**NEWS**, **SYNAPTIC**

# Community Newsletter: Rare genetic variants; shape-shifting microglia; telehealth diagnoses

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Many tweets in the autism research space this week discussed a **study** exploring the role of rare variants in 22 complex traits. The work, published earlier this month in *Nature*, featured “a new method and **insights from nearly 400,000 exomes**,” tweeted study investigator **Daniel Weiner**, a graduate student in **Elise Robinson**’s lab at Harvard Medical School.

> How will rare genetic variation inform our understanding of common disease?
>
> Today in **@Nature**, we’re excited to share our answer to this question,
>
> with a new method and insights from nearly 400,000 exomes:**https://t.co/H3gXTSK6IC**
>
> ???? (1/15):
>
> — Dan Weiner (@danweiner92) **February 8, 2023**

The researchers developed tools to glean heritability and genetic correlations from exome-sequencing data and found that, on average, rare variants contribute to about 1 percent of the 22 traits’ heritability, compared with 13 percent for common variants, Weiner explained.

Genome-wide association studies (GWAS) have long shown how common genetic variants contribute to complex human traits and disease. The new work suggests that “**rare variants are**

**enriched** in the same candidate genes identified by GWAS," noted **Todd Brusko**, professor of pathology, immunology, and laboratory medicine at the University of Florida in Gainesville.

> An important paper regarding rare vs common variants for complex diseases like diabetes. One important take away-rare variants are enriched in the same candidate genes identified by GWAS. **https://t.co/HYf40QBdG6**
>
> — Todd M. Brusko (@Bruskolab) **February 9, 2023**

In a tweet summarizing the paper's takeaways, **Stephen Waggoner**, associate professor of pediatrics at Cincinnati Children's Hospital in Ohio, wrote, "Rare coding variants will **contribute only modestly** to missing heritability and population risk stratification."

> Rare coding variants will implicate a tractable number of large-effect genes, common & rare associations are mechanistically convergent, and rare coding variants will contribute only modestly to missing heritability and population risk stratification**https://t.co/kkD38646Ad https://t.co/PSR2fsVEcQ**
>
> — Waggoner Lab (@LabWaggoner) **February 8, 2023**

Even so, Weiner tweeted that he and his colleagues remain "**optimistic about rare variants** informing understanding of common disease biology."

> ???? Reason 1: Common + rare variants = convergent:
>
> Drugs targeting RV associated genes can benefit many patients, not only the few who carry specific mutations
>
> ???? Reason 2: RV genetic architecture less polygenic -> Disease mechanisms involve attainable number of genes
>
> (14/15)

— Dan Weiner (@danweiner92) **February 8, 2023**

Another paper turning heads on Twitter this week explored how reactive microglia adjust their microtubule cytoskeleton, which entails “remodeling from **acentrosomal to centrosomal arrays**,” tweeted the study’s lead investigator **Francesca Bartolini**, professor of biochemistry at Columbia University.

> Best Valentine gift ever????! A wonderful journey in collaboration with **@SAngelantonio** team and many others without whom this work would have not been possible???? Microglia reactivity entails microtubule remodeling from acentrosomal to centrosomal arrays **https://t.co/lfXonZfANI**
>
> — Bartolini Lab (@BartoliniLab) **February 14, 2023**

When microglia become reactive in response to inflammation or injury, they change their shape dramatically. *Spectrum* has previously covered the link between autism and **microglia** and **microtubule** biology.

**Ghazaleh Eskandari-Sedighi**, a postdoctoral researcher at the University of Alberta in Canada, tweeted that it’s great to see how this work connects her first love from when she started studying the brain — microtubules — with her most recent one: microglia.

> Microtubules were the first proteins I started my adventurous journey of studying brain with, and ever since then I've been closely tracking the amazing work of **@BartoliniLab**. It's great to see how their latest work connects my first love with the most recent one (microglia)! **https://t.co/Pf5LOcZoqM**
>
> — Ghazaleh Eskandari-Sedighi (@GhazalehEsk) **February 14, 2023**

**Meng-meng Fu**, assistant professor of cell biology, development and physiology at the University of California, Berkeley, called the paper a “**must read** for microtubule and microglia enthusiasts.”

> Golgi outposts in microglia!
>
> Must read paper for microtubule and microglia enthusiasts alike ????
> **https://t.co/hwbztI4OE1**
>
> — Meng-meng Fu (@Meng2Fu) **February 14, 2023**

Lastly, scientists weighed in on *Spectrum*'s Deep Dive about how **remote autism assessments** developed during the COVID-19 pandemic may help solve a persistent problem: the long wait families endure to get a diagnosis in the United States.

"Great reading about Telehealth development assessments," tweeted **Adam Guastella**, professor of child and youth mental health and a clinical psychologist at the University of Sydney in Australia. "The next 5 years will see new innovative approaches transforming the science of assessment that overcome disadvantage, isolation and cost for families."

> Great reading about Telehealth development assessments **@Spectrum**
>
> The next 5 years will see new innovative approaches transforming the science of assessment that overcome disadvantage, isolation and cost for families**@becsutherlandSP @alistair_mcewan https://t.co/mj5R7rdFQ7**
>
> — Adam Guastella (@Adam_Guastella) **February 15, 2023**

But others cautioned that telehealth should not replace in-person evaluations entirely. "It may be a useful additional adjunct, but there is so much more to holistic assessment," tweeted **Michael Absoud**, honorary reader in women and children's health at King's College London in England.

> I worry about this replacing in person assessments— it may be a useful additional adjunct, but there is so much more to holistic assessment…
>
> — Michael Absoud (@MAbsoud) **February 15, 2023**

That’s it for this week’s Community Newsletter! If you have any suggestions for interesting social posts you saw in the autism research sphere, feel free to send an email to **michael@spectrumnews.org**.

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