**2.0 Literature Review**

2.1 Canine domestication

The role that early domesticated dogs played in the lives of humans around 10-15,000 years ago is uncertain (Frantz et al., 2016), but the proposed hypotheses generally cast dogs in utilitarian roles (Janssens *et al*., 2018). However, re-evaluation of approximately 14,000-year-old *Canis* remains that were originally found at Bonn-Oberkassel around 100 years ago, revealed evidence that led to a new hypothesis. It is suggested by Janssens *et al*. (2018) that the puppy buried at this site provides evidence of the earliest known emotion driven relationship between humans and dogs. This hypothesis is derived from dental evidence indicating that it is highly likely that the puppy received human care during repeated bouts of severe illness prior to death at a time in its life when it would have had no utilitarian use to humans (Janssens *et al*., 2018). The description by Janssens *et al*. (2018) of the deduced relationship between humans and dogs at Bonn-Oberkassel lends support to Davis and Valla’s (1978) suggestion that evidence from Israeli Natufian fossils provides proof of an affectionate relationship between a puppy and an elderly human 10-12,000 years ago.

These early relationships between humans and dogs appear to be the beginning of our shared evolution, and of two species sharing the same environment; something which has potentially led to us sharing some of the same diseases today (Mazzatenta *et al*., 2017). Canine Cognitive Dysfunction Syndrome (CCDS) has been described as the canine version of human Alzheimer’s disease (Wells Dewey *et al*., 2019) and, as degenerative neurological conditions, both may erode relationships between the sufferer and their carers (Chang *et al*., 2010; Truglio-Londrigan and Slyer, 2018). However, as hypothesised from evidence at Bonn-Oberkassel, the unique characteristics of the domesticated dog stimulate a caring and nurturing response in humans which continues today, even in times of sickness and cognitive decline.

2.2 The role of the modern dog

Many pet dogs in Western societies are considered as one of the family, even as a child or partner substitute (Bradshaw, 2017), and their popularity as pets meant that, in 2017, 24% of United Kingdom (UK) adults owned a dog (PDSA, 2018). It was concluded by Topal *et al*. (1998) that the modern dog-human relationship can be likened to that of the child-parent in terms of attachment theory (Bowlby, 1982). From their review of human-pet bond research, Zilcha-Mano *et al*. (2011) conclude that the factors of proximity seeking, safe haven and secure base behaviour, and separation distress, are often present in tests to observe the human-dog relationship, and that this indicates the presence of an attachment relationship. However, Rehn and Keeling (2016) comment on wide variation in responses within both dog and human samples and recommend focussing on the assessment of individuals and dyads rather than generalising the results of a few to whole populations.

The unconditional love and acceptance that many owners have reported to receive from their dogs may be beneficial to human health and mental wellbeing (Rehn and Keeling, 2016). Dogs often act unprompted as social facilitators, and their requirements for regular exercise and mental stimulation can encourage human exercise and participation in sports (Curl *et al*., 2017). These, and other, factors led Westgarth *et al*. (2014) to conclude that a good owner-dog relationship has proven physical and mental health benefits for humans. However, the work and social commitments of many modern lifestyles are often not compatible with owners spending the amount of time with their dogs that they would ideally like to, and Diverio *et al*. (2016) comment that this could negatively influence the formation of a strong owner-dog bond. Gender differences in commitment to a pet dog in relation to time spent exercising and grooming, both activities that can positively influence the owner-dog bond, were observed by King *et al*. (2009); with females being more likely to show greater commitment. However, although Diverio *et al*. (2016) support this observation, it is possible that cultural factors may contribute to geographical variation in results.

As with any relationship, problems may arise due to a mismatch of needs (McGreevy and Bennett, 2010) or the onset of a health condition, such as CCDS, that is detrimental to the quality of life (QOL) of either, or both, parties (Wittenberg *et al*. 2014). The intensity of many owner-dog relationships as described by Bradshaw (2017), whilst potentially beneficial socially and physiologically (Wells, 2007), can also mean that degradation or loss of the relationship, such as during senescence or at the end of the dog’s life, are felt extremely deeply by the owner (Archer and Ireland, 2011), with potential for harm to mental health (Tzivian *et al*., 2015).

