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Canine olfaction as an alternative to analytical instruments for disease diagnosis: understanding "dog personality" to achieve reproducible results

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Abstract

Recent literature has touted the use of canine olfaction as a diagnostic tool for identifying pre-clinical disease status, especially cancer and infection from biological media samples. Studies have shown a wide range of outcomes, ranging from almost perfect discrimination, all the way to essentially random results. This disparity is not likely to be a detection issue; dogs have been shown to have extremely sensitive noses as proven by their use for tracking, bomb detection and search and rescue. However, in contrast to analytical instruments, dogs are subject to boredom, fatigue, hunger and external distractions. These challenges are of particular importance in a clinical environment where task repetition is prized, but not as entertaining for a dog as chasing odours outdoors. The question addressed here is how to exploit the intrinsic sensitivity and simplicity of having a dog simply sniff out disease, in the face of variability in behavior and response.

Keywords

canine olfaction; scent detection; cancer and disease screening

Introduction

There is no argument that living cells emanate a variety of gas- and liquid-phase compounds as waste from normal metabolism, and that these compounds become measureable from various biological media including skin, blood, urine, breath, feces, etc. [2, 10]. The overarching term for this phenomenon from the perspective of systems biology analysis is "cellular respiration", which has become an important topic for the interpretation and documentation of the human exposome, the chemical counterpart to the genome [22]. There is growing evidence that bacterial cells and human cancer cells, produce different patterns of volatile organic compounds (VOCs) by distinct protein synthesis and changed metabolism [13, 18, 24, 28].

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Cellular level VOCs are likely to have distinctive odours, thus in the last two decades new approaches for analytical detection of VOC's are being studied using targeted analysis with gas chromatography – mass spectrometry (GC-MS), with direct reading instruments including SIFT-MS, PTR-MS, PTR-ToF and IMS, and pattern recognition using sensor arrays commercial known as "electronic noses" [9, 25]. As these chemicals are often expressed in the breath, a wide variety of applications have been developed to assess health state based on such techniques [3].

The analytical instrument approach has limitations in that they can only detect that for which they are programmed, and so the question has arisen if trained dogs can be used to identify breath odour markers of human cancer or other subtle markers of disease in an agnostic manner. Sniffer dogs are known for their incredible ability to detect odours, extracting them from a "complex" environment and recognizing them, a task that is more difficult for current analytical technology. However, the problem is that previous studies on canine scent detection have shown a wide range of outcomes, especially with respect to disease diagnostics [15].

For over a century, humans have relied on trained sniffer dogs to discover illicit substances, explosives, bodies and much else (Figure 1). The exploration of canine scent detection for diseases is relatively new, compared to the use of dogs for other purposes. In 1989, the Lancet published a letter to the editor by Williams and Pembroke describing a dog that was permanently sniffing at a lesion on the thigh of its owner and on one occasion even trying to bite off the lesion. When it finally got excised, it turned out to be a malignant melanoma [27]. Since then, at least 5 studies with high quality and adequate design have been published (double-blind, randomized, controlled) to proof the efficacy of canine scent detection of cancer, sometimes referred as "pet scan" [4, 11, 12, 20, 26]. The results are largely varying, although it is difficult to compare the figures directly, since the studies differ methodically in many aspects. Jezierski *et al* recently reviewed this topic with a focus on the advantages and disadvantages of the method [17].

Possible aspects of divergent results

The varying results still raise questions concerning the reliability of sniffer dogs, especially for cancer detection. It is important to note that the mathematical analyses (typically receiver operator curves (ROC) or sensitivity/specificity parameters) are the same for case-control studies for dogs and for analytical instruments, and so no bias is expected there [5, 7, 21]. However, the main difference between the two techniques is that analytical instruments used for gas chromatography are focused on identifying individual compounds or groups of compounds, generally based on external validation [1, 14], whereas the dog perceives patterns of myriad chemical/biological responses that are sorted against his training set of odours [20]. In short, the dog interprets complex patterns whereas the analytical instruments are more focused. Even instruments designed to mimic olfaction such as the "electronic nose" are relegated to sensor arrays of 16, 32, or 64, whereas the dog has ~200 million olfactory cells [6, 8, 19]. That said, the both canine olfaction and analytical measurements have similar detection sensitivities, respond to airborne chemicals, and require training or calibration to make case-control distinctions. The disparity among results from different studies might not be a detection issue at all, but dependent on intrinsic factors. Dogs can only be trained for a limited set of applications and get tired, thus requiring a high turnover. In contrast to analytical instruments, dogs are subject to boredom, limited attention span, hunger, fatigue and external distractions.

