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Perspective

The role of trained and untrained dogs in the detection and warning of seizures

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ABSTRACT

Seizure unpredictability plays a major role in disability and decreased quality of life in people with epilepsy. Dogs have been used to assist people with disabilities and have shown promise in detecting seizures. There have been reports of trained seizure-alerting dogs (SADs) successfully detecting when a seizure is occurring or indicating imminent seizures, allowing patients to take preventative measures. Untrained pet dogs have also shown the ability to detect seizures and provide comfort and protection during and after seizures. Dogs' exceptional olfactory abilities and sensitivity to human cues could contribute to their seizure-detection capabilities. This has been supported by studies in which dogs have distinguished between epileptic seizure and non-seizure sweat samples, probably though the detection of volatile organic compounds (VOCs). However, the existing literature has limitations, with a lack of well-controlled, prospective studies and inconsistencies in reported timings of alerting behaviours. More research is needed to standardize reporting and validate the results. Advances in VOC profiling could aid in distinguishing seizure types and developing rapid and unbiased seizure detection methods. In conclusion, using dogs in epilepsy management shows considerable promise, but further research is needed to fully validate their effectiveness and potential as valuable companions for people with epilepsy.

1. Introduction

For many people living with epilepsy, the unpredictability of seizure onset is the most debilitating characteristic [1], being a cause of disability and negatively affecting quality of life [2,3]. The major limitations the unpredictability causes, affects many aspects of a person's life; their ability to socialise, carry out everyday activities and maintain a career [4,5]. Being unaware of when a seizure might occur has been shown to increase anxiety, whilst increased anxiety has also been shown to increase seizure frequency [2]. The ability to predict the onset of a seizure could potentially lower these anxieties and allow for the patient to implement preventative measures to limit the impact of the seizure [1]. Amongst the ways of predicting seizures, there has been growing interest in seizure detection dogs [2].

Dogs have been used to assist people with disabilities and improve patients' lives [6]. Both trained and untrained dogs have been used for seizure alerting and detection. This review article aims to identify and evaluate the literature surrounding the use of dogs in epilepsy, their role in seizure detection and alerting, and the potential for future application of dogs for patients with epilepsy.

Moreover, understanding the mechanisms underlying the detection of seizures by dogs may enable the development of strategies to determine if a seizure has occurred [7]. Diagnosis of an epileptic seizure is not always unequivocal, and errors are often made [8]; over 20% of people attending tertiary (specialist) epilepsy clinics do not have epileptic seizures but rather have syncopal or psychogenic events [9]. In addition, people are often unaware of their seizures and may underestimate their frequency [10,11]. Diagnosis is complicated by the lack of reliable diagnostic tests between seizures. For example, electroencephalography (EEG) data collected in the intervals between clinical events have a low sensitivity of only 50% [12] and do not reliably indicate if a seizure has recently occurred.

2. Dogs as modifiers and detectors of human disease

Since the domestication of dogs, their interaction with humans has become increasingly more refined, with selective breeding enhancing desirable traits such as sensitivity to human cues, tameness, as well as

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skills such as hunting or companionship [13]. The varied social-cognitive skills of dogs may be attributable to cohabitation with humans, being able to understand social and communicative human behaviours and being sensitive to emotional cues conveyed by the human face [14]. The value of animal companionship for human health is well-documented [15–17]. While a wide variety of species have been shown to offer therapeutic value to humans, the domestic dog has been utilised considerably more than other species in both experimental and applied settings. Many scientific studies have demonstrated the benefit of companion animals for physical wellbeing in humans, showing that domestic dogs may be able to prevent illness, facilitate recovery and even predict certain underlying health conditions. Hubrecht [18] suggested that pet owners as a group, are healthier than non-owners, while Serpell [6] reported that after only 1 month of owning a dog or cat, there was a significant reduction in the frequency of minor physical ailments in the owners, with dog owners maintaining this decrease in health problems through to a 10-month follow-up; whereas cat owners did not [18].

