

# Behaviour Genetics in the Domestic Dog

Introduction essay, 2013

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## **Abstract**

Through domestication processes and artificial breeding humans have created an extraordinary animal model for the study of behavioural genetics – the dog. Being our faithful companions for at least 30.000 years it is not surprising that dogs have evolved certain social skills making them even better than bonobos and chimpanzees at reading our communicative cues. But this is not all that makes the dog such a good model animal in this case. With great across-breed variation and limited within-breed differences dogs present us with a rather unique opportunity to increase our understanding of both domestication processes as well as the inheritance and genetic aspect of behaviours. Additionally, many analogies between human and dog behavioural problems and diseases give us the possibilities to find new ways within human research. The dog genome sequence was published in 2005 and since then genes involved in several morphological characteristics have been identified. However, surprisingly little has been done on the genetics of canine behaviour. Here, I briefly review a range of studies on breed differences, heritability of canine behaviour as well as methods used within behaviour genetics. Some gene-behaviour associations have already been identified through previous research and are listed here. I also discuss the advantages of using a canine model for the purpose of studying behaviour genetics.

*Keywords: Behaviour genetics, domestic dog, domestication, social behaviour, heritability, breed differences, GWAS*

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# Content

<b>1</b>	<b>THE ORIGIN OF THE DOMESTIC DOG .....</b>	<b>4</b>
<b>2</b>	<b>WHY STUDY THE DOG? .....</b>	<b>4</b>
<b>3</b>	<b>DOMESTICATION AND SOCIAL BEHAVIOUR .....</b>	<b>5</b>
3.1	THE FARM-FOX EXPERIMENT .....	6
<b>4</b>	<b>BREED DIFFERENCES IN BEHAVIOUR.....</b>	<b>7</b>
<b>5</b>	<b>HERITABILITY OF DOG BEHAVIOUR.....</b>	<b>8</b>
<b>6</b>	<b>BEHAVIOUR GENETICS IN DOGS.....</b>	<b>10</b>
<b>7</b>	<b>METHODS IN DOG BEHAVIOUR GENETICS.....</b>	<b>11</b>
7.1	BEHAVIOURAL PHENOTYPING.....	11
7.2	ESTIMATING THE GENETIC CONTRIBUTION OF A TRAIT .....	12
7.3	IDENTIFYING GENES .....	13
7.4	WITHIN-BREED STUDIES.....	14
7.5	ACROSS-BREED STUDIES .....	14
<b>8</b>	<b>CHALLENGES ALONG THE WAY .....</b>	<b>14</b>
<b>9</b>	<b>SUMMARY.....</b>	<b>15</b>
	<b>REFERENCES.....</b>	<b>17</b>

## **1 The origin of the domestic dog**

Our understanding of the origin and evolution of the domestic dog (*Canis familiaris*) has significantly improved since 2005 and the publication of the genome sequence of a female boxer (Lindblad-Toh et al., 2005). Despite their great morphological and behavioural diversity, all modern dog breeds derive from the same ancestor, the grey wolf (*Canis lupus*) (Wayne, 1993). The process of domestication and artificial selection has resulted in the 350-400 different breeds that we see today. It is believed that at least two population bottlenecks have resulted in the modern dog breeds (Lindblad-Toh et al., 2005). The first bottleneck was rather mild and is associated with domestication from wolves and the second is the result of the intensive artificial selection that has produced the great variety of dog breeds. Some indigenous breeds from China and Southeast Asia have relatively high genetic diversity in comparison to younger European and American breeds and are therefore thought to be the basal dog lineages closest connected to grey wolves. However, some recent studies suggest that European wolf populations may be the main contributors to the modern dog population (Savolainen et al., 2002; Pang et al., 2009; Ding et al., 2012; Thalmann et al., 2013).

