‘Bayesian’ theories: Application to mental disorders (CCN Lecture 15)

Peggy Seriès,
IANC, University of Edinburgh

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

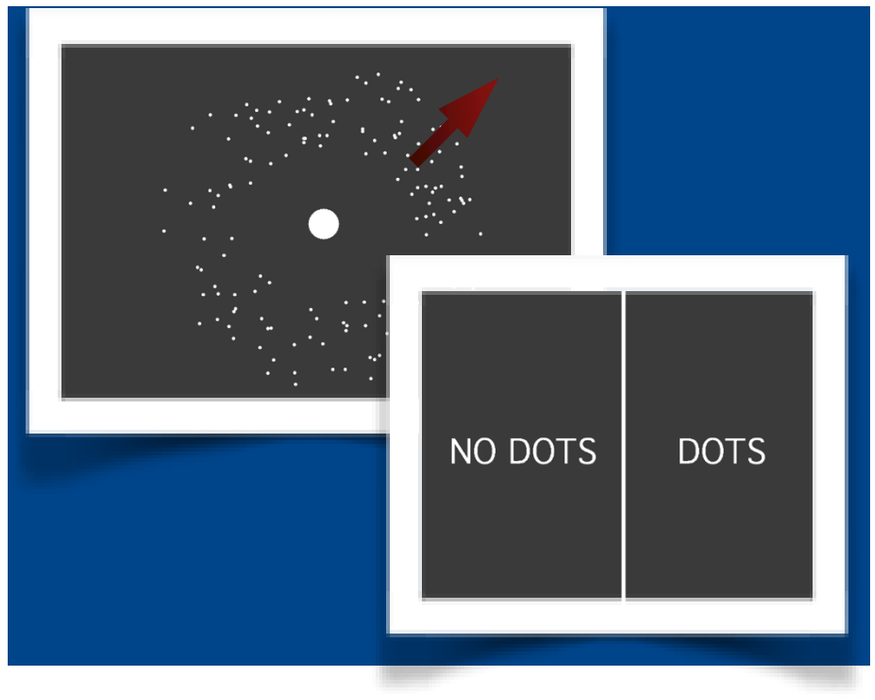
(e.g. pessimistic priors in depression, or priors on controllability, priors on mistrust in borderline).

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

- > a new area of research.

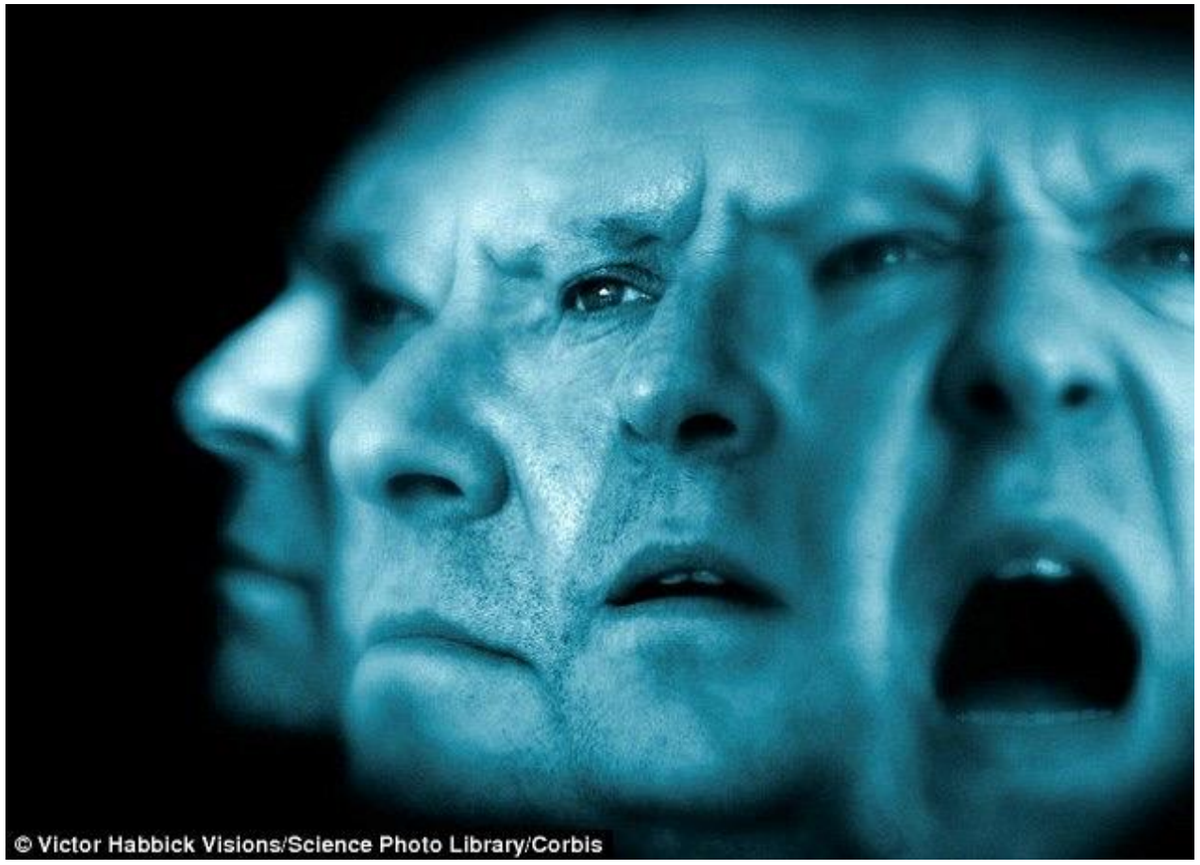
Today's Lecture

- 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)



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- **Negative symptoms** include lack of motivation and becoming withdrawn.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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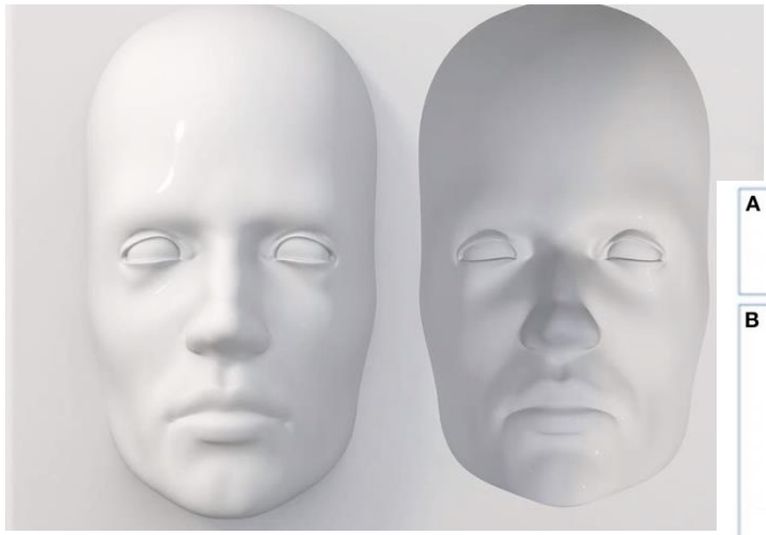
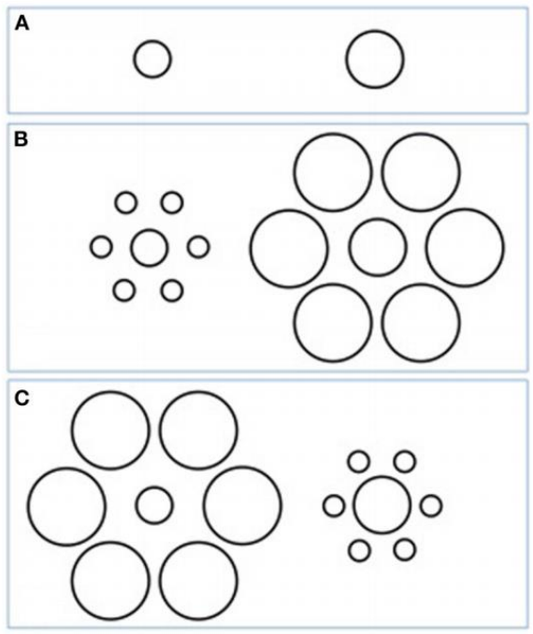
Visual perception in Schizophrenia

• 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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Charles-Edouard Notredame,

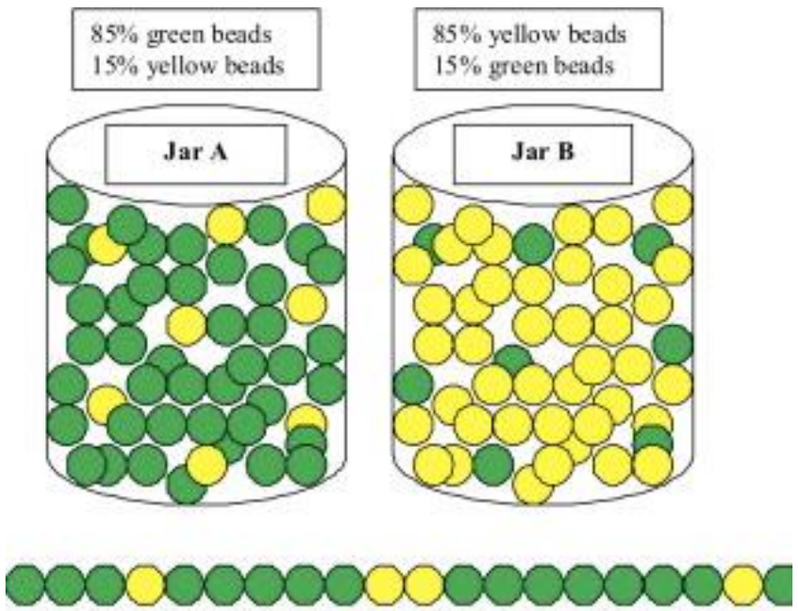
Illusion, namely a mismatch between the objective and perceived properties of an object present in the environment, is a common feature of visual perception, both in normal and pathological conditions. This makes illusion a valuable tool with which to explore normal perception and its impairments. Although 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

Jumping to Conclusions in Schizophrenia

- 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]

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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,

1

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.

