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The relationship between epileptiform discharges and background activity in the visual analysis of electroencephalographic examinations in dogs with seizures of different etiologies

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ABSTRACT

Electroencephalographic (EEG) recordings in 125 outpatient dogs with various epileptiform encephalopathies were acquired under medetomidine sedation using subdermal wire electrodes. The features of canine EEG (background activity [BGA] and epileptiform discharges [EDs]) were assessed, described and compared. The dogs included neurologically healthy controls (N, $n = 19$), dogs with portosystemic shunt (PSS, $n = 9$), dogs with intracranial pathologies (IP, $n = 27$) and dogs with idiopathic epilepsy (IE, $n = 70$).

A visual EEG analysis revealed significantly more pronounced high voltage, low-frequency BGA in the PSS and IP groups in comparison to the N and IE groups (PSS vs. N, PSS vs. IE $P < 0.0001$; IP vs. N, IP vs. IE $P = 0.043$). At least one ED in the recording was found in 47.37% ($n = 9/19$) of the individuals in the N group, 88.9% ($n = 8/9$) of the dogs in the PSS group, 77.78% ($n = 21/27$) of the dogs in the IP group and 61.43% ($n = 43/70$) of the dogs in the IE group. The presence of bilateral symmetric triphasic (BST) waves was significantly higher in the PSS group than in the remaining groups. There was a strong prevalence of spike-waves in dogs with idiopathic epilepsy and of BST waves in dogs with portosystemic shunt. None of the dogs in group N had spike-waves or BST activity. EDs were observed more frequently in high and very high voltage, low frequency BGA than in low voltage, high frequency BGA.

Introduction

Electroencephalography (EEG) is the diagnostic reference standard for humans with a history of seizures (Koutroumanidis and Smith, 2005). The assessment of EEG recordings may be visual or quantitative (qEEG) and includes the description of the background activity (BGA) and superimposed transients, both of which can be physiologic or pathologic (including epileptic discharges, ED).

Canine epilepsy is the most common neurological condition in dogs (Pakozdy et al., 2012). However, unlike in humans with epilepsy, EEG is not routinely used in veterinary medicine due to its technical requirements (De Risio et al., 2015). Numerous interictal EEG recording protocols have been proposed for canine patients (Holliday et al., 1970; Klemm and Hall, 1970; Pellegrino and Sica, 2004) involving different sedation protocols, derivations, electrode types and placement. Recently, investigators have performed EEG recordings without sedation (James et al., 2015, 2016). Most canine EEG reports focus on the detection rate of ED, but do not describe or compare the specificity and character of canine EEG features (BGA and ED) in various epileptiform encephalopathies. There are insufficient data describing the relationship between total and individual EDs. Additionally, the frequency of the occurrence of different types of BGA with seizures of different etiology is unknown. Furthermore, the diagnostic usefulness of photic stimulation, as an EEG activation technique in various canine epileptiform encephalopathies, remains unexamined.

We hypothesized that dogs with different epileptiform etiologies would exhibit different and characteristic ED and BGA during the interictal period when recorded while using photic stimulation. Therefore, we sought to describe and quantify the visually identified ED and BGA in the interictal EEG recordings of dogs with seizures of different etiology, using a simplified, outpatient EEG recording protocol, using medetomidine sedation and photic stimulation. Finally, we assessed the usefulness of photic stimulation

