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New MRI analysis useful in predicting stroke complications caused by clot-busters

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Johns Hopkins researchers have developed a new way of looking at standard MRI scans that more accurately measures damage to the blood-brain barrier in stroke victims, a process they hope will lead to safer, more individualized treatment of blood clots in the brain and better outcomes.

The blood-brain barrier is a unique shielding of blood vessels that limits the passage of molecules from the blood stream into the brain. Without it, the brain is open to infection, inflammation and hemorrhage. Ischemic stroke patients are at risk of bleeding into the brain when there is damage to the barrier. By more accurately identifying areas of damage, the researchers, in a report published in the journal *PLOS ONE*, say they hope to use their new tool to predict and reduce the risk of complications from clot-dissolving drugs used to treat this kind of stroke.

"A better characterization of blood-brain barrier damage opens the door to new approaches to treating stroke patients," says study leader Richard Leigh, M.D., an assistant professor of neurology and radiology at the Johns Hopkins University School of Medicine. "We want to help patients, but we need to make sure our treatments don't make things worse."

In an ischemic stroke, a blood clot is stuck in a vessel, cutting off blood flow to a portion of the brain, which will begin to die the longer the clot remains. When patients come to the hospital within three-to-four hours

of suffering an ischemic stroke, doctors quickly move to give them the intravenous clot-busting drug tPA, hoping that it will dissolve the clot without causing additional damage.

In some people—roughly 6 percent of stroke patients treated in this manner—there already is too much damage done to the blood-brain barrier, and use of the drug causes bleeding in the brain, severe injury and sometimes death. But doctors don't currently know which patients will have this bad outcome. In these situations, if physicians knew the extent of the damage to the blood-brain barrier, they would be able to choose a potentially safer treatment option, Leigh says.

Most stroke patients, Leigh notes, don't get to a hospital within the window for optimal tPA use, and physicians believe it is dangerous to give intravenous tPA to these patients for fear of hemorrhage. Sometimes more aggressive treatment is needed, such as pulling the clot out mechanically via a catheter threaded from the groin area or by directly injecting tPA into the brain.

Before any procedure, these patients traditionally receive an MRI to estimate the risks and benefits of such an aggressive approach. But there has been no reliable way to detect the subtle amount of blood-brain barrier damage that would offer clues about how well the patient would fare under various treatments.

That led Leigh to his efforts to develop new software that uses MRI images already being taken and overlays them with calculations that more precisely measure blood-brain barrier damage.

Animal studies have already shown that blood-brain barrier damage is a predictive marker for risk of hemorrhage.

The use of the new MRI software could mean that for some patients,

tPA could be safely used even if they arrive at the hospital later than safe-use guidelines indicate.

"It's a personalization of medicine," Leigh says. "Rather than lumping everyone together, we can figure out—on a case-by-case basis—who should and who shouldn't get which treatment. In the long run, we can increase the number of patients we can help and decrease the number who have complications."

Leigh and his colleagues say there is more research needed before his software enhancement can be widely used, but "proof of concept" has been established in a review of MRI scans from nine stroke patients with known blood-brain barrier damage. Each patient was found to have a different amount of damage. Leigh and his team are now looking at a larger group to better define the meaning of these variations and how physicians can use this information to choose the best treatment.

Provided by Johns Hopkins University School of Medicine

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