

Evaluation of Cognitive Dysfunction Syndrome (CDS) in dogs and cats following chronic diseases

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Abstract One of the problems of aging in dogs and cats is cognitive dysfunction syndrome (CDS), which is very similar to Alzheimer's disease in humans and can affect the well-being of pets and the quality of human-animal communication. Currently, the most practical way to diagnose CDS in clinical practice is to administer a questionnaire based on cognitive symptoms, which include vocalization, changes in social interaction, changes in sleep/wake cycle, litter box soiling, disorientation, changes in activity level, anxiety, and changes in memory function and past learning. The study of cognitive disorders that may result from medical conditions is a critical area of research in human medicine, and many studies have been conducted to explore this topic. However, the study of such disorders in dogs and cats has received relatively little attention, with only a few studies conducted to date.

A total of 20 clinically affected dogs and cats selected to evaluate their cognitive status. The control group consisted of 10 dogs and 10 cats in similar age and sex. After obtaining the consent of the owners, the samples were evaluated using a questionnaire and the incidence of CDS after chronic diseases was compared with the natural aging process.

According to the results, a significant difference was seen in the activity and change of memory function and prior learning in dogs with underlying disease compared to the control group. In addition, the greatest differences in cats included changes in activity, sleep-wake cycle, and house soiling. On the other hand, anxiety in dogs and social interaction in cats showed the least difference between healthy and patient groups.

It seems important to evaluate behaviors related to cognitive dysfunction syndrome in dogs and cats after chronic diseases using a questionnaire.

Introduction

Thanks to advances in veterinary science and greater public awareness of proper care and nutrition, the life expectancy of pets has increased. Recently, a study based on statistics collected in the United States between 2013 and 2019 showed that the average age of a dog was 12.69 years and that of a cat 11.18 years. [1]. There are currently more than 45 million dogs over the age of 7 in America and Europe [2]. However, as life expectancy increases, so do the problems associated with animal health, such as immune dysfunction, impaired cellular physiology and neoplasia. This issue is of particular importance to clinicians working in the field of small animal internal medicine and requires increased awareness of issues such as proper nutrition in old age, medical and behavioural disorders of this age group. The most common neurological changes that occur in pets as they age include cognitive dysfunction (eventually leading to dementia), motor dysfunction, and vision/hearing disorders [3].

Cognitive Dysfunction Syndrome (CDS) is a progressive and neurodegenerative disease in older dogs and cats that has significant similarities to Alzheimer's disease in humans. CDS can significantly affect the well-being and bond between humans and animals, ultimately leading to a reduction in the life expectancy of pets. The main feature of the disease is the cognitive-based behavioural changes that occur following specific patterns of brain lesions in old dogs and cats. However, CDS is not an inevitable consequence of ageing pets and there are many individual differences. Nelson et al showed that the prevalence of CDS was 28% in 11-12 year old dogs and 68% in 15-16 year old dogs [4]. In a study conducted on 141 cats over 11 years old, the prevalence rate of CDS in cats 11-15 years old was 28% and in cats over 15 years old it was 50% [5,6]. However, the prevalence of CDS appears to be much higher than the cases referred to veterinary clinics. Many pet owners consider the symptoms of CDS to be part of the natural ageing process and do not discuss such cases with the veterinarian. Therefore, CDS is often diagnosed as an incidental finding by the

veterinarian, which reduces the rate of initial referral by owners. Therefore, it is important for the veterinarian to assess the behavioural changes associated with CDS by using Cognitive Dysfunction Syndrome questionnaires when examining older dogs and cats; because of the progressive nature of CDS, early diagnosis and treatment is the main key to its management [3].

Clinical signs in dogs and cats can include deficits in one or more symptoms. These symptoms, often referred to by the acronym DISHAAL, include disorientation, abnormal interactions, sleep/wake cycle disturbances, litter box fouling, changes in activity, anxiety and changes in learning/memory [3]. In addition to the previous signs, recent studies have identified vocalization as one of the most important clinical symptoms observed in cats with CDS [7]. However, not all dogs and cats with CDS will show all of the above, and clinical signs are not limited to these, and changes may be in the form of changes in personal hygiene (such as grooming behavior), changes in appetite, repetitive behaviors, compulsive behavior, aimless behavior, and changes in response to stimuli. On the other hand, some dogs and cats may show only one sign, while others may show several. There is also a wide range in the severity and frequency of occurrence of the same symptoms. It is noteworthy that the occurrence of the above symptoms depends on several factors, including the personality and natural behavior of the animal (being calm, playful, or aggressive), the quality and duration of the relationship with the owner, the history of past events, the presence of other animals in the house, the amount of toys in the house, and other factors. Therefore, it seems that the pet owner is the best criterion for diagnosing such disorders [3].

