Canine Cognitive Dysfunction/ Dementia

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Introduction

The condition known as canine dementia is also known as canine senility, senile dementia, senile cerebral dysfunction, cognitive impairment, and cognitive dysfunction (Beaver 1999). Research advances in this condition have contributed in the understanding of the causes of this clinical condition in dogs. Factors associated with nutrition (such as dietary elements and nutritional supplements) have been shown to be effective in both the prevention and treatment of this disease, which most often afflicts aging dogs. Physical therapy techniques which are currently applied in humans for the treatment of Alzheimer's disease may have a role in the treatment and/or prevention of this condition in dogs.

Behavioral alterations

Older canines, much like older humans, show a variety of symptoms which can be attributed to a decline in their brain function. Canine cognitive disorder is broadly defined as a host of geriatric behavioral changes which cannot be attributed to any other medical condition (Overall 2000). Four categories of behavioral dysfunctions have been characterized and identified as canine cognitive impairment: impairment in orientation or disorientation in home and yard, impairment in social interaction with changes in social interactions with human family members, decline in house training, and alterations in sleep-wake cycles (Table 1) (Bain et al 2001, Adams et al 2000, Neilson et al 2001). A dog is considered to have an impairment in one of these four categories of canine cognitive dysfunction if it exhibits two or more signs of that particular category at least once a week for one month or longer (Bain et al 2001).

Neilson et al (2001) found that castrated male dogs were statistically significantly more likely to develop impairment in orientation than spayed female dogs. The findings also suggested that the processes in the brain responsible for age-related behavioural changes are not different between small and large dogs. They also found that of all dogs 11 to 12 years of age, 28% showed signs of at least one type or category of behavioral impairment, whereas 10% of the dogs showed signs of at least two categories of impairment. Authors of the study also concluded that of all dogs 15 to 16 years of age 68% showed signs of at least one type or category of impairment, whereas 35% of the dogs showed signs of at least two categories of behavioral impairment (Overall 2000). In another study, Bain et al (2001) found that dogs which exhibited some of the signs of any particular category of behavioral dysfunction were likely to display a greater severity of those signs or additional behavioural impairments 6 – 18 months later.

Table 1. Qualification of categories of canine dementia. (Bain et al 2001)[2]

Impairment in orientation
• 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
• Any other sign logically attributed to disorientation
Impairment in house-training
• Started to urinate / defecate in the house without a history of behavioral or medical reason (i.e. incontinence or separation anxiety)
• A decline in signaling to go out or use of the doggie -door.
Impairment in social interaction
• Decline in greeting owners
• Decline in soliciting attention
•A change (increase or decrease) in following owners around the house
Alterations in sleep-wake cycle
• Regularly wakes owner at night by pacing or vocalizing
• Sleeping less at night
• Sleeping more during the day

In addition, other authors have demonstrated that geriatric canines show deficits in memory such as forgetfulness of learned behaviours and habits (Beaver 1999). Other age-related learning dysfunctions have been observed in reversal learning, allocentric spatial learning, spatial learning, spatial memory and object recognition memory (Table 2) (Adams et al 2000). 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 (Adams et al 2000).

Table 2. Definitions of learning disabilities that are age-sensitive in the canine (Adams et al 2000)

Reversal learning:	Similar to object discrimination but after the animal learns one behavior stimuli, then the reward is reversed (i.e. the treat is put under the other object) and the animal must re-learn which object to select in order to be rewarded.
Allocentric spatial learning	The ability to locate an object on the basis of the position of the visual object in reference to a known landmark.
Spatial learning	The ability to locate an object in space.
Spatial memory	The ability of maintaining a limited amount of information for a short period of time in order to reuse a learned behavior.
Object recognition	Using non-matching objects, the dog able to be trained to choose a novel object amongst a choice of familiar objects.

