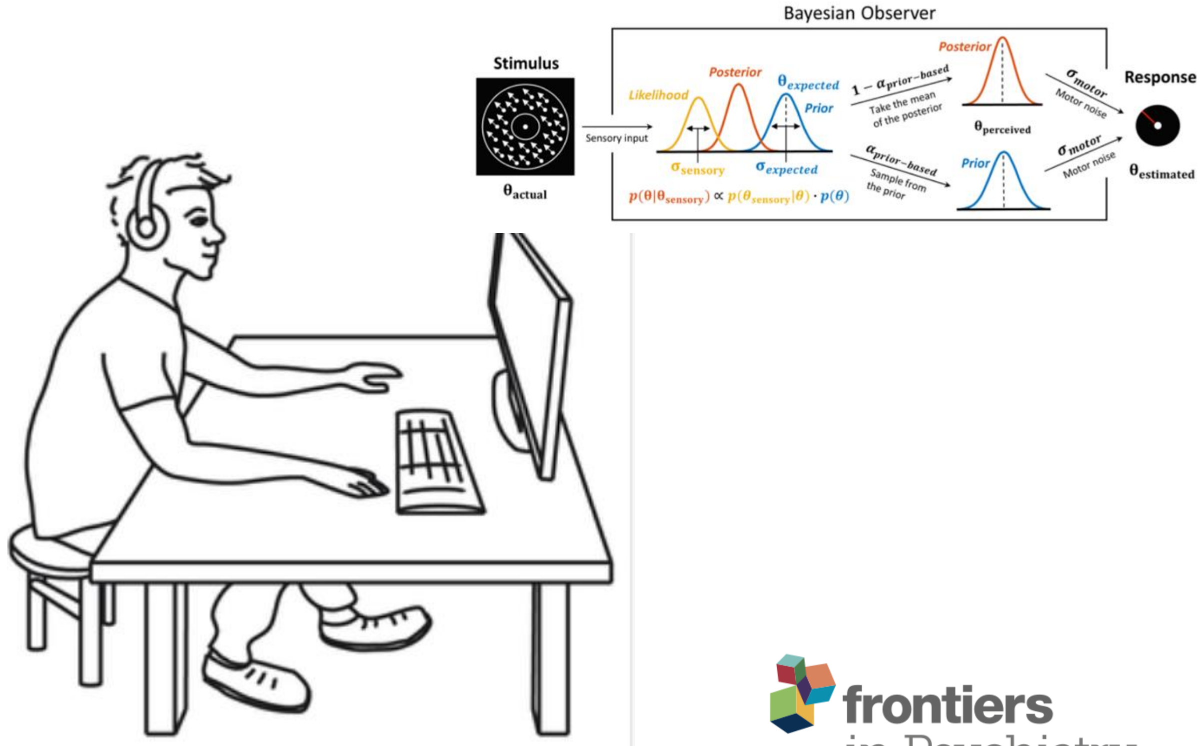
- **Hypothesis 3:** Inflexibility – Priors are more rigid or High and Inflexible Precision of Prediction Errors (HIPPEA) [Van de Cruys et al. 2014]
- In dynamic contexts: Overestimation of environmental volatility [Lawson et al 2016];

"The world is moving too fast"

Clinical interest: providing quantitative tests

If the theories are validated (and specific):

- Provide objective, quantitative, behavioral tests for diagnosis that could be conducted by non-specialists.
- Quantifying parameters at individual level (precision psychiatry)
- Understanding comorbidities (e.g. anxiety) and similarities/differences other disorders (e.g. ASD vs schizophrenia).
- Define learning conditions in which patients can benefit from learning-based therapies.
- fMRI - Neurobiological substrate, provide biomarkers



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

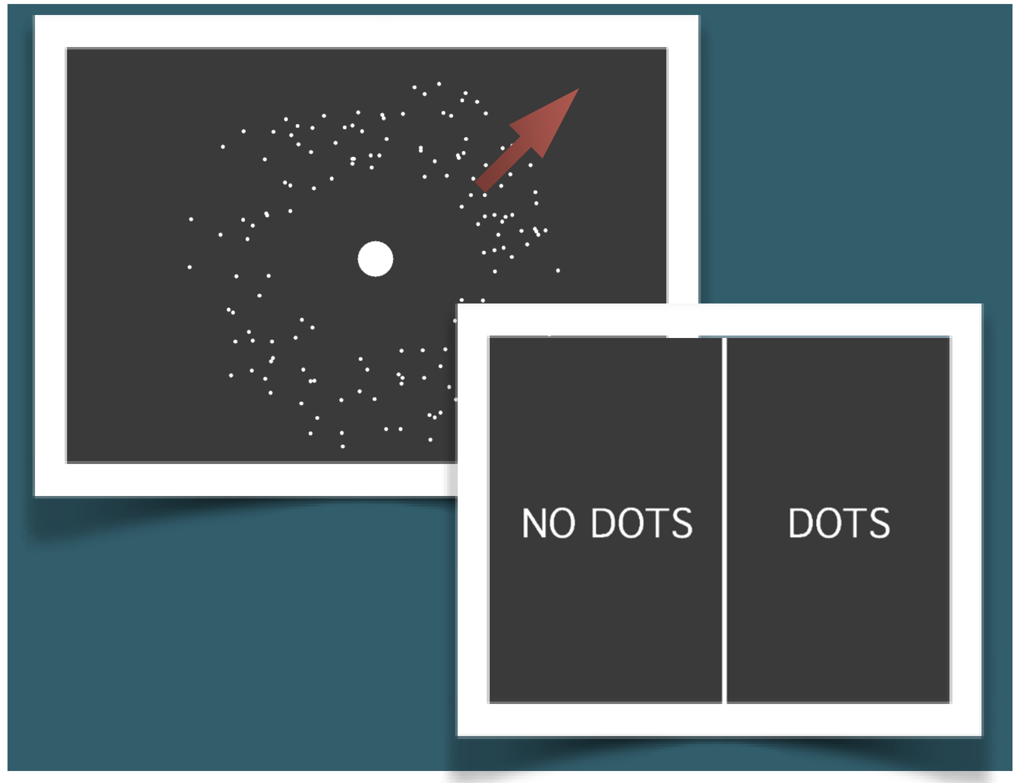
Diagnosis and individualized treatment of autism spectrum disorder (ASD) represent major problems for contemporary psychiatry. Tackling these problems requires guidance by a pathophysiological theory. In this paper, we consider recent theories that re-conceptualize ASD from a "Bayesian brain" perspective, 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?