2.3 Owner expectations and recognition of behaviour problems

Whatever the nature of the individual companionable relationship, owner expectations of their dog’s behaviour can sometimes be unrealistic (Payne *et al*., 2015). There is significant variance in how owners perceive their dog’s behaviour, and this perception can influence an owner’s willingness to attempt to change undesirable behaviours (Pirrone *et al*., 2015). It is suggested by Howell *et al*. (2013) that better understanding of cognitive abilities and innate behavioural traits in dogs may help owners to interpret behaviour more accurately; this could also enable earlier recognition of abnormal behavioural changes that could indicate pathological neurological problems.

The importance of differentiating between maladaptive and malfunctional behaviours in companion animals is stressed by Mills (2003), as they may have different root causes. Maladaptive behaviour in dogs is usually a normal species-specific behaviour that is expressed in a manner that the owner finds inappropriate, for example; barking at passers-by or digging in the garden. Malfunctional behaviours however, usually have a physical or neurological illness behind them and are not normal species-specific behaviours, for example; one-directional circling and pacing due to neurological disease such as CCDS (Bowen and Heath, 2005).

2.4 Association between ageing and behaviour problems

As dogs age, they are often less able to fulfil the expectations of owners due to physiological, and sometimes psychological, changes associated with senescence (Baranyiova *et al*., 2004). Dogs who are suffering pain, for example; due to age related osteo-arthritis, often show decreased interest in petting and may avoid social interactions (Landsberg and Malamed, 2017). Given that King *et al*. (2009) record that the majority of owners want their dogs to enjoy being petted and to be affectionate towards them, age related changes in social interaction could be detrimental to the relationship between an older dog and its owner, and negatively affect QOL for both (Pirrone *et al*., 2015). House soiling, excessive vocalising and aggressive behaviour towards humans and conspecifics are ranked as undesirable behaviours (King *et al.*, 2009), but are all behaviours that may onset due to advancing age (Stelow, 2018). However, Salvin *et al*. (2011b) found that behavioural changes accompanying what is described as successful, or non-pathological, ageing were mild, and that effect on learning and memory was minimal.

Increased age is often positively associated with decreased sensory perception (Szabo *et al*., 2018). For example; hearing loss, which can lead to an increase in vocalisation (Landsberg and Araujo, 2005); and visual impairment, which may cause disorientation and increased anxiety (Jones, 2015). Increased passive behaviour compared to younger dogs during the Strange Situation Test adapted for dogs (Prato-Previde *et al*., 2003) concealed physiological indication, in the form of increased salivary cortisol, that the older dogs were less able to cope with separation from owner than younger individuals (Mongillo *et al*., 2013). It was identified by Landsberg and Araujo (2005) that approximately one in three dogs over the age of nine that are referred for behavioural counselling suffer from separation anxiety. An association of age with separation related behaviours (SRBs) was also observed by van Rooy *et al*. (2018a); although data was not collected on age at commencement of the problem behaviour, therefore, it is not possible to establish a correlation between advanced age and SRBs from this study. The hypothesis that increased age is a contributory factor in anxiety related behaviours is supported by Storengen and Lingaas (2015); although their focus of study was noise related anxiety, correlation between this and increased SRB prevalence was recorded. Dogs that exhibit SRBs as they age may be at increased risk of being relinquished for rehoming, or of being euthanised, as the resultant behaviours such as excessive vocalisation and house soiling, may be difficult for owners to cope with (van Rooy *et al*., 2018a).

2.5 Pathological ageing and CCDS

The biological processes associated with senescence as discussed above could be considered a normal part of healthy ageing (da Costa *et al*., 2016). In this process, despite the observable changes in physical appearance and behaviour that come with advancing age, neurologically the brain is functioning normally as would be expected in a senior dog (Landsberg and Araujo, 2005). Whilst many dogs do not show cognitive decline as they age (Tapp and Siwak, 2006), some develop the degenerative neurological condition CCDS that presents as a gradual cognitive decline over a sustained period, often around eighteen to twenty-four months but sometimes longer (Landsberg and Araujo, 2005). There is significant variability in the age of onset and observable symptoms between affected individuals (Nichol and Head, 2017), however, the condition generally manifests as behavioural changes, impaired memory and learning ability, altered awareness and response to stimuli, disorientation and confusion (Landsberg and Malamed, 2017). The acronym DISHA, which is defined by Landsberg *et al*. (2012) as summarising the classic signs of CCDS, is used frequently in discussions around the diagnosis of CCDS. Additionally, the development of fears, phobias, and generalised anxiety, as well as deficits in memory and learning ability, are accepted as components of CCDS, adding AL to the acronym in some references (Landsberg *et al*., 2012). Table 1 expands on the acronym DISHA(AL).

