Sodium Retention in Mice with Huntington’s Disease

Christa Robey
roby014@umn.edu
Mentor: Dr. Janet Dubinsky  Department of Neuroscience

Why does sodium retention matter?
Huntington Disease (HD) is a devastating neurodegenerative disease characterized by its late onset, involuntary jerky movements, change in cognition and personality. While it is known that Huntington’s disease exhibits an autosomal dominant inheritance pattern with many CAG repeats, the mechanism of pathology is still unknown. Brain shrinkage and increased metabolites in the blood have been observed in transgenic mice with HD. This discovery led our research team to observe important metabolic processes during the onset of HD.

Evidence of Metabolic Change:
• The plasma osmolality increased in the R6/2 transgenic mice significantly by only 9 weeks of age. In contrast, the plasma osmolality of wild-type mice proved to remain fairly constant.
• At the same time, urine osmolarity decreased in transgenic mice.
• The avoidance of saline by the transgenic mice was apparent at 9 weeks, while the overall water consumption increased.
• There was a significant increase in urine volume among the transgenic mice.
• While the overall food consumption increased, the body weight of the HD mice decreased.

Materials and Methods
• R6/2 Transgenic mice were put into metabolic cages (see figure) every 3 weeks.
• Each cohort consisted of five to nine cages containing two mice of like genotype.
• Data was collected twice daily (approximately every 12 hours) for 5 consecutive days.
• On the evening of the third day, a saline bottle was added to determine the preference or avoidance.
• Two way ANOVAS were utilized to determine and provide a quantitative value for the interaction between genotype, age and the interaction between them.

What does this mean?
• The transgenic mice preferred the regular water to the saline water, an unusual behavior for any animal. Wild type mice (as well as animals in general) prefer the sodium infused (saline) water to water alone (Widmaier 454). However, the sodium retention by the transgenic mice, leads them to avoid the saline solution.
• The higher consumption of water, state of polydipsia, by the R6/2 mice is consistent with the sodium retention theory.
• Research conducted and the University of Cambridge suggests that a malfunction in the hypothalamus of the transgenic mice leads to increased levels of serum vesopressin/ADH and xerostomia.
• It is apparent that the R6/2 mice are hypernatremic. MRS, increased plasma osmolarity and salt avoidance are just a few of the statistically significant factors that lead to this conclusion. However, it is not apparent whether or not the hypernatremia is the cause of brain shrinkage in the HD mice.

References:

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