Clinical and Electrodiagnostic Findings in A Cohort of 61 Dogs with Peripheral Nervous System Diseases - A Retrospective Study

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ABSTRACT

The electrodiagnostic examination provides the basis for a diagnostic workup in diseases involving nerve roots, peripheral nerves, neuromuscular junctions and muscles in humans and animals. It is a functional test that enables identification, localization and characterization of the disease within the peripheral nervous system. The study was carried out retrospectively on a group of 61 dogs of different breeds referred for an electrodiagnostic examination because of local or generalized peripheral nervous system impairment. The electrodiagnostic examination consisted of electromyography, electroneurography, F-wave and repetitive nerve stimulation testing. The results of electrodiagnostic studies and their impact on the diagnosis of neuromuscular diseases of different etiology is presented in the study. The lesion was localized to peripheral nerves in 38%, nerve roots in 34%, skeletal muscles in 18% and the neuromuscular junction in 10% of cases. Electrodiagnostics enabled an objective assessment of the extent, distribution and nature of the disease in the study group. However, only when it is used in conjunction with a complete physical and neurological examination and appropriate laboratory or imaging studies, it may be helpful in determining the etiological diagnosis in patients with peripheral nervous system disease.

INTRODUCTION

Electrodiagnostic procedures provide the basis for a functional diagnostic workup in diseases involving nerve roots, peripheral nerves, neuromuscular junctions and muscles in humans and animals (Kimura, 2001). The application of the electrophysiological assessment has been described in veterinary medicine in a variety of neuromuscular disorders, including: ischemic, inflammatory, traumatic, toxic, metabolic, neoplastic and degenerative (Srenk et al., 2010). The predominating symptoms of peripheral nervous system (PNS) impairment include: weakness, flaccid paresis or paralysis affecting one, two or all limbs, decreased muscle tone, hyporeflexia, paresthesias, dysphagia and change of voice (Srenk et al., 2010).

The most commonly used techniques for peripheral neurophysiological examination in veterinary medicine include: electromyography (EMG); electroneurography (nerve conduction velocity, NCV), repetitive nerve stimulation (RNS) and F-wave examination (Cuddon, 2002). EMG is the recording of spontaneous electrical activity produced by skeletal muscles. The normal muscle tissue in an anesthetized animal remains electrically inactive, with the exception of short bursts of electrical activity recorded after insertion of the needle electrode into the muscle (insertional activity, IA) and spontaneous activity at the neuromuscular junctions, called end plate spikes and miniature end plate potentials. Abnormal electromyographic activity includes: fibrillation potentials (FPs), positive sharp waves (PSW), complex repetitive discharges (CRD) and miotonic discharges (Steiss, 2003). Pathological activity may be recorded in either neuropathies or myopathies and it is not possible to distinguish between these two pathologies based only on EMG (Cuddon, 2000).

Nerve conduction velocity (NCV) is an electrodiagnostic test used to measure and record the conduction velocities associated with the electrical stimulation of peripheral nerves. The result of the propagation of motor nerve depolarization is recorded as a compound muscle action potential (CMAP) or M-wave. CMAP is analyzed
Electrophysiological evaluation of the neuromuscular junction is accomplished using the repetitive nerve stimulation test. After a series of supramaximal impulses delivered to the nerve, the amplitudes and areas of sequential CMAPs are measured and should be practically identical from the first to the last. A decrement in consecutive CMAPs, that is greater than 10%, is an indicator of disturbances in neuromuscular transmission (Cuddon, 2000). The nerve root assessment is made using the F-wave recording, which is an antidromic motor nerve depolarization and re-excitation of lower motor neurons in the spinal cord and subsequent orthodromic motor nerve depolarization. The analysis of F wave latency and F ratio may be helpful in the diagnosis of radiculopathy as it is a more precise tool than MNCV to assess diseases that affect proximal segments of the nerve (Cuddon, 1998, 2003). To perform electrophysiological examinations, specialized equipment and well-trained personnel are required (Steiss, 2003). Due to the high diagnostic value, that allows the examiner to confirm the neuroanatomical localization and specify which portion of the PNS is affected, these tests should be carried out on a routine basis in all cases of suspected neuromuscular disorders. However, only when used in conjunction with a complete physical and neurological examination, as well as appropriate laboratory or imaging studies, the etiological diagnosis may be made.

