

Clinical Signs and Management of Anxiety, Sleeplessness, and Cognitive Dysfunction in the Senior Pet

Gary M. Landsberg, DVM, MRCVS^{a,b,*},
Theresa DePorter, DVM, MRCVS^c, Joseph A. Araujo, BSc^{d,e}

KEYWORDS

- Anxiety • Behavior problems • Cognitive dysfunction • Fear
- Night waking • Senior pets

ASSESSING AND MAINTAINING COGNITIVE AND BEHAVIORAL WELL-BEING

Appreciation and compassion for welfare and quality of life, as well as emotional and physical well-being, is important at all stages of our patient's lives, but this becomes particularly complicated in the management of geriatric patients, especially those facing imminent end-of-life decisions. Patience and sensitivity for the pet's emotional state should be part of a comprehensive program for any patient; however, the geriatric hospice patient requires special consideration because changes in anxiety and cognitive function may be further compounded by other medical conditions, sensory perception, medications, and previous learning. For example, if the pet has learned to expect pain and uncomfortable restraint during previous experiences, then the debilitated or compromised pet will be more anxious, defensive, or even aggressive rather than

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^a North Toronto Animal Clinic, 99 Henderson Avenue, Thornhill, ON L3T 2K9, Canada

^b CanCog Technologies Inc, 120 Carlton Street, Toronto, ON M5A 4K2, Canada

^c Oakland Veterinary Referral Services, 1400 South Telegraph Road, Bloomfield Hills, MI, 48302, USA

^d Department of Pharmacology, University of Toronto, 1 King's College Circle, Toronto, ON M5S 1A8, Canada

^e CanCog Technologies Inc, 120 Carlton Street, Suite 204, Toronto, ON M5A 4K2, Canada

* Corresponding author. North Toronto Animal Clinic, 99 Henderson Avenue, Thornhill, ON L3T 2K9, Canada.

E-mail address: gmlandvm@aol.com

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appreciative of even the most compassionate end-of-life care. Behavioral signs are often the first, or only, signs of pain, illness, and cognitive decline (**Table 1**). Therefore, family members need assistance in recognizing the significance of these changes and the importance of reporting these promptly to their veterinarian. Early detection of behavioral changes consistent with disease provides an opportunity for early diagnosis and treatment so that complications might be prevented, further decline might be slowed, longevity might be increased, and welfare issues can be promptly addressed.¹

Both the American Hospital Association and American Association of Feline Practitioner Guidelines specifically refer to the importance of questioning pet owners at each visit as to any changes in health or behavior to improve early recognition of alterations

Medical Condition/Medical Presentation	Examples of Behavioral Signs
Neurologic: central (intracranial/extracranial), particularly if affecting forebrain, limbic/temporal, and hypothalamic; REM sleep disorders	Altered awareness, response to stimuli, loss of learned behaviors, house soiling, disorientation, confusion, altered activity levels, temporal disorientation, vocalization, soiling, change in temperament (fear, anxiety), altered appetite, altered sleep cycles, interrupted sleep
Partial seizures: temporal lobe epilepsy	Repetitive behaviors, self-traumatic disorders, chomping, staring, alterations in temperament (eg, intermittent states of fear or aggression), tremors, shaking, interrupted sleep
Sensory dysfunction	Altered response to stimuli, confusion, disorientation, irritability/aggression, vocalization, house soiling, altered sleep cycles
Endocrine: hyperthyroid or hypothyroid, hyperadrenocorticism or hypoadrenocorticism, insulinoma, diabetes, testicular or adrenal tumors	Altered emotional state, irritability/aggression, lethargy, decreased response to stimuli, anxiety, house soiling/markings, night waking, decreased or increased activity, altered appetite, mounting
Metabolic disorders: hepatic/renal	Signs associated with organ affected: may be anxiety, irritability, aggression, altered sleep, house soiling, mental dullness, decreased activity, restlessness, increase sleep, confusion
Pain	Altered response to stimuli, decreased activity, restless/unsettled, vocalization, house soiling, aggression/irritability, self-trauma, waking at night
Peripheral neuropathy	Self-mutilation, irritability/aggression, circling, hyperesthesia
Gastrointestinal	Licking, polyphagia, pica, coprophagia, fecal house soiling, wind sucking, tongue rolling, unsettled sleep, restlessness
Urogenital	House soiling (urine), polydypsia, waking at night
Dermatologic	Psychogenic alopecia (cats), acral lick dermatitis (dogs), nail biting, hyperesthesia, other self-trauma (chewing/biting/sucking/scratching)

Abbreviation: REM, rapid eye movement.

in physical or behavioral well-being.^{2,3} In addition, ongoing monitoring of behavioral signs can aid in assessing the progress of disease as well as the pet's quality of life and emotional state.

The behavioral focus for pets of any age should be on (1) maintaining positive and healthy social relationships (while avoiding those that are unpleasant); (2) ensuring freedom from stress; (3) providing a sense of control to allow the pet to engage in pleasant, and avoid unpleasant, interactions; and (4) ensuring adequate mental stimulation.⁴ Pets that are elderly, or ill, may be less interested or able to engage in mental, physical, and social stimulation, which could potentially lead to alterations in the type and frequency of activities and interactions that owners provide their pets. However, mental enrichment and physical activity are important in maintaining cognitive health in both humans and pets, and physical activity can be an important component of weight management and for improving mobility.^{5,6} Therefore, a more case-specific approach for designing behavioral strategies may be required for pets that have physical, mental, or behavioral limitations. Interactions that support the human-animal bond are especially critical in pets that are aging and ill because owners need to be responsive and sensitive to their pet's subtle changes in behavior as indicators of pain, welfare, and quality of life. Positive and pleasant shared experiences provide caregivers a sense of accomplishment rather than anguish about their pet's illness.

BEHAVIORAL SIGNS IN SENIOR PETS: ANXIETY, SLEEP-WAKE DISTURBANCES, AND COGNITIVE DYSFUNCTION

Although most pet owners are likely to report more serious signs either because of their obvious health and welfare implications to the pet, or because of the effects they have on the owner-pet relationship, veterinarians must be proactive in asking owners about behavioral signs because those that tend to be more subtle or less problematic to the owners often go unreported.^{7–10} Behavioral signs in geriatric pets that may have the most significance to the owner or the pet include those associated with anxiety, night waking, and cognitive dysfunction syndrome (CDS). Sleep-wake disturbances may be caused by CDS or anxiety, but also for many unrelated reasons, but it warrants special attention in the treatment and management of senior pets.