Archaeological findings of dogs dates back to as far as 12,000 – 14,000 years ago although genetic evidence suggests the dog might have its origin as far back as 100,000 years in Southeast Asia (Vila et al., 1997; Leonard et al., 2002; Pennisi, 2002). However, later studies show evidence of a population split between Chinese indigenous dogs and the grey wolf around 32,000 years ago revealing the dog as the oldest domestic animal that we know of (Thalmann et al., 2013; Wang et al., 2013). They also suggest an initial domestication process through scavenging with humans. Since they identified an initial mild population size reduction subsequent to the split from wolves, possibly resulting in a mild bottleneck prior to the greater genetic bottleneck that is the result from selective breeding. The same initial process is also suggested by (Axelsson et al., 2013) upon finding genes with key roles in starch-digestion that might have been selected for during domestication. This could indicate that the now omnivorous diet of dogs, which could be considered a change of ecological niche, may be the driving force behind the domestication process. Similar adaptive responses to a starch rich diet have been found in humans possibly making this a striking example of parallel evolution in dog and human (Perry et al., 2007; Axelsson et al., 2013).

## **2 Why study the dog?**

There is no doubt that the dog is the domestic animal that have been living with humans for the longest period of time, but dogs have also been living closest to us. Why would we not want to study and learn everything about mans' best friend? But

there are numerous other reasons to study dog behavioural genetics. Because dogs have been selectively bred for centuries for their looks as well as behaviour, they present a rather unique model for the study of behaviour genetics (Jazin, 2007). This selective breeding has resulted in breeds that can be considered genetically relatively isolated populations. Across breeds, we see a great variety of morphological appearances but they also differ in certain behavioural abilities such as herding, pointing and retrieving. In turn, artificial selection on behaviour has resulted in breed groups that differ in personality traits like activity, aggressiveness and emotionality.

The importance of the dog as a model for genetic research has been demonstrated by the fact that it was the fourth mammal to have its genome sequenced (O'Brien and Murphy, 2003). The reason for this was based on the numerous advantages of the canine model for both basic genetics research and genetics research on human diseases. There are many analogies in behavioural variance between dogs and humans. Dogs display differences in behaviours such as aggression, social behaviour, temperament, anxiety levels and even compulsory disorders (Overall, 2000; Jones and Gosling, 2005; Overall et al., 2006). For example, tail-chasing behaviour has been classified and studied as a canine compulsory disorder (CCD) that could be an analogy of obsessive compulsory disorder (OCD) in humans (Irimajiri et al., 2009; Moon-Fanelli et al., 2011). Additionally, polymorphism in the tyrosine hydroxylase (TH) gene has been associated with activity-impulsivity behaviour in German shepherds, similar to ADHD in humans (Kubinyi et al., 2012).

Additionally, the structure of the dog genome is very well suited for genome-wide studies. Dogs share fragments of the genome called linkage disequilibrium blocks (LD blocks) that are statistically linked together, in this case, due to heavy inbreeding (Wall and Pritchard, 2003). A much lower density of single-nucleotide polymorphisms (SNPs) is required for genome-wide association studies (GWAS) in dogs than in humans since the long-range LD within dog breeds extend about 50 times further than in humans (Lindblad-Toh et al., 2005). This means that dog GWAS only requires about 10,000-30,000 SNPs compared to more than 300,000 in human studies. Additionally, the LD blocks differ between dog breeds, depending on historical founder and bottleneck effect, and could therefore be a potential instrument to determine genetic correlates of behavioural differences (Jazin, 2007; Parker et al., 2010).

Another major advantage of using a canine model for genetic mapping of phenotypic traits is that morphological variation seems to be governed by a small number of large effect genetic variants (Boyko et al., 2010).

### **3 Domestication and social behaviour**

Evidence of possible effects of a close relationship and co-evolution between the domestic dog and humans can be found on behavioural traits in both species (Hare and Tomasello, 2005). Through the years, dogs appear to have evolved certain skills

for reading human communicative and social behaviour (Cooper et al., 2003; Miklosi et al., 2004). When comparing these skills to primate studies, it seems dogs even outclass our closest phylogenetic relatives such as bonobos and chimpanzees. For example, dogs perform better than chimpanzees in tasks involving finding hidden food with the help of human communicative cues like pointing and gazing at the hiding place (Itakura and Tanaka, 1998; Miklosi et al., 2003; Hare and Tomasello, 2005). Additionally, dogs, like human infants but unlike chimpanzees, are able to discriminate human communicative behaviours from other similar behaviours such as gazing in the direction of an object but not directly at it (Povinelli et al., 1999; Soproni et al., 2001). In this case, dogs and infants ignored a human's gaze cue if the person was not looking directly at one of two hiding locations.

