Applied Animal Behaviour Science 171 (2015) 138–145

Contents lists available at ScienceDirect

Applied Animal Behaviour Science

journal homepage: www.elsevier.com/locate/applanim

Assessment of severity and progression of canine cognitive dysfunction syndrome using the CAnine DEmentia Scale (CADES)

Aladar Madari[a,1], Jana Farbakova[a,1], Stanislav Katina[b,1], Tomas Smolek[c], Petr Novak[c], Tatiana Weissova[a], Michal Novak[c], Norbert Zilka[c,d,*]

[a] University of Veterinary Medicine and Pharmacy, Komenskeho 73, Kosice, Slovak Republic
[b] Institute of Mathematics and Statistics, Masaryk University, Kotlarska 2, Brno, Czech Republic
[c] Institute of Neuroimmunology, Slovak Academy of Sciences, Dubravska cesta 9, Bratislava, Slovak Republic
[d] Institute of Neuroimmunology, n.o., Dvorakovo nabrezie 45, Bratislava, Slovak Republic

ARTICLE INFO

Article history:
Received 11 February 2015
Received in revised form 21 August 2015
Accepted 23 August 2015
Available online 31 August 2015

Keywords:
Canine cognitive dysfunction syndrome
Canine dementia
Mild cognitive impairment
Annual conversion rate
Staging

ABSTRACT

Cognitive dysfunction syndrome (CDS) represents a group of symptoms related to the aging of the canine brain. These changes ultimately lead to a decline of memory function and learning abilities, alteration of social interaction, impairment of normal housetraining, changes in sleep–wake cycle and general activity. The initial symptoms gradually worsen over time. Despite extensive research, little is known about the staging and phenotypic variability of CDS. We have analysed more than 300 dogs; 215 were selected for the study. We developed a rating scale, CADES – canine dementia scale – containing 17 items distributed into four domains, related to changes in dogs' behaviour: spatial orientation, social interactions, sleep–wake cycles and house soiling. Using CADES, we identified various stages of cognitive impairment: mild cognitive impairment, moderate cognitive impairment and severe cognitive dysfunction. Further, we found that the rate of conversion at 6-months follow-up of normal ageing to mild cognitive impairment was 42%, while conversion rate of mild to moderate cognitive impairment was 24%. At twelve months, the conversion rates almost doubled to 71.45% and 50%, respectively. These findings showed that CADES can be used as a predictor of conversion from normal ageing to mild, and from mild to moderate cognitive impairment. In regards to the four behavioural domains we found that impairment in social interaction was frequently present in dogs with mild cognitive impairment (40%), 67% of dogs with moderate cognitive impairment had affected social interaction and sleep–wake cycles. For severe cognitive dysfunction, the majority of dogs displayed impairment in all four domains, while other two subgroups showed impairment only in three domains. In this study, we have assessed the psychometric properties of the CADES scale, and validated it as a screening tool for CDS. The scale is also suitable for long-term assessment of the progression of cognitive impairment in canines, and potentially as efficacy readout for treatments.

1. Introduction

Cognitive dysfunction syndrome (CDS) represents a serious health problem for aged dogs. It has been estimated that there are more than 30 million senior and geriatric dogs over the age of seven years in the USA and over 15 million in Europe (Bosch et al., 2012). The prevalence of CDS is extremely high, ranging from 28% in 11–12 years old dogs to 68% in 15–16 years old dogs (Neilson et al., 2001). Several prevalence studies have identified that a substantial population of pet dogs are at risk to develop CDS (Azkona et al., 2009; Neilson et al., 2001; Osella et al., 2007). However, a serious impairment of cognitive functions caused by a dementing process has to

Abbreviations: CADES, canine dementia scale; CD, canine dementia; CDS, cognitive dysfunction syndrome; DISHA, disorientation, interaction changes, sleep–wake disturbances, house soiling and activity changes; MiCI, mild cognitive impairment (canine); MCI, human mild cognitive impairment; MMSE, Mini-Mental State Examination; MoCI, moderate cognitive impairment (canine); NA, normal ageing.

* Corresponding author. Tel.: +421 907756744; fax: +421 254774276.
E-mail addresses: aladar_madari@yahoo.com (A. Madari), jana.farbakova@gmail.com (J. Farbakova), stanislav.katina@gmail.com (S. Katina), tomas.smolek@savba.sk (T. Smolek), petr.novak@savba.sk (P. Novak), weissova@uvlf.sk (T. Weissova), michal.novak@savba.sk (M. Novak), norbert.zilka@savba.sk (N. Zilka).

[1] These authors contributed equally to this work.

http://dx.doi.org/10.1016/j.applanim.2015.08.034
0168-1591/

be distinguished from a simple and mild decrease in psychomotor activity that is caused by general ageing of the organism (Osella et al., 2007).

It has been proposed that CDS represents the progressive neurodegenerative disorder of elderly dogs (Landsberg and Araujo, 2005), characterized by cortical atrophy, ventricular widening, meningeal calcification, demyelination, increased lipofuscin accumulation and apoptotic bodies, axonal degeneration, neuronal loss and presence of amyloid beta plaques in various brain areas (Cummings et al., 1996; Borras et al., 1999; Head et al., 2008). However, it is important to note that key features of human Alzheimer's disease neurodegeneration – such as tau neurofibrillary lesions – are usually not present in the senior canine brain (Davis and Head, 2014).

