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Electroencephalographic features of metabolic encephalopathy in dogs

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Summary

The article describes electroencephalographic (EEG) recordings in dogs with diagnosed metabolic encephalopathy (ME) due to a porto-systemic shunt (PSS). A group of 24 dogs underwent an EEG examination according to a uniform recording protocol. Patients were divided into group A, comprising dogs diagnosed with hepatic PSS (n = 12), and control group B, composed of patients with an extracranial neurological disorder without cerebral involvement. All dogs included in the study underwent standard diagnostic procedures, which included a comprehensive metabolic panel and EEG examinations. All EEG recordings were subjected to visual and spectral analysis and were compared.

The visual EEG examination revealed a high voltage, low-frequency background activity in both groups, more pronounced in group A. Random pathological activity of paroxysmal discharges (PD) was found only in group A, consisting of spikes and sharp-and-slow waves. Moreover, the presence of bilateral symmetric triphasic waves was noted only in group A. The EEG features in the dogs with ME were similar to known characteristics of the corresponding human EEG recordings.

Keywords: electroencephalography, EEG, dog, metabolic encephalopathy

Electroencephalography (EEG) is a recording of spontaneous cortical activity, and is used to diagnose functional disorders of the central nervous system (CNS). It is one of the most important tools in the diagnosis of epilepsy in humans. An electroencephalogram may be evaluated visually and quantitatively, as well as by using spectral analysis (quantitative EEG, q-EEG). Two activities are analysed visually: background activity and superimposed transients. Background activity is a setting in which a given normal or abnormal pattern appears and from which such a pattern is distinguished. A superimposed transient is a phenomenon with an abrupt onset, rapid attainment of a maximum, and sudden termination, and it is distinguishable from background activity (18). In veterinary medicine, EEG has rarely been used to diagnose seizures (10, 23). Because of its sensitivity to electrical muscle, cardiovascular and ocular activity, the procedure has its limitations, and requires special preparation when used in animals (3, 13).

Hepatic encephalopathy (HE) in dogs is a metabolic disorder of the CNS resulting from hepatic malfunction of acquired or congenital causes. One of the most common causes of HE is the presence of anomalous hepatic vessels forming a porto-systemic shunt (PSS). As a result of this, blood bypasses the liver, and unaltered constituents of the portal blood flow directly into the systemic circulation, causing clinical symptoms of metabolic encephalopathy (ME). Toxic substances like ammonia, aromatic amino acids (including phenylalanine, tyrosine, and tryptophan), short-chain fatty acids, mercaptan and various biogenic amines, indoles and skatoles, have been incriminated in causing ME. Metabolic encephalopathy in the course of PSS causes functional disturbances of CNS activity due to endogenic intoxication (14). The EEG features of ME in humans are widely described (8, 24), whereas in dogs the characteristics of cortical waveforms during ME remain unclear.

The present study was designed to retrospectively carry out an EEG visual and quantitative analysis (qEEG) of recordings in dogs with diagnosed PSS.

Material and methods

The research material consisted of 24 dogs presented for a neurological consultation to the Department of Internal Medicine and Clinic of Horses, Dogs and Cats, Faculty of Veterinary Medicine, Wrocław University of Environmental and Life Sciences. The study protocol was approved by the Ethics Committee on Animal Trials (permit number

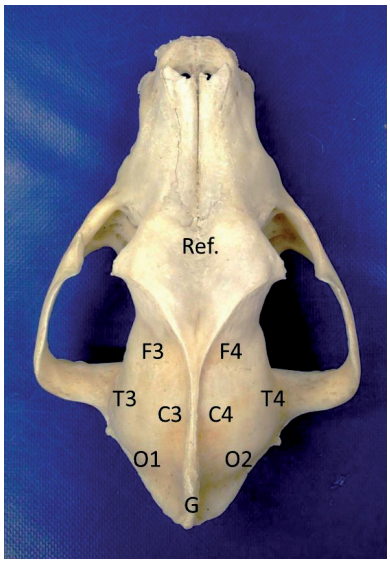

Fig. 1. An 8-channel montage used for the study. Monopolar montage: F3, F4, C3, C4, T3, T4, O1, O2, -Ref., ECG-Ref., Resp-Ref. (reference at the nose). (F – frontal; T – temporal; C – central; O – occipital; ECG – electrocardiography; Resp. – respiration; odd numbers = left hemisphere; even numbers = right hemisphere)

