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Evaluierung neurographischer Parameter bei diabetischer Neuropathie

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1. INTRODUCTION

Diabetes mellitus (DM) and especially diabetic neuropathy (DNP) as complication of the underlying disease lead to a major morbidity and mortality resulting in a huge economic burden for the society (54). Diabetic neuropathy is the most common form of neuropathy in the developed countries of the world, accounts for more admission to hospital than all other diabetic complications combined and is responsible for 50-75% of non-traumatic amputations (54).

Distal symmetric sensimotor polyneuropathy is the most common from of peripheral neuropathy and is the leading cause of lower limb amputation (18). Diabetic neuropathy can result in painful neuropathy, disabling foot ulcers, and death from autonomic neuropathy. (20). Diabetic neuropathy is a set of clinical syndromes that affect distinct regions of the nervous system, singly or combined. The progress of the disease can be silent and go undetected, or be present with clinical symptoms and signs that although non-specific and insidious with slow progression also mimic those seen in many other diseases (54). Diabetic neuropathy is diagnosed by exclusion meaning, that other potential causes of neuropathy should be excluded (54).

Patients suffering from diabetic neuropathy can be present with altered sensation, pain, weakness, or autonomic symptoms. The clinical picture can vary widely and may resemble myelopathy, radiculopathy, muscle disease, or even hyperventilation. As a result of these findings identifying a neuropathy in patients with coexistent problems can be therefore difficult (20). The evaluation and identification of possible causes for neuropathy was improved by the so-called neuropathy symptom profile, which is a questionnaire developed by Dyck et coworkers (14).

For the diagnosis of diabetic neuropathy the tools used differ depending on the aim: from simple clinical tests to screen for diabetic neuropathy to clinical-neurophysiological methods necessary to exclude other diagnoses, stage severity and monitor the course of diabetic neuropathy, to novel investigative techniques, which are highly promising, but their usefulness in the clinical setting remains limited at this time (31).

For the neurologist in usual clinical practice the diagnosis of diabetic neuropathy consists of the anamnesis of the patient, inspection (e.g. ulcera cruris, cutis), clinical tests (investigation of reflexes, sensation, muscle strength) and neurophysiological tests. Diabetic patients suspicious of having a diabetic neuropathy due to symptoms providing hints (e.g. impaired sensation, vibration, etc.) are then usually tested with various neurophysiological tests (motoric and sensory tests of peripheral nerves, electromyography, tests of the autonomous nervous system) to further evaluate their functional status. Combined with the clinical symptoms and

the anamnesis of the patient and by excluding other common causes of neuropathy (e.g. alcohol misuse, drugs, paraneoplasia, etc.) (20) the patient will be analyzed and diagnosed.
Due to the fact, that the measurement of motoric nerve function of peripheral nerves is one of the most valid methods (51) that can be applied in the electrophysiological evaluation of peripheral nerves, this study was designed to measure the motoric function of three peripheral nerves (N. medianus, N. tibialis, N. peronaeus). Combined with the anamnesis of the patient and the results of the neurological examination this neurophysiological test shall help to identify those patients with diabetes mellitus, who are at an early stage of diabetic neuropathy. Those patients should be engaged to have an optimal control of their glucose metabolism with low glycosylated hemoglobin levels, which was proved to keep their disease status or slow down the progression of their diabetic neuropathy (35, 45, 49).

2. PATHOGENESIS OF DIABETIC NEUROPATHY

The pathogenesis of diabetic neuropathy is not completely understood yet despite huge efforts in preclinical and clinical studies (48, 22, 7, 37, 27, 53). This could be related to the fact, that the pathogenesis of peripheral diabetic neuropathy is a very complex and heterogeneous mechanism with involvement of different factors, which are probably not comprehensively known and fully analyzed (53, 54, 27, 48).

Simplified said different concepts are involved in the pathogenesis of DNP so as vascular factors, neurochemical factors and pathobiochemical factors (27). The vascular concept of DNP implies that diabetes-induced endothelial dysfunction with resulting decrease of nerve blood flow and endoneural hypoxia has a key role in functional and morphological changes in the diabetic nerve. Endothelial changes in the vasa nervorum have been attributed to multiple mechanisms, including increased aldose reductase activity, nonenzymatic glycoxidation, activation of protein kinase C, oxidative stress, changes in arachidonic acid and prostaglandin metabolism, and others (27). The neurochemical concept of DNP suggests the importance of similar mechanisms in the neural elements of the peripheral nervous system (PNS) (i.e. neurons and Schwann cells). Other pathobiochemical mechanisms in the peripheral nervous system have also been invoked. These include

1) metabolic abnormalities such as downregulation of the Na^+/K^+-ATPase activity, “pseudohypoxia” (i.e. increase in free cytosolic NADH/NAD^+ ratio attributed to increased conversion of sorbitol to fructose by sorbitol dehydrogenase),
2) changes in fatty acid and phospholipids metabolism,
3) impaired neurotropic support; and

4) dorsal root ganglion and Schwann cell mitochondrial dysfunction and premature apoptosis.

The vascular concept of DNP was also supported by results of pathological tests carried out in autopsy cases in diabetic patients, which revealed focal fascicular lesions likely due to diabetic microangiopathy (22).

The structural changes within the peripheral nervous system in patients suffering from DNP can be classified as

1) nodal structural changes leading to axo-glial dysfunction and paranodal demyelination and
2) axonal structural changes leading to axonal atrophy and fiber loss (37).

The functional changes related to the former mentioned structural changes are for

1) a reduction of the nerve conduction velocity (NCV) and for
2) a reduction of the amplitude of the compound muscle action potential.

The predominant pathological factor in this context seems to be rather the axonal atrophy as main structural abnormality of DNP, as demonstrated in various studies involving both humans and experimental animals (37).

3. CLASSIFICATION OF DIABETIC NEUROPATHIES

The natural course of DNP separates them into two very distinctive entities, namely those which progresses gradually with increasing duration of diabetes and those which remit usually completely. Sensory and autonomic neuropathies usually generally progress, whereas mononeuropathies, radiculopathies and acute painful neuropathies, although symptoms are severe, tend to be short-lived and often recover (54). Acute painful diabetic sensory neuropathies is therefore a separate entity with a favorable prognosis (47) and will be not further addressed in this study.

The progression of DNP is related to the glycemic control in both type I and type II diabetes (54). It seems that the most rapid deterioration of nerve function occurs soon after the onset of type I diabetes and within 2-3 years there is a slowing of the progress with a shallower slope to the curve of dysfunction. In contrast in type II diabetes slowing of nerve conduction velocities can be one of the earliest neuropathic abnormalities and often is present even at diagnosis (57). After diagnosis, slowing of nerve conduction velocity generally progresses at a steady state of approximately 1 m/s per year and the level of impairment is positively correlated with the duration of diabetes. Although most studies have documented that sympto-

matic patients are more likely to have slower nerve conduction velocities than patients without symptoms, these do not relate to the severity of symptoms.

In a long-term follow-up study of type II diabetes patients (29**)** the percentage of patients with electrophysiological abnormalities in the lower limb increase from 8% at baseline to 42% after 10 years: a decrease in sensory and motor potential amplitudes, indicating axonal destruction was more pronounced than slowing of the nerve conduction velocities.

The form of neuropathy found in patients with impaired glucose tolerance (IGT) at early stage of diabetes mellitus is predominantly a small-fiber neuropathy, compared to patients with diabetes mellitus, who had a more involvement of large nerve fibers (42).

3.1 Clinical presentation

The spectrum of clinical neuropathic syndromes described in patients with diabetes includes dysfunction of almost every segment of the somatic peripheral and autonomic nervous system (54). Each syndrome can be distinguished by its pathophysiological, therapeutic and prognostic features. Usually the clinical syndromes be can differentiated into the following items:

- Focal neuropathies
- Diffuse neuropathies
    - Proximal motor neuropathies (diabetic amyotrophy)
    - Distal symmetric polyneuropathy
    - Small-fiber neuropathy
    - Large-fiber neuropathies
- Autonomic neuropathies

3.1.1 Focal neuropathies

Monoreuropathies are rare in comparison with distal symmetric neuropathies. They usually occur primarily in older populations, their onset is often rapid, associated with pain and their course is self-limiting, resolving within 6-8 weeks. One example of this clinical entity would be the carpal tunnel syndrome, which occurs twice as frequently in people with diabetes compared with normal healthy population and its increased prevalence in diabetes can be related to repeated undetected trauma, metabolic changes, or accumulation of fluid or edema with the confined space of the carpal tunnel (55).

3.1.2 Diffuse neuropathies

Proximal motor neuropathies (diabetic amyotrophy) has been for many years considered as a variant of diabetic neuropathy. It can be clinically identified based on recognition of these common features (54):

1) primarily affects the elderly,
2) gradual or abrupt onset,
3) begins with pain in the tighs and hips or buttocks
4) followed by weakness of the proximal muscles of the lower limbs with the inability to rise from the sitting position,
5) begins unilaterally and spreads bilaterally,
6) coexists with distal symmetric polyneuropathy and
7) spontaneous muscle fasciculation, or provoked by percussion.

