



The Canine Cognitive Dysfunction Syndrome: rating scales

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Abstract: “Aging” represents the broad spectrum of changes associated with the passage of time. Among domestic animals, dogs have been extensively studied as a model for neurodegenerative human diseases due to their similarities, especially in terms of pathological alterations. Canine Dysfunction Syndrome (CDS) is still under investigation from diagnostic, clinical, anatomopathological, and therapeutic perspectives. Consequently, numerous authors have developed and validated various rating scales to assess geriatric animals for early and non-invasive diagnosis of CDS. The objective of this review is to offer a comprehensive overview of existing rating scales and to discuss their strengths and limitations.

Key Words: Canine Cognitive Dysfunction Syndrome; aging; dog.

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Introduction

Aging and senescence represent fundamental processes in the life cycle of animal species, encompassing both chronological and physiological aspects of getting older (Hassan, 2022; Coraduzza et al., 2023). While often used interchangeably, these terms hold distinct etymological roots and conceptual nuances. “Aging” represents the broad spectrum of changes associated with the passage of time, encompassing both chronological markers and the myriad physiological alterations that unfold over the lifespan. Conversely, “senescence” delves deeper into the cell, spotlighting the gradual decline in cellular functionality and resilience that accompanies the aging process.

Age-related neurodegenerative diseases in humans

Age-related neurodegenerative diseases bring about a decline in cognitive and motor functions (Mihevc et al., 2019). While commonly associated with older age, these diseases can strike individuals at any stage of life, imposing significant burdens on patients, caregivers, and society. Alzheimer’s disease (AD) is a prominent example, characterized by the gradual build-up of harmful proteins in the brain, leading to cognitive decline (Hardy et al., 2002). Similarly, Parkinson’s Disease (PD) leads to motor symptoms like tremors and stiffness due to the loss of specific brain cells (Obeso et al., 2017). Amyotrophic lateral sclerosis (ALS) affects motor neurons, resulting in muscle weakness and paralysis (Brown et al., 2017). Spinocerebellar ataxias (SCAs) encompass various hereditary disorders affecting movement and coordination (Sullivan et al., 2019). Additionally, age-related depression and cerebrovascular diseases contribute to neurodegeneration, impacting mental and physical health (Djernes, 2006). These diseases share a common thread of neuroinflammation, driven by the immune system, which worsens neuronal damage (Franceschi et al., 2007).

Canine Cognitive Dysfunction Syndrome

Canine Cognitive Dysfunction Syndrome (CDS) reflects the shared vulnerabilities between humans and their dogs, revealing the complexities of aging, neurodegeneration, and cognitive decline (Ciurli et al., 2024). Often called “canine dementia,” CDS affects older dogs with a gradual onset of neurobehavioral symptoms similar to those seen in humans. These symptoms include changes in social behavior, disorientation, and anxiety, causing distress and confusion in affected dogs. However, distinguishing CDS from typical age-related changes poses challenges, as symptoms overlap with those observed in healthy aging dogs. Understanding canine cognition and behavior, along with specific diagnostic tests, is essential for accurate diagnosis (Schutt et al., 2015). While age-related cognitive decline is common in dogs, not all progress to full-blown CDS, highlighting the influence of genetic, environmental, and individual factors. Despite the prevalence of cognitive decline, only a small percentage of affected dogs receive veterinary attention, indicating a lack of recognition and diagnosis of CDS in clinical practice (Landsberg et al., 2010).

Alzheimer's Disease and Cognitive Deficiency Syndrome

The strong similarities between CDS and AD provide valuable insights into the shared mechanisms of neurodegeneration in dogs and humans (Ciurli et al., 2024). Both conditions show similar neuropathological features, such as changes in brain structure like widening of cerebral sulci, ventricular enlargement, and cortical atrophy in key brain areas like the cortex, hippocampus, and limbic system (West et al., 2000; Toepper, 2017; Siwak-Tapp et al., 2008). Additionally, clinical signs of CDS closely resemble those seen in AD, including gradual cognitive decline, changes in behavior, and increased anxiety (Bature et al., 2017). The progression of both diseases follows a similar pattern, starting with a preclinical phase before advancing to overt dementia (Toepper, 2017). Motor dysfunction is also common in both conditions, with dogs affected by CDS showing gait abnormalities and muscle weakness similar to human Parkinson's disease (Mihevc et al., 2019). Furthermore, neuroinflammation plays a role in both diseases, suggesting a shared inflammatory process driven by the immune system. These shared features highlight the potential of studying CDS in dogs to better understand neurodegeneration and develop treatments that could benefit both canine and human populations.