Dogs have an exceptional olfactory discrimination ability, far exceeding that of humans; this remarkable ability can be explained by differences in the canine olfactory system structure and in the number of olfactory receptor cells expressed [19]. The olfactory receptor genes form the largest gene families in mammalian genomes [20], with dog olfactory epithelium expressing up to 20 times more olfactory receptors than that of humans [21] and 40% more of a dogs' brain being devoted to olfaction than that of a humans [22].In addition to their favourable anatomical structure, dogs have been suggested to be the easiest domesticated animal to train to have co-operative interactions with humans [6]; additional other factors such as training protocols, high play and prey drives and a willingness to please can also impact on olfactory capabilities [19]. As a result of their ability to distinguish odours and their trainability, dogs have been used for the detection of illicit substances, explosives, biological scents at crime scenes and in biological safety such as parasite detection [23–25]. The use of service dogs and the establishment of new training procedures have also resulted in their use in a growing spectrum of disabilities [26].

Observations of spontaneous behavioural changes in dogs in response to a human pathology, has led to the reinforcement of these behaviours through training [19]. Over 30 years ago, there was a report of a dog repeatedly sniffing a mole on its owner's leg, which was later found to be malignant [27]. Since then, there has been a burgeoning literature supporting the innate aptitude of dogs to detect and alert people to certain disease states such as cancers, diabetes, and kidney diseases [28–31]. Impressively, Willis and colleagues [28] reported training six dogs to identify a urine sample from a patient with bladder cancer amongst urine from six healthy and disease controls on repeated occasions, yielding a successful cancer identification rate of 41% (95% confidence interval: 26–52%) compared with 14% detection rate expected by chance alone. Such observations have led to dogs being used in the detection and alerting of seizures in patients with epilepsy.

3. Can dogs detect seizures?

For decades it has been documented by people living with epilepsy, that their dogs are able to sense or alert them to their oncoming seizures [32,33]. There have been numerous studies discussing the idea of seizure prediction or alerting by both trained and untrained dogs [34–37]. Specifically trained seizure detection dogs (SDDs) and seizure response dogs (SRDs) can successfully detect when a seizure is occurring or distinguish seizure samples from non-seizure samples [37]. Seizure-alerting dogs (SADs) are specifically trained to alert their owners before a seizure starts, enabling the owner to prepare or take preventative measures [2,38]. Untrained pet dogs living with people with epilepsy have also shown an innate ability to detect and alert their owners to oncoming seizures, without any formal training [37].

It was initially proposed that a SAD was cued by minute gestures or posturing of patients, based on the observation that a primary form of communication for a dog is through facial expressions and body language [39]. Reports of dogs suddenly approaching their owner handlers to alert them despite previously being out of sight of them, suggests an alternative cue, something detectable at a distance, such as a scent [39]. Anecdotal reports have established the distinct ability of dogs to alert to oncoming seizures, often minutes before they occur; allowing patients to prepare themselves and ensure they are in a safe environment [40]. Evidence suggests that dogs can be reliably trained to anticipate seizures and that owning a SAD may even reduce seizure frequency [2,36,41]. However, most of this evidence comes from small series in uncontrolled studies (Table 1). More convincing studies have tested the ability of dogs to distinguish between ictal (during a seizure) and interictal (between seizures) sweat samples [40].

These studies have led to the hypothesis that the detection of seizures by dogs is, at least partly, mediated through a change in chemicals known as volatile organic compounds (VOCs) [37,40], in the breath or sebum of patients with epilepsy. It is thought that the exceptional olfactory ability of dogs enables them to identify these subtle changes, which would go unnoticed by human olfaction [42]. The idea of VOCs changing in different disease states is not novel, with studies successfully showing a correlation between colorectal cancer detection by dogs and altered VOC profiles [43]. VOCs are produced by physiological metabolic pathways, and their production can be altered by different pathological states, creating a distinct profile due to these specific alterations [44]. An existing device known as the electronic nose (eNose) can identify specified VOC profiles and perform aroma classification in certain disease states, such as lung cancer and respiratory diseases [45,46]. Essentially, it is thought that dogs perform a simplified version of this aroma classification, identifying a sudden change in odour, perhaps realising that the VOC profile indicates a potentially harmful event, and then alerting their owners.