Prevalence of Behavior Problems Reported by Owners of Senior Pets

Several studies have examined the prevalence of behavioral signs in senior pets (**Tables 2 and 3**).^{11–13} In a Spanish study of 270 dogs more than 7 years of age presented for behavior problems, 74%, 19.8%, 4.6%, and 1.3% of the owners detected at least 1, 2, 3, and 4 behavior problems, respectively.¹¹ In this same study, although 16% were diagnosed with CDS, the most common signs were related to aggression (53%) and, to a lesser extent, those consistent with fear and anxiety.¹¹ Similarly, when examining the distribution of 103 senior dogs referred to a veterinary behaviorist in another study, in which 7% were diagnosed with CDS, most cases displayed aggression (34%) or signs of fear and anxiety (39%) (see **Table 2**).¹² In 83 senior cats referred for behavioral consultations, most cats displayed signs of marking or soiling (73%); however, cases of aggression (16%), vocalization (6%), and restlessness (6%) were also serious enough to require referral (see **Table 3**).¹² To further examine the distribution of problems reported by owners in senior dogs and cats, the Veterinary Information Network (VIN) database was searched for behavior problems of 50 senior dogs (aged 9–17 years) and 100 senior cats (aged 12–22 years). In the 50 canine cases reviewed from VIN boards, 31 dogs (62%) had signs consistent

Table 2 Canine behavior problem distribution reported by senior dog owner		
Behavior Referral Practice (n = 103 Dogs) >7 y¹² (%)	Spanish Study (n = 270 Dogs) >7 y¹¹ (%)	VIN^a Boards (n = 50 Dogs) (%)
Separation anxiety 30	Aggression family member 32	Anxiety (fear, vocal, salivate, hypervigilant) 74
Aggression to people 27	Cognitive dysfunction 16	Cognitive dysfunction 62
Aggression to animals 17	Aggression to family dogs 16	Separation anxiety 36
Compulsive disorders 8	Barking 9	Wandering 26
Cognitive dysfunction 7	Separation anxiety 8	Night anxiety/waking 22
Phobias 5	Disorientation 6	Noise phobias 18
Anxiety 4	Aggression unfamiliar people 5	Vocalization 14
House soiling 3	House soiling 4	Stereotypic behavior 4
Vocalization 1	Destructive 4	Aggression 2
	Compulsive 4	
	Noise fears and phobias 3	

^a Veterinary Information Network (www.VIN.com).

with CDS, but most of the dogs had signs related to anxiety, including night waking and vocalization (see **Table 2**). In the 100 feline cases reviewed from VIN boards, 27% of the complaints were related to elimination problems, and the most common complaints were vocalization (61%), especially at night, and other signs associated with anxiety (see **Table 3**). Although many of these signs could be caused by underlying medical problems (see **Table 1**), in many of these cases, all possible medical causes were reported to have been ruled out.

Prevalence of Behavior Problems Solicited by Veterinary Inquiry

Although studies on the prevalence of behavior problems reported by owners may be representative of those problems that are serious enough for the owners to seek behavioral guidance, many of the most common behavioral signs that arise in senior pets require a more proactive approach on the part of the practitioner because they often go unreported.

Table 3 Feline behavior problem distribution reported by senior cat owner	
Behavior Referral Practices n = 83^a >10 y (%)	VIN Boards n = 100, Aged 12 to 22 y (%)
House soiling (elimination and marking) 73	Excessive vocalization 61 (night vocal 31)
Intercat aggression 10	House soiling (elimination and marking) 27
Aggression to humans 6	Disorientation 22
Excessive vocalization 6	Aimless wandering 19
Restlessness 6	Restlessness/night waking 18
Overgrooming 4	Irritable/aggressive 6
	Fear/hiding 4
	Clingy (attachment) 3

^a Cases recruited from behavior referral practices Landsberg (n = 25), Horwitz (n = 33), Chapman, Voith (n = 25).

Data from Chapman BL, Voith VL. Geriatric behavior problems not always related to age. *DVM* 1987;18:32.

In one study of dogs aged 11 to 16 years that had no medical signs, 28% of dogs aged 11 to 12 years and 68% of dogs aged 15 to 16 years showed at least 1 sign consistent with CDS.⁸ In a study of 14 dogs with CDS, all dogs visited the veterinarian for a routine annual checkup and the owners reported no behavioral complaints until actively questioned by the veterinarian.⁹ In another recent study, 124 dogs more than 7 years of age were evaluated and 22 were eliminated because of possible medical factors.¹⁰ Of the remaining dogs, 42 had alterations in 1 category and 33 had signs in 2 or more categories associated with CDS.¹⁰ In a recent Spanish study that examined the prevalence and risk factors for age-related cognitive impairment in a population of 325 dogs more than 9 years of age, 22.5% of geriatric dogs were affected.¹³ Females and neutered males were significantly more affected than males and entire dogs, and the prevalence and severity increased with age.¹³ In this study, social interactions and house training were the most impaired categories.¹³ The possible relationship between gonadectomy and an increased prevalence in CDS was previously described.¹⁴ In a large-scale epidemiologic study using Internet survey responses regarding 497 dogs ranging in age from 8 to 19 years, the estimated prevalence of CDS was 14.2%. However, only 1.9% of these dogs were diagnosed with CDS by their veterinarian, exemplifying that CDS is severely underdiagnosed.⁷ In a Hills Market Research study, 75% of owners of dogs more than 7 years of age indicated that their pet had 1 or more signs consistent with CDS when asked, but only 12% had previously reported the signs to their veterinarian (Hills Pet Nutrition. US Market Research Survey, Omnibus study on aging pets. Topeka [KS]: Hills Pet Nutrition; 2000, data on file). In one study of aged cats presented to veterinary clinics for routine annual care, 154 owners of cats aged 11 years and older were asked to report any signs of CDS. After eliminating 19 cats with medical problems, 35% of the cats were diagnosed with possible CDS, and this increased with age: 28% of 95 cats aged 11 to 15 years, and 50% of 46 cats more than 15 years of age, were diagnosed with possible CDS.^{15,16}

CLIENT EDUCATION AND SCREENING

Given the prevalence and underdiagnosis of behavioral problems in senior pets, monitoring and assessing behavioral signs is a critical component of every veterinary visit. The earlier a diagnosis can be made, the greater the opportunity to implement interventions that can positively affect the pet's health, comfort, and perhaps even longevity. Veterinarians and staff must inform clients of the potential health and welfare implications for the pet if these signs go unrecognized or unreported. Specific recommendations for monitoring might also be required based on previously diagnosed health issues and any medications being used. Handouts and web links can be used to further educate owners about the value of regular geriatric evaluations. The use of a questionnaire can be particularly effective in quickly and comprehensively screening for changes in both health and behavior.

HOW HEALTH MAY AFFECT BEHAVIOR AND BEHAVIOR MAY AFFECT HEALTH

Although the presence of gastrointestinal, neurologic, or dermatologic signs, polyuria or polydipsia, altered mobility, or declining sensory function may indicate an underlying medical problem, it is common for behavioral signs to be the first, or only, indication of medical problems (see **Table 1**). Sickness behaviors that may manifest as lethargy and inappetence are usually considered to be passive and in response to debilitation or weakness; this may be a well-organized adaptive process that diverts energy to the immune system to enhance disease resistance and facilitate recovery.¹⁷

When senior pets are presented with a recent onset of a change in behavior, such as house soiling; alterations in social interactions; altered responses to stimuli; changes in activity levels (whether increased or decreased); night waking; excessive vocalization; or an increase in fear, anxiety, or phobias, then possible medical causes of these signs must first be ruled out.

