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Modeling Human Cognitive Aging in the Beagle Dog

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Glossary of Abbreviations

DNMP: Delayed Non-Matching-to-Position Task
DNMS: Delayed Non-Matched to Sample
MCI: Mild Cognitive Impairment
SLL: Spatial List Learning Task
TGTA: Toronto General Test Apparatus

Summary

This paper summarizes what we have learned in the past 20 years about canine cognitive abilities, how these abilities change over time, and how canine cognition compares with human cognition. We have developed a battery of objective neuropsychological tasks to assess several cognitive domains. With respect to learning ability, dogs are proficient in tasks requiring associative learning and acquisition of simple relational rules. We've also examined performance on several tasks that assess executive function. Dogs perform well on two of these — reversal learning and selective attention — and poorly on others — notably tasks aimed at concept learning. On tasks designed to assess working memory, dogs require extensive training and show erratic performance in visual object recognition, but show much higher levels of performance on tasks assessing visuospatial memory. Most of our research has used laboratory-housed Beagle dogs. We have now extended this work to the clinic and have obtained similar data from pet dogs.

Cognitive abilities change with age in a manner that varies with cognitive domain. Tasks that involve complex learning are more sensitive to age than tasks solved more easily. These findings parallel the kinds of age-dependent cognitive changes that are known to occur in humans. There also are notable individual differences, particularly in performance on specific tasks. Some dogs can be characterized as successful agers, while others show a moderate impairment, which may correspond to a human condition known as mild cognitive impairment (MCI). Still other dogs develop more severe impairment, which may correspond to human dementia. These results model many aspects of human cognition, including the cognitive changes associated with human aging and the development of dementia.

Why Study Cognitive Aging in Dogs?

Over the past 20 years, our research program at the University of Toronto, and later at CanCog Technologies, has focused on understanding the process of cognitive aging in the Beagle dog and participating in developing interventions to counteract cognitive decline. Our interest was based on both a desire to understand and characterize canine aging per se and the potential value of the dog as a model of human aging and dementia.

Canine aging represents a uniquely important area of study because of the multiple roles that dogs have in human society, which includes companion animals, guide dogs, military working dogs and odor detection dogs. All these functions are sensitive to the cognitive status of the dog. Furthermore, clinicians have now identified a cognitive dysfunction syndrome in pet dogs that becomes progressively more severe with increased age.[1,2]

With respect to human aging, in some individuals, progressive cognitive decline is a prominent feature that can have devastating effects on quality of life and also impose a significant economic cost to society as a whole. Animal models provide a tool to better understand aging processes and develop interventions. Until recently, cognitive aging models were largely limited to rodents and primates.

Over the past 20 years, much of our work has been focused on understanding canine cognitive abilities and the link among cognition, age and brain changes. The rationale for the specific approach we've taken was based on both parallels between canine and human aging and on practical considerations. When compared to humans, the key features of the canine model include, but are not limited to, similarities in brain pathologies and similarities in the process of cognitive decline. There is now a large body of research on neurobiological changes associated with aging in the dog. We have known for some time that the aged canine brain develops diffuse amyloid plaques similar to the senile plaques seen in Alzheimer's patients.[3] More recent work has established that, like in the human brain, canine plaques contain pathological deposits of beta amyloid protein, following a biochemical pathway virtually identical to that seen in humans.[4] Brain aging in the dog is accompanied by structural changes associated with neuronal loss, including cortical atrophy and loss of white matter[5] and again, like the human brain, can develop cerebrovascular pathology and oxidative damage, processes that model events associated with human brain aging.[6]

This article focuses primarily on the work we've done in characterizing cognition and age-dependent cognitive decline in the Beagle dog. Because a major goal has been to utilize the dog as a model of human aging, we'll start with a brief overview of human cognitive aging. We next describe our work in characterizing canine cognition in the laboratory setting, examining how cognition changes with age and comparing the performance of dogs and humans on similar tasks. We'll also briefly discuss some new work involving development of cognitive assessment technologies for use in clinical settings. We conclude by identifying new target areas for future research.

Features of Human Cognitive Aging

Before we can effectively utilize an animal model of human cognitive aging, we must first identify what aspects of human cognitive aging we hope to model. We can identify three main features: domain specificity; individual differences; and age-associated neuropathology.

Domain Specificity

Human cognition encompasses a set of separate functions or domains, which are at least partially independent. These functional domains include executive functions (higher level functions that control other cognitive processes), visuospatial function, memory, learning of new information (episodic memory), language, and psychomotor function (link between cognitive control and motor function). Evidence of independence is supported by individual differences showing subjects can excel in one domain but do poorly in another, by data obtained from brain imaging studies that highlight differences in underlying brain circuitry, and by evidence showing that processes, such as aging, can be accompanied by greater deterioration in some functions than others. Thus, digit span, which assesses our ability to hold information into memory for a short-time period shows minimal age differences.[7] By contrast, we tend to process information more slowly, have greater difficulty in recalling previous events (episodic memory), and are slower in acquiring new information as we age.

Individual Differences in Impact of Age on Cognitive Abilities

In "successful agers," age-associated cognitive changes are relatively small and have little or no impact on quality of life, although we're apt to complain about memory lapses.[8] Successful agers are distinguished from subjects showing mild cognitive impairment and from a third group that develop dementia. The diagnostic label of MCI covers a wide range of individuals who show some degree of cognitive impairment but are not demented and can function within society. Dementia refers to a more global impairment in more than one cognitive domain that severely impacts the overall quality of life.

