Canine cognitive dysfunction and dementia

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INTRODUCTION

Canine dementia can go by the synonyms of senility, senile dementia, senile cerebral dysfunction, cognitive impairment or cognitive dysfunction.[1] Research is coming closer to understanding the reasons for this disease occurrence. Use of nutrition and supplementation has been shown to be effective in both the prevention and treatment of this disease of aging. As well, physical therapy techniques that are currently applied to the human Alzheimer's disease patient may have a role to play in the treatment or prevention of this very similar disease process in the canine.

Canine Dementia

Aged canines, much like aged humans, show a variety of classical symptoms attributable to a decline in brain function. Canine cognitive disorder is broadly defined as geriatric behavioral changes that are not related to a general medical condition.[5] There have been four identified categories of behavioral dysfunction characterised in canine cognitive impairment; disorientation in home and yard, changes in social interactions with human family members, decline in house training, and alterations in sleep-wake cycles.[2,3,4]. Descriptions of the categories are found in Table 1. To say that an animal has a dysfunction in one of the categories, the animal would need to have the signs of dysfunction ≥ once a week and for one month or more.[2]

Table 1 - Qualification of Categories of Canine Cognitive Impairment (Bain MJ et al)[2]

A dog has impairment in orientation if it has ≥ 2 of the following: ■ Staring into space ■ Getting lost in the house or yard ■ Getting stuck in corners ■ Standing at the wrong door or wrong part of door to go out ■ Another sign that is logically attributed to disorientation	**A dog has impairment in social interaction if it has ≥ 2 of the following:** ■ Decline in greeting owners ■ Decline in soliciting attention ■ A change (increase or decrease) in following owners around the house
A dog has impairment in house-training if it has 2 of the following: ■ Started to urinate / defecate in the house without behavioral or medical explanation (i.e. incontinence or separation anxiety) ■ A decline in signaling to go out or use of the doggie-door.	**A dog has an impairment of the sleep-wake cycle if it has ≥ 2 of:** ■ Regularly wakes owner at night by pacing or vocalizing ■ Sleeping less at night ■ Sleeping more during the day

Table 2 - Definitions of Learning Disabilities That Are Age-Sensitive in the Canine (Adams et al)[3]

Reversal learning:	Similar to object discrimination but after the animal learns one behavior stimuli, then the reward is reversed (ie the treat is put under the other object) and the animal must re-learn which object to selects in order to be rewarded.
Allocentric Spatial Learning	Dogs are able to locate an object by giving them references located on the testers body.
Spatial Learning	The ability to locate an object in space.
Spatial Memory	The process of maintaining a limited amount of info in an active representation for a short period of time in order to re-use a learned behavior.
Object Recognition	Use of non-matching objects. When a dog is given a choice between familiar and novel objects, it will choose the novel object and is rewarded for the correct choice (successful 80 per cent of the time).

Figure 1 - Example of an owner-based cognitive training program carried out at home in an aged dog.

Statistically, Neilson et al found that castrated male dogs were significantly more likely to have impairment in orientation than spayed female dogs. They found no difference between aging brains in small or large dogs however. Of 11 to 12-year old dogs they found that 28 per cent of animals have impairment in ≥1 category (see Table 1 above) and of these, 10 per cent were impaired in ≥2 categories. In 15 to 16-year old dogs, 68% had impairment in ≥1 category, and 35 per cent of these were impaired in ≥2 categories.[4] Adding to these statistics, Bain et al found that dogs with some signs of dysfunction in a category were likely to become severely affected six to 18 months later.[2]

Additionally, it has been shown that aged canines show deficits in memory and forgetfulness of learned behaviours and habits.[1] Other age-related learning dysfunctions have been observed in reversal learning, allocentric spatial learning, spatial learning, spatial memory and object recognition memory.[3] See Table 2. Procedural learning and memory (i.e. where to get food, signs that food is being dispensed and behaviors required to get food) and object discrimination (animal is able to learn which one of two objects hides a treat) are skills that are not affected by aging processes.[3]