These challenges are of particular importance in a clinical environment where task repetition is required, but not as entertaining for the dog as chasing odours outdoors. The question addressed here is how to exploit the intrinsic sensitivity and simplicity of having a dog sniff out disease, in the face of variability in response and behavior. Looking for answers to this question, it seems reasonable to consider experiences gained in other canine olfaction detection fields.

Essentials for canine olfaction detection and confounding factors

Regardless of the individual search target, scent detection is built on 4 main parts:

1. Respect of the individual characteristics of the chosen dogs
2. Precise training
3. Considering of the setup of detection work
4. Considering of the interactions between dog and handler

Some breeds and crossbreeds are considered to be more effective for detection work than others, but the selection of dogs mainly depends on their trainability and eagerness to learn, their performance and preferences by trainers [16]. Experienced sniffing dogs might be beneficial for mastering new tasks, but there is no general recommendation [23]. Obviously, it is important that the handler knows and understands the chosen dogs behavior, even when the animal is naive to detection work.

Training is a fundamental part of odour detection. For cancer detection, training parameters largely orientate on previous sniffing detection fields. They are based on step-by-step learning and recognition of the target scent, supported by positive feedback, thus a reward (e.g. treat or a toy to retrieve). In the past years, the process of canine scent detecting, e.g. for tracking or rescue, has changed in many ways. Nowadays dog handlers try to influence and distract their dogs as little as possible during detection work. As an example, for modern avalanche search, handlers stay at the edge of the avalanche to correct and conduct their dogs only when they obviously leave the search field or loose interest and attention. During training it is also important to include short game/play phases, especially after a success. By doing this, handler and dogs alike are on one level for a brief period, which is important for bonding and interaction. On the other hand, it is essential that the handler always leads and supports the dog taking corrective actions if necessary. A dogs' indication for a positive finding may vary depending on the requested search, but usually should be trained too. Before, during and after training it is crucial that the dogs drink and eat enough and go for a walk regularly. Drinking enough water is not only for quenching the dogs thirst, but reduces a possible elevated body temperature and may reduce the fever for the flavor that might occur during detection work. During detection training an association is being produced between the target odour or odour signature and a positive response mechanism. Thus, detection or identification will always be considered as a sort of game to earn rewards from a dogs' perspective. Exchange of prey (e.g. goodie bits for detected drugs or odour-marked rags) is therefore an important part in the training but also in actual detection work. Furthermore, it seems reasonable to give dogs' the time they need for training and to evaluate their individual performance before advancing to the next level. Even if the dogs' performance was not satisfying, it is important to finish every kind of detection work with a positive experience for the dog.

The setup and site of the actual detection work largely depends on the request and ranges from almost impassable outdoor terrain, crowds of people, airports or tiny lab rooms. For handlers, it is important to always be aware of possible external distractions for dogs. This also includes the handler's positive and negative sensations being transmitted to the dogs. The search for buried people will always be an exceptional, stressful and difficult situation for the handlers and therefore should be trained extraordinary well.

Last but not least, interaction between dogs and handlers play another very essential part in detection work that is often underestimated. Usually, the sniffer dog has a very strong binding to its handler and if trained well, the animals notice every single detail in the body language and behavior of their owner and vice versa as mentioned earlier. For handlers, it is very important to understand and interpret the dogs' behavior precisely. Heavy panting or sluggishness might be signs of fatigue. Head lifting, slowness or running off might indicate a lack of concentration. Coping strategies are playing with the dogs, granting a break and then trying to continue the work. Handlers also need to regard, when dogs are exhausted and further detection work would be only more tiring. But once again, the detection work should always be finished with a positive experience for the animal.

Implications for cancer scent detection

When it comes to canine scent detection for diseases, a lesson learned from the previous studies is that the structure of the experiments is of paramount importance, especially in real double-blind or screening situations. In a clinical environment, task repetition is prized, but not as entertaining for the dog as chasing odours outdoors. It seems reasonable to confront dogs with the pattern odour which should be indicated relatively often, for example the cancer odour. Therefore double blind trials should probably not be performed continuously, since the dogs would either lose their interest in the work or would try to earn a reward, increasing the percentage of false alerts.