CDS rating scales

The challenges posed by CDS in aging dogs highlight the necessity for reliable assessment tools to facilitate early diagnosis and effective management (Ciurli, 2024). CDS Scales, standardized tools designed for the evaluation and quantification of cognitive dysfunction in aging dogs (Maddari et al., 2015), aim to offer an objective and comprehensive assessment of various behavioral changes associated with canine cognitive decline. These scales encompass a series of easily administered tests, including evaluations of spatial orientation, social interaction, and response to specific stimuli. Such scales enable veterinary surgeons to efficiently evaluate cognitive function during routine examinations, thereby facilitating early detection and intervention in dogs experiencing cognitive decline. Several screening questionnaires have been developed for assessing canine cognitive decline:

- Pugliese et al. (2005) introduced a rapid behavioral test assessing CDS severity, correlating each disease stage with modifications in cerebral energy metabolism.
- Rofina et al. (2006) analyzed previous questionnaires, investigating correlations between scores and various cerebral parameters in geriatric dogs.
- Osella et al. (2007) amalgamated previous questionnaires to explore CDS clinical sign prevalence in an elderly dog population.

Salvin et al. (2011) developed the Canine Cognitive Dysfunction Rating scale (CCDR), identifying key behavioral signs based on a survey of over 900 dogs aged 8 years or older.

Madari et al. (2015) devised the CADES for objective cognitive impairment assessment in 215 dogs aged 8 years and older, aiming to create a tool free from owner bias, in contrast to CCDR.

A differentiation of these scales is based on their specific purpose:

1. Pugliese et al. (2005) and Rofina et al. (2006), developed two scales to evaluate the association between common signs of CDS, such as disorientation, hypoactivity, and house-soiling, with measurable neurophysiological changes.
2. Osella et al. (2007) built up a questionnaire with scales from the literature to assess the prevalence of signs of CDS among elderly dogs and follow-up with the patients chosen to evaluate the results achieved by administering a nutraceutical.
3. Salvin et al. (2011) and Madari et al. (2015) aimed to elaborate a scale to assess behavioral changes consistent with CDS, and follow-up the clinical cases.

Pugliese et al. (2005)

The study involved a comprehensive examination of 25 dogs at the veterinary hospital Ars Veterinaria in Barcelona, Spain. A cognitive evaluation was conducted using a test adapted from existing veterinary assessments, employing 16 items that covered various behavioral traits. This test revealed three distinct groups of dogs categorized by age and cognitive status: young controls, those with light cognitive deficits, and those with severe cognitive deficits.

Simultaneously, cerebrospinal fluid (CSF) analysis provided insights into biochemical parameters related to energy metabolism and ionic movements, uncovering notable differences between the groups. The severe cognitive deficit (SCD) group exhibited increased variability in glucose concentration and higher levels of pyruvate, lactate, and potassium. Moreover, the study introduced a novel concept by assessing the ratio of lactate to pyruvate as a potential marker of cognitive impairment. The results indicated a marked increase in this ratio in the SCD group, whilst no significant difference was observed in the light cognitive deficit group.

The discussion section delves into the refinement of the cognitive test by removing 7 items with ambiguous owner evaluations, resulting in a more effective tool for detecting cognitive deficits. Items such as eating, barking, drinking, and self-control were straightforward to comprehend but posed challenges for owners during evaluation. The assessment of aggression proved intricate due to owners hesitating to acknowledge this behavior. Similarly, auto-stimulatory and learned social behavior items presented difficulties in understanding and evaluation for the owners.

The conclusions propose the validated test as a time-efficient tool for discriminating between varying degrees of cognitive impairment in dogs. The parallel increase in lactate and pyruvate levels in CSF is identified as reflective of severe cognitive impairment. The article calls for further studies to determine the applicability of these findings in differentiating cognitive deficits in human patients.

Rofina et al. 2006

The research presents a comprehensive study investigating cognitive dysfunction in dogs and its potential correlation with pathological changes in the brain. The experimental procedure involved the examination of the brains of 30 dogs of various breeds. 14 dogs were females, of which 6 were neutered; 16 dogs were males, of which 8 were neutered. The age range was 0.1 - 19.2 years, with a mean age of 12.03 years. The causes of death/euthanasia were various, but for 19 dogs were related to behavioral changes or aggression. The study collected data on behavior through three questionnaires and conducted necropsies to rule out physical causes for observed behavioral changes.

Additionally, blood tests were performed to assess kidney and liver function, along with glucose levels.

The brains underwent detailed analysis for pathological lesions, including cortex atrophy, amyloid deposition, lipofuscin accumulation, demyelination, and oxidative damage. Notably, the study revealed correlations between cortical atrophy and dementia scores, suggesting a potential link between the loss of cortical tissue and behavioral changes in older dogs. The same relation was suggested for other pathological features such as amyloid deposits and lipofuscin, while oxidative damage seemed to be linked to advanced stages of dementia.

The article delves into the intricacies of canine cognitive dysfunction, emphasizing the necessity for a balanced questionnaire to accurately diagnose behavioral changes. Acknowledging the potential influence of various factors on behavior, the study highlights the need for comprehensive diagnostic criteria to ensure accurate assessments.