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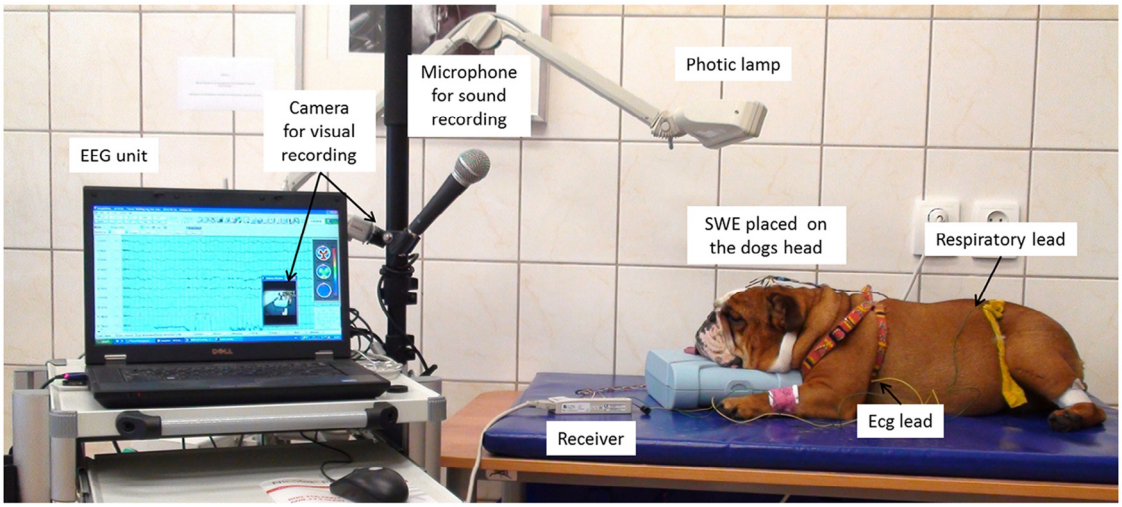

Fig. 1. Electroencephalographic set-up for canine electroencephalographic (EEG) recording. The dog was placed in sternal recumbency with the head slightly elevated so that it could be visualized in the video recording. The examination room was darkened during the EEG acquisition. SWE, subdermal wire electrodes.

in various canine epileptiform encephalopathies in eliciting characteristic ED and BGA and helping differentiate between different epileptiform etiologies.

Materials and methods

Study population

The study was performed at the Department of Internal Medicine and Clinic *for* Horses, Dogs and Cats in the Faculty of Veterinary Medicine at the Wrocław University of Environmental and Life Sciences, Poland. The research material consisted of 125 EEG recordings from dogs. The control group ($n = 19$) consisted of dogs from a closed permanent breeding colony of the Faculty. Dogs with seizures of various origins ($n = 106$) presented for a neurological consultation to the neurological division of the Department of Internal Medicine comprised the study group. The study protocol was approved by the Regional Ethics Committee for Animal Research (Approval number 106/2010, 21 June 2010). Dog owners provided informed consent for their pets to participate in the EEG study. The EEG recordings were only included in the study if the dog underwent the following procedures: (1) a clinical and neurological examination; (2) a comprehensive metabolic blood analysis (complete blood count, differential leucocyte count, sodium, chloride, potassium, calcium, total protein, albumin, globulin, urea nitrogen, creatinine phosphokinase, glucose, cholesterol, lipase, alanine aminotransferase [ALT], aspartate transaminase [AST], alkaline phosphatase, thyroxin, pre and post-prandial bile acids, ammonia, and total bilirubin); (3) MRI of the brain and a cerebrospinal fluid (CSF) analysis (in all the cases excluding the group diagnosed with a portosystemic shunt; PSS); and (4) a readable EEG recording was obtained under medetomidine sedation using a subdermal wire electrode protocol.

Dogs were divided into the following four groups based on the examinations detailed above: control dogs (N, $n = 19$); dogs with portosystemic shunt (PSS, $n = 9$; the results of an EEG analysis in this group were described elsewhere; Wrzosek et al., 2015); dogs with intracranial pathologies (IP, $n = 27$), subdivided into dogs with meningoencephalitis of unknown origin (MUO, $n = 12$) and dogs with intracranial space occupying masses (ICM, $n = 15$); and finally, dogs with idiopathic epilepsy (IE, $n = 70$). Dogs were included in the control group if they were seizure-free and screening examinations were within the reference range. Portosystemic shunts were diagnosed based on the results of bloodwork (increased post-prandial ammonia and/or bile acids, low urea, albumin and total protein concentrations) and confirmed using abdominal ultrasonography. Meningoencephalitis of unknown origin was diagnosed based on the results of MRI (focal or multifocal lesions compatible with meningoencephalitis/encephalitis), negative infectious disease blood or CSF titers, pleocytosis in the CSF (>5 cells/μL; total protein <0.25 g/L) and a positive response to immunosuppressive treatment. Intracranial masses were diagnosed based on the results of MRI and CSF examinations. Dogs with a history of at least two seizures and no changes in any of the above-mentioned assessments, except EEG, were assigned to the IE group.