Table 1: Clinical signs of CCDS classified by the acronym DISHA(AL) (Landsberg *et al*., 2012; Benzal and Rodriguez, 2016).

|  |  |
| --- | --- |
| **Behavioural category from acronym** | **Description of examples of clinical signs** |
| **D**isorientation | Getting stuck behind or under objects, appearing lost in familiar places, walking into walls/doors, going to hinge side of doors, inability to locate dropped food, and blank staring at floor or walls. |
| **I**nteraction | Decreased interest in greeting familiar people/pets, decreased interest in petting, clingy behaviour and need for constant contact, and altered relationships with familiar people/other pets which can incorporate aggressive behaviour towards them. |
| **S**leep | Altered sleep-wake cycles, commonly restless and agitated at night whilst sleeping more during the day. |
| **H**ouse-soiling | House-soiling when previously house trained, decrease/loss of signalling prior to elimination, and elimination in sleeping area. |
| **A**ctivity | Increased: pacing and aimless wandering, air snapping/licking, licking of owner or household objects, increased appetite.Decreased: lack of interest in food or treats, decreased exploration/activity/play, lack of interest in previously enjoyed toys, decreased self-care. |
| **A**nxiety | Unusual vocalisation, restlessness and agitation, generalised or specific anxiety, fears and phobias not present previously or more pronounced, separation anxiety. |
| **L**earning | Decreased ability to perform previously learned tasks, decreased responsiveness to known cues, inability or slowness to learn new tasks/cues. |

The full DISHA(AL) signs checklist is within Appendix 1.

It is believed that structural neurological changes are responsible for the degeneration in cognitive function observed in cases of CCDS. These include; brain atrophy, a decline in neurogenesis (Siwak-Tapp *et al*., 2007), neuro-transmitter abnormalities (Badino *et al*., (2013), the accumulation of beta-amyloid plaques (Araujo *et al*., 2017), mitochondrial dysfunction, and cumulative oxidative damage within the brain and cerebral vasculature (Nichol and Head, 2017). Many of the features identified in pathological brain ageing in dogs have also been identified in human Alzheimer’s disease (Nichol and Head, 2017). Therefore, due to similarities in neuropathological and biomarker changes, CCDS is considered to be a suitable model for research into disease interventions for Alzheimer’s disease (Gilmore and Greer, 2015; Araujo *et al*., 2017). It is possible that the outcomes of this clinical research into human neurodegenerative disease could potentially benefit the treatment of senior dogs with CCDS (Araujo *et al*., 2017). The fact that companion dogs are unique in sharing the same environment so closely with humans is particularly relevant to cross species research into biological ageing (Kaeberlein *et al*., 2016).

2.6 Risk factors of CCDS

Age has been determined as the key risk factor for dogs developing CCDS (Mad’ari *et al*., 2017). Advances in veterinary medicine, and increased knowledge about canine nutrition and behavioural needs, mean that dogs are living longer than in previous generations (Katina *et al*., 2016). However, increased longevity means that anatomical, functional, and neurodegenerative changes in the brain occur more frequently, and these factors have been shown to contribute to the development of CCDS (Mad’ari *et al*., 2017). The accumulation of oxidative damage within the brain, accompanied by a decrease in anti-oxidative activity within the body due to age-related processes, is also proposed as a causative factor in the development of CCDS (Head *et al*., 2009). Investigation into this factor led Katina *et al*. (2016) to conclude that a diet not controlled for size, breed, age, and/or health status, for example; some homemade, or poor-quality commercial, diets was indicative as increasing a dog’s risk of developing CCDS. This conclusion is supported by Head *et al*. (2009) who suggest that poor diet can negatively influence mitochondrial function, which is a key element of anti-oxidative activity in dogs.