Osella et al. 2007

The study conducted by Osella et al. in 2007 aimed to investigate CDS in geriatric dogs and evaluate the therapeutic effects of a nutraceutical called Senilife® (the latest won't be debated further). The methods employed in this research involved a comprehensive survey of 124 geriatric dogs (over 7 years of age) that were not admitted for behavioral complaints. The owners were interviewed to provide information about behavioral signs related to CDS. The study categorized these signs into various groups, such as disorientation, socio-environmental interaction, sleep-wake cycles, house soiling, and general activity. Additionally, physical examinations, laboratory assessments, and sensory evaluations were performed, and further diagnostic tests or consultations were recommended when necessary.

Out of the 124 dogs, 22 were excluded for primary organ failure and/or neurological signs, or because they have been living with the owner for less than 1 year. Out of the remaining 102 subjects:

- 27 dogs expressed aging without any signs of CDS,
- 42 dogs had alterations in 1 category. 25 dogs had alterations in socio-environmental interaction, 16 in sleep-wake cycles, and 1 in house soiling. 18 dogs had general activity changes with 12 dogs being hypoactive. 15 dogs were females, 10 of which were neutered, 15 were males, 2 of which were castrated, and the age range was 8–17 years, with a mean age of 12.61.
- 26 dogs had signs in 2 categories. 13 dogs had alterations in socio-environmental interaction, 16 in sleep-wake cycles, and 2 in house soiling, 20 dogs had general activity changes, with 8 dogs being hypoactive. 13 dogs were females, 8 of which were neutered, 13 were entire males, and the age range was 9–19 years, with a mean age of 12.61.
- 5 dogs had signs in 3 categories. 2 dogs had alterations in socio-environmental interactions, 2 in sleep-wake cycles, 2 in disorientation, and 1 in house soiling. All the dogs showed marked hypoactivity. All the dogs were females, 4 of which were spayed. 2 dogs were 12 years old, while the others were each 13, 14, and 15 years old.
- 2 dogs had signs in all 4 categories. 1 was an 18-year-old female, and 1 was a 16-year-old male.

Therefore, 75 out of 102 dogs had signs referring to CDS.

The document delved into the prevalence of CDS in veterinary medicine and the challenges of early detection. It drew comparisons with human medicine, where standardized neuro-psycho-physiological evaluation scales are used. The authors noted that the questionnaire employed in their study was not a validated scale for a specific diagnosis of CDS but could serve as part of a preliminary global geriatric screen for the condition. The questionnaire was adapted from the research of Kiatipattanasakul et al. (1996), Colle et al. (2000), Pageat (2001), Landsberg et al. (2003), and Pugliese et al. (2005). The article also addressed the need for further research to correlate behavioral, emotional, and cognitive signs with biological markers and post-mortem brain lesion analysis.

Salvin et al. 2011

The study employed a comprehensive approach to investigating the prevalence of CDS in aging dogs, aiming to structure a reliable diagnostic questionnaire. The research involved a survey distributed both online and in hard copy formats to owners of dogs over 8 years of age. The survey collected data on various behavioral aspects, including eating and drinking, changes in activity levels, house-soiling, aggression, and phobias. Owners were asked to report the frequency and changes in these behaviors over the preceding six months. The study aimed to create a reliable diagnostic tool able to identify age-related cognitive impairment in dogs, by analyzing a range of behavioral indicators.

Each item was assigned a score between 1 and 5 depending on the frequency of the observed behavior: 1 for never, 2 for once a month, 3 for once a week, 4 for once a day, and 5 for more than once a day. Dogs with a score higher than 50, were defined as affected by cognitive deficiency.

A total of 957 eligible responses were obtained from owners coming from 11 different countries (mainly Australia, the United States of America, New Zealand, and the United Kingdom), with a mean age of 11 years and 9 months, for the surveyed dogs. The prevalence of CDS in the entire sample was estimated at 12.0%, with rates increasing exponentially with age: 4.4% of 8–10-year-olds, 3.4% of 10–12 year-olds, 18.6% of 12–14 year-olds, and 31% of dogs >14 years. Rates of CDS were similar in males (entire 13.6%; neutered 10.8%) and females (entire 9.7%; neutered 12.7%).

The study developed a Canine Cognitive Dysfunction Rating (CCDR) scale, comprising 13 behavioral items that were observed in 80% of dementia cases, diagnosed by veterinary surgeons. The CCDR scale demonstrated high diagnostic specificity, with a peak of 90% in severe cases of CDS. Indeed, the research aimed to develop a scale able to diagnose CDS rather than predict it or discern it with an “elder behavior”.

One crucial aspect highlighted in the research (already mentioned in chapter 2.1.2) is the under-diagnosis of CDS in aging dogs. The authors stress the common misconception among owners that neurobehavioral changes in older dogs are a normal part of aging, leading to low presentation rates.

The author emphasizes the scale’s potential in early diagnosis, allowing for timely intervention and improved management of CDS. However, a combination of the CCDR scale and veterinary assessment is proposed as a definitive and standardized method for diagnosing CDS in veterinary practice.

In conclusion, this approach hopes to serve as a valuable tool for companion dogs, contributing to the understanding of CDS as a naturalistic model of human AD.