Dogs' ability to read human social behaviours, such as pointing and gazing towards and object, do not seem to change remarkably with age or experience of human contact (Hare et al., 2002; Riedel et al., 2008). When studying the ability of using pointing and gazing cues, puppies with little experience of humans perform as well as puppies with more experience. Additionally, these traits do not seem to be inherited from the wild ancestors of the dog. When comparing human-reared wolves and dogs, wolves were not as skillful as dogs in reading human social cues (Hare et al., 2002; Miklosi et al., 2003). However, when presented with an insolvable task, dogs give up early and start gazing between the human and the task while wolves continues to try and solve the task on their own. This human-directed gazing behaviour could be considered a communicative cue with the purpose of asking for help since it is often observed when the dog is requesting an out-of-reach object from a human (Miklosi et al., 2003; Passalacqua et al., 2011). Human-directed gazing seems to occur more in hunting and herding dog breeds and also increases with age and/or experience suggesting that this behaviour is shaped by both genetic factors and life experience (Passalacqua et al., 2011).

### **3.1 The farm-fox experiment**

Evidence keeps pointing towards dogs' social skills being a product of domestication. This seems even more likely after studying the farm foxes of the Siberian domestication experiments at the Institute of Cytology and Genetics of the Russian Academy of Sciences (ICG) in Novosibirsk, Russia. In 1959, Dr Belyaev and his colleagues started selecting and breeding farmed silver foxes (*Vulpes vulpes*) for what today is the longest running experiment looking at behavioural genetics of domestication (Trut, 1999). This so called "farm-fox experiment" has shown to be a remarkable resource for understanding both morphological and behavioural changes occurring with the domestication process. Foxes were selected only for one criterion – less fearful and human-directed aggressive behaviour (tameness). The second population has been kept as a control group that has been randomly bred in respect of this criterion. Although only selecting on behaviour, morphological changes began to appear in the foxes within few generations. These traits were similar to those distinguishing domestic dogs from wolves including floppy ears, widened skulls,

shortened snouts, shortened and curly tails and alterations in coat patterns (Trut et al., 2009).

Interestingly, foxes selected for tameness also display behavioural similarities of domesticated dogs (Trut, 1999; Kukekova et al., 2012). They are actively seeking human contact, sniffing and licking at humans and starts whimpering to attract attention. Like previously mentioned as a difference between dogs and wolves, tame foxes have developed human social cognitive skills that are not found in the control strain. When compared to age-matched dog puppies, the tame foxes are as skillful at reading human social cues (Hare et al., 2005). However, the foxes selected for tameness are more skilled at reading human social cues than the foxes randomly bred in regards to tameness. These findings confirm the probability that dogs' ability to read human social cues is a product of the domestication process. Also, the research of farm foxes suggests that this ability could have been an incidental by-product of selecting for tameness in dogs (Hare and Tomasello, 2005). Nevertheless, this unique ability of dogs' to read human social communicative behaviour is a remarkable asset in research aiming to broaden the understanding of comparative social cognition as well as the evolution and genetics of human-like forms of communication (Miklosi et al., 2004; Hare and Tomasello, 2005).

#### **4 Breed differences in behaviour**

As far as we know, the 343 dog breeds recognized today by FCI can be placed on four genetically different clusters, based on common ancestry. These are composed of old Asian breeds such as sled dogs and Akita, guard dogs like mastiffs and boxer, herding breeds and sight hounds such as collies and greyhound and at last hunting breeds like terriers, gun dogs and hounds (Parker et al., 2004; Parker and Ostrander, 2005). The most distinct out of these groups is the Asian breeds which are also considered the oldest breeds (Savolainen et al., 2002). However, even breeds within the clusters are more or less closely related to one another and morphological characteristics cannot always be used to tell whether two breeds are closely related or not (Parker et al., 2004).

The earliest and up to date most complete studies of breed differences in canine behaviour was performed by Scott and Fuller starting in 1945 (Scott and Fuller, 1965). They studied the behavioural differences between five dog breeds: Basenji, Beagle, Cocker spaniel, Shetland sheepdog and wirehaired fox terriers. The abilities of the five breeds were studied in numerous ways, looking at everything from social motivation, problem solving tasks, and trainability to special abilities associated with the specific breeds. Dogs were raised in the same environment and studied daily from birth until 16 weeks of age and then regularly at set ages for different tests. Many interesting observations were made e.g. they found that the Basenji performed the best in a problem-solving task followed by the beagle, and the terriers scored the lowest in spatial orientation.

