Electroencephalographic studies in dogs and cats

Thesis
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Electroencephalographic recordings in dogs suffering from idiopathic and symptomatic
epilepsy: diagnostic value of interictal short time EEG protocols supplemented by two
activation techniques. Submitted.

Paroxysmal discharges and photic driving in the electroencephalogram of healthy and
diseased cats under propofol anesthesia. Submitted.

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Department of Science and Culture, Lower Saxony, Germany
To my family
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Chapter 1: General Introduction

Epilepsy is one of the most frequent neurological diseases in dogs and cats (Berendt, 2004). An epileptic seizure is characterized by excessive and/or hypersynchronous and usually self-limited activity of neurons in the brain (Blume et al., 2001). De Lahunta and Glass (2009) differentiate focal, partial and generalised seizures. Whereas focal seizures are without spread and only visible in the EEG, partial and generalized seizures are clinical entities (de Lahunta and Glass, 2009). Partial seizures affect only a part of one cerebral hemisphere (Blume et al., 2001). Simple and complex partial seizures are discriminated by the disturbance of the patient’s sensorium (de Lahunta and Glass, 2009). A generalised seizure is characterised through the involvement of both cerebral hemispheres (Blume et al., 2001).

Epilepsy is defined as a status of recurrent seizures (Berendt, 2004). Etiologically, three different forms of epilepsy or seizures can be differentiated: idiopathic or primary epilepsy, symptomatic or secondary epilepsy and reactive seizures (March, 1998). During a cluster two or more seizures occur within a 24 hour time span (de Lahunta and Glass, 2009). A seizure of 30 minutes or longer duration or recurrent seizures without interictal resumption of baseline central nervous system function are called status epilepticus (Blume et al., 2001; Podell, 1996).

Idiopathic or primary epilepsy is characterised by recurrent, unprovoked seizures without any underlying structural brain disease (for example tumour or encephalitis) and lack of interictal abnormalities (Knowles, 1998; Podell et al., 1995; Thomas, 2010). The prevalence for idiopathic epilepsy is estimated to be around 0.5-5.0 % in
dogs (Berendt, 2004) and 0.5 % in cats (Schwartz-Porsche, 1994). Familial predisposition or different modes of inheritance have been suggested for different breeds as Beagle (Bielfelt et al., 1971), Belgian Tervueren (Oerbauer et al., 2003; van der Velden, 1968), Keeshound (Hall and Wallace, 1996; Wallace, 1975), Vizsla (Patterson et al., 2003), Labrador Retriever (Berendt et al., 2002; Jaggy et al., 1998) and Golden Retriever (Srenk and Jaggy, 1996). Although the first seizure can occur between six month and ten years of age (Thomas, 2010), most dogs suffer from their first seizure, when they are one to five years old (Podell et al., 1995). Due to the fact, that no underlying cause can be found, idiopathic epilepsy is a diagnosis of exclusion (de Lahunta and Glass, 2009; Thomas, 2010). If an animal is particularly young or old and an underlying disease is likely but not proven, the term cryptogenic epilepsy or probable symptomatic epilepsy can be used (Berendt and Gram, 1999; Podell, 2004).

Symptomatic or secondary epilepsy is diagnosed when seizures result from a structural cerebral lesion (March, 1998; Podell et al., 1995). Intracranial causes of seizures can be congenital structural brain diseases, central nervous system (CNS) inflammatory or infectious diseases, intracranial neoplasia, vascular events, acquired structural abnormalities through traumata or degenerative diseases (Podell, 2004).

Reactive seizures can be caused by many different toxins and nearly any disturbance of the metabolism (Brauer et al., 2009) such as hypoglycaemia, hypoxia, hyperosmolality, electrolyte imbalances, hepatic failure and renal failure (O'Brien, 1998).
Dogs and cats that suffer from idiopathic epilepsy can be treated with a small number of antiepileptic drugs (AEDs), of which all but phenobarbital for dogs, have to be rededicated from human medicine for their use in dogs and cats in Germany. Treatment of idiopathic epilepsy should be started when an animal experienced two or more generalised seizures during a six-month-period (Podell, 2004). Phenobarbital, potassium bromide, diazepam (long-time treatment in the cat only) felbamate, gabapentin, zonisamide and levetiracetam are the most frequently used AEDs in veterinary medicine (Potschka et al., 2009).

Dogs suffering from symptomatic epilepsy should be treated aetiologically and, in addition, the seizures themselves should be controlled with anti-epileptic drugs (de Lahunta and Glass, 2009).

It is essential to do an adequate diagnostic investigation of the patient in order to determine the origin of the seizure disorder and to optimise the treatment, which can differ significantly according to the underlying disease (Podell, 1998). It is of major importance to gather the exact history of the patient together with the owner, to do a precise clinical and neurological examination and to thoroughly analyse the patient’s blood for any underlying metabolic disorder. If necessary, further examinations in general anaesthesia have to follow; in particular electroencephalography (EEG), magnetic resonance imaging (MRI) of the brain and cerebrospinal fluid (CSF) analysis (Berendt, 2004).

The EEG has been introduced as a clinical neurological test by Hans Berger at the beginning of the 20th century (Brazier, 2005). The first reports and clinical studies on its use in veterinary medicine came up about 30 years later (Croft, 1962; Fox and
Stone, 1967; Klemm, 1965; Redding, 1964). These mainly focused on animal restraint and technical realisation of EEG in animals and concentrated on dogs. Soon, researches started to record EEGs in dogs and cats only under sedation or general anaesthesia with different anaesthetics, because interpretation of the EEG recordings of conscious animals was often hindered by movement and/or muscle artefacts (Gustafson Beaver and Klemm, 1973). Until the invention of newer imaging techniques as computed tomography (CT) and MRI and introduction of these techniques to veterinary medicine, diagnosis of neurological diseases of the brain often relied on the physical and neurological examination, blood work, CSF tap and EEG (Knecht et al., 1983). In patients with symptomatic epilepsy, CT and MRI improved the pre-mortem diagnosis of structural abnormalities (Podell, 1996) and in patients in which an idiopathic epilepsy is assumed, these techniques can be used to show that no underlying disease can be detected (Thomas, 2010). Due to the widespread acceptance and availability of CT and MRI in veterinary medicine and the fact that until now no universal EEG recording procedure has been found, EEG has become less important in veterinary seizure diagnostics. A survey showed, that nowadays only a few veterinary colleges or private referral practices record EEGs at all (Steiss, 1988) although EEG can be valuable in confirming the diagnosis of canine epilepsy (Berendt et al., 1999). This is especially interesting, when it is not possible to gather a conclusive description of the seizure through the owner or when a complex partial seizure can be mistaken for a syncope (Penning et al., 2009) or a movement disorder (Kube et al., 2006).
Activation techniques are commonly used in human medicine to enhance the diagnostic value of routine EEGs (Mendez and Brenner, 2006). Most often, photic stimulation, hyperventilation, sleep and sleep deprivation are used (Aminoff, 2005; Angus-Leppan, 2007; Mendez and Brenner, 2006). In a retrospective study on 1000 EEGs, activation techniques made a unique diagnostic contribution to prior normal routine EEG in 11% of all patients (Angus-Leppan, 2007). So far, no systematic studies on the use of activation techniques, especially photic stimulation and hyperventilation, during EEG recording have been conducted in veterinary medicine using the same anaesthetic protocol for healthy as well as diseased animals.

Therefore, the aims of this study were to establish a short time EEG recording protocol using the same anaesthetic protocol for healthy and diseased dogs and cats and to determine the diagnostic value of these short time EEG protocols. Special emphasis was taken on the additional use of the muscle relaxant rocuronium bromide to the general anaesthesia with propofol in order to abolish any muscle artefact that would hinder the interpretation of the recorded EEGs and to be able to keep the propofol anaesthesia as light as possible. Furthermore, the benefit of two activation techniques, photic stimulation and hyperventilation, was evaluated for their use in dogs and cats.
Chapter 2: Electroencephalographic recordings in dogs: prevention of muscle artifacts and evaluation of two activation techniques in healthy individuals

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Chapter 3: Electroencephalographic recordings in dogs suffering from idiopathic and symptomatic epilepsy: diagnostic value of interictal short time EEG protocols supplemented by two activation techniques

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3.1 Abstract

In the current study the diagnostic value of short time electroencephalographic (EEG) recordings in epileptic dogs under general anaesthesia with propofol and the muscle relaxant rocuronium bromide was investigated. Two activation techniques, photic stimulation and hyperventilation, were evaluated for their potential to enhance the diagnostic validity of these recordings. Sixty-one dogs suffering from idiopathic and 28 dogs suffering from symptomatic epilepsy were included in the study. Electroencephalograms were recorded using five subdermal EEG electrodes (F3, F4, Cz, O1 and O2). All 89 EEGs were analysed visually, and in addition, 61 of them quantitatively with fast Fourier transformation. Interictal paroxysmal epileptiform activity was found in 25 % of idiopathic and in 29 % of symptomatic epileptic dogs. Quantitative analysis of the EEGs (qEEGs) detected significant differences of frequency analysis in single reading points without any continuous changes of frequency bands. A comparison between healthy and affected brain hemisphere in seven dogs with focal lesions of one hemisphere did not show any significant differences in qEEG analysis. Quantitative EEG analysis was not more sensitive than visual evaluation.

Despite the use of activation techniques, the results of this study show that short time EEG recordings in epileptic dogs can detect interictal epileptic activity in less than one third of all seizuring dogs and is not considered to be a useful screening method.
Keywords: hyperventilation; photic stimulation; propofol; qEEG; rocuronium bromide; seizures
3.2 Introduction

Epilepsy is one of the most common neurological diseases in dogs (Berendt, 2004; Fluehmann et al., 2006). Therefore, electroencephalography (EEG) has been an important diagnostic tool to examine animals with seizures since the early 1960s (Croft, 1962) and a wide variety of reports dealing with different aspects of EEG recording and interpretation have been published in the last five decades.