The existence of different subtypes of MCI provides further evidence of functional specificity. One distinction is between two primary clinical subtypes, based on whether they show a predominant memory disorder. Amnestic MCI is associated with memory disorders; non-amnestic MCI does not have a memory component. Within each of these systems, we can further distinguish subjects that show impairment in only one domain from those that show impairments in multiple domains.[9]

Link to Age-Dependent Brain Pathology

Human cognitive decline is associated with changes in the functioning of brain circuitry and with distinct lesions in the nervous system that disrupt normal functioning of nerve cells. Two such lesions, neurofibrillary tangles, resulting from the accumulation of intracellular hyperphosphorylated tao deposits, and neuritic plaques, linked to accumulation of extraceullar amyloid deposition, are widely thought to be linked to age-dependent cognitive decline, and more specifically to Alzheimer's disease.

Procedures Used in Canine Cognitive Assessment

When we started our examination of canine cognitive aging, previous research had shown that aged dogs develop similar brain pathologies to those seen in aged humans, but there was no work looking at the effects of age on cognition. As a starting point, we were guided by previous research on non-human primates in which neuropsychological strategies had been used to develop cognitive assessment measures and to use these measures to study cognitive aging. This strategy entailed developing tasks that could be linked to known brain circuitry and to distinct functional cognitive domains. Our goal was to develop comparable protocols for use with the dog. We subsequently extended this work to develop novel tasks that were uniquely suited for testing dogs.

General Methods

Toronto General Test Apparatus (TGTA)

Most of our cognitive assessment protocols have utilized a standardized test apparatus that was modified from a testing apparatus used in assessment of primates (called the Wisconsin General Testing Apparatus). The canine version, which we've called the Toronto General Test Apparatus (TGTA), consists of an enclosed chamber with height-adjustable stainless steel bars at the front.[10] The experimenter is separated from the dog by a screen with a one-way mirror and hinged door that can be raised by the experimenter. The apparatus also consists of a sliding Plexiglas tray with three or four parallel food wells that can be covered with a variety of stimulus objects and presented to the animal by the experimenter. The current version of the test apparatus has a number of small modifications to reduce distractions and to simplify the presentation of the tray (see Figure 1). When the experimenter now slides the tray toward the animal, it automatically opens a screen to permit a response by the subject.

Setting up Different Tasks

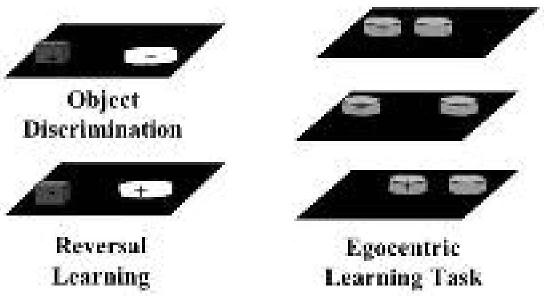
We've developed a standardized training protocol that we use in all our dogs. The dogs are initially trained to find food rewards in open food wells upon presentation of the tray. They then are taught to displace a single object covering a food well to obtain a food reward when the tray containing the object is presented by the experimenter. After learning to respond to a single object, the dogs are repeatedly presented with two distinct objects, only one of which is associated with a food reward. This task, known as object discrimination learning, provides an initial measure of dogs' learning ability.

Dedicated software is used to control timing and randomization procedures, to indicate stimuli and reward locations, to store responses, latencies and comments, and to generate and store back-up electronic files at the end of a cognitive test session. The TGTA and software allowed us to develop a variety of different test protocols, which were designed to provide assessment of domain specific cognitive functions. Figure 2 illustrates examples of how we set up different test protocols.

Learning Versus Performance Test Protocols

The tasks we've used fit into either of two kinds of test protocols. For the first, the animals are naïve to the task and are tested for their ability to learn a rule. The second involves testing the animals on a familiar task, which can be used to assess specific functional abilities such as memory, attention and perceptual ability.

Figure 2



Test paradigms used in assessing discrimination and reversal learning (left panel) and egocentric spatial learning (right panel). In discrimination learning protocol, subjects are presented with two objects, one of which is associated with reward and the other with non-reward. In the reversal task, the associations are switched so that the object initially associated with reward is now associated with non-reward and vice versa. In the egocentric task, subjects are presented with two identical objects using three food wells and are always rewarded for responding to the object closest to their left (or right). Thus, the center well is the correct response when the alternative is to the animal's right, and the incorrect response when the alternative is to the animal's left.

Figure 1

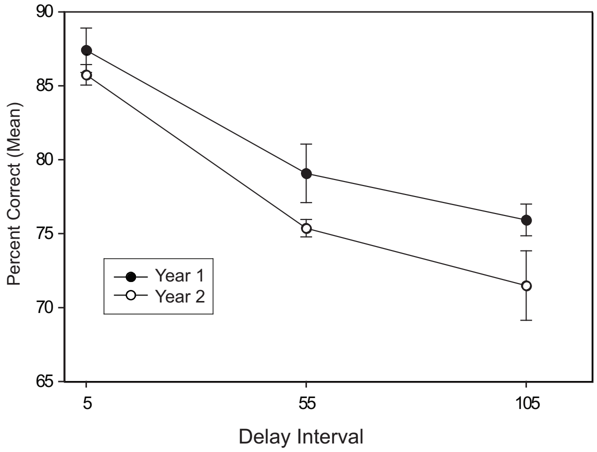
TGTA: This shows the current version of the test apparatus used for cognitive assessment of canines. The supplies on the table are part of the standard equipment used in cognitive testing.

Learning Protocol: In training animals on a new task, our standard training entails testing animals repeatedly, once daily over a fixed block of trials until the animals either achieve a predetermined criterion level of performance or unsuccessfully complete a maximum number of test sessions. Thus, we customarily set an upper limit on the number of days that an animal will be tested before concluding that the animal is unable to learn the task. Our learning criterion typically requires that the subjects first demonstrate performance accuracy of at least 80%, and second, that they can maintain a 70% level of performance over subsequent testing.