The aim of this study was to present the results of electrophysiological studies and their impact on the diagnosis of PNS peripheral nervous system diseases of different etiology in a cohort of 61 dogs.

MATERIALS AND METHODS

The study was carried out retrospectively on a group of 61 dogs of different breeds (37 males and 24 females), admitted to the Department of Internal Medicine with the Clinic of Horses, Dogs and Cats, Wrocław University of Environmental and Life Sciences between February 2010 and December 2012. The age of the dogs at presentation ranged from 2 months to 14 years. All canine patients were referred for an electrophysiological examination because of local or generalized peripheral nervous system impairment.

All the patients underwent a clinical and neurological examination, as well as a blood test (serum biochemical analysis and complete blood count). A cerebrospinal fluid (CSF) examination was performed in 9/61 cases, infectious diseases testing (Toxoplasmagondii, Neospora caninum, Ehrlichia canis, Borrelia burgdorferi Anaplasma phagocytophilum and Ehrlichia canis) in 17/61 and diagnostic imaging was conducted in 22 patients (plain radiography in 14/61 and MRI in 8/61).

Electrophysiological assessment was carried out under general anesthesia. Dogs were premedicated with a combination of medetomidine at a dose of 20 µg/kg and butorfanol at a dose of 0.1 mg/kg administered intramuscularly. General anesthesia was induced using 1-4 mg/kg of intravenous propofol at and a 0.1-0.4 mg/kg dose was used for maintenance.

The examination was performed at an ambient temperature of 22°C using Nicolet Viasys Healthcare portable system electrodiagnostic equipment with Viking Quest version 11.0 software.

The EMG was performed by intramuscular insertions of the standard electromyographic concentric needle electrode into the muscles of the thoracic and pelvic limbs, head and trunk. A subdermal monopolar ground electrode was placed subcutaneously on the tested side of the body. The NCV study, RNS and F-wave assessment were conducted with the use of stimulating needle electrodes, consisting of an anode and cathode; recording concentric needle electrode and a ground electrode, placed between the stimulating and recording electrodes. The measurements were obtained from the sciatic and tibial nerves in animals with suspected generalized PNS disease and para- or monoparesis affecting hind limbs (Fig. 1). The tests were performed over the radial and ulnar nerve in the case of front limb monoparesis with electrode placement according to Walker et al. (1979). The MNCV was obtained using a single supramaximal electrical stimulus with duration of 0.1 milliseconds and the results were compared with those of dogs of a similar age (Walker et al., 1979; Cuddon, 2000). F-wave evaluation was based on the measurement of the minimal latency of recorded F-waves in comparison to expected minimum F-wave latency calculated according to the following formula: 6.03+0.22 x limb length [cm] for the ulnar nerve and 3.45+0.33 x limb length [cm] for the sciatic/tibial nerve. The F ratio for the sciatic/tibial nerve was calculated according to the formula: (LatF–LatM-1)/2LatM and compared to the reference 1.95±0.086 at the hock and 0.88±0.052 at the stifle. RNS was carried out with a series of ten supramaximal impulses delivered to the sciatic nerve, where percent decrement in amplitude and area was calculated for the third, fifth and tenth wave. Sensory nerve conduction was not performed in this study group.

RESULTS

Based on the electrophysiological examination, the distribution of pathological process within the PNS was localised to the peripheral nerves in 38%, nerve roots in 34%, followed by skeletal muscles (18%) and neuromuscular junction in 10% of cases. The cases were classified to the groups based on the etiology and distribution of the pathological process and were put in order depending on the frequency of the disorder. The clinicopathological findings regarding the particular groups are summarized in Table 1.