Prior to the clinical onset of a seizure, it has been reported by Dalziel [39] that SADs innately exhibit behaviours consistent with attention-getting, nurturing and protection. In addition to this behaviour, it is also common for the dogs to remain with the person until the seizure subsides [47,48]. There are also descriptions of dogs who do not alert people to an impending seizure but display nurturing behaviours to the person during and/or immediately after the seizure, suggesting awareness of what is occurring [39]. There has been a growing interest in this area, Table 1 summarises the key publications reporting dogs' alerting behaviours in people diagnosed with epilepsy and those with non-epileptic attacks.

4. Spontaneous seizure detection behaviour of untrained dogs

It has been documented that seizure alerting behaviours may develop spontaneously in dogs living with adults with epilepsy [39]. A qualitative questionnaire [39] revealed that of 29 patients who owned an untrained dog, 9 (31%) reported that their dog responded to a seizure with comforting behaviour, e.g., standing or lying alongside them and sometimes licking the person's face or hands during and immediately after the seizure. Of the 9 patients who reported this behaviour of their dogs, 3 said their dogs alerted them to an imminent seizure, estimating an alert of 3 minutes in advance of a seizure. These alerting behaviours were described as whining, pacing in front of or around the patient, anxious barking, or intense staring.

This relationship between people with epilepsy and their untrained dogs was investigated further [35], surveying families with children affected by refractory epilepsy who had lived with a dog for at least 1 year. Of these 48 families, 20 (42%) reported specific seizure-related behaviours by their dogs, and in 41% of these families, it was felt this behaviour was acquired by the dog from the first seizure. The most common response behaviours noted were licking (59%), protective behaviour without aggression (50%) and whimpering (36%), as shown in Fig. 1. Of all families living with a dog, 20% witnessed anticipatory

Table 1
Below table summarises the existing literature evaluating the role of seizure response dogs (SRDs) and seizure alert dogs (SADs), both formally trained and untrained (adapted and updated from [38]).

Author	N (subjects)	Number and Type of Dog	Dogs' Training Status	Control Group/Condition	Type of Sample	Outcomes
Strong et al., 2002 [34]	10 adults	10 SAD	Trained	None	–	• There was a decrease in seizure frequency following training and pairing of patients with SADs versus prior to being assigned a SAD • Overall seizure frequency had reduced by 43%, with 9/10 subjects showing a reduction of 34% or more
Dalziel et al., 2003 [39]	9 adults	6 SRD and 3 SRD + SAD	Untrained but demonstrate alerting/ responding behaviours	Patients without alerting/ responding dogs	–	• Dogs may spontaneously alert and/or respond to seizures. • Trend on seizure type. • Success depends on the person's awareness and response to the dogs' alerting behaviour.
Kirton et al., 2004 [35]	20 children	13 SRD and 9 SRD + SAD	Untrained but demonstrate alerting/ responding behaviours	Patients without dog, patients with dog without responding/alerting behaviour, patients with SRD	–	• 42% reported specific seizure-related behaviours by their SRDs. • Accuracy of alerting behaviours was high, with a median sensitivity estimate of 80%. • Increase in quality of life for patients with a dog sensitive to seizure
Kirton, 2008 [36]	4 children 18 adults	22	Trained	Retrospective survey (before owning the dog)	–	• Increase quality of life found with SADs. • SRDs developed SAD skills in 59% of cases
Kersting, 2009 [41]	9 adults	9	Trained	Answers reflecting "do not know/cannot judge" impression of the owners	–	• Effective predictions • There was a decrease in the number of seizures when owning a SAD. • An increase in well-being of patients who owned a SAD was noted
Maa et al., 2021 [40]	60 adults	13	Trained	Sweat samples from seizure and non-epileptic seizures (NES) were investigated by the service dogs	Sweat samples	• Dogs had a 93.7% (OR: 14.89, 95%CI: 9.27, 23.90) probability of correctly distinguishing between ictal and interictal sweat samples. • NES population: 18 of the 19 NES events with sweat samples were not associated with identification of the unique seizure scent. • Number of seizures associated with a unique scent prior to the clinical/electrical onset of the seizure.
Powell et al., 2021 [37]	3 adult volunteer epileptics and 19 adult volunteers (dog owners)	19	Untrained	Dogs exposed to odours from 3 phases of epileptic seizures vs non-seizure controls. Evaluated dogs alerting response behaviours to owner	Odours, in the form of sweat	• Seizures are associated with an odour; dogs detect this odour and demonstrate increased affiliative behaviour towards owner (e.g. intense stare)
Catala et al., 2020 [49]	228 children/adults took questionnaire, 72 included in analysis due to incomplete questionnaires.	72	Trained but non-specifically (e.g., trained as a motor assistance dog but developed epilepsy alerting behaviours) or dog spontaneously developed epilepsy-specific behaviours	–	–	• Twenty-two (30.6%) of the 72 dogs were reported by owners to demonstrate seizure-alert behaviours. • The alert behaviour often developed from the first day the pet dog was exposed to a seizure (45.5%), within the first week for 18.2%, one month for 13.6% or after a few months for 22.7%. • Almost half of the owners reported that their pet dogs demonstrated seizure-alert behaviours for each seizure (43.8%).
Catala, 2019 [50]	10 patients recruited, 1 declined, 4 had no	5	Trained	Dogs exposed to seizure samples, exercise samples	Sweat samples	• Dogs were clearly able to discriminate the seizure odours