One task we used frequently is called the delayed non-matching-to-position task (DNMP) and requires the subjects to first learn a specific rule about the location of food and to then hold in memory the location of a test object for a variable amount of time. The task consists of two components: a sample component, in which a stimulus is presented at one of three locations, and a test component, in which identical stimuli are presented at two locations, including the location of the sample. To learn the task, the animals must learn to respond to the new location on the test trial.

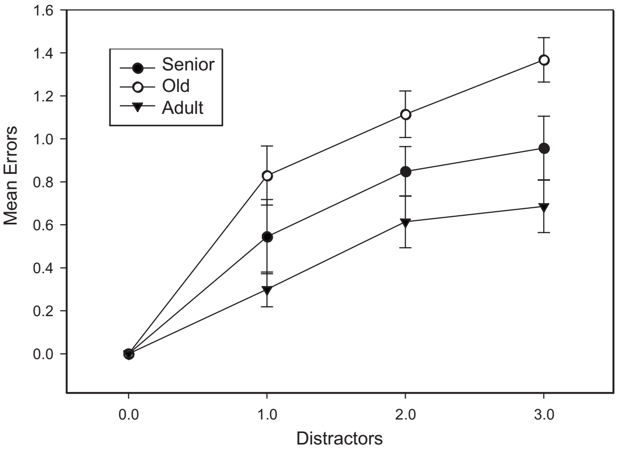
Assessment of Working Memory, Perceptual Abilities and Attention: In the second type of protocol, the animals are tested on a task they have previously learned, but the test conditions are modified to allow assessment of specific cognitive domains. For example, after an animal has learned the DNMP, the time

Figure 3



Performance on the DNMP as a function of delay between presentation of sample and test stimuli. The above data were obtained from the same group of highly experienced six animals one year apart. The results show that accuracy of performance falls off as a function of delay. The performance decrement in the second test year is probably linked to the fact that the animals are one year older.

Figure 4



Performance of adult (3 to 4 years of age), old (8 to 9 years of age) and senior (>10 years of age) dogs on the attention task. Subjects were presented with 0 to 3 distracters. Subjects were tested over seven days, with each condition occurring three times per day. Y-axis indicated mean errors, out of a maximum of eight. Increasing the number of distracters was particularly disruptive for senior dogs.

interval (delay) between presentation of sample and presentation of the test stimuli can be increased, which increases the memory demands required of the animal. The longer the delay, the longer the information must be held in memory and the poorer the animal is likely to perform (see Figure 3).

Cognitive Tests and Capabilities

Task Acquisition

Table 1 summarizes the tasks and cognitive domains that we've studied thus far and what is known about age and species differences. Table 1 reveals that Beagle dogs are capable of learning a wide variety of tasks, which includes associative learning, more complex rule-based learning and psychomotor learning (skill learning). Associative learning requires animals to learn that two events are related and can be assessed using discrimination learning tasks in which subjects are trained to associate a specific object with reward (discrimination learning) and positional learning, in which dogs learn to respond to objects based on location (e.g., egocentric discrimination). Dogs also are capable of more complex learning, including the DNMP (described previously) and utilizing the location of an external cue to determine the location of reward (landmark discrimination). Finally, we've found that dogs can rapidly learn to acquire specific skills (psychomotor learning) in which they learn to perform a new motor response to obtain a reward. We can assess this with a reaching task in which dogs are required to use their paws to pull a coaster toward them, a response that's typically outside their normal behavioral repertoire.

We've also found that dogs can perform at high levels on a set of tasks designed to assess executive function, which includes reversal learning and a new test we've developed to assess selective attention. In reversal learning tasks, dogs are first taught a discrimination learning task, to respond selectively to one of two objects or an object in a specific location. Next, in the reversal phase, the relationship between the objects or location and reward are switched, and the animals must learn to respond to the previously unrewarded object or location. Although most dogs can learn the reversal task, it usually takes about twice as many training trials as does the original discrimination task. In the selective attention task, the animals are presented with a correct object and from 0 to 3 incorrect objects, all of which are identical and serve as distracters. The task requirement is to ignore the incorrect objects and, as Figure 4 shows, we observe that the greater the number of distracters, the greater the number of errors.

A second subset of tasks can be learned by only a small proportion of animals. There are two examples. The first is the delayed-non-matching-to-sample (DNMS), which is intended to provide a measure of recognition memory. The task entails presenting dogs with a single object and allowing them to respond to obtain reward. They are then presented with two objects, the sample object and a second novel object, which is now associated with reward. Thus, this task requires them to remember what the sample object was and then to respond to the novel object. When we initially attempted to train dogs on this task, they were able to perform at better than chance, but they were not able to achieve the learning criterion.[10] We subsequently found that learning could be improved if the objects were first presented to the dog at its near point; when the distance was closer, the dogs probably had difficulty focusing.[14] Nevertheless, even under optimal conditions the task is difficult and only a small proportion of dogs are able to master it.

The second is called spatial list learning task (SLL) and involves three phases. In the first, the dog is presented with a single object in one of three locations. In the second, the dog is presented with two identical objects: one in a new location (the correct response) and one in the same location. On the third trial, the dog is presented with three of the identical objects and must respond to the location that was not used in either of the first two trials. Performance varies with age and memory demands, with aged dogs doing much more poorly than young dogs.

