VIEWPOINT

Helpful hurdles

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Matthew State (left) and Nenad Sestan (right).

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In the past year, we and others have published evidence suggesting that the number of autism risk genes **lies in the hundreds**. Some people see this as disheartening news, but we believe that these genes will converge on a much smaller number of molecular processes that lead to autism spectrum disorders.

What's more, the rapid discovery of an increasing number of *bona fide* autism genes, combined with an emerging map of gene expression and regulation in the normal human brain, offers unprecedented opportunities to unravel the complex biology of autism.

As we outlined in a commentary published 14 September in *Science*, we propose that examining the expression of a set of well-established autism genes during normal brain development will **provide novel and interesting insights** into the autism brain. Identifying where and when the expression of this diverse set of genes converges in time and space will help pinpoint relevant biological mechanisms.

From this perspective, each new autism risk gene discovered offers the potential to hone the focus of our research efforts.

For example, newly discovered autism-associated genes point to the importance of a wide range of biological processes in neurons. However, despite their diverse functions, a subgroup of these genes seem to share the property of being expressed during the same time points and in the same regions of the early developing brain — in particular, when early neural connections are being formed in the cerebral cortex.

We know from studying animal models that these emerging **synapses** are particularly sensitive to genetic and environmental perturbations. We also know that some of these circuits in the cortex take a long time to mature. Indeed, some are not fully developed until early adulthood.

This combination of early vulnerability and extended maturation may, at least in part, account for the observation that some of the genetic regions identified as increasing autism risk also increase risk for other developmental brain disorders, such as schizophrenia.

This approach may also lead to **new treatment strategies**.

For example, evidence from animal models shows that targeting specific genes may reverse autism-like symptoms, **even in adult mice.**

They also highlight the fact that understanding autism's basic biology — though a long, hard and often frustrating road — has the potential to transform our understanding and offer more effective and personalized treatments.

We have every reason to hope that the next several years will bring similarly great strides in the understanding and treatment of autism.

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