In veterinary medicine, diagnosis, prognosis and treatment options for epileptic patients were based on physical and neurological examinations, blood work, cerebrospinal fluid (CSF) taps and EEG evaluation (Knecht et al., 1983) until invention and introduction of newer imaging techniques as computed tomography (CT) and magnetic resonance imaging (MRI). Computed tomography and MRI examination of an epileptic patient improved the diagnosis of symptomatic epilepsy since morphological changes can be visualized by these methods (Podell, 1996). In patients with presumptive idiopathic or cryptogenic epilepsy these imaging techniques can be used to show that no underlying macroscopic structural aetiology can be detected (Thomas, 2010). On the other hand, EEG can be valuable in confirming the diagnosis of canine epilepsy (Berendt et al., 1999) which is of special interest when the seizure description of the owners is not conclusive or complex focal seizures cannot be distinguished from a movement disorder (Kube et al., 2006) or a syncope (Penning et al., 2009). In a study by Jaggy and Bernardini (1998) EEG was capable of localising the seizure focus in 35 % (13/37) of epileptic dogs.

About 20 to 50 % of human epilepsy patients show interictal epileptiform discharges on their first routine EEG (Glick, 2002). Results of EEG investigation vary even more
widely in veterinary medicine. In 20-86% of dogs with seizures, interictal EEG changes can be found (Holliday et al., 1970; Jaggy and Bernardini, 1998; Berendt et al., 1999; Jeserevics et al., 2007).

Since most dogs with seizures do not only undergo EEG recording in general anaesthesia but also MRI and CSF examination, the goal of the current study was to evaluate the diagnostic value of a short time EEG protocol (approximately 15-20 minutes recording time) in epileptic dogs. In this protocol the diagnostic value should be enhanced by the systematic use of two different activation techniques. Such a short protocol could be used routinely as a screening method for seizing dogs or to differentiate complex focal seizures from seizure-like phenomena as movement disorders or syncope.

3.3 Materials and Methods

3.3.1 Dogs

Electroencephalograms of 61 dogs suffering from idiopathic or cryptogenic and 28 dogs suffering from symptomatic epilepsy were recorded in this study. All dogs had a history of generalised seizures, albeit it cannot be excluded that some of them had a focal origin.

Idiopathic epilepsy was diagnosed when no underlying disease capable of inducing seizures was detected based on clinical and neurological examinations as well as routine blood work (complete blood cell count, serum biochemistry) and radiographs. Magnetic resonance imaging (Magnetom Impact Plus, 1.0 Tesla, Siemens) in dogs
EEG in epileptic dogs

suffering from idiopathic/cryptogenic epilepsy did not show any abnormalities and CSF tap results were within reference ranges. In this group dogs from 35 different breeds were examined, of which mixed breed dogs (11), Labrador (5) and Golden Retriever (4) were the most common. There were 27 sexually intact males, 16 neutered males, ten sexually intact females and six spayed females in this group. The mean age was 52 months (range 5-154 months) and the mean weight 23.6 kg (range 6.6-62.0 kg). Thirty-five dogs had not received any anti-convulsive treatment prior to EEG recording, 19 dogs were pre-treated with phenobarbital and 7 dogs with a combination-therapy of phenobarbital and potassium bromide (Tab. 3.1).

<table>
<thead>
<tr>
<th>Subdivisions and number of dogs for visual analysis</th>
<th>Subdivisions and number of dogs for qEEG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without treatment: 35</td>
<td>Without treatment: 28</td>
</tr>
<tr>
<td>With phenobarbital: 19</td>
<td>With phenobarbital: 13</td>
</tr>
<tr>
<td>With phenobarbital + potassium bromide: 7</td>
<td>With phenobarbital + potassium bromide: 4</td>
</tr>
</tbody>
</table>

Tab. 3.1: Study groups for visual and quantitative EEG analysis

Symptomatic epilepsy due to intracranial diseases was diagnosed when abnormalities were found in MR imaging of the brain and/or CSF tap results. Additionally, diagnoses were confirmed with necropsies or histopathologic examination in seven of these dogs. This group comprised 10 intact male, 5 neutered male, 11 intact female and 2 spayed female dogs. Boxer (4 dogs), Jack Russell Terrier, Dachshunds and Pug dogs (each breed 3 dogs) were the most common breeds presented with symptomatic seizures. Mean age and weight of these dogs was 81 months (range 5-194 months) and 19.9 kg (range 2.3-45.0 kg), respectively.
Eleven dogs suffered from diffuse intracranial diseases (e.g. hydrocephalus, encephalitis, meningoencephalitis), nine dogs had lesions in the right cerebral hemisphere, six dogs in the left cerebral hemisphere, and two dogs had centrally located lesions (Tab. 3.1). Localized lesions were identified as (presumptive) neoplasia, suspected ischemic lesions and cysts.

3.3.2 Anaesthetic protocol

Anaesthesia was induced with propofol (mean dose 6.54 mg/kg (range 2.68-13.21 mg/kg); Narcofol®, CP-Pharma Handelsgesellschaft mbH) given intravenously (IV) via an intravenous catheter until endotracheal intubation was possible. Propofol anaesthesia was held at a light plane with a constant rate infusion (CRI) at a mean dose of 0.36 mg/kg/min (range 0.17-0.6 mg/kg/min) determined by the absence of the swallowing reflex and purposeful movements. After intubation, oxygen was delivered via a small animal rebreathing system. In addition to propofol CRI, lactated Ringer’s solution (Sterofundin®, B.Braun Melsungen AG) was administered IV at a rate of 10 mL/kg/h. Dogs were placed in sternal recumbency.

The end-tidal carbon dioxide (EtCO₂) tension, the peripheral oxygen saturation of haemoglobin (S₉O₂) and the pulse rate were constantly measured with a side-stream capnograph and a pulse oximeter clip attached to the tongue and observed on a patient monitor (OxiMax NPB75, Nellcor Puritan Bennett Inc.). After achieving a stable plane of anaesthesia, all but one dog received the peripheral muscle relaxant rocuronium bromide (Esmeron® 10 mg/ml, N. V. Organon) at a mean dose of 0.4
mg/kg IV (range 0.2-0.8 mg/kg) to prevent electromyographic artefacts in the EEG readings as described before (Brauer et al., 2010).

3.3.3 EEG recordings

EEGs were obtained via five subdermal needle electrodes (F3, F4, Cz, O1 and O2; disposable subdermal stainless steel EEG needle, Viasys Healthcare Inc.) as described by Redding (1978). The reference electrode was placed on the bridge of the nose and the ground electrode right caudal to the occipital protuberance. Two subdermal needle electrodes were used to record a lead II electrocardiogram. The EEG (NicoletOne nEEG, Viasys Healthcare Inc.) was recorded with sensitivity = 70µV/cm; time constant = 0.3 seconds; Hf = 70 Hz; Lf = 0.5 Hz; notch filter inserted; impedance of all electrodes < 10 kΩ.

Two activation techniques were used during EEG recording. After obtaining baseline data without any activation, a photic stimulation with a photic stimulator (Photic stimulator, Viasys Healthcare Inc.) placed approximately 20 cm in front of the closed eyes was carried out. The flash frequency was gradually increased in steps of 5 Hz from 5 to 50 Hz and then decreased in the same way. Each flash interval was applied for 8 seconds and followed by a pause of 5 seconds until the next flash interval started. After a stimulation free interval, hyperventilation was started in order to reduce the EtCO₂ tension until a mean value of 24 mmHg (range 18-31 mmHg) was reached in a mean of 231 seconds (range 180-512 seconds). Post hyperventilation EEG recordings lasted for another three minutes.
3.3.4 Visual examination of the EEGs

Monopolar and bipolar montages were used for visual examination of all EEGs. Paroxysmal epileptic activities (e.g., spikes, spike-wave discharges) as well as possible artefacts were determined visually. Background activity was analysed visually for any detectable change during the recording procedure.

3.3.5 Quantitative analysis

Quantitative EEG (qEEG) analysis was performed with monopolar montages. Recordings were divided into the following sections: pre-stimulation phase, photic stimulation (increasing) of 5 Hz, 10 Hz, 15 Hz, 20 Hz, 25 Hz, 30 Hz, 35 Hz, 40 Hz, 45 Hz and 50 Hz, photic stimulation (decreasing) of 45 Hz, 40 Hz, 35 Hz, 30 Hz, 25 Hz, 20 Hz, 15 Hz, 10 Hz and 5 Hz, inter-stimulation phase, beginning of hyperventilation (HV1), middle of hyperventilation (HV2), end of hyperventilation (HV3), beginning of post-hyperventilation (pHV1), middle of post-hyperventilation (pHV2) and end of post-hyperventilation (pHV3). Two to ten two-second artefact free periods of every recording section were visually selected for analysis of background activity using Fast Fourier Transformation (FFT). Spectral bands were 0.5-4.0 Hz for delta, 4.0-8.0 for theta, 8.0-13.0 Hz for alpha and 13.0-30.0 Hz for beta activity. In order to minimize errors through different skull sizes, forms and thicknesses, the relative power of the spectral bands was calculated for every lead and averaged for different study groups.
3.3.6 Statistical analysis

Data of background analysis were compared to prior obtained healthy reference values from our EEG laboratory (Brauer et al., 2010). For statistical analysis of qEEG data, dogs were divided into the following groups: (1) dogs suffering from idiopathic epilepsy without antiepileptic treatment (n=28), (2) dogs suffering from idiopathic epilepsy under phenobarbital treatment (n=13), (3) dogs suffering from idiopathic epilepsy under treatment with phenobarbital and potassium bromide (n=4), (4) dogs suffering from symptomatic epilepsy with diffuse intracranial lesions and (n=9), (5) dogs suffering from symptomatic epilepsy suffering from focal lesions of either the left or right hemisphere (n=7). Goodness of fit for normal distribution of model residuals of all parameters was rejected by visual assessment of normal probability plots and the Kolmogorov-Smirnov test, i.e. data was neither normally nor lognormally distributed. For that nonparametric methods were used for examination of data. Independent samples of relative power values of the spectral bands of the first four groups were compared to healthy reference values by the Wilcoxon Two-Sample Test stratified by lead and event. In the group with repeated measurements of focal lesions of the right or left brain hemisphere, data of the healthy hemispheres were compared to the affected hemispheres with Friedman’s Chi-Square Test (Cochran-Mantel-Haenszel Statistics). Results were considered significant if \( p < 0.05 \). Analysis were carried out with the statistical software SAS, version 9.1 (SAS Institute, Cary, NC).
3.4 Results

3.4.1 Visual analysis

Theta and delta activity dominated the background activity of the EEG and was superimposed by faster alpha and beta activity. There was no visible change in background activity between periods with either photic stimulation or hyperventilation and periods without any stimulation.