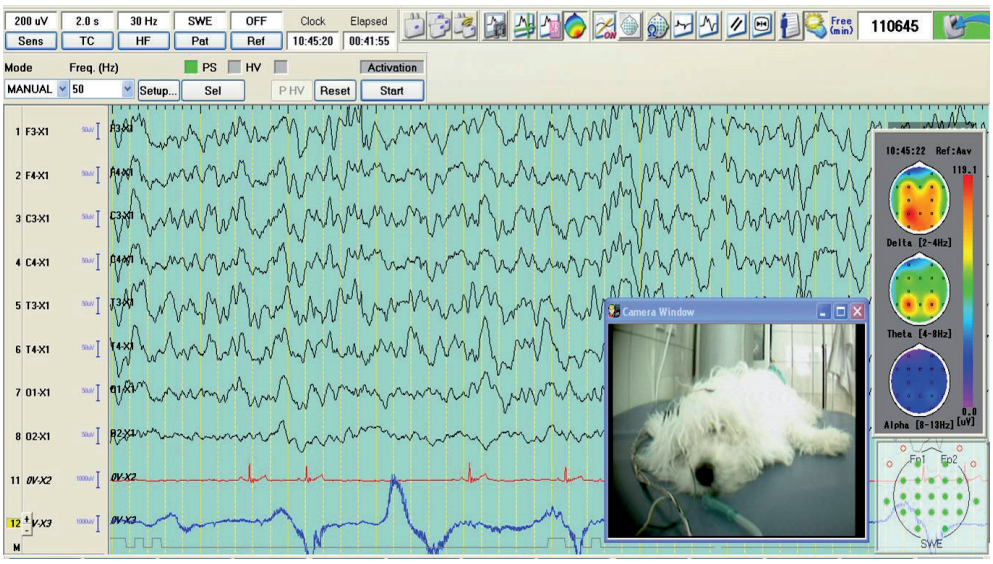

Fig. 2. Representation of a EEG recording with a camera view of the patient, spectral activity visualisation (right side of the figure). A generalized slowing of the recording with spread bisynchronous and asynchronous slow waves is visible (green highlighted)

106/2010). Dogs were divided into a group diagnosed with hepatic PSS (group A, n = 12) and a control group (group B, n = 12) with a diagnosed extracranial neurological disorder, without any involvement of cortical function (e.g., myelopathy). Group A included six Yorkshire terriers, one mixed breed and one dog from each of the following breeds: Bolognese, Bernese mountain dog, West Highland White Terrier, Miniature Schnauzer, Czechoslovakian Wolfdog. Eight of the dogs were male and four were female. Their mean age was 13.9 months (median 12), and their mean weight was 3.81 kg (median 3.1). Control group B included 8 Yorkshire terriers and 4 Beagles. Seven of these dogs were male and five were female. Their mean age was 15.2 months (median 14.8), and their mean weight was 4 kg (median 2.3). A clinical and neurological examination was performed in all animals. Venous blood samples were collected from all the dogs included in the study to evaluate their haematological and metabolic profiles. The following parameters were evaluated: complete blood count, differential leucocyte count, sodium, chlorine, potassium, calcium, phosphorus, total protein, albumin, globulin, urea nitrogen, creatinine phosphokinase (CPK), glucose, cholesterol, lipase, ALT, AST, alkaline phosphatase (ALP), thyroxin, pre and post-prandial bile acids and ammonia, and total bilirubin. All dogs underwent an abdominal ultrasonography to assess hepatic vasculature.

