MedicalXpress

Blood-brain barrier repair after stroke may prevent chronic brain deficits

March 25 2014

Following ischemic stroke, the integrity of the blood-brain barrier (BBB), which prevents harmful substances such as inflammatory molecules from entering the brain, can be impaired in cerebral areas distant from initial ischemic insult. This disruptive condition, known as diaschisis, can lead to chronic post-stroke deficits, University of South Florida researchers report. In experiments using laboratory rats modeling ischemic stroke, USF investigators studied the consequences of the compromised BBB at the chronic post-stroke stage. Their findings appear in a recent issue of the *Journal of Comparative Neurology*.

"Following ischemic stroke, the pathological changes in remote areas of the brain likely contribute to chronic deficits," said neuroscientist and study lead author Svitlana Garbuzova-Davis, PhD, associate professor in the USF Health Department of Neurosurgery and Brain Repair. "These changes are often related to the loss of integrity of the BBB, a condition that should be considered in the development of strategies for treating stroke and its long-term effects."

Edward Haller of the USF Department of Integrative Biology, the coauthor who performed electron microscopy and contributed to image analysis, emphasized that "major BBB damage was found in endothelial and pericyte cells, leading to capillary leakage in both brain hemispheres." These findings were essential in demonstrating persistence of microvascular alterations in chronic ischemic stroke.

While acute stroke is life-threatening, the authors point out that

survivors often suffer insufficient blood flow to many parts of the brain that can contribute to persistent damage and disability. Their previous investigation of subacute ischemic stroke showed far-reaching microvascular damage even in areas of the brain opposite from the initial stroke injury. While most studies of stroke and the BBB explore the acute phase of stroke and its effect on the blood-brain barrier, the present study revealed the longer-term effects in various parts of the brain.

The pathologic processes of stroke-induced vascular injury tend to occur in a "time-dependent manner," and can be separated into acute (minutes to hours), subacute (hours to days), and chronic (days to months). BBB incompetence during post-stroke changes is well-documented, with some studies showing the BBB opening can last up to four to five days after stroke. This suggests that harmful substances entering the brain during this prolonged BBB leakage might increase post-ischemic brain injury.

In this study, the researchers used laboratory rats modeling ischemic stroke and observed injury not only in the primary area of the stroke, but also in remote areas, where persistent BBB damage could cause chronic loss of competence.

"Our results showed that the compromised BBB integrity detected in post-ischemic rat cerebral hemisphere capillaries—both ipsilateral and contralateral to initial stroke insult—might indicate chronic diaschisis," Garbuzova-Davis said. "Widespread microvascular damage caused by endothelial cell impairment could aggravate neuronal deterioration. For this reason, chronic diaschisis poses as a therapeutic target for stroke."

The primary focus for therapy development could be restoring endothelial and/or astrocytic integrity towards BBB repair, which may be "beneficial for many chronic stroke patients," senior authors Cesar V. Borlongan and Paul R. Sanberg suggest. The researchers also

recommend that cell therapy might be used to replace damaged endothelial cells.

"A combination of cell therapy and the inhibition of inflammatory factors crossing the blood-brain barrier may be a beneficial treatment for stroke," Garbuzova-Davis said.

More information: Compromised blood-brain barrier competence in remote brain areas in ischemic stroke rats at chronic stage. Garbuzova-Davis S, Haller E, Williams SN, Haim ED, Tajiri N, Hernandez-Ontiveros DG, Frisina-Deyo A, Boffeli SM, Sanberg PR, Borlongan CV. *Journal of Comparative Neurology*, March 8, 2014. DOI: 10.1002/cne.23582

Provided by University of South Florida