

NEWS

Community Newsletter: Female protective effect, genetic risk factors, identity-first rejection

BY GRACE HUCKINS

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Hi there! I'm **Grace Huckins**, *Spectrum's* editorial intern, your host for the Community Newsletter this week.

Two new preprints on medRxiv have generated a buzz on Twitter. Both look at how common genetic variants, rare variants and sex interact to affect an individual's chances of having autism.

The first paper, from **Elise Robinson's** lab at Harvard University, considers the **relationship between inherited genetic risk** and how autism occurs within families. Siblings of autistic girls are more likely to have autism than the siblings of autistic boys, the researchers found, and non-autistic mothers' genes contribute more to a child's likelihood of having autism than non-autistic fathers' genes do. Together, the team says, these findings "support a [female protective effect] against ASD that includes common, inherited genetic variation."

Study investigator **Emilie Wigdor**, a graduate student at the University of Cambridge in the United Kingdom, broke down the findings in a Twitter thread.

I'm thrilled to present our analyses on the female protective effect (FPE) against autism spectrum disorder (ASD) using the nationally representative Danish iPSYCH resource, SSC+SPARK and UKB: <https://t.co/0zy3tOVAJz> (1/11)

— Emilie Wigdor (@EmilieWigdor) **April 5, 2021**

Meng-Chuan Lai, a clinician scientist at the Centre for Addiction and Mental Health in Toronto, Canada, praised the paper's "elegant analyses."

An important set of elegant analyses on the genetic nature of sex-differential probability of autism. <https://t.co/FaogEPmgUD>

— Meng-Chuan Lai (@mengchuanlai) **April 5, 2021**

The paper answers some questions but raises others, according to **Victoria de Menil**, research director at the Stanley Center for Psychiatric Research in Cambridge, Massachusetts.

Excellent paper supporting a female protective effect in autism. Any guess what mechanisms underly the effect?

— Victoria de Menil (@vdemenil) **April 8, 2021**

The second paper comes from the lab of **Jonathan Sebat**, professor of psychiatry and cellular and molecular medicine at the University of California, San Diego, and examines how various genetic factors **together determine the chances of having autism**. Analyzing males and females separately, the researchers found that females with autism have greater genetic risk scores, on average, than males with autism. "This is consistent with [the] 'female protective effect' in which girls require a genetic load," Sebat wrote in a thread about the paper.

I'm pleased to share our latest preprint. "A phenotypic spectrum of autism attributable to the combined effects of rare variants, polygenic risk and sex". Here is the????I promised!
<https://t.co/m2okuqViPj>

— Jonathan Sebat (@sebatlab) **April 5, 2021**

"What an epic journey of a paper!" tweeted **Samuel Katz**, a postdoctoral fellow at the National Institutes of Health. "So much to process here."

Woah! What an epic journey of a paper.

So much to process here.

Is autism driven by the rare variant "load" (so looking for the specific variants that explain it is futile?). Is data on parental education and age skewed because how the two are connected?

Very interesting. <https://t.co/3SFpfeDjqj>

— Sam Katz (@2Bistheanswer) **April 6, 2021**

David Curtis, honorary professor of genetics, evolution and environment at University College London in the U.K., piped up with an idea for further analysis.

Did you think of trying to pull out effects of X chromosome versus autosomal variants? It would be interesting to know how this related to sex-specific risk.

— Dave Curtis (@davecurtis314) **April 5, 2021**

And **Shai Carmi**, associate professor of medicine at the Hebrew University of Jerusalem in Israel, brought the two "excellent threads" into conversation with each other.

Two excellent threads explaining new preprints in autism genetics.

The papers suggest that autism is due to both high impact de-novo variants + polygenic "load". Females are more protected and both must be high to become affected. <https://t.co/t6yrpB9ESi><https://t.co/kBM1k6zYsb>

— Shai Carmi (@ShaiCarmi) **April 6, 2021**

Our last featured tweet this week provoked strong reactions from both the autistic and science communities. **Kristen Bottema-Beutel**, associate professor of special education at Boston College

in Massachusetts, went viral when she tweeted about having a paper rejected because she didn't use person-first language. Person-first language ("person with autism") places the individual before their identity or diagnosis, whereas identity-first language ("autistic person") leads with the identity label.

A paper about autistic adults on which I am a coauthor was just desk rejected for not using person-first language ????

— Dr. Kristen Bottema-Beutel (@KristenBott) **April 7, 2021**

"NeuroTribes" author **Steve Silberman** tweeted that the publication's decision is out of step with the autistic community, which largely favors identity-first language — for "very good historical reasons."

There are very good historical reasons why many autistic adults reject person-first language, while other disabled communities embrace it. I talk about why in **#NeuroTribes**.

— Steve Silberman (@stevesilberman) **April 8, 2021**

Meghan Ellerden, a physician assistant in Fredericksburg, Virginia, chimed in to give some context about why a scientific journal might impose person-first language, even if the autistic community rejects it.

There's communities and individuals that prefer PFL, but professionals took and adopted it as the only acceptable language around disability in general despite other communities and individuals preferring identify first language.

— Meghan Elliden, PA-C (@mmellden) **April 8, 2021**

Eric Garcia, author of "We're Not Broken: Changing the Autism Conversation," succinctly

captured the sentiments of many responders.

This sucks!!

— Eric Michael Garcia (@EricMGarcia) **April 8, 2021**

That's all for this week! Feel free to get in touch with me at **ghuckins-intern@simonsfoundation.org** with any interesting autism- and autism research-related social media discussions. Have a great weekend!