Neurology Service announce new study funded by American Kennel Club-Canine Health foundation

Magnetic Resonance Imaging (MRI) study of Syringomyelia in Brussels Griffon /Griffon Bruxellois Dogs

www.vet.uga.edu on the neuro page.

Much has been made of breed-related and possible inherited disorders in dogs of recent, not least because the genetic make-up of the dog has now been well-defined opening up possibilities to develop blood tests and determine appropriate breeding programs. In the last couple of years, a disorder of the nervous system has been identified in the Brussels Griffon (BG) breed which may indeed be hereditary and has been shown to be familial (Figure 1.). The disorder has been termed *syringomyelia*. Currently, exactly how common and therefore how concerning this disease is in the breed is unknown. In this article, we will describe what this problem is and how it can be recognized and possibly treated. Additionally, funding for investigation of this disease in the BG has been awarded to the neurology service at the College of Veterinary Medicine, University of Georgia by the Canine Health Foundation (a branch of the American Kennel Club), and so details of the upcoming research project are included. The study is in collaboration with Clare Rusbridge and Penny Knowler in the UK, world renowned for their pioneering work in this disease in Cavalier King Charles spaniels over the last 10 years. Their preliminary investigations in Europe and Australia with BG breed groups have given rise to the need for this study to be pursued. Indeed, this work has encouraged many BG clubs and groups all over the world to financially support further work, and all the veterinarians involved in this venture are extremely grateful for this.

WHAT IS SYRINGOMYELIA?

Syringomyelia (SM) describes an abnormal fluid filled cavity within the spinal cord (Fig 2.). The fluid-filled cavity, or syrinx typically is largest in the neck, but it can affect all regions of the spinal cord. It can vary in size from being hardly noticeable to over 90% of the cross sectional area of the spinal cord. As the cavity gets bigger, the spinal cord in which it sits becomes damaged. Syringomyelia can affect human beings with approximately 90% of people also having what is called a type I Chiari malformation, which is believed to be an underlying cause of the spinal fluid accumulation. A Chiari malformation is a complicated disorder whereby some of the brain is seen to protrude outside of the skull and sit on top of the spinal cord in the neck! The reason for this is often due to the skull being misshaped and smaller than is necessary to house the brain. Simplistically, a small skull leads to a small part of the brain pushing out of the hole at the back of the skull which leads to syringomyelia.

Quite how all the skull and brain defects lead to fluid build-up in the spinal cord is uncertain but it can be thought of as follows. The normal brain continuously produces fluid (cerebrospinal fluid or CSF) to nourish and protect its structures. The fluid normally flows out of the back of the skull and around the spinal cord. The brain can be viewed as a tap which can't be turned off and is attached to a hose pipe. There is a continuous flow of water out of the hose pipe. When there is an abnormality of the skull such as a Chiari malformation, it is as if a thumb is placed over the end or top of the hose pipe. The same amount of water passes through but now with a lot more pressure. This pressure can cause fluid to build up in the spinal cord ultimately resulting in syringomyelia. The only way in this case to stop further build up of the fluid is to either turn the tap off, which can't be completely done or remove the thumb, which when talking about the skull means surgery!

Breeds currently identified with SM include the Yorkshire Terrier, Maltese Terrier, Chihuahua, Miniature Dachshund, Miniature and Toy Poodle, Bichon Frisé, Pug, Shih Tzu, Pomeranian, Staffordshire Bull Terrier, Boston Terrier, Pekingese, Miniature Pinscher, King Charles or English Toy Spaniel and French Bulldogs. Recently the condition has also been detected in the BG. The breed that has been most extensively studied is the Cavalier King Charles Spaniel (CKCS) in which SM is observed in association with a Chiari malformation similar to that seen in humans. Chiari-like malformations, similar to those in people, have been described in dogs of many breeds, but the condition is over-represented in CKCS in which there is a suspected familial/genetic basis.

WHAT SIGNS ARE SEEN IN DOGS WITH SM?