It was concluded by Storengen and Lingaas (2015) that gender and neutering status are significant predictor variables in the development of CCDS, with females and neutered males appearing to be more at risk. This observation suggests that sex hormones, such as oestrogen and testosterone, may have influence on pathological brain ageing (Mood *et al*., 2018). However, Mood *et al*. (2018) comment that increased longevity in females may be contributory to their higher incidence of CCDS, yet Fast *et al*. (2013) detected no significant difference between sexes in either prevalence of CCDS or longevity. Although the sample size utilised by Fast *et al*. (2013) was not large, the study included follow-up data, collected 4 years after the initial data, which adds validity to the conclusions by extending the period of observation. No significant difference in CCDS prevalence between dogs with different neutering status was detected by Katina *et al*. (2016), which casts doubt upon the sex hormone hypothesis. However, the authors comment that the sample included many more neutered than intact dogs and that this may have influenced results. It was concluded by Mad’ari *et al*. (2017) that the variation in methodologies used to carry out studies into risk factors for CCDS, and the frequent use of small sample sizes, may be contributing to the conflicting results obtained in this area.

There is similar debate over the influence, or not, of breed, size, and weight on development of CCDS with contradictory conclusions from some studies (Katina *et al*., 2016). However, it is documented that larger breeds generally live shorter lives (Selman *et al*., 2013), and therefore may have a reduced age risk factor for the development of CCDS, which could account for the apparently higher prevalence within smaller dogs (Azkona *et al*., 2009). Although Salvin *et al.* (2012 p.63) conclude that there is variation in the cognitive ageing process between breeds, the authors’ sample comprised only “successfully aging dogs” and the consensus from reviewing current evidence is that there is no correlation between breed, size and CCDS prevalence (Mood *et al*., 2018).

Chronic anxiety and resultant stress could potentially be risk factors for cognitive decline, and Mad’ari *et al*. (2017) conclude that senior dogs may be more vulnerable to the physiological effects of chronic stress. Effective treatment of anxiety in humans may be protective against the development of neuro-degenerative disease such as Alzheimer’s disease (Gulpers *et al*., 2019). As there are many similarities between the development and progression of CCDS and Alzheimer’s disease, it is possible that this conclusion is relevant for dogs also. The conclusion of Dreschel (2010) that fear and anxiety in dogs is negatively associated with good health and lifespan would support the anxiety risk factor hypothesis. However, the author observed that their internet sample was probably subject to selection bias and that investigation into the physiological and neurological effects of anxiety on dogs is hindered by the many variables present, for example; social and physical environment (Dreschel, 2010).

In common with the conclusion of Carey *et al*. (2018) that there is a positive association between exposure to air pollution and diagnosis of Alzheimer’s disease, Calderon-Garciduenas *et al*. (2008) revealed that ambient air pollution in an urban area, in particular ultrafine particulate matter, is positively associated with neuro-inflammation in children and dogs. Neuro-inflammation is stated by Calderon-Garciduenas *et al*. (2008) as being a key factor in the development of neurodegenerative diseases such as Alzheimer’s disease and is also considered to be a contributory factor in the development of CCDS (Mad’ari *et al*., 2017). Therefore, dogs living in an urban area with high levels of air pollution may be at significantly greater risk of developing CCDS than dogs living in rural areas that are exposed to lower air pollution. However, this hypothesis is, as yet, untested and a large-scale longitudinal study of dogs would be required for further investigation.

2.7 Diagnosis of CCDS

Currently, veterinary diagnosis of CCDS is made by assessment of behavioural signs following the exclusion of any medical conditions or medication side effects (Landsberg *et al*., 2012) and relies heavily on owner observation of signs of abnormal behaviour (Chapagain *et al*., 2017). It was observed by Schneider *et al*. (2010) that dogs may behave differently at home than in a clinic environment. However, the authors also comment that owner reporting of signs and symptoms of CCDS, for example; a decline in learning and cognition and/or reduced QOL, may be subjective (Schneider et al., 2010). This suggestion of subjectivity is supported by Madari *et al*. (2015). Owner-directed questionnaires and behaviour rating scales have been developed to assist in assessing dog behaviour prior to diagnosis of CCDS; these are detailed in Table 2.

Table 2: Questionnaires and behaviour rating scales developed to assess dog behaviour in relation to a diagnosis of CCDS.