Interictal paroxysmal activity occurred in 15 dogs (25 %) suffering from idiopathic epilepsy (Tab. 3.2) and consisted of single spikes, polyspikes and spike slow wave-complexes (Fig. 3.1, Fig. 3.2). Eight dogs (29 %) suffering from symptomatic epilepsy had visible abnormalities in their EEGs (Tab. 3.1, Fig. 3.3, Fig. 3.4). No sudden onset of paroxysmal activity during the application of both activation techniques occurred in any of these dogs.

Fig. 3.1: Eight channel bipolar montage.
Focal spike. Dog no. 9 (Tab. 3.2) suffering from idiopathic epilepsy.
Tab. 3.2: Dogs with abnormal EEG recordings and their final diagnosis based on MRI, CSF examination and/or histopathology.

<table>
<thead>
<tr>
<th>No.</th>
<th>Breed</th>
<th>Sex</th>
<th>Age (months)</th>
<th>Antiepileptic medication</th>
<th>EEG abnormalities</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mixed Breed</td>
<td>mn^a</td>
<td>36</td>
<td>-</td>
<td>1 left frontal spike</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>2</td>
<td>Small Munsterlande r</td>
<td>fn^b</td>
<td>65</td>
<td>-</td>
<td>3 frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td></td>
<td>Dogue de Bordeaux</td>
<td>f^c</td>
<td>6</td>
<td>-</td>
<td>2 right frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>4</td>
<td>Mixed Breed</td>
<td>m^d</td>
<td>25</td>
<td>-</td>
<td>6 right frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>5</td>
<td>Mixed Breed</td>
<td>mn</td>
<td>51</td>
<td>-</td>
<td>right frontal polyspikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>6</td>
<td>Border Terrier</td>
<td>M</td>
<td>58</td>
<td>-</td>
<td>2 spike-wave complexes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>7</td>
<td>Mixed Breed</td>
<td>mn</td>
<td>38</td>
<td>-</td>
<td>2 frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>8</td>
<td>Labrador Retriever</td>
<td>F</td>
<td>5</td>
<td>-</td>
<td>frontal polyspikes and isolated spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>9</td>
<td>Labrador Retriever</td>
<td>M</td>
<td>20</td>
<td>-</td>
<td>1 occipital spike</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>10</td>
<td>Mixed Breed</td>
<td>mn</td>
<td>30</td>
<td>-</td>
<td>1 frontal spike</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>11</td>
<td>Jack Russell Terrier</td>
<td>F</td>
<td>70</td>
<td>phenobarbital</td>
<td>1 right frontal spike</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>12</td>
<td>Cocker Spaniel</td>
<td>F</td>
<td>20</td>
<td>phenobarbital</td>
<td>2 frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>13</td>
<td>Jack Russell Terrier</td>
<td>F</td>
<td>18</td>
<td>phenobarbital</td>
<td>frontal polyspikes and isolated spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>14</td>
<td>Briard</td>
<td>M</td>
<td>20</td>
<td>phenobarbital</td>
<td>9 right frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>15</td>
<td>Tibet Terrier</td>
<td>Fn</td>
<td>72</td>
<td>phenobarbital; potassium bromide</td>
<td>6 frontal spikes</td>
<td>idiopathic epilepsy</td>
</tr>
<tr>
<td>16</td>
<td>Wire-haired Dachshund</td>
<td>F</td>
<td>126</td>
<td>phenobarbital</td>
<td>1 generalised spike</td>
<td>meningoima</td>
</tr>
<tr>
<td>17</td>
<td>Jack Russell Terrier</td>
<td>F</td>
<td>66</td>
<td>-</td>
<td>frontal polyspikes</td>
<td>presumptive neoplasia</td>
</tr>
<tr>
<td>18</td>
<td>Yorkshire Terrier</td>
<td>Fn</td>
<td>25</td>
<td>phenobarbital</td>
<td>right frontal spikes</td>
<td>hydrocephalus internus, syringohydromegaly, atlantoaxial instability</td>
</tr>
<tr>
<td>19</td>
<td>Jack Russell Terrier</td>
<td>M</td>
<td>103</td>
<td>-</td>
<td>20 occipital spikes</td>
<td>hydrocephalus ex vacuo</td>
</tr>
<tr>
<td>20</td>
<td>Wire-haired Dachshund</td>
<td>M</td>
<td>118</td>
<td>-</td>
<td>left frontal spikes</td>
<td>Presumptive meningitis, mild herniation of the cerebellum</td>
</tr>
<tr>
<td>21</td>
<td>Cairn Terrier</td>
<td>M</td>
<td>48</td>
<td>phenobarbital</td>
<td>13 left frontal spikes</td>
<td>mild focal lymphohistiocytic meningitis, presumptive encephalitis</td>
</tr>
<tr>
<td>22</td>
<td>West Highland White Terrier</td>
<td>M</td>
<td>5</td>
<td>-</td>
<td>right frontal polyspikes and single spikes</td>
<td>mild hydrocephalus with increased intracranial pressure</td>
</tr>
<tr>
<td>23</td>
<td>Jack Russell Terrier</td>
<td>Mn</td>
<td>105</td>
<td>-</td>
<td>20 left frontal spikes</td>
<td>moderate hydrocephalus with increased intracranial pressure, occipital malformation</td>
</tr>
</tbody>
</table>

^a neutered male; ^b neutered female; ^c intact female; ^d intact male
Fig. 3.2: Eight channel bipolar montage.
Spike-wave complex. Dog no. 6 (Tab. 3.2) suffering from idiopathic epilepsy.

Fig. 3.3: Eight channel bipolar montage.
Spikes. Dog no. 20 (Tab. 3.2) suffering from a presumptive meningitis and mild herniation of the cerebellum.
Fig. 3.4: Eight channel bipolar montage. Polyspikes. Dog no. 22 (Tab. 3.2) suffering from a mild hydrocephalus and increased intracranial pressure.

3.4.2 Quantitative analysis

EEGs of 45 dogs (28 without treatment, 13 receiving phenobarbital, 4 receiving phenobarbital and potassium bromide) suffering from idiopathic epilepsy, 9 EEGs of dogs suffering from symptomatic epilepsy with diffuse intracranial lesions and 7 EEGs of dogs with lesions in the right or left hemisphere underwent quantitative analysis with FFT. In the other dogs the occurrence of artefacts prevented a complete qEEG analysis.

All EEGs showed prevalence for slow delta rhythms in every derivation. There were no continuous significant changes between qEEG data of dogs suffering from both idiopathic (Fig. 3.5) or symptomatic epilepsy and healthy reference values. A comparison between affected brain hemisphere and healthy hemisphere in dogs with
lesions in only one hemisphere did not show any significant differences between healthy and affected hemisphere (Fig. 3.6).

Fig. 3.5: Relative power values of the Cz electrode.
Relative power values of the Cz electrode (Median) of healthy controls compared to 28 dogs suffering from idiopathic epilepsy (IE) without any anti-epileptic treatment (IE without treatment), 13 dogs suffering from IE under treatment with phenobarbital (IE + pheno) and 4 dogs suffering from IE under treatment with phenobarbital and potassium bromide (IE + pheno + pb). Significant differences were detected at single reading points but without showing any tendency for a continuous change:

delta activity:  IE without treatment: pause (p=0.035)
theta activity:  IE without treatment: a35Hz (p=0.045)
               IE + pheno + pb: b40Hz (p=0.02)
alpha activity:  IE without treatment: b45Hz (p=0.035)
                IE + pheno: a45Hz (p=0.017)
                IE + pheno + pb: b10Hz (p=0.04)
beta activity:   IE + pheno: a45Hz (p=0.032)
               IE + pheno: a50Hz (0.044)
               IE + pheno + pb: b15Hz (p=0.04)
3.5 Discussion

EEG has played a major role in veterinary medicine for further examination of the brain until newer imaging techniques as computed tomography and MRI were established (Podell, 1996). Routine examinations of the brain function with EEG have been done for more than 40 years (Fox and Stone, 1967). Since the early beginning of EEG recording, researchers have investigated different recording techniques and anaesthetic protocols in order to increase the value of EEG recording in dogs. The latest publications from Bergamasco et al. (2003), Pellegrino and Sica (2004) and Jeresevics et al. (2007) focussed on the problem of animal restraint, number of
recording electrodes and qEEG analysis. Yet, no universal EEG recording protocol was found which could be used routinely at every recording facility around the world.

By now there are only few veterinary colleges or private referral practices which are recording EEGs at all (Steiss, 1988). On the other hand, there is still a demand for EEG recording in veterinary medicine, especially when the diagnosis of epilepsy is doubtful or research on new antiepileptic drugs is performed.