Pathological changes

Aging canines show several processes of deterioration in their brain. ß-amyloid plaque deposits have been identified in brains of older dogs (Beaver 1999, Neilson et al 2001, Araujo et al 2005), with the hippocampus and cerebral cortex being primarily affected (Overall 2000, Cotman et al 2002). It has been determined that the amount of ß-amyloid deposition in the brain can be correlated with the severity of cognitive dysfunction in dogs (Overall 2000, Cotman et al 2002). Ventricular dilation, thickening of meninges, vascular changes, a decrease in cerebral volume, as well as an increase in oxidative stress with a reduction in mitochondrial function, and poorer metabolic strategies for mitigating oxidative stress have been identified as characteristic in dogs with canine dementia (Overall 2000, Araujo et al 2005, Cotman et al 2002, Milgram et al 2002). Other studies in dogs have found a correlation between cholinergic tone and memory impairment and dementia (Beaver 1999, Araujo et al 2005). Cotman et al (2002) proposed that the oxidative damage observed in dogs exhibiting signs of CD is likely to play a central and pivotal role in the evolution of the cascade of events that result in canine dementia and cognitive impairment. The authors suggest that since the brain utilizes the greatest amount of oxygen in the body, the oxidative damage observed is likely to begin early in life, but this pathological change is unlikely to induce a substantial neuronal dysfunction until late in life (Cotman et al 2002).

Neuromusculoskeletal function in Canine Dementia

Research in canine dementia has been largely related to the need to develop a disease model for Alzheimer's disease in humans (Adams et al 2000, Overall 2000, Araujo et al 2005). The similarities between canine dementia in dogs and Alzheimer's disease in humans are profound, which has enabled numerous in-depth studies addressing brain function and the effects of certain pharmaceutical, nutritional, and natural treatments for both humans and animals. Therefore, the knowledge obtained from this research can arguably be transferred from humans to dogs.

Franssen et al (1999) found that human patients affected with Alzheimer's disease show significant delays in activation of postural responses to perturbations. These

patients demonstrate 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, and equilibrium, and/or limb co-ordination (Franssen et al 1999, Pettersson et al 2005). Affected humans also suffer from subtle changes in sensorimotor function. These losses and deteriorations result in anxiety, insecurity, a reduction in physical activity, and loss of social contacts (Franssen et al 1999). Falls and injuries commonly afflict such Alzheimer's patients, and this can lead to premature loss of function, deconditioning, fractures, other illnesses as a result of injuries, and early institutionalization (Franssen et al 1999, Pettersson et al 2002, Pettersson et al 2005). Additional motor functional performance deficits other than gait alterations may be present in humans with mild stages of Alzheimer's (Pettersson et al 2002). Patients with Alzheimer's have been found to be significantly less active than healthy subjects of similar ages, have impaired postural control, and had the tendency to cease activities that placed more demands on initiative, interacting with others, and planning (Pettersson et al 2002).

If we endorse the notion that human Alzheimer's disease and canine dementia share similarities in behavioral alterations and pathological changes in the brain, we can speculate that canines affected with this condition are at higher risk of physical deterioration and injury. Neuromuscular awareness, motor control and functional abilities are likely to be diminished in dogs with canine dementia as they are in humans suffering from Alzheimer's disease, and therefore warrant therapeutic intervention.

Nutritional prevention and treatment

As stated previously, oxidative damage and mitochondrial dysfunction in the hippocampus and cerebral cortex are pathological mechanisms which appear to contribute to age-associated cognitive dysfunctions in dogs and humans. We can then speculate that a reduction in neuronal oxidative stress in these regions of the brain may delay a host of 'down-stream' mechanisms which result in neuronal dysfunction, therefore delaying the progression of these cognitive disorder diseases in both species (Cotman et al 2002). It has been demonstrated that anti-oxidants can delay age-related cognitive decline in humans and improve mental/behavioral performance in aged rodents (Milgram et al 2002). Milgram et al (2002) provided evidence demonstrating that age-dependent impairments in dogs can be at least partially reduced by supplementing the diet with a complex mix of anti-oxidants and mitochondrial enzymatic co-factors. This study observed the mental performance of groups of old (8 to 12+ year old) and young (<2 to 4+ year old) dogs in oddity discrimination tasks (object recognition). Table 2. Half of each group was then put on a diet enriched with anti-oxidants, and the other half was fed a non-supplemented diet for a duration of 6 months and served as controls. Results of this study found no difference in oddity discrimination tasks in young dogs. Nevertheless, the study demonstrated a superior performance in oddity discrimination tasks in old animals receiving an anti-oxidant enriched diet when compared to control dogs. The rationales for the benefits attributed to anti-oxidant complex diet supplementation in mental performance are numerous. It is speculated that a complex mix of anti-oxidants better supports a host or network of anti-oxidant reactions in the brain, which require different components. Secondly, anti-oxidants can cause improvement in mitochondrial function, increasing energy levels and cellular efficiency in the brain, as well as decreasing free-radical production and therefore neuronal damage. And lastly, several anti-oxidants also possess anti-inflammatory properties other studies have established correlations between non-steroidal anti-inflammatories (NSAIDs) and a reduction in the incidence of senile dementia in humans. Antioxidants utilized in the Milgram et al (2002) study and their effects at the cellular level are listed in Table 3.