1

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.

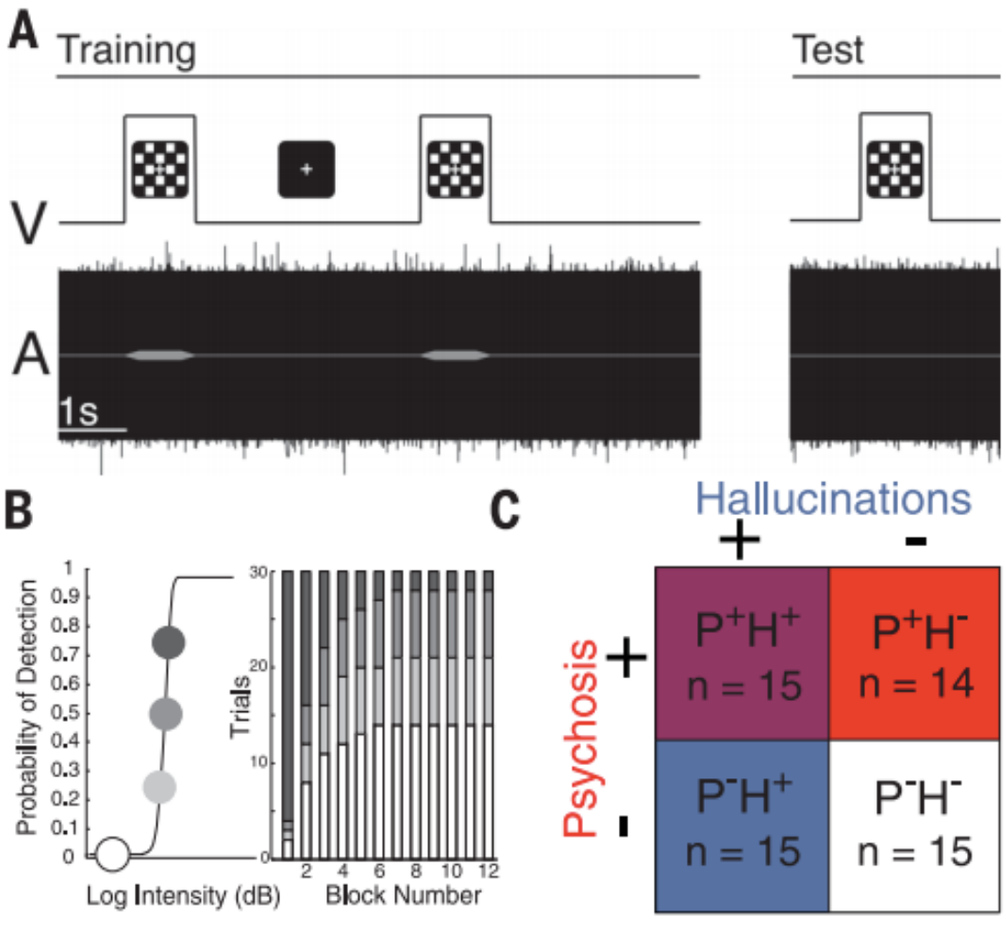
Powers *et al.*, *Science* **357**, 596–600 (2017)

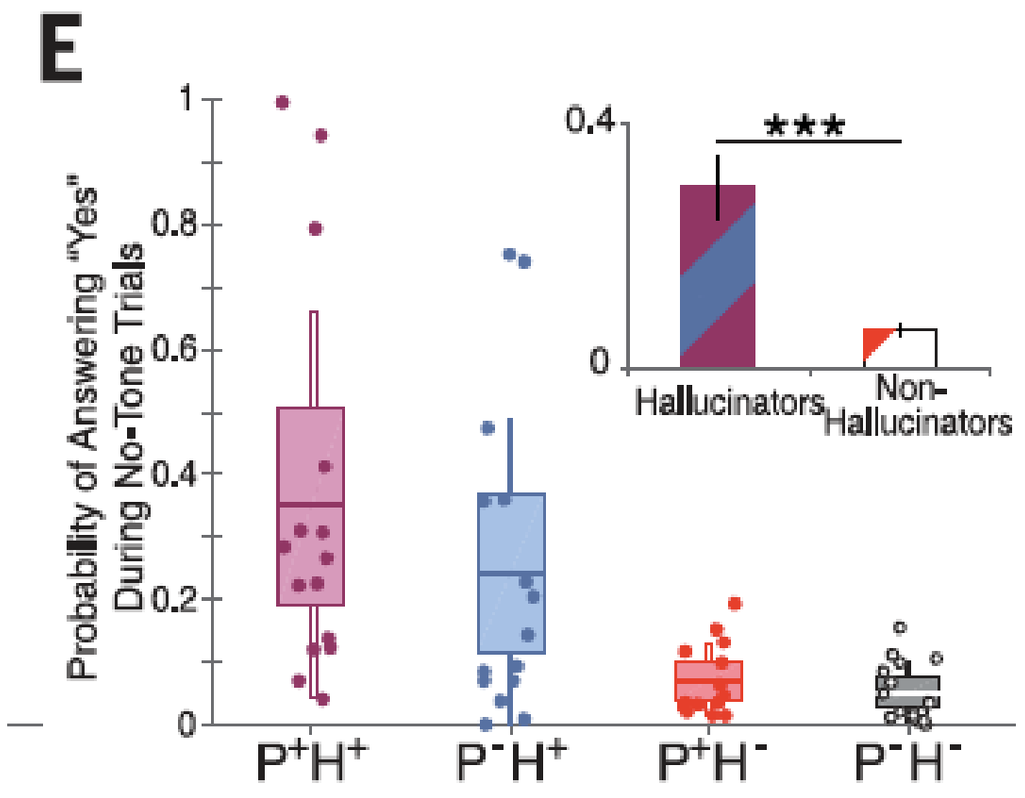
- Participants had to **detect a 1-kHz tone occurring concurrently with checkerboard** visual stimulus

- **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)

1 S tronger 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)

1

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,

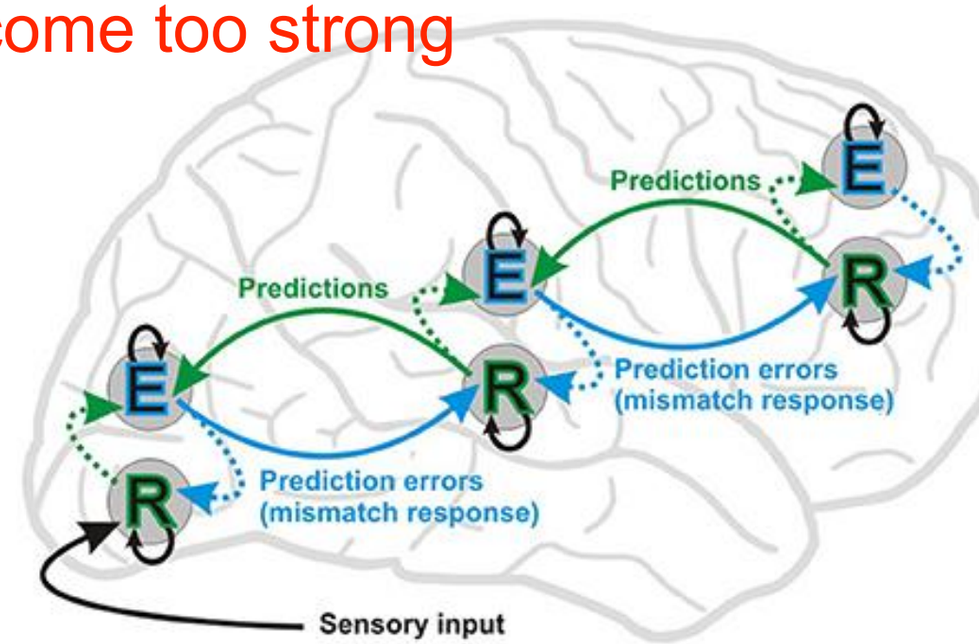
Mismatch negativity, eye movements, force-matching experiments.

