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A medical detection role for dogs

Introduction

The association between humans and dogs is a long and close. Throughout history, dogs have fulfilled a whole range of different functions and the number and diversity is continually expanding. Whilst traditionally dogs have been trained to hunt, herd, guard and as traction animals, in recent years, canine roles have grown to include military, conservation, assisting farmers, even confirming which cows are in oestrus (Johnen et al 2015) and also a range of medical support and disease detection tasks.

As medical usage expands, it is imperative that the value of these dogs is fully objectively assessed, their potential capabilities are optimised and we use these abilities to further our understanding the diseases in question. In the UK, the leading charity training dogs, for both medical assistance and disease detection is Medical Detection Dogs (MDD). The charity receives no state funding and is not only a pioneer of the training but is committed to carrying out empirical research to improve its own and other charities' operations and to inform future medical technologies. The operations of the charity falls under two wings.

Medical Alert Dogs

In the medical alert dog wing, dogs are trained to detect the odours associated with a range of human diseases in controlled environments, and trials are conducted to quantify, understand and improve their performance. Harnessing the ability of dogs to detect odours is no new phenomena. For decades dogs have been used to search out narcotics, explosives and other contraband, and have assisted in law enforcement and humanitarian missions. Medical roles are a more recent development, but have evolved from naturalistic case examples. The first published example of a dog detecting cancer describes a young British woman, who reported to her dermatologist that her dog had been licking, nipping and barking persistently at a suspicious mole on her leg (Williams and Pembroke 1989). The lesion was later confirmed to be malignant. Subsequently, there have been a large number of documented examples of companion dogs seemingly alerting their owners to the onset of cancers, and hence charities have moved on to utilise this apparent sensitivity and to formerly train dogs for the purpose of cancer detection.

Just as when trained to find drugs, or explosives, dogs are conditioned to show a specific responses, such as sitting and staring, when presented with a target odour, in this case a diseased as compared to a control biological sample. The first documented proof-of-principle trial was conducted by Medical Detection Dogs (formerly Cancer and Bio-detection Dogs) and reported in the British Medical Journal (Willis et al 2004). Six dogs of varying breeds were trained to alert to urine samples from individuals diagnosed with bladder cancer, but to ignore samples from other patients and from healthy controls. Overall diagnostic accuracy was 41%, compared to 14% expected by chance alone. However there was considerable variation in the success between dogs, the best dog achieving 56%, whilst two failed to perform above chance level.

In a follow-up study, four dogs underwent rigorous training and double-blind testing and achieved average sensitivities (proportion of positives correctly identified) of 64% and specificities (proportion of negatives correctly identified as such) ranging from 92% for urine samples from young, healthy volunteers, to 56% for samples taken from older patients with non-cancerous urological disease. Interestingly factors such as smoking, gender age, as blood, protein or leucocytes in the urine did not significantly alter the odds of dogs showing a positive response. Together these studies show that specific dogs can be trained to distinguish patients with bladder cancer on the basis of urine odour, supporting the potential use of canine as affordable, precise, and non-invasive detection system.

There have been a number of subsequent studies around the world collaborating these findings but using a range of cancer types, and sample media. Trained dogs have been shown to be able to detect melanoma (Pickel et al 2004), prostate (Taverna et al 2016; Cornu et al 2011; sensitivity 91%, specificity 91%), breast, ovarian (Horvath et al 2013), colorectal (Sonoda et al 2011; sensitivity 97%, specificity 99%) and lung (McCullogh et al 2012; Ehmann et al 2012) cancers from samples of, urine, sweat, breath (McCullogh et al 2012; Sonoda et al 2011), blood (Horvarth et al 2013), stools and from cell cultures (Yoel et al 2015).

These findings suggest there is a characteristic "odour signature" in the air above cancer samples, which is detectable by dogs and potentially could be exploited for diagnosis. Identifying the volatiles that make up this signature and determining whether they are present early enough to improve is now vital (Buszewski et al 2012). Large numbers of patients currently die every year, or undergo invasive surgery unnecessarily as their cancers are not detected sufficiently early. With developments by charities like MDD it is hoped that dogs can, in the future, play a role in early diagnosis and that their abilities can be used to help improve technologies to achieve this aim. For example, the knowledge gained from dog studies suggests the possibility of constructing a bioelectronic-nose, based on canine olfactory receptors (ORs), for the purpose of diagnosing cancer in a more sensitive, specific and cost effective manner than is currently available (Pomerantz et al , 2015).

