VIEWPOINT

Visual system may offer glimpse of autism's effects in brain

BY **MICHAEL-PAUL SCHALLMO, SCOTT MURRAY**

25 OCTOBER 2016

Most people do not associate autism with visual problems. It's not obvious how atypical vision might be related to core features of autism such as social and language difficulties and **repetitive behaviors**.

Yet examining how autism affects vision holds tremendous promise for understanding this condition at a neural level. Over the past 50 years, we have learned more about the visual parts of the brain than any other areas, and we have a solid understanding of how neural activity leads to visual perception in a typical brain.

Differences in neuronal processing in autism are likely to be widespread, and may be similar across brain regions. So pinpointing these differences in visual areas might reveal important details about processing in brain regions related to social functioning and language, which are not as well understood.

Studying vision in autism may also help connect studies of people to those of animal models. Working with animals allows neuroscientists to study neural processing at many different levels — from specific genes and single neurons to small neural networks and brain regions that control functions such as movement or hearing.

But animals do not display the complexity and diversity in language and social functioning that people do.

By contrast, visual brain processes are similar between people and animals. We can use our rich knowledge of how neurons in animals process visual information to bridge the gap between animals and people. We can also use it to test hypotheses about how autism alters neural functioning in the brain.

For these reasons, we see the visual system as a vital avenue of autism research. Using this approach, we have begun to assess a particular theory about brain changes associated with autism, one that could have powerful implications for scientists and clinicians.

Applying the brakes:

Our approach has been to use what we know about small networks of visual neurons to test a theory about people with autism.

We and others have proposed that a process called 'normalization'[1] is unusually weak in these individuals[2].

The term normalization refers to the fact that the activity of neighboring neurons is not independent: One neuron's behavior affects that of its neighbors. When neurons are active, they lower the activity of neighboring neurons by sending suppressive signals to those cells.

For example, making a visual stimulus larger causes more neurons to respond to that stimulus. However, normalization between neighboring neurons causes the cells to suppress one another's activity. This leads to the counterintuitive observation of lower neuronal responses to larger stimuli.

Normalization is carried out by small networks of neurons. Although we are testing the hypothesis that normalization is weak in autism by studying vision, normalization occurs in many brain regions. So this work may generalize to other sensory domains, as well as motor and cognitive ones[1].

Normalization is thought to benefit vision by suppressing the response to less important parts of a visual scene. For example, it is not necessary to have a strong, detailed neural representation of large uniform background regions, such as the sky. Perceiving a small bird flying across the sky may be more important.

Normalization is likely to help maintain a proper balance of excitatory and inhibitory neural activity, calibrating overall activity so it falls in a certain range within these small networks.

In autism, weak normalization might lead to excessively large neural responses within networks or individual neurons, which could disrupt the transmission of information in the brain. However, the effect of this disruption on vision and other functions is not yet fully understood.

To examine whether normalization is unusually weak in people with autism, we are looking at their perception of visual motion. In 2013, researchers showed that in some cases, people with autism are unusually good at perceiving motion, and this counterintuitive result is actually consistent with weak normalization in the visual system[3].

Gone in a flash:

With weak normalization, people with autism would be expected to have greater neural responses in motion-selective visual areas, which could improve motion perception. Starting with this hypothesis, we can predict how weak normalization might affect neural activity or visual behavior, and then look for differences in people with autism.

We are examining the relationship between neural data and perception in people at multiple levels: visual behavior, neural responses and neural chemicals. In our study, a moving image is flashed briefly on a computer monitor, and afterward, participants judge whether it moved to the left or the right. If they answer correctly, the next picture appears for a shorter period of time. This process repeats until we find the minimum amount of time a participant needs to accurately perceive the direction of motion.

We have found that people with autism are able to see this motion in about half the amount of time that typical people do — a surprisingly large advantage. This enhanced ability to see motion appears to be related to greater activity in the visual cortex, as assessed by functional magnetic resonance imaging, and to the concentrations of particular **neurotransmitters** in these regions.

These preliminary results suggest that most young adults with autism show weaker normalization than their typical peers. Interestingly, a small minority of people with autism do not seem to show this difference. This observation raises the exciting possibility of identifying different autism sub-groups based on how well this particular neural circuit is functioning. This work is ongoing, and our findings thus far will be presented at this year's **Society for Neuroscience annual meeting**.

Visual tests:

Understanding the relationship between autism and normalization may help us uncover the role certain genes and neurochemicals play in autism and in the typically developing brain. It also may improve the speed and accuracy of autism diagnosis and predict treatment outcomes.

For example, doctors could give people a visual test designed to detect weak normalization. This measure may prove easier than directly assessing language and social deficits in some children, such as those with hearing difficulties.

Weak normalization may also go along with particular features, such as **sensory sensitivity**. If so, understanding this connection might help clinicians and families develop new strategies to address these challenges. Normalization strength might even predict how well a person will respond to certain drugs or behavioral therapies.

First, however, we need to better understand the relationship between normalization at a neural level and the behavioral traits related to autism. Large scientific studies in people and animals may help us understand the role of particular genes and neurochemicals in this process — and whether this process differs in the various forms of autism.

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