Effect of an Antioxidant-Diet and Cognitive Enrichment on Age-Dependent Cognitive Dysfunction in Dogs

Advanced age in dogs is accompanied by a variety of behavioural changes, which include disorientation, loss of social interactions and housetraining, and disturbances in sleep. Veterinary behaviourists interpret these as symptoms of cognitive impairment, which can be used to characterise canine cognitive dysfunction syndrome (CDS). Both identification of CDS and clinical evaluation of pharmacological interventions have relied on questionnaire data. This methodology involves considerable subjectivity, and is subject to large placebo effects.

Our laboratory has used a neuropsychological perspective to study the problem of age-dependent cognitive dysfunction in dogs. This has necessitated development of a set of laboratory-based tests that provide quantitative measures of various aspects of cognition. From this perspective, cognitive dysfunction manifests itself in the loss of various cognitive functions, which include behavioural flexibility (ability to switch from one response set to another), acquisition new information (learning), increased variability (behavioural instability), and impaired memory. These deficits probably account for the clinical symptoms associated with CDS. Our aim was to investigate the impact of both nutritional and experiential intervention on canine cognition, using the above-mentioned objective and quantitative parameters to measure the efficacy of the interventions.
MATERIALS AND METHODS

In a longitudinal investigation, we evaluated the effect of dietary manipulation and cognitive enrichment on age-dependent cognitive dysfunction in beagle dogs.

The nutritional intervention consisted of feeding a specially formulated food containing a broad spectrum of antioxidants and mitochondrial cofactors (see Jewell et al. p.38). Our interest in this food stems from evidence linking failure to adequately scavenge free radicals to the development of age dependent neuropathology.

The second intervention involved behaviour, and was intended to provide a test of the hypothesis that the rate of decline of age-dependent behavioural dysfunction can be slowed down by use – presumably because of the inherent plasticity of nervous system tissue. In the enrichment condition, a subgroup of dogs was exercised twice a week, pair housed, and given a set of toys, which were alternated weekly. Most importantly, the enriched group received regular cognitive stimulation defined by neuropsychological testing 5 to 6 days per week.

Testing apparatus

In our standard protocol, the sliding tray is presented to the dog with objects covering a food reward present in one of the food wells. FIGURE 1 illustrates the testing apparatus. The correct location of the food reward is determined by a randomised computer program to negate reward location bias. In a discrimination task the dog is presented with a choice of responding to two or three objects that differ in at least one dimension (e.g., size, colour and shape). The dog’s task is to discover and respond to the correct object. To perform accurately on this task, the subject is required to learn which object is associated with reward, and to remember this when tested at a later occasion.

Animals

The experiment started out with a total of 48 aged beagle dogs, which were placed into cognitively equivalent enriched (n=24) and control food groups (n=24), based on baseline performance on a series of neuropsychological tests. Half of the animals in each group were assigned to the cognitive enrichment group. This resulted in four groups of 12 animals each with two variables of either cognitive enrichment or dietary enrichment. We also tested a group of 16 young dogs, 9 of which were on the antioxidant fortified food. The young dogs were all provided with cognitive enrichment.

Study design

During a longitudinal study, three types of learning tasks were evaluated.

1. Landmark discrimination learning tasks

Starting approximately two weeks after being placed on the nutritional intervention, the cognitively enriched groups were tested on a series of landmark discrimination learning tasks. On these tasks, the dogs were presented with two identical objects. To obtain food reward, the animals were required to respond selectively to the odd object. Every animal was tested on a series of four such tasks, which differed regarding the distance of the external cue.

2. Oddity discrimination learning tasks

After approximately 6 months on the fortified or control food, the cognitively enriched groups were trained on a series of oddity discrimination learning tasks. In each such task, the animal was presented with three objects, two identical and one different (FIGURE 1). To obtain reward, the animal is required to respond to the odd object. Every animal was tested on a series of four such tasks, of increasing difficulty based on

Figure 1. Testing apparatus used in assessing discrimination learning. With the animal in the test box, the hinged door is opened and the animal is presented with the sliding tray. The animal is then allowed to select an object, in this instance the animal is presented with a choice of three and is rewarded for choosing the odd object.
similarity of positive and negative objects. Note that performance was task sensitive, with the third and fourth problems clearly more difficult than the first two.

