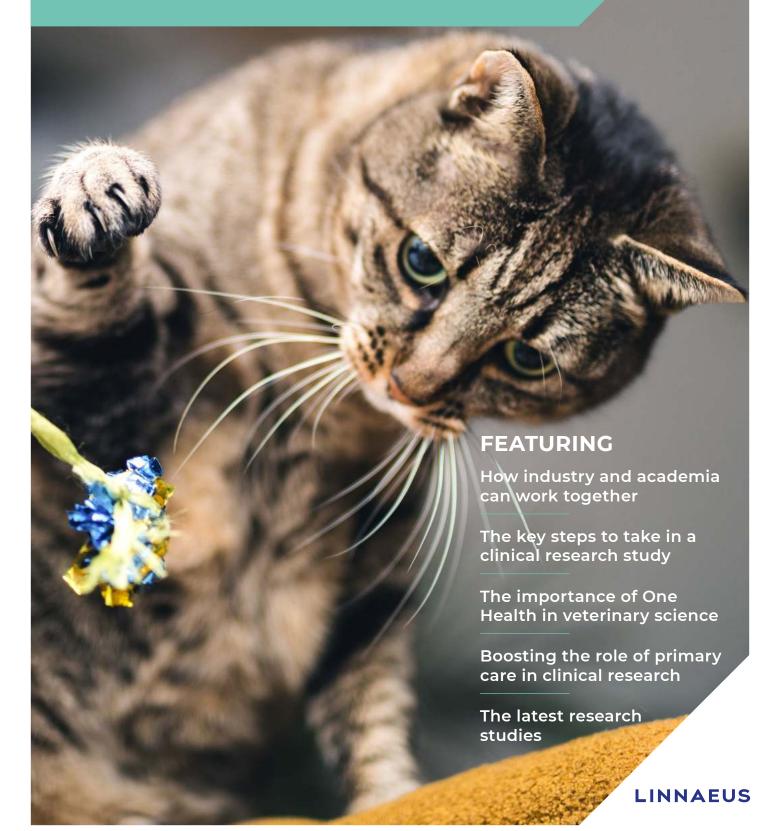
SPARKING THE CLINICAL MIND

How collaboration delivers excellence in research



By Dr Jo Gale, Director of Science Advocacy at Mars Petcare



Welcome to the first in a series of reports celebrating the importance of clinical research in the veterinary profession, in an endeavour to improve the care we deliver to patients.

Sparking the Clinical Mind – How Collaboration Delivers Excellence in Research focuses on the areas where knowledge can be furthered, and it is clear from the perspectives of its authors that different elements of the profession working together is critical. Developing skills and knowledge, and challenging ourselves to improve, can only happen with the guidance and perspectives of others.

The report's first article, by Dr Darren Logan, explores the integration of industry and academia – while Professor Luisa De Risio focuses on the steps and support required to deliver a gold-standard study. Professor Philippe B. Wilson considers how the veterinary profession can involve others in One Health projects, followed by Maureen Geraghty Sathi discussing the challenges and opportunities for primary care clinicians who want to take part in research.

Despite the hurdles faced during the Covid-19 pandemic, many in the profession have still produced excellent research that will help to guide the veterinary industry and support the animals they look after. A number of these studies have been published in open access scientific journals, to the benefit of all. The second half of this report brings together four leading studies from primary care and referral clinicians across the UK, covering a range of conditions seen in practice.

I would like to thank all the authors involved in this report, who have taken the time to lend their expertise to further promote collaboration. I hope you enjoy reading their contributions.





From design to dissemination: the steps a research project needs to take

Dr Luisa De Risio, Clinical Research & Excellence Director at Linnaeus and Professor of Veterinary Neurology at Nottingham Trent University

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Boosting primary care involvement in clinical research

Maureen Geraghty Sathi, Field Medical Director at Linnaeus

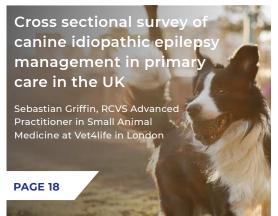
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Randomised clinical trial evaluating the effect of a single pre-appointment dose of gabapentin on signs of stress in hyperthyroid cats

Matthew Gurney, RCVS & EBVS® European Specialist in Veterinary Anaesthesia and Analgesia, and Clinical Director at Anderson Moores Veterinary Specialists

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Perspective: when industry meets academia



By Dr Darren Logan,
Head of Research at the
Waltham Petcare Science Institute
and a member of the Linnaeus clinical studies funding council

Research in the pursuit of knowledge takes many forms; from validating clinical interventions, studying disease progression, to better understanding basic physiology. Underpinning these endeavours is the scientific method. A philosophical process refined over centuries of forming and testing hypotheses through ideation, observation, and experimental measurement, of applying rigour through scepticism and logic. That's the theory, anyway.



Today, however, different disciplines make for a fragmented, often insular research landscape. We class clinical science, industry research and academia as very separate enterprises with their own cultures and customs. We talk of 'transitioning' from one to the other like it involves an irreversible, metamorphic change.

I've experienced this journey personally. After 15 years of leading fundamental research at academic institutions then at the global science centre for Mars Petcare, the Waltham Petcare Science Institute. More recently my team has been collaborating with veterinary colleagues at Linnaeus and other veterinary hospitals and networks, developing and deploying clinical studies to improve the health of pets. My experience of working across this spectrum of research is that the diversity of perspectives and skills that exists is significant and broad. Though, undoubtedly, there is more that connects us than divides us.

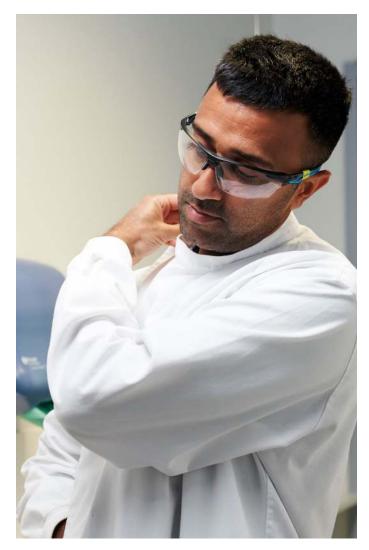
For example, the academic environment is fertile ground for research creativity. I look back (with some envy) to whole days when I had time to read and think. From those untethered thoughts sprouted new ideas, and ideas grew into novel hypotheses. However, unbound creativity is divorced from practical feasibility by its very nature: transformative advances rarely arise from working within the constraints of what is possible today.

On the other hand, even the best hypothesis needs to be tested experimentally to bear fruit, otherwise it simply remains an idea. Further, 'bottom up' ideation can often result in a solution looking for a problem, failing to meet a real practical need. This is where the applied expertise of an industrial researcher comes to the fore.