	Never	Once a month	Once a week	Once a day	> Once a day	Score
How often does your dog pace up and down, walk in circles and/or wander with no direction or purpose?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
How often does your dog stare blankly at the walls or floor?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
How often does your dog get stuck behind objects and is unable to get around?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
How often does your dog fail to recognise familiar people or pets?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
How often does your dog walk into walls or doors?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
How often does your dog walk away while, or avoid, being patted?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
	Never	1-30% times	31-60% times	61-99% times	Always	
How often does your dog have difficulty finding food dropped on the floor?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
	Much less	Slightly less	The same	Slightly more	Much more	
Compared with 6 months ago, does your dog now pace up and down, walk in circles and/or wander with no direction or purpose?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
Compared with 6 months ago, does your dog now stare blankly at the walls or floor?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
Compared with 6 months ago, does your dog urinate or defecate in an area it has previously kept clean (if your dog has never house-soiled, tick 'the same')?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
Compared with 6 months ago, does your dog have difficulty finding food dropped on the floor?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	Multiply by 2 =
Compare with 6 months ago, does your dog fail to recognise familiar people or pets?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	Multiply by 3 =
	Much more	Slightly more	The same	Slightly less	Much less	
Compared with 6 months ago, is the amount of time your dog spends active?	<input type="checkbox"/> =1	<input type="checkbox"/> =2	<input type="checkbox"/> =3	<input type="checkbox"/> =4	<input type="checkbox"/> =5	=
0-39 = Normal 40-49 = At risk 50+ = CCD					Total	=

Image: Canine Cognitive Dysfunction Rating (CCDR), Salvin et al. (2011).

Madari et al. 2015

The study focuses on the development and validation of a rating scale for CDS. The authors address the limitations of existing evaluation schemes for cognitive functions in dogs, highlighting the need for more sensitive instruments to detect early cognitive changes characteristic of CDS. They emphasize the importance of early detection in increasing the chances of successful treatment. To address these concerns, the researchers developed the Canine Dementia Scale (CADES), a questionnaire designed to assess the severity of the disease, identify various stages, and measure the progression of decline over time. The scale was adapted from the previous questionnaires proposed by Osella et al. (2007) and Salvin et al. (2011).

The researchers included 300 dogs above 8 years of age in their sample, visiting the veterinary clinic for vaccinations, parasitological treatments, and common health complaints. To rule out any potential confounding factor, every dog underwent clinical, neurological, orthopedic, X-ray, ultrasound, and ECG examinations as well as blood and urine analyses. A behavioral investigation was

conducted by an experienced professional, and information was collected from pet owners. The scoring system of CADES covered four domains related to changes in behavior: spatial orientation (Domain A), social interactions (Domain B), sleep-wake cycles (Domain C), and house soiling (Domain D). The scale was employed to quantify cognitive decline in dogs.

The authors present the classification of dogs into different cognitive states based on CADES scores: Normal Ageing (NA), Mild Cognitive Impairment (MiCI), Moderate Cognitive Impairment (MoCI), and Severe Cognitive Impairment or Canine Dementia (CD). The study meticulously provides detailed demographic information for each cognitive group, including gender, neuter status, weight, and age range. Among the 56 dogs classified as experiencing Normal Aging (NA), 30 were females, 26 were males, 43 were neutered, and 13 were intact. The age range for this group was 8–13 years, with a mean age of 9.29. In the Mild Cognitive Impairment (MiCI) group, consisting of 80 dogs, 37 were females, 43 were males, 64 were neutered, and 16 were intact, with an age range of 8–14 years and a mean age of 10.15.

The Moderate Cognitive Impairment (MoCI) group, comprising 49 dogs, had 19 females, 30 males, 38 neutered, and 11 intact, with an age range of 8–16.5 years and a mean age of 12.25. The Severe Cognitive Impairment or Canine Dementia (CD) group, with 49 dogs, included 13 females, 17 males, 22 neutered, and 8 intact, with an age range of 9–17 years and a mean age of 13.8.

CADES is the only scale, among the ones mentioned in the dissertation, that aims to differentiate between the cognitive states. For NA, the scores ranged up to 7 points. In MiCI, the scores were between 8 and 23 points, while for MoCI, the range was 24–44 points. The CD group exhibited CADES scores higher than 45 points.

The study explored the phenotypic variability of the cognitive dysfunction syndrome in aged dogs, identifying the domains most commonly affected in each cognitive state. The distribution of impaired domains in each cognitive state was as follows: In the MiCI group, 40% of dogs had impaired Domain B, 12.5% had impaired Domain C, and only 5% displayed impairment of both B and C domains. For the MoCI group, 67% of dogs showed impairment in B and C domains, 8% in A and B domains, and 8% in A, B, and C domains. In the CD group, 67% demonstrated impairment in all four domains, 13% in B, C, and D domains, and 13% in A, B, and C domains.