[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]



2

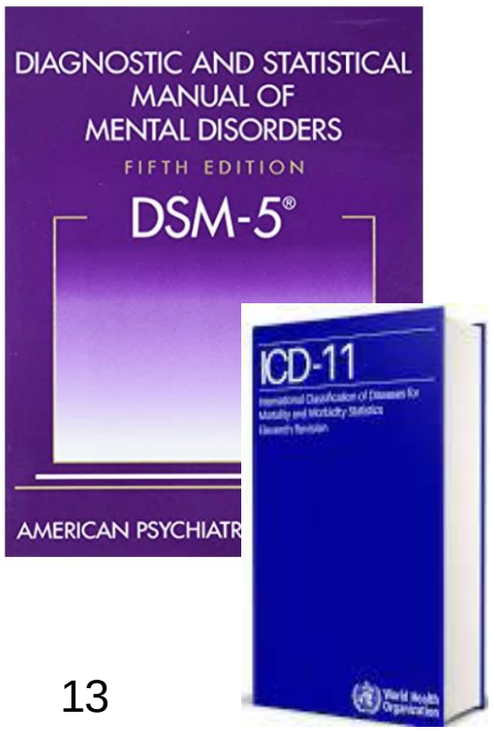
Autism Spectrum Disorder (ASD)

- 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



2

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

Cell PRESS

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

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

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frontiers in HUMAN NEUROSCIENCE

HYPOTHESIS AND TI

doi: 10.3

An aberrant precision account of autism

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****Correspondence:***

Autism is a neurodevelopmental disorder characterized by problems with communication, restricted interests and repetitive behavior. A recent and t provoking article presented a normative explanation for the perceptual symptoms o in terms of a failure of Bayesian inference (Pellicano and Burr, 2012). In respo suggested that when Bayesian inference is grounded in its neural instantiation— predictive coding—many features of autistic perception can be attributed to precision (or beliefs about precision) within the context of hierarchical message in the brain (Friston et al., 2013). Here, we unpack the aberrant precision acc autism. Specifically, we consider how empirical findings—that speak directly or i

CrossMark click for updates

Autism as a disorder of prediction2014

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]

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Richard M. Held, September 5, 2014 (sent for review November 13, 2013; reviewed by Leonard Rappaport, Stephen M. Camarata, and ikhani)

ion of empirical findings accumulated over the past s attests to the diversity of traits that constitute the otypes. It is unclear whether subsets of these traits derlying causality. This lack of a cohesive conceptu- the disorder has complicated the search for broadly rapies, diagnostic markers, and neural/genetic cor- is paper, we describe how theoretical considerations of empirical data lead to the hypothesis that some ts of the autism phenotype may be manifestations

conditional probability $P(B|A, \Delta t)$, the likelihood of transitioning to state "B" given the occurrence of "A" and elapsed temporal duration, Δt. The hypothesis of predictive impairment in autism (PIA) posits that autism may be associated with inaccuracies in estimating the $P(B|A, \Delta t)$ conditional probability.

Fig. 2*A* depicts the PIA hypothesis schematically. Two key parameters characterize any interevent relationship: strength $[P(B|A)]$ and temporal separation (Δt). In this 2D space, rela- tionships toward the lower right may be undetectable, given that

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ELSEVIER

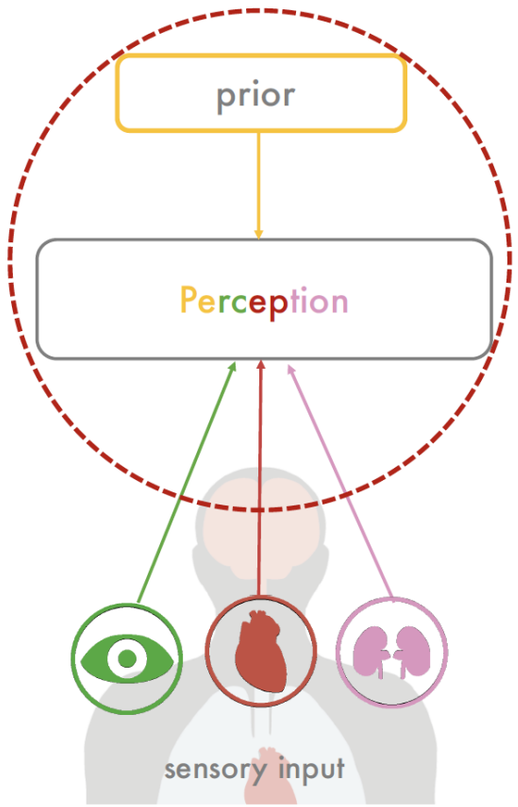
10 years of Bayesian theories of autism: A comprehensive review

Nikitas Angeletos Chrysaitis, Peggy Seriès *

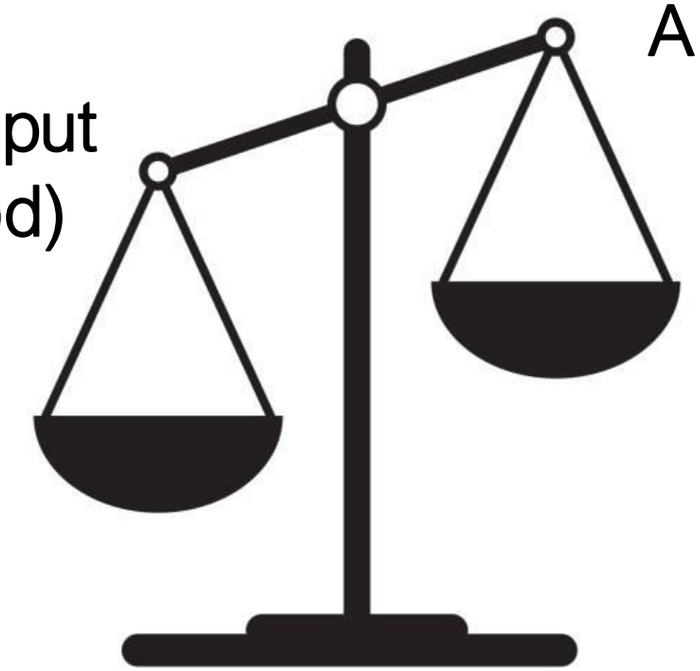
Institute for Adaptive and Neural Computation, University of Edinburgh, 10 Crichton Street, Edinburgh EH8 9AB, United Kingdom

- 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?



Sensory Input
(Likelihood)



A priori expectations
(priors)

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]

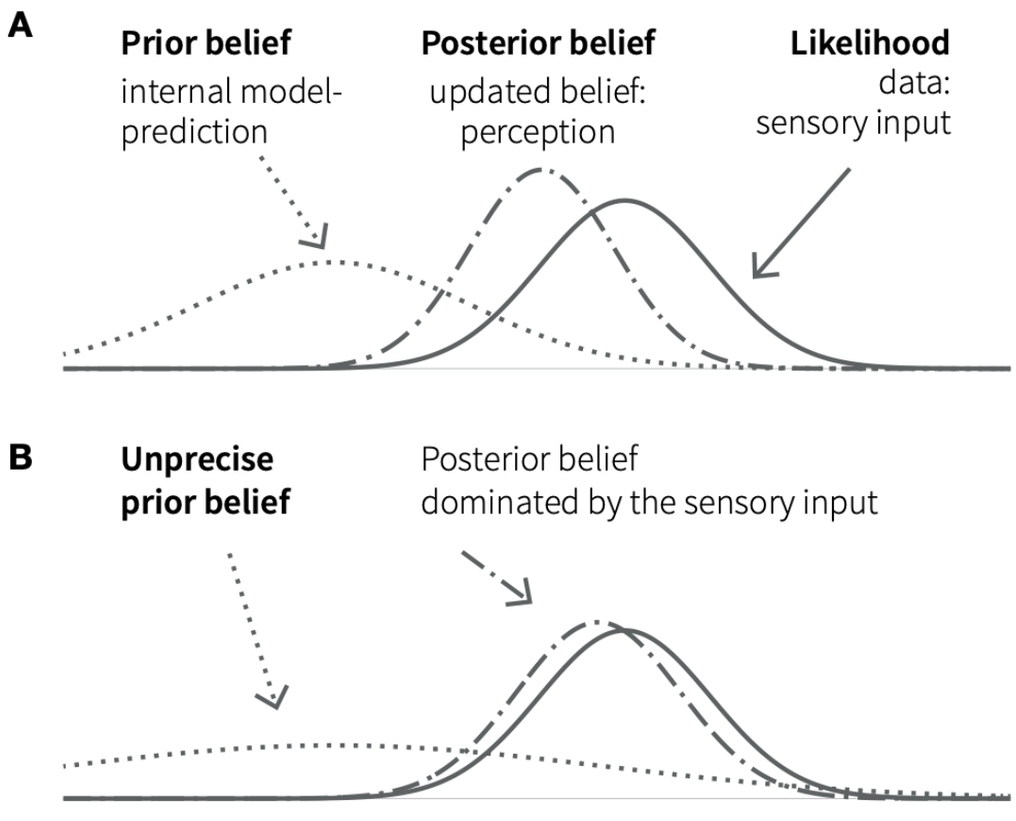
Relatively weaker priors in autism?

