Predicting behavioral changes associated with age-related cognitive impairment in dogs

Melissa J. Bain, DVM; Benjamin L. Hart, DVM, PhD, DACVB; Kelly D. Cliff, DVM;
William W. Ruehl, DVM, PhD, DACVP

Objective—To monitor the progression of age-related behavioral changes in dogs during a period of 6 to 18 months and to determine whether signs of dysfunction in any of 4 behavioral categories can be used to predict further impairment.

Design—Age-stratified cohort study.

Animals—63 spayed female and 47 castrated male dogs 11 to 14 years of age.

Procedure—Data were collected from randomly selected dog owners who were interviewed by telephone twice at a 12- to 18-month interval; data were included if the dog had lived ≥ 6 months between interviews. The interview focused on signs of impairment in the following behavioral categories: orientation in the home and yard, social interactions with human family members, house training, and the sleep-wake cycle. Dogs were determined to have impairment in 0 behavioral categories (on the basis of ≤ 1 sign for each category), impairment in 1 category (≥ 2 signs of dysfunction in that category), or impairment in ≥ 2 categories.

Results—Between interviews, 22% (16/73) of dogs that did not have impairment in a category at the time of the first interview developed impairment in that category by the time of the second interview. Forty-eight percent (13/27) of dogs that had impairment in 1 category at the time of the first interview developed impairment in ≥ 2 categories by the time of the second interview and were significantly more likely to develop impairment in ≥ 2 categories, compared with dogs that initially had impairment in 0 categories. Dogs with 1 sign of dysfunction in orientation were significantly more likely to develop impairment in that category, compared with dogs that had 0 signs of dysfunction in orientation.

Conclusions and Clinical Relevance—Age-related behavioral changes in dogs are progressive. Clinicians should consider trying to predict which dogs are most likely to become progressively impaired during the subsequent 6 to 18 months. (*J Am Vet Med Assoc* 2001;218:1792–1795)

Behavioral changes associated with aging in dogs are becoming a primary concern as dogs increasingly live to old age as a function of better veterinary care, advanced nutrition, and protection from accidental death. The advent of dopaminergic and neuroprotective drugs such as selegiline[a] for treatment of age-related signs of cognitive dysfunction in dogs has also challenged us to research these behavioral changes further. A cross-sectional study from our institution, using a structured interview with randomly selected hospital clients owning dogs that were 11 to 16 years of age, explored the prevalence of signs of dysfunction in the following behavioral categories: orientation in the home or yard, social interactions with human family members, house training, and the sleep-wake cycle.[1] These behavioral categories involve learning and memory and have been referred to as indicators of cognitive dysfunction or cognitive impairment[2,3] and would appear to reflect degenerative changes in the brain such as accumulation of β-amyloid deposits.[4-6] Behavioral categories include the signs of dysfunction for which improvement was reported in the pivotal clinical trial for FDA approval of selegiline for cognitive dysfunction syndrome in dogs.[7]

The prevalence study[1] was undertaken within the background of a large-scale clinical trial that provided data for FDA approval of selegilene for treatment of cognitive dysfunction syndrome in dogs.[7] That trial included extensive physical examinations with hematologic evaluation, blood biochemical analysis, and urinalysis at enrollment and exit stages to rule out medical disorders as probable causal factors in the signs of cognitive dysfunction. In the prevalence study, an extensive telephone interview with owners of dogs, preceded by a review of the hospital records, sought to exclude dogs that had evidence of organ system abnormality that may have contributed to ≥ 1 of the signs of dysfunction.

The purpose of the study reported here was to monitor the progression of age-related behavioral changes in dogs during a period of 6 to 18 months and to determine whether signs of dysfunction in any of 4 behavioral categories can be used to predict further impairment. Because disorientation within the home or environment could be a function of visual or auditory impairment as well as impairment in learning and memory, the degree to which the onset of disorientation during the longitudinal period corresponded with the onset of visual and auditory impairment between the 2 interviews was also determined.

Materials and Methods

Selection of dogs—All the owners of 11- to 14-year-old dogs from a previous prevalence study[1] who could be reached by telephone after 3 attempts (different times of day and week) were contacted 12 to 18 months after the initial interview (interview 1), and a second interview (interview 2) was

conducted that was identical to the initial interview. Owners whose dogs had lived ≥ 6 months beyond interview 1 were interviewed. For each dog still living at interview 2, survival time was recorded as the elapsed time between interviews. For dogs no longer living at interview 2, survival time was recorded as the elapsed time between interview 1 and death. Unless specified otherwise, data were pooled for all ages.

Interview format and questions—Owners were interviewed by a veterinary behaviorist (MJB), using the same structured interview used in interview 1. About 2 weeks prior to the first interview, owners were sent information about possible age-related behavioral changes in dogs. Owners did not know they would be contacted for the second interview. This procedure was used to help to prevent owners from being more sensitized to behavioral changes in the second interview, compared with the first interview.