Typical behavioural changes of CDS include signs of spatial disorientation, an alteration of social interaction, impairment of normal housetraining, changes in the sleep–wake cycle and general activity (Milgram et al., 1994; Cummings et al., 1996) as well as decline of memory function and learning abilities (Landsberg and Araujo, 2005; Azkona et al., 2009; Salvin et al., 2011). Traditionally the clinical signs are described by the acronym DISHA–disorientation, interaction changes, sleep/wake disturbances, house soiling and activity changes (Landsberg et al., 2012).

Finally, it is not known whether behavioural problems of aged dogs represent the continuation or the exacerbation of problems acquired earlier in life, or whether they are characteristic features of age-related dementia.

Rating scales are essential tools for CDS diagnosis, staging, assessment and careful monitoring of the disease symptoms as well as for evaluation of the efficacy of therapeutic strategies. Several rating scales have been developed during the last decade e.g. ARCAD–Evaluation of Age-Related Cognitive and Affective Disorders, CCDR–the Canine Cognitive Dysfunction Rating scale etc. (Colle et al., 2000; Pugliese et al., 2005; Osella et al., 2007; Salvin et al., 2011). An ideal rating scale should fulfil several criteria: (1) easy and quick to administer for an experienced clinician, (2) validated for canine cognitive dysfunction syndrome, (3) covers the CDS-relevant areas of cognition and behaviour, (4) applicable to all CDS severity stages and (5) able to monitor disease progression. The scales should undergo evaluation of their psychometric properties before use. Although a variety of rating scales for CDS (in-person or telephonic) have been developed to monitor cognitive decline in dogs, they did not undergo a proper psychometric validation, therefore their psychometric properties are largely unknown, and their validity in diagnosis, monitoring disease severity or disease progression is limited.

Moreover, there are some practical limitations of the currently used rating scales for CDS. First, the evaluation scheme of published scales is usually based either on the rate of deterioration of cognitive functions or on the frequency of abnormal behaviour. However, these approaches may not be sensitive enough for the early cognitive changes characteristic for CDS. Early detection of cognitive impairment greatly increases the chances for successful treatment (Osella et al., 2007). Second, a telephone-based or on-line cognitive assessment approach could be influenced by subjective evaluation of pet owners, who can either overestimate or underestimate the severity of the disease (Neilson et al., 2001; Azkona et al., 2009; Salvin et al., 2011). We can conclude that there is still a need for better instruments, which are more sensitive to disease staging or changes over time.

In view of the aforementioned points, we developed a validated rating scale for CDS, CAnine DEmentia Scale. It allowed us to assess the severity of disease, identify various stages of the disease and to measure the progression of decline in the follow-up study.

2. Methods

2.1. Clinical examination

In total, 300 dogs above 8 years of age visiting the veterinary clinic for regular vaccination, parasite treatments and various health complaints were included in the study. 85 dogs were ruled out because of other medical causes. 56 dogs were classified as cognitively normal, 159 dogs displayed signs of cognitive impairment. The study population included dogs aged 8–16.5 years, 116 males and 99 females of different breeds and body weight. All pet owners were invited to participate on the follow-up study. For the analysis of the longitudinal measurement, 64 dogs returned for a second assessment after six months and 17 for a third assessment after 12–14 months. To rule out medical causes of behavioural decline, as proposed by Landsberg et al. (2012), all dogs used for this study were assessed by neurological, orthopaedic, X-ray, ultrasound and ECG examinations as well as blood and urine analyses. Dogs found to have systemic illness that could interfere with their cognitive status were excluded from the study.

We obtained fully-informed consents from pet owners. We adhered to a high standard of veterinary care to ensure that all studied dogs received the best care available.

2.2. Behavioural examination

The health status, behavioural changes and neurological abnormalities were evaluated by veterinarians (AM, JF). Behavioural investigation included observation of geriatric dogs by an experienced investigator and collection of information provided by pet owners. The investigator was pro-active in asking about behavioural abnormalities to identify even subtle signs that often go unrecognized by pet owners.

To quantify cognitive decline in dogs, we designed a questionnaire with a novel scoring system (Table 1) – CAnine DEmentia Scale (CADES). The questionnaire (Table 1) was adapted and modified from the questionnaires proposed by Osella et al. (2007) and Salvin et al. (2011). It originally contained 17 items. They were distributed into four domains, related to the type of changes in the dogs' behaviour: A – spatial orientation, B – social interactions, C – sleep–wake cycles and D – house soiling. The frequency of abnormal behaviour was assessed for each item. We used a 5-point scale for easy evaluation of behaviour frequency; 0 points – abnormal behaviour of the dog was never observed, 2 points – abnormal behaviour of the dog was detected at least once within the last 6 months, 3 points – abnormal behaviour appeared at least once per month, 4 points – abnormal behaviour was seen several times per month, 5 points – abnormal behaviour was observed several times a week. Then, the scores from each domain were added up to obtain the quantitative final score that reliably reflected the quantitative evaluation of cognitive decline. The questionnaire was filled out by veterinarians (AM, JF) through interview with the dog owner.

In order to validate information obtained from pet owners or identify unreported clinical signs, we investigated the full spectrum of neurobehavioural symptoms including apathy, anxiety, staring blankly, confused or aimless walking, excessive vocalization, aggression and anxiety symptoms, and signs of compulsive and stereotyped behaviour etc. Furthermore, we addressed response to various commands to test responsiveness of tested dogs, observed a dog's interaction with known (owner and family members) and unknown people (clinical staff) or with other dogs/animals. Finally, we monitored the dogs' behaviour during handling.

2.3. Data analysis

Statistical analyses were performed with R software (R Development Core Team, 2014). Due to the presence of outliers,