In senior pets, especially those receiving palliative care for previously diagnosed health issues, the practitioner must be cognizant that multiple health and behavior issues may coexist. Although a physical examination and diagnostic tests are invaluable in diagnosing and monitoring many medical conditions, the potential for pain and neurologic diseases, including sensory dysfunction and CDS, to contribute to the pet's behavioral signs must also be evaluated. In addition, for pets that are on medication for existing health or behavioral problems, all potential behavioral effects of the medications must also be considered. Pain and illness further contribute to stress and anxiety, just as stress and anxiety can contribute to pain and illness. If a medical cause is diagnosed or suspected, a therapeutic trial may help to confirm the cause by monitoring the pet's behavioral response. Therefore, identifying signs of stress and anxiety (**Box 1**) are critical in the monitoring of both behavioral and medical health as well as animal welfare.

The Effects of Health on Behavior

Any disease that affects the central nervous system or its circulation (eg, cardiac, anemia, hypertension) can affect behavior (see **Table 1**). Both intracranial (eg, degenerative, tumor) and extracranial causes (eg, organ failure, immune diseases, endocrinopathies, circulatory, respiratory) become increasingly common in older pets. A change in personality or mood, awareness, inability to recognize or respond appropriately to stimuli, and loss of previously learned behavior might indicate forebrain or brainstem involvement. Altered responsiveness to stimuli can also arise from sensory or motor dysfunction, as well as pain. Episodic changes in conscious response may be

Box 1

Signs of stress and anxiety

Alteration/change from normal behavior

Reduced activity ←-----→ Increased activity (restlessness)

Increased sleeping ←-----→ Increased nighttime waking

Avoidance of social interaction ←-----→ Increased attention seeking

Reduced feeding and/or drinking

Increased huddling or shivering

Alterations in vocalization (whining, barking, or howling)

Increased irritability and aggression ←-----→ Apathy or reduced response to stimuli

Increased sensitivity or reactivity to stimuli

Depression

Elimination in home

Decreased interest in toys or social play

Increased sensitivity to stimuli including phobia and separation anxiety

Physiologic changes (heart rate, respiratory rate, blood pressure, panting, salivation, other autonomic signs, eg, dilated pupils)

caused by neurologic conditions such as seizures or other clinical conditions such as syncope, acute vestibular dysfunction, tremors, narcolepsy/cataplexy, rapid eye movement (REM) disorder, and movement disorders, all of which may mimic anxiety attacks and result in nighttime waking and which are particularly challenging to distinguish. These disorders must be differentiated by history and, if possible, video recordings of episodic anxiety and especially night waking behaviors.

Any disease that alters hormone levels (thyroid, adrenal, reproductive organs) can also affect behavior. For example, in elderly felines, hyperthyroidism (which can also contribute to behavioral signs of hypertension including vocalization, restlessness, and night waking) can be associated with behavioral signs ranging from appetite stimulation to increased irritability, anxiety, and urine marking.

Self-traumatic disorders including biting, chewing, scratching, licking, or excessive barbering lead to skin lesions and alopecia. Although self-traumatic disorders can have a behavioral cause, when dermatologic diagnostics do not identify a medical cause, hypersensitivity reactions and neuropathic pain must first be ruled out.¹⁸

Pain can be identified by both behavioral and physical signs. Studies have shown that behavioral measures are an accurate means of measuring pain, and pain assessment scoring systems have been developed for both veterinarians and pet owners.^{19–21} Pain can be a contributing factor to many of the behavioral signs associated with CDS, self-traumatic disorders, and anxiety disorders.

Unusual oral behaviors including licking, sucking, pica, smacking lips, and gulping might arise because of partial complex seizures or gastrointestinal disorders. In a recent study of dogs with excessive licking of surfaces, gastrointestinal disorders were identified as a cause in at least half of the dogs.²²

House soiling is often considered a behavior problem but is often precipitated by medical problems. In a retrospective study of cats with problem elimination behavior, 60% of the cats had a history of feline urological syndrome/feline lower urinary tract disease.²³ Inappropriate elimination can be caused by any medical problem, or in response to medications, that causes an increased volume of urine or stool, increased discomfort during elimination, decreased control, or diseases that affect cortical control.

Consider all medications the pet is taking and possible side effects or interactions, because these effects may influence behavior. For example, steroids may cause irritability and pain medications may cause sedation. Conversely, the conditions these medications alleviate may lead to an improvement in the behaviors associated with the medical condition. Monitoring behavioral signs may be a critical component in monitoring drug efficacy.

CDS (discussed later) is generally a slowly progressive disorder that cannot be definitively diagnosed and early symptoms are easily overlooked. Patients undergoing palliative and end-of-life care may have undiagnosed CDS. The challenge for the clinician is to identify evidence of early CDS and distinguish these from signs of illness or medication side effects, because diagnosis of cognitive dysfunction is based on exclusion and confirmed only by characteristic deterioration of cognitive function and the associated progression of symptoms.

The Effects of Stress on Health and Mental Well-being

Although it is common to consider the effects of disease on behavior, acute and chronic stress can also have an impact on both health and behavior.²⁴ Stress is an altered state of homeostasis that can be caused by physical or emotional factors that trigger psychological, behavioral, endocrine, and immune effects that are designed to handle stress.²⁵ In the aging or ill pet, there is a general deterioration in

physical condition; tissue hypoxia; alterations in cell membranes; increased production and decreased clearance of reactive oxygen species; a decline in organ, sensory, and mental function; a gradual deterioration of the immune system; and decreased ability to cope with change. Thus, the senior pet in particular is less able to respond to stress and maintain homeostatic balance.

In humans, there may be a correlation between stress and poor health, including poor immune function, cardiovascular disease, skin disease, asthma, gastrointestinal disorders, and cellular aging. Similarly, in pets, stress may alter immune function, and has been shown to be a contributing or aggravating factor in gastrointestinal diseases, urinary tract disorders in cats, dermatologic conditions, respiratory and cardiac conditions, behavioral disorders, and a shortened lifespan.²⁶ For example, cats with interstitial cystitis (FIC) may have altered bladder permeability and an increase in plasma noradrenaline, whereas cats receiving environmental modification had a significant reduction in FIC, respiratory disease, fearfulness, nervousness, inflammatory bowel disease, and aggression.^{27–29} Fear, anxiety, and stress can also contribute to gastrointestinal signs including anorexia, vomiting, diarrhea, and colitis.