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| --- | --- | --- | --- |
| **Diagnostic tool** | **Key Features** | **Additional information** | **Author(s)** |
| Canine Cognitive Dysfunction Rating Scale (CCDR) | Comprises 13 behavioural items, including 3 sensitive to severity of disease stage | A tool for research and clinical settings for assessment and tracking of cognitive change. 98.9% diagnostic accuracy. Used by the Regenerative Neuroscience Group. | Salvin *et al*. (2011a) |
| Canine Dementia Scale (CADES) | Comprises 17 items over 4 behavioural domains.  | A validated and psychometrically tested clinical screening tool, also suitable for assessment of disease progression.  | Madari *et al*. (2015) |
| Questionnaire ‘C’ | Unnamed questionnaire consisting of 10 graded score behavioural items. | Used in consultation with owners when dogs were at the point of euthanasia for various reasons. Questionnaire scores correlated significantly with post-mortem brain pathology. | Rofina *et al*. (2006) |
| Canine Cognitive Dysfunction Checklist | 30 item behavioural checklist. | No option to grade behaviour. Designed for owners to monitor behaviour prior to veterinarian consultation. | Anderson (2015) |
| DISHAAL Checklist  | 33 item behavioural checklist with grading score and age of commencement for each | A comprehensive diagnostic and behavioural grading tool for both owner and veterinarian use. Appendix 1. | Landsberg *et al*. (2012) |
| Vienna Canine Cognitive Battery | A comprehensive test battery assessing various areas of cognitive function. Designed to be used in conjunction with an owner questionnaire | Developed following two empirical studies of Border Collies and a third using multiple breeds. Assesses 10 areas covering different cognitive functions in around 1-2 hours. Suitable for clinical use.  | Chapagain *et al*. (2017) |

However, Chapagain *et al*. (2017) comment that the design of these diagnostic tools, and the methodology used to establish a total cognitive score, is diverse and that there is little evidence of validity and comparability between current questionnaires. The CCDR (Salvin *et al*., 2011a) and Questionnaire C (Rofina *et al*., 2006) are considered to be comparable in successfully detecting severe and multiple signs of CCDS (Schutt *et al*., 2015). However, Schutt *et al*. (2015) consider the CCDR to be more relevant for clinical use due its design which categorises dogs as; non-CCDS affected; at risk of developing CCDS; and currently affected by CCDS. Detection of mild cognitive impairment in early disease progression is particularly difficult to diagnose using the existing diagnostic tools, and as this is the time when medical intervention can have most benefit, more sensitive diagnostic tools are required (Schutt *et al*., 2015; Chapagain, *et al*., 2017). Establishment of a baseline for normal ageing would be beneficial to future development of improved early/at risk detection techniques (Schutt *et al*., 2015).

Objective spatial learning and memory tasks have been used to measure cognitive decline in laboratory dogs (Adams *et al*., 2000). However, a lengthy pre-task training protocol was required and Chapagain *et al*. (2017) consider this test design unsuitable for use with pet dogs. Recent developments in the field of detecting cognitive decline in ageing dogs include various neurophysiological tests to measure behaviour associated with food seeking, social responsiveness, locomotion and exploration (Chapagain *et al*., 2017). The authors conclude that the best approach to detecting CCDS at all stages, and to measure disease progression, is to combine both owner-evaluated questionnaires and objective neurophysiological test batteries such as the Vienna Canine Cognitive Battery (Chapagain *et al*., 2017). However, the availability of such testing to owners will be reliant upon their chosen veterinarian having sufficient knowledge of CCDS and its diagnosis to recommend them (Bennett, 2012), as well as having access to suitable testing resources.

It was observed by Szabo *et al*. (2018) that it can be difficult to separate the behavioural changes associated with healthy ageing and those arising due to cognitive changes associated with pathological ageing. For example; disorientation in a familiar place may be due to sensory impairment, such as deterioration in vision, in a successfully ageing dog (Jones, 2015); or due to neurological malfunction associated with CCDS progression (Landsberg *et al*., 2011). Additionally, many owners do not appreciate that neuro-behavioural disturbance in a dog’s senior years is not part of normal healthy ageing and this contributes to the conclusion of Salvin *et al*. (2011a) that CCDS is severely under-diagnosed in pet dogs.

2.8 Prevalence of CCDS

As previously identified, there is significant variation in symptom presentation and disease progression between individuals (Head, 2013). This, along with a potential lack of awareness of CCDS amongst owners and the difficulties surrounding definitive diagnosis, can lead to delay in diagnosis which may contribute to the lack of conclusive evidence on the prevalence rate of CCDS within the global pet dog population (Chapagain *et al*., 2017).