EEG recordings were conducted under sedation with 20 µg/kg of medetomidine administered intramuscularly in the triceps muscle. The recordings lasted at least 25 minutes and were conducted until the animals woke up. The EEG examination was carried out with the use of a Nikon - Kodhen unit and the following settings: transverse pages 30 mm/s, 70 µV/cm amplitude, 30.0 Hz high-pass filter (HF.), low-pass filter (Lf.) and 0.016 Hz notch filter. Each recording was carried out in an 8-channel single-pole assembly (F3, F4, C3, C4, T3, T4, O1, O2, -Ref., ECG-Ref., Resp-Ref.), in which the reference electrode was placed on the nose, and a standard bipolar assembly (Fig. 1). The registration of the bioelectric activity of the cerebral cortex was carried out on the surface of the scull by means of subdermal wire electrodes (SWE). All recordings were subjected to visual and spectral analysis, and compared. The spectral bands were defined as delta for the frequency values of 0.5-4.0 Hz, theta for 4.1-8.0 Hz, alpha for 8.1-12.0 Hz and beta for the values between 12.1 and 30.0 Hz. Special emphasis was placed on artefact detection and elimination. Artefacts were noted on the basis of simultaneous visual, ECG and respiratory recordings of the patients, as well as the recordings of their ocular movements, cardiovascular and muscular activity, physiological rhythmic movements and the recording environment (Fig. 2).

Results and discussion

The conducted clinical, neurological and blood examinations revealed no abnormalities in the control group. All dogs in group A were diagnosed with a hepatic PSS on the basis of a medical history of seizures, episodic alterations of consciousness and elevated pre- and post-prandial bile acid and ammonia concentrations. The neurological examination revealed mild to pronounced consciousness abnormalities in group A, ranging from depression to obtundation, diffusely mild decreased conscious proprioception (CP) and a decreased menace response. Cranial nerves and spinal reflexes were considered normal as far as motor and sensitivity performance was concerned. In all dogs from group A, an ultrasonographic examination revealed abnormal hepatic vasculature and a porto-caval shunt.

The visual EEG examination revealed a high voltage, low-frequency (HVLF) background activity in both groups (Fig. 2, 3), which was more pronounced in group A (Fig. 2). Generalized delta activity superimposed with theta activity was seen in most cases, and

a physiological activity of sleep spindles, k-complexes and vertex waves were noted. In group A, random pathological activity of paroxysmal discharges (PD) was found, consisting of spikes, polyspikes, as well as sharp and slow wave complexes (Fig. 4). Moreover, the presence of bilateral symmetric triphasic waves was noted in 9/12 dogs (58%) from group A (Fig. 5), whereas spread bisynchronous and asynchronous slow waves were observed in 10/12 dogs (83%) (Fig. 2).

The slowing of the EEG patterns in different ways can be attributed to numerous etiologies. It is not known why EEG slowing presents in various patterns. A physiological slow-wave pattern with a frequency of 2-5 Hz and voltage of 25--100 µV was described in dogs during the non-REM sleep. In comparison, these values were 8-20 Hz and 5-25 µV in normal alert dogs (16, 22). Generalized slowing due to a dominant delta and theta background activity of the EEG recording was found in control dogs from group B. This was interpreted as a physiological feature of the cortical activity during the medetomidine sedation or non-REM sleep, and is a known and previously reported phenomenon (11, 12). The spectral analysis of the recordings did not deviate from the previously reported sedation pattern as far as superimposed characteristic sleep transients were concerned (3). ME is characterized by a common EEG pattern that includes a generalized slowing of the recording and a bisynchronous and asynchronous slow wave spread (8, 24). A visual evaluation of the EEG recording makes it possible to differentiate the physiological sleep pattern and the ME EEG pathologic pattern (1), which was confirmed in this study. The recordings of EEG in dogs with ME were charac-