Since the questionnaire is currently the only tool used for the clinical diagnosis of CDS, it is recommended that when cognitive dysfunction is suspected, the questions of the questionnaire be asked in different ways to increase the accuracy of the questionnaire and to reduce possible bias. To date, no comprehensive study has been conducted using this questionnaire to evaluate the diagnosis of behavioral disorders following chronic disease in dogs and cats.

Therefore, the present study was designed to investigate the syndrome of cognitive dysfunction after chronic diseases using a cognitive-behavioral questionnaire in dogs and cats.

Materials and Methods

Animals

The present study was conducted on 20 sick dogs and 20 sick cats and 10 healthy dogs and 10 healthy cats in the hospital of the Faculty of Veterinary Medicine of Tehran University of Science and Research. The studied animals were of similar age (more than 5 years). In the animals of the control group, blood tests (CBC) and biochemical tests were normal and no abnormal findings were observed in the clinical examinations. The diagnosis of sick animals was based on the results of blood tests, biochemical factors, and diagnostic imaging after clinical/physical examinations. Dogs in the patient group with Periodontal Disease (3 cases), Mitral Valve Dysfunction (MVD) (2 cases), Chronic Bronchitis (2 cases), Cushing's Disease (2 cases), Inflammatory Bowel Disease (IBD) (2 cases), Chronic Kidney Disease (CKD) (2 cases) urinary tract infection (UTI) (1 case), irritable bowel syndrome (IBS) (1 case), epilepsy (1 case), breast cancer (1 case), diabetes mellitus (DM) (1 case), hypothyroidism (1 case), and chronic hepatitis (1 case). On the other hand, cats in the disease group included CKD (9 cases), hypertrophic cardiomyopathy (HCM) (3 cases), feline infectious peritonitis virus (FIP) (2 cases), asthma (2 cases), periodontal disease (2 cases), feline immunodeficiency virus (FIV) (1 case), and hyperthyroidism (1 case).

Study protocol

So far, several studies have evaluated and standardized questionnaires of cognitive dysfunction syndrome to diagnose CDS in dogs ([8,9] and cats [7]), and it seems that the evaluation of DISHAAL (which includes disorientation, social interaction, sleep cycle, house soiling, activity, anxiety, and learning and memory) symptoms in dogs and VISHDAAL (which includes

vocalization, social interaction, sleep cycle, house soiling, disorientation, activity, anxiety, and learning and memory) symptoms in cats is the main part of these questionnaires. Each section of the questionnaire contained different questions that were scored in the form of 23 questions. Since the questionnaire is currently the only available method that can consider the behavioral variables based on the personality of each animal, whose owner has the most information about the process of its changes, it is necessary to ensure the design of an accurate questionnaire [3]. Therefore, we tried to examine the cognitive factors in different ways, based on previous questionnaires. Thus, the questions related to each section were asked in different ways to minimize the possibility of information loss. In the present study, each of the behaviors related to the CDS was investigated using a questionnaire and its severity was measured from -2 to +2, indicating a severe decrease, a mild decrease, no change, a mild increase, and a severe increase, respectively. After the identification of the studied animals, the relevant explanations were given to the owners of the animals, and after obtaining their consent, the questionnaires were completed according to their answers.

Statistical analysis

The data were analyzed using IBM SPSS Statistics 22 software (Chicago, IL, USA). Descriptive findings of the studied variables, including indicators such as mean, standard deviation, and frequency, were calculated and reported.