It is noteworthy that the various studies carried out around the world have yielded wide ranging results and estimates of detection accuracy. Most previous studies have used relatively small numbers of samples and dogs, and there appears to be significant heterogeneity in performance both between dogs and between studies. This may be partly due to individual characteristics in the dogs, and in the training methods employed, but there is also currently much variability in techniques used during testing. Understanding and optimising this variability, whilst standardising testing is an important future goal. Work at MDD is ongoing to monitor the performance and identify traits which correspond to the very best performing dogs, so in future selection of naive dogs can be even more targeted towards those most likely to ultimately produce the very best detection dogs.

Integral to the work of Medical Detection Dogs is scientific rigour and their testing regimes involve a large number of novel samples which have not been encountered by the dogs during training, as well as double blind testing, in which neither the handler nor the experimenter know the position of the target samples. Varying trials globally have used different regimes, therefore the charity are seeking to find out the optimal robust

presentation. They are currently comparing assessment methods, for example using a 8-stand carousel presentation of samples as compared to, a 4-stand linear array (see Figure 1) and a binary "yes-no" paradigm. They have also worked with universities to produce a novel pressure plate device which shows great promise in discerning the relative certainty of a dog's response when encountering an odour. Through trials using this device, in the future, we may more fully understand which aspects of the cancer odour signature are most important and which most confusing to the working dogs.

This area of work is exciting and very promising and MDD are currently working on a range of NHS approved proof-of- principle trials, exploring dogs' ability to locate breast cancer (from pads that have contacted the skin, breath and urine), and urological cancer; with a prostate cancer trial being ongoing. They have also recently obtained a new grant to work with Durham University exploring the possibility of dogs detecting malaria, from clothes (socks which have been in contact with infected Gambian children. The aim is to find a non-invasive way of detecting malaria that can be used to test large numbers of samples at the same time. Current tests require finger-prick blood collection and laboratory screening. In contrast, the dogs are portable and rapid and so have could have immense life-saving potential around the world.

Medical Alert Assistance Dogs

The other arm of MDD also uses olfactory alerting ability but for day to day support for people living with chronic conditions. Dogs have been used for medical support and assistance since the 1920s when the first guide dog was trained, and assistance dogs for sight impaired people are now commonly used around the globe. Similarly hearing dogs, and dogs trained to increase the independence of people living with physical disabilities are widespread. However, increasingly dogs are being trained to fulfil an alerting role for people living with life-threatening conditions.

More than twenty years ago, charities started to train dogs living with people with unpredictable epileptic seizures to alert their owners, between 10 and 45 minutes prior to an episode. Case studies suggest that these dogs were effective and that new owners experienced a reduction in seizure frequency (Strong et al 1999). Epileptic seizure alert dogs have been demonstrated to improve quality of life of those patients with whom they live (Kirton et al 2008). More recently the use of glycaemic alert dogs for patients living with chronic and debilitating diabetes has started to develop.

This role too stems from naturalistic responses of dogs. Individual case studies suggest that some pet dogs respond to their owners' hypoglycaemic state and a survey showed that of , 65% of dog owners reported some behavioural change in their dogs during hypoglycaemic episodes (Wells et al 2008). Moving on from this, charities have started to formally train dogs for this role and for the past 10 years, MDD has been a major pioneer in this field, and now have in excess of 70 functional dogs living with their owners.

Type I diabetes is a chronic condition affecting about a quarter of a million people in the UK. Hypoglycaemia is a common, potentially life threatening complication in individuals

receiving insulin and is especially hazardous for long-term patients who may have lost the ability to recognise early warning signs. Fear of hypoglycaemia can have a profound effect and people often restrict their lifestyle to an incredible degree to reduce the risk of hypoglycaemic events: this can significantly reduce their psychological wellbeing and quality of life. Some also manipulate injected insulin levels which increases the risk of long-term deleterious consequences of hyperglycaemia including potential renal complications and blindness.

Having a non-invasive early warning system of impending changes in blood sugar level could massively improve patients' quality of life, and this is what glycaemia alert dogs aim to achieve. Dogs are trained to alert their owner when blood sugars deviate from a target range. Alerts include barking, pawing or even fetching a blood testing kit, allowing their owner to test their glucose levels and take appropriate action. As the number of these dogs increases, people living with them anecdotally report great benefits. However one could question whether the dogs are really improving their owners' glycaemic control or whether perhaps they exert a placebo effect, or whether owners simply feel healthier and more active, benefits known to be associated with general dog ownership (Wells 2011).