Criteria for identifying dogs with impairments in the various categories were also the same as in interview 1. During each interview, 3 to 4 specific questions were asked that addressed signs of dysfunction within each behavioral category. The criterion for impairment in a category was that dogs had ≥ 2 distinct signs in that category that were not observed at the time of the previous interview. A dog had impairment in orientation if it had ≥ 2 of the following signs: staring into space, getting lost in the house or yard, getting stuck in corners, standing at the wrong door or wrong part of the door to go out, and another sign that was logically attributable to disorientation. A dog had impairment in social interaction if it had ≥ 2 of the following signs: decrease in greeting owners, decrease in soliciting attention from the owners, and change (increase or decrease) in following owners around the house. A dog had impairment in house training if it had the following 2 signs: started to urinate or defecate in the house with no other behavioral or medical explanation discernible such as urinary incontinence or separation anxiety, and a decrease in signaling to go out or a decrease in use of a dog door. If a dog was strictly an outdoor dog or never house trained, so that learned house training could not be evaluated, the dog was not included in our study. A dog had impairment in the sleep-wake cycle if it had ≥ 2 of the following: regularly waking up the owner at night by pacing or vocalizing, sleeping less at night, and sleeping noticeably more during the day.

To have impairment in a category, a dog had to have the signs of dysfunction for that category ≥ 1 time a week continuously for at least the previous month. The interviewer made an effort to acquire objective information by asking for indicators relating to the signs of dysfunction. Before asking specific questions about signs associated with each behavioral category, the owner was given an opportunity to answer an open-ended question related to that category. Efforts were made to not lead the owners to expect that there was a correct answer to any of the questions asked. As in interview 1, owners were also asked about visual and auditory impairments.

Statistical analysis—Inasmuch as there was no effect of age by sex interaction on impairment in any of behavioral categories in the prevalence study,[1] data in our study from spayed female and castrated male dogs were pooled for analyses unless otherwise indicated. The percentage of dogs with impairment in each category at interview 1 was compared with the percentage of dogs with impairment at interview 2 by use of logistic regression analysis. Changes in signs within a category as well as changes in impairment among categories were analyzed.

A χ^2 test for independence was used to determine whether impairment in 1 category at interview 1 was predictive of impairment in ≥ 2 categories at interview 2, compared with no impairment in any category at interview 1. It was

also determined whether 1 sign of dysfunction in a category at interview 1 was predictive of impairment in the same category at interview 2, compared with 0 signs of dysfunction in that category at interview 1. For dogs that developed impairment in vision and hearing between the 2 interviews, the logistic regression test was used to determine whether there was a significant increase in these impairments. Significance for all analyses was set at $P < 0.05$, using a 2-tailed t-test.

Results

Dogs—Of the 110 (63 spayed females and 47 castrated males) dogs included in our study, 32 were alive at interview 2, and 78 had died but had lived ≥ 6 months after interview 1. Mean survival time for all dogs was 15.2 (± 2.9) months.

Percentages of dogs with impairment in each behavioral category at interviews 1 and 2 were determined for dogs that were 11 to 12 (n = 62) and 13 to 14 years old (48) as of interview 1 (**Fig 1**). Of the 11- to 12-year-old dogs, 23% (14/62) had impairment in ≥ 1 category at interview 1, and 44% (27/62) had impairment in ≥ 1 category at interview 2. The number of 11- to 12-year-old dogs with impairment in ≥ 2 categories increased from 5 to 18% (3/62 to 11/62) between interviews.

Of the 13- to 14-year-old dogs, 48% (23/48) had impairment in ≥ 1 category at interview 1 (Fig 1), and 69% (33/48) had impairment in ≥ 1 category at interview 2. The number of 13- to 14-year-old dogs with impairment in ≥ 2 categories increased from 13 to 36% (6/48 to 17/48) between interviews.

The increase in impairment was significant within all categories ($P < 0.001$) between interviews as well as for the increase in the number of dogs with impairment in ≥ 1 ($P < 0.001$) and ≥ 2 ($P < 0.001$) categories. The increase in dogs with impairment in ≥ 1 or ≥ 2 categories at interview 2 reflected an increase in signs of cognitive dysfunction in dogs that already had some signs or the first appearance of signs in dogs that did not have signs at interview 1. Only 2 dogs reported to have an impairment in a behavioral category at interview 1 did not have impairment in that category at interview 2.