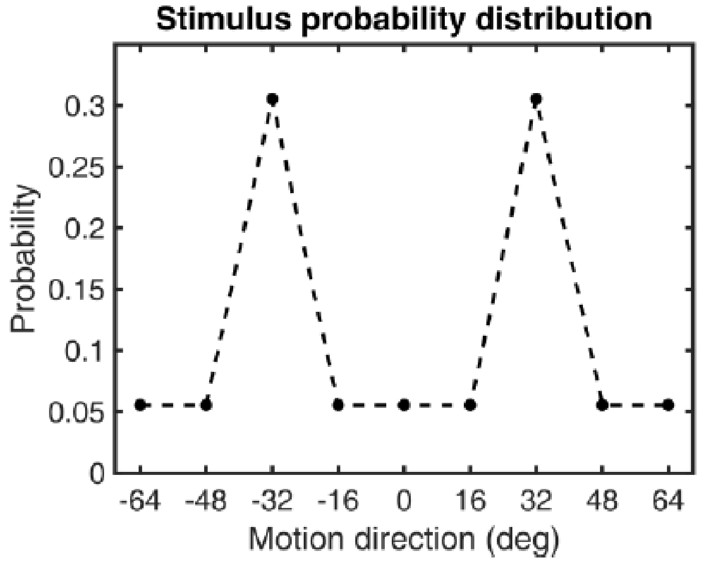
Testing the models with a statistical learning task:

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).

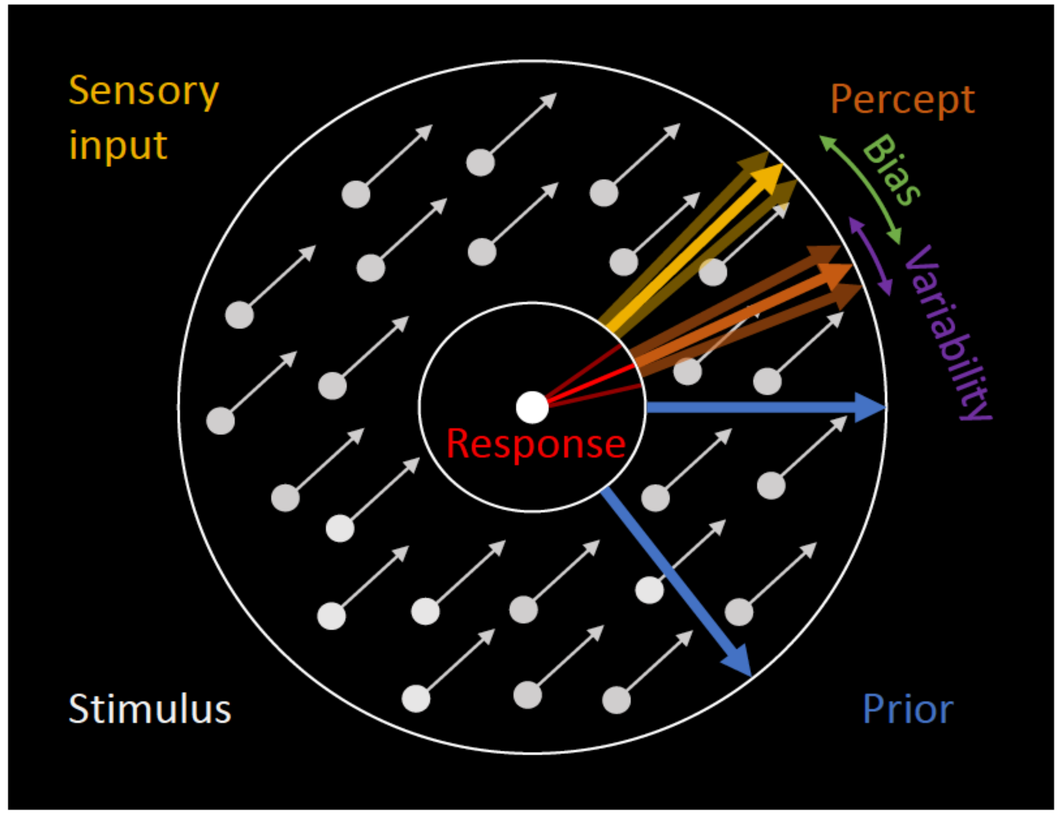


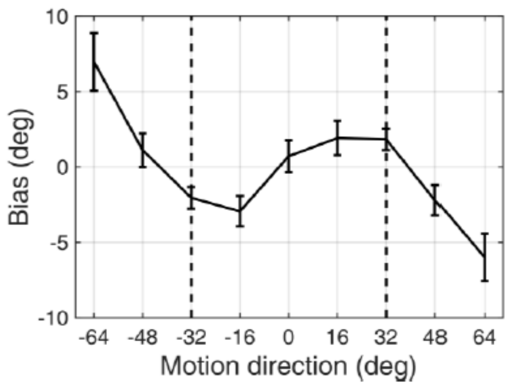
- Two directions of motion are more frequently presented. Are participants going to learn about this? implicitly? how will this change their perception?

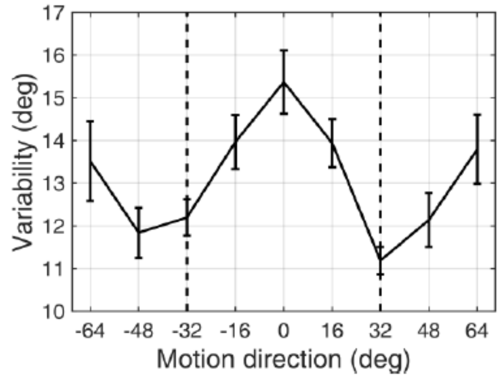


jov an ARVO journal

[Chalk, Seitz, Seriès, JOV 2010]