Since the study of Scott and Fuller, there have been several other studies on breed differences in different types of behaviours. Breed differences have been studied in both morphological characteristics and behaviour related to neoteny (juvenilization) (Houpt, 2007). In this case, breeds were ranked according to their developmental stages based on both the degree of puppy-like features such as a shortened snout as well as of juvenile behaviour. Another example is Goodwin et al. (1997) that investigated variation in communication behaviours of ten different breeds and then ranked them in relation to their similarities to wolves. Here, Siberian husky and German shepherd ranked the highest while the Norfolk terrier and Cavalier King Charles spaniel displayed the least parallels to wolves in communication behaviours.

Even though behavioural differences between dog breeds are often considered as historical remnants from past selection, in many breeds, selection has changed during the last decades (Svartberg, 2006). Personality traits such as aggressiveness, curiosity/fearfulness, playfulness and sociability were used to study breed differences between 31 breeds. Here, data from a standardized behavioural test performed on 13,000 dogs was used. No relationships were found between the historical function of the breed and the breed-characteristic behaviour. Instead they found a positive correlation between the selection for dog show use and social and non-social fearfulness, and a negative correlation to playfulness, curiosity and aggressiveness. In contrast, aggressiveness and playfulness correlated positively for working dogs. Also, more popular breeds have higher scores in playfulness and sociability than less popular breeds. This indicated that a positive attitude towards strangers is a desired trait by dog owners, but a conflicting factor in the selection for dog show use. These results imply that dog behaviour can change with changes in selection pressure and that the current use of the dogs can have a greater impact on their behaviour than their historical use.

## **5 Heritability of dog behaviour**

Specific behavioural traits of hunting dogs such as retrieval, search and pointing have been of great interest to some scientists working with behavioural genetics. These traits are very important for the breeders of high performance hunting dogs and have been selected on for many generations. Because of this, the heritability of these highly demanded behavioural traits is usually the focus of study. Variation in the phenotype ( $V_P$ ) can be expressed as the sum of the underlying genetic ( $V_G$ ) and environmental ( $V_E$ ) variance (Visscher et al., 2008; Wilson et al., 2011). Broad-sense heritability ( $H^2$ ) is defined as the proportion of phenotypic variation in a characteristic that can be explained by genetic or environmental factors ( $H^2=V_G/V_E$ ). However,  $V_G$  contains all genetic factors that can possibly affect the phenotype such as additive (average effects of the alleles) variance ( $V_A$ ), allele dominance within loci ( $V_D$ ) and between loci allele interactions (epistasis) ( $V_I$ ). It is very difficult to estimate  $V_D$  and  $V_I$  and since an individual only inherits one allele from each parent at a certain locus  $V_A$  is the variable mainly explaining parent-offspring resemblance. Therefore, when using an



animal model, it is most often narrow-sense heritability ( $h^2$ ) that is estimated, defined as the proportion of phenotypic variance that can be explained by additive genetic effects ( $h^2=V_A/V_E$ ). If the variation in a trait is completely dependent on genetic variance, the heritability value will be 1 in contrast to 0 if the variation of the trait can be explained by environmental factors only. The higher heritability value, the easier it is to identify genetic differences by molecular genetic methods.

One of the most well known studies trying to identify the genetic contribution to a behavioural trait in dogs was done by Scott and Fuller (1965). The trait of interest, in this case, was barking and they made a Mendelian cross between the Basenji that rarely barks and the Cocker spaniel that barked most frequently of all the different breeds they studied. In contrast to the farm fox experiment, Scott and Fuller did not attempt to accentuate the breed differences by further selection, but relied on the historical selection of each breed. They created a  $F_1$  crossbreed of the Basenji and Cocker spaniel and also continued with making both  $F_2$ 's as well as back-crosses towards the parent strains. The  $F_1$  hybrids barked almost as frequently as the Cocker spaniel parents and the  $F_2$  generation barked slightly less than the  $F_1$ . Individuals backcrossed to Cocker spaniel barked as much as the pure bred parents in contrast to the dogs backcrossed to the Basenji that displayed barking behaviour intermediate to the hybrids and the parents. These results suggest that this trait has a dominant inheritance and that it probably depends on either one or two genes.