Group 1: The most commonly diagnosed disease of the peripheral nervous system in the study group was endocrinological polynuropathy due to hypothyroidism in 20/61 individuals (32.8%). Diagnosis of polyneuropathy was based on electrophysiological findings, which
Table 1a: Clinicopathological findings in the study group. The laboratory test were performed and interpreted according to Shelton (2010)

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Clinical/neurological symptoms</th>
<th>Laboratory investigation/imaging</th>
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<tbody>
<tr>
<td>1</td>
<td>Overweight (13/20), lethargy (12/20), bradycardia (7/20), dermatological signs (4/20), regurgitation (megaeosophagus) in 1/20. Weakness and hyporeflexia (20/20), chronic, progressive para- or tetraparesis (14/20), tetraplegia (5/20), muscle atrophy (12/20), vestibular signs (6/20), facial paralysis (1/20)</td>
<td>total T4 concentration (20/20), ↓FT4 (20/20), ↓cTSH (15/20), hypercholesterolemia (15/20), ↓ALP (8/20), non-regenerative anemia (5/20), ↑CK (4/20) mild ↑CK (1/10); Infectious diseases titers: negative (10/10); CSF: mild ↑protein level (7/10), mild pleocytosis (cell count above 5 cells/mm3) in 2/10 3a and 3b: ↑CK (6/7), ↑AST (6/7) Infectious diseases titers: negative (7/7)</td>
</tr>
<tr>
<td>2</td>
<td>acute tetraparesis to tetraplegia with decreased spinal reflexes (10/10), dys- or aphony (9/10) , muscle atrophy (3/10)</td>
<td>circulating antibodies against type 2M fibers (2/2)</td>
</tr>
<tr>
<td>3a</td>
<td>weakness (5/5), stiff gait (4/5) muscle atrophy (3/5) and myalgia with fever (1/5)</td>
<td>↑ serum ACh receptor antibody concentration (5/6), leukocytosis (2/6), ↑CK and AST (1/6)</td>
</tr>
<tr>
<td>3b</td>
<td>dysphagia, masticatory muscle atrophy and inability to open the jaw (2/2)</td>
<td>degenerative lumbosacral stenosis was confirmed in all 5 dogs by imaging studies (MRI)</td>
</tr>
<tr>
<td>4</td>
<td>exercise-induced weakness (4/6), tetraparesis (1/6), regurgitation and excessive salivation (3/6), ↓palpebral reflex and muscle tremor (1/6)</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>chronic, progressive paraparesis to paraplegia, proprioceptive deficits, hyporeflexia and muscle atrophy in both hind limbs and decreased tail tone in all 5 dogs, urinary and/or fecal incontinence in 2/5 cases</td>
<td></td>
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Table 1b: Clinical/neurological symptoms

<table>
<thead>
<tr>
<th>Study Group</th>
<th>Laboratory investigation/imaging</th>
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<tr>
<td>6a</td>
<td>↓ proprioception in the left (2/3) and right (1/3) front limb, impaired cutaneous sensation of the dorsal, lateral and caudal part of the antebrachium of the affected limb (3/3), ipsilateral Horner syndrome and a lack of the cutaneous trunci reflex (2/3)</td>
</tr>
<tr>
<td>6b</td>
<td>↓ postural reactions in the affected hind limb, muscle atrophy in the caudal part of the thigh, a decreased withdrawal and increased patellar reflex (pseudohyperreflexia) in 2/2.</td>
</tr>
<tr>
<td>7a, 7b</td>
<td>progressive monoparesis, severe muscle atrophy of the front limb (2/2).</td>
</tr>
<tr>
<td>7c</td>
<td>Palpable mass in the axillary area found during the clinical examination (1/2).</td>
</tr>
<tr>
<td>8</td>
<td>history of episodic muscle twitching and vermiform movements of the overlying skin (myokymia) with muscle stiffness (neuromyotonia) in 3/3, hyperthermia and tachypnea (3/3).</td>
</tr>
<tr>
<td>9</td>
<td>↓ proprioception and ataxia in all four (1/3) miotonic attack during the examination (1/3).</td>
</tr>
<tr>
<td>10</td>
<td>tremors in all four limbs observed only while standing.</td>
</tr>
<tr>
<td>11</td>
<td>moderate leukocytosis (due to inspiratory pneumonia), laryngoscopic examination confirmed bilateral laryngeal paralysis.</td>
</tr>
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included: increased IA, multifocal patterns of FPs and PSW on EMG that was found in 60% of dogs in the appendicular muscles. MNC in sciatic/tibial nerves was reduced in varying degrees (20-54 m/s, median value 38 m/s) in all dogs. A prolonged CMAP latency and distal temporal dispersion were found in 80% of patients and decreased CMAP amplitude was recorded in 20% of dogs.