Although stress leads to an immune response intended to enhance defense mechanisms, in some individuals, stressors may contribute to inflammatory dermatoses and endocrinologic factors, which, in situations of stress, may play a role in the pathogenesis of dermatoses such as atopic dermatitis, psoriasis, and urticaria.^{30–32} An increased severity and frequency of skin disorders in dogs with nonsocial fear and separation anxiety has been identified.²⁶ Chronic anxiety, stress, conflict, and frustration may lead to behavioral disorders in humans, including panic disorders, separation anxiety, social and other phobias, obsessive-compulsive disorders, generalized anxiety disorders, posttraumatic stress disorders, impulse control disorders, and sleep disorders, all of which may have animal correlates.³³ Pets that are physically or mentally impaired may find it difficult to deal with the effects of stress. Aging pets may have difficulty with forgetfulness, just as described in people, and the pet may appear confused or stubborn as a result of impaired short-term memory or reduced cognitive abilities. Therefore, although enrichment (discussed later) may have beneficial effects in helping to maintain both physical and mental health, changes in the pet's household or schedule should be made slowly to help the pet cope. When changes must be made, pet owners should pay particular attention to the pet's emotional and behavioral state, as well as its appetite, sleep, and elimination, to gauge whether additional support in the form of behavior therapy or drugs might be warranted.

AGING AND ITS EFFECT ON THE BRAIN

In dogs, frontal volume decreases, ventricular size increases, and there is evidence of meningeal calcification, demyelination, increased lipofuscin and apoptic bodies, neuroaxonal degeneration, and a reduction in neurons.^{34,35} Although not as well defined, similar changes including neuronal loss, cerebral atrophy, widening of the sulci, and an increase in ventricular size are also reported in cats.^{16,36} Perivascular changes including microhemorrhage or infarcts in periventricular vessels have been reported in senior dogs and cats, which may be responsible for some of the signs of cognitive dysfunction.^{16,34,35,37–40} With increasing age, there is also an increase in reactive oxygen species leading to oxidative damage in dogs, which is speculated to also be a factor in aged cats.^{16,41} There may also be a depletion of catecholamines and an increase in monoamine oxidase B (MAOB) activity in dogs.⁴² A decline in the cholinergic system has also been identified in dogs and cats, which may contribute to cognitive decline and, possibly, alterations in motor function, as well as alterations in REM

sleep.^{36,42–45} In dogs, cats, and humans, there is an increased accumulation of diffuse amyloid- β (A β) plaques and perivascular infiltrates of A β .^{16,37–39} Furthermore, increased A β is positively correlated with cognitive impairment in dogs.^{38,39,46} A β plaques in cats older than 10 years are more diffuse than those seen in humans and dogs.^{16,37,40,47,48} The link between CDS and A β disorders in the cat is inconsistent because some studies found a positive link,^{37,47} whereas others show no correlation.^{47,48} Nonetheless, the overall similarity in brain aging among various mammalian species suggests that some level of dementia, and other age-related behavioral changes including anxiety, memory loss (forgetfulness) and sleeplessness, occurs with aging across many species. A video example of a cat performing a memory task in a laboratory model may be viewed online (within this article at www.vetsmall.theclinics.com, May 2011 issue). In this video, the cat is performing a delayed non-matching to position (DNMP) task, which tests memory. Initially, the cat is presented with an object over 1 of 2 possible food wells. The cat must displace the object to retrieve a food reward beneath. After responding, the tray is removed from the cat's view and a delay is initiated (in this case, there is a delay of 90 seconds, but this is sped up in the video). After the delay, the cat is presented with duplicates of the object from the previous presentation. The correct choice, leading to a food reward, is the object in the position not used previously (ie, the nonmatch). To prevent the use of olfactory-based responding, the incorrect object is baited with an unattainable food reward. By increasing the delay between the 2 presentations, memory can effectively be tested by assessing the cat's ability to make the right choice, which is rewarded by food. A long the delay between the first and second presentation results in a poorer performance, which means the cat has an increased incidence of forgetting. Consequently, cats (or dogs) with cognitive impairment score poorly on a memory test, relative degrees of loss or decline in short-term memory may be assessed, and interventions intended to reduce the short-term memory loss effects of cognitive impairment may be assessed in this laboratory model (Video 1).

CLINICAL SIGNS

Anxiety, Stress, and Distress

Signs related to anxiety may indicate impaired cognitive function, compromised health, or pain. Therefore, the recognition of pain, anxiety, memory loss, and stress in pets requires curiosity and sensitivity because these may occur without overt signs, particularly because pets are instinctually driven to avoid revealing obvious signs of stress or vulnerability (see **Box 1**; **Box 2**). Furthermore, species, breed, and individual differences in both the perception and display of anxiety further confounds the problem of accurate assessment. Physiologic monitors may indicate pain so that assessments of changes in heart rate, respiratory rate, and blood pressure are important indicators in pain management, particularly in hospitalized pets. However, these physiologic indicators are not unique to pain and may also be influenced by fear or anxiety. However, more subjective measures are required for pet owners to evaluate pain in the home environment, which needs to be differentiated from other causes of fear and anxiety.^{19–21}

Animals may display anxiety in an array of manifestations but generally these reflect either the absence of normal behaviors or the expression of abnormal or atypical response for the individual animal. An appreciation for the pet's normal display of behaviors provides the foundation for the assessment. New behaviors such as vocalizing, pacing, eliminating in the home, or even panting are readily observed by the attentive caregiver. However, the absence or muted expression of normal behaviors

Box 2**Canine communication: gradient of expression of anxiety**

Subtle low-level anxiety signs:

- Sniffing ground, scratching, urination, or defecation
- Yawning, blinking
- Nose licking or tongue flicking
- Diverting eyes

Low-level anxiety, conflict signs:

- Turning head away,
- So-called wet dog shake (when not wet)
- Momentary lack of motion
- Cowering or crouching

Moderate-level anxiety, conflict signs:

- Freezing (holding still, sitting)
- Turning body away
- Pawing or attention seeking
- Snatching or grabbing offered food
- Quiver of lip
- Tail down or motionless
- Submissive urination

Medium-level anxiety, conflict signs:

- Walking away, retreating
- Weight shifted back
- Creeping
- Ears back

Intense or aroused signs of anxiety, conflict

- So-called whale eye (sideways glance shows white of eye)
- Hackles raised on back
- Tail tucked, body lowered, or crouching
- Lip lift

Reactive signs of anxiety, conflict:

- Staring, orienting toward rather than away
- Weight shifted forward
- Stiffening of body, tightening of muscles
- Snarl or lip lift with teeth exposed

Reactive signs of anxiety, conflict; may include aggression:

- Staring, orienting toward rather than away
- Weight shifted forward
- Stiffening of body, tightening of muscles
- Snarl or lip lift with teeth exposed

