Q&A: How new software is changing our understanding of human brain development

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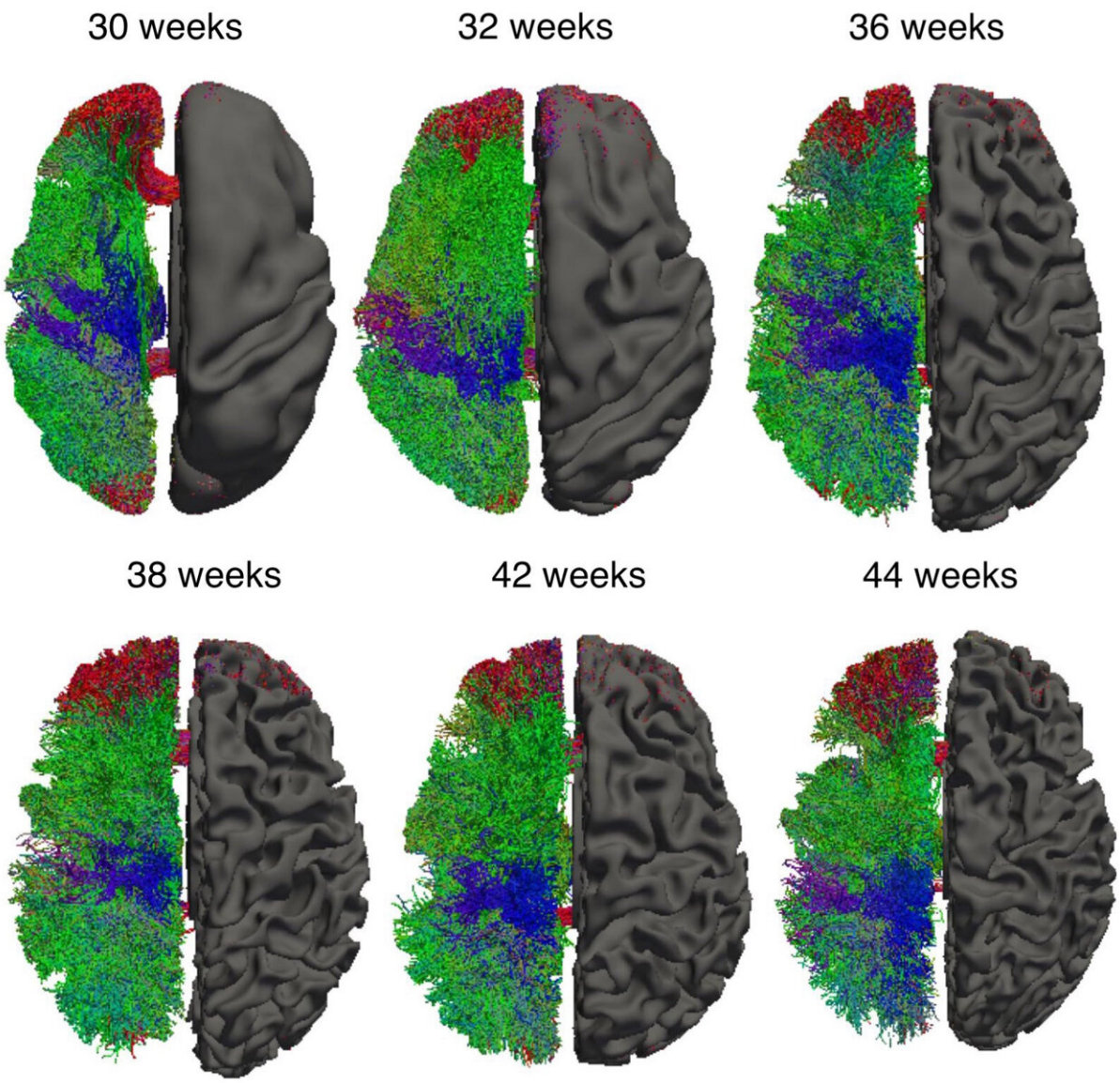

A team including researchers at the University of Washington compared MRIs from 300 babies using new software to compare their brains' white matter and discovered that myelin, a part of white matter, develops much slower after birth. Here, images from six babies born at different times in their terms (displayed above each) show the changes in brain development. Credit: Grotheer et al./*PNAS* 2023

A single brain is unfathomably complex. So brain researchers, whether they're looking at datasets built from 300,000 neurons in 81 mice or from MRIs of 1,200 young adults, are now dealing with so much information that they must also come up with new methods to comprehend it. Developing new analysis tools has become as important as using them to understand brain health and development.