Cognitive Limitations

A third category of tasks are ones for which we have not been able to convincingly demonstrate learning. These include both true oddity task and conditional discrimination tasks. The oddity task involves presenting dogs with three objects, two of which are identical and the correct response is to select the

Table 1. **Summary of tasks used in canine cognitive assessment, domain associated with task, effects of age and comparison with humans (N/A indicates that comparable data is not available).**

Task	Cognitive Domains	Performance of Adult Dogs	Age Effects in Dogs	Normal Humans	Dementia
Discrimination Learning[10,11]	Associative Learning	Acceptable, show learning set	Varies with similarity of objects	Use rule based strategy	Similar to dogs
Reversal Learning[10,11]	Executive Function	Acceptable	Declines with age	No reversal learning effect	Similar data to dogs
DNMP Acquisition[12,13]	Complex Learning	Acceptable	Strongly Correlated	Moderately difficult	Very difficult task
DNMP – Performance[13]	Episodic Working Memory	Generally Excellent	Greater individual differences	Parallels work with humans	N/A
DNMS – Acquisition[10,14]	Recognition memory	Very difficult task	Highly Signficant	Easy task	Difficult
Spatial List Learning[15]	Episodic Working Memory	Very difficult task	Age-Dependent Deficit	No Data	N/A
Landmark Discrimination[16]	Allocentric Spatial	Requires special training	Age-Dependent Deficit	N/A	N/A
Attention Task[17]	Selective Attention	Acceptable	Highly sensitive to age	Similar age-effects in humans	N/A
Concurrent Discrimination (unpublished)	Episodic memory	Yes – varies with difficulty	N/A	N/A	N/A
Oddity (unpublished)	Concept Formation	Difficult or impossible	Difficult or impossible	Very easy task	N/A
Conditional Discrimination (unpublished)	Relational Strategy	Difficult or impossible	N/A	N/A	N/A
Motor Reaching Task (unpublished)	Psychomotor Function	Large majority learn rapidly Some	Small age deficit	Varies with task difficulty	N/A
Concept Extraction[18]	Executive function (Concept Formation)	Show simple concept abstraction	Slower learning in aged dogs	N/A	N/A
Learning Set Performance[19]	Acquisition of Higher Level Rules	Successfully show learning sets	N/A	N/A	N/A

odd object. In the true oddity task, each set of three objects are presented only once. Thus, accurate performance requires the animals to learn the oddity concept. We have shown that dogs can only learn to select the odd object, if they are repeatedly presented with the same three objects,[20] but they are unable to learn the oddity concept when unique object sets are used.

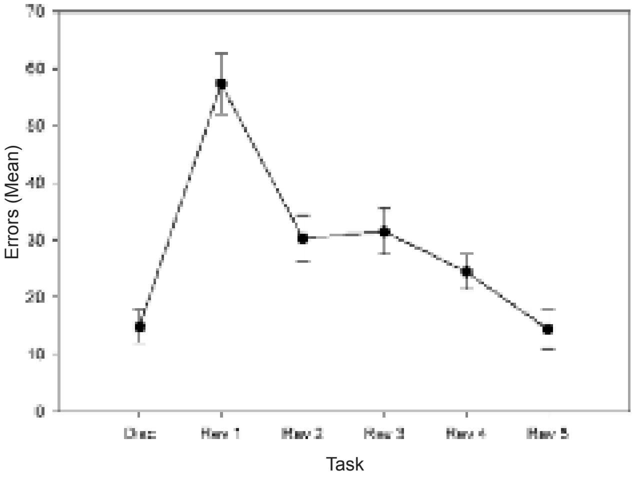
For conditional discrimination, the animals are presented with a choice of two objects, with the correct response being contingent on another event. When we originally set this up, the animals were presented with identical objects in the left and right food well, and one of two objects in the center food well. The rule was to respond to the left when the center object was a circle and to respond to the right when the center object was a triangle. We've been unable to demonstrate learning, despite giving dogs up to 1,000 training trials.

These results suggest that dogs are incapable of acquiring higher level concepts. On the other hand, we have found that dogs are capable of distinguishing objects based on size and of responding based on relative size, thus demonstrating concept abstraction.[18]

Role of Experience

Previous experience is important in two respects. First, animals that have had considerable cognitive experience perform better overall than animals that have had little experience. This is important when looking at age differences in which age-differences are seen most clearly if animals are highly experienced.[21] Thus, experienced young animals learn faster than experienced old animals. Inexperienced young and old animals, by contrast, show a much smaller age-related difference.

Figure 5



Development of a learning set. Beagle dogs were first tested on an egocentric discrimination and subsequently on a series of egocentric reversal tasks. The group showed progressively better performance over successive reversal and eventually learned reversal more rapidly than initial discrimination. Moreover, some animals reach a stage of proficiency in which they can learn the reversal task in a single trial.

One of the reasons that experience is important is because dogs are able to learn general rules that can be used in solving new cognitive protocols. We have known for some time that when dogs are repeatedly tested on the same type of problem, they show progressively better performance and may achieve mastery of the problem.[18] In some cases they become sufficiently proficient to be able to learn the correct response in a single trial. This is an example of the development of a learning set and is illustrated in Figure 5.

Experience also differentiates animals with respect to accumulated knowledge. Dogs that are well-trained on the DNMP at a young age, for example, are apt to perform at reasonably high levels when tested later in life — even at an age when learning the task is very difficult.

Domain Specificity

Several lines of evidence indicate that the tasks we've developed span functionally distinct cognitive domains. First, there are clear differences in the effect of age on task performance, which we've already alluded to and will discuss in more detail in the following section. Second, specific interventions have been found to have different effects on some tasks but not on others. For example, adrafinil, a highly effective stimulant, was found to significantly improve performance on discrimination learning tasks[20] but to impair performance on DNMP.[21]

Another way of demonstrating domain specificity is by testing a group of animals on a battery of tasks and calculating the correlations between tests. Table 2, for example, is based on data from 36 animals, 8 to 15.2 years of age, tested on DNMP at 20 and 90 seconds, a discrimination learning task and two tests of selective attention. The DNMP at 20 and 90 seconds are highly correlated with each other (see Figure 6). At a 20-second delay, the DNMP is weakly correlated with discrimination learning and the "same" attention task. At the high delay, the correlation is even lower. These results suggest that the cognitive processes underlying DNMP performance, discrimination learning and selective attention must be at least partially distinct.