In the current study we wanted to shorten the EEG recording time and therefore the concomitant anaesthesia in epileptic dogs to a minimum and to enhance the diagnostic value of this shortened EEG through adding standardised activation techniques to the recording protocol. The aim was the development of a protocol which can be used in a routine manner. With this protocol interictal abnormalities consistent with epilepsy were found in 15 (25 %) dogs suffering from idiopathic epilepsy and in eight (29 %) dogs suffering from symptomatic epilepsy. Occurrence of interictal paroxysmal epileptiform activity in the EEGs of dogs shows wide variance in the literature. In a study evaluating dogs suffering from idiopathic epilepsy, 20 % of the study population had paroxysmal epileptiform activity in their EEGs (Jeserevics et al., 2007). Epileptiform activity occurred in 9 of 23 investigated dogs (39 %) and abnormal EEG activity in 65 % of the study population which was composed of dogs without extracranial or inflammatory brain diseases (Berendt et al., 1999). Holliday et al. (1970) found abnormalities in the EEGs of 71 % of all investigated dogs with recurrent seizures whereas Jaggy and Bernadini (1998) obtained consistent and characteristic findings in 86 % of the interictal EEGs in dogs with idiopathic epilepsy.
In dogs suffering from intracranial mass lesions, paroxysmal discharges were not detected in the EEGs of six dogs that had clinical seizures (Steiss et al., 1990).

Manifold reasons are feasible for not obtaining more EEGs with interictal paroxysmal discharges in the present study although human studies evaluated, that only up to 50% of human epilepsy patients have interictal paroxysmal discharges on their first routine EEG (Glick, 2002). Anatomical differences between humans and dogs can explain these low numbers. Whereas the human skull is not covered by muscles at most points of EEG recording, the skull of dogs is nearly completely covered by masticatory muscles leading to a larger distance between recording electrode and epileptic discharge resulting in lower amplitudes and possible masking of paroxysmal discharges. On the other hand, using more recording electrodes could cover more of the brain’s electrical activity. Pellegrino and Sica (2004) described a standardized recording protocol using 12 electrodes including two temporalis electrodes going through the temporalis musculature and with direct contact to the skull. Such electrodes were not used in the current study with patients due to the possible damage of blood vessels and nerves by inserting the electrodes (Pellegrino and Sica, 2004).

In human medicine, activation techniques are widely used (Mendez and Brenner, 2006) and it has been shown that they are able to make a diagnostic contribution in 11% of patients with normal routine EEGs (Angus-Leppan, 2007). Since the dog is a valuable translational animal model to study seizures and many common features are described (Berendt and Gram, 1999), the current study aimed to enhance the knowledge in this specific field of comparative medicine. However, the described
activation techniques were not able to numerically enhance the interictal occurrence of paroxysmal activity in the short time protocol.

In human medicine, responses to photic stimulation are described as either normal (no change of EEG rhythms, photic driving) or abnormal (photo-paroxysmal response; Angus-Leppan, 2007). A photo-paroxysmal response is characterized by the occurrence of spike-slow wave and polyspike-slow wave complexes in coherence with the photic stimulation (Mendez and Brenner, 2006). How these abnormalities due to photic stimulation are produced in the human EEG is still unknown (Aminoff, 2005).

In veterinary medicine, photic stimulation has been used before by Holliday et al. (1970) and Goiz-Marquez et al. (2009) to improve the diagnostic value of the EEG. Goiz-Marquez et al. (2009) do not mention if there were more paroxysmal discharges under photic stimulation over 30 seconds and an unspecified flash frequency. Holliday et al. (1970) added photic stimulation at flash rates of 5-25 Hz each for 30-40 seconds to the recording protocols of 13 dogs. In seven of these dogs paroxysmal activity was more common under this activation technique. These different results may be due to different methods of animal restraint. Holliday et al. (1970) just fixed the dogs on a table with adhesive band whereas Goiz-Marquez et al. (2009) used general anaesthesia with propofol in combination with xylazine. In the current study propofol in combination with the muscle relaxant rocuronium (Brauer et al., 2010) was applied. Pharmacological depression of the visual cortex may be an explanation for not attaining more paroxysmal discharges through photic stimulation in epileptic dogs under propofol anaesthesia. Albeit, it has been shown that recording of visual
evoked potentials in dogs was hindered by propofol (Krause, 2003), propofol was chosen in the current study because it is widely used in veterinary studies (Accatino et al., 1997) and has proconvulsive activity (Löscher, 2009). In addition, with propofol the highest number of dogs displaying interictal discharges was found (Jaggy and Bernardini, 1998).

Hyperventilation has not been described before as routinely used activation technique in veterinary medicine. In our protocol dogs were hyperventilated for at least three minutes as recommended by the International League Against Epilepsy (Flink et al., 2002). During our hyperventilation procedure the EtCO2 tension could be measured continuously and a mean value of 24 mmHg (range 18-31 mmHg) was reached. Hyperventilation can lead to a slowing of the background activity in human patients which is considered abnormal when it persists after cessation of the procedure (Aminoff, 2005). It is more effective in patients with generalized seizures and may lead to the occurrence of interictal discharges and can lead to seizures in these patients (Mendez and Brenner, 2006). Although only patients with generalized seizures were investigated in our study, we could not provoke any sudden onset of paroxysmal discharges with our hyperventilation procedure. This may be due to the fact that the dogs were under general anaesthesia, though the level of anaesthesia was kept as light as possible. A slowing of the background activity, respectively a change in the qEEG analysis, could have been masked by the overall slowing of the EEG activity through anaesthesia. On the other hand, non pharmacologic hyperventilation of a dog is not possible without general anaesthesia.
Interictal EEG recording is an essential part of the pre-operative assessment of human epilepsy surgery candidates (Kuzniecky and Devinsky, 2007). Epilepsy surgery has been shown to have a beneficial effect in cases of medically uncontrolled human epilepsy patients (Kuzniecky and Devinsky, 2007) as it is four times more likely as medical treatment alone to transform drug resistance into full drug response (Schmidt and Stavem, 2009). Unfortunately, epilepsy surgery has not been used for treatment of drug-resistant epileptic dogs so far but it may be an option (Bagley et al., 1996), when the pre-operative assessment could be improved and epileptic foci identified (Berendt, 2004). Unfortunately, our results in a large number of dogs show that short time interictal EEG recording under general anaesthesia with propofol is only capable to deliver information concerning the seizure focus in a limited number of patients. Therefore, future research in this field should concentrate on modifications of the mode of restraint, use of other activation techniques (e. g. pharmacological activation with ketamine or chlorpromazine) during EEG recording and particularly on other methods to determine the seizure focus (e. g. intracranial electrodes combined with video EEG monitoring, positron emission tomography, single photon emission computed tomography, magnetoencephalography).

All investigated dogs in the current study underwent further diagnostic procedures such as MRI and/or CSF examination. Final diagnoses or presumptive diagnoses in cases of symptomatic epilepsy without pathological examinations were based on these further procedures and/or pathological examinations. In all of these cases EEG recording did not have an impact on any decision concerning prognosis and treatment for the patient.
Conclusions

In the present study the diagnostic value of short time EEG recording using two activation techniques in a large number of epileptic dogs was evaluated. In about 25% of the dogs interictal discharges occurred. This number could not be enlarged by the systematic use of photic stimulation or hyperventilation. Quantitative EEG analysis was not more sensitive than visual evaluation. Therefore, we do only recommend EEG recording in dogs suffering from atypical seizure like phenomena and not for the systematic search of a seizure focus.

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3.7 Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.
3.8 References


Chapter 4: Paroxysmal discharges and photic driving in the electroencephalogram of healthy and diseased cats under propofol anesthesia

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Short title: EEG in cats

Keywords: hyperventilation; photic stimulation; propofol; rocuronium bromide; seizure

List of abbreviations:

CRI constant rate infusion  CSF cerebrospinal fluid
EEG electroencephalogram  EtCO₂ end-tidal carbon dioxide
FeLV feline leukemia virus  FIV feline immunodeficiency virus
GABA γ-aminobutyric acid  IE idiopathic epilepsy
MAO monoamine oxidase  MRI magnetic resonance imaging
NMDA N-methyl-D-aspartate  SE symptomatic epilepsy
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4.1 Abstract

Background: No data on healthy cats and cats with seizures using the same anesthetic and EEG recording protocol exist.

Objectives: Evaluation of the diagnostic value of EEG recording in cats suffering from seizures under special consideration of photic stimulation and hyperventilation.

Animals: Six healthy cats and 13 cats with a history of seizures.

Methods: EEGs in healthy cats were recorded in light (mean dose of 0.23 mg/kg/min) and deep (mean dose of 0.7 mg/kg/min) propofol anesthesia whereas EEGs in diseased cats were recorded in a propofol anesthesia which was kept as light as possible (mean dose of 0.39 mg/kg/min).

Results: Paroxysmal discharges were detected in six of 13 cats suffering from seizures (two cats with idiopathic epilepsy, four cats with symptomatic epilepsy). Activation techniques did not enhance the diagnostic value of the EEGs. Photic driving was detected in one of six healthy cats under light, in five of six healthy cats under deep propofol anesthesia and in 11 of 13 diseased cats.

Conclusions and clinical importance: EEG in cats suffering from seizures can be recommended because it can add unique information to the diagnosis. Systematic use of activation techniques does not seem to increase the diagnostic yield of the recorded EEGs and should only be used after careful consideration. Further investigation on the origin of photic driving under propofol anesthesia is needed and could lead to the development of a reliable animal model to investigate drug effects on the EEG.
Epilepsy in cats has an estimated prevalence of 0.5 % and is less commonly observed than in dogs\textsuperscript{1}. In addition, idiopathic epilepsy seems to occur more frequently in dogs than in cats\textsuperscript{1-3}. Furthermore, in cats symptomatic epilepsy due to intracranial diseases are observed more frequently than reactive seizures or idiopathic epilepsy\textsuperscript{3-6}.

