Cognitive Dysfunction

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Background

Cognitive dysfunction syndrome (CDS) is a chronic, progressive disease characterized by neuronal loss and neuroaxonal degeneration.[1,2] In dogs, CDS has some similarities to human Alzheimer's disease in neuroanatomic pathology.[3] Treatments include environment and behavior modification, comorbidity considerations, and medication for possible anxiety and agitation.

The prevalence of CDS in dogs and cats is fairly high. Reportedly, 28% of dogs 11 to 12 years of age and 68% of dogs 15 to 16 years of age show at least one sign associated with CDS.[4] In laboratory settings, dogs begin showing impairment in specific learning and memory tasks as early as 6 to 8 years of age.[5] The clinical presentation in cats is more ambiguous, although they may begin to show signs consistent with cognitive dysfunction at approximately 10 to 11 years of age. One study reported that 50% of cats older than 15 years of age had possible CDS.[5,6]

Screening patients 10 years of age or older as part of routine examination can allow for treatment to slow CDS progression or address signs that may distress patient and caregiver. Anxiety (eg, restlessness, fear or phobias, separation anxiety) can be a common sign of CDS. The most common signs in dogs are alterations in social interaction and a break in housetraining.[7] Altered social interactions may reflect an increase in neediness (ie, a dog seeks the owner more often) or the opposite (ie, a dog appears more aloof and disinterested in engaging the owner). In cats, the most common signs are vocalization (often at night)

MORE ▶

How I Treat Cognitive Dysfunction

- ❑ Treat and manage comorbid medical conditions.
- ❑ Provide environment and behavior modification.
- ❑ Provide nutritional support.
- ❑ Provide pharmacologic support.

CDS = cognitive dysfunction syndrome

and housesoiling without medical cause.[8] One of the most troubling signs for caregivers is the potential change in sleep–wake cycles: patients may remain awake throughout the night and pace, whine, or vocalize. Patients may also show anxiety or fear (agitation) that may result from disorientation.

Classically, the signs of CDS in dogs have been described with the acronym *DISH-A*:

- **D**isorientation (eg, wandering, going to the hinged side of doors, appearing confused)
- Social **I**nteraction changes
- **S**leep–wake cycle changes
- **H**ousetraining breaks (when previously housetrained)
- **A**ctivity level changes (decreased or increased)

Diagnosis

In patients with positive CDS responses on screening, a more detailed behavioral history can provide key information regarding areas of concern (see **How I Diagnose CDS**). It is important to include specific questions about when problem behaviors are most frequently observed, whether there are identifiable triggers for behaviors, and whether signs of anxiety are present.

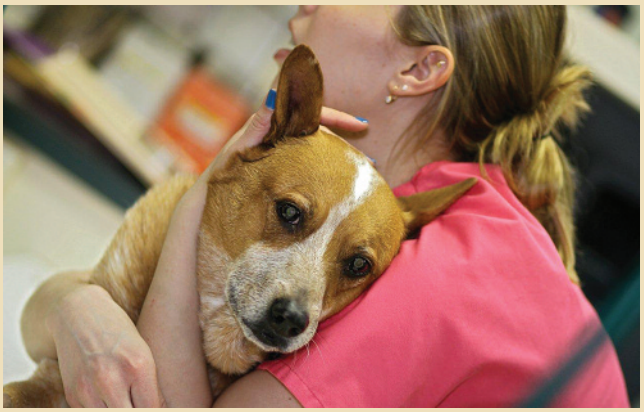
How I Diagnose CDS

- ❑ Screen older patients for early signs.
- ❑ Obtain a thorough behavioral history.
- ❑ Rule out other medical (eg, intracranial, extracranial) causes of the behavior.

A clear and consistent rating scale for each of the signs can help caregivers and veterinary personnel track changes over time. Having caregivers videotape behaviors can also provide insight on severity. The patient may be afflicted with several disease processes that can complicate CDS diagnosis and/or treatment. Chemistry panels, hematology profiles, and urinalyses can help determine whether other medical conditions exist. Imaging or advanced diagnostics may be needed to rule out other neurologic or painful conditions (see **Potential Medical Causes of Behavioral Changes**).

Potential Medical Causes of Behavioral Changes

- Other neurologic diseases (eg, pituitary macroadenoma, forebrain disease)
- Endocrine diseases (eg, hyper- or hypoadrenocorticism, hyper- or hypothyroidism, diabetes mellitus) can present with behavioral signs, including housesoiling (secondary to polyuria and/or lower urinary tract infection), increased vocalization (hyperthyroidism in cats), irritability, aggression, and lethargy.
- Painful conditions (eg, osteoarthritis, neoplasia, dermatologic disorders) in which patients have difficulty finding comfortable resting positions and may appear restless, anxious, irritable, or aggressive
- Metabolic disorders (eg, renal or hepatic dysfunction) can trigger behavioral signs (eg, disorientation, mental dullness, irritability, aggression, housesoiling).
- Hypertension can cause anxiety, restlessness, changes in activity level, confusion, and disorientation.
- Adverse effects from medications can affect behavior (eg, steroids can increase water intake and contribute to housesoiling, irritability, aggression).
- Sensory loss (eg, vision, hearing) can lead to confusion, disorientation, changes in movement, irritability, and housesoiling.



