Does a Calcium-Binding Protein Used In Combination With an Antioxidant Provide Neurotherapeutic Benefits to Aged Canines With Cognitive Decline?

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Introduction

- Canine cognitive dysfunction (CCD) is a neurobehavioral syndrome caused by physical and chemical alterations in the brain. CCD can be distinguished by changes in sleep/wake patterns, general activity, social behaviors and interactions, and a steady decline in cognitive function.
- There are many similarities between CCD and Alzheimer’s disease (AD). This includes deficits in cognition, behavior, and calcium regulation. Humans and canines also have similar brain physiology. This makes dogs affected by CCD suitable animal models for studying the effects of mild cognitive impairment and dementia in humans.
- Neutricks is a prescription medicine that is given to dogs experiencing behavioral changes due to age. The active ingredient, apoaequorin (AQ), has been shown to provide calcium-buffering proteins that could protect the brain against damage caused by aging. Studies have shown that a combination treatments are the most effective for treating neuronal disorders, especially when using antioxidant therapies for the treatment of CCD (Head 2010).
- The proposed study will examine if apoaequorin, along with combination of an antioxidant (AOX) supplement, provides any neurotherapeutic benefits to canines with CCD. Studying CCD could help develop tools for screening patients to determine their risk for AD and aid in the development of neurotherapeutic treatments and procedures for amyloid-beta (Aβ) related neurodegenerative diseases.

Review of Literature

- Clinical signs of cognitive decline can be described by DISHA (disorientation, interaction changes, sleep/wake disturbances, house soiling and activity change). The cause of cognitive decline is the combination of disease and aging (Ossella et al. 2007).
- An assessment tool, the CCD Rating scale (CCDR), was developed to correctly differentiate CCD symptoms from normal aging symptoms. Formed from a combination of 13 behaviors, from a survey for owners of senior dogs, that were diagnosable by a veterinarian as CCD when irregular which are similar to different phases of AD (Salvin et al. 2011).
- Canines are able to suffer from the same age-related cognitive disorders humans do. The aged canine brain also displays similar pathological changes observed in the aged human brain (Canudas et al. 2014). Cortical atrophy, increased ventricular volume, reduction in neurogenesis, cerebrovascular pathology, and oxidative damage are all observed in both humans and aged canines (Cotman and Head 2008).

- The calcium hypothesis is that amyloid metabolism is the product of the up-regulation of calcium signaling by improvement of the entry of external calcium into the cell and the responsiveness of the channels that release calcium from the cells internal sources. This could cause the effects of AD like memory loss and neuronal cell death. (Berridge 2010). Calcium dysregulation is often associated with the development of AD, therefore it is possible that the symptoms associated with CCD or AD, can be attributed to changes in intracellular calcium inside of the brain (Milgram et al. 2015).
- Head (2010) studied if the effects of an AOX combination diet increased cognition and reduced neuropathy in canines. The results showed that old dogs on the AOX diet performed better on difficult tasks than old dogs on the control diet. Improvements in cognition were observed in visual discrimination, reversal learning, spatial memory, and reduced Aβ quantities and toxic oxidative stress biomarkers in their brains.
- Underwood et al. (2011) showed that individuals given AQ had improved memory, delayed recall, and verbal and visual learning in comparison to the individuals that were a part of the control.

Hypotheses

- AQ will have neurotherapeutic benefits that improve or prevent the symptoms/prognosis of CCD.
- AQ will provide lasting benefits to the canine.
- Combination therapy (AQ/AOX) will provide further benefits to the canines than individual therapies (AQ, AOX).

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Research Design

1. Obtain 120 Dogs
2. Assess behavior with CCDR
3. Divide into treatment groups (Fig. 1)
4. Dogs will receive treatment for 30 days
5. Upon 30 day mark: CCDR assessment
   - Variable-delay nonmatching-to-position task (DNMP)
   - Discrimination task
   - Attention task
6. Continue treatments and repeat assessments at every 6 month period for 2 years

Expected Results

- Dogs will show improvements in spatio-temporal memory, delay nonmatching, and reversal learning (n=10)
- Dogs will show discrimination, reversal learning, and attention task (n=20)
- Dogs will receive treatment for 30 days
- Upon 30 day mark: CCDR assessment
- Continue treatments and repeat assessments at every 6 month period for 2 years

Literature Cited