In a bustling clinical practice where extensive thinking time is a luxury, hypotheses more often arise from empirical observation; the recognition of a real-world issue. Feasibility is important when the subjects are pets owned by busy clients, and the study is being conducted around routine care.

For most clinical scientists, pragmatic study design is paramount, but this too can lead to problems. Most vets have developed a good instinct for understanding how to complete studies in their busy clinics, though few are formally trained in the statistical powering or randomisation techniques necessary to ensure that their approach is scientifically robust.

My experience of working across this spectrum of research is that the diversity of perspective and skills that exists is significant and broad.



I have grown to believe these disciplines need to work together more often and more effectively. A deep understanding of veterinary or customer pain points can guide ideation. Innovative studies can fail if not constructed around the practical reality of a clinical trial, but that study also needs to be designed and analysed with statistical rigour. Multi-disciplinary research collaborations are not without their tensions, but embracing the diversity each discipline offers is our best chance of transforming the future health and wellbeing of pets – which is what we all want to achieve.

ABOUT THE AUTHOR

Dr Darren Logan is Head of Research at the Waltham Petcare Science Institute, where he leads a diverse team of over 80 scientists and vets with the aim of improving the health and wellbeing of pets.

After obtaining a PhD in genetics from the University of Edinburgh and undertaking postdoctoral training at The Scripps Research Institute, he joined the faculties of the Wellcome Sanger Institute and the Monell Chemical Senses Center, leading research teams in animal behaviour and their senses. Darren was the first recipient of the Verne Chapman Award from the International Mammalian Genome Society, appointed a Wellcome Fellow in 2010 and an EMBO Young Investigator in 2014. He is a scientific adviser to Fifth Sense, the charity for people affected by smell and taste disorders.

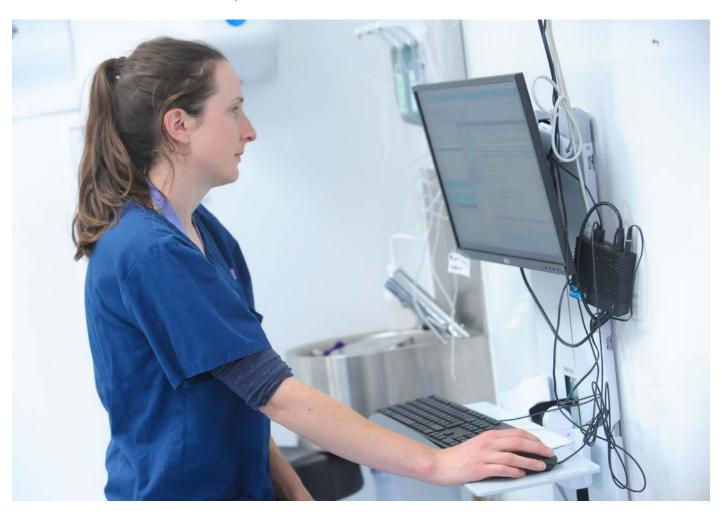
From design to dissemination:

the steps a research project needs to take



Dr Luisa De Risio, Clinical Research & Excellence Director at Linnaeus and Professor of Veterinary Neurology at Nottingham Trent University

The excellence of care provided by the veterinary profession is underpinned by evidence-based practice, with high-quality clinical research leading to better outcomes for our patients and clients.



We consistently strive to improve animals' health and wellbeing – and this commitment should always be reflected in our research activities, from the lightbulb moment of our study idea to the dissemination of our findings. A well-designed and ethical study with rigorous data analysis will make a valuable contribution to the evidence base for veterinary science.

Having identified the research topic, perhaps after reading about a specific area of interest or being inspired by a clinical case, the first step is to form a good research question. This should be answerable and reasonably focused. It should also be considered whether it has already been reliably answered by other researchers.

Thoroughly searching and critically appraising veterinary literature is a vital step in understanding what has been studied about a topic to date. It enables the development of a question that furthers current knowledge and can deliver clinically relevant and applicable findings. The EBVM Toolkit¹ by RCVS Knowledge offers support in exploring a clinical question by locating and critically appraising the available evidence.

A well designed and ethical study with rigorous data analysis will make a valuable contribution to the evidence base for veterinary science.

Answering a research question requires robust study design. Clinical studies undertaken in practice are commonly observational, including cross-sectional studies, cohort studies, case-control studies and case reports, or interventional, such as randomised controlled clinical trials. The choice of study design is based upon what will most appropriately answer the research question.

Constructing a detailed methodology is the crucial next step. Carefully consider the inclusion and exclusion criteria, sample size required to achieve statistical significance, and patient recruitment feasibility; this applies to retrospective and prospective study. For clinical trials, randomisation and blinding should also be factored in.

Guidance from a biostatistician can be invaluable in the planning stage of a study. Waltham Petcare Science Institute, for example, provides this support at Linnaeus. There are also free resources available online, including sample size calculators. Clinical research needs to be conducted in compliance with the regulatory framework of the country in which the work is being undertaken and adhere to recognised ethical standards.

Opt for open access journals if possible, which enable research to be disseminated more widely.

In the UK, the RCVS provides guidance to help the veterinary profession determine which studies can be conducted as part of clinical veterinary research (CVR) and when ethical review is required.² CVR is when routine veterinary procedures are performed for the benefit of the patient, with the concurrent intention to generate new knowledge that helps to advance veterinary healthcare. Research may also involve veterinary surgeons, veterinary nurses or pet owners to seek their views on various aspects of veterinary practice.

Review and approval by an independent ethics review panel (ERP), like the RCVS ERP in the UK,³ ensures that the investigators have adhered to ethical and legal standards and followed research best practice, including a robust experimental design.

Following data collection, most studies require statistical analysis. The analysis plan should include identification of primary and secondary outcome measures, how missing data will be handled and the justification of statistical tests to be used. Again, it can be highly valuable to have support from a biostatistician.

When writing up and disseminating findings, note that reporting guidelines are widely available through sites such as Equator Network.⁴ They list the information required to ensure the authors provide a thorough account of what was done, their conclusions and how these apply to clinical practice. It is advisable to select a target journal before drafting a manuscript, as their guidelines and formats vary. Peer-reviewed titles provide the strongest endorsement of your findings. Opt for open access journals if possible, which enable research to be disseminated more widely and support evidence-based veterinary practice.

Involving others throughout the research process provides additional insight and guidance. Their different perspectives may challenge a study, but it will become stronger as a result. There are many opportunities for collaboration across the veterinary profession – with your colleagues, peers in the UK and overseas, universities and industry.

When undertaking research, financial and practical support is also available through many organisations. At Linnaeus, the clinical research team provide advice on every step of the study process to ensure that our colleagues can realise the full potential of their work.

By designing an achievable and impactful study, and taking advantage of the guidance available, your work could make a hugely positive difference to many lives.



