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Global MRI data offers hope for improving treatment of brain injuries

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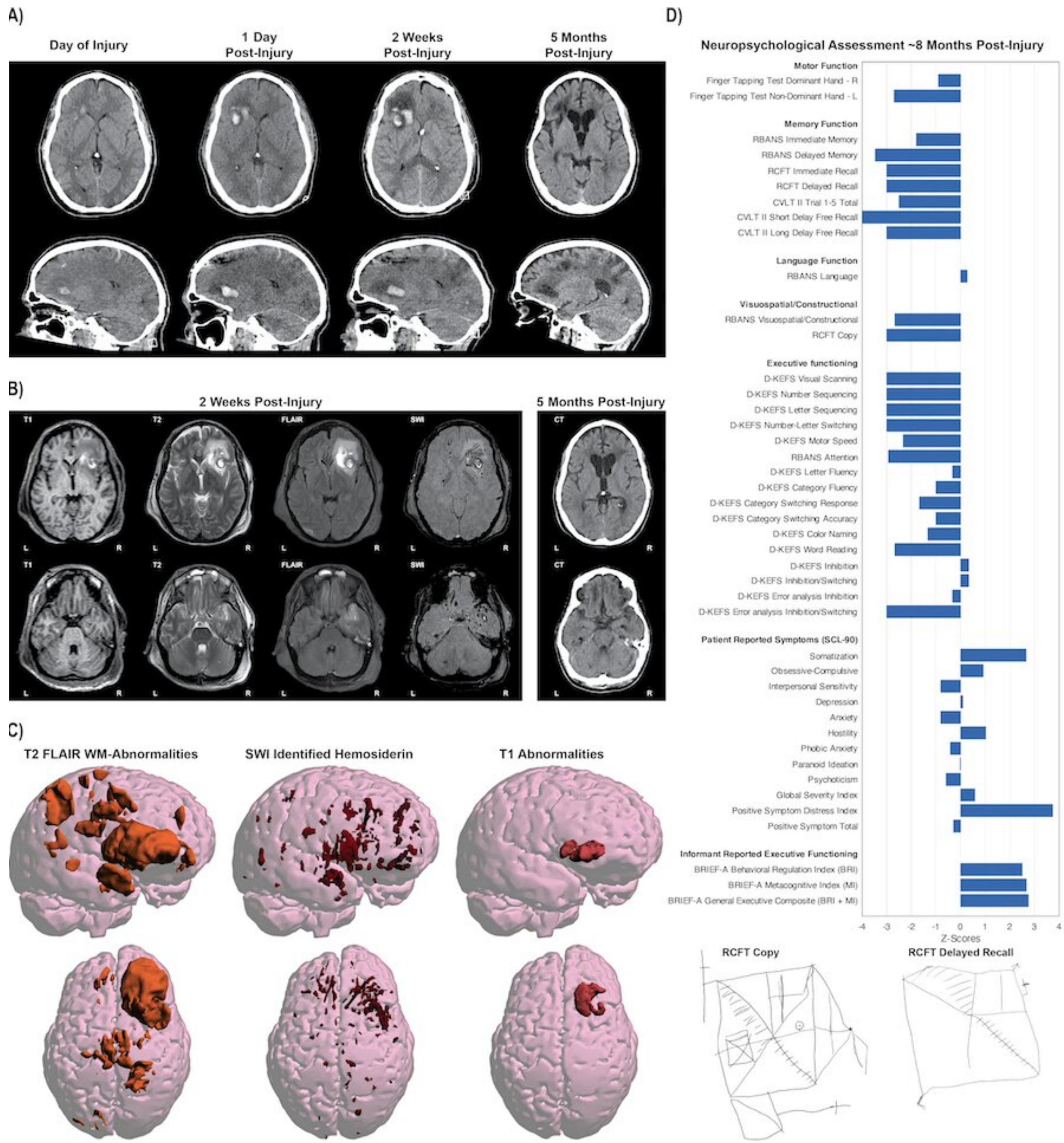

This illustration show the complexity of the data obtained from one single patient with moderate/severe traumatic brain injury. Different imaging approaches and techniques have their own unique sensitivity in assessing different aspects of neuroanatomy and neuropathology. What can be seen on images also changes with time since injury. Data from comprehensive clinical and functional assessments using a range of other tools is also important for evaluating patient outcome. Through data harmonization and large-scale analyses of data combined across multiple research sites, the ENIGMA Brain Injury will develop and test methods and procedures for making sense of the complexity in this data Credit: Olsen et al., Brain Imaging and Behavior, 2020

Traumatic brain injury is a major cause of disability and can have major consequences for patients and their loved ones. Patients can suffer a range of physical, cognitive, behavioral and emotional problems.

