A Fetching Model for Understanding the Mammalian Mind

Genetics & the Natural History of Pointing

by Mark Neff, Ph.D.

TGen & The Van Andel Institute

INTRODUCTION

When it comes to pointing, the most knowledgeable biologists are breeders, owners, and handlers who have dedicated decades to understanding the behavior of their dogs. The hard-earned insights that make the difference in breeding and training a dog to compete may now enable scientists to better understand how genes influence behavior.

A study is underway in my laboratory to map the genes for pointing. Investigating how genes hardwire the brain for instincts like pointing will bring to light fundamental principles of neuroscience. This research is important because understanding the normal biology of natural behavior is a prerequisite to understanding the abnormal biology of human mental illness and psychiatric disease.

What follows is an overview of pointing behavior from a geneticist's perspective. Several points are particularly relevant to the proposed research. First, selectively bred characteristics, like pointing behavior, are generally tied to genes of large effect. This is because artificial selection acts on observable differences, and these tend to result from major gene influences. Second, there are roughly 50 breeds worldwide that possess a discernible degree of pointing instinct. Although there is variation in intensity and style across breeds, each shows a considerably greater proclivity for pointing than the typical non-pointing breed. A key question is whether pointing breeds have inherited *identical* genes from common ancestors. It is possible that the instinct evolved independently many times, and that genes for pointing are unique to a given breed. The more likely explanation, however, is that pointing took a single evolutionary path, and that the genes for pointing are shared across breeds through lineal descent. This is the principal thesis upon which our research is based, and it is addressable by modern DNA analysis.

BACKGROUND

The natural history of the domestic dog is punctuated by biological innovation, by the seemingly sudden appearance of novel characteristics that became prized for centuries. Coat textures that protected hunting dogs from harsh climates; functional action patterns that permitted shepherd dogs to manage a flock; and even the special desire and determination to rescue mountaineers from an avalanche are all examples of such natural ingenuity.

The animals that acquired these attributes had a tremendous evolutionary advantage, and were rewarded with a disproportionate transmission of their genes to the next generation. The dogs by our sides today are the most recent descendants of extraordinary animals whose lineages and legacies have remained unbroken for centuries.

Evolutionary change is constant, and the texture and fabric of breed histories is rich with the tradition of modification, of refining talents and combining them with new traits. Value-added characteristics could stem from spontaneous mutations, but the process of mutation is exceedingly rare. More commonly,

pre-existing characteristics were acquired from the gene pools of other landraces and geographical isolates. By directing crosses, breeders could draw upon standing variation to adapt (customize) their dogs to climate, terrain, and task. This historical shuffling of genes to create new combinations of traits served as the basis for breed diversification and differentiation. Mounting evidence supports this view, that breeds differ not because of unique mutations, but because of unique combinations of shared mutations, which are found in other, related breeds.

THE POINTING BREED FAMILY TREE

The historical emergence of pointing instinct in the dog illustrates a classic example of biological innovation. Most breed histories suggest that the progenitor was a breed native to Spain, the Perdiguero Navarro. Although the true ancestor of pointing dogs is lost to antiquity, it is probable that the natural history of pointing was punctuated by a small number of mutational events. The first pointing dog would have possessed only one of these genes. The instinct of these dogs was presumably much less intense than that which has been cultivated in the hundreds of years since that time, but the founding behavior was desirable enough to have been deliberately bred and intentionally propagated.

As these 'flash' pointers became more recognized for their utility in the field, dogs may have been exported to other regions in continental Europe. Breeders in these locales would not have forsaken their local dogs for Mediterranean imports, but they may have selectively imported a small number of their genes. In this way, landraces that excelled at hunting, and that had been adapted to the regional geography for centuries, could be given one new characteristic – pointing instinct.

Over time, a few spontaneous mutations arose that strengthened and intensified the early pointing behavior. And once again, as word would spread about the tremendous performance of a new strain, breeders would work to capture the new genes and introduce them into their bloodlines.

A migration of pointing instinct across Europe and into the British Isles is consistent with an increase in pointing intensity in the geographical distribution of breeds. The Mediterranean dogs tend to exhibit a less pronounced point than their British counterparts. If the previous methods of breeding were more commonly practiced, genes that arose later in the evolution of pointing would likely make their way back to the early pointing breeds, such that all pointing dogs might perform more similarly.

