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Highly reliable brain-imaging protocol identifies delays in premature infants

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Infants born prematurely are at elevated risk for cognitive, motor, and behavioral deficits—the severity of which was, until recently, almost impossible to accurately predict in the neonatal period with conventional brain imaging technology. But physicians may now be able to identify the premature infants most at risk for deficits as well as the type of deficit, enabling them to quickly initiate early neuroprotective therapies, by using highly reliable 3-D MRI imaging techniques developed by clinician scientists at The Research Institute at Nationwide Children's Hospital. The imaging technique also facilitates early and repeatable assessments of these therapies to help clinicians and researchers determine whether neuroprotective treatments are effective in a matter of weeks, instead of the two to five years previously required.

The researchers—experts in brain imaging and anatomy—developed a protocol for using the special imaging technique to study the development of 10 brain tracts in these tiny patients, work published online January 24 in *PLOS ONE*. Colorful 3-D images of each tract revealed the connections of the segments to different parts of the brain or the spinal cord. Each of the 10 tracts is important for certain functions and abilities, such as language, movement or vision.

"Developing a reliable and reproducible methodology for studying the premature brain was crucial in order for us to get to the next step: assessing neuroprotective therapies," said Nehal A. Parikh, DO, principal investigator in the Center for Perinatal Research at Nationwide Children's and senior author on the paper. "Now that we have this

protocol, we can improve the standard of care and evaluate efforts to promote brain health within 8 to 12 weeks of beginning the interventions. That way, we can quickly see what really works."

The study tested a detailed approach to measuring brain structure in extremely low birth weight infants at term-equivalent age by comparing their diffusion tensor tractography (DTT) scans to those of healthy, full-term newborns. DTT is a special MRI technique that produces 3-D images and is able to detect the brain's structure and more subtle injuries than earlier forms of the technology.

The research team is the first to confirm differences in the fibrous structure of the 10 tracts between healthy, full-term infant brains and those of premature babies. Although the imaging technology is regularly used in adults, the tiny head size and lack of benchmark measurements in healthy infants meant that the use of DTT in premature infants was previously uncharted territory. With the detailed technique developed by Dr. Parikh's team, the images can now be reproducibly processed and reliably interpreted.

"This protocol opens the field to far greater use of the methodology for targeting and assessing therapies in these infants," said Dr. Parikh, who also is an associate professor of pediatrics at The Ohio State University College of Medicine. "We already have studies underway using our DTT segmentation methodology to measure the effectiveness of early neuroprotective interventions, such as the use of breast milk or skin-to-skin contact while premature babies are in intensive care."

As imaging technology continues to be refined, the goal of targeted therapies based on the specific region of the brain with a delay or injury will become reality, Dr. Parikh predicted. For example, if an infant's DTT scan indicates an under-developed corticospinal tract—the region of the brain controlling motor ability—physicians could immediately

begin proactive physical therapies with the baby instead of waiting until the delay manifests itself. A repeat DTT scan a few months after beginning the therapy could then detect whether the therapy is effectively improving the structure of that brain tract.

"Because cognitive and behavioral deficits cannot be diagnosed until school age, there is an urgent need for robust early prognostic biomarkers," said Dr. Parikh. "Our work is an important step in this direction and will facilitate early testing of neuroprotective interventions."

Provided by Nationwide Children's Hospital