Cognitive function declines with age

- Like humans, dogs naturally develop signs of cognitive decline (Milgram et al. 1994; Head 1995; Tapp et al. 2003), and with age brain atrophy in dogs often resembles that seen in the human Alzheimer’s brain.
- The aged canine brain shows accumulation of human-type Aβ, but not tau (Cummings 1996; Head et al. 1998). In addition oxidative damage to proteins and lipids, caspase activation and other mitochondrial impairments are present.
- Over the past several years, we have used the aged canine as a model to evaluate the effect of “lifestyle changes” on these risk factors.
- This has led to identification of diet and exercise as two major contributors to improving cognitive decline with age.

Diet for the aging brain

- **Antioxidants**
  - dl-alpha tocopherol acetate: 1050 ppm (20 mg/kg - 800 IU/day)
  - Stay-C (ascorbyl monophosphate): 100 ppm (~100 mg/day)
  - Spinach, carrot granules, tomato pomace, citrus pulp, grape pomace: 1%
  - Increased ORAC by 50%, equivalent to 4-5 servings of fruits and vegetables/day

- **Mitochondrial cofactors**
  - dl-Lipoic acid: 135 ppm (2.7 mg/kg)
  - l-carnitine: 300 ppm (6 mg/kg)
  - dl-alpha tocopherol acetate: 1050 ppm (20 mg/kg - 800 IU/day)
  - dl-Lipoic acid: 135 ppm (2.7 mg/kg)
  - l-carnitine: 300 ppm (6 mg/kg)

Diet and enrichment improve brain aging – results from a 3-year study

**Behavior results**

- Play toys
- Kennel-mate
- 3x/wk exercise
- Cognitive experience

**Molecular results**

- Reduced amyloid pathology (Pop et al.)
- Reduced protein oxidation levels (Opii et al., 2008)
- Improved mitochondrial function (Head et al., 2009)
- Reduced caspase 3 production (Snigdha et al., 2012)

Exercise alone can facilitate cognition

- Concurrent Discrimination Task measures ability of animals to remember object-object associations in the presence of active interference
- Day 1: preference testing, Day 2: baseline performance, followed by 10 min exercise and retesting Day 3: re-testing 24 h after the preceding day’s exercise

Exercise can facilitate cognition even when diet is already optimal

- Physiological function improves with nutrient level and then plateaus off for most nutrients
- Effect of exercise on a reversal learning task in animals that showed no additional improvement with diet supplements

Conclusions

- Exercise rather than further dietary supplements (when diet is optimal) would better serve brain health in aging.
- Exercise results in an increased number of synapses and higher protein levels, reflecting synapse growth.

Future Directions

- Extend investigations to human studies, in a new trial called EXERT
- Evaluate the molecular mechanisms that underlie the effects of exercise in the aging brain
- Investigate possible epigenetic mechanisms underling synaptic changes observed with exercise

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