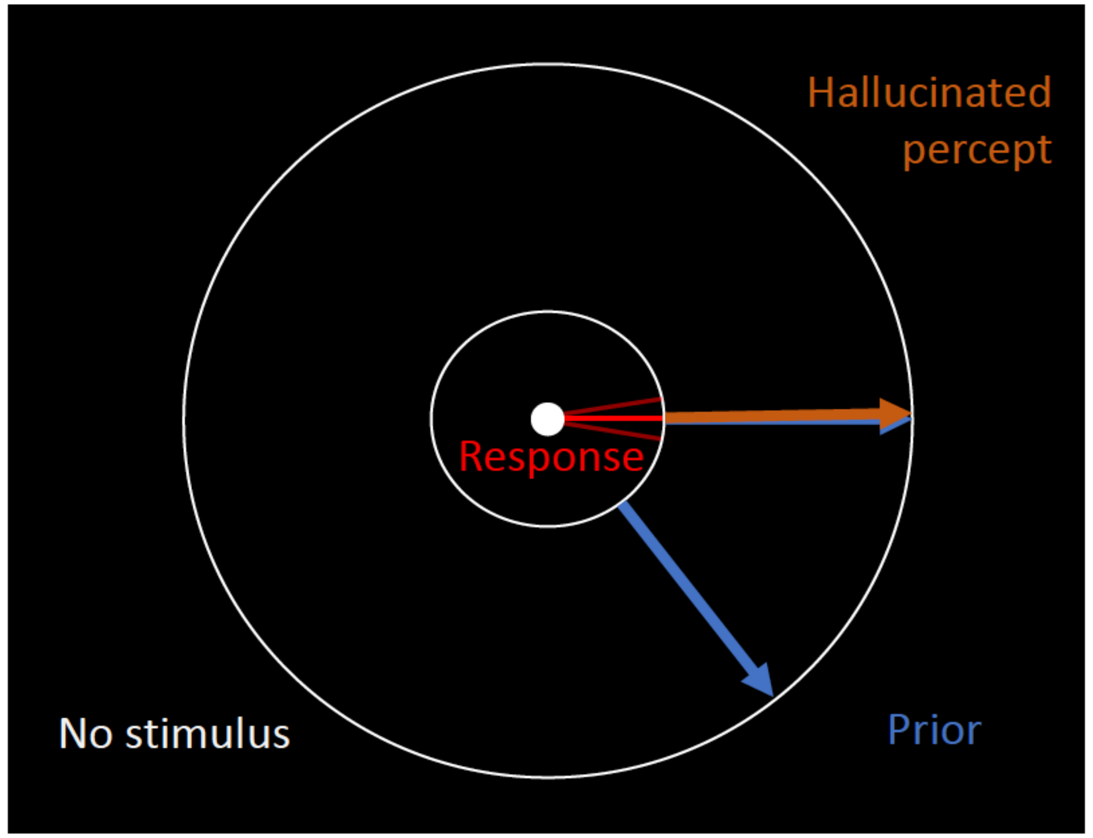


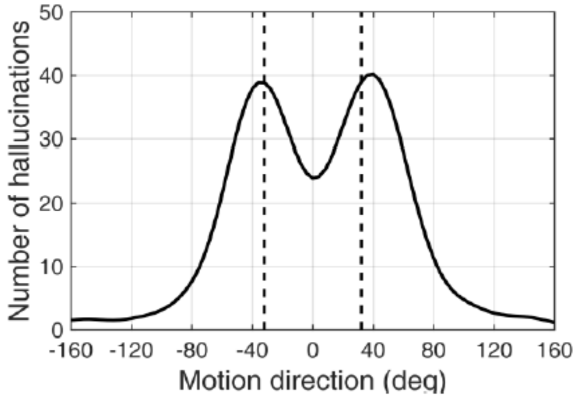




Biases:

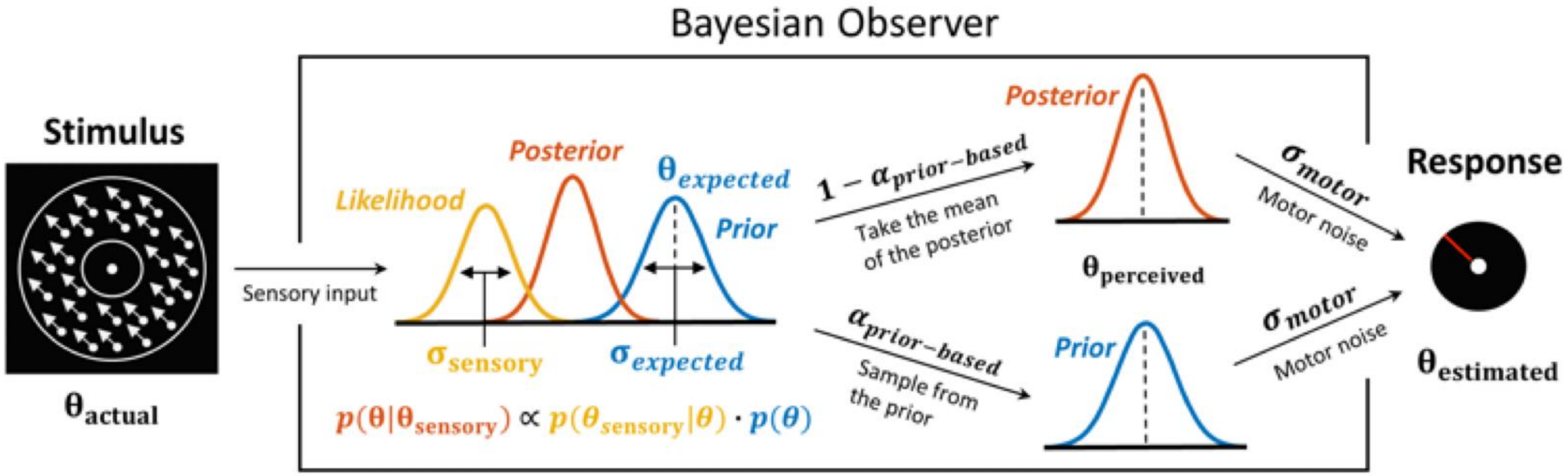
participants perceive motion direction as being more similar to frequent directions than really is