We've also examined performance of the tasks combined by converting data into Z scores. The results reveal relatively small groups of high-performing and low-performing animals, and a larger group performing closer to average, suggesting a distinction between dogs that show global cognitive impairment and dogs that show more selective deficits to specific cognitive domains.

Table 2. **Correlation matrix between four cognitive assessment measures and age.**

	AGE	DNMP 20 (Accuracy)	DNMP 90 (Accuracy)	DISCR (Errors)	ATTENT SAME	ATTENT DIFF
AGE	1.00	-0.12	0.12	0.41	0.26	0.07
DNMP 20 (% correct)	-0.12	1.00	0.86	-0.23	-0.19	0.01
DNMP 90	0.12	0.86	1.00	-0.08	-0.08	-0.06
DISCR (errors)	0.41	-0.23	-0.08	1.00	0.71	0.16
ATTENT SAME (errors)	0.26	-0.19	-0.08	0.71	1.00	0.38
ATTENT DIFF (errors)	0.07	0.01	-0.06	0.16	0.38	1.00

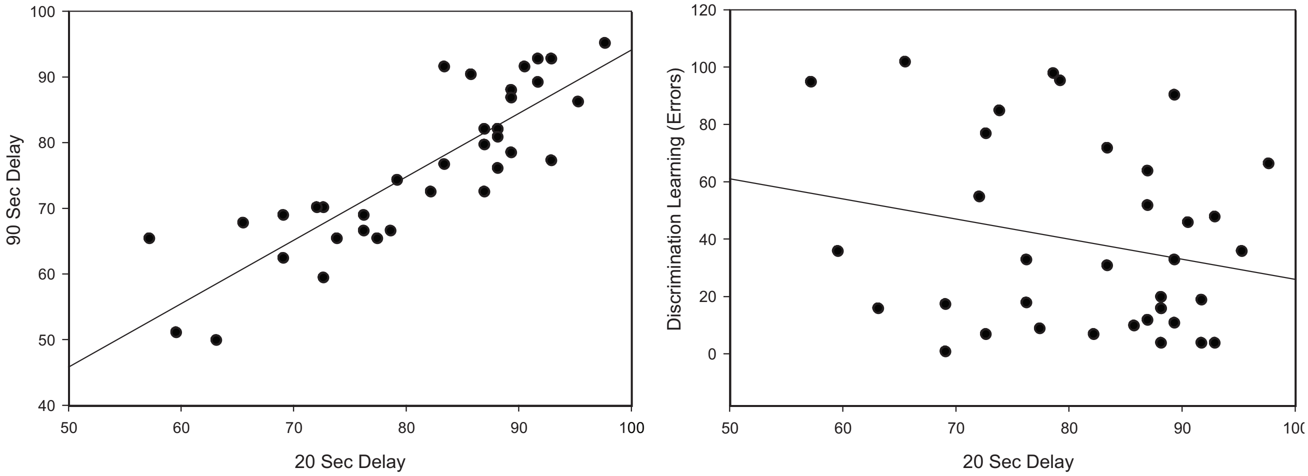
Individual Differences and Changes Associated with Age

We have completed a substantial amount of work dealing with cognitive changes associated with age. We typically begin to see impairment in Beagles as young as 5 years of age, depending on task and previous experience. The differential sensitivity to task is summarized in Table 1.

Simple discrimination learning shows relatively little change with age — dogs generally perform quite well at learning to distinguish objects that differ in more than one dimension (e.g., size, shape and color). Performance, in general, deteriorates when dogs are required to discriminate more similar objects. For example, we see significant age differences when dogs are tested on a size discrimination learning task, in which the dogs are asked to discriminate between two red blocks that differ in size, but not in color or shape.[11] Age differences also are enhanced when dogs are tested on an oddity discrimination task in which they are required to learn to select the odd object when the animals are given a choice of responding to one of three, with two being identical and incorrect.[22] This is a discrimination learning problem, rather than a concept learning problem, because the dogs are repeatedly tested with the same object set.

Reversal learning tasks also tend to show greater age sensitivity than discrimination learning,[10,11] indicating an executive function deficit. Greater age differences are seen in more complex learning in which animals are required to learn a more general rule. Figure 7 illustrates the effect of age on

Figure 6



Acquisition of DNMP as a Function of Age Range. Scatter plots showing relationship between performance on the DNMP at 20-second delay with a highly correlated task (performance at 90-second delay – top panel) and with performance on a discrimination learning task (bottom panel). Note that although the correlation with discrimination learning is low, the highest performing dogs tended to acquire the discrimination learning task more rapidly.

acquisition of DNMP, a task that shows marked age sensitivity. Note also that the spread of scores increases with age. This is a reflection of individual differences among aged groups, which can be subdivided into dogs that show successful aging and are high performing, dogs that show impairment, and dogs that differ from young dogs by more than two standard deviations and may be classified as demented.[23]

The DNMP also can be used to demonstrate age differences in memory capacity. When training experience is equated between young and old animals, the young animals perform more accurately and show greater improvement with practice. However, with extended practice a subset of old animals are able to show further improvement. A second subset, aged impaired animals, show substantial impairment at long delays.[24]

Clinical Assessment of Cognitive Ability in Companion Animals

Although the number of aged pet dogs is huge, the total population of aged laboratory-housed dogs is small. Furthermore, restricting our sample to Beagle dogs neglects the huge potential diversity that exists among different breeds. To increase the available population of dogs and to obtain evidence about the effect of breed, we have recently developed a portable cognitive test apparatus and accompanying protocol for use in the clinical setting. This project was initially designed and carried out by Dr. Paolo Mongillo over the course of a year sabbatical taken at CanCog in Toronto. Preliminary data were first presented in 2009 by Dr. Mongillo at the annual Meeting on Canine Cognition and Aging in Niagara-On-the-Lake, Ontario. The test box was similar to our standard test apparatus with a few modifications to increase its portability and to enable testing of larger breeds.