Here, a digression is necessary. An exchange of genes between landraces was relatively common for thousands of years. Only recently has the concept of formal registries and closed gene pools begun to dominate breeding. Of course, it must be kept in mind that kennel clubs and the modern breeding practices they espouse were never intended to ensure the performance of dogs. Indeed, registries were established as a conservation effort, a means to preserve breeds that were on the verge of being lost to posterity. In many cases, the threat of extinction was because the breed had lost their functional purpose, or they were simply no longer able to compete with other breeds performing similar tasks. The divergence continues, and today almost every breed includes stratified sub-populations - field, show, and pet dogs. Interestingly, each sub-population should be considered purebred, but they breed true for different characteristics. Ironically, few dogs are truly reminiscent of the breed populations that existed prior to the mid-1800s. Selective breeding has continued, and so has the concomitant evolution of the dogs.

THE GENETIC BASIS OF POINTING

Pointing instinct is tied to differences in genes. The behavior has responded to selective breeding, and breeds differ in striking ways for the instinct. It is possible that this seemingly complex behavior is tied to hundreds of genes of small, indistinguishable effects. If this were the case, the causative genes for pointing might be undetectable with current genetic technologies. But such a complex genetic architecture is highly unlikely. Traits and characteristics that have been selectively bred are almost always tied to a small number of genes of very large effect.

The genetics of corn establishes a precedent. Maize was domesticated and developed by selective breeding, transforming an American grass called teosinte into one of the most important cereals in the history of civilization. Of course, selective breeding can only be applied to observable, recognizable differences in each generation. This predicts that there are a small, manageable number of genes that define the major differences between teosinte and corn. Gene mapping experiments have shown this prediction to be correct. A single gene, for instance, converted a plant with multiple tassels and a single ear to a plant with multiple ears and a single tassel.

The relative genetic simplicity of complex traits and behaviors in the dog will be no less astounding. Pointing instinct is expected to follow this theme, and be tied to a few gene differences that account for most of the difference between pointing dogs and non-pointing dogs. Although there are likely to be many genes that modify pointing and influence a dog's intensity, style, and drive, it is probable that there are only 3-5 genes specifying the primary instinct.

MAPPING POINTING GENES

The natural history of pointing breeds, and the recent development of stratified breed populations, provide several research opportunities to identify major genes governing the instinct. New technologies permit analyses of more than 100,000 letters in the genetic code, thereby providing remarkably detailed DNA profiles of individual dogs. This scale and resolution can make visible the molecular signatures of selective breeding over a historical timeframe.

The DNA footprints of selection can be detected in two ways. First, if pointing evolved once, and the genes for pointing are shared by common descent across pointing breeds, then the DNA profiles of hundreds of dogs can be compared to locate the few regions that are identical in DNA sequence. Blood samples from 50 outstanding pointing dogs from 15 top-tier breeds are expected to provide the sample size and statistical power for sieving out regions of the genome that are shared by chance, and leaving only the regions that have been mutually selected across breeds.

This approach is unlikely to identify more than 2-3 of the major genes involved. But once a few genes have been located, subsequent experiments can be designed with this information in mind to focus mapping on secondary genes of smaller effect.

A second, complementary set of experiments leverage the availability of stratified sub-populations within breeds, which can differ profoundly in their degree of pointing instinct. Contrasting the DNA profiles of field dogs with show-bred dogs, and perhaps even the intermediate 'dual champion' dogs, will identify regions of the genome that have been subjected to differential selection -- high in the field-bred dogs, and low or non-existent in the show-bred dogs.

WHY STUDY POINTING?

The National Institutes of Health, the nation's primary funding agency for biomedical research, declared the 1990s "the decade of the brain and behavior." During that time, a great deal was learned about neuroscience – much was learned about the biophysics of synaptic transmission and the rules of axonal guidance in neuronal development. But little progress was made in identifying the genes responsible for psychiatric diseases like Alzheimer's, schizophrenia, addiction, and bipolar disorder. Since then, progress in these areas has been made, but the general principles by which genes influence mood and behavior have remained elusive.

A complex system like the brain can be broken in myriad ways, both direct and indirect. Mental illnesses reflect broken minds. The potential biological uniqueness of each case presents an enormously complicated problem for clinicians and researchers alike. There are simply too many ways to mechanistically 'break' the mind.