**Group 2:** The second most commonly diagnosed disease in the study group was acute canine polylradiculoneuritis (ACP) with a prevalence of 10/61 (16.4%). Electromyographic findings in the described group revealed FPs and PSW in appendicular muscles in all individuals and CRDs in 60% of dogs. Abnormal EMG activity in axial muscles was found in 20% of group 2 the patients in this group. MNCV in the sciatic/tibial nerve was decreased (30-49 m/s, median value 42 m/s) in 30% of dogs. Increased CMAP latency and temporal dispersion was found in 50% of dogs and decreased CMAP amplitude was presented in all patients. F-wave was not recordable in 30% and increased latency and F-ratio was found in 70% of dogs.

**Group 3:** Myositis was found in 7 patients (11.5%). Five dogs were presented with generalized inflammatory myopathy (subgroup 3a), and in two cases a diagnosis of masticatory muscle myositis (MMM) was made (subgroup 3b). The electrodiagnostic examination revealed moderate to severe pathological changes in electromyography: increased IA, multifocal patterns of FPs and PSW in all dogs and CRD in 2 dogs in subgroup 3a. In two dogs with MMM, the same EMG changes were found only in the masticatory muscle group.

**Group 4:** Six dogs, that is 9.8%, were diagnosed with a junctionopathy i.e. generalized, acquired myasthenia gravis (MG). The electrodiagnosis in this group was based on the repetitive nerve stimulation, as the results of other electrodiagnostic tests were normal. A significant decline in the amplitude of the successive potentials (>-12%) was recorded in all of the myasthenic patients with a range 19-25% for the 3rd, 25-40% for the 5th and 35-83% for the 10th consecutive CMAPs.

**Group 5:** Radiculopathy due to compression (i.e. lumbosacral stenosis) was diagnosed in 5 of 61 dogs (8.2%). Pathological changes were found bilaterally in 40% and unilaterally in 60% of the dogs. The electromyographic examination revealed moderate increases in spontaneous activity in the muscles of the caudal thigh and all the muscles distal to the stifle in the affected limbs in all dogs. Increased F-wave latency and F-ratio was found in all patients. In 60% of the cases decreased CMAP amplitude was detected. In one case a decreased MNCV in the sciatic nerve (42 m/s) was additionally recorded.
**Group 6:** Peripheral nerve injury causing monoparesis was found in 5/61 patients (8.2%). There were 3/5 cases of brachial plexus avulsion (subgroup 6a). The electrodiagnostic investigation was performed more than 5 days after injury. The EMG revealed significant denervation (increased IA, FPs, PSW) in all muscles of the affected forelimb in one dog and in the remaining two cases muscles supplied by radial and ulnar nerves were affected (triceps muscle, extensors of the carpus and digits, flexor carpi ulnaris and interosseous muscle). Ulnar and radial CMAP and F-wave were not recordable in one case. MNCV and CMAP amplitudes were decreased in radial (40-52 m/s) and ulnar nerves (32-37 m/s) in the two remaining cases.

Subgroup 6b consisted of 2 cases of iatrogenic sciatic nerve trauma. The EMG revealed increased IA, FPs and PSW in caudal muscles of the thigh and muscles located distally to the stifle. The MNCV evaluation revealed a decreased motor sciatic/tibial nerve conduction velocity (34 m/s and 48 m/s), decreased CMAP amplitudes in both cases and temporal dispersion in one dog.

**Group 7:** There were three patients (4.9%) in the study group diagnosed with a neoplastic disease of peripheral nerves, including two cases of a nerve sheath tumor (7a, 7b) and one poorly differentiated fibrosarcoma involving the sciatic nerve (7c). **Subgroup 7a:** On EMG there was moderate spontaneous activity (FPs and PSWs) in the muscles of the forelimb, including the triceps muscle and extensors of the carpus and digits. The radial nerve examination revealed slowed MNCV (32 m/s) with decreased CMAP latency and amplitude. **Subgroup 7b:** Moderate denervation changes were found in all muscles of the affected limb. Radial nerve CMAP was not recordable. Ulnar nerve MNCV and CMAP amplitude were markedly decreased (25 m/s) and F-wave latency was prolonged. **Subgroup 7c:** A severe denervation on EMG (FPS, PSWs) was found in the semitendinosus, semimembranosus, biceps femoris muscles and muscles of the crusc. CMAP and F-wave were not recordable in the sciatic/tibial nerve.