Predicting changes in behavior—Thirteen of 27 (48%) dogs that had impairment in 1 category at inter-
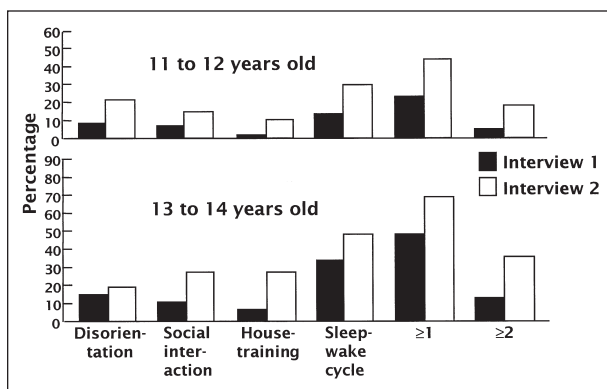

Figure 1—Percentage of 11- to 12-year-old (n = 62) and 13- to 14-year-old (48) dogs with impairment in each of 4 behavioral categories at interviews 1 and 2 as well as impairment in ≥ 1 and ≥ 2 categories. Ages are as of interview 1. There was a significant ($P < 0.05$) increase in impairment in each category and degree of impairment between interviews when data from dogs of all ages were combined.

view 1 had impairment in ≥ 2 categories at interview 2, whereas only 8 of 73 (11%) dogs that did not have impairment in any category at interview 1 had impairment in ≥ 2 categories at interview 2. Thus, impairment in 1 category was significantly ($P = 0.012$) predictive of impairment in ≥ 2 categories 6 to 18 months later.

There was a significant increase in the progression of disorientation in dogs that had 1 sign of dysfunction in that category, compared with dogs that had 0 signs (**Fig 2**; $P < 0.001$). Dogs with 1 sign of dysfunction in social interaction or house training at interview 1 often developed impairment in those categories at interview 2, compared with dogs that had 0 signs of dysfunction, but this difference did not reach significance for social interaction ($P = 0.052$) or house training ($P = 0.058$). The difference in progression between dogs with 1 sign of dysfunction in the sleep-wake cycle, compared with dogs with 0 signs, was insignificant ($P = 0.319$).

Changes in visual and auditory impairment—The onset of impairment in visual or hearing function between interviews was evident from comparing cross-sectional data of the 2 interviews for both age groups (**Fig 3**). One dog that was considered to have visual
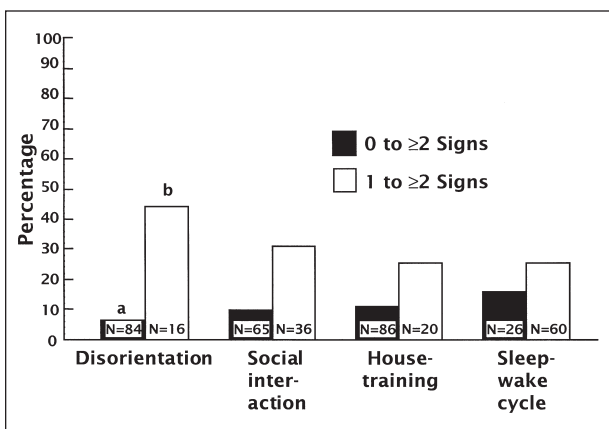

Figure 2—Percentage of dogs with 0 or 1 sign of dysfunction in each of 4 behavioral categories at interview 1 that had ≥ 2 signs of dysfunction in that category at interview 2. [a,b]Different letters within a set of bar graphs indicate significant differences ($P < 0.05$).
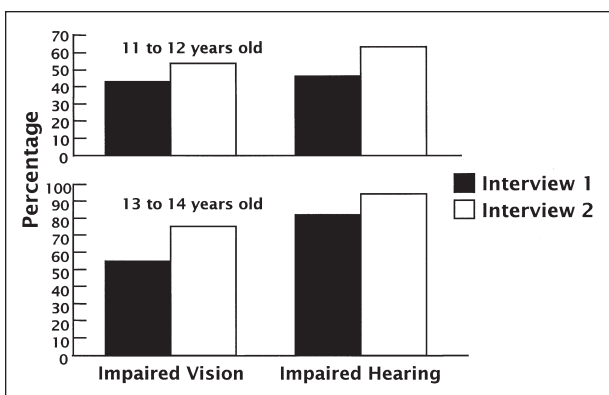

Figure 3—Percentage of 11- to 12-year-old (n = 62) and 13- to 14-year-old (48) dogs with impairment in vision and hearing at interviews 1 and 2. Increases in visual and auditory impairment between interviews were significant ($P < 0.05$) across age groups. Ages are as of interview 1.

impairment at interview 1 was reported to not be visually impaired at interview 2. Results of logistic regression analysis indicated that between interviews, there was a progressive significant increase in impairment in visual ($P < 0.001$) and hearing ($P < 0.001$) function.