The most common signs associated with SM in people are pain, weakness, muscle wasting and spinal curvatures. The pain typically is more marked on one side of the neck, shoulder and arm; it has been described as having a burning, aching quality. There can also be pain at the base of the skull or back of the neck – in some cases this pain is made worse by coughing, sneezing, stooping or other positions. There is considerable variation of clinical signs that relate to the Chiari-like malformation and SM in the dog. The most common clinical sign is neck pain or intermittent, non-specific discomfort. Affected dogs may suddenly scream and/or lie with the head on the ground between the paws after jumping up or during excitement. It is also common to sleep with the head in unusual positions, for example elevated. Discomfort often appears worse in the evening and early morning or when excited and can be associated with defecation or may vary with weather conditions. A classic clinical sign is scratching at the neck and shoulders which may represent a reaction to possible burning sensations in the skin; typically this occurs on one side only, while the dog is walking and often without making skin contact. Such behaviour is often referred to as an "air guitar" or "phantom" scratching. Additional signs include varying degrees of weakness and

incoordination (failure to track when trotting), head shaking and ear twitching, muscle wasting and abnormal curvature of the neck.

HOW CAN SM BE DIAGNOSED?

The abnormality of the skull cannot be accurately felt through the skin. X-rays of the skull may suggest CM but cannot confirm this or SM. The diagnosis of SM and CM requires advanced imaging of the brain and neck, made possible with magnetic resonance imaging (MRI) (Fig 2.). Abnormalities of the skull, brain and spinal cord can all be clearly seen with this test, although a one hour general anesthesia is necessary. The size of the spinal cord cavity can be accurately measured and has been shown to be related to how severe the pain is in individual dogs.

WHY STUDY THIS DISEASE IN THE BG?

Preliminary evaluations of the BG suggest that there are a few dogs with CM and / or SM. In affected dogs, a definitive cause for the SM has not been identified and an association with CM has not been established. Based on these preliminary evaluations of BG dogs we expect to identify some of this breed affected with SM using MRI and deduce how common it may be in the BG. We anticipate that these affected dogs will manifest similar clinical signs as has been reported in dogs with CM / SM. Many of the BG dogs with SM will appear clinically normal to their owners. Additionally, we anticipate that some of the dogs with SM may demonstrate clinical signs different from those which has been previously documented in dogs with CM / SM. Characterizing the clinical signs associated with SM in the BG should allow owners and veterinary health care professionals the ability to not only identify other affected individuals but it also should allow for earlier therapeutic intervention preventing morbidity and mortality in affected dogs. Defining the morphological abnormalities in SM in the BG may provide insights into the underlying cause for SM and it should lead to appropriate therapeutic options for affected dogs. Finally, this study should enable BG breeders the opportunity to preemptively alter the perpetuation of a disease process in the breed. If corrective measures are taken early enough, wide spread perpetuation of SM within the breed can be avoided. DNA will be collected for studying the genetics in association with the University of Montreal, Clare Rusbridge, Penny Knowler and the Animal Health Trust, UK.

HOW CAN I FIND OUT IF MY DOG WOULD QUALIFY FOR THE STUDY?

The study will target AKC registered Brussels Griffon dogs *with or without* clinical signs from as many US states as geographically possible. Full 5 generation pedigree information must be provided but the AKC has agreed to help with this pursuit. Dogs will

be selected from as diverse breeding lines as possible. Priority will be given to dogs over 5 years of age which are related, with some showing signs and some normal; but dogs > 18mths may be accepted if related to older dogs within the study. Litters of normal dogs are also valuable, especially if they are known to be related to dogs showing signs. Dogs should not be receiving treatment for any other diseases and should be medically suitable for general anesthesia; therefore, dogs over 10 years may not be suitable. However dogs as old as 12 years have undergone MRI. Questions regarding enrolment or requests for enrolment can be addressed through abgstudy@uga.edu

WHAT WILL HAPPEN TO MY DOG DURING THE STUDY?