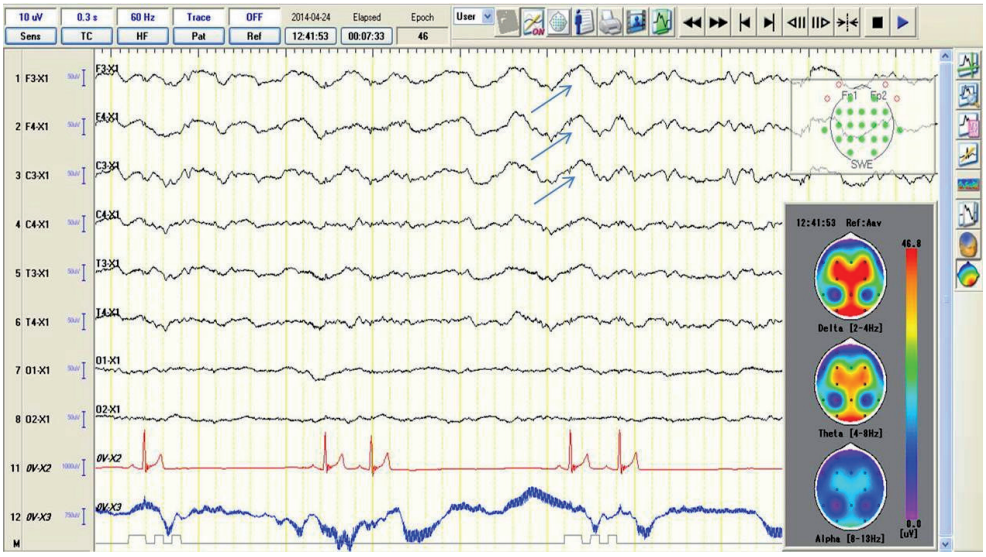

Fig. 3. EEG of a healthy dog – group B. A generalised background of high voltage, slow activity (HVSA), with delta waves (arrows) in the frontal and central leads

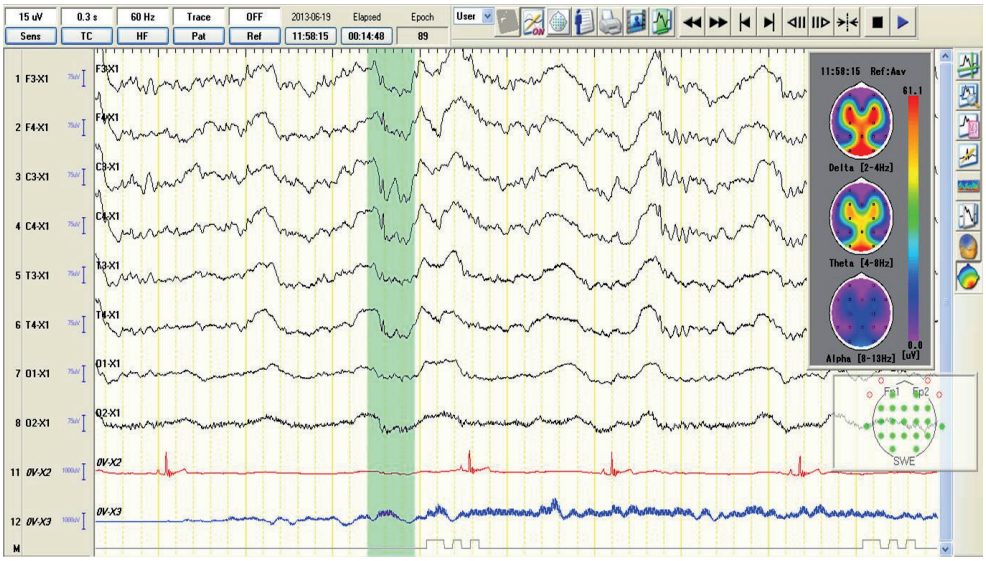

Fig. 4. Paroxysmal epileptiform discharges of a spike-slow wave (green highlighted) in the C3 lead in a dog from group A

