Researchers investigate altered neural computation in autism

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

(Medical Xpress)—In recent decades, autism diagnoses have dramatically increased in prevalence, and people with autism in the United States are now believed to number one in 68. Correspondingly, an increasing number of research efforts seek genetic, epigenetic,

neurological and other foundational causes of autism.

Autism affects individuals at cognitive, motor, and perceptual levels, and because symptoms vary in degree between individuals, it is conceived as a spectrum disorder. Since it manifests with a heterogeneous set of symptoms, rather than impacting individual neural systems, researchers at Baylor College of Medicine speculated that autism may arise from global differences in neural computation. They've published the results of their study in the *Proceedings of the National Academy of Science*.

"Divisive normalization" is regarded as a canonical computation that occurs throughout the brain. This kind of computation divides the activities of individual neurons by the combined activity of the neuronal population in which they are embedded. It basically controls the ratio of neural excitation to inhibition (E/I), and is implicated in a wide range of functions including sensory encoding and decision making. Hypothetically, E/I is imbalanced in the brains of people with autism.

There's a lot of evidence from previous autism research pointing toward this imbalance. Excitatory glutamatergic and inhibitory GABAergic neurons coordinate to create an E/I balance that is essential for normal brain activity. Among other things, the E/I balance is responsible for the critical timing of neurodevelopmental stages and computations in the primary visual cortex. The authors note that experience-dependent neural plasticity is altered in mice lacking GAD, an enzyme that helps to convert glutamate to GABA. The connection is further reinforced by biochemical analyses and the presence of susceptibility gene candidates.

To test the idea, the researchers simulated a population of neurons in the primary visual cortex, and compared this nonlinear neural network's response properties before and after divisive normalization. The framework of altered divisive normalization predicts that autism will broadly affect processes requiring so-called "cognitive marginalization,"

involved in such functions as social cognition and visual searching, and the researchers observe that reducing the inhibitory function of divisive normalization can account for the perceptual symptoms of autism.

The differing expression of divisive normalization across brain regions can account for the phenotypic diversity of autism symptoms between individuals. The authors write, "Qualitative differences between individuals should occur when alterations in divisive normalization have an impact on different brain areas. Quantitative differrences should instead reflect the extent to which divisive normalization is affected."

The study strongly implicates the neuronal milieu—the specific regions where neurons are embedded—as a basis of autism. Further, the framework of altered divisive normalization points the way toward further investigations of neural computation and autism symptomology, and the authors note that it may have applications in studies of schizophrenia and aging. "We suggest that computational perspectives can play an important role in the future of mental health research, providing insights that will aid in understanding and treating complex disorders such as autism," they write.

More information: "A computational perspective on autism." *PNAS* 2015 ; published ahead of print July 13, 2015, DOI: 10.1073/pnas.1510583112

Abstract
Autism is a neurodevelopmental disorder that manifests as a heterogeneous set of social, cognitive, motor, and perceptual symptoms. This system-wide pervasiveness suggests that, rather than narrowly impacting individual systems such as affection or vision, autism may broadly alter neural computation. Here, we propose that alterations in nonlinear, canonical computations occurring throughout the brain may underlie the behavioral characteristics of autism. One such computation,

called divisive normalization, balances a neuron's net excitation with inhibition reflecting the overall activity of the neuronal population. Through neural network simulations, we investigate how alterations in divisive normalization may give rise to autism symptomatology. Our findings show that a reduction in the amount of inhibition that occurs through divisive normalization can account for perceptual consequences of autism, consistent with the hypothesis of an increased ratio of neural excitation to inhibition (E/I) in the disorder. These results thus establish a bridge between an E/I imbalance and behavioral data on autism that is currently absent. Interestingly, our findings implicate the context-dependent, neuronal milieu as a key factor in autism symptomatology, with autism reflecting a less "social" neuronal population. Through a broader discussion of perceptual data, we further examine how altered divisive normalization may contribute to a wide array of the disorder's behavioral consequences. These analyses show how a computational framework can provide insights into the neural basis of autism and facilitate the generation of falsifiable hypotheses. A computational perspective on autism may help resolve debates within the field and aid in identifying physiological pathways to target in the treatment of the disorder.