The condition is now recognized as being secondary to a variety of causes unrelated to diabetes but which have a greater frequency in patients with diabetes than the general population. It includes patients with chronic inflammatory demyelinating polyneuropathy (CIPD), monoclonal gammopathy, circulating GM1-antibodies and antibodies to neuronal cells and inflammatory vasculitis (40). It was formerly thought to resolve spontaneously in 1.5 to 2 years but now, if found to be immune-mediated, can resolve within days with immunotherapy (54).

Distal symmetric polyneuropathy (DSP) is the most common and widely recognized form of diabetic neuropathy. The onset is usually creeping but occasionally rapid, following stress or initiation of therapy for diabetes. It can be either sensory or motor and involve small fibers, large fibers or both (54). There is now evidence that distal symmetric polyneuropathy can be accompanied by loss of cutaneous nerve fibers that stain positive for the neuronal antigen PGP9.5 as well as impaired neurovascular blood flow (39). There are however a variety of ways in which small fiber neuropathies can be present.

Small fiber neuropathy can be differentiated between acute and chronic painful form. For acute painful neuropathy some patients develop a predominantly small-fiber neuropathy, which is manifested by pain and paresthesia early in the course of diabetes. It can be associated with the onset of insulin therapy and has been termed “insulin neuritis” (43). By definition it has been there for less than 6 months. Symptoms are often exacerbated at night and are manifested in the feet more than the hands. Spontaneous episodes of pain can be severely disabling. The pain varies in intensity and character. Chronic painful neuropathy persist by definition longer than 6 months and becomes disabling. This condition can result in

tolerance to narcotics and analgetics and finally to addiction. It is extremely resistant to all forms of intervention, and more frustrating for both patient and physician.

Large-fiber neuropathies can involve sensory or motor nerves or both. These tend to be neuropathies of signs rather than symptoms. Large fibers subserve motor function, vibration perception, position sense and cold thermal function. Unlike the small fibers these are myelinated, rapidly conducting fibers that begin in the toes and have their first synapse in the medulla oblongata. They tend to be affected first because of their length and tendency in diabetes for nerves to “die back”. Because they are myelinated, they are the fibers represented in the electroneurograph and subclinical abnormalities in nerve function are readily detected. The symptoms can be minimal; sensation of walking on cotton, floors feeling “strange”, inability to turn the pages of a book or inability to discriminate among coins.
Most patients with DSP have, however, a “mixed” variety of neuropathy with both large and small fiber damage. In the case of distal symmetric polyneuropathy, a “glove and stocking” distribution of sensory loss is almost universal (55). Early in the course of the neuropathic process, multifocal sensory loss also might be found. In some patients, severe distal muscle weakness can accompany the sensory loss resulting in an inability to stand on the toes or heels. Some grading systems use this as a definition of severity.

3.1.3 Autonomic neuropathies

Diabetic autonomic neuropathy can involve any system in the body. Involvement of the autonomous system can occur as early as the first year after diagnosis and major manifestations are cardiovascular, gastrointestinal, and genitourinary system dysfunction (55). Reduced exercise tolerance, edema, paradoxic supine or nocturnal hypertension and intolerance to heat due to defective thermoregulation are a consequence of autonomic neuropathy. Silent myocardial infarction, respiratory failure, amputations and sudden deaths are hazards for the diabetic patients with cardiac autonomic neuropathy (50). Therefore, it is vitally important to make this diagnosis early so that appropriate intervention can be instituted.

4. DIAGNOSIS OF DIABETIC NEUROPATHIES

The diagnosis of diabetic neuropathy in clinical practice requires the neurological history and physical examination in combination with neurophysiological testing as a criterion standard for diagnosis and measurement of severity (31).
The assessment of neuropathy can be carried out using different tools: one example would be the Michigan Neuropathy Screening Instrument, which is an eight-point assessment that relies on clinical examination of the feet, the presence or absence of foot ulcerations, the assessment of vibratory sensation in the great toes, and grading of ankle reflexes (38).

A more sophisticated and detailed tool would be the neurological symptom score and neuropathy impairment score by Dyck et al (13), which was also used in the Diabetes Control and Complication Trial (DCCT) (44). These classifications are however time-consuming and therefore inconvenient in daily practice (41).

The 1988 San Antonio conference on diabetic neuropathy and the 1992 conference of the American Academy of Neurology (2, 3) recommended that at least one variable from each of the following five categories are measured to classify diabetic neuropathy: symptom profiles, neurologic examination, quantitative sensory test (QST), nerve conduction study and quantitative autonomic function testing (QAFT) (54). The least reliable measure is the neurologic symptom score. The quantitative sensory test and quantitative autonomic function test are objective indices of neurologic functional status. Combined, these tests cover vibratory, proprioceptive, tactile, pain, thermal and autonomic function (54). Nevertheless these tests are also quite time-consuming and therefore for daily practice maybe not useful.

The validity respectively reproducibility of different diagnostic measures in diabetic patients was evaluated by Dyck et coworkers (15), the results showed that the neurologic disability score (NDS), vibratory and cooling thresholds, compound muscle action potential, sensory nerve action potentials, and motor nerve conduction velocities achieved the most reliable results.

Perkins (31) stated in his review, that screening for diabetic neuropathy is justified as it offers the patient with diabetes a crucial opportunity to actively alter the course of suboptimal glycemic control prior to significant morbidity associated with the natural history of neuropathy. For screening purposes three fundamental issues need to be addressed (31):

1) Specificity,
2) confirmatory diagnosis and
3) appropriateness of screening.

The first issue specificity need be addressed, since distal symmetrical sensimotor deficits may arise from such conditions as uremic, toxic, alcoholic, familial, paraneoplastic, and/or nutritional neuropathy (17). The second issue is still in discussion, the criterion standard to diagnose diabetic neuropathy (DNP) is not finalized yet. The most objective test in the evaluation of DNP are the physical examination, quantitative sensory testing and nerve conduction studies (NCS). It is generally agreed, that at least two objective tests are required for a diagnosis for research purposes (6). Nerve conduction studies are the least subjective of these tests since they are independent of patient psychophysical interpretation and they provide reliable, quantitative measures of nerve function. The lack of sensitivity for isolated small fiber neuropathy is however a criticism of the use of nerve conduction studies alone, although the clinical importance of this form of neuropathy is likely insignificant in the context of DNP, in which the progressive loss of all nerve fibers is observed.(16). The third issue ad-

dresses the common prerequisites to justify the necessity for the screening for certain subjects so as the relevance of the disease, the consequences of the natural course of the disease, the possibility to positively influence the course of the disease and the availability of a simple and accurate test suitable for diabetes or primary care.

Another proposal for the screening of large numbers of diabetic patients from Simmons et al (38) proposes the use of inexpensive, rapid methods e.g. the use of monofilaments to measure touch sensitivity and the use of tactile circumference discrimination.

Meijer et coworkers (25) tested the possibility to differentiate between three patient groups (group 1: diabetic patients with diabetic foot ulcers; group 2: 24 diabetic patients without clinical neuropathy; and group 3: 21 control subjects without diabetes) with the diabetic neuropathy score (DNS), the diabetic neuropathy examination score (DNE), and their relationship with cardiovascular autonomic function testing (CAFT) and electrodiagnostic studies (EDS). Both scores were able to discriminate between group 1 and group 2 significantly ($p<0.001$). The diabetic neuropathy examination score discriminated also between group 2 and group 3 ($p<0.05$). Spearman's correlation coefficients between both scores and cardiovascular autonomic function testing and electrodiagnostic studies were high.

Perkins et coworkers (32) investigated the diagnostic value of four different simple sensory tests (the 10-g Semmes-Weinstein monofilament examination [SWME], superficial pain sensation, vibration testing by the on-off method, and vibration testing by the timed method) as screening tests for peripheral neuropathy in the diabetes clinic. Therefore these tests were carried out in 478 subjects with independent blinded evaluations compared against the criterion standard of nerve conduction studies. The results gained were convincing for superficial pain sensation testing, Semmes-Weinstein monofilament examination, or vibration testing by the on-off method.

The value of nerve fiber conduction velocity distributions as additional diagnostic criteria for diabetic neuropathy was evaluated by Cummins et coworkers (10). He found a shift of towards slower conduction velocities in diabetic patients with minimal or no clinical neuropathy, but these findings were obtained in the elbow-to-axilla segment of the N. medianus.

The conduction slowing observed in diabetic patients was also evaluated by Herrmann et coworker (19) in comparison to patients suffering from amyotrophic lateral sclerosis (ALS), where a form of neuropathy with a loss of large axons is observed. The findings suggested that the nerve conduction velocity slowing was due to an amplitude-dependent mechanism in both diabetic patients and ALS patients in the upper and lower extremities, consistent with a loss of large myelinated fibers. In addition in diabetic patients also a significant amplitude-independent slowing in intermedia but not in distal nerve segments was found, supporting that an additional demyelinative component could be observed.

The influence of aging to changes of the compound muscle action potential (CMAP) in pa-

tients without clinical neuropathy was investigated by Kurokawa (24). He found, that the amplitude of the compound muscle action potential was lower in older patients, however the compound muscle action potential ratio (proximal CMAP/distal CMAP) did not change with age. The compound muscle action potential duration or interval and the corresponding ratio was not different in groups of patients with different age, but the compound muscle action potential area was smaller in older patients, the area ratio nevertheless remained almost constant.