Sensory input unaffected

Hypothesis 1
Weaker / flatter Priors

Lower precision

π_{prior}



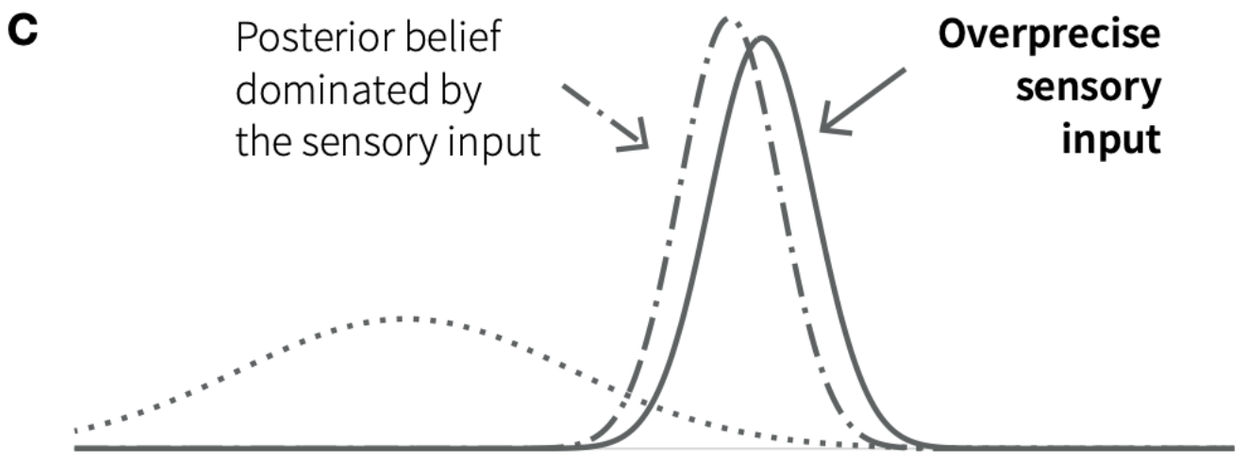
Relatively weaker priors in autism?

Hypothesis 2
Sensory information more precise

Higher precision

$\pi_{likelihood}$

prior expectations unaffected

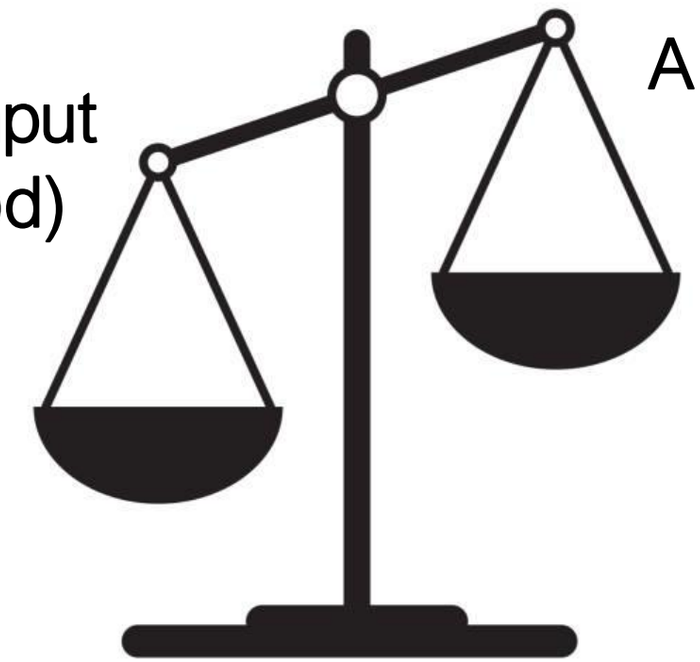


2 Predictive Coding: Increased weight on prediction error

Sensory Input (Likelihood)

Relatively higher precision

$\pi_{likelihood}$



A priori expectations

Relatively lower precision

π_{prior}

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"

Original Article

autism

Autism
1–12

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

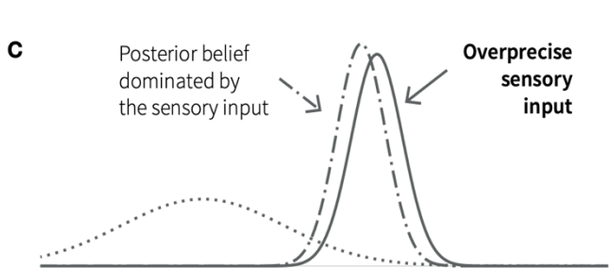
Greta Krasimirova Todorova, Rosalind Elizabeth Mcbean Hatton, Sarveen Sadique and Frank Earl Pollick

Abstract

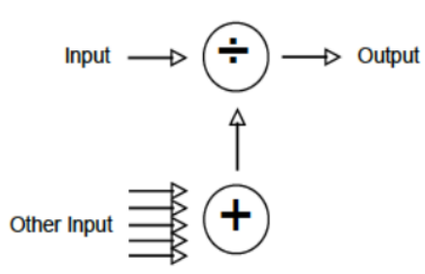
Little attention has been given to the voice of autistic individuals during the development of theories that are trying to explain the condition. This can often make individuals feel that they have to fit into the theory's definition, rather than it fitting into their experience. We aimed to understand 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.

2 Multi-scale computational approach

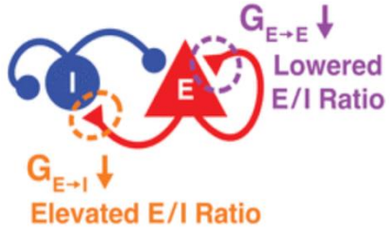
Computational → Algorithm → Neural Instantiation



Impaired inference



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



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

2023

Trends in Cognitive Sciences

CellPress

Opinion

A theory of autism bridging across levels of description

Jean-Paul Noel [1,3,*,@] and Dora E. Angelaki [1,2,4]

Autism impacts a wide range of behaviors and neural functions. As such, theories of autism spectrum disorder (ASD) are numerous and span different levels of description, from neurocognitive to molecular. We propose how existent behavioral, computational, algorithmic, and neural accounts of ASD may relate to one another. Specifically, we argue that ASD may be cast as a disorder of causal inference (computational level). This computation relies on marginalization, which is thought to be subserved by divisive normalization (algorithmic level). In turn, divisive normalization may be impaired by excitatory-to-inhibitory imbalances (neural implementation level). We also discuss ASD within similar frameworks, those of predictive coding and circular inference. Together, we hope to motivate work unifying the different accounts of ASD.

In need of a new kind of theory of ASD

ASD is a heterogeneous neurodevelopmental condition of unknown etiology. It impacts a wide range of functions, from social and communicative faculties [1] to motor behaviors [2] and sensory processing [3]. Similarly, a wide range of genetic [4] and environmental [5] factors have been

Highlights

Autism is a pervasive condition broadly afflicting perceptual, cognitive, social, and motor function.

There are a large number of theories of autism spectrum disorder (ASD), and these span the gamut in terms of levels of description: behavioral, algorithmic, and neural instantiation.

Here we attempt to close the gap between different theories (causal inference, marginalization, divisive normalization, excitatory-to-inhibitory ratio balance, and predictive coding) and levels of description.

Clinical interest: providing quantitative tests

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

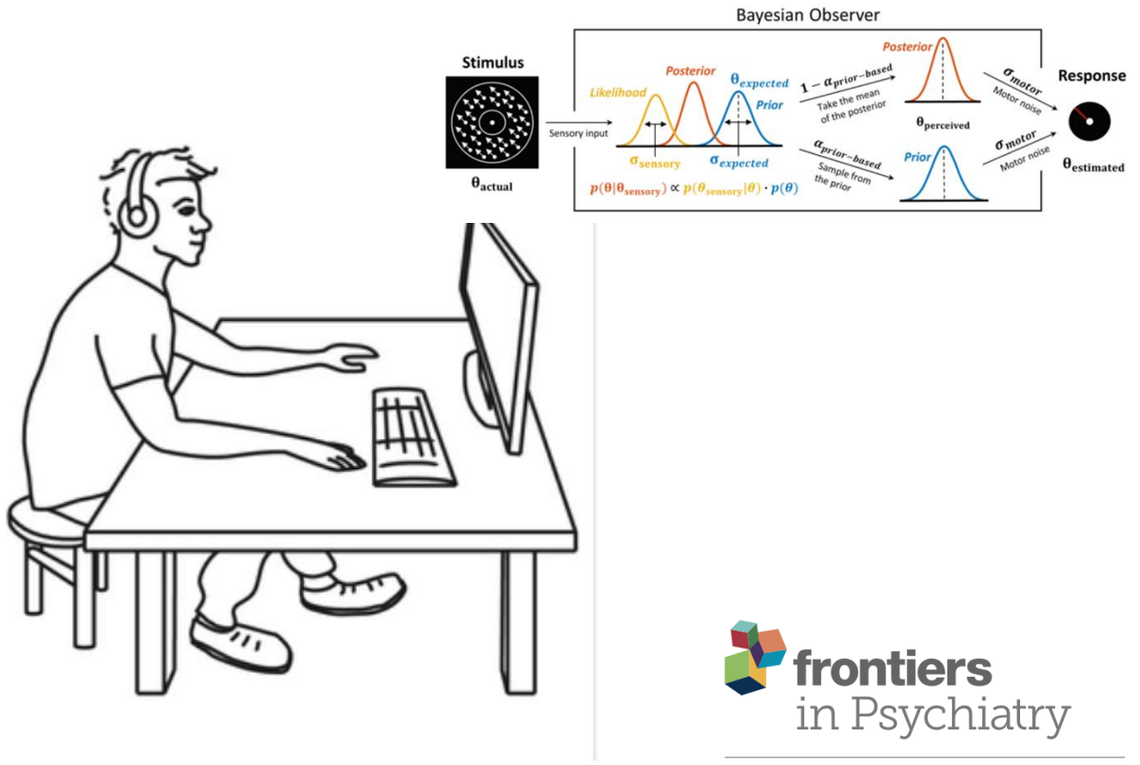
- Provide objective and quantitative, behavioral tests facilitating diagnosis that could be conducted by non-specialists.