The test procedure was also modified to allow training on several tasks within a short time frame. We therefore used a less stringent learning criterion, in which subjects were deemed to have learned when they obtained a string of five consecutive correct responses. Thus far, we've obtained complete data on four tasks from 11 pet dogs and 8 laboratory-housed Beagles: reward approach learning; object approach learning; discrimination learning; and reversal learning. As shown in Figure 8, these data show very similar results from pet and laboratory-housed dogs, and validates the use of this technique for objectively assessing cognition in clinical trials.

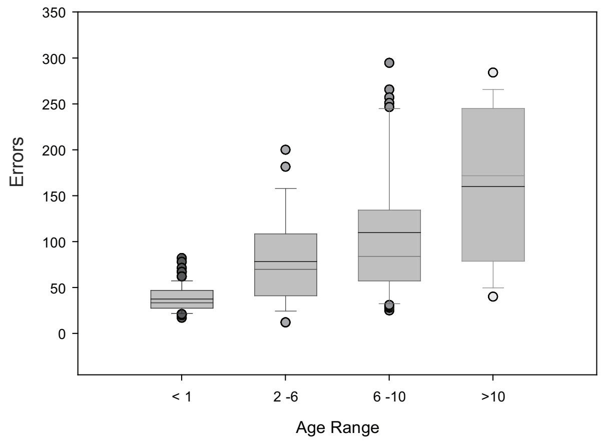
Cognitive Assessment in Human Populations Using Parallel Testing Protocols

One of our goals in examining dogs as a potential model for human cognitive decline is to develop tasks that are translational, which require age-related task differences to predict how different human populations will respond. To advance this goal, we have developed a battery of test protocols that we can use to assess human subjects, and we have used these to obtain preliminary data from various human populations including Down syndrome,[25] children with Fragile X disorder,[26] autistic children, aged populations,[27] and patients with dementia. The specific tests were set up in a manner that paralleled the setup used in canine assessment. Thus, we developed a specialized test apparatus (Figure 9) and dedicated software based on the canine model adapted for testing humans. The learning criterion we used was the same as used in the clinical testing of pet dogs. That is, a subject was deemed to have learned a task if it obtained five consecutive correct responses.

Figure 10 shows data we've obtained from several different populations of human subjects on an object discrimination and reversal learning task. The left-hand panel illustrates that performance is impacted by age and that the tasks are also sensitive to cognitive impairment. One notable result was that both the oldest of the normals (> 70) and Alzheimer's patients performed more poorly on the reversal task than the original discrimination, illustrating a reversal learning deficit consistent with that seen in dogs. Younger human subjects, by contrast, learn the reversal task more quickly than the original discrimination. The right-hand panel demonstrates that these tasks can also be used to detect developmental abnormalities, as evidenced by the extremely poor performance of the Fragile X group on the reversal learning task.

Figure 11 compares groups of humans on two tasks, DNMP and DNMS, and for comparative purposes shows how dogs perform on the same two tasks. Note that DNMS is acquired more rapidly than DNMP by all groups of human subjects,

Figure 7



A box and whisker plot showing acquisition of DNMP task as a function of age group. The Y-axis represents errors to achieve a criterion level of performance at a delay of 5 seconds. The boundaries of the box represent the 25th and 75th percentiles. The whiskers indicate the 10th and 90th percentiles. The solid line shows the median, and the fainter line shows the mean. Note that both mean errors and variability (spread) increase as function of age.

while for dogs, it's the opposite. These species differences probably reflect the importance of object recognition to the human and accompanying specializations in the human brain. Overall, these results suggest that the tasks we've developed in dogs can also be used in assessment of human subjects and that they can be used to detect abnormalities. Moreover, human subjects showing cognitive impairment or dementia are more impaired on DNMP than DNMS, suggesting that the canine DNMP, in particular, can serve as a transformative model for human assessment.

General Discussion

The research we have completed thus far has accomplished several goals. First, it's provided us with an extensive database to better understand the cognitive capabilities of the dog. Second, it's provided several age-validated model systems that can be used to assess the effectiveness of potential interventions and hopefully further our ability to develop treatments for dementia and Alzheimer's disease. Finally, the work has helped us understand how cognitive capabilities change over the course of aging.

What Have We Learned About the Cognitive Capabilities of the Dog and the Effects of Age?

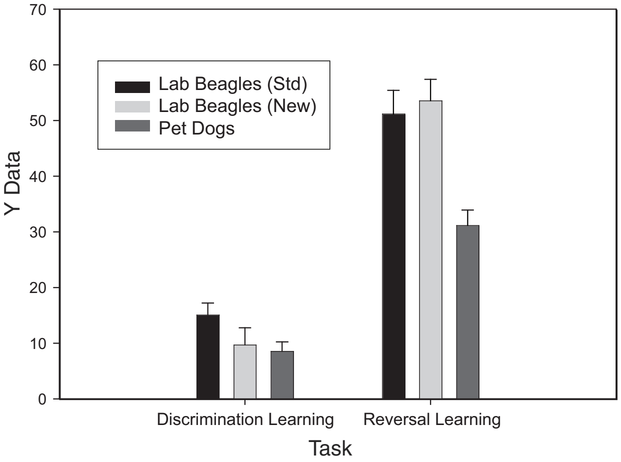
Cognitive Capabilities of Dogs

There is an accumulating literature on what dogs are and are not capable of doing. Most of this work, however, has been done with small sample sizes and is subject to alternate interpretations based on the dogs' ability to utilize cues associated with the tester. Our focus, therefore, has only been on the work that's been done by our group. We've discovered that the cognitive capabilities of dogs are extensive but are also limited by their sensory and motor capabilities. While dogs are capable of learning a DNMS task, it is a very difficult task, particularly for aged dogs. We suspect that the difficulty of this task reflects limitations in the dogs' visual system, which is better designed to detect movement and location than to detect complex shapes and objects. This suggestion is consistent with evidence that dogs are more capable of learning a recognition.