The study also investigated the rate of conversion from normal aging to mild cognitive impairment and from mild cognitive impairment to dementia over a 12-14-month period. The conversion rate from normal aging to mild cognitive impairment was 42%, while the conversion rate from mild to moderate cognitive impairment was 24%. Notably, 85% of dogs suffering from MoCI remained stable for 6 months. In the 12–14-month follow-up, 71.4% of initially classified NA dogs were diagnosed with MiCI, and 50% of originally MiCI subjects converted to MoCI. Intriguingly, dogs that converted from MiCI to MoCI within one year obtained more than 10 points in the first testing session (12–21 points). Importantly, none of the initially cognitively normal dogs deteriorated to dementia over one year.

To conclude, the authors emphasize the sensitivity of the scale to early cognitive changes, making it a valuable tool for both diagnosis and monitoring of cognitive decline in dogs. The phenotypic variability findings underscore the complexity of CDS in dogs, with social interactions and sleep-wake cycles being the most commonly affected domains.

Domain	Item
A. Spatial orientation	1. disorientation in a familiar environment (inside/outside)
	2. to recognize familiar people and animals inside or outside the house/apartment
	3. abnormally respond to familiar objects (a chair, a wastebasket)
	4. aimlessly wandering (motorically restless during day)
	5. a reduced ability to do previously learned task
	6. changes in interaction between man/dog, dog/other dog (playing, petting, welcoming)
B. Social interaction	7. changes in individual behavior of dog (exploration behavior, play, performance)
	8. response to commands and the ability to learn new task
	9. irritable
	10. expression of aggression
C. Sleep-wake cycle	11. abnormally responds at night (wandering, vocalization, motorically restless)
	12. switch over from insomnia to hypersomnia
	13. eliminate at home at random locations
	14. eliminate in its kennel or sleeping area
D. House soiling	15. changes in signalization for elimination activity
	16. eliminate indoors after a recent walk outside
	17. eliminate at uncommon locations (grass, concrete)
Total score (A + B + C + D) = 0 - 95	
Clinical stage:	
- Normal aging (Score 0–7),	
- Mild cognitive impairment (8–23),	
- Moderate cognitive impairment (24–44),	
- Severe cognitive impairment (45–95)	

Canine Dementia Scale (CADES):

Frequency: 0 points – abnormal behaviour of the dog was never observed, 2 points – abnormal behaviour of the dog was detected at least once in the last 6 months, 3 points – abnormal behaviour appeared at least once per month, 4 points – abnormal behaviour was seen 2–4 times per month, 5 points – abnormal behaviour was observed several times a week, Madari et al. (2015).

Discussion

Analysis and methodologies of previous studies

The effectiveness of scales in assessing CDS varies, each presenting strengths and limitations. This is also due to the different purposes defined in each study. Pugliese et al.'s scale (2005) offers an interesting insight into CDS severity through CSF analysis, correlating biochemical parameters with cognitive impairment. However, the study's limitation is its small subject size, involving only 25 dogs. The reliance on CSF analysis, while informative, may not be practical for routine clinical use due to the invasive nature of the procedure and associated costs. Despite these limitations, the emphasis on biochemical markers adds valuable information to the understanding of cognitive impairment.

Rofina et al.'s scale (2006), which correlates cognitive dysfunction with pathological changes in the brain, faces challenges with a relatively small subject pool of 30 dogs. The study's strength lies in its exploration of neurobiological correlations, shedding light on the intersection of behavioral symptoms and brain pathology. However, the limited number of subjects raises concerns about the representativeness of the findings for the broader population of aging dogs with cognitive dysfunction.

Salvin et al.'s CCDR (2011), despite its extensive subject sample of over 900 dogs aged 8 years or older, relies on a questionnaire. The subjective nature of owner responses introduces a potential source of bias, impacting the accuracy of the scale. While providing a broad overview, its effectiveness in precisely assessing cognitive states may be limited compared to more objective measures. The reliance on owner observations might not fully capture the subtleties of cognitive decline, especially in cases where owners may not recognize or report certain behavioral changes accurately.

Madari et al.'s CADES (2015) stands out for its meticulous methodology, involving a diverse set of examinations, including blood and urine analyses, clinical, neurological, orthopedic, X-ray, ultrasound, and ECG examinations. This comprehensive approach ensures a thorough assessment of cognitive decline in aging dogs, covering domains such as spatial orientation, social interactions, sleep-wake cycles, and house soiling. The inclusion of 215 dogs aged 8 years and older adds statistical robustness to the findings, allowing for a nuanced classification of cognitive states. The study's focus on the rate of conversion between different cognitive states over a 12–14-month period emphasizes the scale's sensitivity to early cognitive changes, further validating its utility for both diagnosis and monitoring.

In comparison, while each scale contributes to our understanding of CDS, scales like CCDR, Pugliese's, and Rofina's, provide valuable insights, but face limitations in terms of reliance due to questionnaires or small subject sizes, impacting their overall effectiveness. Moreover, Pugliese and Rofina's studies were not focused on validating a diagnostic method. Indeed, the aim was to examine possible associations between behavioral symptoms and neurological clinicopathological signs. In contrast, CADES appears to be a more comprehensive and objective tool, offering a detailed assessment of cognitive states in aging dogs. The inclusion of additional examinations strengthens its validity and reliability.

