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SUPPLEMENTATION WITH A NOVEL LIPID EXTRACT IMPROVES FRONTAL LOBE LINKED COGNITIVE DEFICITS IN AN AGED BEAGLE MODEL OF ALZHEIMER'S DISEASE

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BACKGROUND:

Aged dogs demonstrate several parallels with Alzheimer's disease including both domain-specific cognitive decline and neuropathological changes. Moreover, canine aging is associated with biomarker signature patterns that are consistent with Alzheimer's disease progression. Therefore aged dogs can be used for preclinical evaluation of therapeutics under development for Alzheimer's disease.

The current study sought to evaluate the effectiveness of supplementation with a novel lipid extract (Bioiberica S.A.U., Barcelona, Spain) on improving or attenuating cognitive deficits in aged Beagle dogs and improving biomarkers related to Alzheimer's disease progression.

METHODS:

- Performance across discrimination learning, delayed non-matching to position (**DNMP**), **and selective attention tasks** were used to establish two cognitively-balanced groups of aged Beagle dogs (N=12 per group) at baseline (Figs. 1, 2 and 3).

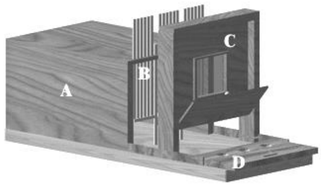

Fig. 1. Schematic of canine cognitive test apparatus. A) Chamber in which dog is located for testing. B) Gates that can be adjusted to permit only the head of the dog to reach the test tray. C) Barrier with one-way mirror allowing the tester to observe the dog and with a gate that is raised when test tray is presented. D) Test tray with food reward wellls over which objects are placed. Tester slides the tray after lifting gate.

Fig. 2. DNMP test. Task consists of a sample presentation, a delay, and a choice presentation. Choice of the non-sample position results in reward (indicated by positive sign).

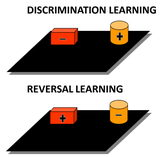

Fig. 3. Discrimination and reversal learning. The dog must choose one of two objects to receive a food reward (the positive object) until a learning criteria is reached. Subsequently, the previously correct object is no longer rewarded and the dog must learn to repsond ot the other object during reversal learning.

- Dogs received either a **supplement containing** a **proprietary lipid extract** (Bioiberica S.A.U., Barcelona, Spain; Mean age ±SD = 9.9 + 2.6 y) or a **placebo control**, in gelatin capsules (Mean age ± SD = 7.0 ± 0.5 y) daily **for 6 months** by oral administration.
- **Changes in cognitive function** were evaluated using the delayed non-matching to position task (DNMP), selective attention, discrimination retention, reversal learning and spatial discrimination and reversal learning tasks.
- Additionally, **treatment effects on brain metabolism were assessed with magnetic resonance imaging (MRS)** both at baseline and six months following treatment.

RESULTS:

- A significant (p=0.02) **decline in DNMP performance was seen in placebo-treated dogs, but not in dogs receiving the supplement** (Fig. 4)**.** This suggests that the **treatment attenuated short-term memory decline** that occurs over several months in aged dogs.
- The supplement group also demonstrated significantly (p=0.01) **improved performance on the most difficult spatial discrimination and reversal task pattern** (Fig. 5) **and on reversal learning** (p=0.04) compared to placebo (Fig. 6), which **reflects improved executive function**.
- **MRS** revealed significantly (p=0.048) higher levels of **frontal lobe glutamate and glutamine in the treatment group after 6 months,** compared to placebo (Fig. 7).

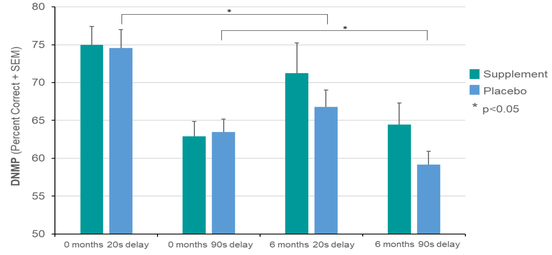

Fig. 4. DNMP performance in each study group.

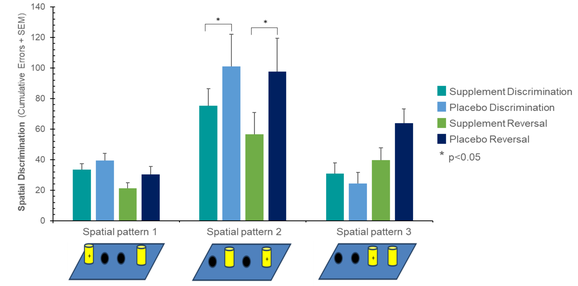

Fig. 5. Spatial discrimination performance in each study group.

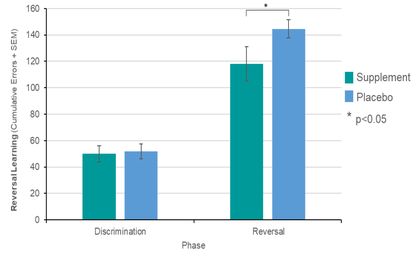

Fig. 6. Reverse learning scores in each study group.

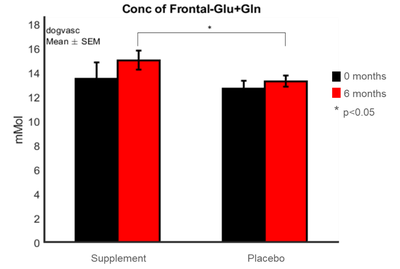

Fig. 7. MRS frontal lobe glutamate and glutamine levels in each study group.

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AP and ST are employees of Vivocore Inc. NWM is an employee of CanCog Technologies Inc.
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The protocol was approved in accordance with the guidelines of the Ontario Ministry of Agriculture, Food and Rural Affairs and the Canadian Council on Animal Care.

CONCLUSIONS:

The oral administration of a novel lipid extract for six months in aged dogs showed beneficial effects on cognitive function, especially attenuating memory decline and improving executive function, which encourages further testing of this novel lipid extract as a potential tool for the management of Alzheimer's disease.