

## A Neurology patient's best friend: not letting sleeping dogs lie or shaking dogs shake

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Photo taken from University of Bern Institute of Genetics:

[http://www.genetics.unibe.ch/content/rubrik/obermann\\_head\\_bobbing/index\\_eng.html](http://www.genetics.unibe.ch/content/rubrik/obermann_head_bobbing/index_eng.html)

It is widely known that dogs or other pets benefit the healing process in patients with all types of disease. Most large hospitals or medical centers have some form of pet therapy program. Recently, dogs have become our best friends in more ways than we have imagined. Beyond companionship, happiness, and love some of our furry friends have actually provided some key insights into neurologic disease. This has come about from collaborations between veterinarians and clinicians in looking at neurological diseases that are prevalent in certain breeds of dogs, diseases that in some cases resemble human neurological disorders.

### Dogs and neurologic disease

Probably the most stunning example of a genetic discovery in dogs that relates to human disease relates to a group of sleepy Doberman Pinschers. In 1999, Stanford scientist and current director of the Stanford Center for Narcolepsy, Emmanuel Mignot, capped a tour de force of work by identifying a gene responsible for the sleepiness in these Dobermans. The story of the sleepy Dobermans starts almost 30 years earlier. In the early 1970s, Dr. William Dement, considered by some to be the father of sleep research and author of the popular book "The Promise of Sleep", identified a group of Doberman

Pinschers and Labrador Retrievers that would spontaneously doze off in the middle of activities and sometimes collapse when they got excited, such as when they were being served food. We know these as some of the classic signs of a condition called narcolepsy. Dr. Dement established a breeding colony for these dogs at the sleep research center to study narcolepsy. Dr. Mignot, a narcolepsy researcher from France, traveled to Stanford and inherited this colony in the 80's and initiated what many scientists thought was a foolhardy task at the time - Identifying the gene associated with the narcolepsy in dogs. He did just that after many years identifying mutations of a gene called Orexin receptor 2 causing the sleepiness in these dogs. Perhaps even more surprising, at about the same time, in parallel research done by Dr. Yanagisawa at the University of Texas Southwestern who was looking at genes that were thought to be important for feeding behavior in mice found that when his mice were bred to have an absence of this gene, called Orexin, the mice also had altered day/sleep cycles and would suddenly collapse. The gene turned out to be one that directly interacts with the gene identified by Dr. Mignot. Subsequently, problems in these gene products were then identified in many humans with narcolepsy.

In science, there are at times reciprocal relationships between animals and man. An interesting example of this has recently emerged in epilepsy research. In this case, dogs trying to detect seizures in patients and in reverse, researchers trying to detect seizures in epileptic dogs.

A research collaboration between researchers at the Mayo Clinic, University of Pennsylvania, and Neurovista Corporation have created a novel implantable device wirelessly linked to an external recording unit which is currently being tested in dogs with canine epilepsy. Certain dogs are prone to epilepsy that shares a lot of characteristics with human epilepsies that are difficult to control with medications. The goal of this type of work would be to try to predict seizures before they happen. A practical application of this type of work is that if an epileptic patient knew that they were going to have seizure in advance they could take precautions or perhaps even try to abort the seizure by taking extra medications. On the flipside, there has been a small but growing interest in the possibility of seizure alert dogs- that is, dogs that have been trained to alert to or respond to seizures in patients. This is usually predicated on the idea that there may be subtle behavioral changes in patients who are about to have



a seizure although this is not known for sure. Other theories hypothesize dogs having keener senses and detecting changes in respiratory rate, heart rate, odors, or other such features. This area has been fraught with controversy however and there have only been a few limited studies. It remains to be seen if seizure alert dogs are practical.

It is often beneficial to have animal models of disease both for learning about the disease and for screening potential treatments. Dogs are generally not practical animal models as they have long lifespan, care intensive, and they have a special place in the human heart. It would not be considered kind or ethical to breed certain disease traits as is performed in yeast, flies, worms, fish, and mice. However, preexisting conditions that have naturally become more prevalent as a result of breeding for the purposes of owning pets can be useful for the study of those conditions.