Due to the fact that idiopathic epilepsy in the cat is less common, all diagnostic options have to be used to rule out possible underlying seizure origins to find the best treatment for the presented animal\textsuperscript{7}. These diagnostic investigations are in particular: good history taking, physical and neurologic examination, complete blood cell count, serum biochemistry, tests for feline leukemia virus (FeLV) and feline immunodeficiency virus (FIV), radiographs of the thorax and abdomen, magnetic resonance imaging (MRI) and/or cerebrospinal fluid (CSF) analysis\textsuperscript{3}.

Another important diagnostic tool in seizure diagnostics, especially in human medicine, is the electroencephalographic (EEG) recording of the electrical brain activity\textsuperscript{8}. However, EEG recording has become less important in veterinary medicine after the introduction of computed tomography and MRI\textsuperscript{9}. Nevertheless, major advantages of EEG recording compared to MRI are the possibility to detect the seizure focus and to control treatment regimes\textsuperscript{10}. Another benefit of EEG is the potential to detect abnormal brain activity which may be helpful to differentiate between seizure and seizure-like phenomena\textsuperscript{11} or a movement disorders\textsuperscript{12}.

In the past feline EEG research has focused on healthy cats and different anesthetic protocols\textsuperscript{13,14} as well as individual descriptions of pathologic patterns of the EEG activity\textsuperscript{15-17}. Therefore, the first aim of the current study was to compare EEGs of
healthy cats and those suffering from seizures using the same anesthetic drug for both groups.

The additional application of activation techniques is a common procedure in human medicine in order to increase the diagnostic value of the EEG\textsuperscript{8}. In a large retrospective study on 1000 human EEGs, the authors found that one or more activation techniques were used in 85.5 % of the recorded EEGs\textsuperscript{18}. Thus, the second aim of our study was to evaluate the diagnostic usefulness of photic stimulation and hyperventilation in interictal feline EEG recordings.

4.2 Materials and Methods

4.2.1 Healthy cats

Six clinically healthy domestic short hair cats from a cat colony of the University of Veterinary Medicine Hannover were investigated. Mean age and weight were 49 months (range 22-106 months) and 4.65 kg (range 3.7-5.3 kg), respectively. Physical and neurological examination as well as complete blood count and serum biochemistry prior to anesthesia did not reveal any abnormalities. All procedures fulfilled the requirements of the German Animal Welfare Act and were approved by the Federal State Office for Consumer Production and Food Safety of Lower Saxony, Germany (AZ 09/1792).
4.2.2 Cats with seizures

In addition to the examination of healthy cats, 13 EEGs of cats suffering from recurrent seizures were recorded. Animals underwent physical and neurological examination as well as routine blood work and thoracic and abdominal radiographs prior to anesthesia. After EEG recording cats were further investigated by MRI of the brain and/or CSF tap examination. Final or presumptive diagnosis was established based on these examination results and in one cat on necropsy of the euthanized animal.

Four domestic short hair cats with a mean age and weight of 31 months (range 10-73 months) and 4.33 kg (range 3.3-5.3 kg) suffered from presumptive idiopathic epilepsy. One of these animals was pretreated with phenobarbital. No abnormalities were found on physical and neurological examinations as well as routine blood work, thoracic and abdominal radiographs, MRIs of the brain and/or CSF taps.

Nine cats (eight domestic short hairs and one Turkish van) with a mean age and weight of 63 months (range 14-199 months) and 4.37 kg (range 1.25-6.0 kg) displayed abnormalities on physical examination, neurologic examination, complete blood count, serum biochemistry, MRI and/or CSF examination which were indicative for symptomatic epilepsy (Tab. 4.1). Two animals with symptomatic epilepsy were pretreated with phenobarbital, three with diazepam and one with phenobarbital and diazepam.
Table 1: Cats suffering from symptomatic epilepsy and their final diagnosis based on MRI, CSF examination and/or histopathology.

<table>
<thead>
<tr>
<th>No.</th>
<th>Breed</th>
<th>Sex</th>
<th>Age (months)</th>
<th>Antiepileptic medication</th>
<th>EEG abnormalities</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DSH</td>
<td>Mn</td>
<td>34</td>
<td>-</td>
<td>none</td>
<td>presumptive meningoencephalitis</td>
</tr>
<tr>
<td>2</td>
<td>DSH</td>
<td>Fn</td>
<td>112</td>
<td>phenobarbital + diazepam</td>
<td>none</td>
<td>presumptive encephalitis</td>
</tr>
<tr>
<td>3</td>
<td>Turkish Van</td>
<td>Mn</td>
<td>17</td>
<td>diazepam</td>
<td>3 left frontal spikes</td>
<td>feline infectious peritonitis</td>
</tr>
<tr>
<td>4</td>
<td>DSH</td>
<td>F</td>
<td>15</td>
<td>diazepam</td>
<td>generalised spikes</td>
<td>presumptive right hippocampal necrosis</td>
</tr>
<tr>
<td>5</td>
<td>DSH</td>
<td>Fn</td>
<td>90</td>
<td>-</td>
<td>3 right frontal spikes</td>
<td>presumptive meningioma</td>
</tr>
<tr>
<td>6</td>
<td>DSH</td>
<td>Mn</td>
<td>9</td>
<td>phenobarbital</td>
<td>10 left occipital spikes</td>
<td>feline immune deficiency virus infection</td>
</tr>
<tr>
<td>7</td>
<td>DSH</td>
<td>Mn</td>
<td>14</td>
<td>phenobarbital</td>
<td>none</td>
<td>presumptive left hippocampal necrosis</td>
</tr>
<tr>
<td>8</td>
<td>DSH</td>
<td>Mn</td>
<td>25</td>
<td>-</td>
<td>none</td>
<td>presumptive bilateral hippocampal necrosis</td>
</tr>
<tr>
<td>9</td>
<td>DSH</td>
<td>Mn</td>
<td>199</td>
<td>diazepam</td>
<td>none</td>
<td>presumptive neoplasia with herniation of the forebrain and cerebellum</td>
</tr>
</tbody>
</table>

DSH: domestic short hair cat; m: intact male; mn: neutered male; f: intact female; fn: neutered female

4.2.3 Anesthesia

In the healthy animals anesthesia was induced with propofol. A mean dose of 6.85 mg/kg (range 5.67-8.11 mg/kg) was needed until endotracheal intubation was possible. General anesthesia was maintained with propofol constant rate infusion (CRI) during EEG recording. In three of the six healthy cats, anesthesia was first held at a light plane until the first EEG recording period of 18-24 minutes (mean 20 minutes) was finished. Propofol CRI was then increased to 0.7 mg/kg/min. Thirty minutes later, another EEG recording period (mean 17 minutes) was started. In the other three healthy cats, propofol CRI was first held at high propofol rates of 0.7 mg/kg/min. After the first EEG recording period of 17-19 minutes (mean 18 minutes), propofol CRI was stopped. It was restarted at a lower level thirty minutes after cessation and another EEG recording period (mean 17 minutes) followed. It was
randomized whether animals started with low or high propofol CRI. Mean doses for light and deep propofol anesthesia were 0.23 mg/kg/min (range 0.13-0.33 mg/kg/min) and 0.7 mg/kg/min. In order to avoid muscle artifacts in the EEG, 0.6 mg/kg rocuronium bromide was administered before the first EEG recording period. During anesthesia, lactated Ringer’s solution was administered IV at a rate of 5 ml/kg/h. Peripheral oxygen saturation of hemoglobin, pulse rate and end-tidal carbon dioxide (EtCO₂) tension were constantly measured and monitored on a multiparameter monitor.

Cats suffering from seizures were also anesthetized with propofol for EEG recording, but general anesthesia was kept as light as possible (based on clinical assessment of reflex activity). The animals underwent one EEG recording period of 14-21 minutes (mean 17 minutes) before further investigation with MRI and/or CSF examination. Mean induction and maintenance doses of propofol were 8.87 mg/kg (range 5.77-15.15 mg/kg) and 0.39 mg/kg/min (range 0.3-0.61 mg/kg/min). All but one cat received rocuronium bromide in a dose of 0.4 mg/kg IV for prevention of muscle artifacts.

4.2.4 EEGs

EEGs were recorded with a mobile electroencephalograph. Cats were placed in sternal recumbency and five subdermal needle electrodes (F3, F4, Cz, O1 and O2) were placed over the calvarium in order to record the EEG. Acquisition parameters for EEG recording were: sensitivity = 70µV/cm; time constant = 0.3 seconds; Hf = 70 Hz; Lf = 0.5 Hz; notch filter inserted; impedance of all electrodes < 10 kΩ; reference
electrode on the bridge of the nose; ground electrode caudal to the external occipital protuberantia. Another two subdermal needle electrodes were used to record a lead II electrocardiogram. EEG recordings lasted for 14-21 minutes (mean 17 minutes) in diseased cats and twice 17-24 minutes (mean 18 minutes) in healthy cats.

The EEG recording procedure was supplemented by two activation techniques. First an intermittent light stimulation was carried out with a photic stimulator placed approximately 20 cm in front of the eyes. Flash frequency started at 5 Hz, increased in 5 Hz steps until 50 Hz was reached and decreased again down to 5 Hz. Each frequency was applied for 8 seconds. After a stimulation free period of about three minutes, hyperventilation was started in order to reduce the EtCO₂ tension to a mean value of 25 mmHg (range 18-34 mmHg) within a mean duration of 211 seconds (range 180-373 seconds). Another three minutes were recorded after cessation of hyperventilation (post hyperventilation period).