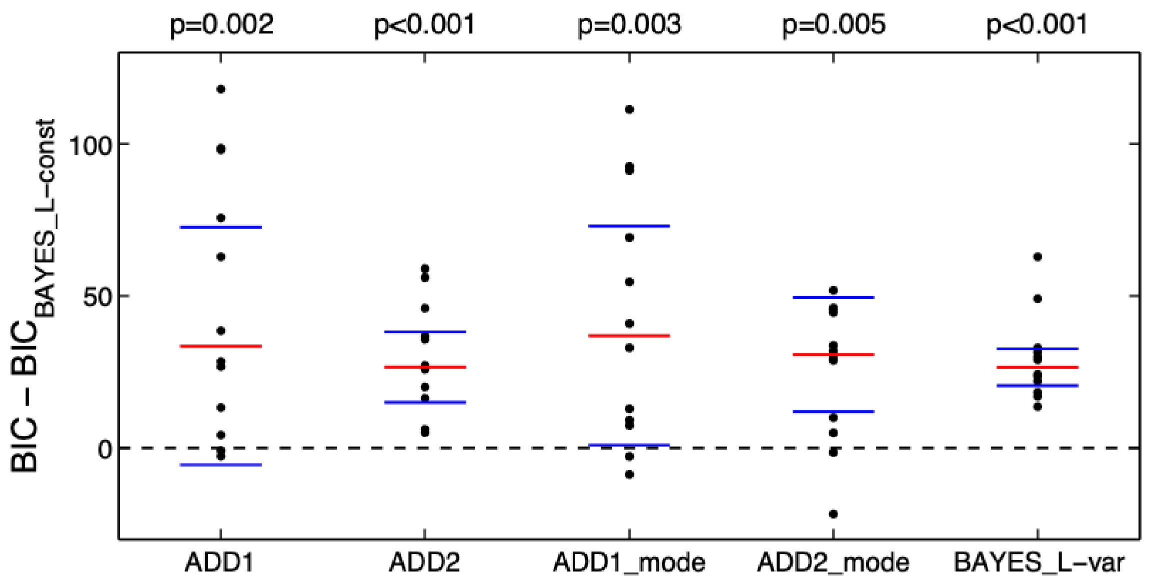




"Hallucinations":

participants sometimes perceive frequent motion direction even when it's not there





- **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**

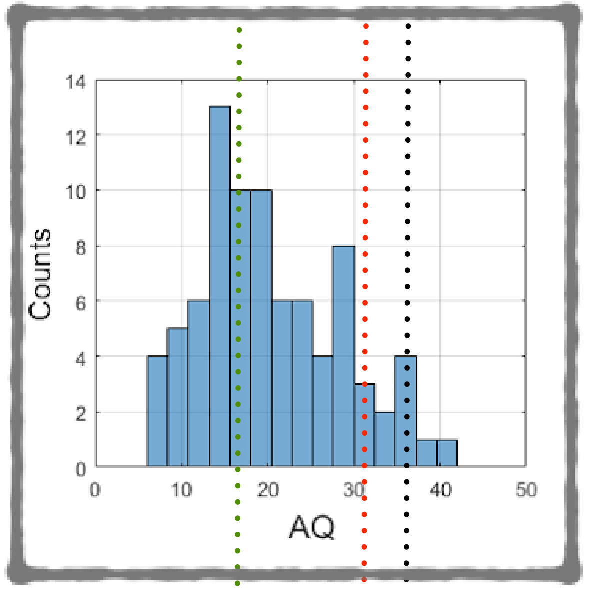
Fast, implicit learning of stimulus statistics modulates perception -- compatible with the construction of Bayesian priors and Bayesian inference.

Q: How do participants with individual differences behave in this task?

Autistic traits: weaker impact of the prior

Povilas Karvelis

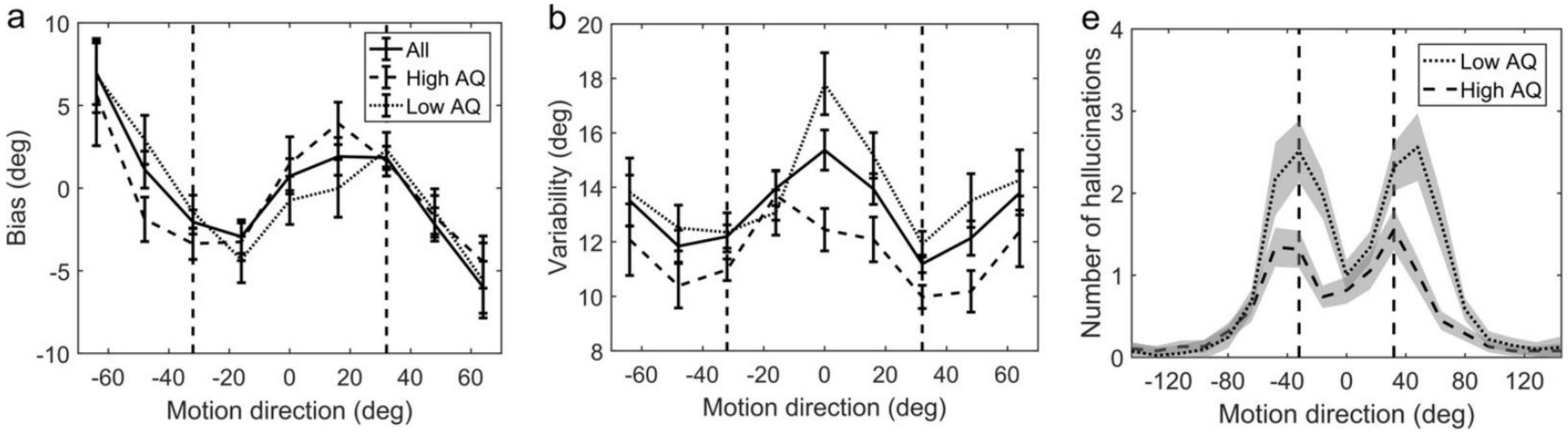
- 83 healthy participants scored for schizotypy (RISC & SPQ) and autistic traits (AQ)



- High AQ show less bias, are more precise in estimations, fewer hallucinations.

Correlations between AQ and those measures were stat. significant.