Of 16 dogs not visually impaired at interview 1 but reported as visually impaired at interview 2, only 2 (13%) also had impairment in orientation, and conversely, of 12 dogs that became disoriented between interviews, only 2 (17%) acquired visual impairment. Similarly, there was little correspondence between onset of auditory impairment and onset of disorientation. For auditory impairment, 4 of 17 (24%) dogs that became hearing impaired also became disoriented, while 4 of the 12 (33%) dogs that became disoriented also became hearing impaired in the interval between interviews.

Discussion

Impairment in the behavioral categories of orientation, social interactions, house training, and sleep-wake cycle, reflecting a loss of memory and learning, is increasingly likely as dogs advance in years. A significant increase in the prevalence of dogs with impairment in each category was apparent in a time span of 6 to 18 months. The increase in perceived prevalence of the signs of dysfunction recorded between interviews could partially reflect increased sensitivity of the owners to noticing behavioral changes. However, this effect should have been minimal, because prior to interview 1, the owners had been sent an information sheet advising them of the types of age-related behavioral changes that may develop. No intervening contact was made with owners between interviews, and the owners did not know they would be contacted for interview 2.

For our longitudinal study, data were obtained on dogs that survived a mean of 15.2 (± 2.9) months after interview 1. Almost all dogs in our study had progressive impairment or impairment that stayed the same over time. Only 2 dogs that were considered to have impairment in a category at interview 1 did not have impairment in the same category at interview 2. This finding indicates that the behavioral changes, which were considered markers of cognitive function, reflect a decrease in function of the brain areas responsible for memory and learning. A progressive deterioration in behaviors related to memory and learning is what one would expect over time in dogs suffering from cognitive dysfunction syndrome. Neuropathologic findings and types of signs of dysfunction in aging dogs and in humans with Alzheimer's disease are similar.[1-6,8,9]

The progression of signs of cognitive dysfunction in some dogs in our study could also have been influenced by an organ system abnormality other than brain degeneration. Although most old dogs have ≥ 1 major organ system disorder, data from the clinical trial with selegilene,[7] resulting in improvement in the signs of dysfunction of orientation, social interaction, house training, and sleep-wake cycle, suggest that the signs of cognitive dysfunction in our study were more likely a reflection of deterioration in the brain than in other organ systems, because selegilene, with dopaminergic and neuroprotective properties, would be expected to primarily affect brain function.

Results of our study indicate that dogs with some signs of dysfunction in a behavioral category were much more likely to become severely affected 6 to 18 months later than dogs with few or no signs, a concept that also applies to Alzheimer's disease.[10,11] In a clinical setting, this information can be used to predict which dogs are most likely to progress to a severe degree of impairment. Most at-risk dogs are those that have impairment in 1 category. In our study, 48% (13/27) of dogs with impairment in 1 category progressed to have impairment in ≥ 2 categories, whereas those with impairment in 0 categories were only a fifth as likely to progress to this severe degree of impairment. Dogs with 1 sign of dysfunction in orientation were significantly more likely to develop impairment in that category, compared with dogs that had 0 signs of dysfunction in orientation. Dogs with 1 sign of dysfunction in social interaction or house training at interview 1 often developed impairment in those categories at interview 2, but compared with dogs that had 0 signs of dysfunction, this difference did not reach significance. In our study, 1 sign of dysfunction in the sleep-wake cycle was clearly not predictive of progressive impairment in that category. This finding may reflect that compared with other behavioral categories, the sleep-wake cycle is the least clearly related to memory and learning.

Although disorientation would logically result from visual or auditory impairment, there was little correspondence between the onset of disorientation and the onset of visual or auditory impairment between interviews, revealing that in most instances, disorientation probably reflected deterioration of cerebral function much more than visual or auditory impairment. However, we believe that visual and hearing impairment would probably impact the severity or frequency of disorientation.

Because data in our study comprised the responses of owners over the telephone about behavioral changes in their dogs, one would expect some discrepancy between the actual changes in behavior, as may be assessed in a laboratory, and the owners' reports. Among the procedures that were used to reduce this discrepancy or the effects that such a discrepancy would have on data analysis was the use of a conservative evaluation system for classifying a dog as impaired in a behavioral category. This method may have excluded some dogs that had age-related impairments in memory and learning.

In terms of indications for medical and behavioral intervention in aging dogs, findings from our study suggest that dogs that would be candidates for pharmacologic treatment such as with the dopaminergic and neuroprotective drug, selegilene, would be those with 1 sign of dysfunction in orientation in the home or yard, social interactions, or house training. Such dogs are likely to develop more signs in these categories and eventually more severe stages of cognitive dysfunction. However, it is important in evaluating dogs that have signs of cognitive dysfunction to determine, to the degree possible by a thorough medical evaluation, that the signs are not caused in whole or in part by deterioration in some organ system other than deterioration of the brain. Treatment of signs of cognitive dysfunction is just one aspect of the care needed for maintaining the health and welfare of aging dogs.

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