CDS = cognitive dysfunction syndrome, MAOI = monoamine oxidase inhibitor

How I Treat Cognitive Dysfunction

Treat and manage comorbid medical conditions.

Provide environment and behavior modification.

- Inform caregivers that treatment and management options are designed to slow CDS progression, but complete resolution may not be possible.
  - CDS is chronic and progressive, and the goal is to maintain function and quality of life for both patient and caregiver for as long as possible.
- Provide opportunities for engagement throughout the day to help maintain a normal sleep–wake cycle.
  - Opening the blinds or windows can help keep patients awake during the day.
- Provide physical and mental stimulation.
  - Enrichment (eg, training, play, exercise, toys) can help boost and maintain cognitive function.
  - Puzzle and food toys are forms of enrichment.
  - Structured and consistent playtime and exercise reinforce routines and are important for lowering stress and promoting cognitive health.
- Provide modified and alternative toileting opportunities for older patients.
  - This may include multiple, low-sided litter boxes for cats and provisions for dogs to go out often or have designated elimination areas within the home.
- Avoid marked changes in schedules, environments, and routines if possible.
- Train *settle* techniques for dogs using a dedicated mat.
  - Training when dogs are not agitated can condition a calm response that can be useful when dogs become more anxious or restless.

Provide nutritional support.

- Supplemented canine diets can provide fatty acids, additional antioxidants to combat the reactive oxygen species that increase with age, and alpha-lipoic acid to support mitochondrial function.[9]
- A diet enriched with medium-chain triglycerides has been shown to improve cognitive function in geriatric dogs.[10]
- Other nutritional supplements may be added to regular diets: L-theanine (for anxiety), *S*-adenosyl-L-methionine (SAMe),[11] phosphatidylserine,[12] and antioxidants.
  - SAMe, an endogenous methyl donor used to decrease oxidative stress by stimulating brain glutathione, has been shown deficient in humans with Alzheimer's disease.

  - Phosphatidylserine, a phospholipid component of the cell membrane, has several effects on acetylcholine and acetylcholinesterase, though data on its use in humans is mixed.
  - Formulations for phosphatidylserine and antioxidant mixtures exist.

Provide pharmacologic support.

- Selegiline hydrochloride (Anipryl, online.zoetis.com/us), a monoamine oxidase inhibitor (MAOI), is currently approved in the United States for CDS treatment in dogs.
  - It has not been approved for use in cats but has been used off-label.
  - In the author's experience, if improvement or stabilization is seen within the first month, improvement may continue in the following month or may plateau.
  - If no improvement is seen, the patient may benefit from another medication that addresses clinical signs.
  - MAOIs cannot be combined with other serotonergic drugs or other MAOI-containing products, including some antiparasitic products that include amitraz.
- Fluoxetine or sertraline
  - Both are selective serotonin reuptake inhibitors (SSRIs) that can help treat anxiety in geriatric patients.
  - Neither can be used with an MAOI.
- Sleep aids (eg, melatonin, benzodiazepines, trazodone)
  - Targeted therapy at bedtime can help reset the sleep–wake cycle, providing patients and caregivers with rest. ■ cb

See **Aids & Resources**, back page, for references & suggested reading.

A Comment on Cognitive Dysfunction

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Human cognition may be defined as the mental process of *knowing* or *possessing judgment*. This definition includes "that which comes to be known through perception, reasoning, or intuition." Animal cognition, meanwhile, is more difficult to define.

The study of animal cognition is largely empirical; the practice of science in this area relies on theoretic arguments and assumptions. Although there are arguments against animal minds, cognitive scientists studying animals largely accept that animals are minded, cognitive beings. Most owners feel strongly that their pet is capable of cognitive function; how they reach this conclusion includes a degree of anthropomorphism (ie, attribution of human characteristics or behavior to an animal or object).

Cognitive ethology is concerned with the influence of conscious awareness and intention on the behavior of an animal. Three different views exist towards whether a science of cognitive ethology is even possible: some deny any possibility of success in cognitive ethology, proponents keep an open mind about animal cognition and the utility of cognitive ethological investigation, and skeptics stand somewhere in between.

As a veterinary neurologist, I accept that a form of cognition exists in animals. I know *of* cognition in animals, but I know little *about* cognition in animals. Cognition (broadly defined) includes all the ways in which animals receive, process, and retain information and determine how (if at all) to respond. (It is the word *determine* that causes veterinary neurologists to hesitate.)

Regardless of species, it is unarguable that cognition is an aspect of brain function (more specifically, cerebral function). It follows that cognitive dysfunction is an aspect of cerebral dysfunction, caused by numerous conditions, particularly in older cats and dogs. Signs of cerebral dysfunction include behavior alterations, altered mental status, seizures, circling, and hemiparesis. Altered behavior may be the only clinical sign present in an animal with cerebral dysfunction. Cognitive dysfunction syndrome is diagnosed by eliminating other causes (ie, liver disease, brain neoplasia, cerebral stroke) of cerebral dysfunction.

It is thus the responsibility of every veterinarian to offer a comprehensive extracranial and intracranial workup of an older patient with signs of cerebral dysfunction, even when alterations in behavior are the sole presenting complaint, particularly if the behavior changes are of recent onset. ■ cb