People who fall and hit their head, or who are in traffic accidents or suffer other head injuries, often undergo an MRI if doctors suspect a brain injury. But it can be difficult to predict from an MRI exactly what kinds of issues, if any, will arise from the trauma.

Now, researchers hope that research on newer and more advanced MRI methods will benefit this patient group even better than today. However, progress to date has been limited by relatively small studies and has lacked standards for sharing and analyzing this data across research centers.

"A major challenge in the research is to figure out which injury characteristics and which changes in the brain caused by the injury can predict how patients will recover and what follow-up they need. A big part of the challenge is that individual patients are so different," says

Alexander Olsen. He is an associate professor at the Norwegian University of Science and Technology's (NTNU) Department of Psychology and a neuropsychologist at St Olavs Hospital.

The goal of the researchers is to combine and analyze large data sets on brain imaging from around the world to see if they can find connections that aren't discernible in single studies from individual centers.

The main ENIGMA project is based at the University of Southern California, and Olsen is co-leader of a subgroup focused on moderate to severe brain injuries with Frank Hillary from Penn State University.

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"By pooling our resources, in terms of data, computational power and intellectual expertise, we'll be able to tackle some of the big unanswered questions in our field, such as how sex impacts outcome, whether there are subtypes within the broader patient population, or how to handle lesions in neuroimaging data," said Emily Dennis, who is co-principal investigator for ENIGMA's main group on brain injuries. This main brain injury group is made up of 170 researchers from 13 countries.

"Lots of brilliant scientists around the world have been working on these questions, and made a lot of progress, but this has been limited by the size of our individual samples," she said.

Part of the challenge here is that people's brains are so very different, as different as individual fingerprints, says Erin Bigler, a professor emeritus at Brigham Young University and adjunct professor in neurology and psychiatry at the University of Utah. Bigler has been involved with traumatic brain injury research for 50 years with more than 200 published papers on the subject.

"Traumatic brain injury is often referred to as the most complex disorder affecting the most complex organ," he said.

Add to that the fact that the brain contains roughly 300 billion brain cells that decode 100 trillion messages to enable us to think and act, and it's easy to see why researchers need lots of data from lots of different brains and brain injuries, Bigler said.

"Very large sample sizes are essential, otherwise it would be impossible to embrace all of this variability," he said.

To start, the ENIGMA project will apply different types of advanced analysis methods to MRI data already collected in collaboration with researchers from the United States, Europe, Australia, the Middle East, South Africa and South America.

MRI images today can tell clinicians the size of the injury and the kind of injury it is. But Olsen's research group is working with research-based MRI methods that use more advanced algorithms and statistics.

"We're working to develop better and more standardized ways of summarizing and making sense of the MRI data, and we hope to contribute to breakthroughs in research that will benefit patients," Olsen says.

The heterogeneity in methods and ways of analyzing, along with the heterogeneity of the patient group, has made this kind of standardization impossible so far. Making progress in methods development can only happen through an international collaborative project of this magnitude that includes several thousand datasets.

Another advantage of this effort to combine data that might otherwise seem impossible to combine— what researchers call "data harmonization"—is that it can enable researchers to use old data that has been already collected, says Penn State's Hillary.

"Data aggregation is vital in imaging and genetics research, where data sets and statistical power in any one lab are small, but combining data from labs around the world offers new possibilities to understand brain disorders and may accelerate science," he said.

"Our effort is getting a 'second life' from data that have already been collected," Dennis added.

The knowledge and analysis methods that are developed will be shared openly with all interested researchers. Where the individual research groups approve it, arrangements will also be made for the enormous datasets to be open access.

The working group NTNU Open Data at the NTNU University Library will look into how to facilitate data sharing among researchers in a good and appropriate way.

"Our ultimate goal for sharing the MRI data we collect is to make it public and available wherever possible. There are important reasons why not everything can be open access, but we want the data to be shared in a responsible way as openly and freely as possible according to the laws and practices in the various places," Olsen says.

Olsen notes that it is a challenge to share all data openly. Researchers can still perform analyses where data is not shared, but include the results of analyses carried out locally at each site in meta-analyses. The next step, however, is to carry out mega-analyses.

"Mega-analyses would require sharing the data, and different parts of the world have differing practices for what's legal. A whole separate part of our work involves studying and creating solutions for access so that it will be easier for researchers to navigate that landscape. This is where NTNU Open and others come in with their expertise," Olsen says.

As things stand today, no one can be identified only from an MRI image of the brain. But Olsen believes that in this type of research we have to consider the theoretical possibility of this happening sometime in the future.

"You have to balance the risk with the possible benefits for patients and research," he says.

More information: Alexander Olsen et al, Toward a global and reproducible science for brain imaging in neurotrauma: the ENIGMA adult moderate/severe traumatic brain injury working group, *Brain Imaging and Behavior* (2020). DOI: 10.1007/s11682-020-00313-7

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