OPINION

Slippery SNPs

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About a year ago, researchers in Australia published a study with an **incredible claim**: A new genetic test, screening for 237 common genetic markers, could predict autism with more than 70 percent accuracy.

The study, published in *Molecular Psychiatry*, was widely reported in the popular press with its claims **largely unquestioned**. But as SFARI.org reported at the time, some experts were **strongly skeptical**.

For one thing, larger studies had looked for common variants, known as single nucleotide polymorphisms, or SNPs, that **up the risk of autism** — and had come up short.

“The data look interesting but really need to be tested independently before I would believe the results were scientifically sound,” geneticist **Stephen Scherer**, director of the Centre for Applied Genomics at the Hospital for Sick Children in Toronto, told me at the time. “There is much room for error, both in study design and interpretation, and too much at stake here to get this wrong.”

As it turns out, the study was indeed wrong. Last week, **Benjamin Neale** and his colleagues from Massachusetts General Hospital reported in the same journal that the 237-marker panel **does not predict** autism risk — not by a long shot.

The Australian researchers designed their panel based on screening 732 individuals with autism from the **Autism Genetic Resource Exchange** database and 123 controls. They validated those markers in another sample, comprising 525 children with autism from the **Simons Simplex Collection** and 2,620 population controls from the Wellcome Trust in the U.K. (The Simons Simplex Collection is sponsored by SFARI.org’s parent organization.)

Other scientists raised their eyebrows at those sample choices because the autism and control groups are of different ethnicities. As geneticist **Daniel Geschwind** and his colleagues pointed out in a **commentary** a couple of months after the Australian study came out, the controls hail from a relatively homogenous population in the U.K., whereas the individuals with autism are of a more mixed ancestry.

Neale's new study provides even more ammunition. He and his colleagues analyzed the top 30 autism-linked SNPs reported in the original study (because, apparently, the Australian researchers **refused to disclose** the other 207 SNPs used in their panel).

Neale's team looked for those SNPs in more than 5,000 individuals with autism enrolled in the **Psychiatric Genomics Consortium** and as many controls. None of the 30 SNPs are associated with autism, either individually or in combination, their study found.

Having reported the SFARI.org article last year, and now following the reactions to the Neale paper, I find it surprising that the original study ever made it through the peer-review process. It went against everything we've learned from the past five years of rigorous (and expensive) research in autism genetics.

We know now that **hundreds of genetic variants**, of **all different flavors** — big, small, rare, common, inherited, spontaneous — not to mention epigenetic glitches and environmental factors, contribute to autism risk.

To suggest otherwise — and especially to claim that this complex disorder boils down to a set of 237 common variants — is extraordinary. As Carl Sagan liked to say, extraordinary claims require extraordinary evidence.