To summarize: Nerve conduction studies remain the most reliable, accurate, and sensitive measure of peripheral nerve function (1). These have long been a gold standard for the diagnosis of all neuropathies (11) and are, most simply considered, an extension of the clinical neurological examination. The nerve conduction study findings correlate with the clinical endpoints (32), and the nerve potential amplitudes reflect the degree of nerve fiber loss (34). Standardized methods improve the reliability of testing such that nerve conduction studies have the lowest degree of variance of all tests in diabetic neuropathy (51). The prevalence of abnormal nerve conduction velocities increases with duration of diabetes (1), and disease severity correlates with glycemic control (21). Only small changes in parameters are observed In intervals as long as 5 years, particularly in the setting of acceptable glycemic control (45). The small changes in conduction velocity are readily demonstrable, but amplitude changes are more difficult to show due to higher variability of this measures (9). Two potential disadvantages must be considered for the use of nerve conduction studies: the limit of availability of nerve conduction testing for routine diagnostic evaluation and the insensitivity for the identification of small fiber neuropathy (16).
All these findings are interesting for further diagnostic measures for early detection of diabetic neuropathy in patients suspicious of having diabetic neuropathy and need to be re-evaluated in this patient population in a comparison to a “normal” population without diabetes and clinical signs for any form of neuropathy.

5. THERAPY OF DIABETIC NEUROPATHY

This section describes the treatment of diabetic neuropathy without considering the treatment of symptomatic diabetic neuropathy.

Despite huge efforts for clinical research in treatment of DNP the value of intensive glycemic control remains as the most important issue in this context (30).

The Diabetes Control and Complications Trial showed that maintenance of an intensive therapy intervention, resulting in a mean hemoglobin A1 concentration of 7.2%, as compared

with conventional therapy, resulting in a mean of 9.1%, reduced the risk of neuropathy by 60% (95% CI: 38% to 74%) (44). A weakness of this and other studies of the effect of glycemic control is that they used surrogate measures for the improvement (or slowing of progression) of neurologic function (28). Most used sensory or motor nerve conduction studies and some used vibration perception thresholds. Whether such measures correlate reliably with neuropathy symptom scores, neurologic examination, quality-of-life, neuropathic complications (foot ulcers and amputation), and mortality remains controversial. Nevertheless: as a result of these studies patients should be treated with a goal of glycated hemoglobin less than 7% (30).

Measures other than improved glycemic control and symptomatic control of painful symptoms can improve the prognosis for patients with DNP. Beside glycemic control other approaches to treat DNP so as aldose reductase inhibitors (ARI), which aims to protect nerves from the effects of overactivity of the polyol pathway caused by chronic hyperglycemia (8). Several substances were clinically tested with negative results for various reasons (negative clinical results, side effects, poor study data quality).

Neurotropins such as nerve growth factors used to stimulate the growth of nerves, which demonstrated encouraging results in preclinical and early clinical studies (4), failed also in phase III clinical trials, due to poor efficacy results or side effects observed (8).

Anti-oxidant therapy (e.g. alpha-lipoic acid) which shall improve the blood flow is still in clinical investigations and need to be reconsidered.

Summarizing it can be stated, that beside optimal glycemic control no other convincing therapy option consists for the treatment of DNP. Beside this specific approaches more common measures as preventing of known toxic substances (e.g. alcohol, prevention of vitamin deficiencies, certain drugs), reduction of known risk factors (e.g. hypertension, hypercholesterolemia, smoking) and prevention of complications (podiatry, hygiene, appropriate stockings and shoes, weight reduction) need to be considered also (26).

6. AIM OF THE STUDY

Due to the high risk for foot ulceration in patients with distal symmetric polyneuropathy, which may lead to lower limb amputation and high financial burden for the society it is mandatory to optimize the early diagnosis of these disease (46). The early identification of the neuropathic process in diabetic patients is justified as it offers the patient a crucial opportunity to actively alter the course of suboptimal glycemic control prior to significant morbidity associated with the natural course of neuropathy in these patients (31). It is likely that effective intervention will be possible only during the subclinical or early phase of dysfunction in diabetic patients

(5).

The impact and diagnostic value of determination of motor nerve conduction velocities (mNCV) as early diagnostic tool for diabetic neuropathy is well accepted. (41, 23). This non-invasive and easy-to-generate method is frequently used in neurophysiological examinations. In general the assessment of this diagnostic tool in terms of reproducibility and validity as a prerequisite for comparing analyzes demonstrates, that this tool used professional is able to be utilized for diagnosis and staging of diabetic neuropathy (33, 51). A comparative study investigating whether it is sufficient to test only one side of peripheral nerves for nerve conduction velocity analyses revealed, that in patients with diabetic neuropathy interside symmetry can be considered (33). Therefore it is acceptable for studies in this field to rely on data collected in patients from one side. Parameters usually applied for the testing of peripheral motor nerves are the determination of the maximum nerve conduction velocity, amplitude of the compound muscle action potential (CMAP), latency and F-wave latency (12). It can be assumed, that these parameters could become pathological not in the early course of disease but in later stages.

Therefore the aim of this study was to determine, whether there are additional ways in analyzing the neurophysiological status of the peripheral nerve system in the case suspected diabetic neuropathy in an early stage of disease. The determination of the maximum motor nerve conduction identifies only demyelination of the fastest nerve fibers, which represent only a minority of the profile of the complete nerve (41). Up to now it is still in discussion, whether DNP is based on a loss of nerve fibers or a process of demyelinisation or on both, and if both processes are involved, which of both are involved in the beginning of the process (52, 23).

Therefore a study was carried out comparing two groups of patients to test additional parameters for the evaluation of peripheral motor nerve function beside the parameters already mentioned above. In the group 1 inpatients of the Neurologische Universitätsklinik Marburg were included, who

1) had no diabetes mellitus,
2) had no clinical signs of any neuropathy,
3) were not suspected to have any alcohol abuse,
4) gave their informed consent for the tests carried out.

In group 2 patients

1) having impaired glucose tolerance or manifest diabetes mellitus,
2) clinical signs of distal symmetric DNP and
3) with informed consent

were included and investigated. The parameters tested additionally beside the parameters

already mentioned are described and defined in the section 8.2 Neurophysiological investigation (8.2). Summarized following characteristics of the compound muscle action potential shall be analyzed:

1) Since the usual nerve conduction velocity determination analyzes only the fastest nerve fibers, additionally the nerve conduction velocities of the other characteristic CMAP markers shall be analyzed in order to further characterize not only the fastest nerve fibers, but also slower-conducting nerve fibers.
2) The changes of the characteristics of the CMAP (amplitudes, intervals, areas) from distal to proximal stimulation due to dispersion of the CMAP (24, 56) will be evaluated by calculation of the quotient of the corresponding proximal and distal values (e.g. proximal maximum amplitude divided by distal maximum amplitude).
3) The area under the curves (distal and proximal) of the CMAP provide further information about the quantity of nerve fibers tested and shall be therefore analyzed.
4) Intervals of the CMAP (distal and proximal) further characterize the function of peripheral nerves and shall be therefore analyzed.
5) In addition to the maximum amplitude of the compound muscle action potential also parts of the amplitude (positive/negative amplitude) shall be analyzed.

The Zero-Hypothesis for this study will be therefore defined as following:

For the support of the diagnosis of diabetic neuropathy other parameters (as described above) than maximum nerve conduction velocity and compound muscle action potential amplitude do not differentiate with statistical significant results between healthy persons and patients suspicious of having diabetic neuropathy.

7. STATISTICAL ISSUES

All relevant data collected for the neurophysiological investigations were transferred into a data table (Excel 2000) and analyzed by a statistician program (SPSS 11.5). A non-parametric test (Mann-Whitney test) was applied to compare the parameters for both patient groups. In addition descriptive statistical parameters (mean, standard deviation [SD], median, minimum, maximum, percentile 25/50/75) were provided for both patient groups. Relevant results of the analysis were transferred into boxplots.

8. PATIENTS AND METHODS

8.1 Patients

All patients included in this study were inpatients of the Neurologische Universitätsklinik Marburg. In order to comply with ethical standards to study was evaluated and accepted by the ethical committee of the Universitätsklinik Marburg before initiation. All patients gave their informed consent prior recruitment. The further details of the ethical background of the study are summarized in section Ethical issues (13.2).

All patients who have participated in this study were examined after following scheme:

1) Common anamnesis
2) Anamnesis for diabetes mellitus
3) Anamnesis for neuropathic symptoms (NS)
4) Neurological examination for neuropathic deficits (ND)

For group 1 following items were checked before recruitment:

1) Patients with diabetes mellitus were excluded
2) Patients with clinical symptoms for any neuropathy were excluded
3) Patients with suspicion of having any alcohol abuse were excluded
4) Patients have to give their written informed consent

In group 1 32 female and 35 male patients were included. The average age (±SD) was 49 years(±28 years).

For patients of group 2 following items were checked prior recruitment:

1) Patients need to have at least impaired glucose tolerance test results or manifest diabetes mellitus
2) Patients with clinical signs of neuropathy
3) Patients with written informed consent.

