

TOOLBOX

Mathematical method may flag potential autism genes

BY MARISSA FESSENDEN

20 MAY 2015

©iStock.com/lvcandy

A new mathematical method confidently ranks genes based on their likely impact in a disorder. The approach, described 6 April in the *Journal of Computational Biology*, may help researchers home in on important autism genes¹.

Sequencing studies have **unearthed a surfeit of genes** that might be involved in autism. But understanding the role of these genes, and of mutations in their sequences, in a disorder is expensive and time-consuming.

Researchers use statistical tools to derive clues to a gene's involvement in a disorder. One clue, for example, might be a gene's proximity on the chromosome to other genes with known ties to the disorder. The new method considers more of these characteristics and can rank more genes with greater statistical confidence than other methods do.

The approach relies on an algorithm that pulls information from more than 35 existing databases. These databases detail everything known about a given gene, such as how it's regulated and how it interacts with other genes. These pieces of information, called annotations, act as digital labels for each gene.

In a test of the method, researchers 'trained' the algorithm using 48 genes that were strongly

linked to autism and intellectual disability before 2010. They then analyzed 475 genes discovered after 2010 to mimic the discovery of new gene candidates. The algorithm generated a list of 190 genes ranked by their likelihood of contributing significantly to either disorder. Of these, 124 have known ties to one or both conditions.

This approach detected more candidates from the dataset than did two similar statistical tools, **Endeavour** and **PINTA**. It also gave stronger statistical backing for the ranked genes with the greatest influence.

The method also flagged 25 genes not previously linked to either disorder. The researchers scoured the literature for those genes and turned up some weak associations with autism. The new analysis, however, makes them attractive enough to study further, the researchers say.

For example, one of the new genes, called ATCAY, is involved in the development of the outer layer of the cerebellum. Mounting evidence suggests this structure at the back of the brain **may play an important role in autism**.

The researchers plan to integrate the method into the Lynx database, an **online** gene analysis platform, later this month.

References:

1. **Xie B.** *et al. J. Comput. Biol.* **22**, 313-323 (2015) **PubMed**