- 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

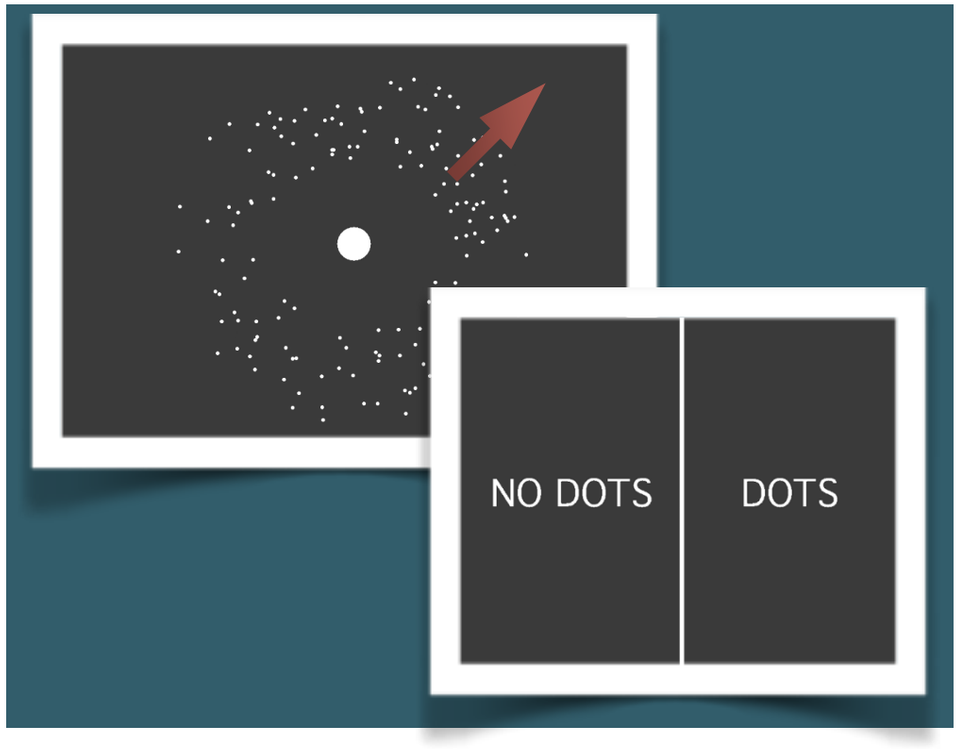
Can we quantitatively test & refine current theories & make them clinically relevant?

- 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?

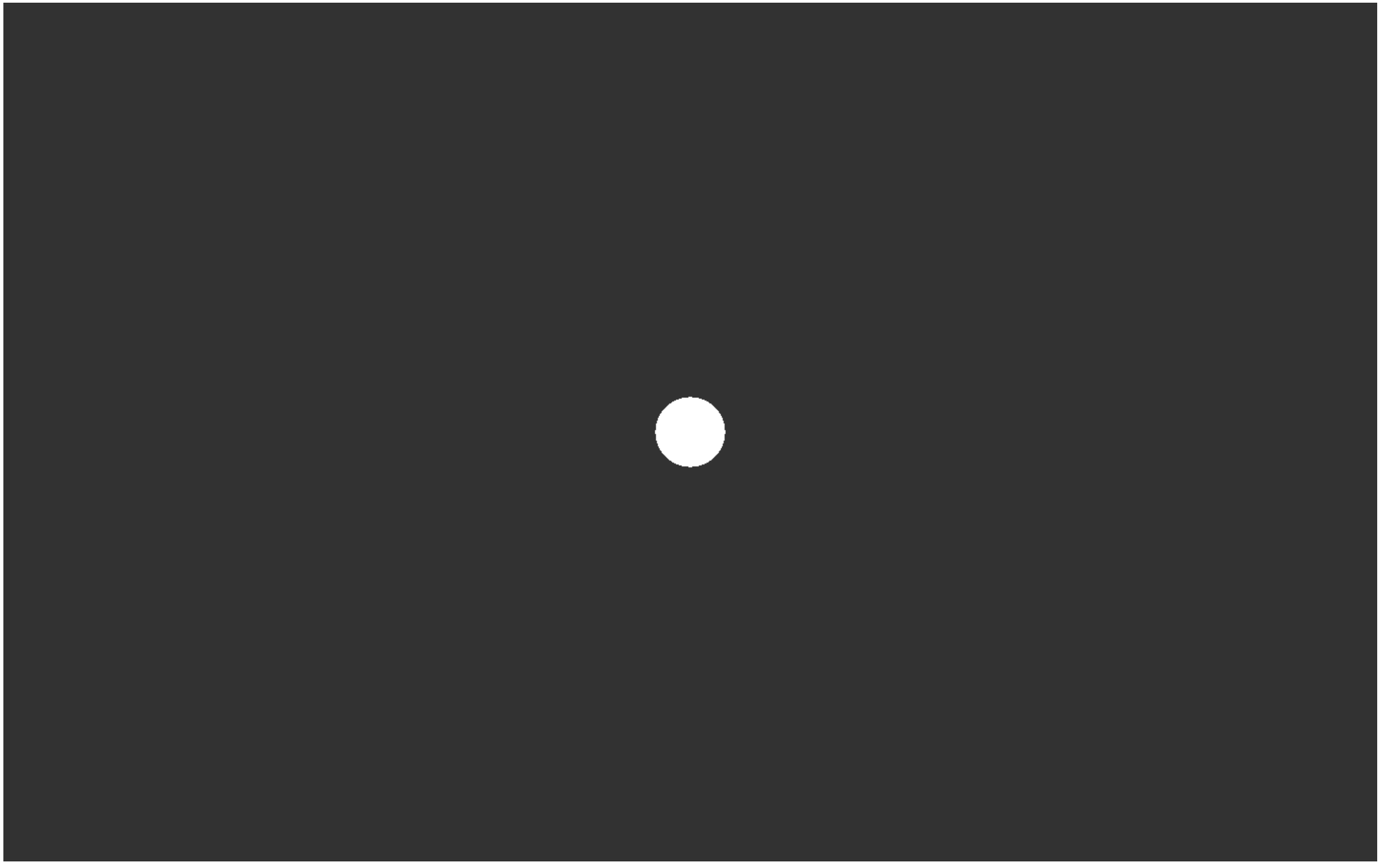
Testing the models with a statistical learning task:

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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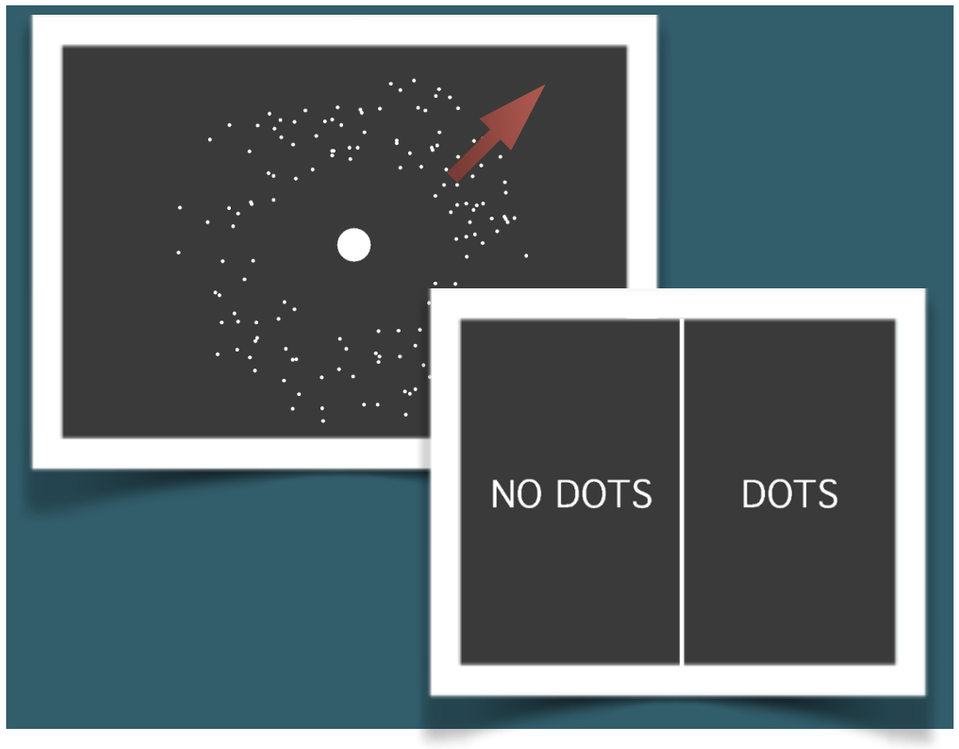
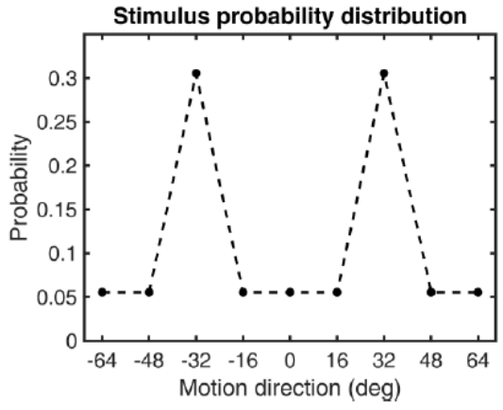
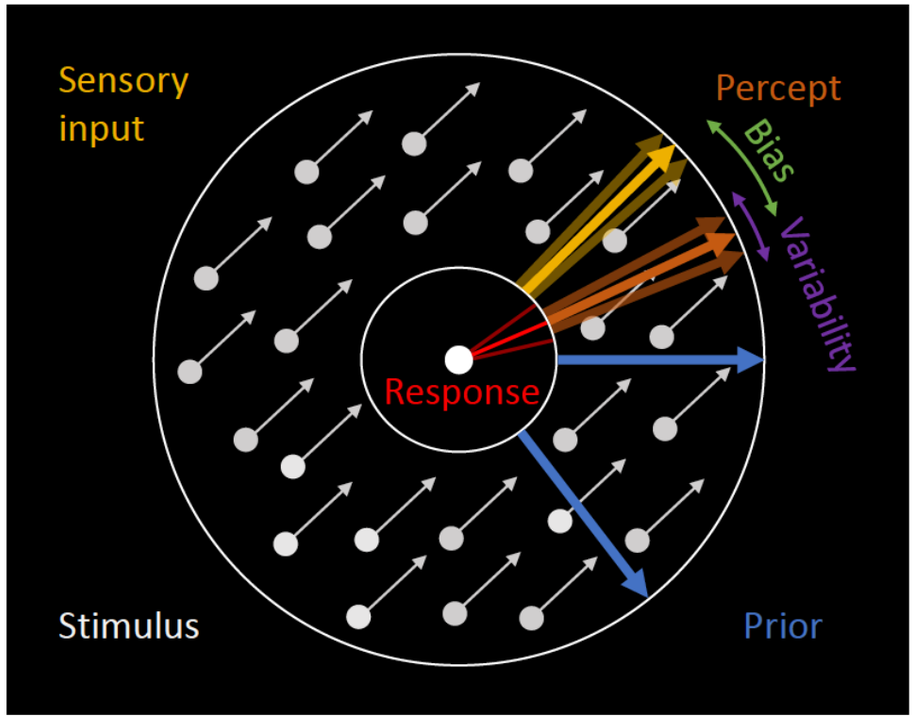
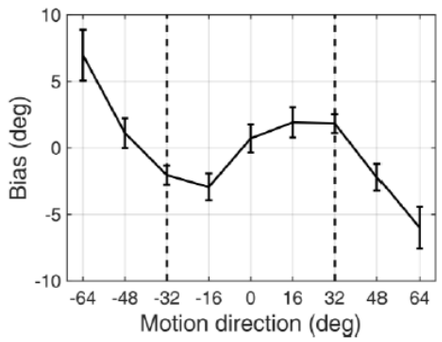


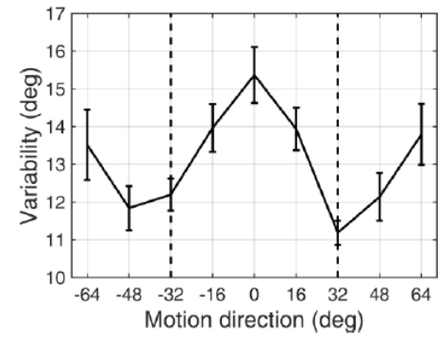
- Two directions of motion are more frequently presented. Are participants going to learn about this? implicitly? how will this change their perception?



[Chalk, Seitz, Seriès, JOV 2010]

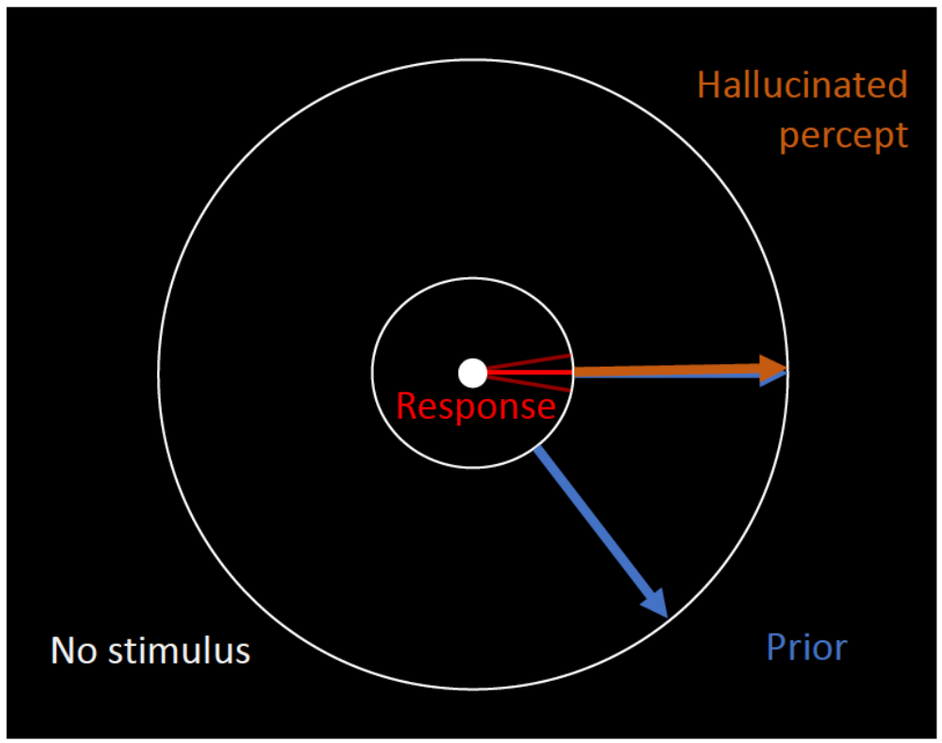


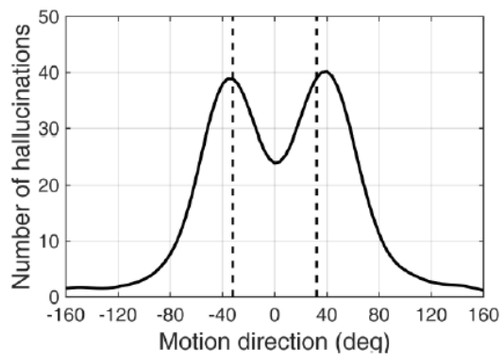




Biases:

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

[Chalk, Seitz, Seriès, 2010]

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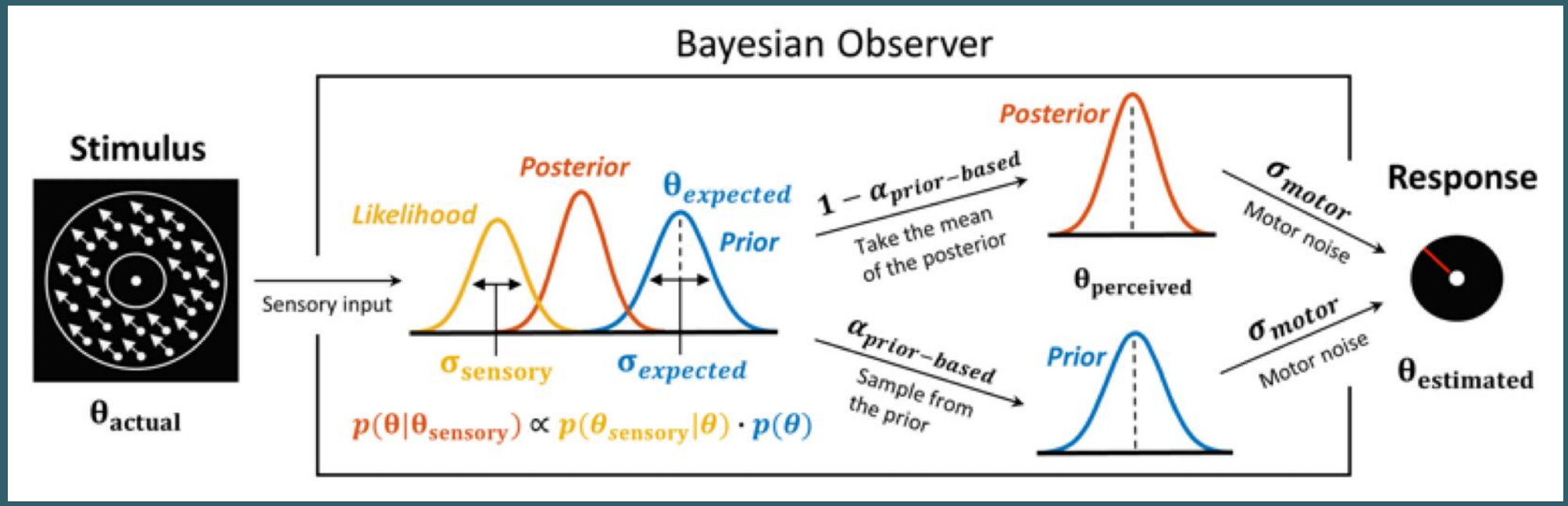