Growl
 Vicious barking
 Lunging forward
 Erect, tall stance (tail may be in motion)
 Bite (may range from single inhibited bites to multiple or uninhibited bites)

requires keen observation. The dog that fails to bark when someone comes to the door may be suffering from severe pain, memory loss, anxiety, or poor health. Moreover, clients rarely complain when their dog ceases to steal food off the counter, jump up during greeting, or chase the family cat, and the absence of these undesirable behaviors may be important determinants in an accurate diagnosis. Although the onset and progression of signs of fear or anxiety may be immediate when the stimulus approaches quickly or appears unexpectedly, most pets begin expressing subtle signs of anxiety such as yawning, nose licking, or momentary immobilization (see **Box 2**). If the threat either increases in intensity or persists, the pet may show signs of increased anxiety that may lead to avoidance and retreat or could escalate to threats (growling) or defensive aggression (fight or flight). Pain, illness, and cognitive dysfunction may also result in reduced tolerance and an increase in avoidance or aggression; however, pets that are ill or painful may be more likely to maintain their position (especially a resting or hiding location) and use aggression rather than avoidance as a strategy to remove the threat. Reduction of anxiety, along with pain control, should reduce the frequency and intensity of aggressive displays. **Box 2** shows a gradient of anxiety expression beginning with mild responses, escalating to aggression.⁴⁹

Behaviors to consider when assessing anxiety include posture, facial expression, ability/willingness to walk or move around, tendency to lie down and sleep, position when in its bed or crate, locations of rest or sleep, appetite, demeanor, mental status, greeting behavior, and vocalization. Specifically, alterations in social interactions including decreased play with family members or other pets, decreased interest in chase or tug games, hiding or seeking seclusion, increased sleep or altered quality of sleep, and decreased interest in play toys (**Fig. 1**) may indicate pain or an underlying medical concern. Pain, illness, changes in sensory perception, and unfamiliar contexts may all reduce a pet's tolerance and thus result in an incremental increase in the expression of intense conflict-based or anxiety-based signs. If the underlying health problem can be managed or resolved, there may be a return to normalcy. However, because many conditions in the patient in palliative care cannot be resolved, monitoring for improvement in signs is an important component of assessing response to therapy and patient welfare.

Cognitive Dysfunction Syndrome

Cognitive dysfunction is a neurodegenerative disorder of senior dogs and cats that is characterized by gradual cognitive decline and increasing brain disorders.^{1,16,34,35,37–39,50–53} The development and validation of neuropsychological tests for assessing canine cognitive function in a laboratory setting, including discrimination learning, oddity discrimination learning, reversal learning, and spatial memory, has been instrumental in documenting age-related cognitive differences (**Fig. 2**).^{1,5,34,35,50–52} Recently, the canine test apparatus and protocols have been modified for use in cats. Preliminary data show age differences, with senior cats being impaired relative to normal adults.^{15,53} This feline battery should also prove



Fig. 1. This dog has lost interest in manipulating food toys; the cognitive, social, and exploratory changes in behavior with cognitive impairment may depend on observing the absence of normal activities. (Courtesy of Theresa DePorter, DVM, Bloomfield Hills, MI.)

instrumental in determining the relationship between brain disorders and CDS in cats as well as in the development of therapeutic interventions.

Based on clinical signs alone, CDS has been traditionally diagnosed in dogs 11 years of age and older. However, dogs show impairment in the spatial memory task as early as 6 to 8 years of age.⁵¹ Laboratory studies have identified altered sleep-wake cycles, increased stereotypy, and decreased social contact with humans in dogs with cognitive impairment.⁵⁴ In cats, based on more limited data, cognitive and motor performance seem to decline starting at approximately 10 to 11 years of age, but functional change in the neurons of the caudate nucleus have been seen by 6 to 7 years of age.^{55–57}

To diagnose CDS, veterinarians must rely on owner history. Only with careful questioning is it likely that signs will be detectable in the earliest stages of development. The diagnosis was initially based on the following clinical signs: (1) disorientation, (2) altered interactions with people or other pets, (3) altered sleep-wake cycles, and (4)



Fig. 2. Neuropsychological testing. In the attention task, the dog must find the food under the correct (different) object when 0, 1, 2, or 3 incorrect objects (distracters) are presented concurrently. (Courtesy of CanCog Technologies Inc., Toronto, ON; with permission.)

house soiling, which are represented by the acronym DISH. In addition, because activity may decline, increase, or become repetitive (stereotypical) in pets with CDS, an A for activity has been added to DISH (DISHA).¹ Although age-related impairments in learning and memory are arguably the most important hallmark of cognitive decline, the average pet may appear minimally challenged as its learning and memory declines, currently limiting the use of this measure in a clinically meaningful way; by contrast, neuropsychological testing can show changes many years earlier than behavioral questionnaires and may provide an important measure in the future if it can be adopted for use with the average pet. In addition, anxiety seems to be associated with brain aging and cognitive decline. In humans with Alzheimer disease and other age-related dementias, anxiety, troubled sleep, and agitation may be associated with cognitive decline and frontal lobe dysfunction.^{58,59}

Clinically, a questionnaire is generally used to assess whether a pet may have signs consistent with CDS (**Table 4**).¹ However, further work is ongoing to develop standardized and validated questionnaires for the assessment of CDS in dogs and cats. One recent publication based primarily on an Internet questionnaire of 957 dogs produced a standardized rating scale that measured both severity for confusion (staring blankly, getting stuck), repetitive activity, recognition of familiar people and pets, avoidance of patting, and ability to find food, as well as changes in the previous 6 months in recognition of people, confusion, activity, and finding food.⁶⁰ Another scale, the Age-related Cognitive and Affective Disorders (ARCAD) scale, has been developed in France.¹ In cats, clinicians tend to assume that CDS has parallel signs to those seen in a dog, which requires additional research to confirm. Once potential CDS signs are identified, any medical condition that might cause or contribute to the signs must first be ruled out. Because senior pets often have multiple health issues, the diagnosis of a medical problem does not rule out the possibility of concurrent CDS. The clinician is required to use best judgment in an attempt to determine the contribution of medical or drug factors to the behavioral signs.

MANAGEMENT AND TREATMENT OPTIONS

Management of Nighttime Waking and Anxiety

Many of the common behavioral presenting complaints in senior pets are related to anxiety, including an increased prevalence of separation anxiety, phobias, excessive vocalization, aggression, and waking at nights. Because disruption of nighttime rest is detrimental to the elderly and debilitated patient and to the family caring for their pet, it is one of the most common presenting complaints for behavior problems in senior dogs and cats (see **Table 1**).

For night waking in dogs and cats, CDS and neurologic diseases, pain, an increased need to eliminate, sensory decline, hypertension, and the behavioral effects of drugs are some of the more common contributing factors. In addition, when signs of anxiety, fears, and phobias are exhibited at night, then the added sleep disruption for the owner can severely affect the owner's level of tolerance and the bond between pet and owner. Further compounding the problem is that, even if the underlying cause can be identified and controlled or resolved, once the pet's sleep cycle is altered, a combination of medical therapeutics, cognitive therapeutics, behavioral modification, and environmental management, as well as drugs (discussed later and in **Table 5**), to reduce anxiety and help reestablish normal sleep cycles may all be required concurrently.