Table 3 illustrates the variation in a sample of prevalence rates established by empirical study.

Table 3: CCDS prevalence rates from a range of studies.

|  |  |  |  |
| --- | --- | --- | --- |
| **Author(s)** | **Notes on study** | **Prevalence rate detected in sample by dog age** | **Clinical diagnosis rate** |
| Neilson *et al*. (2001) | Telephone interview, sample of 180 age stratified dogs. | 11-12 years: 28%15-16 years: 68% | Not available  |
| Azkona *et al*. (2009) | Telephone interview, sample of 325 dogs. | 9-17 years: 22.5% | Not available  |
| Salvin *et al*. (2010) | Online questionnaire, 497 samples selected randomly from 957 responses. | 8 years and older: 14.2% | 8 years and older:1.9% |
| Mood *et al*. (2018) | Questionnaire delivered face to face, incorporated CCDR scale, sample of 234 dogs. | 7-16 years: 8.9% | Not available |

The relatively low clinical diagnosis rate observed by Salvin *et al*. (2010) could be an indication of either how few owners seek veterinary assistance for the observable symptoms or, potentially, a lack of awareness of the condition amongst veterinary surgeons (Bennett, 2012). There are potentially several reasons behind the variation in detected prevalence of CCDS to date. It has been shown that age is a significant predictor of CCDS (Mad’ari *et al*., 2017), therefore, the inclusion of a dis-proportionally large quota of older dogs within a sample may alter results and potentially lead to overestimation of prevalence. It was commented by Mood *et al*. (2018) that a lower average age of dog relative to previous studies, small sample size, perceived high rate of owner awareness, and geographical region may have contributed to the substantial difference in their results compared to previous studies. Additionally, accurate representation of prevalence rate may be harder to achieve using an online survey, as in the study of Salvin *et al*. (2010), than in the telephone interview scenario used by both Azkona *et al*. (2009) and Neilson *et al*. (2001), or face to face interview as used by Mood *et al*. (2018). This is due to potential uncontrolled demographic bias within a convenience-based internet sample. However, Salvin *et al*. (2010) discuss how large sample size and community-based recruitment mitigated this issue by increasing generalisation within their sample. The use of telephone interviews could lead to over-estimation of CCDS prevalence, as medical causes cannot be excluded if the owner does not declare them, although similar issues could potentially arise with any non-face to face data collection method as no veterinary examination or health history is available to researchers (Katina *et al*., 2016).

Despite careful design of individual data collection projects, it is difficult to empirically compare results obtained from different sampling methods due to variance in sample criteria (Szolnoki and Hoffmann, 2013). The selection of age stratification criteria in several studies is discussed by Szabo *et al*., (2016); predetermining a particular age for the start of senescence that applies to the whole dog species has been common practice to date. However, this method does not account for the variation in life span between breeds (Szabo *et al*., 2016). Piotti (2018) recommends adopting the American Animal Hospital Association’s canine life stages definitions of Puppy, Junior, Adult, Mature, Senior and Geriatric (AAHA, 2012), which would assign a dog to the category of Senior at whatever age was 75% of expected life span for the breed (AAHA, 2005). To allow for mixed breeds, the use of the mathematical formula utilising height and weight proposed by Greer *et al*. (2007) can be used to calculate a predicted life span. The range of behaviours taken into account by the evaluation criteria chosen may also be influential on the prevalence rate calculated (Chapagain *et al*., 2017).

2.9 Preventative measures and treatments

Whilst CCDS is currently incurable, it is possible to retard progression of symptoms and to improve QOL of the dog, and subsequently the owner, by using a combination of available treatments (Benzal and Rodriguez, 2016). However, disease progression varies between individuals and therefore, some treatments may be more successful in some dogs than in others (Landsberg and Malamed, 2017). Additionally, early diagnosis and prompt treatment will give the best results in slowing decline (Landsberg and Malamed, 2017). However, as the disease progresses, treatment protocols may need to be adjusted to remain effective for as long as possible and therefore close monitoring by owner and veterinarian is recommended by Denenberg and Landsberg (2017). It is suggested that there are currently four treatment modalities which target; “improving brain metabolism, enhancing neuronal transmission, reducing oxidative damage, and helping to maintain neuronal integrity” (Denenberg and Landsberg, 2017 p.129). Options within the categories of; nutritional treatment, both via diet and nutraceutical supplements; environmental enrichment; and drug treatments are discussed by Benzal and Rodriguez (2016).

