

**Gwangju Institute of Science and Technology** 

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## Professor Hyoung-Ihl Kim's collaborative research team identifies the mechanism of 'functional dissociation' that occurs after strokes

□ The mechanism of 'functional dissociation' that occurs after strokes has been identified. GIST (Gwangju Institute of Science and Technology, President Kiseon Kim) Department of Biomedical Science and Engineering Professor Hyoung-Ihl Kim collaborated with Institute of Basic Science (IBS) Director Chang-joon Lee and the Korea Institute of Science and Technology (KIST) and found that the abnormal change of 'astrocyte cells'\* is a key factor in functional dissociation that occurs after a stroke.

 $\ast$  astrocyte: small cells that form the glial that supports nerve tissue and has protrusions that diverge in various directions

Stroke is a condition in which the blood vessels in the brain are blocked or burst, causing damage to the part of the brain where blood is not supplied. It is a serious disease that leaves various aftereffects such as motor, language, and consciousness disorders depending on the damaged brain area, but there is no clear treatment yet. Stroke causes functional changes not only in the brain but also in other remote areas, which is called 'diaschisis.' When functional dissociation occurs, the activity of brain neurons decreases, causing brain metabolism and function to deteriorate, but the mechanism of occurrence is unknown.

□ In a previous study, researchers revealed that when a stroke occurs in the white matter of the brain, ultrafine neurodegeneration occurs in the motor cortex\* area that is far away from it. In this study, the researchers investigated the principle that astrocyte cells, a type of brain nerve cell, suppresses the activity and metabolism of other nerve cells in the area of neurodegeneration\*\*, causing disfunction.

\* motor cortex: area in the brain responsible for motor function

\*\* neurodegeneration: gradual structural or functional damage to nerve cells

- Astrocytes are star-shaped non-neuronal cells that occupy the largest number in the brain. The condition that increases the number and size of astrocytes and affects peripheral neurons is called 'reactive astrocyte cells,' which are considered to be the main causes of various brain diseases such as Parkinson's disease, Alzheimer's disease, and paralysis. This is because reactive star cells secrete the inhibitory neurotransmitter 'GABA,' which inhibits the activity and metabolism of nearby nerve cells, preventing them from functioning properly.
- □ The researchers observed the brains of mice inducing a stroke in the white matter to determine how reactive astrocyte cells affect the pathology of the stroke. As a result, it was confirmed that GABA was overproduced in the motor cortex and brain functions deteriorated. This means that when a stroke occurs, reactive astrocyte cells over-secret GABA, causing the function of peripheral nerve cells to deteriorate, causing dissociation.
  - MAO-B inhibitor, which the researchers developed and transferred technology to Neurobiogen, is a drug that inhibits MAO-B, an enzyme mainly present in mitochondria of astrocyte cells. MAO-B is a key enzyme in the production of GABA in astrocytes, and the MAO-B inhibitor prevents the production of GABA in astrocytes.
  - The efficacy of KDS2010 was also confirmed. As a result of using KDS2010, GABA secretion of astrocytes was reduced, so that the functional dissociation of the motor cortex was alleviated and the motor-sensory function was restored. In addition to examining the principle of suppressing GABA production in astrocyte cell regulation to alleviate functional dissociation, the efficacy of selfdeveloped therapeutics was also demonstrated by experiments.
- □ GIST Professor Hyoung-Ihl Kim, a neurosurgeon, said, "This research solved the mystery of functional dissociation and presented one of the first treatment methods for neurological diseases, including strokes. It will be a new indicator in

the development of various neurological brain disease treatments with dissociation."

- IBS Director Chang-joon Lee said, "In this study, the principles of functional dissociation inducing not only stroke but also various brain diseases such as migraines, brain tumors, and encephalitis were investigated. It is expected that astrocyte cell control will open a new path to the treatment of various neurological brain diseases with functional dissociation."
- $\Box$  The results of this research were published in *Cell Reports* (IF 8.109) on July 8, 2020.

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