It is important to determine the precise pattern of aberrant nighttime waking. Some pets may be slow to settle and go to sleep compared with others that go to sleep and

Table 4
Cognitive dysfunction screening checklist

	Score: None, 0; Mild, 1; Moderate, 2; Severe, 3
Confusion – awareness – spatial orientation	Age First Noticed
Gets stuck or cannot get around objects	
Stares blankly at walls or floor	
Decreased recognition of familiar people/pets	
Goes into wrong side of door; walks into door/ walls	
Relationships – social interactions	
Decreased interest in petting/avoids contact	
Decreased greeting behavior	
In need of constant contact, overdependent, clingy	
Altered relationship with other household pets – less social	
Altered relationship with other household pets – fear/anxiety	
Aggression – family members – unfamiliar people –	
Family pets – unfamiliar pets – other:	
Response to stimuli	
Decreased response to auditory stimuli (sounds)	
Increased response, fear, phobia to auditory stimuli	
Decreased response to visual stimuli (sights)	
Increased response, fear, phobia to visual stimuli	
Decreased responsiveness to food/odor	
Activity/anxiety – increased/repetitive	
Pacing/wanders aimlessly	
Anaps at air/licks air	
Licking owners – household objects –	
Vocalization	
Increased appetite (eats quicker or more food)	
Restless/agitation	
Activity – apathy/depressed	
Decreased interest in food/treats	
Decreased exploration/activity	
Decreased interest in social interactions/play	
Decreased self-care (hygiene)	
Sleep-wake cycles; reversed day/night schedule	
Restless sleep/waking at nights	
Increased daytime sleep	
Learning and memory – House soiling	
Indoor elimination at sites previously trained	

(continued on next page)

Table 4 (continued)	
	Score: None, 0; Mild, 1; Moderate, 2; Severe, 3
	Age First Noticed
Decrease/loss of signaling	
Goes outdoors, then returns indoors and eliminates	
Elimination in crate or sleeping area	
Learning and memory – work, tasks, commands	
Impaired working ability – decreased ability to perform task	
Decreased responsiveness to familiar commands and tricks	
Inability/slow to learn new tasks	

Adapted from Landsberg GM, Hunthausen W, Ackerman L. The effects of aging on the behavior of senior pets. Handbook of behavior problems of the dog and cat. 2nd edition. Saunders; 2003. p. 273; with permission.

then wake multiple times a night. Although rare, some pets may be unable to settle for the entire night. It is also important to determine the dogs daily routine: some dogs sleep more during the day or early morning or throughout the evening but then keep family members awake at night. Cats are naturally more active at night, especially around dawn, so nighttime waking is not necessarily an abnormal behavior in the cat. However, a change in previously established sleep patterns, increased activity, disorientation, and vocalization may be related to abnormal conditions, such as medical conditions, pain, or cognitive dysfunction. Furthermore, cats may be territorially reactive to activities by felines outside the home. Noise phobias may occur all the time but be more problematic at night, presumably because of reduced ambient noise, which may lead to an apparent random or unpredictable pattern of nighttime waking when the stimulus is not audible to the people. When nighttime waking is mentioned by families, it is important to regard this as an immediate and serious concern; it is essential to resume normal nighttime sleeping patterns promptly to assure the welfare of family and pets.

Consideration of the pet's medical health issues, the pet's daily routine, and the pattern of nighttime waking, aids in both diagnosis and the development of treatment recommendations. For example, if a dog is not waking up the family until 5 AM, then modifications to the bedtime routine are not likely to be helpful and may be counterproductive. Pets that cannot settle, but then eventually sleep all night and into the morning, may benefit from changes to prebedtime routine. It is important to inquire about the desired sleeping pattern for family members because variations or unusual patterns in their routine will affect the timing of recommendations.

Basic recommendations begin with a consistent and predictable bedtime routine. Use family habits or the dog's previous sleeping patterns as a guide. For dogs, massage or gentle petting while the pet is resting in desired sleeping area may promote the atmosphere and routine essential for sleeping. Turn off the TV and at least dim the lights, though some elderly pets benefit from a night light as their vision deteriorates. Recommend a pheromone collar or a pheromone diffuser in the sleeping area of the dog or cat, respectively. Provide a comfortable place to sleep; again, first consider the pet's previous pattern of rest before making recommendations. Most

	Dog	Cat
Alprazolam ^a	0.02–0.1 mg/kg twice to 4 times a day	0.125–0.25 mg/cat once to 3 times a day
Diazepam ^a	0.5–2 mg/kg once to 4 times a day	0.2–0.5 mg/kg twice a day to 3 times a day
Oxazepam ^a	0.2–1 mg/kg once to twice a day	0.2–0.5 mg/kg once to twice a day
Clonazepam ^a	0.1–1.0 mg/kg twice to 3 times a day	0.02–0.2 mg/kg once to twice a day
Lorazepam ^a	0.025–0.2 mg/kg once to 3 times a day	0.025–0.05 mg/kg once to twice a day
Melatonin	3–9 mg/dog	1.5–6 mg/cat
Diphenhydramine ^a	2–4 mg/kg	1–4 mg/kg
Fluoxetine	1.0–2.0 mg/kg once a day	0.5–1 mg/kg once a day
Sertraline	1–5 mg/kg once a day or 2.5 mg/kg divided twice a day	0.5–1.5 mg/kg once a day
Buspirone	0.5–2.0 mg/kg once to 3 times a day	0.5 to 1 mg/kg twice a day
Trazodone	2–5 mg/kg as needed up to 8–10 mg/kg twice to 3 times a day	Not determined
Phenobarbital ^b	2.5–5 mg/kg twice a day	2.5 mg/kg twice a day
Gabapentin ^b	10–30 mg/kg twice to 3 times a day	5–10 mg/kg once to 3 times a day
Potassium bromide ^b	10–35 mg/kg daily or divided twice a day	Not recommended
Selegiline	0.5–1 mg/kg once a day in the morning	0.5–1 mg/kg once a day in the morning
Memantine	0.3–1 mg/kg once a day	Not determined
Amantadine	1.25–4 mg/kg by mouth once to twice a day	3 mg/kg by mouth once a day

^a Use single dosing before sleep or anxiety-evoking event, up to maximum daily dosing for control of ongoing anxiety.

^b Doses are for seizure control: dose and frequency may need to be adjusted when used for other applications (pain management, behavior therapy) or if combined with other drugs.

pets benefit from a specific preferred resting area; for dogs this may be near family members such as in the bedroom, with a crate or tether or with the door closed (if the dog tends to wander or soil at night). Some dogs select another location removed from family members. Provision of a heated bed may ease pain and sensory discomfort caused by cold.