**Group 8:** Myokymia and neuromyotonia was diagnosed in 3/61 of dogs (4.9%). The group included two Parson Russell Terriers (PRT) littermates and a Jack Russell Terrier (JRT). Neuromyotonic discharges of variable amplitudes (doublet, triplet and multiplet) with a high intraburst frequency were visible on EMG in the muscles of the limbs and trunk in all dogs. In one dog these abnormalities were additionally found in the muscles of the head. NCV, RNS and F wave examination were unremarkable in these cases.

**Group 9:** An orthostatic tremor was electrodiagnostically confirmed in one Great Dane (1.6%). Electrodiagnostic assessment in this patient was unremarkable when performed under general anesthesia. EMG recordings, when obtained without sedation on the standing dog, showed continuous discharges of muscle activity of irregular amplitude in the appendicular muscles. Continuous rapid burst firing occurred synchronously with the visible tremors.

**Group 10:** A laryngeal paralysis and polynueuropathy complex was diagnosed in one Rottweiler (1.6%). Electrodiagnostic examination showed increased IA, PSW and FPs in all appendicular muscles and the intrinsic laryngeal muscles. A slightly decreased MNCV (40 m/s) with decreased CMAP amplitude in sciatic/tibial nerve was recorded in this dog.

**DISCUSSION**

The results presented in this study show a variety of clinical and electrodiagnostic findings in a heterogeneous cohort of dogs with neuromuscular diseases. Electrodiagnostic assessment contributed to an antemortem diagnosis of PNS diseases in all cases in the presented group.

The most common cause of peripheral nervous system disease in 61 canine patients in this study was primary hypothyroidism. Neurological manifestations of this endocrinopathy in dogs have been previously reported although they were considered uncommon (Fors, 2008; Parry 2013). Fluehmann et al. (2006) reported that 19.5% of all PNS diseases in dogs had either metabolic or toxic etiology compared to 34.4% of cases in this study. The exact mechanism of hypothyroid-associated polyneuropathy remains unknown. However, two major hypotheses suggest that the accumulation of mucopolysaccharides in the endoneurium and perineurium of the peripheral nerves and an impairment of axonal transport due to decreased mitochondrial ATPase activity could be responsible for the hypothyroid-associated polyneuropathy (Rossmeisl, 2010). Electrodiagnostic findings in this study group were consistent with both demyelination (the presence of temporal dispersion, prolonged latency and slowed MNCV) and axonal impairment (decreased CMAP amplitude) of the peripheral nerves (Fig. 2). A nerve biopsy would be helpful to achieve a definitive diagnosis in Group 1 but it was not performed due to financial constraints. Electrodiagnostic tests could be repeated in the future in the hypothyroid group in order to monitor the function of peripheral nerves and evaluate the efficacy of a replacement therapy (Kececi and Degirmenci, 2006).

Acute canine polyradiculoneuritis, polymyositis, and acquired myasthenia gravis are common immune-mediated diseases, affecting different parts of the peripheral nervous system (Evans et al., 2004; Cuddon, 1998). These diseases may have a common clinical and neurological manifestation (Khorzad et al., 2011). The electrodiagnostic evaluation was found to be a very helpful diagnostic tool in differentiating which portion of the PNS was affected by the disease. In the group 3 (polymyositis) the pathological changes were found only during EMG (Fig 3). In the group 2 (ACP), there were minor EMG changes, with marked MNCV and F-wave abnormalities, whereas in the group 4 (MG), the characteristic changes mainly concerned the RNS test (Fig 4). These findings are not specific with regard to the cause of the disease, however they aided in steering further diagnostic tests (such as serum ACh receptor antibody concentrations in suspected MG or CSF collection in ACP).
The assessment of ventral nerve root compression can be achieved using electrodiagnostic techniques, particularly the F wave examination (Cuddon, 2003). The severity of nerve roots compression due to lumbosacral stenosis was evaluated in five dogs in this study. The functional testing of nerve roots using F-wave examination together with EMG study was particularly useful in differentiation this disorder from orthopedic diseases, e.g. hip dysplasia. Electromyography is clinically useful in differentiating denervation atrophy and muscle atrophy due to disuse. In combination with F-wave changes, which enables the assessment of the subtle conduction changes, it is indicative of nervous system involvement, not an orthopedic problem (Cuddon, 2003).

