Healthcare Innovations
How practice has changed

HERSTON HEALTH PRECINCT SYMPOSIUM 2021

DISC-0031

6 - 10 September 2021
Education Centre
RBWH

Nicotine exposure reduces uptake of transthyretin-thyroxine by placental trophoblasts

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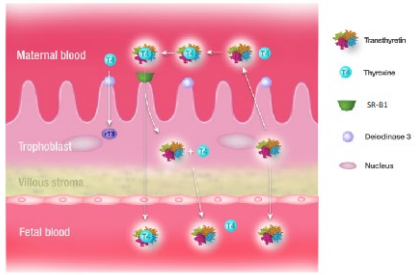
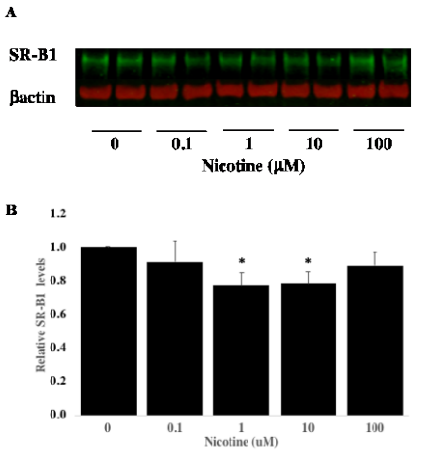
BACKGROUND Placental trophoblasts synthesize, secrete and take up the thyroid hormone binding protein transthyretin, providing a route for maternal thyroxine to enter the placenta. Transthyretin is involved in thyroxine transport in other tissues such as the choroid plexus. Nicotine alters transthyretin function in rat choroid plexus. If nicotine has an effect on the function of transthyretin in trophoblasts, then it may directly affect placental transfer of thyroxine to the developing fetus. This may explain some of the impacts of smoking on fetal growth, development and placental function.

METHODS Trophoblasts were cultured in the presence of 0 – 100uM nicotine for up to 24 hours prior to protein extraction and Western blot analysis. Live uptake of Alexa-labelled transthyretin by trophoblasts was measured using an Essen Incucyte Zoom incubator. Nicotine (0-100uM) and/or thyroxine (10uM) were added to assays to assess any changes in Alexa-transthyretin uptake.

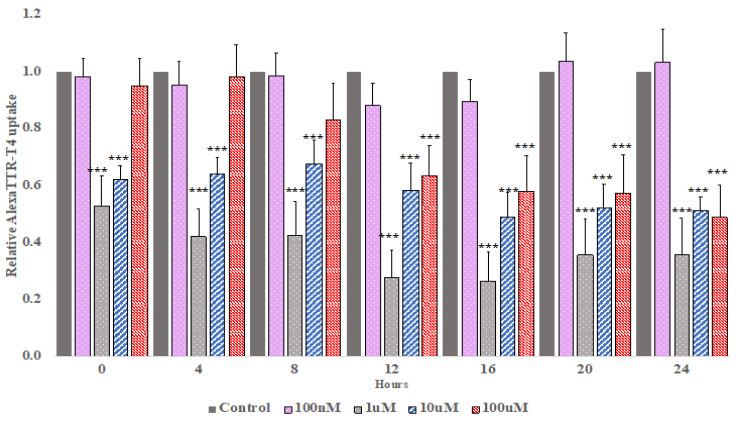


Model of transthyretin synthesis, secretion and uptake in human placenta Transthyretin bound to thyroxine (T4) is rapidly endocytosed by placental trophoblasts through SR-B1

RESULTS



Nicotine treatment reduces SR-B1 protein levels in HTR8 trophoblast cells. Treatment with 1uM or 10uM nicotine for 24 hours significantly reduces SR-B1 levels in HTR8 cells. A) A representative Western blot showing depletion of SR-B1 protein following treatment with 1 and 10uM nicotine for 24 hours. B) Mean relative levels of SR-B1 protein in four sets of nicotine treated cell lysates quantified using ImageJ software. βactin used as a loading control. *p<0.05, n=4.



Treatment with 1uM, 10uM and 100uM nicotine all significantly reduced uptake of AlexaTTR-T4 in HTR8 cells. 100nM nicotine had no effect. Uptake by nicotine co-treated cells were compared to untreated cells (given a value of 1) at each time point. The experiment was carried out in duplicate (each individual value from an average of 9 reads across the well) and four times (n=8), twice for 1uM nicotine (n=4). ***p<0.005

CONCLUSION Nicotine may reduce Alexa-transthyretin-thyroxine uptake by reducing levels of SRB1. However, the rapid effect on uptake suggests that nicotine may interfere with thyroxine binding to transthyretin. The data suggest that nicotine exposure during pregnancy reduces transport of transthyretin-thyroxine to the developing fetus. This may contribute to the adverse effects of smoking on the fetus and pregnancy viability.