In group 2 9 female and 12 male patients were included, the average age (±SD) was 68 years (±17 years). The average time elapsed (±SD) since diagnosis of diabetes mellitus or impaired glucose tolerance (IGT) was 12.1 years (±7.3 ys). In 2 of 21 cases type I diabetes mellitus was diagnosed, in 7 cases type II diabetes mellitus, in 12 cases unknown. 6 Patients suffered from insulin-dependent diabetes mellitus (IDDM), 6 from non-insulin-dependent diabetes mellitus (NIDDM), 9 cases unknown. The results of nerves investigated were available in 18, 19 respectively 15 cases (N. medianus, N. tibialis, N. peronaeus). In 19 out of 21 pa-

tients symptoms of diminished or altered sensation could be observed, in 2 patients the reduction or absence of reflexes was the only symptom of DNP.

The difference with regard to the average age between group 1 and group 2 could have some impact on the results, since it is known that age of patients could influence the nerve conduction (36) or CMAP amplitude (24). This issue will be considered later in the section Discussion (10).

The definition of the gender of the patients is as following: 1 means female, 2 means male.

The detailed information about patients in group 2 is provided in the following table 1:

Table 1 Details of patients in group 2

Patient No.	Initials	Sex	Age at examination	DM type	Diabetes mellitus duration (ys)	NIDDM or IDDM	Symptoms of diabetic neuropathic symptoms/deficits, diabetes mellitus information, antidiabetic medication (if known)	N. medianus	N. tibialis	N. peronaeus
1	HK	2	74	n.k.	n.k.	n.k.	Pallanesthesia legs, distal pronounced hypesthesia and hypalgesia, Achilles tendon reflex -/-	X	X	X
2	AE	1	20	I	23	IDDM	Hypesthesia left upper leg lateral and ventral	X	X	X
3	LB	2	30	I	20	IDDM	Pallhypesthesia, Achilles tendon reflex reduction on both sides	X	X	X
4	BH	2	66	II	5	NIDDM	Pallhypesthesia 4/8 at both lower legs, Achilles tendon reflex -/-, Euglucon 2-0-1	X	X	X
5	JW	2	64	II	n.k.	n.k.	Distal symmetric hypesthesia in both lower legs (middle lower legs), pallhypesthesia 5/8	X	X	X
6	HH	1	82	II	n.k.	n.k.	Achilles tendon reflex -/-, paresthesia and hypesthesia in both lower legs	X	X	-
7	EH	2	67	II	10	NIDDM	Pallhypesthesia 4/8, stocking-like hypesthesia both lower legs, Glyko-Hb 9,5 mg/dl, Euglucon 1-1-0	X	X	-
8	JK	1	86	II	10	NIDDM	Paresthesia both feet, pallhypesthesia 5/8, Achilles tendon reflex reduction on both sides, dietetic treatment of diabetes mellitus	X	X	X

Patient No.	Initials	Sex	Age at examination	DM type	Diabetes mellitus d<<uration (ys)	NIDDM or IDDM	Symptoms of diabetic neuropathic symptoms/deficits, diabetes mellitus information, antidiabetic medication (if known)	N. medianus	N. tibialis	N. peronaeus
9	WS	2	65	n.k.	30	n.k.	Pallanesthesia both lower legs, hypalgesia on both arms and legs		X	X
10	AM	2	69	II	2	NIDDM	Distal symmetric pallhypesthesia. 4/8, Euglucon 2-0-0	X	X	X
11	HH	1	78	n.k.	n.k.	IDDM	Pallhypesthesia on both legs 6/8, Achilles tendon reflex -/-, Depot H 24-0-12	X	-	-
12	GM	1	82	n.k.	n.k.	n.k.	Pallhypesthesia 5/8 at both lower legs, distal symmetric hypesthesia in both lower legs, pathological oral glucose tolerance test	X	X	X
13	GP	2	73	n.k.	n.k.	n.k.	Pallhypesthesia lower legs, Achilles tendon reflex -/-, diabetic metabolism	X	X	X
14	AB	1	68	IIb	n.k.	NIDDM	Pallhypesthesia both feet, Achilles tendon reflex reduction on both sides, posture sense dysfunction both feet, Euglucon 2-0-0	X	X	-
15	EW	1	80	n.k.	>10 ys.	NIDDM	Pallhypesthesia distal lower extremities, patella tendon reflexes and Achilles tendon reflexes -/-, Euglucon 1-0-0	-	X	X
16	RL	2	54	n.k.	9	IDDM	Mild pallhypesthesia on both lower legs, Achilles tendon reflex reduction on both sides	-	X	X

Patient No.	Initials	Sex	Age at examination	DM type	Diabetes mellitus duration (ys)	NIDDM or IDDM	Symptoms of diabetic neuropathic symptoms/deficits, diabetes mellitus information, antidiabetic medication (if known)	N. medianus	N. tibialis	N. peronaeus
17	GG	2	62	n.k.	approx. 8 ys.	NIDDM	Paresthesia feet, posture sense dysfunction both feet, Achilles tendon reflexes -/-	X	X	X
18	GS	2	65	n.k.	approx. 11 ys.	IDDM	Pallhypesthesia, patella tendon reflexes -/-, Achilles tendon reflexes -/-, Depot H 36-0-10	X	-	-
19	KG	2	71	n.k.	n.k.	n.k.	Pallhypesthesia lower extremities, patella tendon reflex reduction on both sides, Achilles tendon reflexes -/-	X	X	-
20	KK	1	73	n.k.	9	n.k.	Achilles tendon reflexes -/-	X	X	X
21	JS	2	87	n.k.	14	IDDM	Achilles tendon reflexes reduced on both sides, pallhypesthesia, Depot H 30-0-16, Euglucon 1-0-1	X	X	X
Sum per nerve (n=)								**18**	**19**	**15**

(n.k. not known; DM diabetes mellitus; IDDM insulin dependent diabetes mellitus; NIDDM non-insulin dependent diabetes mellitus; ys years; no. number; sex: 1 = female, 2 = male)

8.2 Neurophysiological examinations

The measurements were carried out with an usual device for neurophysiological examinations (Neuropack 4 by Nihon Kohden/Japan).

Following parameters of the device were kept up during all measurements:

- Sensitivity of the amplifier 5 mV
- Upper filter frequency 3 kHz
- Lower filter frequency 20 kHz
- Delay time 0 ms
- Stimulation frequency 1 Hz
- Stimulation duration 0.2 ms
- Stimulation type: single

Following parameters were changed during the measurements:

- Analysis time (X axis) from 20-50 ms depending on the length of the CMAP.
- Analysis amplitude (Y axis) 1-5 mV/DIV depending on the amplitude of the CMAP.
- Stimulation intensity: beginning with 20 mA increased in steps of 5 mA until no change of the CMAP could be observed (maximum 99mA).

The parameters were determined on the Nn. medianus, tibialis and peronaeus on one side of the patients. Before carrying out the measurements the temperature of the skin was determined by a sensor and eventually corrected with the help of a red light lamp (if surface temperature was < 32 ^{o}C). During testing the patients were lying on a stretcher.

The skin of the patients was cleaned with an alcoholic pad and the surface electrodes (Ag/AgCl 13mmx7mmx1,5mm) were fixed after application of electrode gel.

The different electrode was fixed above the muscle belly, the indifferent electrode was fixed above the tendon of the muscle (see figure 1). To get an optimal compound muscle action potential the position of the different electrode was corrected if necessary. The grounding electrode was moistened and connected to the wrist (N. medianus) or the ankle (N. tibialis, N. peronaeus). Following nerves were tested:

Table 2 Tested nerves

Nerve	Muscle for recording	Stimulation distal	Stimulation proximal
N. medianus	M. abductor pollicis brevis	Radial wrist	Elbow near the brachial artery
N. tibialis	M. extensor digitorum communis	Upper part behind the medial malleolus	Middle part of the popliteal space
N. peronaeus	M. extensor digitorum brevis	Ventral side of the distal lower leg	Near the capitulum fibulae

The stimulation sides were marked and the corresponding distance was measured in mm by a tape-measure. All neurophysiological examinations were printed and stored via hard disk.
The examinations were analyzed for following variables:

- Nerve conduction velocities (NCV1-4) of the compound muscle action potential (CMAP)
- Intervals of the CMAP (distal and proximal)
- Amplitudes of the CMAP (distal and proximal)
- Areas of the CMAP (distal and proximal)
- Quotients of the before mentioned variables (each proximal parameter divided by distal parameter).