Heritability of hunting related behavioural traits, as well as personality traits, has been investigated in flatcoated retrievers in Sweden (Lindberg et al., 2004). Behavioural traits were observed during a hunting behaviour test carried out by the Swedish Flatcoated Retriever club during a period of eight years. Dogs were exposed to standardized hunting situations during which several behavioural and personality traits were scored. Heritabilities for the different behaviours mostly varied between 0.1 and 0.4. Looking at the three different personality traits scored, the heritability estimates had values of 0.49 for excitement, 0.28 for willingness to retrieve and 0.16 for independence (S.E was 0.08-0.12).

Working dogs have also been studied with the goal to estimate the heritability of behavioural traits. The heritability values vary significantly between different studies. For example, a study in Swiss army dogs (German Shepherds) based on seven traits, observed during working tests, found very low heritability estimates (Ruefenacht et al., 2002). In this case the traits investigated were affability, disposition for self-defense, disposition for self-defense and defense of the handler, disposition for playful fighting, courage, ability to meet with sudden auditory stimuli and disposition for forgetting unpleasant episodes. In contrast, rather high estimates of heritability were found in a Swedish study on eight-week-old German shepherd puppies bred for the purpose of working dogs (Wilsson and Sundgren, 1998). High heritability was found on the traits activity ( $0.53\pm 0.13$ ), tug of war ( $0.48\pm 0.11$ ) and contact

(0.42±0.10) while the values of other behavioural traits studied varied between 0.27 – 0.20.

There are also studies on pet dogs that have been investigating heritability of e.g. dominance and aggression behaviour. The additive genetic component and heritability of dominant aggressive behaviour was studied in English Cocker Spaniel puppies (Perez-Guisado et al., 2006). Highly significant differences were found between sexes and aggressive behaviours were also significantly different between coat colors. In this study dominant-aggressive behaviours were more pronounced in golden coloured individuals, less in particoloured and black furs in the middle. Heritability estimates were 0.20 on sire and 0.46 on dam, implying genetic and environmental maternal effects is an important factor in dominant aggressive behaviour in these dogs. By using the Canine Behavioural Assessment and Research Questionnaire (CBARQ) on Golden Retrievers, factor analysis has revealed that aggressive behaviour can be separated into the three different groups of stranger-directed aggression, owner-directed aggression and dog-directed aggression (van den Berg et al., 2006). In a following study on aggression in Golden Retrievers, very high heritability was estimated for human-directed aggression (0.77) and dog-directed aggression (0.81) (Liinamo et al., 2007). Additionally, the correlation between these types of aggressive behaviour was low and therefore, in genetic studies, these needs to be treated as separate traits.

Similarly to Scott & Fuller as mentioned earlier, another pet-dog study used a cross between two breeds with different behaviour. In this case, they were looking at the staring behaviour of border collies and water friendliness of Newfoundlands (McCaig, 1996). In the F<sub>1</sub> generation pups were very similar to each other both in their appearance and behaviour. However, in the F<sub>2</sub> generation the pups started to vary more in size and behaviour with different combinations of the behavioural characteristics of the parental animals. This typical inheritance pattern suggests a rather substantial genetic factor underlying these traits.

## **6 Behaviour genetics in dogs**

Behaviour, regardless of innate or learned, is always a product of both genetic and environmental factors, nature and nurture (Houpt, 2007; Jensen, 2007). Sensory organs receiving sensory stimuli, interpreted by the central nervous system and transformed into muscle activity, are all processes controlled by genetic factors. However, information processing and the development of the dog depend on environmental input and therefore behaviour is finally a result of both genes and environment. The type of behaviour that scientists are usually most interested in studying is those performed by the animal even without previously acquired knowledge or instruction and are inherited from one generation to the next. These behaviours are influenced by genetic variation but they can also be greatly modified

by the environment. For example, dog's hunting abilities have clear genetic components but can be encouraged, shaped and trained in different ways.

Very generally, behaviour can be defined as the actions of an organism as a response to the environment (Jensen, 2007). And in this case, the environment means anything other than the inherited factors. Therefore, behaviour can be a response to external influences such as climate or social interactions, but also internal influences such as hormones, pathogens and nutrients. With this in mind, it is not difficult to imagine all the challenges ethologists meet in defining specific behaviours and controlling for environmental influences.

