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Exercise induced collapse (EIC) in Labrador retrievers

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Exercise induced collapse (EIC) is a term that describes a form of exercise intolerance seen in young Labrador retrievers after strenuous exercise. Although the first report of EIC dates back to 1993, the first citation in the veterinary literature is very recent (2008).1 According to the authors, affected dogs sometimes develop an abnormal gait or collapse when subjected to strenuous exercise, but the underlying cause has not been well established. Affected dogs usually tolerate mild-moderate exercise but occasionally become ataxic and collapse after 5 to 15 minutes of intense exercise, especially when accompanied by excessive excitement or stress.2

The pattern of the clinical signs (described by the aforementioned authors as “collapse”) is poorly characterised, as demonstrated in a survey carried out by 225 owners of dogs with a history of EIC (Table 1).1

<table>
<thead>
<tr>
<th>Description</th>
<th>% of dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rear limbs floppy/dragged</td>
<td>78</td>
</tr>
<tr>
<td>Wobbly, uncoordinated</td>
<td>60</td>
</tr>
<tr>
<td>Falling to side/balance problem ≥ 1 episode</td>
<td>68</td>
</tr>
<tr>
<td>Rear limbs only affected</td>
<td>82</td>
</tr>
<tr>
<td>All four limbs affected ≥ 1 episode</td>
<td>18</td>
</tr>
<tr>
<td>Forelimb rigidity ≥ 1 episode</td>
<td>18</td>
</tr>
<tr>
<td>Dazed/disoriented ≥ 1 episode</td>
<td>23</td>
</tr>
<tr>
<td>Loud/excessive panting ≥ 1 episode</td>
<td>19</td>
</tr>
<tr>
<td>Generalised seizure during 1 episode</td>
<td>3</td>
</tr>
</tbody>
</table>

The physical activity that appears to trigger the event is also poorly defined and includes retrieving toys (46%), retrieval training on land (43%), upland hunting (25%), excitement during play with other dogs (22%), retrieval training in water (12%) and waterfowl hunting (2%).1 Some factors seem to contribute to the onset and development of clinical signs, including excitement (83%), heat and humidity (31%), use of live birds in training or hunting (25%), stress during training (13%) and competition with other dogs (9%).1

In the examination of the pedigree of 326 dogs, 169 individuals appeared to be affected, with nine of these appearing to have an affected parent. Males and females were equally represented, excluding an X-linked mode of inheritance. Six of the nine affected parents had full phenotypic information. One affected parent mated with another affected parent producing two affected and two unaffected offspring. In three families, an affected dog produced multiple affected second and third generation offspring. The pedigree analysis was most consistent with an autosomal recessive mode of inheritance, although a dominant disorder with partial penetrance or a polygenic disorder could not be excluded.1

Median age of dogs when they presented the first episode of collapse was 12 months. 10% of dogs had experienced more than 25 episodes of collapse and seven had died during a collapsing episode. Three of these individuals had generalised seizure just before death.3 However, the authors do not report whether or not these dogs underwent a cardio-vascular investigation to rule out, for example, episodic arrhythmias or a right-to-left shunting persistent ductus arteriosus (reversed PDA). Although the authors failed to report in their first paper that most EIC dogs will experience spontaneous resolution of the clinical signs and will not show any further collapsing episodes during adult life, in a most recent publication they state: “Five years have passed since the 14 dogs with EIC were evaluated. One dog was euthanized immediately following evaluation. Six dogs were adopted to pet homes where they no longer participate in the trigger activities associated with the collapse, and five dogs have not collapsed since relocation. Three dogs remained with their owners and episodes of collapse reportedly occur if they are allowed to engage in trigger activities. One dog has not had activity limited, but episodes of collapse have become very infrequent. Three dogs were lost on follow-up. No dogs have developed progressive systemic or neurological disorders and all are considered by their owners to be healthy aside from the EIC”.2

The mechanism of EIC has not been determined yet, although “a mutation in dynamin 1 gene (DNM1) was recently suggested as the causal mutation of EIC in Labrador retrievers. A genetic test for the mutation is now available through the Veterinary Diagnostic Laboratory at the University of Minnesota”.2 The DNM1 mutation has been described in an elegant study published in 2008 by the same research group.3
My major criticism about the above discoveries is about the arbitrary stratification operated by the authors to achieve a significant association. Dogs were divided into six groups (presumed EIC, recurrent collapse, single collapse, atypical collapse, alternative collapse, and no collapse). Further arbitrary selection is observed in the alternative collapse group where “other potential causes of repeated collapse” were listed, such as cardiac arrhythmia, laryngeal paralysis, lactic acidemia, and metabolic myopathy. Moreover, 9% of dogs without a history of collapse resulted homozygous for the mutation, which was explained by the owners as insufficient exercise or excitement to trigger collapse.