The different stimulation sites are described by addition of a prefix (distal = D / proximal = P) to the marker (e.g. PL1). Intervals were shortened as IL, amplitudes as A, areas as AR, and quotients as prefix with Q (example QAR = quotient area).
The parameters evaluated are defined and explained in the following figures 1-8:

Figure 1 Schematic picture of the neurophysiological examination of the N. medianus

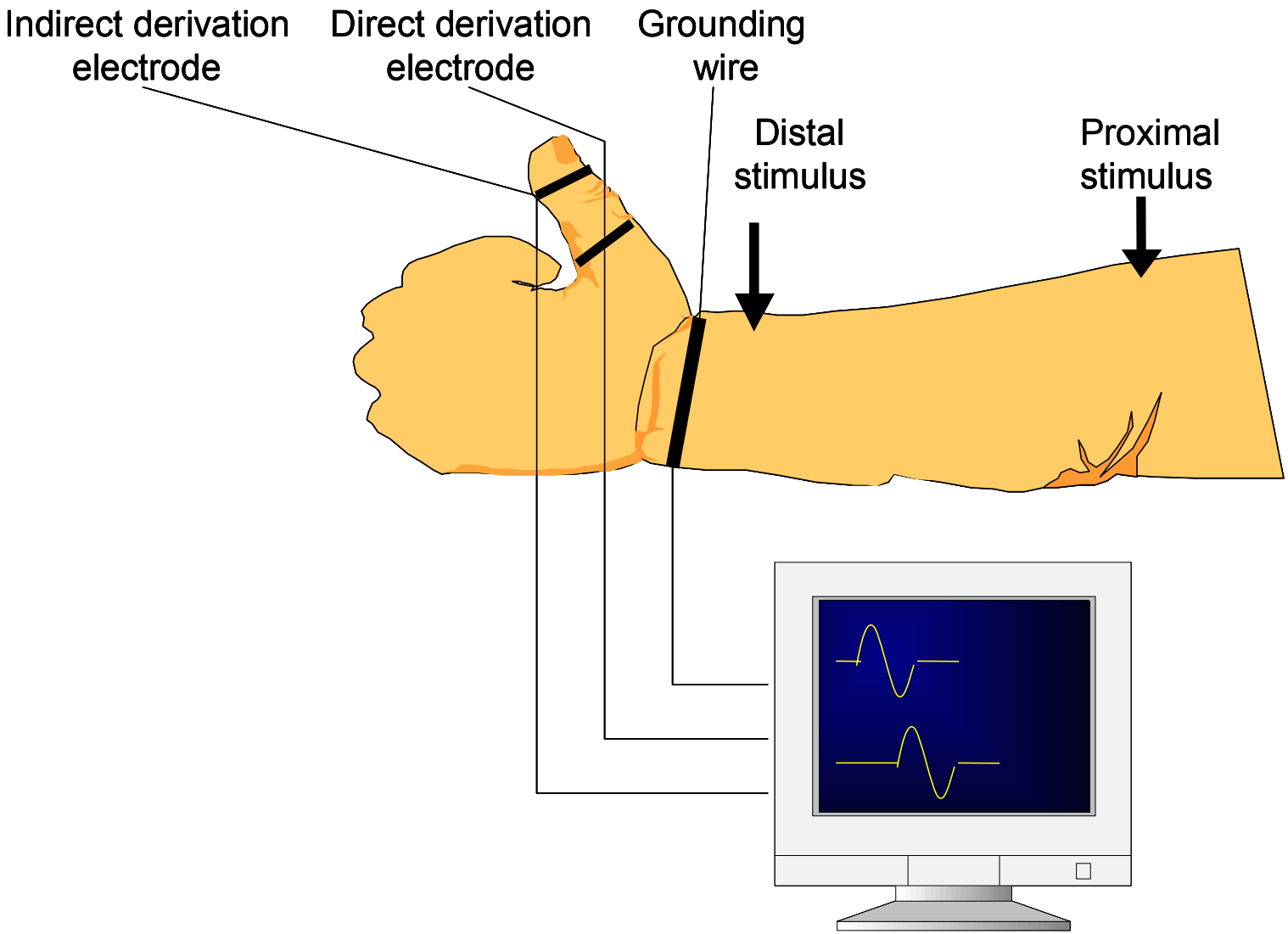
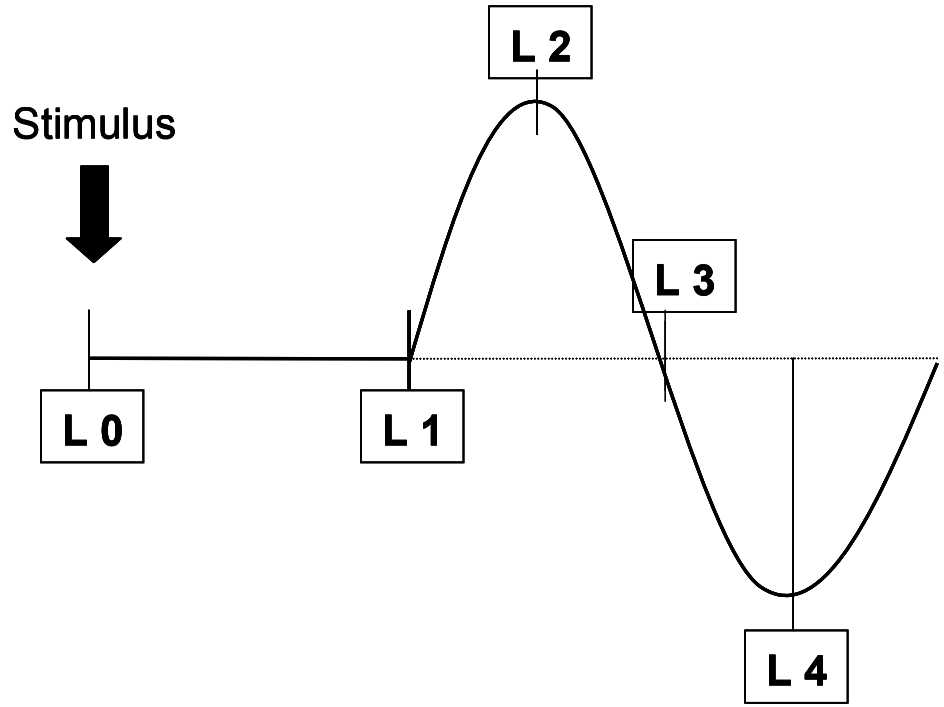


Figure 2 Definition of the different markers in the compound muscle action potential (CMAP)



Marker	Definition of the position
L0	Stimulus
L1	Beginning depolarization from the basic potential
L2	Zenith of the CMAP
L3	Reversal point of the CMAP
L4	Nadir of the CMAP

Figure 3 Definition of the different parameters of the compound muscle action potential (CMAP)