▶ compatible with the idea of them relying less on expectations



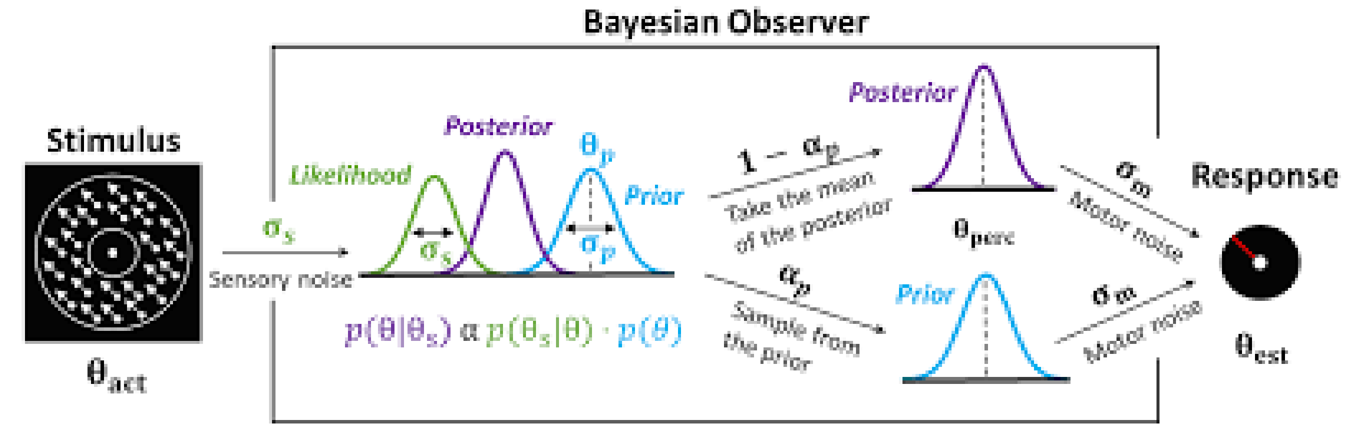
eLife

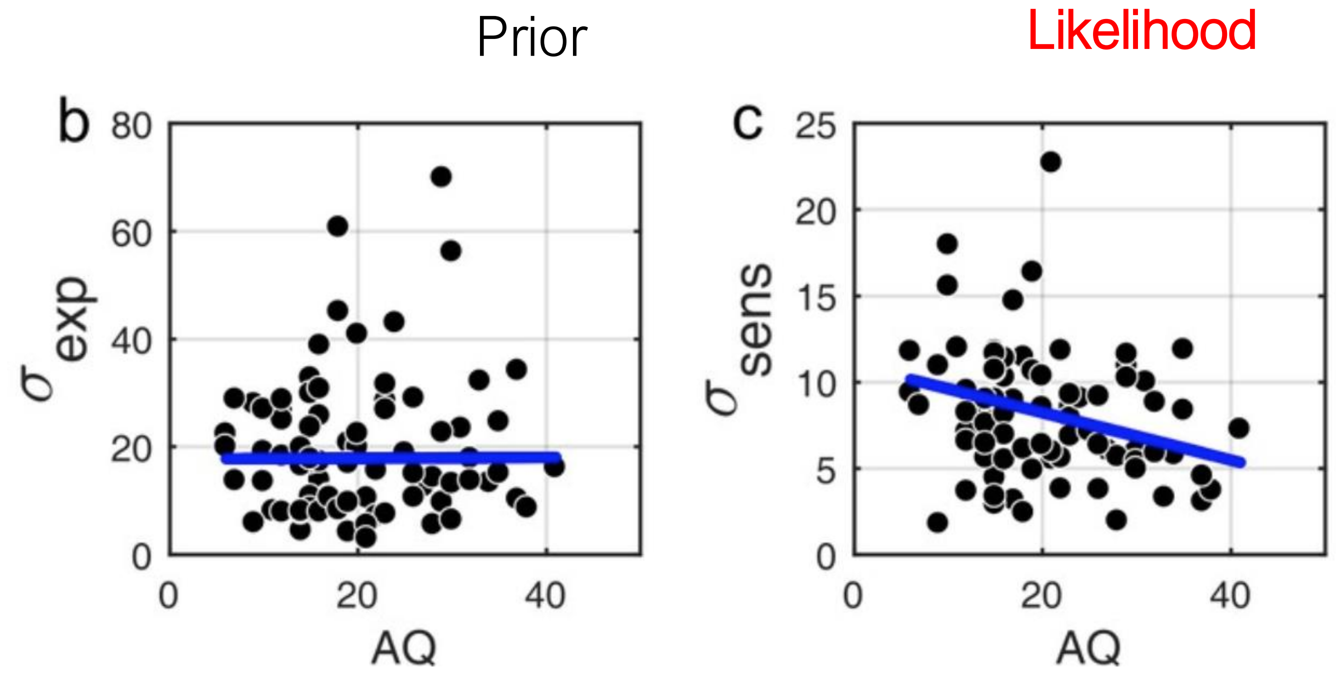
[Karvelis, Seitz, Lawrie and Seriès, 2018]

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 support the (debated) "enhanced sensory precision model".



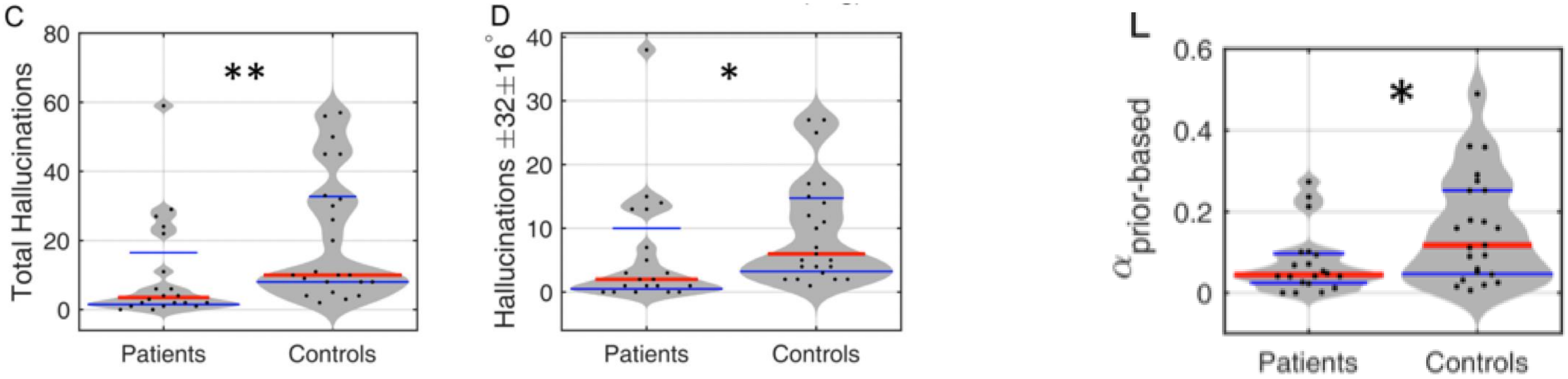


eLife [Karvelis, Seitz, Lawrie and Seriès, 2018]

SCZ: intact stat. learning but fewer “hallucinations”

Vincent Valton

- 25 individuals with psychosis (DSM-IV schizophrenia, *n* = 21; or schizoaffective disorder, *n* = 4) — 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



