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DRD2 is associated with fear in some dog breeds

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# **ACCEPTED MANUSCRIPT**

#### 1 DRD2 is associated with fear in some dog breeds

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#### **ABSTRACT**

- 10 Behavioral problems occur frequently in dogs and represent a significant threat to dog welfare.
- Anxiety, phobias and fears comprise the majority of canine behavioral conditions. The identification
- of an association between specific behavioral phenotypes and genetic variants of candidate genes
- would be a valuable tool in selection for dogs less susceptible to anxiety and fear, which may improve
- animal welfare. The DRD2 gene encodes the dopamine receptor 2. In this study, we found 8 SNPs in
- the DRD2 gene of the Havanese, a breed that shows large variation in a behavioral phenotype that
- manifest itself as a tendency to react fearfully by withdrawing in social situations. Significant
- associations were detected between two SNPs in exon 2 of the DRD2 gene and increased social fear in
- Havanese dogs (n=158), as evaluated through observation by an external evaluator (respective allelic
- odds ratio: 4.35, 4.07) and through owner questionnaires (respective allelic odds ratio: 1.96, 2.2).
- Because different types of fear related behavioral disorders commonly co-occur, the SNPs in exon 2
- 21 were also investigated for possible association to noise reactivity in 5 breeds: Havanese (n=121), collie
- 22 (n=94), Irish soft coated wheaten terrier (n=44), Nova Scotia duck tolling retriever (n=33) and
- standard poodle (n=29). Significant associations were detected between SNPs in exon 2 of the DRD2
- 24 gene and noise reactivity in the Irish soft coated wheaten terrier (respective allelic odds ratio: 2.64,
- 25 2.88) and collie (allelic odds ratio: 3.03). The same SNP alleles were associated with the beneficial
- phenotypes in the three breeds.
- 27 Keywords: Havanese, dopamine, anxiety, social fear, noise reactivity, provocative behavioral
- 28 evaluation

## 29 **INTRODUCTION**

- 30 Behavioral problems occur frequently in dogs (Bamberger and Houpt, 2006) and represent a
- 31 significant threat to dog welfare. Behavioral problems are an important cause of both dog
- 32 abandonment (Scarlett et al., 1999) and euthanasia (Houpt et al., 1996). In one study from the United
- 33 States, at least one behavioral reason was recorded for 40% of relinquished dogs and behavioral
- reasons accounted for 27% of single-reason canine relinquishments (Scarlett et al., 1999). In one set of
- 35 UK shelters, problematic behavior was responsible for 34.2% of relinquishments (Diesel et al., 2010),
- 36 which is similar to the 35% calculated for purely behavioral relinquishments in the US (Dolan et al.,
- 37 2015). The most recent data indicate that 20% of 3.3 million shelter dogs in the US are euthanized
- 38 (ASPCA, 2018), with dogs with behavioral concerns especially at risk. (Marston et al., 2004) reported
- 39 that 54% of 4,846 relinquished dogs in three shelters in Australia were euthanized for temperament,
- 40 aggression or other behavioral problems. Behavioral problems pose the single largest health and
- 41 longevity threat to modern pet dogs (Dreschel, 2010).
- 42 Various types of anxiety constitute a large portion of these behavioral issues, including anxiety in
- 43 general, various phobias, separation anxiety, noise reactivity and various social and environmental
- 44 fears. (Bamberger and Houpt, 2006) found that anxiety, phobias and fears comprise well over 20% of
- 45 cases presented at a large university behavioral clinic. Fear aggression towards owners (5.2%) and

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