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Table 1 (*continued*)

Author	N (subjects)	Number and Type of Dog	Dogs' Training Status	Control Group/Condition	Type of Sample	Outcomes
	seizure. Overall 5 samples			and calm activity samples – evaluated ability to detect the seizure scent		from odours of the same patient outside seizures and for all patients tested. • There is indeed a seizure-specific odour across individuals and types of seizures.
Martinez-Caja et al., 2019 [51]	227 responses from children/adults with seizures, 132 from dogs alerting spontaneously	247 (data from 147 analysed)	Trained and untrained	Survey patients with trained vs untrained dogs responding behaviours	–	• Most of the participants identified behavioural changes in their dogs before their perceived onset of seizures, and this was associated with the presence of preictal symptoms. • The presence of seizure-alerting behaviour may have a positive influence on the bond between the owner and the dog.
Ortiz et al., 2005 [52]	1 child, 1 adult	2 SADs	Trained	2 patients with seizures, evaluated if dogs alerted prior to seizure onset	–	• "Seizure dogs'' were not as effective as previously thought in predicting seizure activity. In the patient with frontal lobe epilepsy, the dog exhibited abnormal behaviour, predicting a seizure before the only spell during which the dog was awake. In the patient with nonepileptic seizures, the dog's behaviour was thought to be reinforcing the patient's psychogenic events and leading to an increase in these events.