Aged canines show several consistent processes of deterioration in the brain. ß-amyloid plaque deposits have been found in the aged canine

brain.[1,4,6] The hippocampus and cerebral cortex are primarily affected and the amount of ß-amyloid deposition can be correlated with the severity of cognitive dysfunction in dogs.[5,7] These dogs display ventricular dilation, thickening of meninges, vascular changes, a decrease in cerebral volume, an increase in oxidative stress with a reduction in mitochondrial function and poorer metabolic strategies for mitigating oxidative stress.[5,6,7,8] Other studies have found a correlation between cholinergic tone and memory impairment and dementia.[1,6] Cotman et al proposed that the oxidative damage probably plays a central and pivotal role in the evolution of the cascade of events that results in canine dementia and cognitive impairment.[7] Importantly, since the brain uses the greatest amount of oxygen, the oxidative damage can begin early in life. However, it is unlikely to induce substantial neuronal dysfunction until late in life.[7]

Neuromusculoskeletal function and canine dementia

Research has been directed towards the use of a canine model of dementia as a parallel to human Alzheimer's disease.[3,5,6] The similarities are profound, which has enabled in-depth studies into brain functioning and creation of pharmaceutical, nutritional and natural treatments for both humans and animals. We can then also transfer our understanding of Alzheimer's patient profiling and management to the canine patient. Franssen et al[9] found that human patients affected with Alzheimer's disease show significant delays in activation of postural responses to perturbations. They have a slowing of gait and movement (described as a "cautious gait") associated with a real or perceived instability. This can be attributable to a loss of balance, equilibrium and limb co-ordination.[9,11] Affected humans also see subtle changes in sensorimotor function. These losses and deteriorations result in anxiety, insecurity, a reduction in physical activity and loss of social contacts.[9] Falls and injuries can lead to premature loss of functioning, deconditioning, fractures, sickness, and early institutionalization.[9,10,11] Motor performance is affected already in mild stages of Alzheimer's and functional performance other than gait may be impaired.[10] Mild Alzheimer's patients were found to be significantly less active than healthy subjects, had impaired postural control and ceased activities that placed more demands on initiative, interacting with others and planning.[10]

It is clear that if human Alzheimer's disease and canine dementia are similar in pathology, that canine's affected with this condition are at risk of physical deterioration and injury. Neuromuscular awareness, control and abilities are likely diminished in both populations and warranting of intervention.

Nutritional prevention and treatment

As stated previously, oxidative damage and mitochondrial function are fundamental mechanisms contributing to age-associated cognitive dysfunction. A reduction in oxidative stress may retard various 'downstream' mechanisms resulting in neuronal dysfunction.[7] Anti-oxidants can delay age-related cognitive decline in humans and improve performance in aged rodents. The age-dependent impairments can be at least partially reduced by maintenance on food fortified with a complex mix of anti-oxidants and mitochondrial enzymatic co-factors as seen in the study by Milgram et al.[8] The study observed performance in oddity discrimination tasks (described as object recognition in Table 2) in old and young dogs, half of each were put an a diet enriched with anti-oxidants and half were on a controlled diet for a duration of 6 months.

The results found a clearly superior performance of the animal on the enriched diet compared to the controlled aged dogs. There was no difference in the young dogs' performance however. The rationale for the supplementation is as follows:

1. A complex mix of anti-oxidants will support a network of anti-oxidants requiring several components that act together for effective function.
2. Improvement of mitochondrial metabolic functions can decrease free-radical production and improve mitochondrial energetics and efficiency.
3. Many anti-oxidants also have anti-inflammatory properties, and other studies have found an association between NSAID use and reduced incidence of dementia in humans.

The list of antioxidants utilized in the Milgram et al study and purported effects are listed in Table 3. de Rivera et al[13] continued the Milgram study over a five –year period. All animals on the anti-oxidant diet learned the required testing task and had significantly fewer errors than those on the control diet. Landsberg reported that improved cognitive performance can be seen as early as two to eight weeks after onset of therapy.[14]

Table 3 - Anti-Oxidants for the Prevention and Treatment of Canine Dementia (Zicker et al 2005)[12]

Vitamin E	Lipid soluble and protects cell membranes from oxidative damage.
Vitamin C	Maintains oxidative protection for soluble phase of cells and prevents vitamin E from propagating free radical production.
Alpha-lipoic acid	A co-factor for mitochondrial respiratory chain enzymes, (pyruvate and alpha ketoglutarate dehydrogenases) and is an anti-oxidant capable of redox recycling other anti-oxidants and raising glutathione levels
L-carnitine	Is a precursor to acetyl-L-carnitine, which is involved in mitochondrial function.
Beta-carotene	Is an anti-oxidant that may improve some aspects of immune function.
Fruits and Vegetables (spinach, tomato pomace, grape pomace, carrots & citrus pulp)	Are rich in flavonoids and carotenoids.

