ABSTRACT

The doctoral thesis titled "Electroencephalographic Research in Epilepsy of Companion Carnivores" is structured in accordance with current regulations into two parts: the first part, titled "The Current State of Knowledge," represents 20% of the entire work, while the second part, "Personal Contributions," details the results obtained during the study period and constitutes the remaining 80%. In addition to these two parts, the thesis includes a table of contents, an introduction, an abstract, a list of bibliographic sources, a list of abbreviations, a list of figures, a list of tables, and a list of publications. The thesis contains 51 figures and 5 tables and references 182 bibliographic sources.

The first chapter of the thesis begins by defining epilepsy and systematically describes the known forms of epilepsy and the variety of clinically defined epileptic seizures, as described in veterinary literature.

Chapter 2 focuses on summarizing key aspects related to the origin of EEG signals and the technical characteristics necessary for EEG acquisition, sedation protocols, electrode setups, and types of electrodes used for EEG recording, artifact detection, and data interpretation. EEG is the standard method used for investigating brain function and is particularly valuable for understanding the pathophysiology of epileptic seizures. Therefore, the information obtained from EEG plays a crucial role in confirming the diagnosis of epilepsy and assessing the effectiveness of antiepileptic treatment.

In the third chapter, the experimental setting is presented - within the Medical Clinic and Neurology service, Faculty of Veterinary Medicine, "Ion Ionescu de la Brad" University of Life Sciences, Iași. The purpose of the doctoral thesis "Electroencephalographic Research in the Epilepsy of Pet Carnivores" is to investigate the bioelectric activity using electroencephalographic techniques in epileptic dogs, both visually and quantitatively.

Chapter 4 consists of two subchapters, serving two objectives: to visually analyze the baseline activity in healthy, anesthetized dogs and to facilitate the recognition and exclusion of EEG recording artifacts, then to detect and interpret overlapping transient events (physiological graphoelements). The second subchapter aims to evaluate cerebral coherence in healthy dogs, in the context of very few

studies concerning quantitative electroencephalographic analysis in dogs, whether clinically healthy, with behavioral disorders, or encephalopathies. Moreover, in this study, we compared the interhemispheric coherence values obtained using different types of electrodes: needles and discs in dogs without neurological pathologies, without sedation or anesthesia, but in a waking state. We obtained an average coherence below 0.6 on all analyzed channels, results that might be due to the fact that EEG recordings were performed only in awake dogs. In this state, coherence does not necessarily manifest in a single frequency band but can vary across multiple bands. In our study dogs, coherence above 0.4 was observed only on frontopolar channels, especially in the delta and theta frequency bands, when EEG traces were recorded using needle electrodes, which could suggest that the recorded values might be directly related to the type of electrode used in acquisition. Since in electroencephalographic studies concerning behavior and degenerative brain diseases, particular attention is given to frontal channels, these results could have significant implications in canine neurology and applied neuroscience.

Chapter 5 combines the visual analysis of electroencephalography by thoroughly describing interictal epileptic discharges (IEDs) found in dogs with convulsive seizures under general anesthesia, with an attempt to quantify and discover certain patterns and predispositions for the manifestation of these paroxysmal transient events based on the etiology and semiology of the epileptic syndrome. Thus, EEG recordings from 62 dogs of different breeds and ages, with focal, generalized epileptiform seizures, or a history of status epilepticus, regardless of the antiepileptic medication received and diagnosed according to IVETF with idiopathic, structural, or reactive epilepsy, were included. The category of idiopathic epileptics was the most represented (n=32), followed by structural epileptics (n=20) and reactive epileptics (n=10). Following visual analysis, detection of IEDs (spikes, polyspikes, spike-wave complexes), and their quantification over at least 20 minutes of EEG recording, in dogs with idiopathic epilepsy, an average of 6.8 ± 0.825 (mean ± standard error) spike-type IEDs were quantified. Polyspikes and spike-wave complexes were fewer, with an average of 3.656±1.196 and 3±2.117 IEDs, respectively; statistical tests showed that spike-type discharges were the most frequently encountered, with recorded values for these IEDs being highly statistically significantly different from those of spike-wave ($p< 0.001$) and polyspike ($p < 0.001$) types. Interestingly, when comparing the values of polyspike and spike-wave IEDs, even though polyspikes apparently predominated, no statistical difference could be identified between them ($p = 0.171$).

In patients with structural epilepsy, the incidence of interictal epileptic discharges was higher, with an average of 15.45±4.511 spikes, 12.5±6.072 polyspikes, and 15.25±5.330 spike-wave complexes observed. As can be seen, the standard error limits are very wide, reflecting the difficulty in identifying a

characteristic pattern for structural epilepsy (possible causes can be the type and size of the lesion, the mode of pathology organization – focal/diffuse/multifocal, etc.). Given the large variation in the standard error limit, we cannot exclude reaching statistical significance in groups with a larger number of dogs with structural epilepsy or in groups formed from a homogeneous canine population in terms of lesions (e.g., structural epilepsy with exclusively tumoral or exclusively non-infectious inflammatory substrate).

EEG trace analysis in the 10 dogs with reactive epilepsy highlighted the presence of IEDs as follows: 17.9±8.055 spikes, 10.8±6.117 polyspikes, and 6.6±2.381 spike-wave complexes, with the highest standard error recordings. Similar to structural epilepsy, for this group of patients, standard error values varied widely. Being the expression of a functional neuronal alteration and not the presence of a lesion in the brain parenchyma, this variation may depend on the type and stage of the primary disease, the medication used, etc.

The highest IED values were obtained in patients with a history of status epilepticus (n=13): 16.076±6.258 spikes, 11.692±4.979 polyspikes, and 16.923±6.955 spike-wave complexes. This observation reflects that even if the patient has exited visible convulsive activity, if the seizure is prolonged (in this case, status epilepticus), the brain's bioelectric activity remains altered for a long period.

Another conclusion that could be important and useful for diagnosing patients with idiopathic epilepsy is that through data correlation (even in the absence of demonstrating direct causality), the presence of only spikes on a short-term EEG recording in a patient with epileptic symptoms, negative for other diagnostic tests, is sufficient for diagnosing idiopathic epilepsy.

The study constituting chapter 6 of this thesis describes a new type of epileptic activity in a Bichon dog with symptoms clinically mimicking CIHTS. This syndrome represents a benign condition characterized by episodic, uncontrolled, horizontal ("no-no"), vertical ("yes-yes"), or rotational head movements in dogs; it affects young adults, occurs when a dog is at rest, and stops upon applying a stimulus. This condition could be an expression of partial epilepsy. To date, there are a limited number of idiopathic head tremor cases where an electroencephalographic recording has been performed.

In this study, we describe a dog with clinical symptoms of idiopathic head tremor, in which a new pattern of interictal epileptic discharges was identified, represented by a rhythmic brain activity consisting of high-voltage (up to 400 volts) spike-wave complexes, with a very low frequency (1.5-2 Hertz) that coincided with the "yes-yes" movements described in the anamnesis. These types of discharges are encountered in human epileptology as specific graphoelements for absence seizures, such as the Lennox-Gastaut syndrome, manifested by moments of disconnection from the environment and cognitive deficits.

Another clue that this manifestation represents a new type of epileptic syndrome is the favorable response to anticonvulsant therapy with Phenobarbital for more than 2 years, during which the patient was under our observation.

This study contributes to the sparse literature on idiopathic head tremor syndrome in dogs and the possibility that affected patients may actually be epileptic, developing partial motor seizures, electroencephalographically similar to the Lennox-Gastaut syndrome in humans.