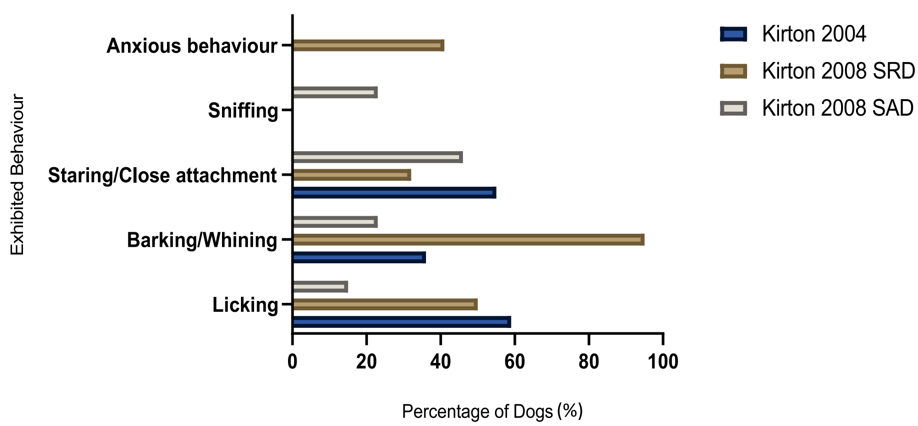

Fig. 1. Common behaviours of seizure alert and seizure response dogs. The most common spontaneous behaviours exhibited by seizure alert dogs (SADs) and seizure response dogs (SRDs) in studies by Kirton et al [35,36]. The most common behaviour demonstrated by SRDs was barking/whining, with 95% of dogs warning their owners in this way. A further 50% and 41% responded to the seizures with licking and anxious behaviours respectively. The most common alerting behaviour was staring/close attachment (46%) followed by barking/whining and sniffing, both at 23%.

behaviours from the dogs prior to the seizure onset, with the median anticipation time of 2.5 minutes.

The accuracy of these alerting behaviours was high, no dogs demonstrated anticipatory behaviour without a subsequent seizure, yielding a median sensitivity of 80%.

The study also detailed very individual protective alerting behaviours from the dogs, specific to the type of seizure the owner was experiencing, such as licking during an absence seizure, but protective positioning to prevent injury to the owner before a drop attack. In one case it was reported that anticipation of seizures by the dog was as early as 5 hours prior to onset [35].

5. Seizure detection abilities of trained versus untrained dogs in patients

Strong et al. [53] investigated the ability of both trained and untrained dogs to detect the onset of a seizure. Patients were recruited and allocated an untrained dog, with a comparison made of their seizure frequency before and after being allocated the dogs. In all cases, the dogs, within 6 months, were able to successfully detect and indicate imminent seizures. As training progressed, each of the dogs were able to provide an accurate prediction of a seizure within time periods ranging from 10 minutes up to 45 minutes. In addition, the frequency of seizures in all of the patients was reduced following completion of the dog training.

Strong et al. [34] further explored the role of seizure alert dogs, by pairing patients who had a confirmed diagnosis of epilepsy with tonic-clonic seizures, with a trained SAD. Baseline seizure frequency for each subject was recorded over a period of 12 weeks, followed by a further 12 weeks in which each subject entered a training period with their prospective SAD. For a further 24 weeks after training the seizure frequency was recorded, with results showing an overall seizure frequency reduction of 43% with 9 out of 10 patients demonstrating a reduction of 34% or more, 4 out of 10 showed a 50% or greater reduction, and only one showed no improvement. This study also showed that the presence of SADs providing a behavioural warning of seizure onset, can be of huge benefit for epilepsy patients, particularly with tonic-clonic seizures, allowing the patient to move to a safe space prior to the seizure. The increased self-confidence that SADs offer in providing an early warning sign could widely improve patient quality of life.

These studies by Strong et al. [34,53] have demonstrated the beneficial nature of dogs in a domestic setting for the alerting of imminent seizures, regardless of their training status. Both the untrained dogs and the already certified SADs exhibited successful detection of upcoming seizures, alerting their owners prior to onset and in the case of the SADs, reducing seizure frequency by 43%.

6. Can dogs distinguish between epileptic seizure and non-epileptic seizure samples?

As described above, there is evidence that both trained and untrained dogs can detect and alert their owners to imminent seizures. The following studies investigated if dogs have the ability to correctly identify a seizure sample taken from a patient, distinguishing these samples from control samples.

Reports of dogs alerting to an imminent seizure support the idea that they do not necessarily require training in order to alert, nor to distinguish seizure samples from non-seizure or control samples. This was demonstrated in a separate study looking at the response of 19 untrained pet dogs to human epileptic seizures. None of the dogs had previous exposure to epileptic patients, nor had they previously witnessed a seizure. All 19 dogs demonstrated significant behavioural changes concomitant with attention-seeking activities and engaged in more affiliative behavioural changes when confronted with the epileptic sweat samples compared to the control odours [37].