EEGs were examined visually in mono- and bipolar montages. Paroxysmal epileptic activities (e.g. spikes, spike-wave discharges) as well as possible artifacts were determined and marked. Background activity was analyzed for any visually detectable changes during the recording procedure.

4.3 Results

4.3.1 Healthy cats

None of the healthy cats showed any paroxysmal discharges in the EEG. Visually, background activity under light propofol anesthesia was dominated by theta and delta
activity superimposed by faster alpha and beta activity (Fig. 4.1A). In deep propofol anesthesia, burst suppression pattern occurred in all six animals (Fig. 4.1B).

**Fig. 4.1A:** EEG of a healthy cat in light propofol anesthesia. Slow delta and theta rhythms dominate the EEG.

**Fig. 4.1B:** EEG of a healthy cat in deep propofol anesthesia. A burst suppression pattern occurred at high propofol rates of 0.7 mg/kg/min.
Background activity did not change under hyperventilation neither in light nor in deep anesthesia. Photic stimulation induced photic driving in one cat under light anesthesia and in five animals in deep anesthesia (Fig. 4.2). Photic driving occurred in all these animals at lower flash frequencies of 5 Hz and 10 Hz and only in one cat at higher frequencies of up to 45 Hz (Fig. 4.3).

**Fig. 4.2: Photic Driving at 5 Hz and 10 Hz in a healthy cat.**
4.3.2 Cats suffering from seizures

Spikes were detected by visual analysis in two EEGs (50%) of cats with presumptive idiopathic epilepsy and in four of nine cats (44%) with symptomatic epilepsy (Fig. 4.4). There was no sudden onset of paroxysmal activity during the use of activation techniques. Background rhythms in the EEGs of three cats with symptomatic epilepsy were marked by burst suppression patterns. All other EEG background rhythms of cats suffering from seizures were dominated by slow delta and theta rhythms which were superimposed by faster alpha and beta activity. Background activity did not visually change during hyperventilation of these cats but photic stimulation induced photic driving in all but two epileptic cats (85%, 11/13 cats).

Fig. 4.3: Percentage of cats with photic driving in response to different flash frequencies.

IE=idiopathic epilepsy (4 cats), SE=symptomatic epilepsy (9 cats), deep=deep anesthesia (6 cats), light=light anesthesia (6 cats). Flash frequency was first increased in steps of 5 Hz from 5 to 50 Hz and then decreased in the same manner. Cats show photic driving most often at lower flash frequencies of 5 Hz and 10 Hz. Only cats suffering from symptomatic epilepsy and healthy controls in deep propofol anesthesia showed photic driving at higher flash frequencies.
Whereas cats suffering from idiopathic epilepsy showed it only at lower flash frequencies of 5 Hz, 10 Hz and 15 Hz, in animals suffering from symptomatic epilepsy photic driving occurred also at higher frequencies of 20 Hz (4 cats), 25 Hz (3 cats) up to 45 Hz (2 cats) and 50 Hz (1 cat; Fig. 4.3, Fig. 4.5).

Fig. 4.4: Cat suffering from seizures due to symptomatic epilepsy.
Left occipital spike.
4.4 Discussion

In the current study interictal paroxysmal discharges consistent with seizures due to different causes could be detected in half of the animals (2/4 cats) with idiopathic and in 44% (4/9 cats) of symptomatic epileptic cats. Albeit activation techniques did not enhance the diagnostic value of these short time recordings, the phenomenon of photic driving was detected in five of six healthy cats in deep propofol anesthesia and 11 of 13 diseased cats. Although the occurrence of photic driving did not contribute to classification of the underlying disease of recurrent seizures, this phenomenon warrants further consideration in research projects on epileptic cats.

Only a few studies on EEG recordings in cats exist in the literature. Gustafson Beaver and Klemm\textsuperscript{13} described the disadvantages of manual restraint or restraint with light sedation and presented EEGs in healthy cats under general anesthesia with sodium thiopental and pentobarbital. About 35 years later, Wrzosek et al.\textsuperscript{14}
investigated the effect of medetomidine sedation on the EEG of healthy cats. Both studies wanted to offer a method that could be further used in routine clinical EEG investigation of cats suffering from intracranial diseases. In addition to these two publications, some authors included a few cats besides a large number of dogs in their EEG studies on animals with neurological diseases\textsuperscript{15-17}. In the study from Croft in 1962\textsuperscript{15}, two of the three investigated cats suffered from seizures. In one of them the EEG was not further described, in the other one the EEG was normal. In his study from 1972, Croft\textsuperscript{17} recognized abnormal EEGs in all six investigated animals suffering from space-occupying lesions in the brain. In 1968, Klemm\textsuperscript{16} reported that the EEG of one cat suffering from seizures showed generalized spikes and sharp waves. To the authors’ knowledge, the current study is the first study investigating EEGs in healthy cats and cats suffering from seizures with the same anesthetic protocol. In addition, it is the first report on the systematic use of two different activation techniques in this species.

No paroxysmal discharges in the EEGs of healthy cats were found in the current study, which is consistent with the results of Wrzosek et al.\textsuperscript{14}. Albeit the use of general anesthesia for restraint, the recording of abnormal EEG activity in six of 13 cats (46\%) suffering from seizures was possible.

The occurrence of paroxysmal discharges in the EEGs of epileptic dogs varies amongst laboratories between 20-86 \textsuperscript{10,21-23}. In the current study, more than half of all investigated cats did not show any abnormal activity in their EEGs although they had a history of generalized seizures as described by the owners. In human medicine, activation techniques are used to increase the diagnostic value of the
EEG and were effective in 11 % of all patients with normal routine EEG. In the current study, we adapted two activation techniques that have been successfully used in human medicine to the EEGs in diseased cats in order to provoke paroxysmal discharges.

Although both techniques, photic stimulation and hyperventilation, did not induce any sudden onset of paroxysmal discharges in any of the investigated cats, 11 of 13 diseased cats displayed EEG recordings with photic driving at least at low flash frequencies of 5 Hz and 10 Hz. Interestingly, four of six healthy cats developed this phenomenon only at deep levels of propofol anesthesia, whereas just one cat showed it also at a light plane of propofol anesthesia. In contrast, in healthy beagle dogs and dogs suffering from seizures that have been studied with the same anesthetic and activation method protocol before, none of the investigated dogs showed photic driving at any flash frequency.

Abnormal reactions to photic stimulation are so-called photoparoxysmal responses which are marked by spikes and wave activity or polyspikes and are only elicited in about 0.5 % of normal subjects and about 7 % in epilepsy patients. A normal reaction to photic stimulation can be a rhythmic activity in the EEG which is also called photic driving. Not all normal humans show such a pattern in their EEG and sometimes it occurs at specific flash frequencies only. It has been demonstrated that differences in amplitudes of more than 50 % have to occur simultaneously to other EEG abnormalities to be suspicious for underlying structural lesions. On the other hand, an asymmetry in the development of driving response is often correlated with ipsilateral focal slowing and the presence of structural lesions.
To the authors’ knowledge, no reports on photic driving in humans in general anesthesia with propofol exist. It has been reported that photic driving due to photic stimulation is increased by enhancement of central cholinergic states and decreased by induction of central adrenergic states\textsuperscript{28}. Vogel et al.\textsuperscript{29} suggested that this is a result of monoamine oxidase (MAO) inhibition or stimulation because they could show that the EEG driving response decreased at lower plasma MAO activities.

Drug effects on photic driving have also been described in relation to schizophrenia patients as they have a decreased sensitivity to photic stimulation in the alpha range\textsuperscript{30} which resolves under treatment with clozapine\textsuperscript{31}. The authors propose that photic driving at the range of the alpha frequency band could reflect the thalamic function in sensory information processing in schizophrenia\textsuperscript{31}. The effect of clozapine in the EEG may be caused by a direct blockade of the dopamine receptors in the striatal neuronal pathway\textsuperscript{31}.

Propofol has manifold mechanisms of action as it directly activates $\gamma$-aminobutyric acid A (GABA\textsubscript{A})-receptors, inhibits the N-methyl-D-aspartate (NMDA) receptor and reduces extracellular glutamate levels through either inhibiting Na\textsuperscript{+}-channel dependent glutamate release or through enhancing the glutamate uptake\textsuperscript{32,33}. In addition, propofol decreases the firing rate and the burst activity of dopamine neurons in the substantia nigra, probably mediated via the activation of GABA\textsubscript{B}-receptors\textsuperscript{34}, resulting in a reduced dopamine terminal efflux\textsuperscript{35}. Concerning the results of the current study, the frequent occurrence of photic driving in healthy cats in deep propofol anesthesia may therefore be a result of GABA\textsubscript{B}-receptor activation. The
presented results indicate that the cat might be a reliable animal model to investigate drug effects on the driving response in the EEG.

Photic driving occurred also in 11 of thirteen diseased cats although anesthesia with propofol was kept as light as possible with a mean propofol CRI dose of 0.39 mg/kg/min. The development of photic driving in these animals might be due to the slightly higher propofol dose (0.39 mg/kg/min compared to 0.23 mg/kg/min in the healthy cats) or due to changes of neurotransmitters in context with the underlying diseases. Further interpretation of these results should be cautious because of the low number of investigated cats. Future research should therefore focus on examination of cats suffering from recurrent seizures in light and deep propofol anesthesia.

The mechanism by which hyperventilation provokes changes in the EEG is still unclear and several theories have been discussed. It can lead to spike-wave discharges in patients that suffer from generalized epilepsies and to enhanced focal abnormalities in patients with partial epilepsy. In a study on 580 EEGs with hyperventilation as activation procedure, epileptiform activity was seen in 72 epileptic patients. Generally, hyperventilation seems to be more effective in generalized epilepsy than in focal epilepsy. In the present study, hyperventilation did not contribute to diagnostic outcome in all investigated cats which may be due to the low number of animals or due to the fact that they were under general anesthesia.