#### Dogs and tremor

Head tremor has been noted in several dog breeds including boxers and bulldogs among some. Anecdotally, there are a plethora of youtube videos taken by owners showing examples of different kinds of head tremors. In addition, there are many different types of tremor syndromes in dogs, perhaps the better known of these is shaker dog syndrome. Just as in humans, there are many different types of tremors seen in animals. The question has been posed by patients and physicians alike, whether there is an animal form of essential tremor and if these can shed any light on what scientists know about essential tremor. It's hard to know if any of these tremors is at all related to essential tremor in humans but there have been a few studies.

Recently, a head tremor in the Southern Sea Otter, Goldie, was examined by a group of researchers at Columbia University led by Dr. Elan Louis in collaboration with the Monterey Bay Aquarium. They found that Goldie's head tremor and pathology resembled several aspects of essential tremor and published their results in the journal Movement Disorders in 2004. An article about this study appeared in the June 2005 edition of the Spikes and Spasms newsletter. More recently, a group of researchers and veterinarians from Germany have undertaken a large

scale study in Doberman Pinschers with head tremor with the goal of characterizing the natural history, inheritance, and clinical characteristics of their head tremor. In the November 2011 issue of the journal Movement Disorders, research led by veterinarian Dr. Martina Wolf and Dr. Andrea Fischer of the Center of Veterinary Clinical Sciences at Ludwig-Maximilians-University of Munich examined an inherited episodic head tremor syndrome in Doberman Pinscher dogs that in some ways resembles some aspects of essential tremor.

The research team recruited Doberman Pinschers for their study by putting announcements on their clinic home page and in internet forums between 2009 and 2010. In the end, they were able to recruit 87 dogs that met the criteria of their study. Information on these dogs were collected through interviews with owners, questionnaires,

videos, and basic blood lab studies and examination. Five of the dogs had more extensive neurologic examinations including MRI, spinal tap, and electromyography.

One consequence that essential tremor patients are quite familiar with is that in about 20-26% of the dogs in this study, there seemed to be distress after the episode of head tremor and

owners noted that their dog seemed to be tired, ashamed, tried to hide, or in need of affection afterwards. In some cases the dogs even tried to stop their head tremor with their paws or by pressing their head against an object.

Though the head tremor exhibited by these Dobermans resemble essential tremor in some ways, there are some key differences and the authors note this. One of the key differences is that the head tremor they observed was episodic or what some clinicians call "paroxysmal", meaning that it is present for limited durations and not constant whereas the tremor in essential tremor patients tends to be constant, though it can be minimal and only apparent with exacerbating factors. In these particular dogs, head tremor was only seen with a median of every 60 days and median duration was about 3 minutes though could range all the way up to 3 hours. In addition, in about two thirds of the dogs, these head tremors could be distracted or interrupted if the owner pet or talked to the dog. In almost 40% of the dogs, the head tremor had a particular precipitant like stress, fatigue, illness, or excess

**"A particular gene in these breed of dogs could potentially shed light on causes of head tremor in humans."**



excitement. It was also noted that in some cases head tremor was accompanied by abnormal posturing of the head, a symptom familiar to some patients with dystonia. It might be the case that the head tremor seen in these Dobermans is actually closer to other types of head tremor including dystonic head tremor or some of the paroxysmal dyskinesias.

The symptoms did appear to be familial or hereditary as the pedigrees of 60 of the affected dogs could be traced back to one common sire in the 1960s. One of the most exciting aspects of these findings is that if a particular gene were identified in these breed of dogs, it could potentially shed light on causes of head tremor in humans, much like the sleeping dogs' effect on narcolepsy research. Researchers would then screen that particular gene in available pedigrees to see if there were any possible links to essential tremor or other tremor disorders.

Will we see some of the same types of reciprocal relationships in essential tremor that we have seen in dogs with narcolepsy or epilepsy? Will we learn more about treating tremor in dogs and will we learn more about our own tremor from dogs? It remains to be seen, but perhaps the dog will become a patient's best friend in ways that we have not imagined.

To learn more about the study of head tremor in Doberman Pinschers please visit

[http://www.genetics.unibe.ch/content/rubrik/dobermann\\_head\\_bobbing/index\\_eng.html](http://www.genetics.unibe.ch/content/rubrik/dobermann_head_bobbing/index_eng.html)

## About the Author

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