Other treatments for canine cognitive dysfunction syndrome include ginko biloba (which may improve memory loss, fatigue, anxiety and depression), and high intake of fruits and vegetables (that have antioxidant and anti-inflammatory properties).[14] As well, omega 3 fatty acids (which promote cell membrane health and reduce inflammation), L-deprenyl (a monoaine oxidase-ß inhibitor which limits free-radical loading) and anticholinesterase drugs (which enhance cholinergic function) have been reported to aid in aged dog cognition.[14,15] However, in regards to nutritional support for this problem, the greatest amount of research has been in anti-oxidant therapy.

Physical therapy perspectives in the treatment of canine dementia

In the human field of medicine, Alzheimer's patients are examined by physical therapists, occupational therapists and speech and language therapists who evaluate their practical skills.[11] It has been found that cognitive activity may delay the clinical onset of Alzheimer's disease, and 'stimulation' programs exist in rehab facilities to target this goal.[16] In the canine realm, 'old-dog' socialisation classes could be created in canine rehabilitation settings that would include basic obedience training, scent discrimination tasks (i.e. scented dumbbell retrievals), and obstacle courses that require the animal to follow their owner through a course (that is, much like a safety-modified agility course) would target this cognitive training in the dog. Additionally, owners could be advised of the benefits of cognitive training and how to challenge their dogs at home (i.e. hide and seek games with the owner or toys or treats). These techniques could be used as both preventative or after onset of dementia (Figure 1).

Exercise has been known to modify brain function, although the mechanism by which it does so is unknown.[17] Compared with no exercises, physical activity was associated with a lower risk of Alzheimer's disease and dementia of any time.[17] Walking results in a release of Acetylcholine in the hippocampus of rats.[18] As well, there

Figure 2 - Laurie is using a mini trampoline to specifically challenge the proprioception of this aged dog and enhance both muscular strength and proprioception.

Figure 3 - Laurie is using a home-made obstacle course to improve cognitive function in an exercise program designed for this dog.

is an inverse relationship between physical activity and ß-amyloid deposits in mice brains.[19] Therefore physical activity might be a useful strategy in therapeutic management by delaying loss of neuromusculoskeletal functioning and the usual complications of the dementia. Regular exercise should be promoted by physiotherapists in the treatment of all dogs, especially those that are aged. Specialised exercise programs can be designed to safely exercise dogs after individual physiotherapy assessments are completed and take into account other orthopedic, neurological or medical problems (Figure 2, Figure 3). Swimming or underwater treadmill walking for example could be great modes of exercise that do not impart the same concussive forces on potentially arthritic joints of older animals.

Another interesting prevention/ treatment strategy for cognitive impairment has been used with mice. Exposure of mice with Alzheimer's disease to an 'enriched environment' reduces cerebral ß-amyloid pathology versus mice in standard conditions.[19] Brain functioning can also be positively affected in demented patients by tactile stimulation and 'unisensory stimuli techniques' (such as bright lights).[18] This information could be translated to the canine patient as a need to educate the owner on the importance of new toys, walks in new areas or areas with plenty of diversified smells, interaction with humans or other animals and/or use of a 'doggie-daycare' facility on a semi-regular basis. Therapy for this condition could include massage, TTouch techniques, or sensori-motor tactile stimulation (that is zig-zag petting, clapping or tapping the animals body, brushing against the lay of the hair, compressing or tractioning the joints including the spine or other forms of manual therapies). Light therapy could be conducted utilizing Light Emitting Diodes in a therapeutic setting or perhaps the owner could construct a situation where lights could blink at home (i.e. with fiber optic Christmas lights or new-age 'light' decorations) for selected periods of time.

Conclusion

It is exciting to consider that nutritional supplementation and possibly physiotherapy techniques or advisement could serve to prevent, delay or treat canine dementia. Physiotherapy is not likely a treatment option readily thought of by traditional veterinarians for the management of canine cognitive disorders. However, physiotherapists could prove to be useful resources in the care of the older canine in the treatment or prevention of this disease.

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