Intranasal deferoxamine affects memory loss, oxidation, and the insulin pathway in the streptozotocin rat model of Alzheimer's disease


PII: S0022-510X(17)30462-8
Reference: JNS 15452
To appear in: Journal of the Neurological Sciences

Received date: 30 January 2017
Revised date: 29 June 2017
Accepted date: 19 July 2017


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Intranasal deferoxamine affects memory loss, oxidation, and the insulin pathway in the intracerebroventricular streptozotocin rat model of Alzheimer’s disease

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Abstract
Accumulation of metal and the accompanying increase in oxidative stress and inflammation plays an important role in neurodegenerative disease. Deferoxamine (DFO) is a metal chelator found to be beneficial in several animal models of neurodegenerative disease and insult including Alzheimer’s disease, Parkinson’s disease, stroke, and subarachnoid hemorrhage. In this study, we determine whether intranasally (IN) administered DFO is beneficial in the intracerebroventricular streptozotocin (ICV STZ) rat model of sporadic Alzheimer’s disease, which is different from previous models in that it exhibits dysregulation of insulin metabolism as well as oxidative stress and inflammation. Surgical induction of the model included ICV injections of either STZ or citrate buffer (sham in rats), which were treated IN with either saline or DFO (n=10-15/group). Treatment started either before or after injection of STZ to induce the model, and continued throughout the study. IN treatment continued three times per week for three weeks before behavior tests started followed by eventual euthanasia with tissue collection. Spatial memory tests with the Morris water maze showed that STZ rats treated with IN DFO both before and after model induction had significantly shorter escape latencies. Pre-treatment with IN DFO also significantly decreased footslips on the tapered balance beam test. Brain tissue analyses showed DFO treatment decreased oxidation as measured by oxyblot and increased insulin receptor expression. These results further support the potential of IN DFO for use as a treatment for Alzheimer’s disease, and show benefit in a non-amyloid/tau rodent model.

Keyword(s): Intranasal, deferoxamine, streptozotocin, GSK3β, oxidation, insulin

Disclosure for all authors: W.H. Frey II and L.R Hanson are co-inventors on a patent application owned by HealthPartners Institute regarding the use of intranasal deferoxamine for the treatment of Alzheimer’s disease and other neurodegenerative diseases.

Abbreviations: AD: Alzheimer’s disease; BBB: blood-brain barrier; ICV: intracerebroventricular; IN: intranasal; STZ: streptozotocin; GSK: glycogen synthase kinase; IR: insulin receptor; IDE: insulin degrading enzyme; IL6: interleukin 6

1. Introduction
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