Applications in the clinical environment

Implementing cognitive dysfunction scales in a veterinary practice holds significant potential for enhancing the quality of care provided to aging dogs. The purpose of incorporating these scales revolves around early detection, accurate diagnosis, and effective management of canine cognitive decline. The benefits encompass improved patient outcomes, enhanced owner awareness, and the potential for proactive intervention. In order to obtain the best output, more than one scale could be involved in the process of identifying, diagnosing, and monitoring patients affected by CDS.

The CCDR can serve as an initial screening tool due to its accessibility and ease of administration. Veterinary practices can integrate CCDR into waiting rooms, phone calls, or routine check-ups, allowing for quick assessments of cognitive function in aging dogs. While the reliance on owner-reported data raises concerns about potential bias, the scale's widespread use and large sample size facilitate its integration into regular practice, providing a preliminary indication of cognitive health.

On the other hand, the CADES offers a more comprehensive approach, making it suitable for more in-depth assessments. Veterinarians can incorporate CADES into consultations with geriatric patients, conducting a thorough examination that includes clinical, neurological, orthopedic, and imaging assessments. The scale can contribute to an accurate diagnosis and monitoring of cognitive decline. CADES can be particularly valuable in cases where owners comply in treating their pets, giving useful insights through time.

Conclusions

The profound bond between dogs and humans, nurtured over millennia, has been underscored by the enduring companionship they share (Pörtl et al., 2017; Jung et al., 2018). This connection, as evidenced by a plethora of studies (Carlone et al., 2019; Mariti et al., 2013a; Mariti et al., 2013b; Mariti et al., 2014; Mariti et al., 2017; Mariti et al., 2018; Mariti et al., 2020; Riggio et al., 2021; Riggio et al., 2021a; Riggio et al., 2021b; Riggio et al., 2021c), highlights the enduring and unique nature of the human-dog relationship. This bond adds complexity and emotional significance to our comprehension and management of age-related neurodegenerative diseases since they are a common pressing concern in both humans and pets.

AD, PD, ALS, SCAs, age-related depression and cerebrovascular disease, and canine CDS share common traits that can lead to the study of dogs as possible models for future research and therapies. Noteworthy similarities include protein aggregates, neuroinflammation, cognitive decline, and motor dysfunction (Hardy et al., 2002; Franceschi et al., 2007; Salvin et al., 2011; Mihevc & Majdic, 2019).

The connection between CDS and AD is underscored, revealing shared pathological features like cerebral changes, beta-amyloid and neurofibrillary tangle accumulation, and neuronal loss (Toepper, 2017; West et al., 2000; Siwak-Tapp et al., 2008; Bature et al., 2017).

The assessment of CDS through various scales is explored, each with distinct strengths and limitations. Pugliese et al.'s scale (2005) delves into CDS severity through a quick-testing questionnaire combined with cerebrospinal fluid analysis, offering insights into biochemical parameters correlated with cognitive impairment. Rofina et al.'s work (2006) correlates cognitive dysfunction with brain pathology, providing neurobiological correlations. Salvin et al.'s CCDR (2011), with over 900 dog owners interviewed, created the first comprehensive questionnaire. Madari et al.'s CADES (2015) stands out for its thorough methodology involving diverse examinations, ensuring an accurate assessment of cognitive decline. Comparatively, CADES emerges as a more comprehensive and objective tool, incorporating various examinations for detailed assessments. While CCDR, Pugliese's, and Rofina's scales offer valuable insights, limitations like reliance on questionnaires or small subject sizes impact their overall effectiveness. Future research is suggested to combine the strengths of these scales, integrating objective measures with larger, diverse populations to enhance precision in CDS assessment in veterinary practice. Moving to applications in the clinical environment, the implementation of cognitive dysfunction scales in veterinary practice holds promise for improving care for aging dogs. CCDR could serve as an initial screening tool due to its accessibility, while CADES offers a more comprehensive approach for in-depth assessments, contributing to accurate diagnosis and monitoring, particularly valuable in cases where owners actively participate in their pet's treatment. Future studies in the field could explore several avenues to advance our understanding

and assessment of cognitive decline in aging dogs, with a comparison focus on human AD. One potential area of research involves the integration of multiple cognitive dysfunction scales, aiming to provide a more nuanced and holistic understanding of the cognitive states in aging dogs.

Addressing the impact of owner education and awareness on the recognition and reporting of behavioral changes associated with CDS is also a relevant area for investigation. Understanding and mitigating potential biases introduced by subjective owner responses in certain scales could improve the accuracy of assessments. Large-scale population studies are essential to increase the diversity and representativeness of subjects. This approach could enhance the generalizability of findings and contribute to the development of more universally applicable assessment tools.