Conclusions

Generally, the present study shows that the diagnostic value of the EEG in epileptic cats is higher than in dogs using the same recording protocol. We therefore
recommend recording EEGs in cats that suffer from seizures since it can add unique information to the diagnosis, because cats display more often symptomatic or atypical seizures. EEG recordings might be of particular importance in animals with unclear forms of seizures. Furthermore, feline EEG in combination with photic stimulation under propofol anesthesia may be a promising animal model to investigate drug effects on the EEG.

4.5 References


4.6 Endnotes

a Magnetom Impact Plus, 1.0 Tesla, Siemens, Erlangen, Germany

b Narcofol®, CP-Pharma Handelsgesellschaft mbH, Burgdorf, Germany

c Esmeron® 10 mg/ml, N. V. Organon, BHOss, Netherlands

d Photic stimulator, Viasys Healthcare Inc., Madison, Wisconsin

e Sterofundin®, B.Braun Melsungen AG, Melsungen, Germany

f Fabius Tiro, Dräger, Lübeck, Germany

g NicoletOne nEEG, Viasys Healthcare Inc., Madison, Wisconsin

h Disposable subdermal stainless steel EEG needle, Viasys Healthcare Neurocare Group, Madison, Wisconsin

i Brauer et al., unpublished data
Chapter 5: General Discussion

The aim of the current study was to find a practical anaesthetic protocol for short-time EEG recording during routine clinical work-up of epileptic dogs and cats. Most sections of the EEGs should be interpretable and not be masked by muscle artefacts. Furthermore, the diagnostic value of these short-time EEGs with the addition of two standardised activation techniques to the recording protocol was evaluated.

Electroencephalography has been used for examination of epileptic dogs and cats for almost 50 years (Croft, 1962). A universally used EEG recording protocol has not been established so far, although many researchers focused on finding the best recording method. Many veterinary EEG laboratories use their own recording and anaesthetic protocol with different numbers of EEG electrodes and different anaesthetic regimes (Berendt et al., 1999; Bergamasco et al., 2003; Croft, 1962; Fox and Stone, 1967; Gustafson Beaver and Klemm, 1973; Holliday et al., 1970; Jaggy and Bernardini, 1998; Jeserevics et al., 2007; Klemm, 1965; Klemm and Hall, 1974; Redding, 1964; Wrzosek et al., 2009). The latest publications also analysed qEEG data in order to optimize the diagnostic output of their EEGs (Bergamasco et al., 2003; Jeserevics et al., 2007; Wrzosek et al., 2009).

Due to the nature of dogs and cats it is seldom possible to record artefact-free EEGs without anaesthetic restraint of the animal (Gustafson Beaver and Klemm, 1973). We therefore recorded the EEGs under general anaesthesia with propofol which had been used before as single anaesthetic by Bergamasco et al. (Bergamasco et al., 2003) and in combination with medetomidine by Accatino et al. (Accatino et al., 1997) and Jaggy and Bernardini (Jaggy and Bernardini, 1998) and proven to be a reliable
anaesthetic for this purpose which still enables to record paroxysmal discharges in 86% of all recorded EEGs (Jaggy and Bernardini, 1998). When anaesthesia is kept as light as possible in order to prevent the suppression of brain activity artefacts caused by masticatory muscle movement increase again. In order to measure useful sections of interpretable EEGs, a muscle relaxation with rocuronium bromide was introduced in the current study. This medication had been used in dogs and cats before for surgical interventions (Auer, 2007; Auer and Mosing, 2006). The administration of rocuronium bromide in the current study led to better interpretable, muscle artefact free EEG recordings. In addition, hyperventilation was facilitated through the overall relaxation of the animals. Relaxation of the eye muscles led to centrally located eye balls and allowed photic stimulation without rotated eyes through general anaesthesia. The use of rocuronium bromide as an adjunct to general anaesthesia with propofol for EEG recording in dogs and cats can thus be recommended.

Propofol anaesthesia in dosages of 70 mg alters the human EEG to diffuse slow theta or delta activity or polyphasic waves whereas isoelectric lines are not reached until dosages of 140 mg are administered (Hufnagel et al., 1990). Bergamasco et al. (Bergamasco et al., 2003) showed that IV infusions of propofol in dosages of 0.5-0.9 mg/kg/min lead to a prevalence of slow delta rhythms in the canine EEG and that there is a significant increase in absolute but not relative delta activity towards the end of the recording period of about 20 minutes. The current study showed that relative delta activity levels also dominate when lower mean CRI dosages of 0.36
mg/kg/min (seizuring dogs) to 0.37 mg/kg/min (healthy beagles) are used and rocuronium bromide is added to the recording protocol.

The use of propofol for general anaesthesia especially in epileptic patients has been widely discussed in human medicine (Borgeat et al., 1994; Hufnagel et al., 1990; Reddy et al., 1993; Wang et al., 1997) and its pro- and anticonvulsive properties have also been demonstrated in veterinary medicine (Heldmann et al., 1999; Loscher, 2009; Smedile et al., 1996; Steffen and Grasmueck, 2000). Waldner et al. (Walder et al., 2002) suggested, that the pro- or anticonvulsive effects of propofol reflect the cerebral propofol concentration. Borgeat at al. (Borgeat et al., 1994) hypothesised that low propofol doses lead to subcortical excitatory-inhibitory center imbalances. This supported our hypothesis, that propofol can be used for general anaesthesia while diagnosing paroxysmal discharges. Using the combination of propofol and rocuronium bromide, none of the healthy beagle dogs and none of the healthy cats in the current studies developed EEG abnormalities. Interictal paroxysmal discharges consistent with epilepsy were found in 15 (25 %) dogs suffering from idiopathic epilepsy and in eight (29 %) dogs suffering from symptomatic epilepsy, whereas two cats (50 %) suffering from idiopathic epilepsy and four cats (44 %) suffering from symptomatic epilepsy showed spikes in their EEGs. These results show that paroxysmal discharges are not totally suppressed by general anaesthesia with propofol albeit the diagnostic output of EEG, especially in dogs, is low.

Activation techniques are routinely used during standard scalp EEG in human medicine in order to increase the diagnostic yield of the EEG recording (Mendez and
Brenner, 2006). Besides sleep and sleep deprivation, photic stimulation and hyperventilation are the most frequently used methods (Angus-Leppan, 2007).

For humans, normal (no change of EEG rhythms, photic driving) and abnormal responses (photo-paroxysmal response) to photic stimulation have been described (Angus-Leppan, 2007). The occurrence of spike-slow wave and polyspike-slow wave complexes in connection to the photic stimulation is called photo-paroxysmal response (Mendez and Brenner, 2006). Only a few veterinary EEG laboratories have described the use of photic stimulation before (Goiz-Marquez et al., 2009; Holliday et al., 1970). However, the diagnostic value of this activation technique was neither evaluated in dogs nor in cats using a standardised protocol.

In a study of Holliday et al. (Holliday et al., 1970) seven of 13 investigated dogs showed more paroxysmal activity under photic stimulation. Dogs and cats in the current study did not show an enhancement of paroxysmal activity as a consequence of photic stimulation. These divergent results may be due to different methods of animal restraint. Whereas propofol was used to immobilise the animals in the current study, Holliday et al. (Holliday et al., 1970) fixed the dogs with adhesive band on a table and recorded EEGs without pharmacological manipulation. A pharmacological interaction of propofol with the visual cortex may be the reason for the failure of photic stimulation to induce any paroxysmal discharges. Propofol has been chosen for the current study because it has proconvulsant properties (Löscher, 2009). In addition, under propofol anaesthesia higher numbers of abnormal EEGs compared to other anaesthetics were described (Jaggy and Bernardini, 1998).
A rhythmic activity of the EEG as reaction to photic stimulation is called photic driving (Aminoff, 2005; Kasteleijn-Nolst Trenite et al., 1999). This pattern does not arise in every human and some people develop photic driving in their EEGs only at specific flash frequencies (Aminoff, 2005). None of the dogs in the current study showed photic driving during photic stimulation with various flash frequencies, whereas 11 of 13 diseased cats showed photic driving at least at low flash frequencies of 5 Hz and 10 Hz. In addition, four of six healthy cats developed this phenomenon only at deep levels of propofol anaesthesia, whereas just one cat showed it also at a light plane of propofol anaesthesia. It has been shown that the photic driving response is decreasing as a consequence of MAO inhibition (Vogel et al., 1974; Vogel et al., 1969). Photic driving is also decreased in schizophrenic patients and appears again under treatment with clozapine probably blocking dopamine receptors in the striatal neuronal pathway (Jin et al., 1990; Jin et al., 1995). Schwieler et al. (Schwieler et al., 2003) reported, that propofol might decrease the firing rate and the burst activity of dopamine neurons in the substantia nigra probably via the activation of GABA\textsubscript{A}-receptors, resulting in a reduced dopamine terminal efflux (Nissbrandt et al., 1994). This could be a possible mechanism by which propofol enhances the photic driving response in cats under deep propofol anaesthesia in the current study. Although only a light plane of anaesthesia was achieved in the diseased cat, 11 of 13 these animals also developed a driving response. This finding might be due to the slightly higher propofol dose (0.39 mg/kg/min compared to 0.23 mg/kg/min in the healthy cats) or due to unknown neurotransmitter changes through the underlying diseases.
The effect of hyperventilation on canine and feline EEGs has not been described before. In human medicine hyperventilation can lead to an activation of the EEG in 60% of all patients with drug-resistant epilepsies (Schuler et al., 1993) and is more effective in generalised epilepsies than in focal ones (Mendez and Brenner, 2006). In patients suffering from generalised seizures hyperventilation can induce spike-wave discharges whereas focal abnormalities can be accentuated in patients with partial seizures (Aminoff, 2005). The mechanisms for induction of paroxysmal EEG responses after hyperventilation have not been found so far (Aminoff, 2005). It has been suggested that systemic hypocapnia with alkalosis leads to an ischemia and hypoxia within the brain, but more subtle mechanisms may be of greater importance (Patel and Maulsby, 1987).