Advise families that punishment or scolding will not ease nighttime waking but will contribute to the pet's anxiety and confusion. However, unless the dog's medical needs require that it be attended to during the night, giving any form of attention (feeding, walks, allowing onto the family bed, or even scolding) may further reinforce the behavior. For dogs with extreme difficulty sleeping accompanied by increased activity at night, tethering or crating the pet might be considered. A head halter may help a dog settle if it has been trained to it already. Comfort wraps such as the Anxiety Wrap (Animals Plus, LLC) or Thundershirt (Thundershirt) may reduce agitation and allow rest. The Calming Cap (Premier Pet Products) may be useful to help a dog settle, but some form of confinement should be used to prevent wandering because the

dog's visual ability is reduced. In the morning, open blinds to allow natural sunlight early in the morning and consider the benefits of getting the pet outdoors. Exposure to natural light may help maintain a night-day cycle. The long walks the family took when the pet was healthy could be replaced by quiet time together in the outdoors; quality time on park benches or picnic blankets should replace long, strenuous walks in dogs with weakness or pain. Increased daytime enrichment with several quality interactive sessions, feeding toys (as demonstrated by a senior cat and a dog on videos online (within this article at www.vetsmall.theclinics.com, May 2011 issue); (Videos 2 and 3) and a final interactive play session before bedtime may help encourage better nighttime sleep while promoting the human-animal bond. Further discussion of drugs or natural alternatives to reduce anxiety and help reestablish nighttime sleep are discussed later.

Management of CDS

Although both environmental enrichment and therapeutic options are useful in improving the signs, and perhaps slowing the decline, of CDS, the first consideration is the treatment of any other concurrent medical problems, including the management of pain and discomfort. Any medications that are essential in the treatment of the pet's medical health need to be considered in the use and selection of therapeutic agents for CDS. Because it is increasingly likely that geriatric and palliative care patients will require multiple medications or supplements, the veterinarian should take responsibility to advise owners of potential interactions (both beneficial or harmful) of those medications and supplements dispensed as well as those that the owner may obtain from other sources.

Maintaining a regular, predictable daily routine and providing the pet with control to engage in pleasant, and avoid unpleasant, interactions may help to reduce stress and anxiety and maintain temporal orientation.² Canine studies have also shown that, not only is mental stimulation an essential component in maintaining quality of life, but that continued enrichment in the form of training, play, exercise, and novel toys can help to maintain cognitive function and perhaps slow cognitive decline.⁵ This is analogous to human studies in which education, brain exercise, and physical exercise have been found to delay the onset of dementia. Concurrent use of diets and supplements for improving cognitive function may help the pet better engage in enrichment activities as well as, perhaps, provide some level of neuroprotective effect.

Because medical problems may preclude the pet from engaging in some forms of enrichment, owners should find alternative forms of social activities (eg, short walks, tug toys, find-and-see games, reward training) and various forms of object play (eg, food manipulation toys, chew toys) that are within the pet's physical and mental capabilities (Figs. 3 and 4). A video of the cat in Fig. 3 is available online (within this article at www.vetsmall.theclinics.com, May 2011 issue) that illustrates play in a senior cat (Video 4). Owners should also have realistic expectations, or be advised, as to the limitations that might be achieved in improving the behavior of a senior pet based on the pet's physical health and cognitive function. Accommodations may also need to be made to the owner's schedule or the pet's environment to address such needs. For example, dogs may require more frequent trips outdoors, a dog walker, or an indoor elimination area if they have medical conditions leading to polyuria or incontinence, whereas ramps and physical support devices may be required to help address mobility issues. For cats, more litterboxes, or more frequent cleaning, may be required to treat house soiling caused by polyuria, whereas ramps, litterboxes with lower sides, larger litter boxes, or relocation of litterboxes may be required for cats with mobility problems. Provision of nonslip surfaces or rugs may provide stability and avoid an



Fig. 3. A food-filled toy, hanging from the doorway, can be used to encourage and stimulate both physical and mental activity to acquire food. (Courtesy of Gary Landsberg, DVM, MRCVS, Thornhill, Ontario, Canada.)

anxiety-causing event such as falling or slipping. As sensory acuity, sensory processing, and cognitive function decline, adding new odor, tactile, and sound cues (provided there is some residual hearing) might help the pet better navigate its environment and maintain some degree of environmental familiarity and comfort.

Therapeutic Options for Sleeplessness and Anxiety

In addition to the control of medical problems including CDS, and the use of behavior modification and environmental management, pharmacologic or natural therapeutics



Fig. 4. Mental enrichment for the senior pet may be provided in the form of food puzzle toys. Manipulation of the toy by oral or physical means allows release of the food, which immediately rewards the exploratory behavior of a novel item. (Courtesy of Theresa DePorter, DVM, Bloomfield Hills, MI.)

may be required to reduce anxiety and aid in reestablishing normal sleep-wake cycles (see **Table 5**). Melatonin, although not sedating, may be useful as part of a bedtime routine ritual and may be best given 30 minutes before bedtime; melatonin should not be redosed at other times of day when used to establish nighttime sleeping patterns. Some medications, such as diphenhydramine, phenobarbital, or trazodone, which may be given for other indications or solely for sleep support, may provide useful sedation if dosed before bedtime provided they do not cause excessive sedation or incoordination that lasts into the daytime. For the dog or cat that has difficulty settling at night but then sleeps well, situational use of anxiolytics that may promote sleep may be beneficial as adjunctive therapy to behavior modification. Benzodiazepines may be useful because of rapid onset of short-acting anxiolytic and sedative effects. In senior pets, especially if liver function might be compromised, clonazepam, lorazepam, or oxazepam might be preferable to alprazolam or diazepam because they have no active intermediate metabolites. Because pain may contribute to unsettled sleep or night waking, consider pain management products. Gabapentin might be a consideration as an adjunctive therapy for pain management as well as for its behavioral calming effects.

For senior pets with generalized anxiety, noise phobias, or separation anxiety that is not restricted to nighttime anxiety, consider drugs with fewer side effects, such as buspirone and selective serotonin reuptake inhibitors such as fluoxetine and sertraline. Paroxetine and tricyclic antidepressants have varying degrees of anticholinergic effects and may therefore be less desirable. Natural compounds that have been shown to be beneficial in reducing anxiety and perhaps help pets to settle at night include suntheanine (Anxitane, Virbac), honokiol and berberine extracts (HarmonEase, VPL), α -casein (Zylkene Intervet/Schering-Plough Animal Health), pheromones (DAP and Feliway, CEVA Animal Health), and lavender essential oils.⁶¹

Drug Therapy for CDS

There are many medications available for treatment of cognitive dysfunction but data to support efficacy is variable and in some cases minimal (see **Table 5**). Selegiline (Anipryl, Pfizer Animal Health) was the first product approved for the treatment of CDS in dogs. Selegiline (which is also licensed in Europe under the brand name Selgian, CEVA Animal Health) is a selective and irreversible inhibitor of MAOB in the dog.⁶² It may act by enhancing dopamine and other catecholamines in the cortex and hippocampus and has been shown both in the laboratory and clinical setting to improve signs related to CDS. Selegiline is considered to be neuroprotective, potentially by increasing efficiency of superoxide dismutase and catalase for improved free radical scavenging, which may decrease nerve damage/degeneration.⁶³ Selegiline is not licensed in cats; however, it has been used off label at the same dose with anecdotal reports of improvement in CDS-like signs.⁶⁴ Selegiline may require from 2 to 6 weeks of administration to show clinical improvement. It should not be used concurrently with other monoamine oxidase (MAO) inhibitors including amitraz (Mitaban, Upjohn, Preventic Allerderm/Virbac), selective serotonin reuptake inhibitors, tricyclic antidepressants, narcotics, and dextromethorphan. Selegiline should be used cautiously with drugs that might enhance serotonin transmission, such as buspirone, trazodone, and tramadol.