Previously, dogs were of little interest to ethologists studying the causes of behaviour since they were often considered artificially bred animals (Kubinyi et al., 2011). However, many researchers have now realized that if scientific questions are asked in the right way, the study of dog behaviour could lead to valuable insights in e.g. behavioural genetics. In fact, dogs share several similarities to the human social system and can therefore represent better models than the traditionally used rodents. However, one of the most extensive studies of behavioural genetics in canids is not made in the domestic dog but in the farm foxes in Siberia (Kukekova et al., 2012). Thanks to the great similarities between the fox and the dog genome, most that is learned about foxes can also be applied to dogs.

## **7 Methods in dog behaviour genetics**

### **7.1 Behavioural phenotyping**

Different approaches have been used for behavioural phenotyping and assessment of behavioural breed differences in dogs (Spady and Ostrander, 2008). These different methods have both positive and negative aspects that should be considered. Typical traits of interest are those defining specific breeds, such as herding and hunting behaviours but there are also other behaviours of interest such as the obsessive-compulsive disorder-like tail chasing behaviour seen in bull terriers (Moon-Fanelli and Dodman, 1998).

A fast way of behaviour phenotyping a large set of dogs is by the use of owner questionnaire surveys (van den Berg et al., 2006; Liinamo et al., 2007; Duffy et al., 2008). Questionnaires can be used on their own or as a way of validating behavioural tests. This method can provide more detailed information about the dogs' tendency to display specific behaviours in a variety of situations during an extended time period. However, in comparison to behavioural observations, dog owner surveys can potentially be more subjectively biased. One of the most frequently used questionnaires in dog behaviour studies was developed by researchers at the Center for the Interaction of Animals and Society at the University of Pennsylvania and is called CBARQ (Canine Behavioral Assessment & Research Questionnaire).

Expert opinion based surveys are not as commonly used and involves the rating of different traits in dog breeds by an “expert” such as a veterinarian or a dog trainer (Hart and Miller, 1985). Obviously, these opinions can be subjectively biased depending on the kind of experience the expert has with the different dog breeds. Also, this method cannot be used to identify individual variation within a breed.

Behavioural observations and test batteries can be very accurate and the testing environment can be controlled for. However, to individually test and score many individuals can be very time consuming and it has been questioned whether a controlled test environment properly reflects dogs typical behaviour (van den Berg et al., 2003). An example of a behaviour that is perhaps better studied by other means than behaviour tests is aggression. In a Swedish study, dogs were tested in a standardized behavioral test called DMA (dog mentality assessment) and questionnaires were later sent out to the owners of dogs taking the test (Svartberg, 2005). Correlation between the scores on the behavioural test and the owner survey was found for most traits except for aggression. Some validation of aggression tests have been presented (Planta and De Meester, 2007). However, there is often a large percentage of cases (>20%) where dogs with a history of biting passes the aggression tests (Kroll et al., 2004).

## **7.2 Estimating the genetic contribution of a trait**

There are several different ways in which the genetic contribution to a behavioural trait can be estimated. Heritability, as mentioned earlier, is a parameter estimating how much of the difference measured in a trait that can be accounted genes or environment (Visscher et al., 2008; Wilson et al., 2011). However, this parameter does not tell us anything about the number or the type of genes or environmental factors involved.

One of the methods that can be used to study the genetic contribution to variation in a behavioural trait is by hybridization, i.e. the cross between two breeds to produce hybrids (Scott and Fuller, 1965). An example of this approach is the experiment performed by Scott and Fuller. As mentioned earlier, Scott and Fuller investigated breed differences between five different breeds. The greatest behavioural differences were found between the Cocker spaniel and the Basenji and therefore, these two breeds were crossed to produce F<sub>1</sub> and F<sub>2</sub> hybrids (Scott and Fuller, 1965). When looking at the trait barking, the F<sub>1</sub> hybrids were very much like their cocker parents while the Basenji phenotype started appearing in the F<sub>2</sub>s. These F<sub>1</sub> hybrids were then backcrossed with the parental lines and again the offspring performed intermediate to the F<sub>1</sub> and the parental population. This is a nice example of the existence of a genetic component of behaviour.