Dogs and cats in our study were hyperventilated for at least three minutes as recommended by the International League Against Epilepsy (Flink et al., 2002). It did not cause any changes of the EEG neither in healthy nor in diseased dogs and cats although only patients with generalized seizures were investigated in our study. This may be due to the fact that the animals were kept under general anaesthesia, though the plane of anaesthesia was kept as light as possible. A slowing of the background activity, respectively a change in the qEEG analysis, could have been masked by the overall slowing of the EEG activity through the anaesthesia.

In conclusion, the present study showed that rocuronium bromide is a useful adjunct to anaesthesia during canine and feline EEG recording because the interpretation of the EEGs is not impaired by muscle artefacts. The background rhythm of all EEGs under general anaesthesia with propofol was characterised through slow delta and
theta activity that was superimposed by faster alpha and beta activity. Paroxysmal discharges occurred in the EEGs of 25 % of dogs with idiopathic epilepsy, 29 % of dogs with symptomatic epilepsy, two of four cats with idiopathic and in four of nine cats (44 %) with symptomatic epilepsy. The number of dogs and cats with paroxysmal discharges in their EEG could not be enhanced by the systematic use of photic stimulation and hyperventilation. Quantitative EEG analysis in dogs did not add any unique information to the diagnosis. In contrast to dogs, the majority of cats developed photic driving under photic stimulation which might be of particular importance for further research studies on the pharmacological interference of photic driving.
Chapter 6: Summary

Brauer, Christina:

Electroencephalographic studies in dogs and cats

This study was performed to improve a standard anaesthetic protocol for canine electroencephalography (EEG), to adapt this protocol to feline EEG recording and to evaluate the effect of photic stimulation and hyperventilation on the EEG in these species.

Ten clinically and neurologically healthy beagle dogs and six healthy cats were used as references. Normal dogs were anaesthetised with propofol given intravenously with average doses of 7.5 mg/kg for induction and 0.37 mg/kg/min constant rate infusion (CRI) for maintenance. In healthy cats general anaesthesia was induced with propofol with an average dose of 6.85 mg/kg. EEGs in these cats were then recorded under low (average dose of 0.23 mg/kg/min) and high (average dose of 0.7 mg/kg/min) doses of propofol CRI. In dogs (n=89) and cats (n=13) suffering from seizures, a light plane of anaesthesia was maintained with propofol CRI at mean doses of 0.36 mg/kg/min (dogs) and 0.39 mg/kg/min (cats) after induction of anaesthesia with mean doses of 6.54 mg/kg for dogs and 8.87 mg/kg for cats. Rocuronium bromide (0.4-0.6 mg/kg IV) was used as a peripheral muscle relaxant in order to prevent electromyographic artefacts.

EEGs were recorded digitally using five subdermal needle electrodes (F3, F4 Cz, O1, O2). Photic stimulation and hyperventilation were performed during the EEG recording to evaluate two activation techniques commonly used in human EEG
laboratories. Monopolar and bipolar montages were analysed visually. In addition, a quantitative EEG analysis with Fast Fourier Transformation (FFT) was performed in all healthy and 61 of the epileptic dogs.

The use of rocuronium bromide produced EEGs without any electromyographic artefacts during the EEG recording procedure. Interictal paroxysmal epileptiform activity was found in 25% of idiopathic and in 29% of symptomatic epileptic dogs. Paroxysmal discharges were detected in six of 13 diseased cats (two cats with idiopathic epilepsy, four cats with symptomatic epilepsy). Photic stimulation did not provoke a photo-paroxysmal reaction in the EEG of any animal. Hyperventilation did not lead to enhanced paroxysmal activity in the EEGs as well. Photic driving was detected in one of six healthy cats under light, in five of six healthy cats under deep propofol anaesthesia and in 11 of 13 diseased cats.

Quantitative analysis of the EEGs in healthy dogs did not show any significant differences of EEG frequencies during the whole recording procedure. In dogs suffering from seizures, qEEGs detected significant differences of EEG frequencies in single reading points without any continuous changes of the frequency bands. In seven dogs with focal lesions of one hemisphere, a comparison between healthy and affected hemisphere did not show any significant differences in the qEEG analysis.

The current study showed that rocuronium bromide is a valuable adjunct to anaesthesia during canine and feline EEG recording. Despite the use of activation techniques, short time EEG recordings in epileptic dogs can detect interictal epileptic activity in less than one third of all seizuring dogs. In contrast, EEG in cats suffering
from seizures can be recommended because cats suffer more often from symptomatic seizures and the probability that EEG can add unique information to the diagnosis is higher than in dogs. Systematic use of activation techniques does not seem to increase the diagnostic yield of the recorded EEGs and should only be used after careful consideration. Further investigation on the origin of photic driving under propofol anaesthesia in cats is needed.
Chapter 7: Zusammenfassung

Brauer, Christina:

Untersuchungen zum Elektroenzephalogramm bei Hunden und Katzen

Ziel der vorliegenden Studie war es, ein bereits für die EEG-Aufzeichnung bei Hunden verwendetes Narkose-Protokoll für die Anwendung bei Hunden und Katzen zu optimieren und den diagnostischen Nutzen von zwei während der EEG-Aufzeichnung durchgeführten Provokationsmethoden zu ermitteln.

Mittels zehn gesunder Hunde und sechs gesunder Katzen wurden Referenzwerte ermittelt. Die Narkose wurde bei den gesunden Hunde mit durchschnittlich 7,5 mg/kg Propofol eingeleitet und anschließend mit einer total intravenösen Anästhesie (TIVA) von durchschnittlich 0,37mg/kg/min Propofol aufrecht erhalten. Die durchschnittliche Dosis zur Anästhesieeinleitung bei den gesunden Katzen betrug 6,85 mg/kg. Bei diesen Tieren wurden EEGs einmal in flacher (durchschnittlich 0,23 mg/kg/min) und einmal in tiefer (durchschnittlich 0,7 mg/kg/min) Propofol TIVA aufgezeichnet. Zur Erhaltung einer möglichst flachen Narkose, bei den an Krampfanfällen erkrankten Tieren, dienten mittlere Propofol Dosierungen von 0,36 mg/kg/min (Hunde) und 0,39 mg/kg/min (Katzen), nachdem die Narkose mit durchschnittlichen Dosierungen von 6,54 mg/kg (Hunde) und 8,87 mg/kg (Katzen) eingeleitet wurde. Rocuronium (0,4-0,6 mg/kg) wurde intravenös verabreicht, um Muskelartefakte im EEG zu unterbinden. Die EEGs wurden mittels fünf subkutaner Ableiteelektroden (F3, F4, Cz, O1, O2) aufgezeichnet. Während der EEG-Aufzeichnung wurden sowohl eine Fotostimulation als auch eine Hyperventilation durchgeführt, um den diagnostischen Nutzen von zwei
Provokationsmethoden, die routinemäßig in der Humanmedizin verwendet werden, bei Hunden und Katzen bewerten zu können. Im Anschluss wurden die EEGs sowohl in mono- als auch bipolaren Montagen ausgewertet. Zusätzlich wurden die EEGs der gesunden Hunde und die von 61 erkrankten Hunden mittels Fast Fourier Transformation quantitativ untersucht.


Die quantitative EEG Analyse konnte keine signifikanten Unterschiede in den einzelnen Frequenzbändern in den EEGs der gesunden Hunde nachweisen. Bei den an Krampfanfällen erkrankten Hunden, zeigten sich signifikante Unterschiede nur an wenigen Punkten der Frequenzanalyse ohne erkennbares Muster oder Tendenz. Ein Vergleich der Frequenzanalyse zwischen erkrankter und nicht betroffener Hirnhälfte bei den an fokalen Läsionen erkrankten Hunden konnte ebenfalls keine Unterschiede nachweisen.
Chapter 8: References


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References


Chapter 9: List of abbreviations

AEDs  antiepileptic drugs

°C  degree Celsius

CBC  complete blood count

CNS  central nervous system

CRI  constant rate infusion

CSF  cerebrospinal fluid

CT  computed tomography

dl  decilitre

EEG  electroencephalogram

e.g.  exempli gratia

et al.  et alii

EtCO₂  end-tidal carbon dioxide

FFT  fast Fourier transformation

FeLV  feline leukaemia virus

Fig.  figure

FIV  feline immunodeficiency virus

GABA  γ-aminobutyric acid

h  hour
List of abbreviations

IV     intravenous
kg     kilogram
l      litre
MAO    monoamine oxidase
mg     milligram
ml     millilitre
mmol   millimole
µmol   micromole
MRI    magnetic resonance imaging
NMDA   N-methyl-D-aspartate
%      percent
Tab.   table
U      units
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DECLARATION

I herewith declare that I autonomously carried out the PhD-thesis entitled

Electroencephalographic studies in dogs and cats.

I did not receive any assistance in return for payment by consulting agencies or any other person. No one received any kind of payment for direct or indirect assistance in correlation to the content of the submitted thesis.

I conducted the project at the following institutions:

Department of Small Animal Medicine and Surgery, University of Veterinary Medicine Hannover, Hannover, Germany.

The thesis has not been submitted elsewhere for an exam, as thesis or for evaluation in a similar context.

I hereby affirm the above statements to be complete and true to the best of my knowledge.

___________________
(Christina Brauer)