Propentofylline (Vivitonin, Intervet/Schering-Plough Animal Health) is licensed in some European countries for the treatment of dullness, lethargy, and depressed demeanor in old dogs. Propentofylline may increase blood flow to the heart, skeletal muscles, and brain. It inhibits platelet aggregation, inhibits thrombus formation, has bronchodilator action, and improves the flow properties of erythrocytes. It has a direct

effect on the heart and reduces peripheral vascular resistance, thereby lowering cardiac load. Although not licensed in cats, it has been anecdotally reported to be useful.¹⁶

Drugs that may enhance the noradrenergic system, such as adrafinil and modafinil, might be useful in older dogs to improve alertness and help maintain normal sleep-wake cycles (by increasing daytime exploration and activity).^{65,66} However, dose and efficacy in dogs has not been established. Other new treatment strategies may include the *N*-methyl-D-aspartate receptor antagonist memantine or hormone replacement therapy.⁶⁷

Because the elderly are particularly susceptible to the effects of anticholinergic drugs, it is prudent to consider therapies with less anticholinergic effects and those that are less sedating for both dogs and cats; however, although drugs that enhance cholinergic transmission might be beneficial for senior dogs, there is limited evidence available for dose schedule recommendations.⁶⁸

Nutritional and Dietary Therapy for CDS

Another strategy in the treatment of CDS is to use dietary supplements to improve antioxidant defense and reduce the toxic effects of free radicals. In humans, several studies have found that dietary management may reduce the risk, or delay the onset, of dementia. For example, a high intake of fruits and vegetables, nuts, whole grains, and vitamins E and C may decrease the risk for cognitive decline and dementia.^{69,70} In dogs, a senior diet (Canine b/d, Hills Pet Nutrition) has been shown to improve the signs and slow the progress of cognitive decline. It is supplemented with a combination of fatty acids, antioxidants (vitamins C and E, β -carotene, selenium, flavonoids, and carotenoids), as well as DL- α -lipoic diet and L-carnitine, which are intended to enhance mitochondrial function.^{5,71,72} The diet improved performance on several cognitive tasks when compared with a nonsupplemented diet, beginning as early as to 2 to 8 weeks after the onset of therapy. After 2 years, a control group (no enrichment, control diet) showed a dramatic decline in cognitive function, whereas those in either the enriched diet or the environmental enrichment group continued to do better than controls.^{71,72} However, the combined effect of the enriched diet plus the enriched environment provided the greatest improvement.⁵ More recently, Purina One Vibrant Maturity 7+ Formula (Nestlé Purina PetCare), a diet that uses botanic oils containing medium-chain triglycerides (MCT) to provide ketone bodies as an alternate source of energy for aging neurons, has also been shown to significantly improve cognitive function in senior dogs.⁷³ Supplementation with MCTs has been shown to improve mitochondrial function, increase polyunsaturated fatty acids, and decrease amyloid precursor protein in the parietal cortex of aged dogs.^{74,75} Cognitive diets for cats have not yet been developed, although canine cognitive diets are generally nutritionally sound for cats.

Several clinical trials have shown improvements in clinical signs associated with CDS in dogs using dietary supplements containing phosphatidylserine, a membrane phospholipid.^{10,76,77} One product, Senilife (CEVA Animal Health) was tested on dogs using a memory task after administration of 60 days of either a placebo or the product.⁷⁸ An example of a cat performing a memory task in a laboratory model may be viewed online (within this article at www.vetsmall.theclinics.com, May 2011 issue) and is discussed earlier (see Video 1).

There is also a video online (within this article at www.vetsmall.theclinics.com, May 2011 issue) showing a dog performing the variable-object discrimination test, which examines selective attention. In this task, the correct object is presented with 0 to 3



Fig. 5. Senior pets may show profound physical changes such as graying of hair around the face and muzzle that can be recognized effortlessly as a sign of aging, but the cognitive changes are more subtle and oblige our intuitive and thoughtful compassion for our aging pets. (Courtesy of Theresa DePorter, DVM, Bloomfield Hills, MI.)

identical incorrect objects (distracters). Performance declines as distracter number increases (Video 5).

Performance accuracy was improved in the treated group compared with baseline, and dogs receiving the supplement in the first portion of the study maintained their improved performance.⁷⁸ The product also contains *Ginkgo biloba*, an MAO inhibitor and free radical scavenger, vitamin B6 (pyridoxine), vitamin E, and resveratrol, which may protect against oxidative damage and reduce β -amyloid secretion. The tested product was an earlier formulation excluding resveratrol.

S-Adenosyl-L-methionine (SAME; Novifit, Virbac), is found in all living cells and is formed from methionine and ATP. SAME may help to maintain cell membrane fluidity, receptor function, and the turnover of monoamine transmitters, as well as increase the production of glutathione.⁷⁹ In a recent placebo-controlled trial, greater improvement in activity and awareness was reported in the SAME group after 8 weeks.⁸⁰ Both Sen-life and SAME have label claims for use in cats, but there are no published studies to support their efficacy in improving signs of CDS in cats.

SUMMARY

The assessment and consideration of the senior dog's and cat's quality of life is complicated by age-related changes in health and behavioral signs. Physical signs of old age may be obvious (Fig. 5), but mental and cognitive changes require more careful observation. Changes in behavior may represent the earliest indications of medical problems, or disorders of the central nervous system, and these may be bidirectional. Moreover, diagnoses of CDS and other age-related behavioral problems are underdiagnosed and affect a substantial portion of aged companion animals. Therefore, the primary caregiver must establish the contribution of medical problems, as well as the effects of concurrent medications and pain, to behavioral signs consistent with age-related behavioral problems such as CDS, sleep disturbances, and anxiety. This article describes potential treatment regimens to address age-related behavioral problems, as well as a framework for investigating differential diagnoses. Overall, early identification of changes in behavior are essential for the adequate treatment and management of both medical and behavioral problems, as well as for monitoring outcomes.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at [doi:10.1016/j.cvsm.2011.03.017](https://doi.org/10.1016/j.cvsm.2011.03.017).

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