One Health in veterinary science: a forward vision



By Prof Philippe B. Wilson,
Professor of One Health
at Nottingham Trent University
and a member of the Linnaeus clinical studies funding council

One Health is a collaborative approach that aims to deliver optimal health and wellbeing outcomes for people, animals and the environment. As a result, adopting this concept in clinical research creates huge opportunities for our work to benefit not only veterinary science, but also human health and the natural world.



This is a significant opportunity for us all; One Health can address a wide range of issues, from the causes of climate change through to endemic diseases. According to the World Health Organisation, some 60% of emerging infectious diseases reported globally are zoonoses. Over 30 new human pathogens have been detected in the last three decades, 75% of which have originated in animals.⁵

Undertaking a One Health initiative requires collaboration – and lots of it. From setting the objectives through to funding bids and the dissemination of results, a wide range of expertise from other scientific fields is required.

There can be hesitancy in working with several partners on a project, but this is where we need to be fearless in bringing people together. As well as needing input from human clinicians and environmental scientists, the inclusion of social science is equally valuable; there is little point in delivering an outcome if there is no uptake. The social sciences support us in ensuring our interventions or initiatives are sufficiently palatable to the end user.

There can be hesitancy in working with several partners on a project, but this is where we need to be fearless in bringing people together.

The key to One Health initiatives is to bring an interdisciplinary approach to projects straight from the outset, and then stay on the path laid out. This is important in maintaining a vision for the overall aim in a large consortium project, so we are not distracted with tangential outcomes. For this, communication and clarity are key.

I previously worked on a truly multidisciplinary approach to addressing the early detection of breast cancer. The sandpit session I initially participated in involved splitting us into teams, with attendees ranging from chemists to oncologists, engineers and social scientists and even nuclear physicists. We had three days to develop a viable project but spent the first morning simply trying to speak the same language. The team ended up translating our ideas into layman's terms and then working them up together. However this also highlighted the shared impact and achievements that this could achieve.

The insights of others also help us to understand what is feasible for clinicians and scientists in very different settings. For example, a visit to a leading NHS secondary care accident and emergency department highlighted the need for quick and reliable clinically actionable metrics for differential diagnosis: clinicians had £80 to spend on tests

per bed and therefore working by process of elimination through simple and fast tests was the only way to proceed. Therefore, a complex piece of kit which conceptually may have offered a highly detailed diagnosis for a specific cancer would have fallen out of the clinical pathway in this setting. Conversely, a simple, RAG (red, amber, green) rating equivalent test for common metabolic conditions would offer the clinicians a fast transition to related clinical pathways.

This perspective helped to secure a common language goal between specialities and most importantly, ensure any interdisciplinary outcomes were actionable for the end user. This is the premise of the One Health mentality and approach.

The challenge of bringing together a truly One Health team is to avoid a focus solely on medicine, ensuring that the environment is represented too. Doctors and veterinary surgeons may instinctively align, while the range of disciplines within environmental sciences is far broader than the different branches of medicine. Taking a One Health approach requires time identifying the right people across all three spheres.

Veterinary science has natural links with human medicine and the environment, which strongly position this profession centrally within the domain of One Health. At The Royal Society of Medicine One Health meeting in December 2021, the vast majority of attendees were veterinary professionals. This was a huge opportunity for us working in the veterinary space to take the lead in delivering multidisciplinary projects that benefit our patients, humans and the planet.

Veterinary science has natural links with human medicine and the environment, which strongly position this profession centrally within the domain of One Health.

We cannot be experts in everything – particularly when it comes to One Health – but we can bring people together to identify our grand challenges and confront the issues we face today. There are already excellent networks to engage with, such as the UK One Health Coordination Group⁶ and the Royal Society of Medicine's Comparative Medicine Council,⁷ but we must ramp up efforts to engage peers across the different scientific branches to make an impact and deliver actionable outcomes across the professions.



Boosting primary care involvement in clinical research



By Maureen Geraghty Sathi, Field Medical Director at Linnaeus

As a Field Medical Director I support Clinical Directors in a range of primary care practices across Linnaeus. I am also the group's primary care research lead: collating, supporting and encouraging research within these practices; and witnessing the hugely positive benefits their involvement can bring.



Within Linnaeus we produce between two and three research studies on average from our primary care practices each year. Of these, some are clinical studies and others non-clinical, such as leadership research. However, this volume does not reflect the high interest in research within our primary care teams, which are passionate about contributing to evidence-based medicine and helping to raise the quality of care our industry delivers.

Indeed, research undertaken in the primary care environment – and thereby including those patients, practitioners and their perspectives - is crucial to evidence-based practice.

Typically, primary care practitioners will collaborate on a study that may be based within a referral centre and is usually led by a specialist. Yet the number of clinicians in primary care developing their own research projects is increasing. Within Linnaeus we are also seeing more primary care practices auditing their outcomes for a particular condition and benchmarking these data against referral sites to measure their quality of care, which we actively encourage.

To encourage more primary care teams to undertake clinical research, the veterinary profession must understand and overcome the barriers that may prevent this. Our initial enquiries suggest finding time to conduct research, identifying or securing funding, lack of knowledge of how to undertake research and difficulty in collecting data within the primary care setting may all contribute.

The number of clinicians in primary care who are developing their own research projects is increasing.

In response to these challenges, specific support is needed for those with an interest in research in a primary care setting. From education to practical advice and funding – there are many steps throughout the research process where guidance from employers, peers, colleagues and membership organisations can really help.

Funding is of course a critical element of any research project, and there may already be options available within a primary care practice or group – for example, Linnaeus's Open Access Publication Charge (OAPC) fund covers the fees to publish a research paper in an open access scientific journal. Open access is important as it means the research is available for anyone to view free of charge (i.e. not behind a paywall), which maximises accessibility of the research findings so we can all learn from it.

External grants to fund research are also available from organisations such as British Small Animal Veterinary Association (BSAVA) PetSavers.⁸ Critically, primary care practitioners need to be aware of these opportunities and the applications required.

Ongoing engagement between primary care and referral centres also remains important as this creates opportunities for specialists and primary care practitioners with similar interests and skillsets to spark conversations about different projects and identify potential co-researchers. Joining networks of shared interest either within your organisation or through groups such as the Small Animal Medicine Society9 or regional groups within the BSAVA10 will help to broaden expertise and spark ideas.

They require opportunities for education, practical advice and funding throughout the entire research process.

Once a research project is identified, the challenge to collecting and collating data is ensuring this data is consistent. Having a unified coding system within groups or practices will greatly increase opportunities to extract and analyse meaningful data from electronic health records, providing researchers with valuable access to large data sets.

The exploration of these data through research based in primary care practices is of significant value. Most patient contacts will begin and end within primary care, meaning that the broad spectrum of both disease and patient subjects within the population is represented. In addition, use of primary care data avoids bias that can occur when using data only from referral populations. A further benefit is the ability to explore long-term disease progression and outcomes, with pets often attending one primary care practice for their whole lifetime. Linnaeus is currently implementing a unified coding system across its estate, which is expected to be hugely valuable across the group.