Results

As shown in Figure 1, the amount of sleep changed in 12 dogs in the patient group; two dogs with mitral valve insufficiency and one dog with hypothyroidism had a severe increase in daytime sleepiness. In the control group, only two dogs with mild increases in daytime sleepiness were reported. The amount of social interaction decreased in 14 sick dogs, including one dog with periodontal disease, one dog with mammary cancer, and one dog with chronic hepatitis, on

Table 1: Standard questionnaires of cognitive dysfunction syndrome to diagnose CDS in dogs

Questions	Sig. decrease	Mild decrease	No change	Mild increase	Sig. increase	Never seen
Change in weight						
Appetite						
Drinking						
Time spent grooming						
Time spent sleeping during the day						
Time spent sleeping at night						
Vocalisation at night						
Vocalisation during the day						
Affection with people in the house						
Tolerance of handling						
Aggression towards animals or people						
Wanting to spend time outdoors						
Activity levels/time spent playing						
Tolerance of being left alone						
Tolerance of other animals in the house						
Willingness to jump up or down (including climbing stairs)						
Aimless activity (e.g. pacing, staring into space)						
Repetitive or compulsive behaviour (e.g. grooming, licking inanimate objects)						
Agitation and restlessness						
Passing faeces in house outside litter tray						
Passing urine in house outside litter tray						
Vomiting (including fur balls)						
Diarrhoea						
Constipation						
Vision loss						
Hearing loss						
Hair loss or hair thinning						