3. Size discrimination learning task and reversal learning task

After one year on the enriched or control food, all dogs were tested on both a size discrimination learning task, and on a reversal learning task. The size discrimination task evaluated the animals’ ability to learn to distinguish two objects that differed only in size in order to locate a food reward. In the reversal task, the association between the particular object associated with the reward in the size discrimination task was switched. We used errors committed as a measure of learning.

RESULTS AND DISCUSSION

1. Landmark discrimination learning tasks

The results of the first part of the study are shown in FIGURE 2. The young dogs acquired the task significantly more rapidly (p < 0.001 for the initial task, and p < 0.05 for the other tasks), indicating that this task is particularly useful in identifying age-dependent cognitive impairment. When we then looked at the effect of food, we found that the aged animals on the test food learned the initial phase of the landmark task with significantly fewer errors than the animals on the control food (p < 0.025). The animals on the test food also performed more accurately on the subsequent testing, but the differences were not statistically significant.

2. Oddity discrimination learning tasks

We found robust effects of age on all tasks (p < 0.05 for all tasks), that indicates that the tasks were sensitive to age-dependent cognitive impairment (FIGURE 3B). We also found that old animals on the fortified food performed better than those on control food for all tasks evaluated. This difference achieved statistical significance on the last two tasks (p < 0.001 for task 3 and p < 0.05 for task 4) as indicated in FIGURE 3A.

3. Size discrimination learning task and reversal learning task

In the size discrimination task an animal was rewarded for approaching the smaller of two objects during the initial discrimination learning task, during the reversal task it was now rewarded for approaching the larger of the two objects. The reversal task, therefore, provides a measure of cognitive flexibility.

When we compared old and young dogs, we found marked differences in favour of the young animals on both tasks, indicating that the tasks are sensitive to age-dependent cognitive impairment. We also found effects of the food intervention. On the size discrimination learning task, the aged dogs receiving the antioxidant fortified food made fewer errors than the aged dogs on the control food. By contrast, we found no significant effect of food on learning ability of young dogs.

The food intervention also improved performance on the reversal task (n=24) (FIGURE 4A), but larger improvement in performance was observed in the group (n=23) provided with environmental enrichment (FIGURE 4B). When the subgroups of the trial were...
compared the largest improvement occurred in the group receiving both treatment regimens the environmental enrichment plus the special diet (FIGURE 5). Impairment on reversal tasks is indicative of behavioural inflexibility. This result, therefore, indicates that dietary enrichment is maximally effective in reducing this inflexibility if the food enrichment is also coupled with environmental enrichment.

CONCLUSION

In summary, we have found first, that age can markedly affects learning ability, second that age-dependent cognitive deficits can be alleviated by food intervention with a broad spectrum of antioxidants and mitochondrial cofactors, and third that cognitive enrichment can also partially alleviate the development of age-dependent cognitive dysfunction. These conclusions are based on data obtained from a variety of neuropsychological tests, conducted over one year.

Figure 3. Oddity discrimination learning as a function of food (A) and age (B). Each animal was given a score based on total number of errors committed before achieving a predetermined performance criterion.

Figure 4. Long-term effects of food (A) and cognitive enrichment (B) on object reversal and size reversal learning. Figure 4 compares animals on the control food with animals on the enriched food on baseline object reversal learning test before starting the treatment and on size reversal learning after one year on enriched food.

Figure 5. Combined effect of food and cognitive enrichment on object reversal and size reversal learning. Figure 5 compares the four groups of aged animals (on the same tasks as in figure 4) before starting the treatment and after one year on environmental enrichment. (A-C) combined dietary and environmental enrichment, (A-E) dietary enrichment and control environment, (C-E) control diet and environmental enrichment, (C-C) control diet and control environment.

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