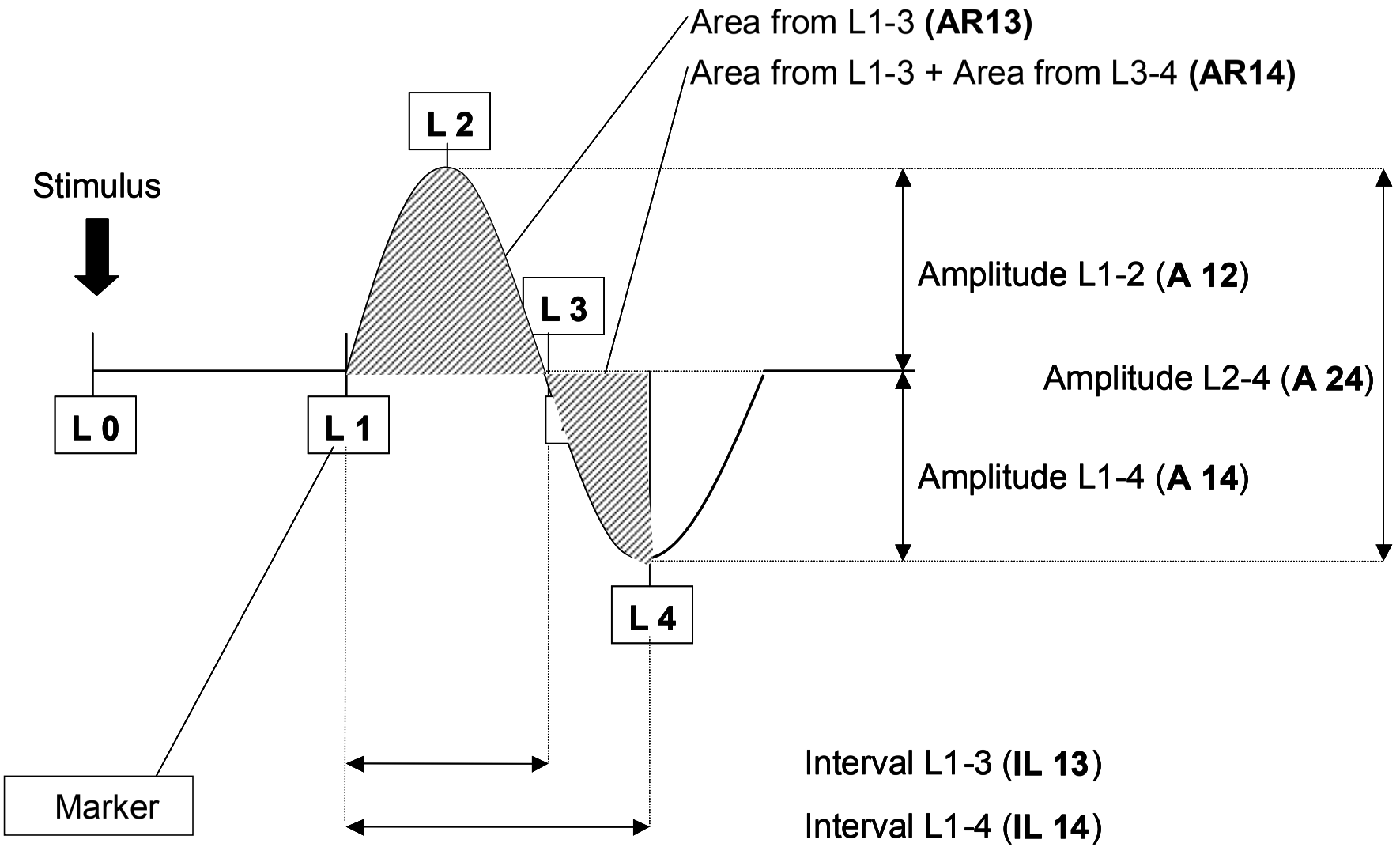
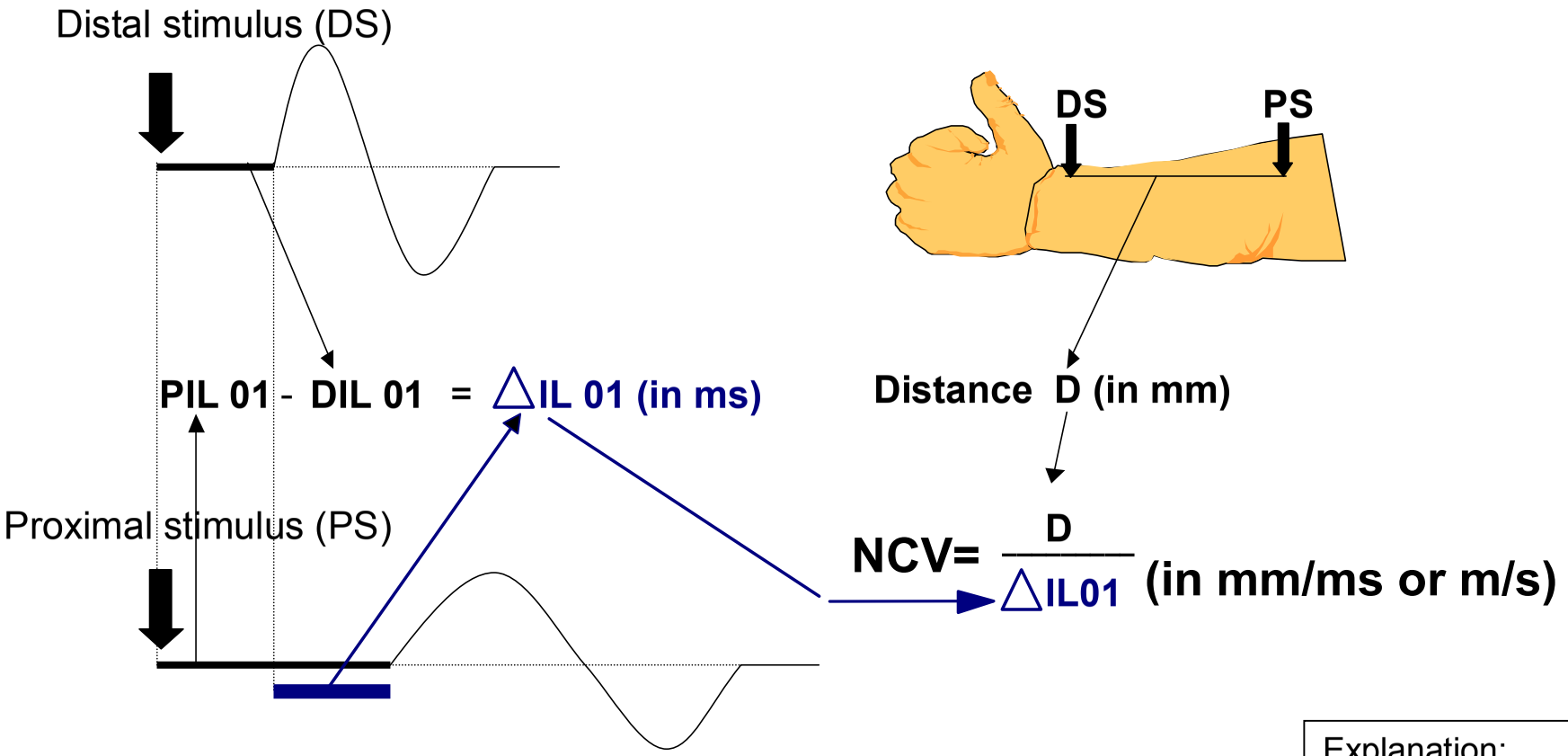


Figure 4 Schematic picture of the determination of the nerve conduction velocity (NCV)



Example: PIL01= 6.8 ms, DIL01 = 3.3 ms, ⇨ △ IL01 = 3.5 ms

Distance = 189mm, ⇨ $\frac{189\ mm}{3.5\ ms}$ = 54 mm/ms or 54 m/s

Explanation:

DIL = distal interval

PIL = proximal interval

Figure 5 Schematic picture of the determination of nerve conduction velocity 1-4 (NCV 1-4)

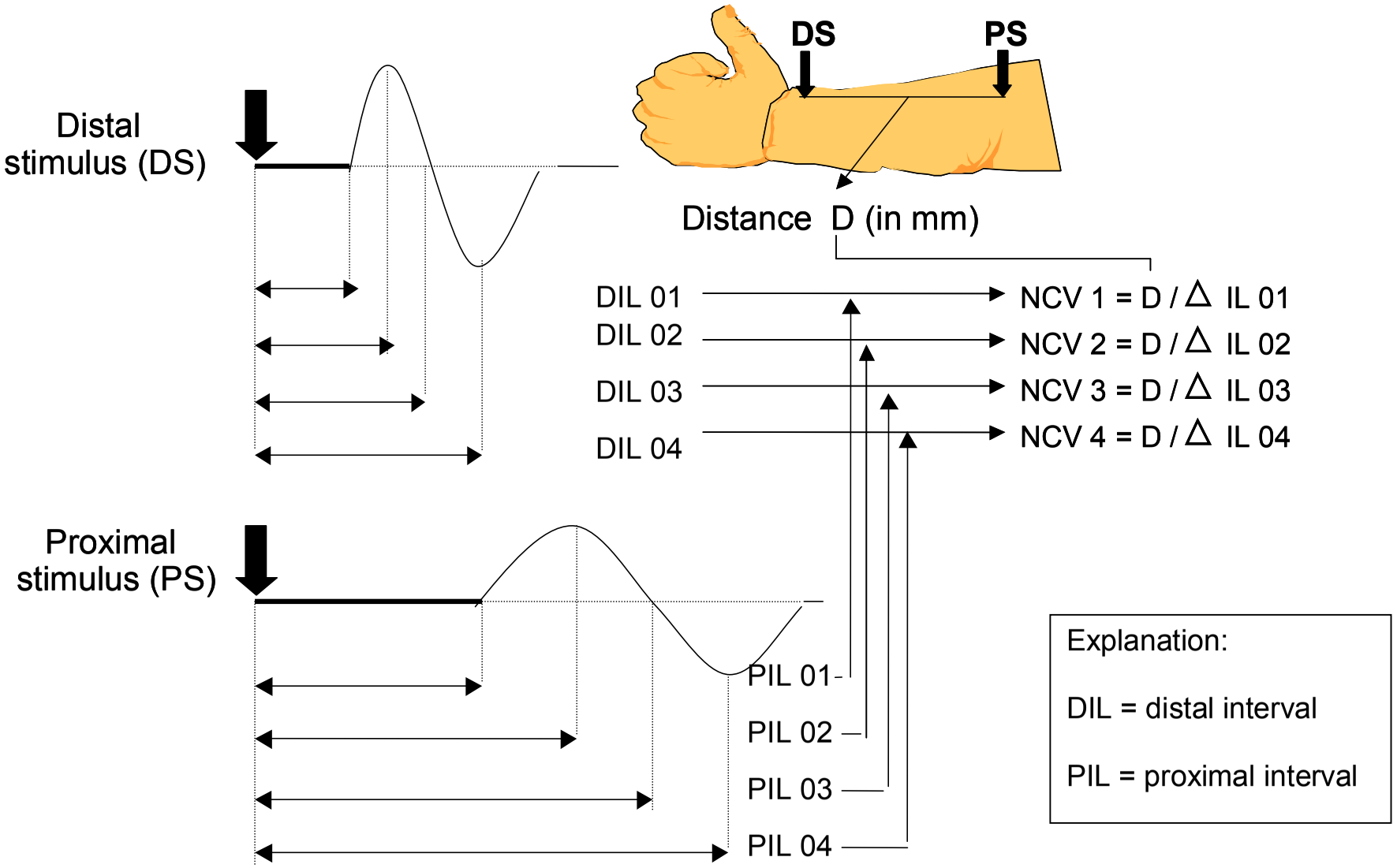


Figure 6 Schematic picture of the determination of the interval quotients (QIL)

