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Researchers find HIV protein may impact neurocognitive impairment in infected patients

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A protein shed by HIV-infected brain cells alters synaptic connections between networks of nerve cells, according to new research out of the University of Minnesota. The findings could explain why nearly half of all patients infected with the AIDS virus experience some level of neurocognitive impairment.

The research was published in the current volume of the *Journal of Neuroscience*.

"The synaptic changes didn't appear to be a symptom of nerve death," said Nicholas Hargus, Ph.D., lead author on the paper and a post-doctoral fellow in the Department of Pharmacology in the University of Minnesota Medical School. "Instead, the changes appeared to be a protective response resulting from the over-excitation of the network by the HIV protein transactivator of transcription (Tat). Essentially, the neuroprotective mechanism has gone awry."

HIV-associated neurocognitive disorders (HAND) are an indirect result of HIV, as the disease itself does not infect neurons. Tat has been shown to contribute heavily to the development of HAND in patients. Hargus and Stanley Thayer, Ph.D., professor in the Department of Pharmacology, wanted to learn more about the relationship between Tat and HAND to better understand how to treat the disorders.

Researchers replicated the impact of the Tat in a rat model and tracked the changes to the synaptic proteins. They found changes in both inhibitory and excitatory synapses were initiated by specific Tat binding activity. This discovery indicated a pharmacological change due to exposure to Tat.

"We found drugs altering synaptic transmission between nerve cells reversed the synaptic changes induced by Tat," said Thayer. "In the future, this could provide a target for the development of drugs to act upon and improve cognitive function in patients."

Ongoing experiments are investigating the relationship between drug-induced changes in synaptic connections and the changes in cognitive function. In the future, high throughput approaches to assess synaptic function will be developed for evaluating drug candidates.

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