There are still hurdles for primary care vets or nurses wishing to take part in research, which must continue to be addressed. Creating pathways for sharing information, and building a culture that welcomes auditing while encouraging curiosity, helps to encourage primary care teams to take part in research activity. The value they bring is certainly worth it.





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CLINICAL RESEARCH STUDIES ACROSS LINNAEUS
ARE UNDERWAY OR PUBLISHED TO DATE

STUDIES BY LINNAEUS ASSOCIATES WERE PUBLISHED OR PRESENTED AT VETERINARY CONFERENCES IN 2021

CLINICAL RESEARCH STUDIES AWARDED FUNDING
BY LINNAEUS TO PUBLISH IN OPEN ACCESS
JOURNALS IN THE FIRST HALF OF 2022

THE FOLLOWING SUMMARIES COVER RESEARCH PROJECTS BY LINNAEUS CLINICIANS PUBLISHED RECENTLY IN

SCIENTIFIC VETERINARY JOURNALS

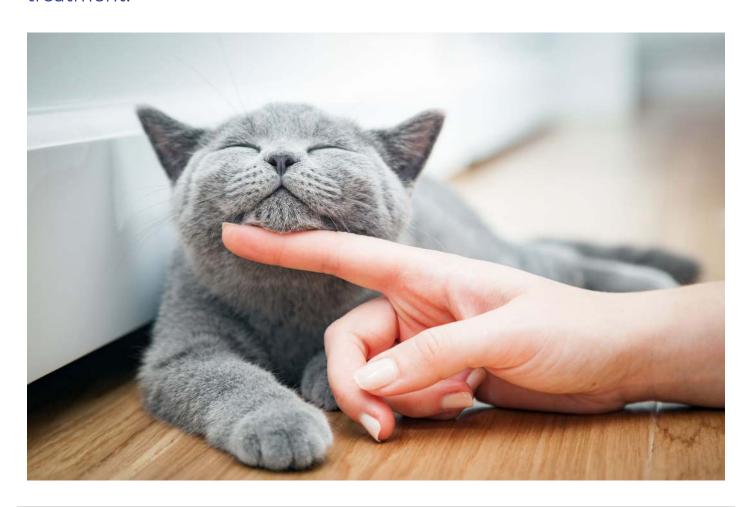
Randomised clinical trial evaluating the effect of a single pre-appointment dose of gabapentin on signs of stress in hyperthyroid cats



By Matthew Gurney, RCVS & EBVS® European Specialist in Veterinary Anaesthesia and Analgesia and Clinical Director at Anderson Moores Veterinary Specialists in Hampshire

Contribution to the field

In the hyperthyroid cats presenting at our clinic, we recognise stress is a welfare issue. With the knowledge from this study, we have the information available to share with vets in practice to enable them to prescribe gabapentin to these cats prior to travel for veterinary treatment.



Introduction

A study in healthy cats undergoing transportation to a veterinary clinic followed by veterinary examination has documented a positive benefit of gabapentin in reducing stress. That study recommended a dosage of 20 mg/kg gabapentin administered two to three hours prior to the veterinary visit to provide maximum stress-reducing benefit without adverse sedation.

Oral administration of gabapentin has been documented to reduce signs of stress in cats as part of a trap–neuter–return programme, ¹² with a dosage range of 9.2–47.6 mg/kg. The greatest effect was seen at two hours post-treatment. Stress is a component of hyperthyroidism¹³ and methods to reduce such stress are likely to be advantageous to the patient.

We hypothesised that hyperthyroid cats medicated with gabapentin at home would show reduced transport stress scores and improved compliance with handling upon arrival at the veterinary clinic compared with cats in a placebo group.

Objectives

This study aimed to evaluate the safety and efficacy of gabapentin as an anxiolytic in hyperthyroid cats.

Gabapentin was chosen for this study as a result of clinical experience based on the work of Van Haaften et al,¹¹ and in the absence of a licensed product for this purpose in cats or another non-licensed medicine with documented efficacy at the time of study design. The study had ethics approval from the Association of Veterinary Anaesthetists' Ethical Review Committee.

Stress is a component of hyperthyroidism and methods to reduce such stress are likely to be advantageous to the patient.

Methods

Cats with hyperthyroidism referred to the Feline Hyperthyroid Centre at Anderson Moores Veterinary Specialists for radioactive iodine (RAI) treatment were eligible for this study. We enrolled 47 cats with confirmed hyperthyroidism, with randomisation performed using the random draw method.

Temperament was assessed by cat owners at the recruitment stage to verify if there were differences between groups that could affect the results and this question was asked again at admission for RAI treatment.

Each cat owner allocated a temperament score and a transport stress score at their first visit. For the second visit the cat owner (blinded to treatment) administered either liquid gabapentin at 20 mg/kg (to 22 of the cats) or an



indistinguishable placebo solution (to the remaining 25 cats) one hour before leaving home. A second stress transport score was allocated by the cat owner at this visit.

Upon admission a compliance score was independently assigned by two veterinary nurses blinded to treatment, who were experienced in working in a cat-only environment using low-stress handling techniques. Excess blood from routine blood draw was analysed for gabapentin plasma concentration from cats in the gabapentin group.

Results

Mean compliance scores were significantly different between cats in the treatment group compared with placebo (P = 0.019).

There were no significant differences in baseline transport stress score between groups (P = 0.13), but significant differences were noted in the second transport stress score between cats medicated with gabapentin compared with placebo (P = 0.018).

Further sedation was required to complete the procedures in 24% of cats in the placebo group compared with 9% in the gabapentin group (P = 0.25). Mean plasma gabapentin concentrations were 10.1 mg/l (range 1.7-22.7) in the gabapentin group within one to three hours post-administration.

Conclusions and relevance

Hyperthyroid cats medicated with 20 mg/kg gabapentin one hour prior to leaving home were more relaxed during transport and more compliant with veterinary procedures than cats administered a placebo solution.

ABOUT THE AUTHORS

Matt Gurney, Clinical Director, and Lou Gower, Registered Veterinary Nurse, Anderson Moores Veterinary Specialists. The study has been published in the open access peer-reviewed scientific journal Journal of Feline Medicine and Surgery: https://journals.sagepub.com/doi/ full/10.1177/1098612X221091736

ACKNOWLEDGEMENTS

Statistical analysis was conducted by Dr Tim Sparks, Waltham Petcare Science Institute, UK. Laboratory analysis was conducted by Synlab UK. The fee for publishing the paper in an open access journal was funded by Linnaeus's Open Access Publication Charge initiative.

Cross sectional survey of canine idiopathic epilepsy management in primary care in the United Kingdom



By Sebastian Griffin, RCVS Advanced Practitioner in Small Animal Medicine at Vet4life in London

Contribution to the field

This study is the first of its kind in the UK to investigate via an online questionnaire how primary care veterinary surgeons diagnose and treat canine idiopathic epilepsy (IE). There is limited information on these aspects and a greater understanding can help improve outcomes for veterinary surgeons, their patients and their clients.

