Dogs as a Model for Mucopolysaccharidosis: Measuring Learning Ability

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What are the Mucopolysaccharidoses?

• A major class of lysosomal storage disorders
• 7 types, some with sub-types
• Each form missing an enzyme that helps break down glycosaminoglycans (GAG)
• GAG accumulation inhibits cellular function
• Can change physical and mental development
• Autosomal or X-linked recessive inheritance

(Neufeld & Muenzer, 2001)
MPS IIIB

- Mutation in NAGLU gene
- Reduced or no activity of N-acetylglucosaminidase (NAGLU)
- No breakdown of GAG heparan sulfate
- Heparan sulfate accumulates in lysosome
- Interferes with normal lysosomal/cell processes
- Affects central nervous system

http://click4biology.info/c4b/7/images/7.6/chain.gif
MPS IIIB in People

• Normal at birth
• Symptoms begin between ages 2-6
• Lag in development in comparison to peers
• Progressive decline in function
• Death typically occurs in teenage years

(National MPS Society, 2011)
Behavior Study of MPS IIIB Dogs

• Now:
  • Use unaffected control animals
  • Use different mazes to test learning and behavior

• Goals:
  • Characterize decline in cognitive function
  • Document learning deficits in MPS IIIB dogs
  • Help develop treatments (enzyme infusion)
  • Test behavior and learning in treated and untreated animals
Basic Test Protocol

• No animals under 3 months of age tested
• Routine socialization under 3 months of age
• Daily acclimation with maze until comfortable and performing
• Allow 10-15 minutes of exercise before test
• Withhold feed on test day until after test
T-Maze

- Assess learning ability through reversal learning
- 3 phases of testing: preference, preference reinforcement, reverse learning
- 1: Run 9 trials to decide preferred arm
- 2: Reward preferred arm until dog consistently chooses it (meets criterion)
- 3: Reward other arm until criterion met

Sanders, et. al (2011)
Results

• N = 2 unaffected control animals
• Average of 11.2 incorrect choices before criterion
• Modifications in process to assist and comfort animals
• Attempt to align with natural behavior
• Continue study with a larger sample size
• More control, affected, and treated animals
Future Tests

• Foraging maze
  • Evaluates spatial memory and changes in memory and behavior (Mendl et. al, 1997)

• Radial arm maze
  • Evaluates spatial and working memory (Craig et. al, 2012)

http://btc.psych.ucla.edu/ram.htm
Overall Goals

• Gain a comprehensive comparison using multiple mazes
• Document changes in memory and learning in affected animals
• Monitor changes throughout animal lifetime
• Compare ability of normal animals to affected animals
• Test animals receiving enzyme treatment to record benefits
• Provide background for similar canine studies
Sources


Questions?

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