A second limiting aspect is the amount of information that dogs are required to retain. One example that illustrates this is the concurrent discrimination task. When we first tried to test dogs on this protocol, we used 10 different object pairs and did not find any dog that learned all the pairings. To the contrary, it was not clear whether the dogs were able to learn much of anything as there was simply too much information. We have now retested a group of animals with only three object pairs, and this made the task solvable; seven of eight animals were able to learn all the problems over a 37-day test period.

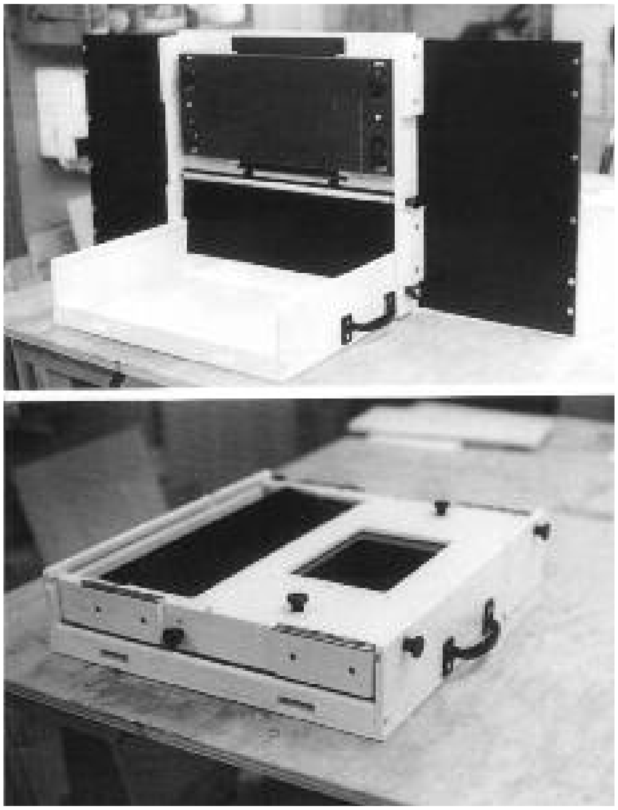
A third limiting factor is the nature of the problem that the animal is asked to solve. Dogs appear to be incapable of learning tasks if the rule is abstract and requires the animals to learn a novel concept, such as oddity or conditional respond-

Figure 8



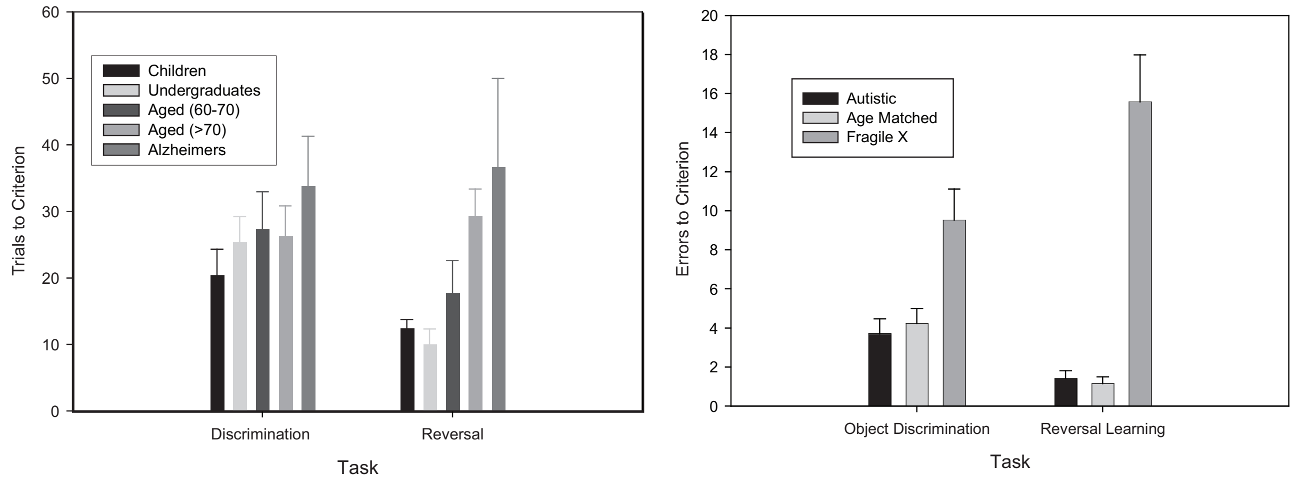
Discrimination and reversal learning in pet and laboratory dogs. This figure compares laboratory Beagle dogs trained on a discrimination and reversal learning task using our standard training procedures with laboratory and pet dogs trained using modified test procedures.

Figure 9



Portable cognitive test apparatus used in assessment of human cognition, which was modeled after the apparatus used in assessment of dogs.