Study patients will be evaluated through the Veterinary Teaching Hospital (VTH) of the University of Georgia or other participating centers in the USA which are currently being confirmed. Each study patient will be under the care and supervision of a board certified veterinary neurologist. Other centers in Australia and Europe can potentially be involved in this study but funding would need to be determined locally. The evaluation of each dog will consist of several steps:

Step 1: Clinical Evaluation

A thorough history will be collected at the time of admission to the VTH. A clinical scoring sheet will be filled out to assess the clinical signs, including frequency of scratching, frequency of vocalization and limb paresis. Neurological examinations will be performed by a board certified veterinary neurologist. Examination results will be recorded in the medical records of each study patient. Blood tests and urine samples will be collected for general health assessment pre-anesthetic. Blood samples will also be stored along with AKC pedigree information for future research in to the potential inherited nature of this disorder.

Step 2: Magnetic Resonance Imaging (MRI)

The MRI unit will be operated by a certified MRI technologist. Image planning will be done under the guidance of a board certified veterinary neurologist and will be exactly the same for each center involved. The imaging procedure will take approximately 45 minutes for each dog. Each dog's images will be stored as electronic files on a secure server. All MR imaging will be performed under general anesthesia by a board certified veterinary anesthesiologist who is aware of the breeds' sensitivity to anesthesia. A general anesthesia is necessary for the MR to enable an expedient, comfortable and safe study which would not occur under a heavy sedation. The premedication used will

consist of a midazolam, glycopyrrolate, hydromorphone combination administered intravenously; induction of anesthesia will be achieved with propofol and anesthetic maintenance will be accomplished using inhalational isofluorane and constant oxygenation. The MR facility at the University of Georgia is complete with state of the art MRI compatible anesthesia equipment which enables constant physiological monitoring during the procedures.

Lumbar spinal cerebrospinal fluid will be collected from all study patients immediately after the MR imaging, under general anesthesia using routine techniques. This will be important to evaluate the possible role of inflammation in this disease which may prove to be valuable in the determination of future treatments. However, concern about this test should not discourage participation and can be discussed on an individual basis. This procedure will take no more than 10 minutes to perform. Cerebrospinal fluid will be assessed by a board certified veterinary clinical pathologist. At the conclusion of the evaluation of each study patient, dogs will be recovered from anesthesia, appropriately cared for under the supervision of board-certified anesthesiologist and will be able to go home the same day.

Step 3: MRI Grading

Once the study is complete, all the MRIs will be evaluated and statistics will be used to investigate how common SM and CM are, and whether they are associated with any clinical signs. The study is completely confidential. The initial results of an individual dog's tests can be discussed with the owners on the day of the scan. Further evaluation of the results for the purpose of the study may take several weeks. Since CM/SM has been shown to have a hereditary basis in the Cavalier King Charles Spaniels, the MRI report will also provide a grading in line with the CKCS recommended breeding guidelines (Table 1).

Further Questions and Donations

Further questions about the study, dog enrolment and the techniques used can be forwarded to the researchers at the University of Georgia, College of Veterinary Medicine, through the links provided on the website or at the following email address abgstudy@uga.edu . All communications will be dealt with in the strictest confidence.

The ABGA, AKC-CHF and the researchers involved in this grant (#1004) would like to encourage study participants and interested parties to make a donation of $100 toward the study, as continued funding for this project is necessary and ongoing. Donations can be arranged through Meg Prior (meg@megpriorconsulting.com) or the AKC-CHF through Erica Werne (EAW@akcchf.org).

Links

American Kennel Club Canine Health Foundation http://www.akcchf.org/

American Kennel Club http://www.brussels-griffon.info/

American Brussels Griffon Association http://www.brussels-griffon.info/

University of Georgia Bioimaging (MRI) Research Center (BIRC)
http://www.uga.edu/psychology/BIRC/index.html

Figure 1. A Brussels Griffon with Syringomyelia or without Syringomyelia?