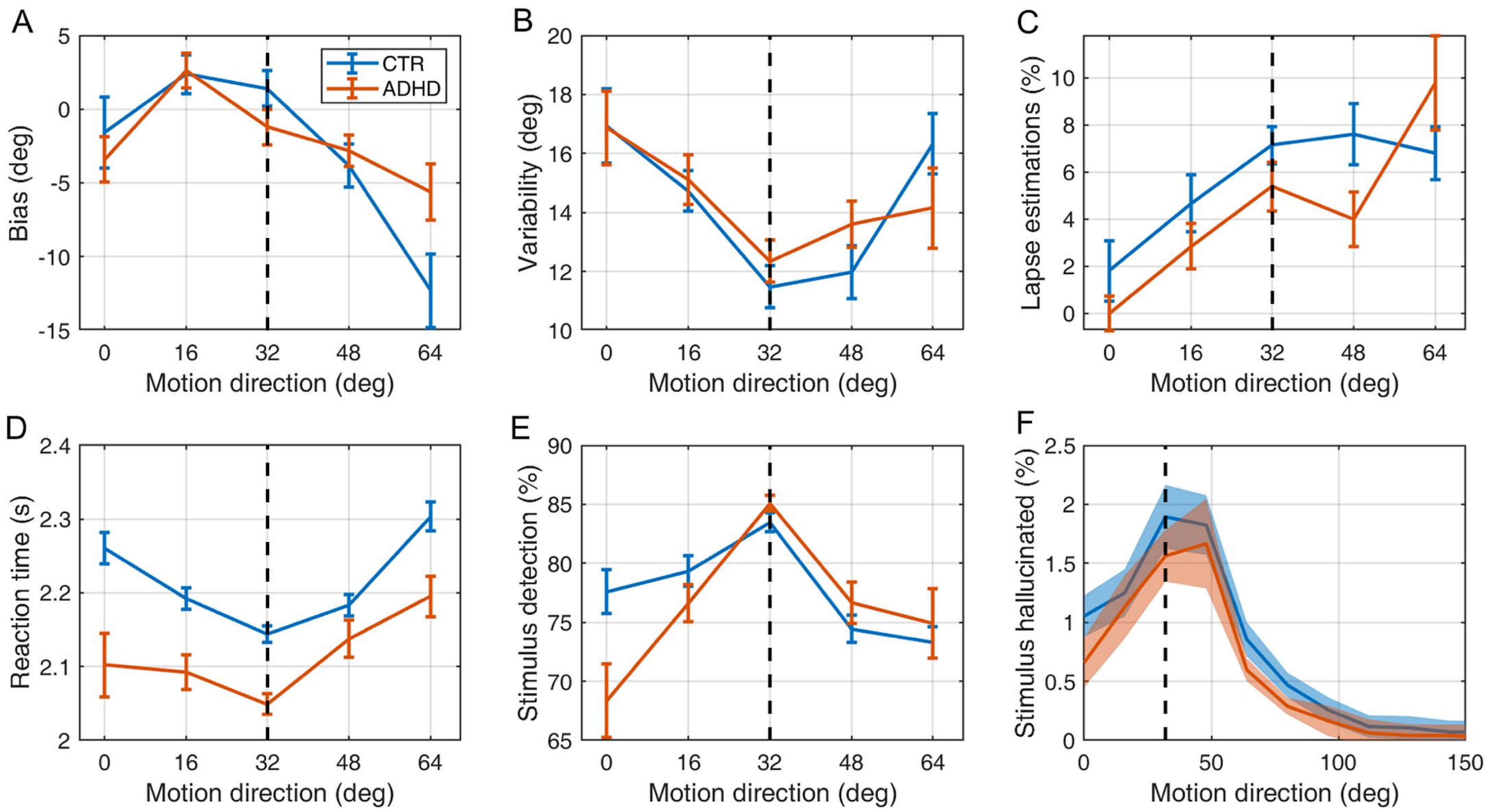
BRAIN A JOURNAL OF NEUROLOGY

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

ADHD: Intact statistical learning and prior integration

Katie Richards

- 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

- <u>(Intermediate) Conclusion from our work:</u>

  Some (subtle) evidence for the current theories (weaker impact of prior, enhanced sensory precision in ASD), with contrasting features in ASD vs Schizophrenia – and new insights on mechanisms.

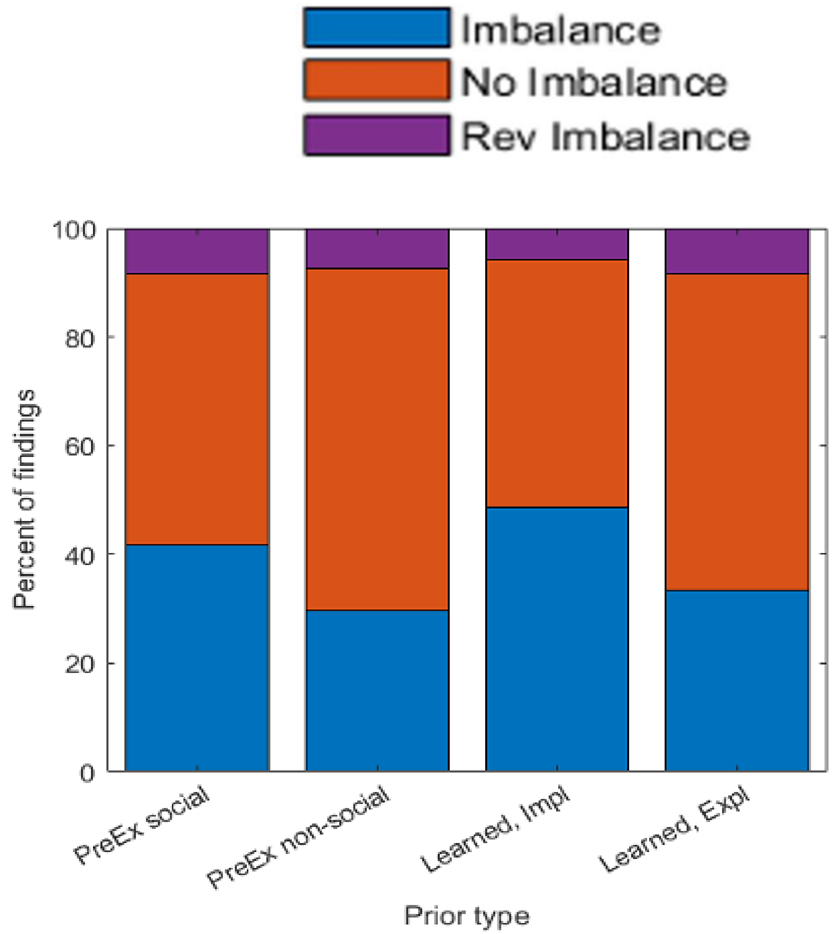
- **What should the next step be?**
- **How/when can we translate the theories to the clinic?**

