

Abstract

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Detection of increased scyllo-inositol in brain with magnetic resonance spectroscopy after dietary supplementation in Alzheimer's disease mouse models.

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OBJECTIVE: There is evidence that inositol isomers may help protect against formation of toxic fibrils of Abeta fragments in Alzheimer's disease mouse models. Scyllo-inositol is one of the more promising inositol isomers for the potential treatment of Alzheimer's disease (AD) and can be detected using MRS in human subjects.

METHODS: In this manuscript we demonstrate using MRS, in two different mouse models of AD (APP x PS1 and APP x PS1 x tau), that we could detect increased scyllo-inositol in the hippocampus and frontal cortex in mice fed water supplemented with 16.5 mg/L of scyllo-inositol equivalent to about 3.3 mg/kg/day. We used both brain extracts using solution MRS as well as intact brain tissue using high resolution magic angle spinning (HRMAS) to ensure that any membrane-associated scyllo-inositol would be detected.

RESULTS: By brain extracts we detected a 3.0 fold increase in scyllo-inositol in the scyllo-fed AD mice compared to normal diet ($p < 0.001$). Using HRMAS we detected a 2.2-2.4-fold increase in scyllo-inositol ($p < 0.001$). Scyllo-inositol treatment was associated with an increase in glutamine in hippocampus. The concentrations of scyllo-inositol were higher in the hippocampus than in the frontal cortex. Mice have a smaller concentration of scyllo-inositol than humans (ca. 100 microM vs. 500 microM in humans).

CONCLUSION: Given the ease with which scyllo-inositol can be measured in human MRS data with high signal to noise ratios, these data suggest that MRS will prove useful for evaluation of inositol treatment trials in AD subjects.

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