Introduction

IE is the most common chronic neurological disease found in dogs and can significantly impact the quality of life for pets and their owners. Affecting many breeds of dog, this complex condition includes recurrent epileptic seizures and behavioural and cognitive co-morbidities, while remission is rare. I can lead to a shortened lifespan but effective treatment can prolong life expectancy.

This study will help to inform future educational and support strategies for primary care veterinary surgeons (including by veterinary neurology specialists), allowing a more targeted, clinically applicable and clinically relevant approach to professional development. Improving the confidence and skills of primary care vets in treating a lifelong condition like canine IE benefits the patients and their caregivers, who can find the condition very distressing.

Objectives

The aims of this study are to gain insight on how primary care vets in the UK diagnose and treat canine IE and what they perceive as challenges in its management.



Methods and results

The anonymous online survey took place between October 2021 and January 2022, with 235 primary care vets responding. The questionnaire asked about the type of practice the respondent worked in, any relevant postgraduate qualifications, how many years' experience they had in practice and the participant's canine IE caseload. Participants were asked how they diagnose canine IE, how they select anti-seizure drugs (ASDs) and how they assess outcomes.

IE is the most common chronic neurological disease found in dogs and can significantly impact the quality of life for pets and their owners.

The questionnaire also explored which information sources respondents access when deciding on canine IE treatment, challenges faced when managing these cases and areas in which more support could be provided.

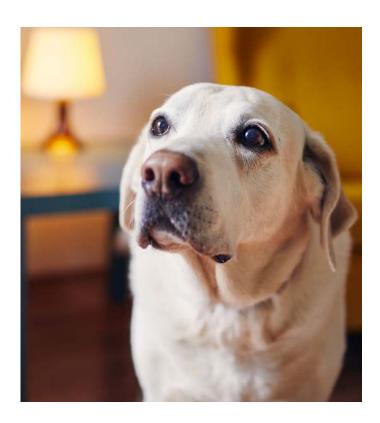
More than 94% of participants (222) managed fewer than ten canine IE cases per year, with 88% (206) administering phenobarbital as their first line ASD. The reported mean initial phenobarbital dosage was 2.1 mg/kg (standard deviation = 0.71) every 12 hours.

While 53% (125) of respondents recommended neutering in canine IE, 47% (110) did not. In addition, 53% (125) did not endorse any additional treatments for canine IE beyond use of ASDs.

Regarding other interventions, recommendations to owners of dogs with IE included: a diet containing medium chain triglyceride (23% (55) respondents); environmental modification (nearly 13% (30) respondents); and medium chain triglyceride supplements (almost 7% (16) respondents).

Conclusions and relevance

In this study participants found managing client expectations to be most challenging alongside canine IE emergency management. The results of this study represent a starting point to inform educational resources and support strategies to improve quality care of canine IE in primary care. The results of this study have informed resource development for Associates across Linnaeus and the owners of dogs with IE.



In this study
participants found
managing client
expectations to be
most challenging
alongside canine
IE emergency
management.

ABOUT THE AUTHORS

Sebastian Griffin, an Advanced Practitioner in Small Animal Medicine at Vet4life in London, led the research. He collaborated with Fabio Stabile, a RCVS and EBVS® European Specialist in Veterinary Neurology at Southfields Veterinary Specialists in Essex, and Luisa De Risio, Clinical Research & Excellence Director at Linnaeus and Professor of Veterinary Neurology at Nottingham Trent University. Sebastian, Fabio and Louisa are all members of the Linnaeus clinical board and are working to develop educational resources based on the results of this study.

The study has been published in the open access peerreviewed scientific journal *Frontiers in Veterinary Science*:
https://www.frontiersin.org/articles/10.3389/
fvets.2022.907313. The article is co-authored by
Sebastian Griffin, Fabio Stabile and Luisa De Risio.

Changes in retinal vascular diameters in senior and geriatric cats in association with variation in systemic blood pressure



By Andra-Elena Enache, RCVS and EBVS® Specialist in Ophthalmology at North Downs Specialist Referrals in Surrey

Introduction

Systemic arterial hypertension (SAH) in cats can lead to blindness and injury to tissues. Sustained hypertension can cause target organ damage (TOD) with the eyes, kidneys, brain, heart and vasculature as the organs most at risk. Various publications have shown most cats are presented late in their disease and already have signs of TOD. Therefore, early diagnosis and regular monitoring of response to treatment are the key factors for successful management of this condition.

Diagnosis of SAH is made upon serial blood pressure (BP) measurements and regular monitoring. The Internal Society of Feline Medicine and American College of Veterinary Internal Medicine guidelines recommend annual screening of cats aged seven and nine years or older, respectively. 19-26

Objectives

The purpose of this study was to assess whether changes in retinal vascular diameters of senior and geriatric cats were associated with varying BP. If sustained hypertension is associated with retinal arteriolar narrowing, then objective measurement of arteriolar diameters might be a useful tool in differentiating truly hypertensive cats from those with situational hypertension.

This prospective observational study investigated the retinal vessel diameters in senior and geriatric cats of varying systolic blood pressure (SBP) status and evaluated retinal vascular changes in hypertensive cats after treatment.



Methods

Following their BP measurement (sphygmomanometer and non-invasive Doppler), physical examination, blood and urine testing and fundus photography, cats with a median age of 14 years (range 9.1–22 years) were categorised into five groups:

- Group 1: healthy normotensive (SBP <140 mmHg) cats (n = 40)
- Group 2: pre-hypertensive (SBP 140–160 mmHg) cats (n = 14)
- Group 3: cats with chronic kidney disease (CKD) and normotensive (n = 26)
- Group 4: cats with CKD and pre-hypertensive (n = 13)
- Group 5: hypertensive (SBP >160 mmHg) cats (n = 15)

Colour fundus images (Optibrand ClearView®) were assessed for hypertensive lesions. Retinal vascular diameters and bifurcation angles were annotated and calculated using the Vascular Assessment and Measurement Platform for Images of the Retina annotation tool (VAMPIRE-AT®).²⁷ When available, measurements were obtained at three and six months after amlodipine besylate treatment. Persons who evaluated the fundus images were unaware of the cats' blood pressure and treatment status.

Results

Retinal changes, more commonly intra-retinal haemorrhages and subretinal exudates, were detected in ten hypertensive cats. Arteriole and venule diameters decreased significantly with increasing age (-0.17 \pm 0.05 pixels/year [P < 0.001]; -0.19 \pm 0.05 pixels/year [P = 0.001]).