Multiple trials have demonstrated tangible benefits in sample populations fed a diet supplemented with anti-oxidants such as vitamins E and C, free radical scavengers, and a range of other neuroprotective substances. For example; Heath *et al*. (2007) observed significant improvements in disorientation, interaction with owner, and house soiling behaviour within the treatment group administered the dietary supplement Aktivait. See Appendix 2 for details of Aktivait’s composition. It is commented by Dowling and Head (2012) that a combination of antioxidants consumed as part of the diet appears to be more effective than when administered as a nutraceutical supplement. However, Heath *et al.* (2007) discuss the issue of owner reluctance to alter a senior dog’s diet, particularly in dogs with other health conditions or where weight control considerations are relevant, and conclude that for these cases in particular, a nutraceutical supplement would be beneficial. This conclusion of Heath *et al*. (2007) is supported by Galan *et al*. (2014), who administered Aktivait supplement to healthy laboratory dogs and concluded that the supplement led to an improvement in brain metabolism. A diet rich in anti-oxidants and mitochondrial cofactors is believed to be a primary factor in prevention of CCDS and as a therapeutic strategy to delay cognitive decline in dogs already diagnosed with the condition (Katina *et al*., 2016). Due to the decline in cerebral glucose metabolism observed in ageing dogs by London *et al*. (1983), the addition of medium-chain triglycerides to the diet, for example; coconut oil, is recommended by both Pan *et al*. (2010) and Katina *et al*. (2016) as a way to provide the brain with a source of ketones as an alternative to glucose for cerebral metabolism.

However, Denenberg and Landsberg (2017) comment that for optimum effect, any dietary supplementation should be accompanied by a programme of cognitive enrichment. Continued social enrichment as a dog ages can assist in maintaining cognitive function and may even slow the cognitive decline associated with CCDS (Landsberg *et al*., 2011). It is recommended that owners play games with their dogs, use age appropriate food puzzle toys, take regular walks and engage the dog in positive reinforcement training appropriate to its physical and cognitive abilities (Landsberg *et al*., 2011). Environmental enrichment and the establishment of predictable routines may also help to reduce stress and anxiety and maintain temporal and spatial orientation (Landsberg *et al*., 2011).

Pharmaceutical medications may also be utilised to treat some clinical signs of CCDS, particularly anxiety and sleep disturbance (Denenberg and Landsberg, 2017). Table 4 details some of the veterinary medicines commonly used to alleviate symptoms of CCDS.

Table 4: Veterinary medicines used in the treatment of CCDS (Crowell-Davis and Murray, 2006; Denenberg and Landsberg, 2017)

|  |  |  |  |
| --- | --- | --- | --- |
| **Pharmaceutical medication** | **Modality** | **Symptom target** | **Contra-indications** |
| Selegiline hydrochlorideProduct name: Selgian | Selective irreversible monoamine oxidase (MAO) B inhibitor.If no improvement within 2 months, treatment is discontinued | General cognitive decline. Emotional disorders generally, including anxiety and depression  | Administration of other MAO inhibitors, selective serotonin reuptake inhibitors, tricyclic antidepressants, pregnancy and lactation |
| PropentofyllineProduct name: Vitofyllin | Neuroprotective action and improvement of peripheral and cerebral circulation  | Mental dullness and lethargy  | Dogs under 2.5kg in weight, hypersensitivity to substance, pregnancy and lactation |
| Benzodiazepines for example; diazepam | Depression of central nervous system | Anxiety and sleep disturbance | Hypersensitivity to substance, pregnancy and lactation |

The use of any of the medications listed in Table 4 within the UK would be subject to the Veterinary Medicines Regulations and may require use of the Prescribing Cascade process (British Veterinary Association, 2018). Complementary therapies such as the use of Dog Appeasing Pheromone (DAP) products (Mills *et al*., 2006), Bach Flower Remedies (Scott and Mariani, 2007), and aromatherapy, for example; use of lavender oil, (Wells, 2006) may also be beneficial for some dogs in reducing stress and anxiety and aiding night time sleep (Landsberg *et al*., 2011).