A team including researchers at the University of Washington recently used new software to compare MRIs from 300 babies and discovered that myelin, a part of the brain's so-called white matter, develops much slower after birth. The researchers published their findings Aug. 7 in the *Proceedings of the National Academy of Sciences.*

UW News spoke with senior author Ariel Rokem, a UW research associate professor in the psychology department and a data science fellow in the eScience Institute, about the paper and his research approach.

What topics do you research and how?

Ariel Rokem: My group works in neuroinformatics, which focuses on building methods and software for analyzing neuroscience data. We focus specifically on MRI measurements in human brains. A brain is made out of a big network of connections between different areas.

Within our brains, we have these big bundles of connections called white matter that contain lots of axons, which are the long, branching parts of neurons that let them talk to each other across pretty large distances. So we use MRI to find these bundles in every person in a study and then make sense of the tissue within these bundles. From that, we can find differences between people who have certain diseases and those who don't, or differences in development or cognitive abilities.

How does this approach differ from how brain research was practiced historically?

AR: For many years, researchers would take test subjects over to their local hospital or MRI center and collect some data. And people still do this. In fact, we have one of these scanners at the new UW Center for Human Neuroscience, which I am part of. But more recent approaches involve collecting much larger amounts of data. For example, it would be hard for anyone here in the department at the UW to collect data from more than 1,000 individuals. But a few years ago, the National Institutes of Health funded what's called the Human Connectome Project to do exactly that—get a sample of 1,200 healthy, grown-up people, and collect pretty large amounts of data on each of them. In neuroinformatics we take those kinds of datasets and develop the tools to study them.

What discoveries have these methods led to within brain science?

AR: Our recent paper is a good example. Our team used a large, openly available dataset from the Developing Human Connectome Project, which collects data from newborn infants in the first few days of life. We were looking at how white matter develops in these scans of more than 300 babies. My collaborator and lead author Mareike Grotheer, at

the Philipps University of Marburg, had previously taken software for finding white matter bundles in adults and adapted it to work on babies' brains. In this study, we scaled her approach up using cloud computing. We were looking at how myelin, a fatty sheath that insulates axons, grows in white matter.

We know from other studies that abnormal myelin development is associated with many developmental and mental health disorders, from chronic depression to schizophrenia. But before this study we still didn't know how birth changes the course of myelin development.

We had several hypotheses that we wanted to test. One is, well, that it doesn't matter when exactly you were born; it just matters how much time passed from conception to when you're scanned. Another was that it matters only how long after conception you were born, and it didn't matter how long after birth you were scanned. And we had a third hypothesis that says both of these things matter: how long the baby spent gestating in the mother's womb, and how much time passed from birth until the time of the scan. So we were comparing scans from babies who were born at different gestational ages, ranging from very early premature birth, up to babies who were born a couple of weeks after the full term of 40 weeks. Because we had this large dataset to work with, we could really chart how babies' brains change in the first few days and weeks of life.

We found that the data supports that both the gestational age at birth and the gestational age at time of scan mattered, but there's an inflection point right at birth. Right then, development of these bundles that we were looking at slows down dramatically. It's a basic fact, but we didn't know this until now, and we found it by examining publicly available data. This has implications for our basic understanding of early-life brain development, and implications for the ways that we might mitigate the adverse effects of premature birth. Perhaps, for instance, creating a

"womb-like" environment after birth could offset this slowed development and give the brains of premature babies more time to develop.

What are you looking to investigate with these methods moving forward?

AR: We're starting to ask questions about brain connections related to autism spectrum disorder and to schizophrenia. We're also now part of the UW's ACT Study, or the Adult Changes in Thought Study. It's been around for almost 30 years, following a large cohort of people in the Seattle area as they are aging. In the recent round of that study, we've added MRI measurements. We're developing methods to make inferences about white matter bundles in people who are aging.

Additional co-authors on this paper are David Bloom, a former UW post-baccalaureate student in the psychology department; John Kruper, a UW doctoral student in the psychology department; Adam Richie-Halford, a former UW postdoctoral researcher in the psychology department; Stephanie Zika and Vicente A. Aguilera González at Philipps University of Marburg; and Jason D. Yeatman and Kalanit Grill-Spector at Stanford University.

More information: Mareike Grotheer et al, Human white matter myelinates faster in utero than ex utero, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2303491120

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