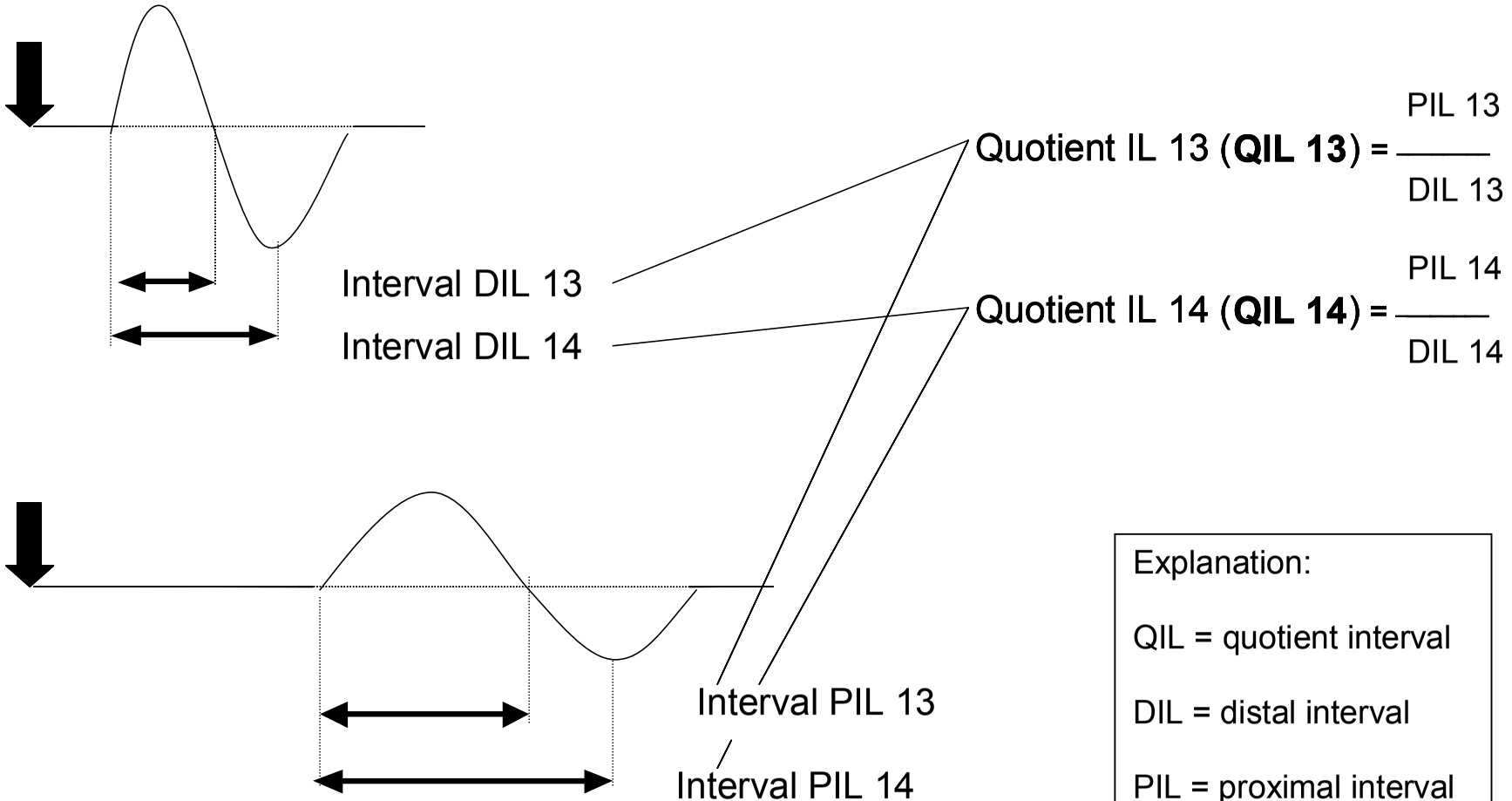
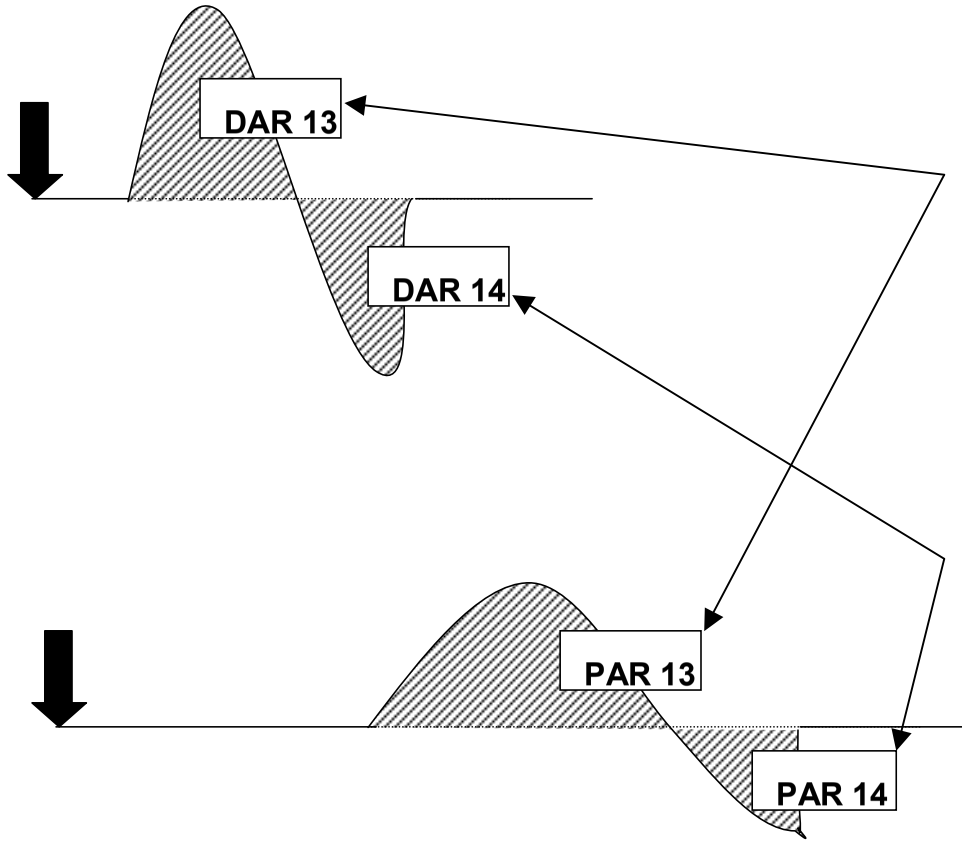


Figure 7 Schematic picture of the determination of the area quotients (QAR)



Quotient AR 13 **(QAR13) =** $\frac{\text{PAR 13}}{\text{DAR 13}}$

Quotient AR 14 **(QAR14) =** $\frac{\text{PAR 14}}{\text{DAR 14}}$

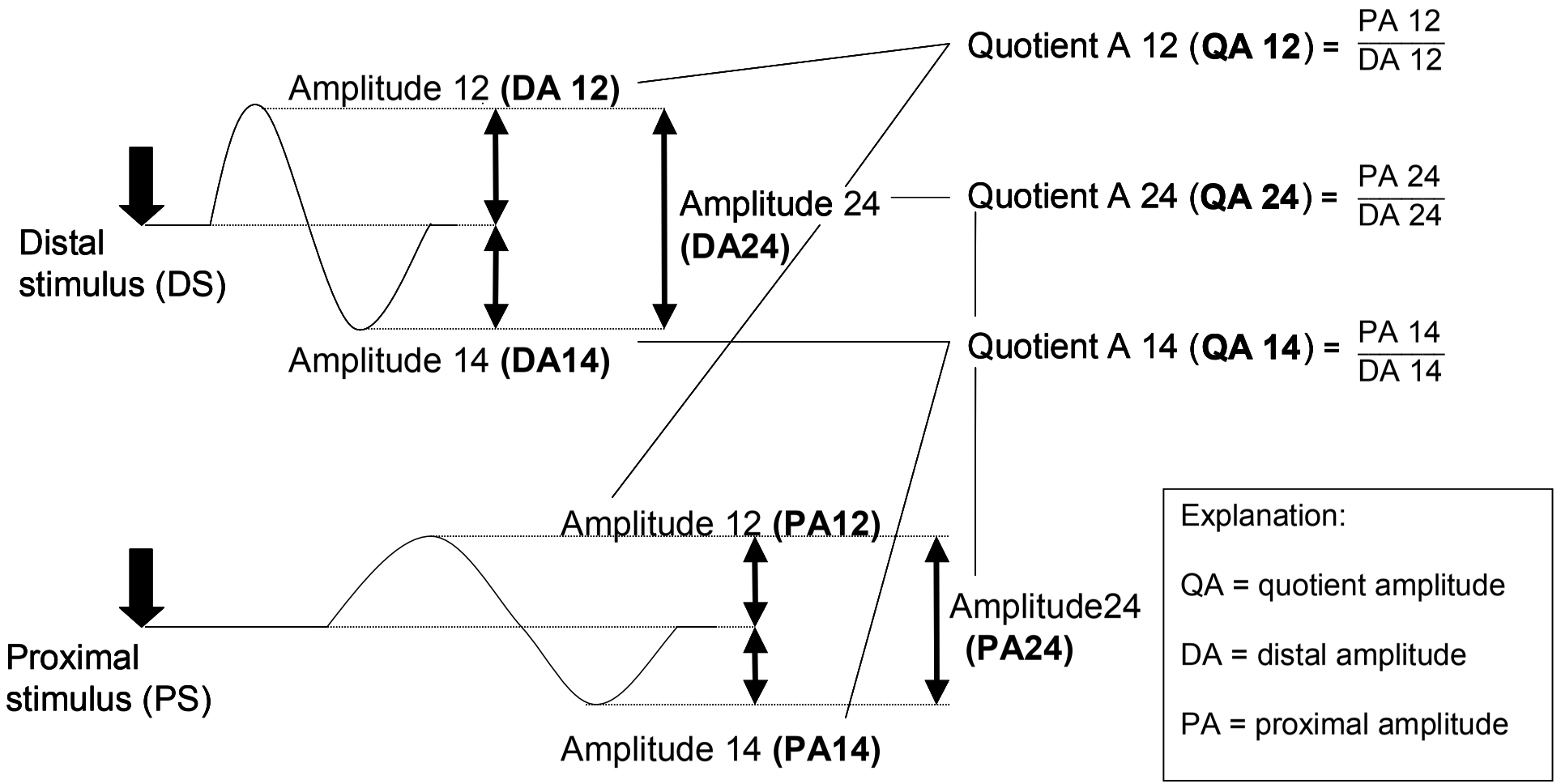
Explanation:

