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The relationship between motor recovery and synaptic density changes after ischemic stroke: Imaging study with 11C-UCB-J PET

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Stroke is one of the most common causes of death and disability worldwide. The physiological process of recovery after stroke is still not fully understood. On positron emission tomography (PET), one of the methods used to image this process, ipsilesional activation is associated with a favorable prognosis in terms of the recovery of motor functions.[1]

In the recent past, a radioligand named 11C-UCB-J, which binds to synaptic vesicle protein 2A (SV2A) located at presynaptic terminals, has been developed for detecting synaptic density in PET imaging. This radioligand reflects the structural correlation of synaptic function. Therefore, the changes observed with 11C-UCB-J are independent of neuronal activation.

In their articles published in Annals of Neurology in 2023, Michiels et al.[2] visualized the changes in synaptic density during the recovery phase after ischemic stroke with the help of 11C-UCB-J PET/magnetic resonance imaging (MRI). For this purpose, changes in ischemic lesions, peri-ischemic areas, and unaffected ipsilesional and contralesional gray matter were examined using 11C-UCB-J PET/MRI in 13 patients who suffered ischemic strokes at one and six months after the stroke. Additionally, the phenomenon of crossed cerebellar diaschisis was investigated. Lastly, brain regions potentially affecting upper extremity motor recovery during the poststroke recovery process were identified, and the change in relative standardized uptake value ratio (ΔSUVR) compared to the centrum semiovale was examined with 11C-UCB-J.

In the study, a decrease in 11C-UCB-J SUVR was observed six months after ischemic stroke in the lesion (ΔSUVR=–1.0, $p<0.01$) and in the peri-ischemic region (ΔSUVR=–0.31, $p=0.02$). Additionally, crossed cerebellar diaschisis was detected in 85% of the patients at six months. Contrary to the literature, Michiels et al.[2] did not observe an increase in radioligand uptake in areas thought to be associated with motor recovery. Instead, a significant decrease was found in the ipsilesional supplementary motor area (ΔSUVR=–0.83, $p=0.04$).

In conclusion, contrary to general belief, this study found that synaptic density further decreased in the ischemic lesion and peri-ischemic area six months after a stroke. The demonstration that there is no increase in synaptic density in regions thought to be associated with motor recovery is an important finding. However, the limitations of this study include the small number of patients, the heterogeneous nature of the patient population, and the lack of dynamic imaging in the subacute phase.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

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