Figure 2a. A normal canine MRI of the head and neck

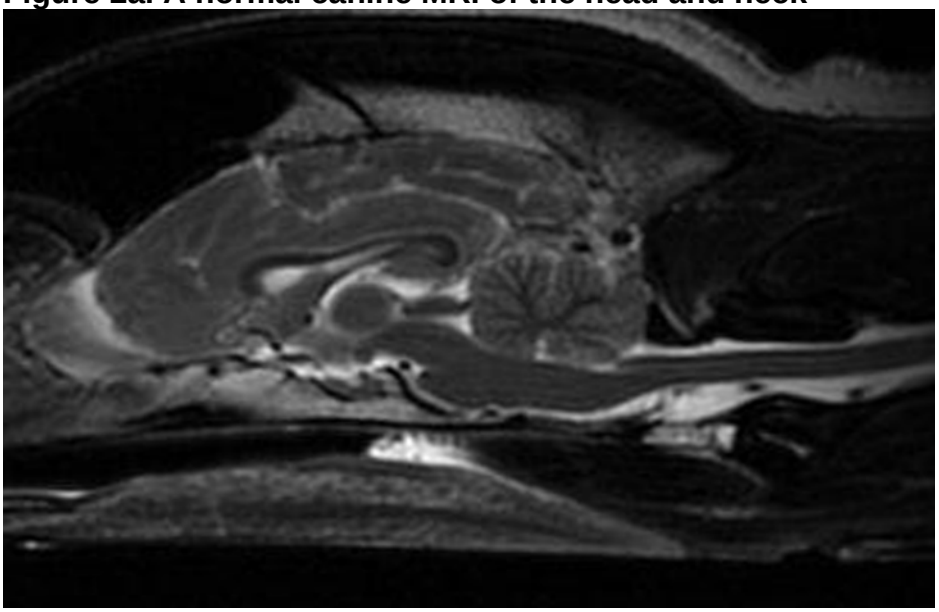

Figure 2b. An MRI of the head and neck of a Brussels Griffon with Chiari-like abnormality and syringomyelia

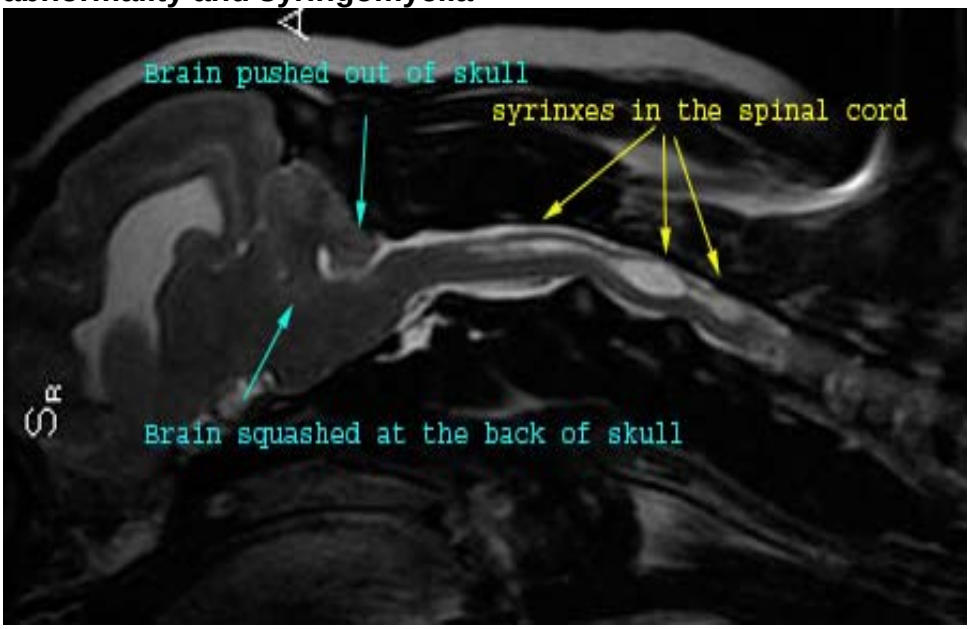

Table 1. International Syringomyelia Conference Nov 2006
Revised CKCS MRI screening and breeding recommendations

Grade	AGE (YEARS)	SYRINGOMYELIA	BREED TO
A	**Over 2.5**	**Absent or less than 2mm central canal dilatation in the C2-C4 region only**	**A, C, D**
C	**Under 2.5**	**Absent**	**A** Re scan after 2.5years
D	**Over 2.5**	**Present but asymptomatic**	**A**
E	**Under 2.5**	**Present but asymptomatic**	**NO**
F	**Any**	**Present and symptomatic**	**NO**