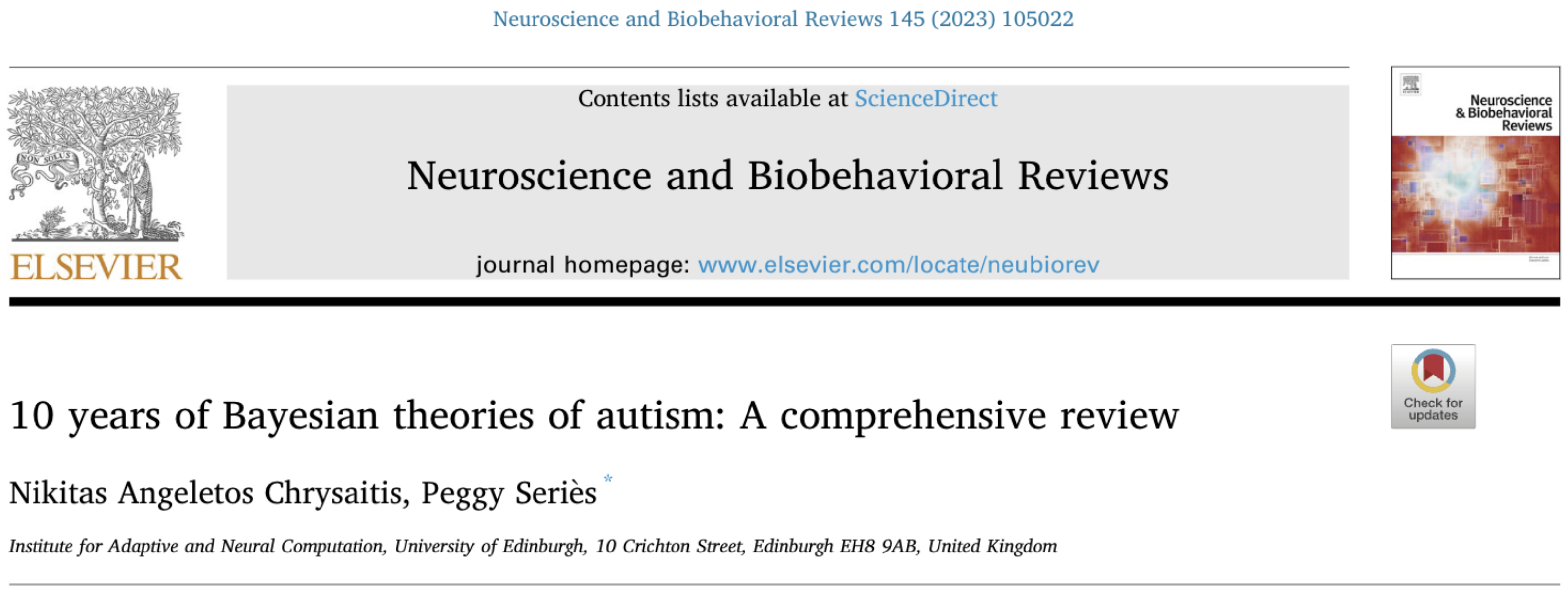

are we there yet?

10 years of Bayesian theories of Autism

Nikitas Angeletos Chrysaitis

- 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

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10 years of Bayesian theories of autism: A comprehensive review

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10 years of Bayesian theories of Autism

Nikitas Angeletos Chrysaitis

- Meta-analysis: 86 articles in [2012-2021] on autism and Bayesian or predictive coding (in title, abstract or keywords)
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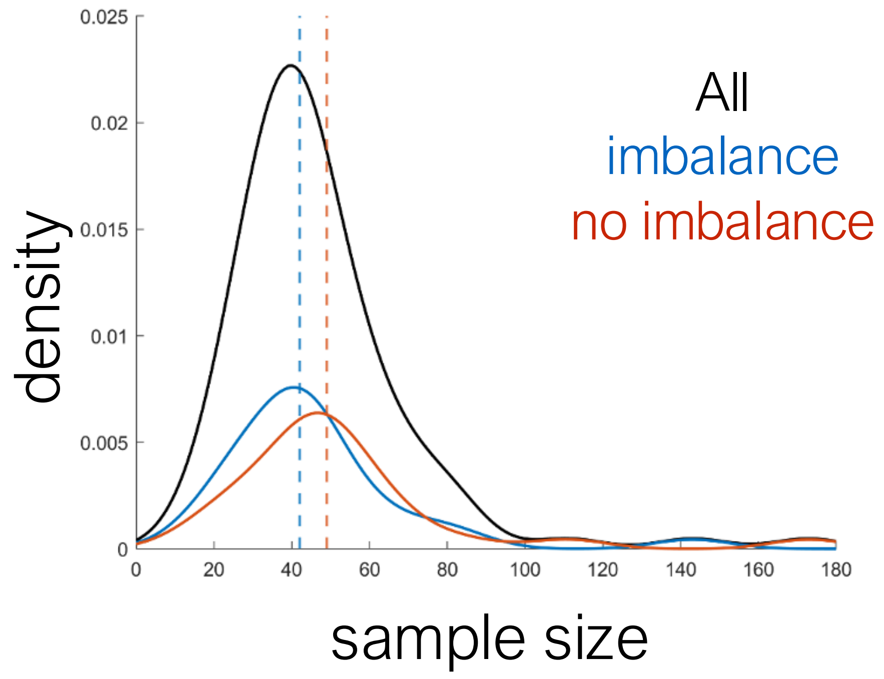
- Surprisingly, contrary to the popularity of theories, the experimental results **do not clearly show a general imbalance** between likelihood and priors.
- A little more evidence for the learned priors and social conditions.