Treatments currently in development include; stem cell therapy (Regenerative Neuroscience Group, 2012), and an immunotherapy vaccine (Davis *et al*., 2017). The stem cell therapy appears to have successfully reversed disease progression in two dogs diagnosed with CCDS (Power, 2018). However, this is still at the clinical trial stage and requires specialist individualised treatment (Avila-Robinson *et al*., 2019). Therefore, this therapy may not become available to all pet dogs even in the future. An immunotherapy vaccine, designed to clear existing beta-amyloid accumulation in the brain, has been investigated for use in combination with environmental enrichment, to slow any further beta-amyloid accumulation (Davis *et al*., 2017; Head, 2017). It was concluded that this combination of treatments slowed cognitive decline in laboratory dogs (Davis *et al*., 2017; Head, 2017). However, the authors recommend that this treatment would need to be administered before significant cognitive decline was observed, ideally at around 6 to 8 years of age. Considering that many dogs are not presented to veterinarians until clinical signs of CCDS are moderate to severely advanced (Denenberg and Landsberg, 2017), late opportunity for administration may be a barrier to successful implementation of this, and other, potentially beneficial therapy combinations (Wells Dewey *et al*., 2019).

2.1.1 The owner-ageing dog relationship

As dogs age they often become less appealing to their owners (McGeevy and Bennett, 2010). It was revealed by Marinelli *et al*. (2007) that increased length of relationship between dog and owner shows correlation with a reduction in owner attention to the dog’s needs. The authors also link the observation that older dogs in their sample received less medical assistance with the hypothesis that owners have a low awareness of the care needs of geriatric dogs (Marinelli *et al*., 2007). However, Mongillo *et al*. (2013) conclude that the attachment of aged dogs to their owners remains intact. At this stage in life a dog needs the care and support of their human more than ever but often this is when the owner disengages from the relationship (McGreevy and Bennett, 2010). It is possible that the experience of declining health, and/or death, of a previous pet may negatively influence the owner’s bond with a subsequent ageing dog (Zilcha-Mano *et al*., 2011). However, Mongillo *et al*. (2013) support the conclusions of Marinelli *et al*. (2007) that owners may fail to modify how they interact and relate with their dogs as they age due to a lack of understanding of the physiological and psychological changes associated with ageing.

2.1.2 Owner influence on diagnosis

Several studies have concluded that early diagnosis of CCDS is vital to enable treatment to start before significant neurological degeneration has occurred (Wells Dewey *et al*., 2019). As owner reporting has been shown to be important in the diagnostic process, owner awareness of the existence of CCDS may influence whether a dog is diagnosed at the early stage of disease progression or not (Bennett, 2012). CCDS has been the subject of an increase in clinical research and media interest during the past twenty years (Bennett, 2012). However, information from research studies does not always filter down to owners quickly and, as observed by Anderson (2015), many owners are still not aware that the condition exists. Even if an owner is aware of the existence of the condition, they may not be willing to consult a veterinarian about behavioural signs observed that may be indicative of the condition (Osella *et al*., 2007). The Bayer Veterinary Care Usage Study demonstrates that there are multiple factors that may deter an owner from consulting a veterinarian (Volk *et al*., 2011). These factors include; owners believing that regular health check-ups are unnecessary, the cost of veterinary care, and the prevalence of internet usage to find information relating to health conditions of humans and their pets without consulting trained professionals (Volk *et al*., 2011).

It is suggested by Bowen and Heath (2005) that owners may be fearful of mentioning behavioural problems observed in their older dogs as these could potentially be serious and even an indicator for euthanasia. This suggestion is supported by Christiansen *et al*. (2016) who comment that as CCDS is a disease of old age and can be compared so closely to Alzheimer’s disease, some owners with experience of Alzheimer’s disease may find it especially difficult to approach their veterinarian if they feel euthanasia is going to be suggested as an option. In conclusion, Landsberg (2014) reports that just 12% of dog owners report potential signs of CCDS to their veterinarian.

This study aims to assess current awareness of CCDS amongst dog owners and to determine what, if any, factors are influential upon owner awareness of this disease. Additionally, the study aims to examine owner attitudes towards ageing pet dogs, and towards the potentially altered care requirements of an older dog. By collecting data such as this, it may be possible to evaluate any apparent influence of owner awareness, attitude to ageing dogs, and owner-dog relationship on the use of potentially preventative measures, timely diagnosis of CCDS, and the management and treatment of clinical signs of the condition.

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