An important limitation in these types of study originates from the lack of objective parameters to assess the physical condition of these dogs. It is well known that exercise causes significant acute alterations in rectal temperature (BT), pulse rate (HR), blood lactate (BL) and other physiological parameters in healthy dogs. However, until recently, there were no available data originating from standardised studies where test-retest reliability has been assessed.

In our recent publication, Dr Marcora and I assessed the reproducibility of a non-invasive exercise test in healthy Labrador retrievers and evaluated BL, HR and BT responses that occur during and after incremental exercise in this breed. In this study, we demonstrated that differences between tests may exist even under the strictest controlled conditions, such as environmental temperature, humidity, intensity of exercise, diet, time of the day, etc. Therefore, the standardised field tests conducted by other groups present several limitations, with little scientific accuracy and clinical utility.

Another important finding in our study was a prolonged recumbency and temporary inability to regain the quadrupedal posture in most dogs during the recovery period. This resembled the typical features of exercise-induced collapse described by Taylor et al. We interpreted these signs as an extreme physiological condition (exertional fatigue or exhaustion). Thus, this could be attributed to a variety of reasons. Exercise-induced changes in muscle action potential, extracellular and intracellular ions, and intracellular metabolites reduce the ability to produce force (peripheral fatigue).

Changes at spinal and supraspinal level due to alterations in brain metabolism and neurotransmitters, or inhibitory afferent feedback from type III and IV muscle afferents can also reduce the ability of the CNS to activate the locomotor muscles (central fatigue). It is also possible that, in these dogs, the increased pulmonary blood flow and capillary pressure during intense exercise induced the activation of pulmonary C fibers (or J receptors). This activation can evoke a somatomotor reflex (the J reflex) that provides potent inhibition of limb muscles in animals but not humans. In contrast with what has been observed in people, incremental exercise did not appear to induce abrupt increases in BL concentration in Labrador retrievers, although significant variation was observed between test stages. Moreover, in humans, BL concentrations would be expected to decrease during recovery after intense exercise. However, in our study, BL values remained stable after a 20-min recovery period in all dogs. Blood lactate concentration during exercise is the result of lactate production by the contracting muscle, lactate transport from the muscle to the vascular bed, as well as intracellular and hepatic clearance. Assuming that lactate clearance would continue during recovery and that lactate production in the muscle would cease after termination of the exercise, it can be speculated that the modest increase of lactate values observed in Labradors depends on a slow transport of this compound from muscle to blood. This could be caused by a low muscular density of proteins involved in lactate transport (i.e., monocarboxylate transporter) and/or intracellular lactate clearance.

According to the EIC test patent owners, breeders need to be selective in their breeding, avoiding the production of dogs that actually have EIC. They advise that all breeding dogs should be tested, and if carrier dogs are bred they should only be bred to dogs that are genetically clear of EIC so that affected puppies will not be produced. They also advocate avoidance of intensive exercise and, in some cases, the use of phenobarbital to decrease the dog's level of excitement or anxiety.

I kindly (but strongly) disagree with the above approach. I have now managed to successfully treat dozens of Labrador (and non Labrador) dogs with a history of EIC. First of all, it is necessary to rule out an underlying cardiac abnormality. Afterwards, the exercise capacity should be assessed on a validated treadmill test to obtain baseline values of BL, HR and BT.

A field test would offer limited value due to its poor repeatability. Furthermore, a well-designed exercise prescription, primarily based on interval training, is normally sufficient to improve the physical ability of the dog to undergo intense training. The exercise prescription can be designed based on the results of the exercise test. It is mandatory to maintain a good communication with the dog's owners and make sure that the prescribed exercise is recorded on a diary. Finally, owners' expectations need to be carefully evaluated. Sometimes, owners force their dogs to undergo exhausting exercise even several times a day. Under these circumstances, young excitable dogs are at higher risk of "collapse" because they tend to exercise above their physical capacity.

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