These potential areas for future research aim to address current limitations, enhance the precision of CDS assessment, and contribute to a more comprehensive understanding of cognitive decline in both aging humans and dogs.

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References

- Bature F., Guinn B.A., Pang D., Pappas Y. Signs and symptoms preceding the diagnosis of Alzheimer's Disease: a systematic scoping review of literature from 1937 to 2016. *BMJ Open*. 7: e015746; 2017. doi:10.1136/bmjopen-2016-015746.
- Brown R H, Al-Chalabi A. Amyotrophic Lateral Sclerosis. *New England Journal of Medicine*. 10.1056/NEJMra1603471
- Ciurli L., Casini L., Cecchi F., Baragli P., Macchioni F., Curadi C., Gazzano V., Capsoni S., Gazzano A. The Canine Cognitive Dysfunction Syndrome: epidemiology, pathophysiology and diagnosis. *Dog Behavior*. <https://doi.org/10.4454/db.v9i2.169>
- Coradduzza D., Congiargiu A, Chen Z, Zinellu A, Carru C, Medici S. Ferroptosis and Senescence: A Systematic Review. *International journal of Molecular Science*. 10.3390/ijms24043658
- Djernes K. Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatrica Scandinavica*. 10.1111/j.1600-0447.2006.00770.x
- Franceschi C., Capri M, Monti D, Giunta S, Olivieri F, Sevini F, Panourgia MP, Invidia L, Celani L, Scurti M, Cevenini E, Castellani GC, Salvioli S. Inflammaging and anti-inflammaging: a systemic perspective on aging and longevity emerged from studies in humans. *Mechanisms of Ageing and Development*. 10.1016/j.mad.2006.11.016
- Hardy J, Selkoe D J. The amyloid hypothesis of Alzheimer's disease: progress and problems on the road to therapeutics. *Science*. 10.1126/science.1072994
- Hassan M H. Comparative Senescence and Lifespan. *IntechOpen*. 10.5772/intechopen.105137
- Obeso A., Stamelou M, Goetz CG, Poewe W, Lang AE, Weintraub D, Burn D, Halliday GM, Bezard E, Przedborski S, Lehericy S, Brooks DJ, Rothwell JC, Hallett M, DeLong MR, Marras C, Tanner CM, Ross GW, Langston JW, Klein C, Bonifati V, Jankovic J, Lozano AM, Deuschl G, Bergman H, Tolosa E, Rodriguez-Violante M, Fahn S, Postuma RB, Berg D, Marek K, Standaert DG, Surmeier DJ, Olanow CW, Kordower JH, Calabresi P, Schapira AHV, Stoessl AJ. Past, present, and future of Parkinson's disease: A special essay on the 200th Anniversary of the Shaking Palsy. *Movement Disorders*. 10.1002/mds.27115
- Jung C. & Pörtl D. Scavenging hypothesis: lack of evidence for dog domestication on the waste dump. *Dog Behavior*. 4: 41-56; 2018.
- Landsberg G., Nichol J., Araujo J.A. Cognitive dysfunction in cats. A syndrome we used to dismiss as 'old age'. *J. Feline Med. Surg*. 12: 837-48; 2010. doi: 10.1016/j.jfms.2010.09.004.
- Madari A., Farbakova J., Katina S., Smolek T., Novak P., Weisssova T., Novak M., Zilka N. Assessment of severity and progression of canine cognitive dysfunction syndrome using Canine Dementia Scale (CA-DES). *Appl. Anim. Behav. Sci*. 171:138-145; 2015.