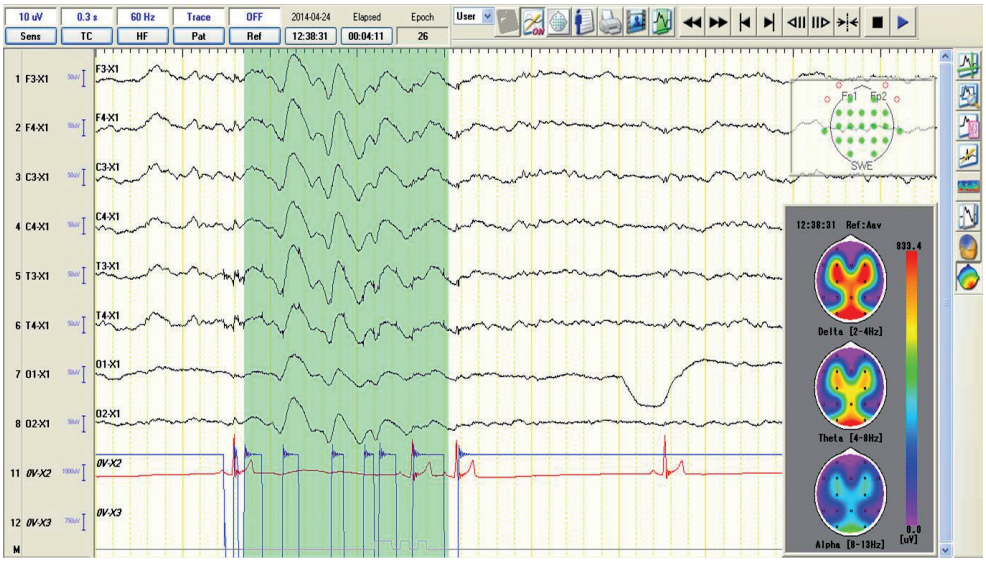

Fig. 5. Bilateral symmetric triphasic waves (green highlighted) in a dog from group A

terized by a diffuse slowing with significantly higher amplitudes than those of the dogs from the control group. Bisynchronous and asynchronous slow waves were found as far as triphasic waves in most dogs with metabolic encephalopathy.

Bisynchronus slow waves are observed in human patients with focal structural lesions and a co-existent toxic or metabolic encephalopathy (1, 8), and should be differentiated from unilateral slow-wave activity. In the dogs in this study, a symmetrical diffuse slowing was observed, which implies a metabolic dysfunction. Increased delta activity is well recognized in human electroencephalography as FIRDA or OIRDA (occipital intermittent rhythmic delta activity) that can progress with the disease to generalized polymorphic delta activity (PDA) (24). Although some EEG recordings in dogs from group A may have resembled the FIRDA pattern, no OIRDA or PDA was found. In humans, triphasic waves (TWs) have been described as bilateral and frontal, with posterior spread and the presence of a clear anterior maximum (14, 15). The name of the pattern refers to the shape and sharpness of the wave. TWs may be misinterpreted as vertex or epileptiform spike waves. TWs classically correlate with clinical hepatic encephalopathy, but their presence has been recognized in all forms of ME (14, 21). Since TWs are also seen in nonconvulsive status epilepticus, it was speculated that the presence of TWs in the course of ME indicates nonconvulsive status epilepticus (5, 19). The presence of diffuse EEG slowing with slow waves is not specific for ME, and differential diagnoses should include conditions such as a postictal state, diffuse meningitis, increased intracranial pressure, drug intoxication, severe hyponatremia or advanced dementia (2, 4, 15). Diffuse EEG slowing should be distinguished from focal slowing, as the latter implies an underlying focal cortical dysfunction. In this study, the dogs from group A did not show any feature of CNS asymmetrical disease, and PSS was diagnosed according to accepted standards (6).

Generalized spikes or sharp waves may occur in toxic-metabolic encephalopathy, with a background of widespread bisynchronous and asynchronous slow waves (8). Occasionally, the appearance of generalized epileptiform activity is seen in repeated and regular intervals and may form complexes resembling spike-and-wave discharges. Paroxysmal discharges of spikes and sharp waves together with a background activity of generalised synchronic or asynchronic slow waves were described in human electroencephalography (7), and may resemble the decrease in intracortical inhibition due to the presence of neurotoxic compounds in the brain of PSS patients (6, 9). There are a few theories regarding the direct cause of cortical activity changes during hepatic encephalopathy, and different mechanisms have been proposed. Several neurotoxic compounds derived from intestinal degradation, such as ammonia, amino acids (especially aromatic amino acids: phenylalanine, tyrosine, and tryptophan), short-chain fatty acids, mercaptan and various biogenic amines, indoles and skatoles, have been implicated in causing HE (6). These compounds are convulsant in animals (17, 20), and may modulate cortical excitability by acting as GABA-A receptor antagonists and NMDA receptor agonists, thus shifting cortical circuitry towards greater excitability (6, 14). In this study, these compounds were not examined in the cerebro-spinal fluid.

The study shows that electroencephalography can be useful in differentiating the aetiology of seizures in dogs. The EEG features in the dogs with ME caused by PSS strongly correlated with known characteristics of the corresponding human EEG recordings.

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