The work of Milgram et al (2002) was extended for an additional 5-year study by de Rivera et al (2005), and found that all animals on the anti-oxidant diet learned the required testing task and had significantly fewer errors than those on the control diet. Landsberg (2005) reported that improved cognitive performance can be seen as early as 2 – 8 weeks after onset of therapy.

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) (Landsberg 2005). 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

Table 3. Anti-oxidants for the prevention and treatment of canine dementia (Zicker 2005)	
Antioxidant	**Cellular effects**
Vitamin E	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	Acts as 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-caritine	Involved in mitochondrial function as a precursor to acetyl-L-carnitine.
Beta-carotene	Improves some aspects of immune function as an antioxidant.
Fruits and vegetables (spinach, tomato pomace, grape pomace, carrots and citrus pulp)	Are rich in flavonoids and carotenoids which act by absorption of oxygen radicals.

loading) and anticholinesterase drugs (which enhance cholinergic function) have been reported to aid in aged dog cognition (Landsberg 2005, Ikeda-Douglas et al 2005). 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 field of medicine, Alzheimer's patients are examined by physical therapists, occupational therapists and speech and language therapists who evaluate their practical skills (Pettersson et al 2005). Rehabilitation facilities implement cognitive activities which may delay the clinical onset of Alzheimer's disease (Olazaran et al 2004). For the same purpose, geriatric canine socialization classes could be established in canine rehabilitation clinics that might 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 (i.e. much like a safety-modified agility course). 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.

Exercise has been known to modify brain function in humans (Sutoo and Akiyama 2003). Although the mechanism by which it does so is unknown, compared with no exercises, physical activity was associated with a lower risk of Alzheimer's disease and dementia (Sutoo and Akiyama 2003). There is an inverse relationship between physical activity and ß-amyloid deposits in mice brains (Nelson 2005). Physical activity might be a useful strategy in therapeutic management by delaying loss of neuromusculoskeletal functioning (posture, balance, co-ordination), motor performance and activity levels. Regular exercise should be promoted by animal rehabilitation physiotherapists in the treatment of all dogs, especially those that are aged. Specialized 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. 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.

Exposure of mice with Alzheimer's disease to an enriched environment reduces cerebral ß-amyloid pathology versus mice in standard conditions (Nelson 2005). Brain functioning can also be positively affected in demented patients by tactile stimulation and 'unisensory stimuli techniques' (such as bright lights) (van Dijk et al 2005). Enriching a dog's environment might include educating dog owners on the importance of new toys, walks in different areas or in areas with plenty of canine -appealing odours, interaction with humans or other animals and/or use of a doggie-daycare facility on a semi-regular basis. Tactile and sensory therapy for ca-

nine dementia could include massage or other sensorimotor tactile stimulation techniques (i.e. zig-zag petting, clapping or tapping the animals body, brushing against the lay of the hair, manually compressing or distracting the joints). 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

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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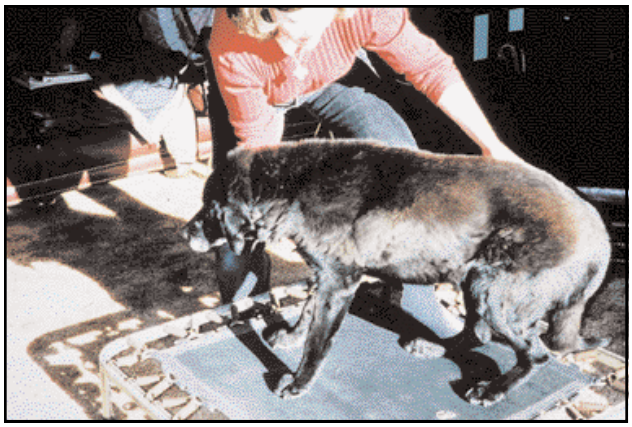

Figure 2 - Laurie is using a mini trampoline to specifically challenge the proprioception of this aged dog and enhance both muscular strength and proprioception.

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

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