A relatively low number of animals with posttraumatic peripheral nerve injury (8.2%) was examined in this study. Traumatic events affecting PNS are very common (Fluehmann et al., 2006) and, possibly, the large number of affected dogs that were involved in vehicle accidents or iatrogenic trauma were not referred for a neurological consultation and electrodiagnostic tests. Assessing MNCV at least 5 days after injury may be helpful in differentiating between benign focal nerve injury (neurapraxia) and complete axonal or nerve separation (axonotmesis, neurotmesis). If the nerve is stimulated below the lesion, an animal with neurapraxia has normal CMAP and motor nerve conduction velocities. Axonotmesis and neurotmesis results in decreased or absent CMAP with or without a decrease in motor nerve conduction velocities, depending on the severity of the lesion (Kimura, 2001). This differentiation is important at the early stage of the disease, since dogs with neurapraxia have a better prognosis and may be monitored through a repeated MNCV study and electromyography (Cuddon, 2003; Korte et al., 2011).

Neoplastic disease of the peripheral nervous system was found in 3.3% of all studied cases and it was less common than reported previously (Fluehmann et al., 2006). Electrodiagnostic testing was helpful in the evaluation of the exact distribution of PNS neoplasia. Together with advanced imaging, such as MRI, it allows to precise surgical planning (Platt et al., 1999).

In some breed-related diseases, electrodiagnostic findings were very specific and, together with characteristic clinical signs and history, were sufficient to confirm the diagnosis. Myokymia and neuromyotonia has been mainly reported in the Jack Russel Terrier, although it has also been described in other breeds of dogs and in a cat (Bhatti et al., 2011). The histopathological examination of the central nervous system, peripheral nerves and muscles of the affected JRTs did not provide diagnostic value and it was stated that it would be valuable to screen every JRT for myokymia and neuromyotonia on the basis of a history, clinical examination and EMG (Vanhaesebrouck et al., 2010).

The orthostatic tremor (OT) in Great Danes is another example of a disorder in which nerve and muscle biopsies fail to confirm any abnormalities. A definitive diagnosis of OT requires documentation of the characteristic tremor pattern during a conscious electromyographic examination (Garosi et al., 2005).
The laryngeal paralysis-polyneuropathy complex was first described in Rottweiler dogs by Mahony et al. (1998). In this study, the owners’ main complaints were respiratory distress and stridor in the dog. Neurological and electrodiagnostic evaluation revealed a concurrent polyneuropathy. Surgical correction of the laryngeal paralysis in young animals should be considered with caution and preferably receded by electrodiagnostic evaluation to rule out a more generalized polyneuropathy (Mahony et al., 1998).

Conclusion: Electrodiagnostic studies enabled an objective assessment of the extent, distribution and nature of the peripheral nervous system diseases in our patients and indicated the direction of further investigations. Taking into consideration the number of the affected animals, a greater need for an accurate diagnosis and hence, an appropriate treatment of veterinary patients, electrophysiological examinations will play an important role in the clinical veterinary practice and research.

REFERENCES


Reduced reflexes indicate peripheral nervous system problems, whereas increased reflexes suggest a central nervous system disorder, particularly when seen in combination with spasticity and increased tone. An important caveat is that in acute spinal cord injury, there can be an initial reduction in reflexes because of spinal shock. In a similar companion study, these investigators studied lower limb NCSs in healthy elderly persons. The American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) supports the Occupational Health and Safety Administration rule that mandates the use of gloves and universal precautions. Clinical and Electrodiagnostic Findings in A Cohort of 61 Dogs with Peripheral Nervous System Diseases - A Retrospective Study. Article. Full-text available. The electrodiagnostic examination provides the basis for a diagnostic workup in diseases involving nerve roots, peripheral nerves, neuromuscular junctions and muscles in humans and animals. It is a functional test that enables identification, localization and characterization of the disease within the peripheral nervous system. The study was carried out retrospectively on a group of 61 dogs of different breeds referred for an electrodiagnostic examination because of local or generalized peripheral nervous system impairment.