A possible model for screening practice using canines would involve trials where there is always a cancer odour pattern in the lineup of samples, which would create the opportunity to earn a reward and would reinforce a dog's motivation. Confirmed "non-cancer" control odour samples should also be presented in the lineup in order to check the dogs' performance. The position of the control and pattern samples in the lineup could be single-blind i.e. not known to the dog handler but known to an investigator. Some test samples in the lineup would be from patients who are screened for cancer, for example smokers or other patients at risk. Indications of these test-samples would not be rewarded, so there is no possibility that the dog would be rewarded for a false alert. The drawback of this screening model is that cancer and non-cancer pattern samples should be systematically exchanged to avoid memorization of odours. Such model sustains the motivation of dogs and has not been systematically tested before. On the contrary, this method is very time-consuming and probably not applicable for a universal screening test.

Summary

Scent detection is not an easy task for both dogs and handlers, and there are many factors to bear in mind. Still, it has become an important method for searching for exceptional things that escape the notice of all but the most targeted instruments. Using trained dogs for cancer detection clearly has great potential, although further double-blind tests with respect to the above mentioned points are required.

Dogs have an extraordinarily sensitive and specific olfaction sense. However, unlike analytical instrumentation, they are subject to boredom, fatigue, and an incentive to gain reward for minimum effort much like the humans they work with. As such, researchers, trainers, and practitioners of canine-based diagnostics should recognize these personality aspects of dogs and develop specific controls and guidelines to assure that the dogs are working to the best of their olfaction abilities.

In conclusion, we suggest that the concept of sniffer dogs as a replacement or a confirmatory complement to cancer diagnostic screening for global application has great merit. In fact, canine olfaction could become a preferred methodology for disease diagnosis in emergency situations (infection epidemics) and in places where high-tech instrument-based analysis is unavailable. Certainly training dogs and subsequently maintaining their interest, health, and performance remains a time-consuming process. However, if one keeps in mind the “dog personality” aspect, canine olfaction can become a robust tool in fighting the battle against cancer and infectious disease.

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References

[1]. Aggio RB, de Lacy Costello B, White P, Khalid T, Ratcliffe NM, Persad R and Probert CS 2016 The use of a gas chromatography-sensor system combined with advanced statistical methods, towards the diagnosis of urological malignancies Journal of breath research 10 017106 [PubMed: 26865331]

[2]. Amann A, Costello Bde L, Miekisch W, Schubert J, Buszewski B, Pleil J, Ratcliffe N and Risby T 2014 The human volatilome: volatile organic compounds (VOCs) in exhaled breath, skin emanations, urine, feces and saliva Journal of breath research 8 034001 [PubMed: 24946087]

[3]. Amann A and Smith D 2013 Volatile Biomarkers, 1st Edition: Non-Invasive Diagnosis in Physiology and Medicine: Elsevier)

[4]. Amundsen T, Sundstrom S, Buvik T, Gederaas OA and Haaverstad R 2014 Can dogs smell lung cancer? First study using exhaled breath and urine screening in unselected patients with suspected lung cancer Acta oncologica 53 307–15 [PubMed: 23957595]

[5]. Baker SG 2003 The central role of receiver operating characteristic (ROC) curves in evaluating tests for the early detection of cancer J Natl Cancer Inst 95 511–5 [PubMed: 12671018]

[6]. Bikov A, Lazar Z and Horvath I 2015 Established methodological issues in electronic nose research: how far are we from using these instruments in clinical settings of breath analysis? Journal of breath research 9 034001 [PubMed: 26056127]

[7]. Brenner H and Savitz DA 1990 The effects of sensitivity and specificity of case selection on validity, sample size, precision, and power in hospital-based case-control studies Am J Epidemiol 132 181–92 [PubMed: 2192549]

[8]. Buszewski B, Rudnicka J, Ligor T, Walczak M, Jezierski A and Amann A 2012 Analytical and unconventional methods of cancer detection using odor Trends Anal Chem 38 1–12

[9]. Cumeras R, Figueras E, Davis CE, Baumbach JI and Gracia I 2015 Review on ion mobility spectrometry. Part 1: current instrumentation The Analyst 140 1376–90 [PubMed: 25465076]

[10]. de Lacy Costello B, Amann A, Al-Kateb H, Flynn C, Filipiak W, Khalid T, Osborne D and Ratcliffe NM 2014 A review of the volatiles from the healthy human body Journal of breath research 8 014001 [PubMed: 24421258]

[11]. Ehmann R, Boedeker E, Friedrich U, Sagert J, Dippon J, Friedel G and Walles T 2012 Canine scent detection in the diagnosis of lung cancer: revisiting a puzzling phenomenon The European respiratory journal 39 669–76 [PubMed: 21852337]

