Hippocampal insulin resistance linked to neuroplasticity

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(HealthDay)—Hippocampal insulin resistance may be a key mediator of cognitive deficits, independent of glycemic control, according to an experimental study published online July 27 in *Diabetes*.

Claudia A. Grillo, Ph.D., from the University of South Caroline School of Medicine in Columbia, and colleagues examined the functional role of hippocampal insulin receptors (IRs) independent of metabolic function. Using a lentiviral vector expressing an IR antisense sequence (LV-IRAS), the authors generated a model of hippocampal-specific insulin resistance.

The researchers found that LV-IRAS effectively downregulated IR expression in the rat hippocampus with no effect on body weight,

adiposity, or peripheral glucose homeostasis. In LV-IRAS-treated rats, hippocampal neuroplasticity was impaired. In LV-control, but not in LV-IRAS, rats, high frequency stimulation evoked long-term potentiation in brain slices. In the hippocampus of LV-IRAS rats, GluN2B subunit levels were reduced, as was the basal level of phosphorylation of GluA1. These deficits in synaptic transmission correlated with spatial learning impairments.

"Importantly, these learning deficits are strikingly similar to the impairments in complex task performance observed in diabetic patients, which strengthens the hypothesis that hippocampal insulin resistance is a key mediator of cognitive deficits independent of glycemic control," the authors write.

More information: Abstract
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