10 years of Bayesian theories of Autism



- no obvious patterns differentiating the positive results to the negative results or inverse imbalance (sample size, effect size).
  More imbalance 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, refine our theories and computational methodology

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:

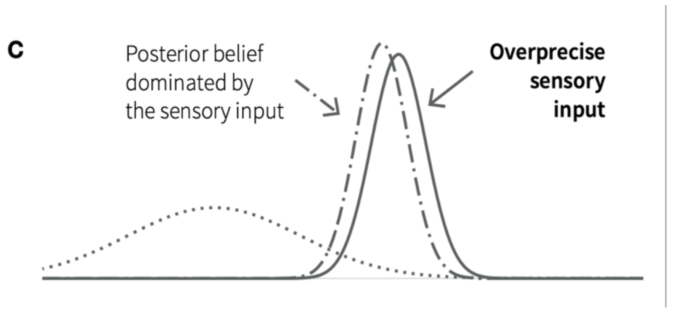
- A more nuanced, hierarchical picture
- Dynamic updating and volatility are now centre stage
- Heterogeneity and comorbidities are taken seriously.
- Developmental approach?
- Stronger computational modelling + neuroimaging or neurophysiological integration

4

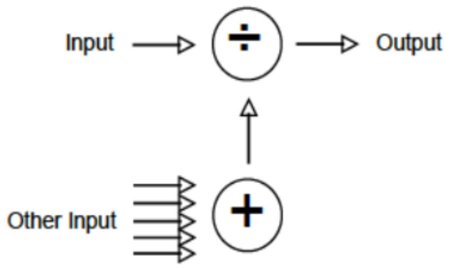
Moving forward: link with the neurobiological substrate

With Renato Paredes

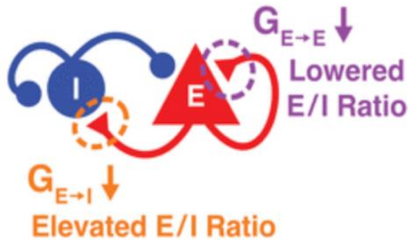
Using neural network models



Impaired inference



Decrease in divisive normalization [Rosenberg, Patterson & Angelaki PNAS 2015]



Increased ratio of cortical excitation to inhibition (E/I balance)

Fitting behavioural data with neural networks models and relating differences in E/I balance and feedforward/feedback connectivity with differences in multisensory integration and causal inference in SCZ and ASD

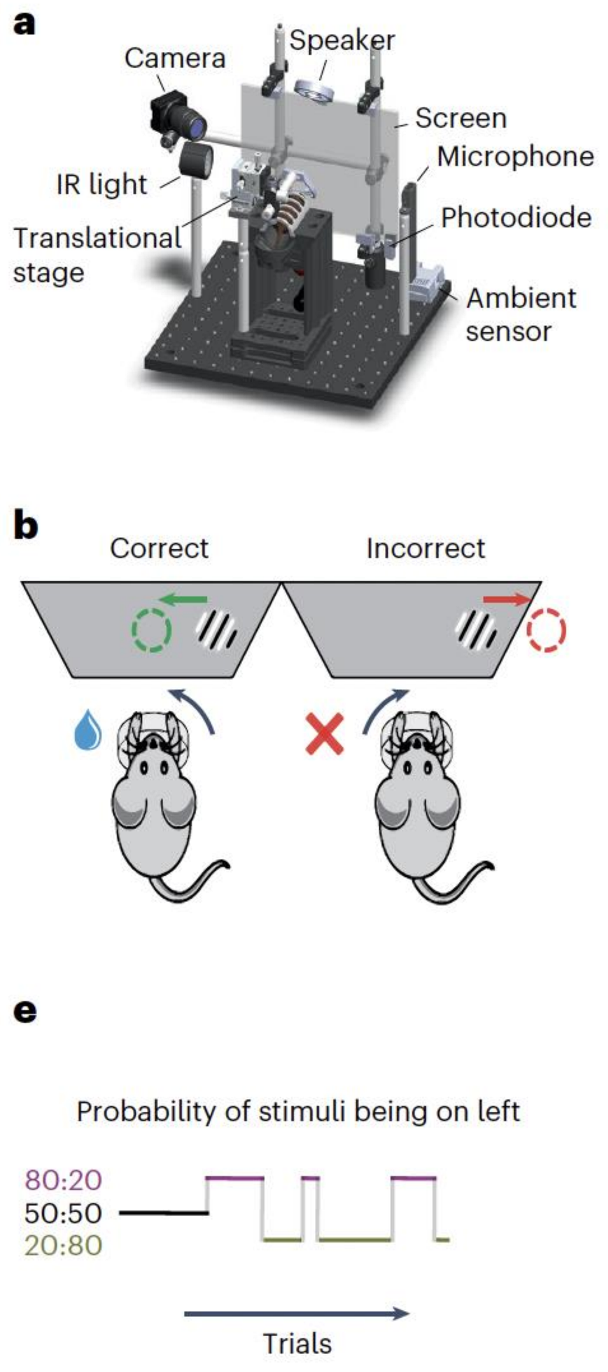
Paredes et al 2020
Noel et al 2021
Paredes et al 2024 in prep

4 Moving forward – combining computational approaches with animal models and electrophysiology

- A recent example: Noel et al 2025, combine state-of-the art genetics, neurophysiology, behaviour and computational models

- Impaired update of priors in autism models compared to wild-type.

  - global shift in prior encoding from sensory to frontal cortices in ASD models.



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A common computational and neural anomaly across mouse models of autism

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Check for updates

Jean-Paul Noel[1,2,3,4], Edoardo Balzani[5], Luigi Acerbi[6], Julius Benson[7], The International Brain Laboratory*, Cristina Savin[7] & Dora E. Angelaki[7,8]

Computational psychiatry studies suggest that individuals with autism spectrum disorder (ASD) inflexibly update their expectations. Here we leveraged high-yield rodent psychophysics, extensive behavioral modeling and brain-wide single-cell extracellular recordings to assess whether mice with different genetic perturbations associated with ASD show this same computational anomaly, and if so, what neurophysiological features are shared across genotypes. Mice harboring mutations in *Fmr1*, *Cntnap2* or *Shank3B* show a blunted update of priors during decision-making. Compared with mice that flexibly updated their priors, inflexible updating of priors was associated with a shift in the weighting of prior encoding from sensory to frontal cortices. Furthermore, frontal areas in mouse models of ASD showed more units encoding deviations from the animals' long-run prior, and sensory responses did not differentiate between expected and unexpected observations. These findings suggest that distinct genetic instantiations of ASD may yield common neurophysiological and behavioral phenotypes.

Conclusions

Bayesian models shows great potential in autism and schizophrenia:

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

Computational approaches still in development.

Need to refine still crude theories, & improve standards to validate them and make them useful for the clinic.

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