[12]. Elliker KR, Sommerville BA, Broom DM, Neal DE, Armstrong S and Williams HC 2014 Key considerations for the experimental training and evaluation of cancer odour detection dogs: lessons learnt from a double-blind, controlled trial of prostate cancer detection BMC urology 14 22 [PubMed: 24575737]

[13]. Filipiak W, Filipiak A, Sponring A, Schmid T, Zelger B, Ager C, Klodzinska E, Denz H, Pizzini A, Lucciarini P, Jamnig H, Troppmair J and Amann A 2014 Comparative analyses of volatile organic compounds (VOCs) from patients, tumors and transformed cell lines for the validation of lung cancer-derived breath markers Journal of breath research 8 027111 [PubMed: 24862102]

[14]. Gasparri R, Santonico M, Valentini C, Sedda G, Borri A, Petrella F, Maisonneuve P, Pennazza G, D'Amico A, Di Natale C, Paolesse R and Spaggiari L 2016 Volatile signature for the early diagnosis of lung cancer Journal of breath research 10 016007 [PubMed: 26857451]

[15]. Hackner K, Errhalt P, Mueller MR, Speiser M, Marzluf BA, Schulheim A, Schenk P, Bilek J and Doll T 2016 Canine scent detection for the diagnosis of lung cancer in a screening-like situation Journal of breath research 10 046003 [PubMed: 27677188]

[16]. Hall NJ, Glenn K, Smith DW and Wynne CD 2015 Performance of Pugs, German Shepherds, and Greyhounds (Canis lupus familiaris) on an odor-discrimination task J Comp Psychol 129 237–46 [PubMed: 26010195]

[17]. Jezierski T, Walczak M, Ligor T, Rudnicka J and Buszewski B 2015 Study of the art: canine olfaction used for cancer detection on the basis of breath odour. Perspectives and limitations Journal of breath research 9 027001 [PubMed: 25944810]

[18]. Kalluri U, Naiker M and Myers MA 2014 Cell culture metabolomics in the diagnosis of lung cancer-the influence of cell culture conditions Journal of breath research 8 027109 [PubMed: 24861817]

[19]. Kateb B, Ryan MA, Homer ML, Lara LM, Yin Y, Higa K and Chen MY 2009 Sniffing out cancer using the JPL electronic nose: a pilot study of a novel approach to detection and differentiation of brain cancer Neuroimage 47 Suppl 2 T5–9 [PubMed: 19362154]

[20]. McCulloch M, Jezierski T, Broffman M, Hubbard A, Turner K and Janecki T 2006 Diagnostic accuracy of canine scent detection in early- and late-stage lung and breast cancers Integrative cancer therapies 5 30–9 [PubMed: 16484712]

[21]. Phillips M, Cataneo RN, Cummin AR, Gagliardi AJ, Gleeson K, Greenberg J, Maxfield RA and Rom WN 2003 Detection of lung cancer with volatile markers in the breath Chest 123 2115–23 [PubMed: 12796197]

[22]. Pleil JD. Cellular respiration: replicating in vivo systems biology for in vitro exploration of human exposome, microbiome, and disease pathogenesis biomarkers. Journal of breath research. 2016; 10:010201. [PubMed: 26954510]

[23]. Polgar Z, Kinnunen M, Ujvary D, Miklosi A and Gacsi M 2016 A Test of Canine Olfactory Capacity: Comparing Various Dog Breeds and Wolves in a Natural Detection Task PloS one 11 e0154087 [PubMed: 27152412]

[24]. Schroeder W. Volatile S-nitrosothiols and the typical smell of cancer. Journal of breath research. 2015; 9:016010. [PubMed: 25749837]

[25]. Smith D, Spanel P, Herbig J and Beauchamp J 2014 Mass spectrometry for real-time quantitative breath analysis Journal of breath research 8 027101 [PubMed: 24682047]

[26]. Sonoda H, Kohnoe S, Yamazato T, Satoh Y, Morizono G, Shikata K, Morita M, Watanabe A, Morita M, Kakeji Y, Inoue F and Maehara Y 2011 Colorectal cancer screening with odour material by canine scent detection Gut 60 814–9 [PubMed: 21282130]

[27]. Williams H and Pembroke A 1989 Sniffer dogs in the melanoma clinic? Lancet 1 734

[28]. Zhu J, Bean HD, Wargo MJ, Leclair LW and Hill JE 2013 Detecting bacterial lung infections: in vivo evaluation of in vitro volatile fingerprints Journal of breath research 7 016003 [PubMed: 23307645]

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Figure 1.:
Trained sniffer dogs are commonly used for different kind of purposes, like search and rescue, detection of illicit substances or for scientific studies.