Another approach, which has the potential of showing the clearest contribution of genes to a trait, is by artificial selection. An example of this is the farm-fox experiment in Siberia (Kukekova et al., 2012). Foxes were selected for tameness for several generations, creating a population that differed from the original population in

their behaviour towards humans. If the environment is constant and the behaviour selected for still is modified in the selected population, the behaviour trait has a clear genetic component. Depending on the development of the trait over generations, estimates can be made on whether there are just a few or several genes involved. This method can also be complemented with making an  $F_1$  and a backcross population between the selected and the original population in order to study the pattern of inheritance of the trait of interest.

It may not always be practical to cross the studied populations but there is an alternative method that involves measuring the same trait in multiple individuals from different dog breeds (Jazin, 2007). If a correlation is found this could possibly indicate a common genetic mechanism behind the measured trait. This method has been utilized in a study comparing the genetic correlation structure of 16 behavioural traits in German shepherds and Rottweilers (Saetre et al., 2006). The pattern of co-inheritance was similar for the studied traits. A principal component accounting for over 50% of the additive genetic variation was found, which indicates a shared genetic component behind most of the traits. In this case, only aggression seemed to be inherited independently of the other traits.

### **7.3 Identifying genes**

As soon as the genetic contribution to a trait has been recognized, it is possible to start looking for the genes that might be involved. There could be analogies between the canine gene that you are looking for and other species like humans and mice. Therefore, if you are particularly interested in a certain behaviour that has been previously studied in other species, you could search for the analogous sequence in the dog and base your study on a candidate gene approach. If you have instead identified a behavioural variation but do not have any candidate genes, a Genome-Wide Association Study (GWAS) can be used to find loci associated to the trait. In contrast to the candidate gene approach that only targets SNPs in a limited number of selected genes, GWAS identifies associations between behaviours and genes across the entire genome (Hall and Wynne, 2012). A GWAS usually identifies a region that can be studied further by fine-mapping and a candidate gene study. Long fragments of LD-blocks, as previously mentioned, characterize the dog genome and can be of great use in association studies (Lindblad-Toh et al., 2005). These are statistically associated fragments with limited recombination that are shared within dog breeds. LD-blocks can be very useful since they limit the number of genetic markers (SNPs) needed to complete a GWAS.

It is very unlikely that the behavioural trait studied is controlled by only one single gene, but rather that it is a quantitative trait controlled by multiple genomic regions each contributing with a small phenotypic variation. These genomic regions containing genes involved in quantitative traits are called quantitative trait loci (QTL) (Mackay, 2001).

#### **7.4 Within-breed studies**

Some gene-behaviour associations have already been identified and are summarized in Table 1. A common feature of these studies is that they are all analyzing a behavioural trait segregating within breeds. Different molecular approaches and methods have been used within the studies, however, it has been noted whether they were GWAS or candidate gene based. For example, I previously mentioned a study by van den Berg et al. (2006) that identified high heritability of aggressive behaviour in Golden Retriever dogs. Since alterations in brain serotonin metabolism previously had been described in aggressive dogs, they decided to evaluate three serotonin receptor genes and a serotonin transporter gene further by the candidate gene approach (van den Berg et al., 2008). On the other hand, Dodman et al. (2010) did not have candidate genes for canine compulsive disorders (CCD). Instead, a GWAS had to be performed to search for associations in the entire genome. After identifying a region associated with CCD, fine-mapping revealed the gene CDH2 as a possible gene involved in compulsive behaviour.

#### **7.5 Across-breed studies**

If the behavioural variation studied does not segregate within a breed but is instead a common variation between different breeds it is preferably analyzed through an across-breed GWAS (Vaysse et al., 2011). The difference between the across and within breed designs is that in the across-breed design the samples represents the mean value of a breed instead of the individuals. This approach has been used by Vaysse et al. (2011) to identify the genomic region associated with a behavioural phenotype named boldness in dogs. They compared 19 non-bold breeds to 18 bold breeds and found significant associations at two SNPs on chromosome 10 and the peak significance for the trait was situated within an intron of the gene HMGA2.