A study by Maa et al. [40] supports the idea that dogs can distinguish an epileptic seizure sample from a control sample and further investigated whether dogs had the ability to also distinguish seizure events from NES. In 18 of the 19 NES events, there was no detection of a unique scent by the dogs, compared to a correct identification of ictal from interictal sweat samples in 93.7% of the epileptic events.

The role of dogs in the above studies has led to the support of a seizure-related VOC or VOCs preceding a seizure event; where Powell et al. [37] proposed that the VOCs are associated with seizures rather than specific to epilepsy while Maa et al. [40] propose that epilepsy has a distinctive and unique odour. This VOC or group of VOCs could be used clinically for prospective training of dogs to further help them recognise differences between seizure states and tailor their training to match the specific needs of the owners.

7. Conclusions, limitations and future perspectives

In conclusion, the scientific literature surrounding the topic of seizure alert and seizure detection dogs has revealed circumstantial evidence supporting the use of trained and untrained dogs in people with epilepsy. Although the majority of the included studies demonstrated positive outcomes, represented by reductions in seizure frequency, prewarning of oncoming seizure activity and improved quality of life, there is a lack of well-controlled, prospective studies to demonstrate how effective seizure detection dogs are.

Although evidence has been in favour of pet dogs responding with nurturing behaviour to their owners' seizures or forewarning them to an oncoming event, there have been concerns over the possession of untrained dogs and their potential for aggression. One case report suggested that there is a risk of untrained dogs behaving in a dangerous or aggressive manner, with non-epileptic seizures seemingly increasing in frequency as a result of the dogs alerting behaviour [52]. However, this behaviour has not been seen in dogs specifically trained as SADs [54] and is not reflective of the findings of the other studies in this field [35–37,39,49,51].

Although encouraging, the included literature presents drawbacks. In order to reduce the confounding factor of personal bias, a behavioural scale related to the most common alerting behaviours would be beneficial to standardise reported outcomes [51]. With the literature included in this review, the variation of reporting methods would make this unachievable as 6 relied on questionnaires, one was a video recording of patients, and the remaining 4 were experimental.

As a result of inconsistencies across the studies of reported timings of alerting behaviours, comparisons of the studies are hard to make, this is however, to be expected given the studies explored were both qualitative and quantitative in nature. Maa et al. [40] and Catala et al. [50] explored the possibility that epileptic seizures emit an epilepsy-specific odour, whereas Powell et al. [37] tried to demonstrate that dogs predict seizures by responding to VOCs associated with seizures. Although all 3 studies applied rigorous scientific methodologies and reported measured outcomes, inconsistencies are not uncommon in these circumstances. A prospective study would be required with documentation of every seizure and every time the dog warned of a seizure in order to calculate sensitivity and specificity of seizure detection dogs. To further validate timings, a more controlled research setting, such as video-EEG telemetry where seizures could be monitored in real time, would be required.

The existing literature has demonstrated the presence of a scent, detectable by both trained and untrained pet dogs which precedes the onset of epileptic seizures. The scent in most of these studies evoked a significant behavioural change from the dogs, providing time for the owners to take precautionary measures prior to seizure onset. The literature demonstrates good evidence of the ability of dogs to discriminate interictal from ictal sweat, however, the sensitivity is low at 72% [40].

In order to further support and enhance the results of these and future studies, there is the need for a systematic approach to distinguishing the epileptic from the non-epileptic samples, using biomarker detection. This would allow for the development of a targeted training programme for seizure detection dogs, with the possibility to significantly reduce accidents and injuries associated with unexpected seizure occurrences. It is therefore necessary for detailed prospective studies evaluating the composition of breath and sweat prior to and following a seizure. This could be achieved by advances in VOC profiling, allowing the further validation of self-reported response behaviours by dog owners or their carers, and paving the way for a rapid and unbiased identification of seizure type and thus permitting faster diagnoses and more reliable treatment plans.

CRediT authorship contribution statement

Grace C. Luff: Writing – original draft, Writing – review & editing. **Ilaria Belluomo:** Writing – original draft, Writing – review & editing. **Eleonora Lugarà:** Writing – original draft, Writing – review & editing. **Matthew C. Walker:** Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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