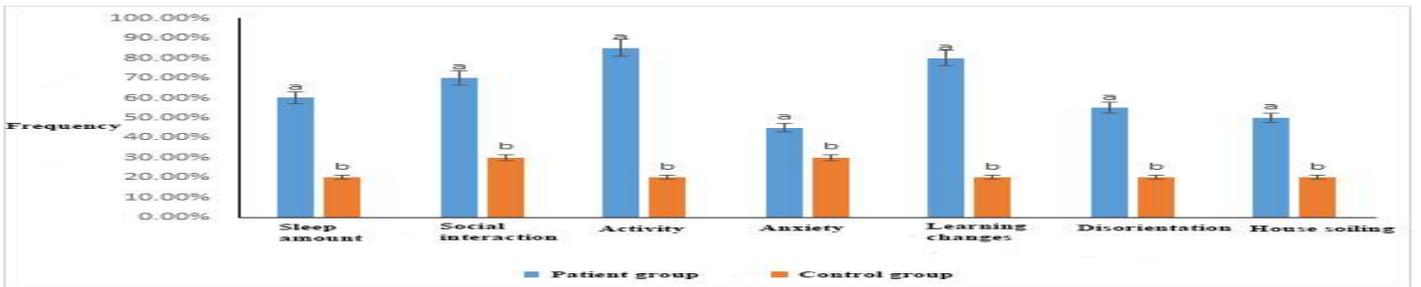


Fig. 1 Changes of different parameters of DISHAAL questionnaire in studied dogs

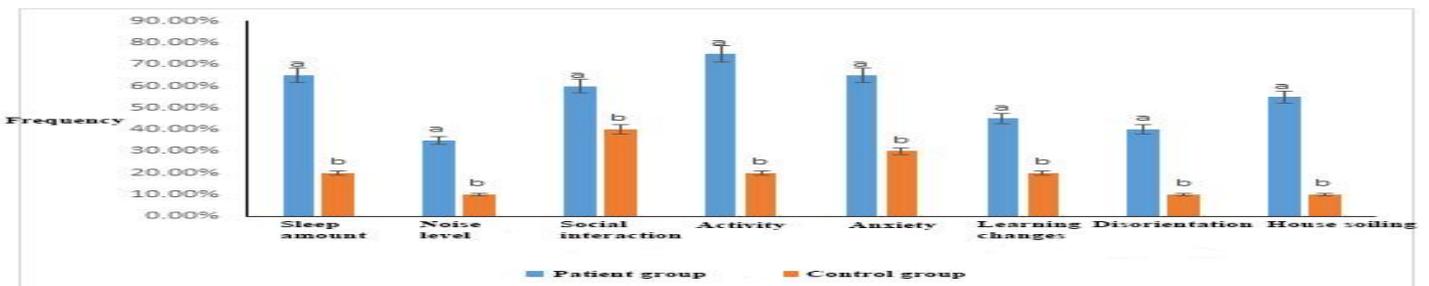


Fig. 2 Changes of different parameters of VISHDAAL questionnaire in studied cats

the other hand, the owners of 3 dogs in the control group reported a mild decrease in social interaction. The amount of activity decreased in 17 sick dogs, of which two dogs with mitral valve insufficiency and one dog with chronic bronchitis had a severe decrease in daily activity. On the other hand, a slight decrease in activity level was observed in two dogs in the control group. Mild anxiety was reported in 9 dogs with underlying disease, while 3 dogs in the control group showed symptoms associated with mild anxiety. A decrease in the implementation of previous training was observed in 16 dogs with underlying disease, including a severe decrease in one dog with chronic hepatitis and one dog with breast cancer. On the other hand, two dogs in the control group showed a mild decrease in this symptom. Spatial perception and orientation were altered in 11 sick dogs, including one dog with chronic hepatitis with a severe decrease in spatial position perception. There was also a slight decrease in this symptom in two control dogs. Household fouling was mildly increased in 10 dogs with underlying disease and mildly increased in only two dogs in the control group.

As seen in Figure 2, sleep was altered in 13 cats with underlying disease, of which one cat (with hyperthyroidism) had a slight decrease, nine had a slight increase, and two cats with CKD and one with HCM had a large increase in the amount of nocturnal sleep. On the other hand, only two cats in the control group showed a slight increase in the amount of sleep. Vocalization was slightly increased in 7 cats with underlying disease, while only one control cat showed a slight increase. A decrease in social interaction was observed in 12 cats with underlying disease, of which 3 cats with CKD showed a severe decrease, while 4 control cats showed a mild decrease in social interaction. Activity was altered in 15 cats with underlying disease, including 4 cats with CKD, 2 cats with HCM, and 1 cat with FIP with a severe decrease and 1 cat with hyperthyroidism with a mild increase. In the control group, only two cats showed a mild decrease in activity. Anxiety-related symptoms were observed in 13 cats with underlying disease, including two cats with CKD with severe increases in anxiety. On the other hand, mild anxiety was observed in only 3 cats in

the control group. A mild reduction in previous training was observed in nine cats with underlying disease, whereas two cats in the control group showed a mild reduction. A decrease in the ability to navigate and perceive spatial position was observed in 8 cats with underlying disease, this change was severe in one cat with CKD, while a mild decrease was observed in one cat in the control group. House soiling was reported as mild in 11 cats with underlying disease, while only one control cat showed this symptom.

Discussion

For two decades, the study of CDS has attracted the attention of researchers due to its many similarities with Alzheimer's disease in humans. On the one hand, the increasing trend of Alzheimer's disease has been such that the number of people suffering from Alzheimer's disease has been announced to be about 55 million people worldwide in 2020, and it is estimated that it will reach 78 million people by 2030 and more than 139 million people by 2050 [10]. On the other hand, the limitations of laboratory models and the high cost of unsuccessful testing of about 190 possible drugs in clinical cases of Alzheimer's disease [11] show the importance of investigating the relationship between CDS and Alzheimer's disease. Therefore, some studies have investigated CDS in dogs [12] and cats [13] as a model to study human Alzheimer's disease. Histopathologic studies of dogs and cats with CDS have shown extensive brain changes similar to those seen in AD, including progressive atrophy of the cerebral cortex and basal ganglia, loss of neurons in specific areas such as Purkinje cells in the cerebellum, enlargement of the lateral ventricles, widening of the cerebral furrows, vascular and perivascular changes, lipofuscin accumulation, amyloid deposition, and tau hyperphosphorylation [3].

As mentioned above, the likelihood of CDS increases with age, but it appears that CDS in dogs and cats is not just a primary disease caused by aging and, like dementia in humans, is divided into primary and secondary types. Human studies have shown the association of various

chronic diseases, including thyroid disease, congestive heart failure, chronic kidney disease, diabetes mellitus, liver disease, cancer, and the use of various medications with cognitive decline and impairment [14]. Nearly 60% of the elderly with a chronic condition have reported some type of impairment to their physician [15], compared with only 25% of older people without a chronic condition [16].