Myself and co-authors sought to study these dogs empirically and quantify their potential benefits for the first time. In a paper published three years ago (Rooney et al 2013), we investigated whether seventeen trained dogs reliably responded to their owners' hypoglycaemic state, and whether owners experienced tightened glycaemic control, and wider psychosocial benefits. Since obtaining their dog, all clients reported positive effects including reduced paramedic call outs, decreased unconscious episodes and improved independence. Some described dramatic life changes, now being able to stay in the house alone or go on holiday for the first time. Owner-recorded data from 17 partnerships showed that dogs alerted their owners, with significant, though variable, accuracy at times of low and high blood sugar. Comparison of routine blood glucose records showed significant overall change after owners obtained their dogs. This study highlighted the potential value of alert dogs, for increasing glycaemic control, client independence and consequent quality of life and even reducing the costs of long-term health care.

It also pointed out the variability in dog performance, and so an ongoing challenge in the field (as well as bio detection) is to identify those factors which best predict working ability, and hence reject less appropriate dogs before investing large amounts of time and money in their training. We are currently examining the expanded cohort of over 70 dogs (trained by MDD) to try to identify factors which correlate to a dog's specificity and sensitivity of responding and hence we aim to improve selection and training. The mechanism by which dogs are able to detect changes in blood glucose also poses an important question. Since dogs are initially trained using remote breath samples, it is likely that there is an odour signature associated with falling and rising glycaemic levels. Indeed controlled studies have recently confirmed dogs ability dogs to a identify perspiration samples from patients whose blood sugars were low as compared to normal (Hardin et al 2015). However when operational, some dogs appear to respond to glucose changes even before they have reached out-of-range levels, and many owners report the dogs responding ahead of continuous glucose monitoring systems (technology which samples glucose from interstitial fluid). By understanding which volatiles the dogs use to achieve this, it is hoped we will not

only be able to target training towards the most relevant compounds, but potentially also work to improve current technologies.

As well as diabetes the charity has trained alert dogs to live with people suffering from a range of other chronic conditions including Addison's disease (also known as primary adrenal insufficiency or hypoadrenalism), and more recently for PoTS (Postural Tachycardia Syndrome) - an abnormal response by the autonomic nervous system, abnormally high increase in heart rate and altered blood supply to the brain on standing. This results in symptoms, including dizziness, fainting, tiredness and palpitations. They have also trained dogs to alert to minute airborne levels of nut allergens, which can trigger a life-threatening anaphylaxic episodes in their Nut allergic owners**.**

How are the dogs trained?

All dogs for medical alert and bio-detection within the Medical Detection Dog charity are trained using the principles of positive reinforcement. Primarily the target scent and the required behavioural response are paired using rewards, usually food and human attention. So whenever the dog shows the required response in the presence of the target odour it is rewarded. Gradually the dog is trained to distinguish between increasingly similar but distinct odours until it is reliably alerting only under the target conditions. In the case of medical alert assistance dogs, the dogs live with their owners and are in their presence the vast majority of the time. When the dogs are fully functional they will be registered Assistance Dogs UK, afforded the same treatment as dogs like guide and hearing dogs for example they can be taken into public places (shops and restaurants) and even travel on planes accompanying their owners. For this reason, the dogs have to reach high standards of behaviour and qualify as a working dog. This is an important aspect of their training. When it comes to the reliability of the dogs at their alerting tasks, as yet there is no universal agreed standard. So whilst MDD have high requirements and insist on dogs being reliable and their owners providing large amounts of data to show this prior accreditation, some newer organisations may not have such high standards. As the discipline of medical alert dogs grows, accreditation of medical alerting function is important to ensure dogs are all equally able to fulfil their life protecting role. .

How are the dogs kept healthy and happy?

The link between positive wellbeing and productivity has been long been established for human, Leverhulme and Lord Cadbury back in Victorian times acknowledged the fact that happy well-kept workers were more productive. For livestock the link between productivity and welfare is also well established, happy cows with kind stock people produce more milk (Waiblinger et al 2002) whilst sheep which are least stressed by the journey to slaughter Dalmau et al 2014) and poultry killed more humanely produce better quality meat Terlouw, et al 2015). When it comes to working dogs, positive welfare is similarly vital, and at Medical Detection Dogs keeping the dogs happy and stress free is a priority. For this reason, the charity has a no-kennelling policy. Kennelling is known to be stressful for trainee working dogs (Rooney et al 2006), and those dogs which respond most to this stress tend not to do

well training (Rooney et al 2009). Training methods based on positive rewards, have been demonstrated to produce more obedient dogs WITH fewer potential behaviour problems For these reasons, as well as from an ethical standpoint of wanting to do the best for this incredible animals, Medical Detection Dogs aims to prioritise its dogs health and well-being.

For more information
https://www.medicaldetectiondogs.org.uk

The charity receives no government funding and relies entirely on charitable donations.

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