The arteriole and venule diameters (table) of normotensive cats in group 1 were significantly smaller than those of pre-hypertensive cats (groups 2 and 4). Furthermore, the arteriole bifurcation angles of pre-hypertensive cats in group 2 were significantly narrower than those of normotensive cats (groups 1 and 3). Post-treatment measurements obtained in six hypertensive cats showed the vessel diameters decreased significantly approaching the values of the normotensive cats.

Group number	Type of cat in group (number)	Arteriole diameter adjusted mean ± standard error (SE) (pixels)	Venule diameter adjusted mean ± standard error (SE) (pixels)
1	Healthy normotensive (40)	6.3 ± 0.2	8.9 ± 0.2
2	Pre-hypertensive (14)	7.6 ± 0.3	10.1 ± 0.4
3	Cats with chronic kidney disease and normotensive (26)	6.9 ± 0.2	9.5 ± 0.3
4	Cats with chronic kidney disease and pre-hypertensive (13)	7.4 ± 0.3	10.0 ± 0.4
5	Hypertensive (15)	7.0 ± 0.3	9.8 ± 0.4

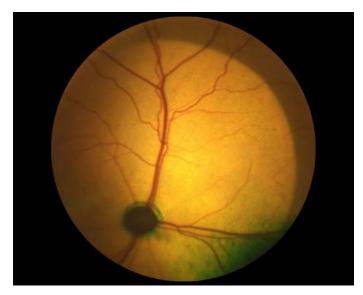
Using a computer-assisted imaging method for objective measurement of retinal vessel calibres from photographs, the diameters of retinal arterioles and venules were found to be narrower with increasing age. This study showed elderly cats had decreased vascular diameters, however an association of vessel diameter with hypertension was not observed.

The VAMPIRE-AT® may be useful to monitor the treatment effect on the retinal vasculature over time. Further studies are required to investigate the prognostic value of retinal vascular assessment in the senior and geriatric cats for early diagnosis of SAH.

Elderly cats had decreased vascular diameters, however an association of vessel diameter with hypertension was not observed.

Conclusions

Increased age was associated with decreased vascular diameters. Longitudinal studies are warranted to assess whether changes in vessel diameters are a risk indicator for hypertension in cats.



Source: Royal Veterinary College Archive

ABOUT THE AUTHORS

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Owner reported breathing scores, accelerometry and sleep disturbances in brachycephalic and control dogs: a pilot study



By David Barker MRCVS, RCVS Advanced Practitioner in Small Animal Surgery at Paragon Veterinary Referrals in Yorkshire

Introduction

Brachycephalic obstructive airway syndrome (BOAS) is characterised by increased upper respiratory noise as a result of elongated and thickened soft palate, stenotic nares and aberrant nasal turbinates. Consequential changes occur secondary to these anatomical abnormalities, including laryngeal collapse and eversion of laryngeal saccules, exacerbating upper respiratory tract noise. The characterised by increased and eversion and eversion of laryngeal saccules, exacerbating upper respiratory tract noise.

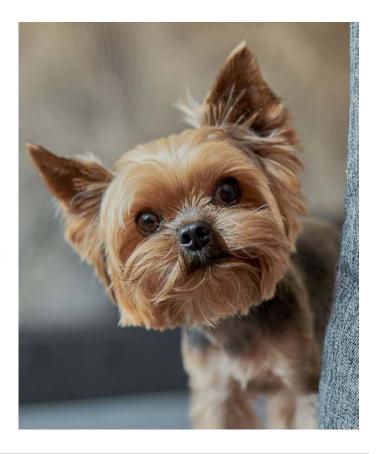
In addition to observed dyspnoea, brachycephalic dogs can suffer from chronic fatigue, hypoxia and decreased sleep quality.³²

In people, it is recognised that a lack of, or poor quality, sleep results in decreased concentration, poorer problemsolving ability and exhaustion. This has also been linked to reduced healing, imbalances in endocrine control, glucose regulation and cardiovascular function.³³ It has been shown that total sleep deprivation greatly affects the health of rats.³⁴ Thus it is equally plausible that poor quality and lack of sleep may have similar consequences in dogs.

Objectives

The aim of this study was to determine owner perceived and actual daily activity, and time sleeping, in brachycephalic and non-brachycephalic dogs – and to measure their quality of sleep.

We hypothesised that brachycephalic dogs would be less active as a consequence of reduced sleep quality. We further hypothesised that brachycephalic dogs would have more disturbed sleep and an increased 'owner-reported breathing score' (ORBS) when compared with control non-brachycephalic dogs.



Methods

The study involved 20 brachycephalic and 15 control dogs. There were no differences between median age and weight. Their owners completed a questionnaire regarding typical daily activity, sleep patterns and an ORBS. The owners were asked to grade the frequency of respiratory noise at rest, while walking, during strenuous activity and while asleep. They also graded the type of respiratory noise in the same four scenarios.

Respondents recorded how long their dog slept on an average day and how long their dog was active on an average day. They were then asked how often the dog seemed unwilling to take part in activity and appeared unwilling to go for a walk.

Length of activity and sleep were determined via accelerometer use. One hour of normal home sleep was also recorded for each dog via a video camera, with a veterinary observer subjectively scoring their sleep quality by counting the number of sleep disturbances due to respiratory issues.

We hypothesised that brachycephalic dogs would be less active as a consequence of reduced sleep quality. ""

Results

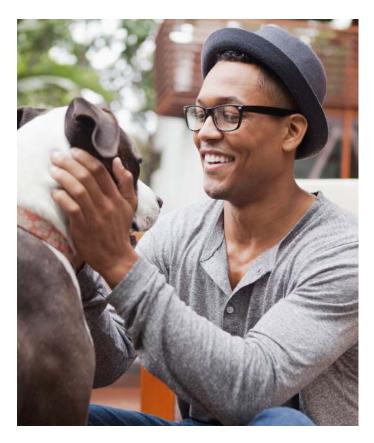
Owners reported brachycephalic dogs to be less active (P = 0.022) and have higher levels of stertor (P < 0.001)compared with control dogs. Brachycephalic dogs also experienced increased sleep disturbance compared with control dogs (P = 0.001) and video sleep score was positively correlated with increased sleep disturbance $(r^2 = 0.47, P = 0.007).$

For the brachycephalic dogs, the video-sleep-score was significantly higher than the owners' perception as taken from the ORBS (P = 0.04). There was no difference in this score for the control group (P = 1.00).

There were no differences in active and sleep times based on accelerometry between groups.

Conclusions

Our results show that brachycephalic dogs have more disturbed sleep, which may have negative implications on welfare, but there were no differences in activity or length of sleep between groups.



Owners may underestimate disturbed sleep or may perceive disturbed sleep to be normal. 99

There is evidence that signs suggestive of BOAS as assessed by ORBS are correlated with poorer sleep quality, indicating reduced sleep quality is part of BOAS.

Owners may underestimate disturbed sleep or may perceive disturbed sleep to be normal and client education may engender an acknowledgement that stertor at rest and during sleep are part of a BOAS complex and warrant veterinary attention.

