Preliminary data from intranasal delivery of thyroid hormone to wild-type and Mct8 deficient mice

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Numerous studies indicate that the severe psychomotor retardation in MCT8 deficiency is likely due to impaired TH transport across the blood-brain-barrier (BBB). The nasal cavity provides a direct and non-invasive route to the brain that can be used to deliver chemical therapy. We have performed preliminary studies in mice to evaluate intranasal delivery as a potential route to administer TH directly into the brain without affecting systemic TH concentrations.

Wt and Mct8KO mice were treated with a highly concentrated solution of T4. Though several experimental data indicate an increase in brain T4, the level of TH in plasma, as well as the expression of Dio1 in liver increased. This result indicates that intranasal administration of T4 does not deliver TH selectively to the brain and that it will actually aggravates the already existing TH excess in peripheral tissues of MCT8 deficient patients. In addition, as mice express the T4 transporter Oatp1c1 at the BBB, it is not possible to determine if the observed T4 effects on the brain are the consequence of intranasal or systemic delivery of T4.

We therefore used bovine serum albumin (BSA), that binds TH with high affinity, previously described as means to enhance substance brain delivery without reaching the systemic circulation, as well as a vasoconstrictor. Unfortunately neither of these manipulations were able to prevent or even reduce the TH reaching the systemic circulation after intranasal administration.