- Mariti C., Ricci E., Zilocchi M., Gazzano A. Owners as a secure base for their dogs. *Behaviour*. 150: 1275–1294; 2013a.
- Mariti C., Ricci E., Carlone B., Moore J. L., Sighieri C., Gazzano A. Dog attachment to man: A comparison between pet and working dogs. *J. V. B.* 8: 135-145; 2013b.
- Mariti C., Carlone B., Ricci E., Sighieri C., Gazzano A. Intraspecific attachment in adult domestic dogs (*Canis familiaris*): Preliminary results. *Appl. Anim. Behav. Sci.* 152: 64-72; 2014.
- Mariti C., Carlone B., Votta E., Ricci E., Sighieri C., Gazzano A. Intraspecific relationships in adult domestic dogs (*Canis familiaris*) living in the same household: A comparison of the relationship with the mother and an unrelated older female dog. *Appl. Anim. Behav. Sci.* 194: 62-66; 2017.
- Mariti C., Carlone B., Sighieri C., Campera M., Gazzano A. Dog behavior in the Ainsworth Strange Situation Test during separation from the owner and from the cohabitant dog. *Dog Behavior*. 4: 1-8; 2018.
- Mariti C., Lenzini L., Carlone B., Ogi A., Gazzano A. Does attachment to man already exist in 2 months old normally raised dog puppies? A pilot study. *Dog Behavior*. 6: 1-11; 2020.
- Mihevci S., Majdic G. Canine Cognitive Dysfunction and Alzheimer Disease – Two Facets of the Same Disease? *Frontiers in Neuroscience*. 2019. doi.org/10.3389/fnins.2019.00604
- Osella M.C., Re G., Odore R., Girardi C., Badino P., Barbero R., Bergamasco L. Canine cognitive dysfunction syndrome: prevalence, clinical signs and treatment with a neuroprotective nutraceutical. *Appl. Anim. Behav. Sci.* 4: 297-310; 2007.
- Pageat P. Description, clinical and histological validation of the A.R.C.A.D. score (evaluation of age-related cognitive and affective disorders). En: Lynne Seibert DVM, MS editors. Newsletter of the American Veterinary Society of Animal Behavior. Third International Congress on Behavioural Medicine; Boston 7-8 de Agosto de 2001.
- Pugliese M., Carrasco J.L., Andrade C., Mas E., Mascort J., Mahy J. Severe cognitive impairment correlates with higher cerebrospinal fluid levels of lactate and pyruvate in a canine model of senile dementia. *Prog. Neuropsychopharmacol. Biol. Psychiatry*. 29: 603-10; 2005. doi: 10.1016/j.pnpbp.2005.01.017.
- Riggio G., Noom M., Gazzano A., Mariti C. Development of the dog attachment insecurity screening inventory (D-aisi): A pilot study on a sample of female owners. *Animals*. 11: 3381; 2021a.
- Riggio G., Piotti P., Diverio S., Borrelli C., Di Iacovo F., Gazzano A., Howell T., Pirrone F., Mariti C. The dog-owner relationship: Refinement and validation of the Italian c/dors for dog owners and correlation with the laps. *Animals*. 11: 2166; 2021b.
- Riggio G., Gazzano A., Zsilák B., Carlone B., Mariti C. Quantitative behavioral analysis and qualitative classification of attachment styles in domestic dogs: Are dogs with a secure and an insecure-avoidant attachment different? *Animals*. 11: 1-23; 2021c.
- Riggio G., Mariti C., Sergi V., Diverio S., Gazzano A. Serotonin and tryptophan serum concentrations in shelter dogs showing different behavioural responses to a potentially stressful procedure. *Veterinary Sciences*. 8: 1-10; 2021. Doi 10.3390/vetsci8010001.
- Rofina J.E., van Ederen A.M., Toussaint M.J.M., Secrève M., van der Spek A., van der Meer I., Van Eerdenburg F.J.C.M., Gruys E. Cognitive disturbances in old dogs suffering from the canine counterpart of Alzheimer's disease. *Comparative Study Brain Res.* 19;1069(1): 216-26; 2006. doi: 10.1016/j.brainres.
- Salvin H.E., McGreevy P. D., Sachdev P.S., Valenzuela M.J. The canine cognitive dysfunction rating scale (CCDR): A data-driven and ecologically relevant assessment tool. *Vet. J.* 188: 331-6; 2011. doi: 10.1016/j.tvjl.2010.05.014.
- Schütt T., Toft N., Berendt M. Cognitive dysfunction, progression of age-related behavioral changes, biomarkers, and survival in dogs more than 8 years old. *J. Vet. Intern. Med.* 29: 1569-77; 2015. doi: 10.1111/jvim.13633.
- Siwak-Tapp C.T., Head E., Muggenburg B.A., Milgram N.W., Cotmana C.W. Region specific neuron loss in the aged canine hippocampus is reduced by enrichment. *Neurobiol. Aging*. 29: 39–50; 2008.
- Sullivan R., Yau WY, O'Connor E, Houlden H. Spinocerebellar ataxia: an update. *Journal of Neurology*. 10.1007/s00415-018-9076-4.
- Toepper M. Dissociating Normal Aging from Alzheimer's Disease *J. Alzheimers Dis.* 57: 331-352; 2017 doi: 10.3233/JAD-161099.
- West M.J., Kawas C.H., Martin L.J., Troncoso J. C. The CA1 region of the human hippocampus is a hot spot in Alzheimer's Disease. *Ann. N. Y. Acad. Sci.* 908: 255-9; 2000. doi: 10.1111/j.1749-6632.2000.tb06652.x.

La sindrome da disfunzione cognitiva canina: scale di valutazione

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Sintesi

L'“invecchiamento” rappresenta l'ampio spettro di cambiamenti associati al passare del tempo. Tra gli animali domestici, i cani sono stati ampiamente studiati come modello per le malattie neurodegenerative umane a causa delle loro somiglianze, soprattutto in termini di alterazioni patologiche. La sindrome da disfunzione canina (CDS) è ancora oggetto di studio dal punto di vista diagnostico, clinico, anatomopatologico e terapeutico. Di conseguenza, numerosi autori hanno sviluppato e convalidato varie scale di valutazione per valutare gli animali geriatrici per la diagnosi precoce e non invasiva della CDS. L'obiettivo di questa revisione è quello di offrire una panoramica completa delle scale di rating esistenti e di discuterne i punti di forza e i limiti.

