

Subcortical Band Heterotopia (SBH) in Rat Offspring Following Maternal Hypothyroxinemia: Structural and Functional Characteristics. M Gilbert¹, R Ramos², D McCloskey³, J Goodman⁴, A. Johnstone¹. US Environmental Protection Agency, RTP, NC, ²NY Institute of Technology College of Osteopathic Medicine, Old Westbury, NY, ³CUNY, Staten Island, NY, ⁴NY State Institute Basic Research, Staten Island, NY.

Thyroid hormones (TH) play crucial roles in brain maturation, neuronal migration, and neocortical lamination. Subcortical band heterotopia (SBH) represent a class of neuronal migration errors in humans that are often associated with childhood epilepsy. We have previously reported the presence of SBH in a rodent model of low level hypothyroidism induced by maternal exposure to propylthiouracil (PTU). Here we examined the dose-response characteristics of this developmental malformation, the connectivity of heterotopic neurons with other brain regions, and their functionality. Pregnant rats were exposed to varying concentrations of PTU through the drinking water (0, 1, 2, 3, 10ppm) from gestational day 6 to postnatal day 21, producing graded levels of TH insufficiency. Dose-dependent increases in the volume of the SBH present in the corpus callosum were documented, with clear presence at concentrations of PTU that resulted in only minor, not statistically reliable, reductions in maternal serum T4. SBH contain neurons, oligodendrocytes, astrocytes, and microglia. Both monoaminergic and cholinergic processes were prevalent in the SBH. Tracer studies revealed anatomical connectivity of SBH neurons to cortical neurons and synaptic functionality of these anatomical connections was verified by *ex vivo* field potential recordings. SBH persisted in adult offspring despite rapid return to euthyroid status at termination of exposure, and adult offspring displayed an increased sensitivity to seizures induced by the convulsant pentylenetetrazol. A number of features of this model are attractive to the investigation of molecular mechanisms of cortical development, effectiveness of therapeutic intervention in hypothyroxinemia during pregnancy, and of the impact of very modest TH imbalance that accompanies exposure to environmental contaminants. (*Does not reflect EPA policy*)