- **Behaviour is consistent with Bayesian model:**

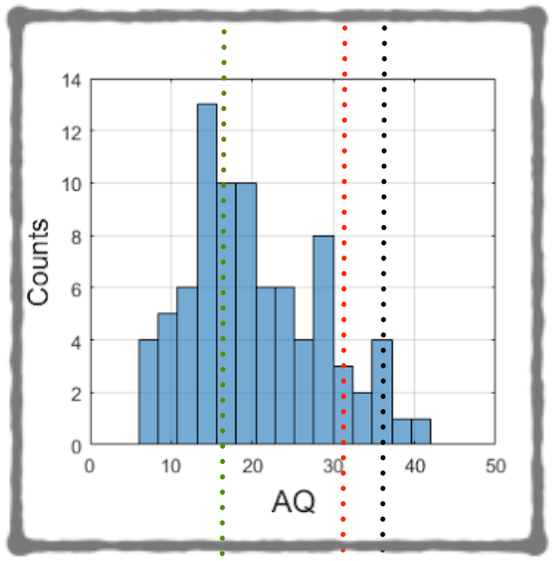
  Participants combine a noisy estimate of the motion direction with a prior belief which represents an estimate of the stimulus distribution
- **We can recover the shape of likelihood and priors for each participant**

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)

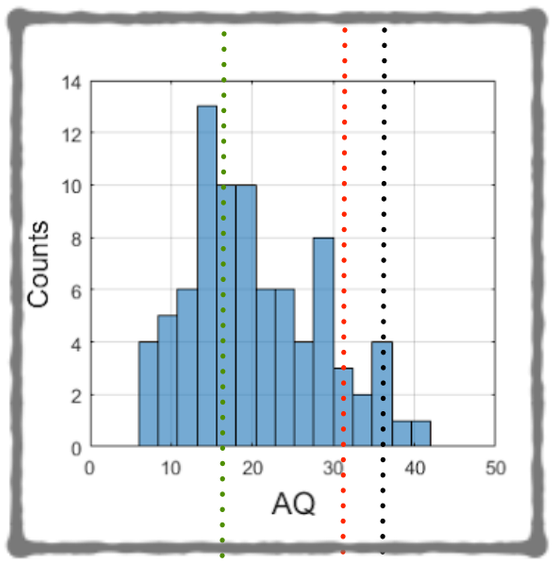


eLife

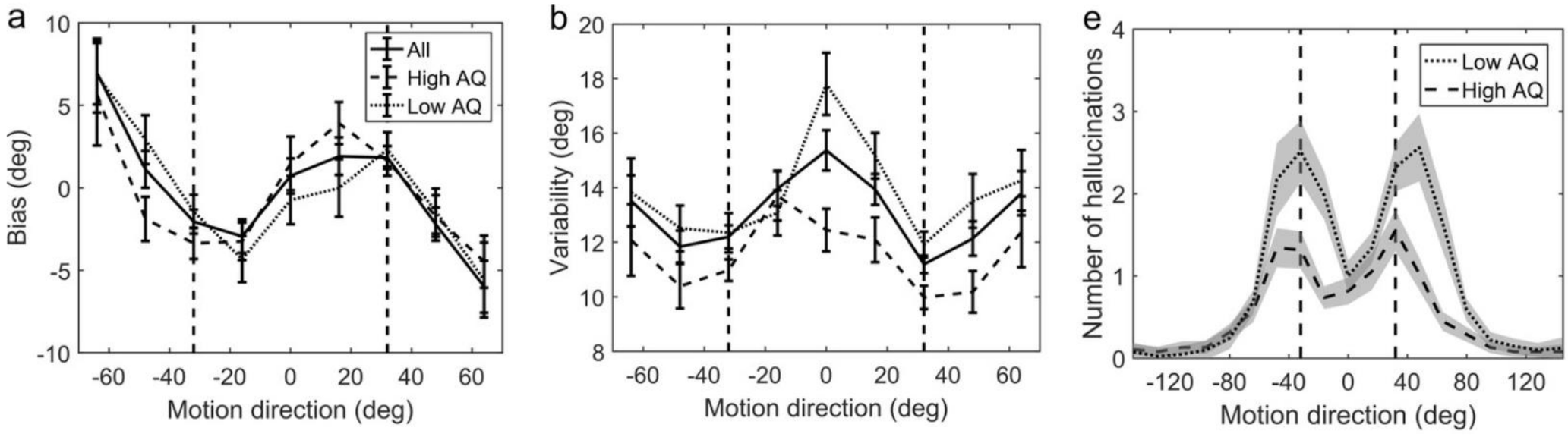
[Karvelis, Seitz, Lawrie and Seriès, 2018]

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.



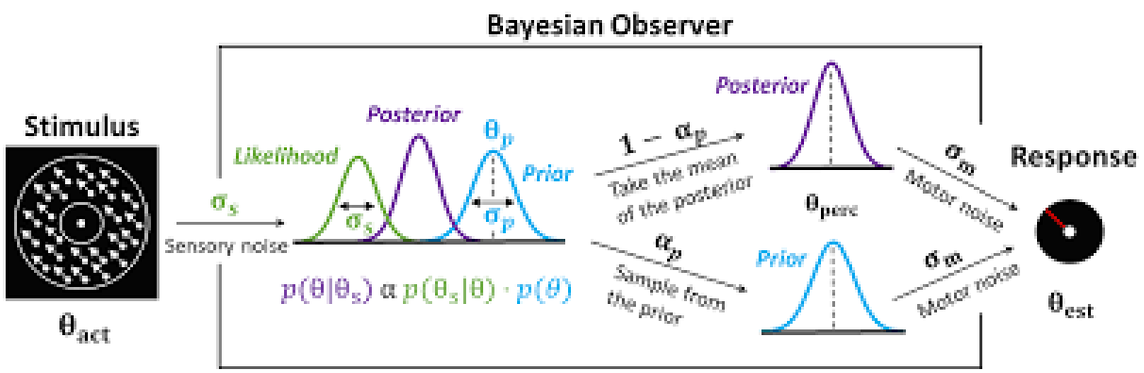
- compatible with the idea of them relying less on expectations

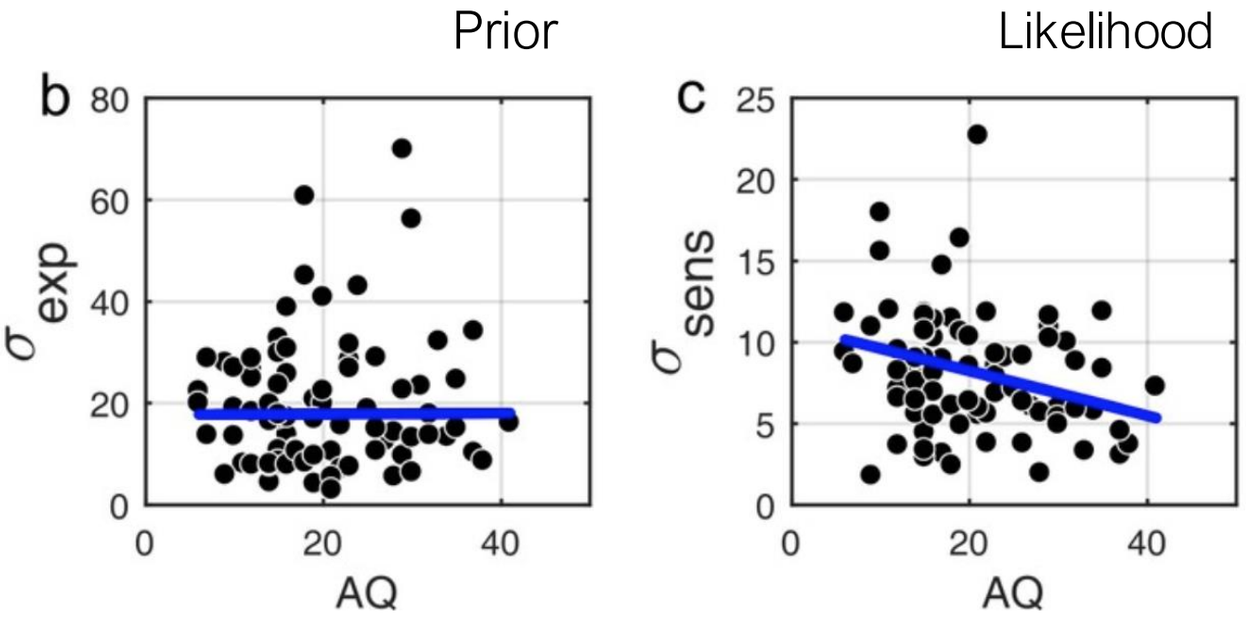


eLife [Karvelis, Seitz, Lawrie and Seriès, 2018]

3 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.

