



# Reply to Lawson et al.: A synergistic approach to mental health research

Perception and action reflect the interplay of immediate sensory information and knowledge derived from past experience (“priors”). Together, sensory information and priors enable us to form predictions about our environment (e.g., guessing what a friend will say next) and select appropriate behavioral actions (e.g., a response that keeps the conversation going). Recent efforts to understand the phenotypic consequences of autism suggest that the disorder may alter the ability to make such predictions (1–4). As Lawson et al. (5) discuss, this idea can be framed as an imbalance in the relative “precision” (reliability or certainty) of sensory information and priors. The sensory precision of your friend’s words is greater if the conversation occurs in a quiet room than a noisy restaurant. The precision of the prior (what you expect to hear) is greater if you are hearing a story for the fifth time. An increase in the precision of sensory evidence relative to the precision of priors may account for a number of behavioral characteristics observed in autism.

If this hypothesis is correct, then what neurophysiological changes might be responsible for the behavioral characteristics of autism? Several (nonexclusive) possibilities include: (i) narrower neural tuning functions resulting in increased sensory precision (1); (ii) neural responses that more closely reflect the sensory environment because of a decrease in the precision of priors (2); (iii) reduced habituation to repeated sensory stimulation (3), consistent with a decreased capacity to selectively attenuate sensory precision (5);

and (iv) reduced inhibition from the neural population that decreases the effect of priors (4). Behavioral predictions associated with these possibilities are qualitatively similar, in part because they derive largely from computationally inspired considerations capturing the idea that the brain’s ability to “contextualize” sensory representations is reduced in autism. Moreover, such changes may result from alterations in diverse physiological processes, including lateral inhibition within a brain area (4) and feedback from high-level areas (5). To accurately bridge physiology and behavior, explicit computational models are needed to interpret empirical data (4). The power of such models lies in the ability to generate refined predictions capable of teasing apart subtle differences between hypotheses.

Along these lines, it is important to emphasize the synergistic role that computational and empirical (e.g., genetic, behavioral, and animal model) approaches can play in mental health research. Computational approaches provide frameworks for analyzing and interpreting large (often noisy) empirical datasets, as well as creating precise predictions, spanning multiple levels, from cellular to behavioral. A large component of President Obama’s Brain Initiative also capitalizes on the same need and promise for the future. As our understanding of mental health disorders improves, it will become increasingly important to develop explicit computational models that make precise, testable predictions that can be vetted experimentally. Our recent work

toward developing a computational model of autism is an early step in this direction (4). Looking forward, computational modeling can provide a valuable tool for bridging the complexities of the genetic and environmental factors that give rise to mental health disorders and the resulting phenotypic consequences.

**ACKNOWLEDGMENTS.** This work was supported by Integrative Graduate Education and Research Traineeship Training Grant 43413-1 (to J.S.P.), and Simons Foundation Autism Research Initiative 247992 (to D.E.A.).

**Ari Rosenberg<sup>a,1</sup>, Jaclyn Sky Patterson<sup>b</sup>, and Dora E. Angelaki<sup>b</sup>**

<sup>a</sup>Department of Neuroscience, University of Wisconsin School of Medicine and Public Health, University of Wisconsin–Madison, Madison, WI 53705; and <sup>b</sup>Department of Neuroscience, Baylor College of Medicine, Houston, TX 77030

- 1 Qian N, Lipkin RM (2011) A learning-style theory for understanding autistic behaviors. *Front Hum Neurosci* 5:77.
- 2 Pellicano E, Burr D (2012) When the world becomes ‘too real’: A Bayesian explanation of autistic perception. *Trends Cogn Sci* 16(10): 504–510.
- 3 Sinha P, et al. (2014) Autism as a disorder of prediction. *Proc Natl Acad Sci USA* 111(42):15220–15225.
- 4 Rosenberg A, Patterson JS, Angelaki DE (2015) A computational perspective on autism. *Proc Natl Acad Sci USA* 112(30):9158–9165.
- 5 Lawson RP, Friston KJ, Rees G (2015) A more precise look at context in autism. *Proc Natl Acad Sci USA* 112:E5226.

Author contributions: A.R., J.S.P., and D.E.A. wrote the paper.

The authors declare no conflict of interest.

<sup>1</sup>To whom correspondence should be addressed. Email: ari.rosenberg@wisc.edu.