### **8 Challenges along the way**

Defining a behavioural phenotype is not always the simplest task when it comes to determining the genetic contribution to a complex trait (Hall and Wynne, 2012). More general behavioural phenotypes such as shyness/boldness and activity/impulsivity are often assessed through a battery of tests generating huge amount of phenotypic data. To be able to make a comprehensive overview and define the interesting phenotypes a factor analysis or principle component analysis (PCA) is often utilized. For example, Svartberg and Forkman (2002) used factor analysis to reveal five narrow traits named “playfulness”, “curiosity/fearlessness”, “chase-proneness”, “sociability” and “aggressiveness” and a broad factor combining all of these (except for “aggression”) and relates to shyness/boldness.

However, there are limitations of these models that sometimes can be overlooked (Hall and Wynne, 2012). Firstly, behaviours that factor together do not necessarily have a common genetic foundation. A complex behavioural trait may have numerous causal pathways that neither the factor analysis nor the PCA can discriminate.

Secondly, these models cannot distinguish shared genetic causes from shared environmental factors. Therefore, behavioural tests can factor together due to common environmental cues instead of the genetic basis of the phenotypes. Also, it is not yet clear in which manner gene-factor associations actually translate back to gene-behaviour associations. Obvious ways of avoiding these problems would be to look at more specific and clear-cut behaviour phenotypes or to design an approach trying to account for the environmental variables.

Another problem we find when studying behavioural genetics in dogs is the great similarities between the wolf and the dog genome (Jazin, 2007). In fact, the dog genome is almost identical to that of the wolf even though we see such great variation in both physiological and behavioural traits (Kirkness et al., 2003). This suggests that the difference may not be in the gene structure but more likely in the expression of the genes. For example, a study found increased expression of genes in the human brain in comparison to the chimpanzee, indicating that the determinant behind behavioural differences, in this case, is due to brain gene expression (Gu and Gu, 2003). This mechanism could also have been important in the evolution of behaviour in other species such as the dog.

## **9 Summary**

The dog is a useful model animal for studying behaviour genetics for numerous reasons. Their unique morphological and behavioural variance has so far been surprisingly unutilized in comparison to the potential applications within human research. Previous studies have shown the heritability of complex traits and some gene-behaviour associations have already been identified. By the use of good phenotypic measurements and environmental factors accounted for, the study of dog behaviour genetics may greatly improve our understanding of how genes influence behaviour.

**Table 1:** Genes associated with behaviours from within-breed studies.

Behaviour	Breed	Sample size	Approach	Genes associated	Genes not associated	Citation
Activity/impulsivity	German Shepherd	189	Candidate gene	DRD4	-	Hejjas et al. (2007b)
Attention deficit	Belgian Tervueren	59	Candidate gene	DAT, DBH, DRD4	TH	Hejjas et al. (2007a)
Activity	Labrador Retriever	81	Candidate gene	slc1A2, COMT	DRD2, TH, DBH, htr1A, ht21b, DRD4, MOAB	Takeuchi et al. (2009a)
Impulsivity	German Shepherd	96	Candidate gene	DRD4	-	Hejjas et al. (2009)
Activity/impulsivity	German Shepherd	104	Candidate gene	TH	-	Kubinyi et al. (2012)
Aggression (human directed)	English Cocker Spaniel	50 cases, 81 controls	Candidate gene	DRD1, htr1d, htr2c, slcA1	DRD2+3, DBH, htr1A+B+D+F, htr2A+B+C, MAOA, MAOB, GAD1	Våge et al. (2010)
Aggression	Shiba Inu	77	Candidate gene	slc1A2	DRD2+4, TH, DBH, htr1A, ht21b, COMT, MOAB	Takeuchi et al. (2009b)
Aggression	Fawn-coloured Akita Inu	100	Candidate gene	AR	-	Konno et al. (2011)
Aggression (human directed)	Golden Retriever	49 cases, 49 controls	Candidate gene, linkage analysis	-	htr1A+B, htr2A, slc6A4	van den Berg et al. (2008)
CCD	Doberman Pincher	92 cases, 68 controls	GWAS	CDH2	-	Dodman et al. (2010)
Tail chasing	Bull Terrier	40 cases, 28 controls	Candidate gene	-	CDH2	Tiira et al. (2012)
Tail chasing	German Shepherd	11 cases, 16 controls	Candidate gene	-	CDH2	Tiira et al. (2012)
Tail chasing	Staffordshire Bull Terrier	7 cases, 5 controls	Candidate gene	-	CDH2	Tiira et al. (2012)



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