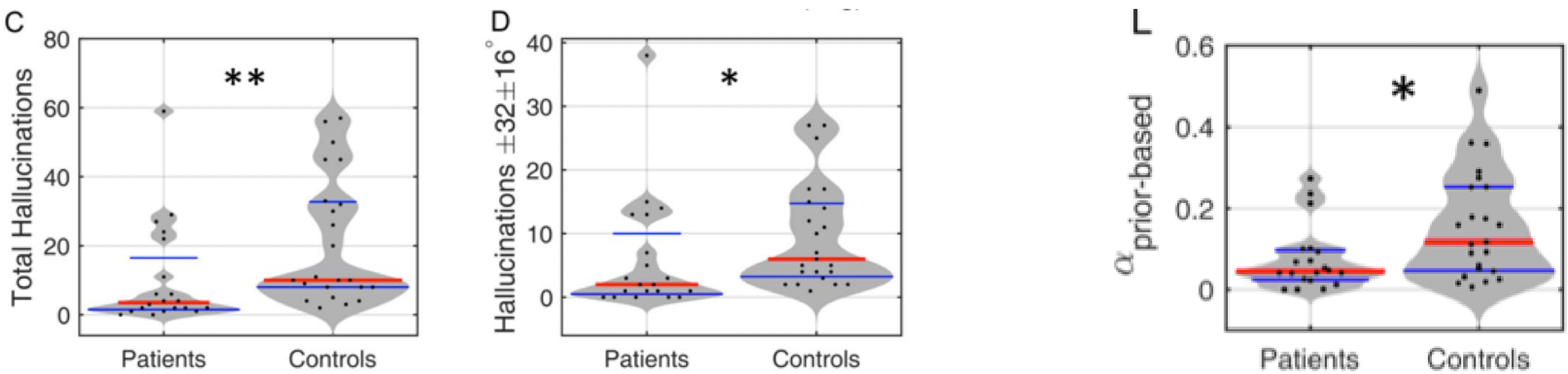




eLife [Karvelis, Seitz, Lawrie and Seriès, 2018]

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



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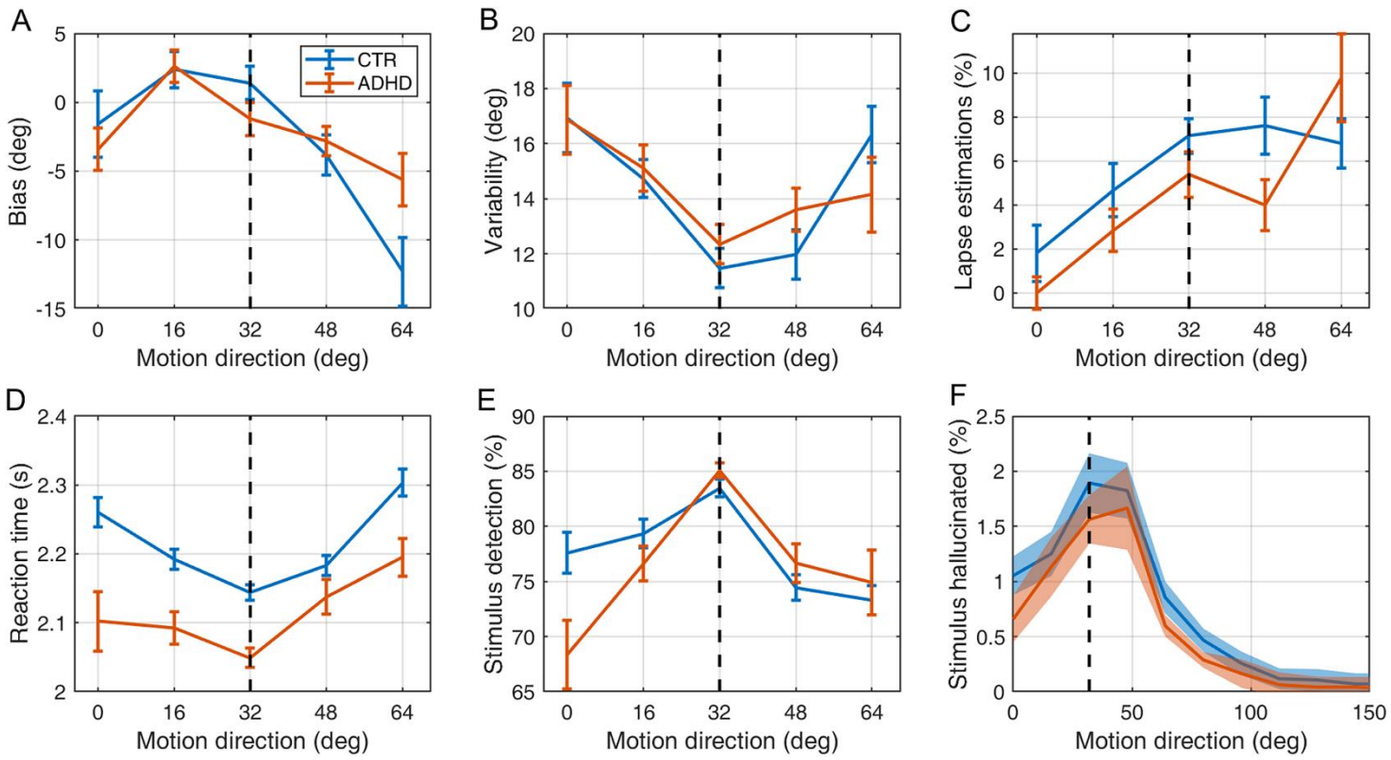
[Valton, Karvelis, Richards, Seitz, Lawrie and Seriès, 2019]

ADHD: Intact statistical learning and prior integration

- 20 ADHD vs 30 controls,

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

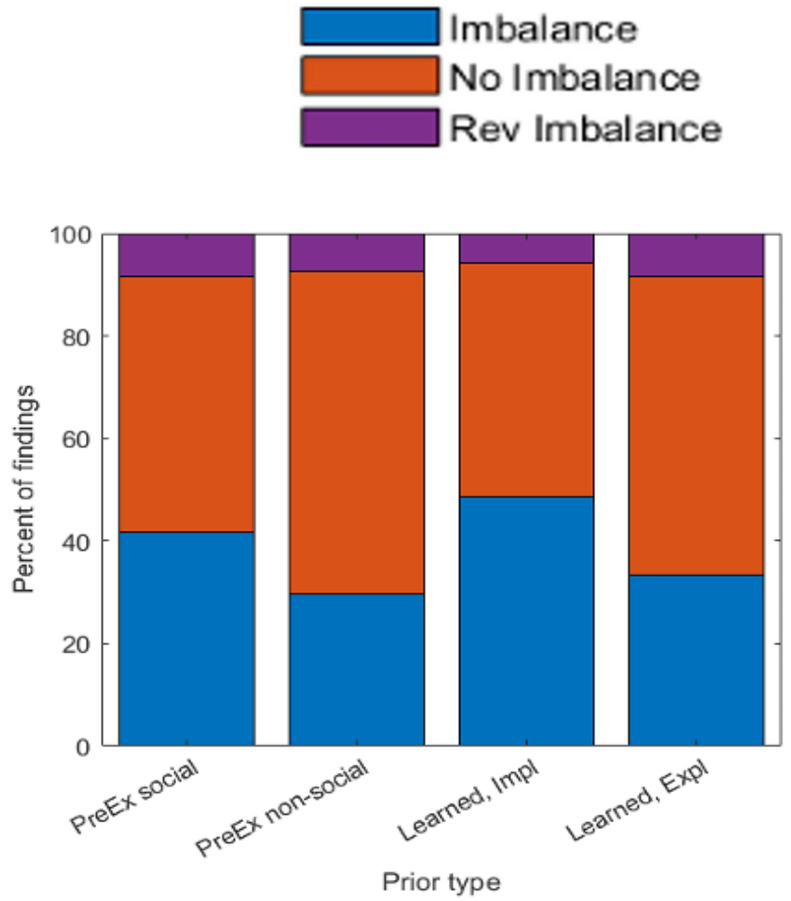
- Intact Statistical learning and inference;
- No difference between groups



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

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

Nikitas Angeletos Chrysaitis, Peggy Seriès *

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

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

- 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.

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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 and theorists is being refined.