ABOUT THE AUTHORS

David Barker, Paragon Veterinary Referrals; Emily Tovey, Bristol Veterinary School, University of Bristol; Dr Andrea Jeffery, Linnaeus; Emily Blackwell, Bristol Veterinary School, University of Bristol; Michael S. Tivers, Paragon Veterinary Referrals.

The study has been published in the peer-reviewed scientific journal Veterinary Record, https://bvajournals. online library.wiley.com/doi/10.1002/vetr.135.

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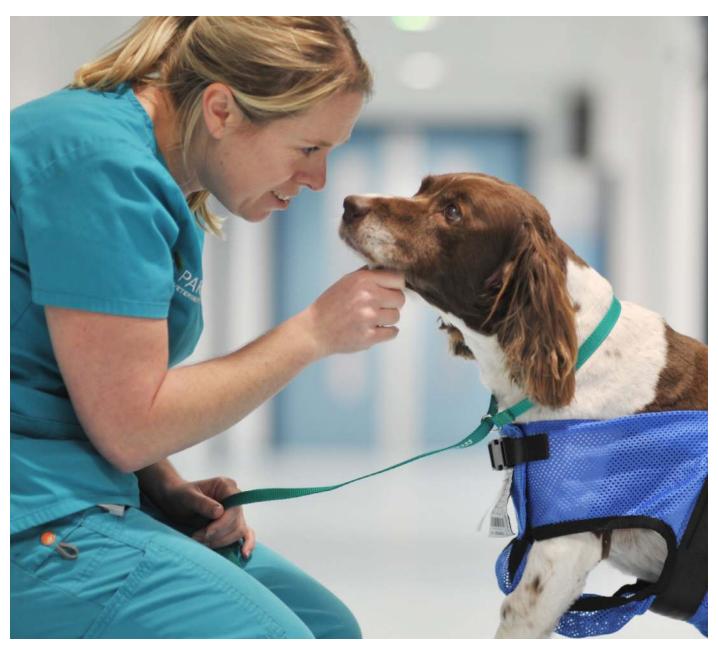
The authors would like to thank PitPatPet Limited for the donation of accelerometers used in this study.

Clinical research at Linnaeus

Linnaeus is a partnership of highly respected veterinary practices across the UK and Ireland, comprising some of the most dedicated vets and nurses in the profession. It delivers high-quality animal care to create a better world for pets.

Linnaeus aims to be globally recognised for its contribution to improving animal health and advancements within the veterinary profession. To accomplish this, it is committed to conducting high calibre clinical research that produces reliable, relevant and clinically applicable findings that directly impact animal health and welfare.

Linnaeus is part of the Mars Veterinary Health and Mars Petcare family, which offers a huge network of global experts and specialists to work with.



Commitment to excellence

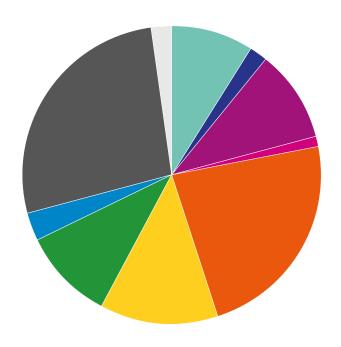
Clinical research ideas stem from clinical practice. They are focused on the needs of patients and their owners to improve the diagnosis, treatment, prognosis and prevention of naturally occurring disorders in patients.

Clinicians at Linnaeus are leaders in their fields and their research outputs contribute directly to the body of evidence that supports decision-making by veterinary professionals and pet owners. Their findings are disseminated nationally and internationally to benefit the wider veterinary and scientific community and the general public.

Experts from a range of specialisms are working on research projects at Linnaeus. The 850 studies underway or completed at the group predominantly cover surgery (27%), internal medicine (23%) and neurology (13%).

The goal of Linnaeus and Mars Veterinary Health is to lead the veterinary industry in meeting and exceeding the guidelines established for clinical studies involving clientowned pets, and sociological studies seeking input from veterinary professionals and pet owners. The clinical research is conducted following informed client consent and in compliance with the UK regulatory framework and Mars privacy35 and research policies. 36

Study discipline



Discipline	Percentage %
Anaesthesiology	9
Cardiology	2
Diagnostic Imaging	10
Emergency & Critical Care (Ecc)	1
Internal Medicine	23
Neurology	13
Oncology	10
Ophthalmology	3
Surgery	27
Other	2

Supporting clinical research

The Linnaeus clinical research team coordinates and supports clinical research activities across the group. This includes assistance with study design, ethical approval, statistical analysis, manuscript preparation and publication, grant application and internal funding.

Clinical research training is provided by mentoring, formal teaching and tailored resources.

The clinical research team also facilitates collaboration with academic institutions in the UK and abroad - and within the Mars Petcare ecosystem, which comprises scientists in areas including genetics, metabolomics and artificial intelligence.

Research grants are available from the Linnaeus fund for clinical research projects, which is overseen by its clinical studies funding council and includes representatives from the Waltham Petcare Science Institute, Mars Veterinary Health and Nottingham Trent University. Its Open Access Publication Charge (OAPC) initiative covers the fees for Associates to publish in prominent peer-reviewed veterinary journals, enabling papers to be accessed freely across the profession for the benefit of pets and their owners in all parts of the world.

For more information about clinical research at Linnaeus, visit www.linnaeusgroup.co.uk/medical-and-nursing. More details about working at Linnaeus can be found at <u>www.linnaeusgroup.co.uk/careers</u>.

Working together

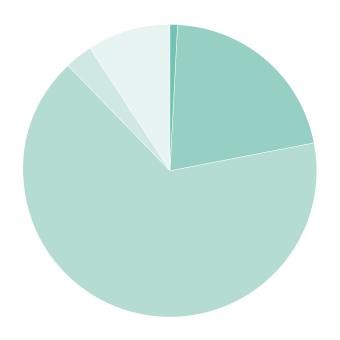
Linnaeus research projects include fruitful collaborations between primary care and referrals within the group, generating large sets of valuable data and supporting its commitment to the effective translation of research evidence into clinical practice.

Diplomate Veterinary Surgeons and residents at Linnaeus most commonly lead research projects, accounting for a combined 87% of the group's studies. Primary care clinicians and interns are also working on research, with veterinary nurses contributing to a number of studies.

Vets and nurses at Linnaeus review and critically appraise scientific literature - in veterinary and human medicine - on their topic of interest, deepening their knowledge and helping provide gold standard care to patients.

The Linnaeus clinical board enables its practice teams to offer the highest standards of client service and patient care. Chaired by its Chief Medical Officer Professor Séverine Tasker, it comprises clinical veterinary and nursing Associates as well as support services, ranging from new graduates to Clinical Directors and from analytic scientists to Patient Care Assistants, who are chosen for their skills, engagement and commitment. The board includes highly experienced Veterinary Surgeons and Registered Veterinary Nurses representing more than 25 disciplines.