Another body of human research has shown that older people who are hospitalized have higher rates of dementia and cognitive impairment than other older people. In 2009, Sampson et al. showed that 42% of patients hospitalized for medical reasons had dementia. The study also found that the death rate among people with dementia was significantly higher than among others [17]. Another study found that 43% of older people who are hospitalized for medical reasons have cognitive disorders. However, many of them are undiagnosed [18].

Many studies have shown cognitive impairment caused by conditions in populations with CHF [19], CKD [20], DM [21], chronic obstructive pulmonary disease (COPD) [22], hypertension [23], and cancer [24]. Taylor et al. showed that Subjective Cognitive Decline (SCD) is observed in patients with chronic disease (such as CHF, CKD, COPD, stroke, etc.) to a greater extent and intensity than others, so that in the population of people over 65 years of age, cognitive impairment was reported in 10%, 13%, and 21% of those with one, two, and three or more chronic diseases, respectively [25]. Therefore, it seems that the management of chronic diseases plays an important role in reducing cognitive disorders, and the assessment of cognitive status is an essential part of the management process of chronic diseases [26].

Although research on CDS in dogs and cats has not identified disease as an important underlying factor in the occurrence of cognitive dysfunction, the importance of investigating such a relationship seems to have been recognized by researchers in the early part of the last decade. Silva et al. showed that the incidence of CDS symptoms in elderly dogs with Cushing's disease was higher than in the control group, and that these changes were observed particularly in

memory, anxiety, obsessive-compulsive behavior, and depression [27]. Studies have shown that long-term use of corticosteroids affects cognitive levels and causes behavioral changes in dogs [28]. Therefore, it appears that in addition to chronic diseases, long-term use of medications requires monitoring of cognitive levels and related behavioral changes. Human studies have also examined the relationship between Cushing's disease and cognitive decline [29]. One study showed that as the severity of periodontal disease in dogs increased, so did the CDS score, which was determined by evaluating the DISHAAL factors. It has also been found that dogs with CDS have a higher risk of periodontal disease [30]. Previously, periodontal disease has been reported as one of the underlying factors in the onset and progression of Alzheimer's disease in humans [31]. In previous studies examining brain lesions caused by feline immunodeficiency virus (FIV) [32], Azadian and Gunmore used tests based on problem solving and visuospatial working memory to show that older cats with FIV suffer from reduced cognitive function more than young healthy cats, and their visual memory is impaired as opposed to their problem solving ability [33]. Previous studies have also shown that the human immunodeficiency virus (HIV) causes cognitive impairment in infected individuals, with a reported prevalence of 15-64% [34]. As mentioned above, few studies have investigated the syndrome of cognitive dysfunction in underlying diseases in dogs and cats. The present study, in agreement with previous studies, shows that it is important to investigate factors related to cognitive function in underlying diseases. This issue becomes important because most underlying diseases occur in old age, which may itself lead to more severe cognitive impairment.

Neuropsychological testing examines learning and memory related disorders that may be involved in CDS. However, because such tests require trained personnel, standard methodology, equipment necessary for cognitive assessment, sufficient time, and the continuous presence of the animal, they are not considered a suitable option for the clinical diagnosis of CDS [3]. Therefore, the use of a questionnaire seems

to be the most practical method to clinically evaluate Cognitive Function Deficiency Syndrome.

Conclusion

In the present study, we evaluated CDS using a questionnaire in dogs and cats with underlying disease compared to healthy cases. According to the results, there was a significant difference in activity and performance of previous training in dogs with underlying disease compared to the control group. Also, the greatest differences between healthy and sick cats included changes in activity, amount of sleep, and litter box fouling. On the other hand, in the present study, anxiety in dogs and changes in social interaction in cats showed the least difference between healthy and diseased groups. The importance of this issue is that cognitive disorders affect the quality of the human-animal relationship and the well-being of pets, and in the case of such disorders following disease, the comorbidities also need to be managed. Considering the importance of cognitive status in daily life and the quality of communication between the pet and its owner, it is recommended that specialists working in the field of small animal internal medicine pay attention to the monitoring of behaviors related to CDS, using relevant questionnaires in cases of chronic diseases.

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Not applicable

Conflict of interest

Authors declare that there is no conflict of interests.

Ethical approval

For this type of study, formal consent is not required.

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