EEG recording

All the EEG recordings were performed using medetomidine sedation (Narcostart, Animedica) at a dose of 20 mcg/kg, administered IM into the right triceps muscle. The recordings were performed prior to the general anesthesia necessary for MRI and CSF examinations. The examined dogs were placed in sternal recumbency in order to facilitate videometry (Fig. 1). The videometry was performed to record possible dog movement during the recording. The recordings lasted approximately 30 min and were carried out with the use of a Nikon Kohden EEG unit using the following settings: sensitivity, 70 μV/cm; bandpass filter, 0.5–30.0 Hz; a 0.3 s time constant; and a notch filter 60 Hz inserted. Each recording was carried out using a 14-channel referential montage (F3, F4, C3, C4, T3, T4, O1, O2, -Ref., the reference electrode was placed on the frontal bone while the ground electrode was inserted in the neck and in a standard bipolar montage [F3-C3, C3-T3, T3-O1, F4-T4, C4-T4, T4-O2]; Fig. 2). The ECG-Ref. electrode was placed subcutaneously at the left 5th intercostal space near the chondrocostal junction. Subdermal wire electrodes (Ives EEG Solutions[1]) were used. The 3 mm, Ag-Ag/Cl electrode recording tip was positioned on the skull surface. Light stimulation using a photic stimulator, at an initial stimulation frequency of 0.5 Hz, was conducted after 5 min of EEG recording (Fig. 1). The frequency gradually increased to 60 Hz, then steadily decreased to the base point, over a 5 min period. All EEGs were subjected to visual analysis (Polaris one ver. 1.4.1.0; Nihon Kohden Europe). The recordings were blindly studied by a board certified veterinary neurologist (MW). The background activity (BGA) was defined at the moment before the photic stimulation and all EDs were noted and recorded on a transient annotation list (Fig. 3). The physiological transients (sleep spindles, K-complexes) were identified, but not quantified in this study. All the marked transients were assessed blindly by two medical epileptologists (ED, EG). The analysis of the recordings was performed using simultaneous referential and bipolar montages (Figs. 3–5). Special emphasis was placed on the detection and the differentiation of ED from the artifacts including muscle activity, movements, ocular movements or blinks, together defined as 'muscle artifacts'. The BGA was defined based on the visual assessment and the frequency measurement (Fig. 3). If the frequency was higher than 8 Hz (and the amplitude ranged from 10 to 40 μV), the BGA was defined as low-voltage, high frequency (LVHF; Fig. 3A). If the frequency ranged from 4 to 7 Hz (40–140 μV), it was classified as high-voltage, low frequency (HVLF; Fig. 3B). If the frequency was lower than 4 Hz (amplitude >140 μV), it was classified as very high-voltage, low frequency (V-HVLF; Fig. 3C). The nomenclature currently accepted by the International Federation of Societies for Electroencephalography and Clinical Neurophysiology (IFSECN; Chatrian et al., 1974; Nordli et al., 2011) was used to define the epileptiform discharges. A spike was defined as 'a transient wave, clearly distinguished from the BGA, with a pointed peak at conventional paper speed and a duration from 20 to under 70 ms; with a generally negative main component' (Fig. 4). A sharp wave was defined as 'a transient wave, clearly distinguished from the BGA, with a pointed peak at conventional paper speed and a duration from 70 to 200 ms; with a mostly negative main component', and a spike wave was defined as 'a pattern consisting of a spike followed by a slow wave' (Fig. 5). Polyspikes and polysharp waves were combinations of multiple spikes and sharp waves (Fig. 4). We localized ED based on the highest amplitude of the discharge in a reference montage, and reversed polarity in a bipolar montage recording (Fig. 4). Bilateral symmetric triphasic (BST) waves were identified as a low amplitude negative deflection (upwards), followed by a main large positive (>70 μV; downwards) and followed by a long, slow, broad slow-rising negative deflection (upwards; Fig. 6), of a diffuse and bilateral synchronous localization (Kaplan, 2004; Kaplan and Sutter, 2015).

[1] See: Ives EEG Solutions. http://www.iveseegsolutions.com/swe.html (Accessed 5 March 2017).