Position of principal investigator on study



Position of principal investigator	Percentage %
Veterinary Nurse	1
Resident	21
Diplomate Veterinary Surgeon	66
Veterinary Surgeon	3
Intern	9





Page 6: From design to dissemination: the steps a research project needs to take

- 1. https://knowledge.rcvs.org.uk/evidence-based -veterinary-medicine/ebvm-toolkit
- 2. https://www.rcvs.org.uk/news-and-views/news/newrcvs-guidance-to-help-profession-navigate-clinical-and/
- 3. https://www.rcvs.org.uk/who-we-are/committees/ standards-committee/ethics-review-panel/
- 4. www.equator-network.org/reporting-guidelines

Page 9: One Health in veterinary science: a forward vision

- 5. www.emro.who.int/fr/about-who/rc61/zoonoticdiseases.html
- 6. www.bva.co.uk/media/3145/bva_one_health_in_action_ report_nov_2019.pdf
- 7. www.rsm.ac.uk/sections/comparative-medicine-section

Page 12: Boosting primary care involvement in clinical research

- 8. https://www.petsavers.org.uk/Apply-for-funding
- 9. www.samsoc.org
- 10. www.bsava.com

Page 16: Randomised clinical trial evaluating the effect of a single pre-appointment dose of gabapentin on signs of stress in hyperthyroid cats

- 11. Van Haaften, KA, Eichstadt-Forsythe, LR, Stelow, EA, et al. Effects of a single preappointment dose of gabapentin on signs of stress in cats during transportation and veterinary examination. J Am Vet Med Assoc 2017; 251: 1175-1181.
- 12. Watson, N, Murray, JK, Fonfara, S, et al. Clinicopathological features and comorbidities of cats with mild, moderate or severe hyperthyroidism: a radioiodine referral population. J Feline Med Surg 2018; 20: 1130-1137.
- 13. Pankratz, KE, Ferris, KK, Griffith, EH, et al. Use of single-dose oral gabapentin to attenuate fear responses in cage-trap confined community cats: a double-blind, placebo-controlled field trial. J Feline Med Surg 2018; 20: 535-543.

Page 18: Cross sectional survey of canine idiopathic epilepsy management in primary care in the **United Kingdom**

- 14. Kearsley-Fleet, L., O'Neill, D.G., Volk, H.A., Church, D.B. and Brodbelt, D.C., 2013. Prevalence and risk factors for canine epilepsy of unknown origin in the UK. Veterinary Record, 172(13), pp.338.
- 15. Heske, L., Nødtvedt, A., Jäderlund, K.H., Berendt, M. and Egenvall, A., 2014. A cohort study of epilepsy among 665,000 insured dogs: incidence, mortality, and survival after diagnosis. The Veterinary Journal, 202(3), pp.471-476.
- **16.** Armaşu, M., Packer, R.M.A., Cook, S., Solcan, G. and Volk, H.A., 2014. An exploratory study using a statistical approach as a platform for clinical reasoning in canine epilepsy. The Veterinary Journal, 202(2), pp.292-296.
- 17. Packer, R.M., Shihab, N.K., Torres, B.B. and Volk, H.A., 2014. Clinical risk factors associated with anti-epileptic drug responsiveness in canine epilepsy. PLoS One, 9(8), p.e106026.

Page 20: Changes in retinal vascular diameters in senior and geriatric cats in association with variation in systemic blood pressure

- 18. Barnett KC and Crispin SM. Feline ophthalmology. An atlas and text. Philadelphia, PA: WB Saunders, 1998.
- 19. Acierno MJ, Papich M, Brown S, et al. ACVIM consensus statement: guidelines for the identification, evaluation, and management of systemic hypertension in dogs and cats. J Vet Intern Med 2018; 32: 1803-1822.
- 20. Stepien RL. Feline systemic hypertension: diagnosis and management. J Feline Med Surg 2011; 13: 35-43.
- **21.** Jepson RE. Feline systemic hypertension: classification and pathogenesis. J Feline Med Surg 2011; 13: 25-34.
- 22. Conroy M, Chang Y, Brodbelt D, et al. Survival after diagnosis of hypertension in cats attending primary care practice in the United Kingdom. J Vet Intern Med 2018; 32: 1846-1855.
- 23. Stiles J, Polzin D and Bistner SI. The prevalence of retinopathy in cats with systemic hypertension and chronic renal failure or hyperthyroidism. J Am Anim Hosp Assoc 1994; 30: 564-572.
- 24. Maggio F, DeFrancesco TC, Atkins CE, et al. Ocular lesions associated with systemic hypertension in cats: 69 cases (1985–1998). J Am Vet Med Assoc 2000; 217: 695-702.
- 25. Young WM, Zheng C, Davidson MG, et al. Visual outcome in cats with hypertensive chorioretinopathy. Vet Ophthalmol 2019; 22: 161–167.
- **26.** Taylor SS, Sparkes AH, Briscoe K, et al. ISFM Consensus guidelines on the diagnosis and management of hypertension in cats. Journal of Feline Medicine and Surgery. 2017;19(3): 288-303.
- **27.** Cirla A, Drigo M, Ballerini L, et al. VAMPIRE® fundus image analysis algorithms: Validation and diagnostic relevance in hypertensive cats. Vet Ophthalmol 2019: 22: 819-827.

Page 22: Owner reported breathing scores, accelerometry and sleep disturbances in brachycephalic and control dogs: a pilot study

- 28. Aron D, CroweD.Upper airway obstruction. General principles and selected conditions in the dog and cat. Vet Cli North Am Small Anim Pract. 1985;15:891-917.
- **29.** Meola SD. Brachycephalic airway syndrome. Topics Companion AnimMed. 2013;28:91-96.
- 30. Roedler FS, Pohl S, Oechtering GU. How does severe brachycephaly affect dog's lives? Results of a structured preoperative owner questionnaire. Vet J. 2013:198:606-610.
- 31. Bowlt K, Moore A. Surgery of the upper respiratory tract Part 2: brachycephalic obstructive airway syndrome (BOAS). Companion Anim. 2009;14:19-26.
- **32.** Packer RM, Hendricks A, TiversMS Impact of facial conformation on canine health: Brachycephalic obstructive airways syndrome. PLoS One. 2015;10(10):e0137496.
- 33. Van Cauter E, Spiegel K, Tasali E. Metabolic consequence of sleep and sleep loss. SleepMed. 2008;9:S23-28.
- 34. Everson CA, Bergmann BM, Rechtschaffen A. Sleep deprivation in the rat: III Total sleep deprivation. Sleep. 1989;12(1):13-21.

Page 24: Clinical research at Linnaeus

- 35. https://www.mars.com/privacy
- **36.** https://www.mars.com/about/policies-and-practices/ our-animal-research-policy

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 Referrals in Surrey
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