Figure 10



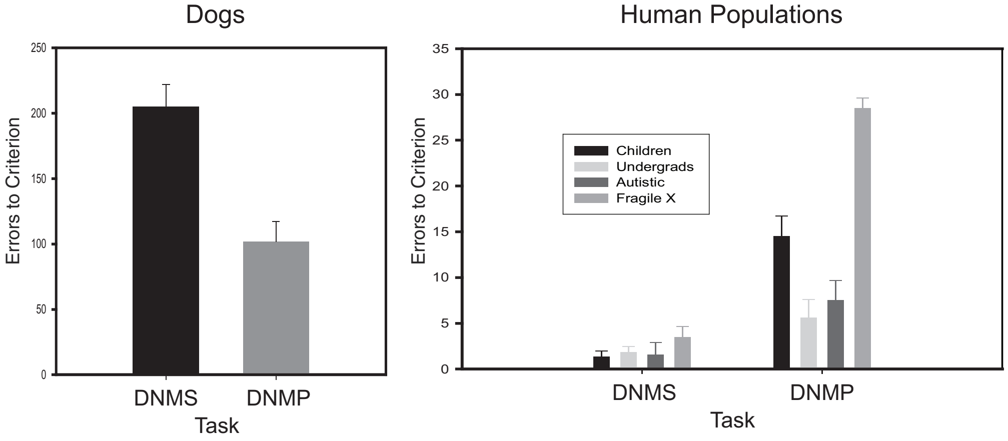
Trials to criterion on an object discrimination and reversal learning task for groups of human subjects that differ in age and level of cognitive function.

ing. This conclusion, however, may be constrained by the specific task or modality. Pietrzykowska and Soltysik[29] were able to train dogs on an auditory task in which they were presented with two tones and were required to make a particular response to the second tone only if it was the same as the first. They were able to solve the task, suggesting the ability to learn the concept of "sameness." However, the same dogs were unable to learn the same type of task when presented with photic stimuli.[30]

Distinction Between Fluid and Crystallized Intelligence

Another key factor determining the performance of dogs is their previous cognitive test history; dogs show the ability to benefit from experience. Psychologists studying human cognition have found it useful to distinguish between knowledge that we've acquired, which is referred to as crystallized intelligence, and the ability to think logically and solve problems in novel situations, which is referred to as fluid intelligence. The distinction can also be made for the dog, but it seems clear that their level of fluid intelligence is far below that of the human. Thus, their inability to learn oddity or conditional discrimination tasks indicates limited fluid intelligence. By contrast, once dogs have had experience learning discrimination and reversal problems, they are able to solve subsequent problems more rapidly. Further evidence that dogs have high levels of crystallized intelligence is demonstrated by the fact that once dogs are trained on DNMP, they retain it and are able to perform at reasonably high levels up until they reach advanced age; this is despite the fact

Figure 11



DNMP and DNMS learning in human and canine groups. The left panel shows that dogs make many more errors in learning DNMS than in learning DNMP. In this experiment, the animals were given a maximum of 400 trials to learn each of the tasks, and the majority of dogs failed. The left-hand side compares four groups of human subjects – undergraduate students, autistic children, age-matched controls, and children with Fragile X syndrome. All the human groups showed very rapid learning of DNMS. All the groups learned DNMP more slowly, and there were much greater group differences.

that aged dogs are generally unable to learn the task or do so only after extensive training.

Use of the Dog as a Model of Human Cognitive Aging

A major goal of our research program with dogs was to develop assessment protocols that could be used to predict how human subjects would respond to therapeutic interventions designed to improve cognitive function. Evidence supporting the use of the dog includes similarities in brain pathology associated with aging and general parallels in the process of cognitive decline.

On one hand, individual tasks are not always going to be comparable. We've seen that dogs perform significantly better on memory tests of visuospatial function than object recognition, while the opposite is true for humans. This difference probably relates to differences in the functioning of the canine and human visual system. On the other hand, there also are qualitative differences between human and canine cognitive capabilities, as evidenced by the inability of dogs to acquire concepts, such as oddity, that are easily demonstrated in humans.

Perhaps the more interesting comparisons between dogs and humans are those linked to neurobiological disorders, including developmental disorders associated with pathological brain aging. For example, dogs, aged humans, children with Fragile X disorder, and patients with dementia all show reversal learning deficits, which is indicative of executive function deficits and suggest that dogs can model both human developmental disorders and pathological cognitive aging.

Future Directions

There are two new research areas that we hope to pursue in future studies — breed differences and social cognition. Breed differences in canine intelligence is of general interest but has not yet been systematically evaluated using objective techniques.[31] We hope to increasingly participate in clinical assessment of canine cognition, with the goal of obtaining a large database of cognitive performance on our tasks as an outcome of clinical testing.

Regarding social cognition, this relates directly to the nature of interactions between dogs and other dogs, particularly between dogs and humans, and is an active area of investigation. One aspect that has not yet been critically examined, however, is how social cognition is affected by age. We're planning collaborations with Dr. Lisa Lit to investigate social cognitive interactive behaviors in dogs. This includes the possibility of using the dog as a model for social behaviors relevant to disorders such as autism.

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Q&A Discussion

Q: Dr. Barb Kitchell, Michigan State University: How did you control for olfactory cues in the way that the objects were placed or positioned for the dogs, since they are so much more acute in the olfactory sense?

A: Dr. Milgram: What we did, what we do routinely, is we have a coaster and an object placed on top of the coaster. On the bottom of the coaster we stick food so that the amount of food between the two wells is equivalent. They can’t get at it because if they knock the coaster down it’s under the coaster, not in the well. And to demonstrate that we have controlled for olfactory cues, we’ve done further work and have shown that dogs actually are unable to learn if the odor is hidden. What some of the dogs did, and what we also had to control for, was that some dogs would lick one coaster and use that as a cue. The only way we could control that was wiping off the top of the coaster, which we do after every trial. So basically we masked the odor by presenting the food in both wells.

Q: Dr. Ake Headhammer, Sweden: I'm glad to see that you are interested in going on to breed differences. I wonder if you have been thinking of comparing Beagle dogs selected for laboratory use compared to Beagles selected for hunting. Have you seen any differences between genders?

A: Dr. Milgram: We have never seen gender differences. And we've looked really hard. As far as using dogs that are bred for hunting, we hadn't really planned to do a direct comparison. When we started this research in the '90s, our old dogs were all retired hunters. We now get the dogs from commercial breeders, so we've actually had a lot of experience with both retired hunters and those bred for laboratory use. And basically we've never seen any real differences between them, and that's sort of interesting because these dogs would have had a lot of experience in the real world.