The same complexity that confounds an understanding of human mental illness similarly constrains the evolution of behavioral diversity. Most alterations are likely to be mal-adaptive; only a select few functional changes are positive, and represent an extended, specialized, or otherwise evolved mind. Such adaptive variation, such as pointing, can serve as a more precise probe of the inner workings of the mind. Pointing setters and herding collies do not have broken minds, they have adapted minds, and studying these variants can help elucidate the basic rules governing the genetics of behavior.

THE FASCINATING BIOLOGY OF THE DOG

Resolving the genetics of pointing is unlikely to directly benefit the breeding programs with competitive dogs. The resolution of gene mapping only permits identifying genes of large effect, and these are genes that have already been genetically fixed within the top-tier breeds. DNA tests built around any of the early discoveries are unlikely to be of much help. Identifying genes of lesser strength will require a substantial improvement in genetic technologies.

Research into the basis of pointing may still be of interest, however. Field trialing enthusiasts are presumably fascinated by their dogs' behaviors, probably even more so than the academic in the laboratory. There are many interesting questions one can ask. What was the antecedent behavior in the wolf from which pointing was derived? Are there early experiences or environmental influences that strengthen the behavioral outcome? These questions and many more are addressable with genetic knowledge of pointing.

In addition, there are many variations on the pointing theme and modifications to the primary pointing pattern that can be informed upon with the initial study. Moreover, the tools and approaches used to map pointing genes can similarly be applied to related traits of interest, such as the natural difference between all-age dogs that run 'large', shooting dogs that handle more kindly, and gun dogs that work close. Identifying causal genes would translate into DNA tests of predictive value to breeders. Young gun dog puppies of exceptional talent could be given to hunters, while the puppies expected to be shooting dogs or all-age dogs could be kept and trained for field trial championships.

The same approach can be applied to many other traits relevant to pointing, including gait, tail carriage, flagging, scenting ability, stamina, endurance, intelligence, biddability, and many more. Studies of these characteristics and their genetic underpinnings are logical extensions of the research foray into the genetics of pointing.

Participation of Field Enthusiasts

The most exceptional pointing dogs in the world are enlisted into the books of several different registries, including the American Field and American Kennel Club. Enthusiasts can support the effort to map the major genes for pointing in several ways. The simplest is by contributing blood samples and pedigree records from top pointing dogs. The cost of blood draws can be reimbursed; the shipping can be billed to a Federal Express account number. Thus, there is no cost to participate.

Additionally, there is a collective knowledge base amongst breeders and handlers that is crucial for making sense of any genes that may be mapped. The most knowledgeable dog biologists are not researchers in laboratories, but field trial enthusiasts who have dedicated decades to understanding the biology of their dogs. Such hard earned insights make the difference in breeding a dog to compete. These same insights will be necessary to fully understand the biology and behavior of these dogs. The hope is that geneticists and avid field trialers can share their fascination of these remarkable dogs, and work together to answer basic questions in biology, with the potential to address fundamental problems neuroscience.

About The Author

Dr. Mark Neff is a classically trained geneticist. He earned his Ph.D. from the University of Virginia where he studied the cellular mechanisms that guard against cancer. He has more than 15 years of experience in canine genetics, beginning as a Human Genome Distinguished Postdoctoral Scholar at UC Berkeley in 1993. He worked with Dr. Jasper Rine on the first Dog Genome Project. Dr. Neff is now Director of the Program for Canine Health and Performance. This unique program is aligned across two different non-profit research agencies, the Van Andel Research Institute (VARI) in Grand Rapids (MI) and the Translational Genomics Research Institute (TGen) in Phoenix (AZ). In addition to directing the program, Dr. Neff also heads The Laboratory of Neurogenetics and Canine Behavior, and holds the position of Associate Professor at both VARI and TGen.

This research is made possible by the voluntary submission of blood samples from dogs exhibiting intense pointing instinct. There is no cost to participate; blood draws can be reimbursed, and the costs of shipping can be billed to the recipient with FedEx. To enroll your dog in the study, please contact:

TGen

Van Andel Research Institute®

Mark W. Neff, PhD
Director
Center for Canine Health & Performance
The Van Andel (VARI) & The Translational Genomic Research Institutes (TGEN)
Emails: mneff@tgen.org, mark.neff@vai.org