



Abstract Type : Oral presentation

Abstract Submission No.: A-0576

Abstract Topic : Basic Research

The GLP-1 Receptor agonist ameliorates cognitive impairment following long-term AKI

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Objectives : Previous studies have shown that glucagon-like peptide-1 (GLP-1) receptor agonists can mitigate cognitive defects associated with Alzheimer's disease. Epidemiological studies suggest that the risk of cognitive impairment increases following AKI. We hypothesize that GLP-1 receptor agonists may attenuate long-term cognitive impairment after AKI.

Methods : AKI was induced using kidney ischemia-reperfusion injury (IRI). Mice underwent sham operation and mice that received phosphate-buffered saline after IRI served as negative controls. Mice with fecal microbiota transplantation (FMT) after IRI were designated as positive controls. The experimental group consisted of mice receiving IRI followed by weekly administration of the GLP-1 receptor agonist (dulaglutide). Body weight and fasting blood glucose levels were measured monthly, and at three months post-IRI, we assessed cognitive function using the Y-maze spontaneous alternation test.

Results : There was no consistent or significant trend in monthly body weight among the mouse groups. At one month after IRI, FMT group had significantly reduced blood glucose levels compared to IRI group. At two months after IRI, the GLP-1 receptor agonist treated group showed significantly reduced blood glucose levels compared to the IRI group. At three months after IRI, no significant change showed among mice groups. In the behavioral test, the IRI group exhibited significantly lower spontaneous alternation values compared to the non-IRI group, indicative of impaired spatial working memory. Both FMT or the GLP-1 receptor agonist administration tended to show improved spontaneous alternation compared to the IRI group.

Conclusions : This pilot study suggests that administering the GLP-1 agonist may exert beneficial effects on long-term cognitive impairment following AKI. Further investigations, including comprehensive structural and behavioral brain analyses, are warranted to elucidate the underlying mechanisms and validate these observations.