QAR = quotient area

DAR = distal area

PAR = proximal area

Figure 8 Schematic picture of the determination of the amplitude quotients (QA)



9. RESULTS

In the following sections the results of the testing of the three different nerves (N. medianus, N. tibialis, N. peronaeus) are presented. As a rule comparisons were carried out between group 1 and group 2, shortened as GR 1 and GR 2. The complete tables with all analyzed data (frequencies with descriptive statistics, ranking, results of Mann-Whitney tests, boxplots) are summarized in section 13.1 Listing of tables/boxplots (13.1). In this section only the results of the Mann-Whitney tests for the analyzed parameters are presented together with relevant boxplots. The prefixes D and P before the variables characterize them either as distal or proximal stimulated. The single characteristics of the variables were defined in section 8.2. Neurophysiological examinations (8.2). Results for asymptomatic significance as shown below are qualified to be statistical significant, if the values provided were < 0.05.

9.1 N. medianus

9.1.1 Distal and proximal intervals, amplitudes and areas

The testing of proximal and distal intervals (IL13 and IL14) and distal areas (DAR13 and DAR14) showed insignificant results. For distal amplitude DA14 also insignificant results were obtained, whereas proximal amplitude PA14 and proximal area PAR13 and PAR14 showed significant results. Amplitudes (A12, A24) showed both significant results for distal and proximal stimulation. The switch from insignificant results to significant results, which can be demonstrated here in some cases from distal to proximal stimulation, could be explained by the probably stronger influence of dispersion in proximal stimulation due to longer distance from the stimulation point to the derivation point. The best results in terms of differentiation between group 1 and group 2 can be achieved be focusing on the amplitudes (maximum amplitude of the CMAP = A24 and amplitude of the first part of the CMAP = A12), which can be seen in the boxplots below.

Distal variables

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	570,000	595,500	398,000	454,000	390,500	435,500	448,500
Wilcoxon W	2848,000	766,500	569,000	625,000	561,500	606,500	619,500
Z	-,355	-,081	-2,205	-1,603	-2,286	-1,728	-1,586
Asymp. Sig. (2-tailed)	,723	,936	,027	,109	,022	,084	,113

a. Grouping Variable: GR

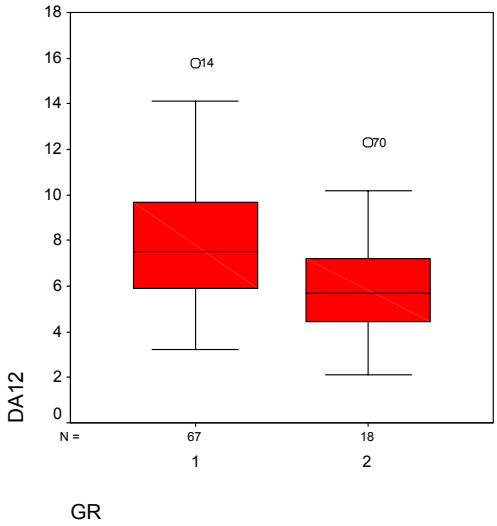
Proximal variables

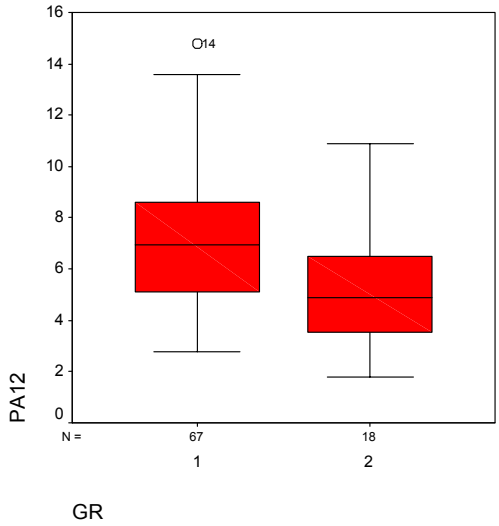
Test Statistics[a]

	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	527,000	558,500	351,500	382,500	353,000	386,500	412,500
Wilcoxon W	2805,000	2836,500	522,500	553,500	524,000	557,500	583,500
Z	-,818	-,479	-2,705	-2,372	-2,689	-2,262	-1,979
Asymp. Sig. (2-tailed)	,413	,632	,007	,018	,007	,024	,048

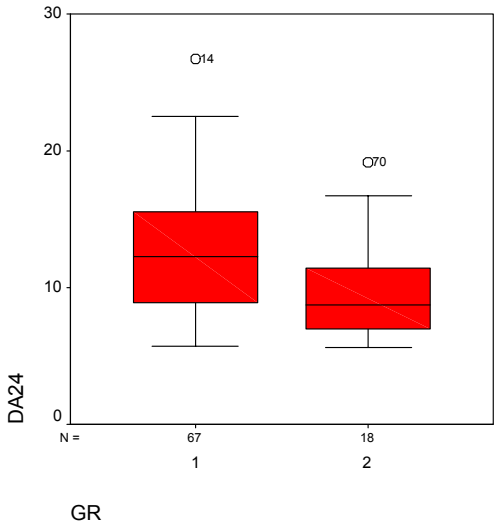
a. Grouping Variable: GR

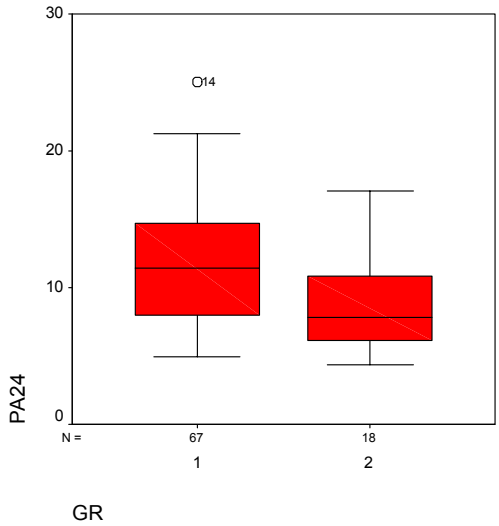
Boxplots for distal positive amplitude 12 (DA12) and proximal positive amplitude 12 (PA12)



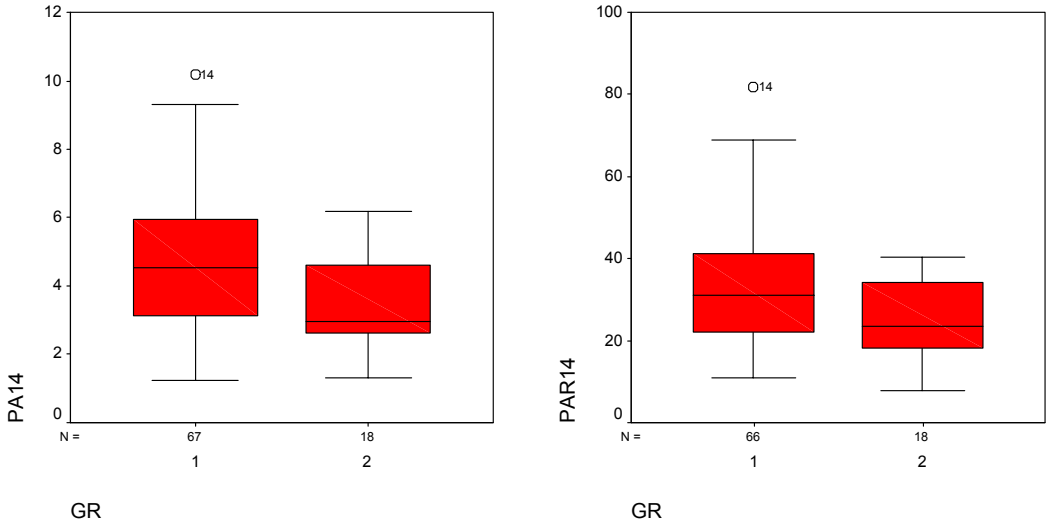


Boxplots for distal maximum amplitude 24 (DA24) and proximal maximum amplitude 24 (PA24)

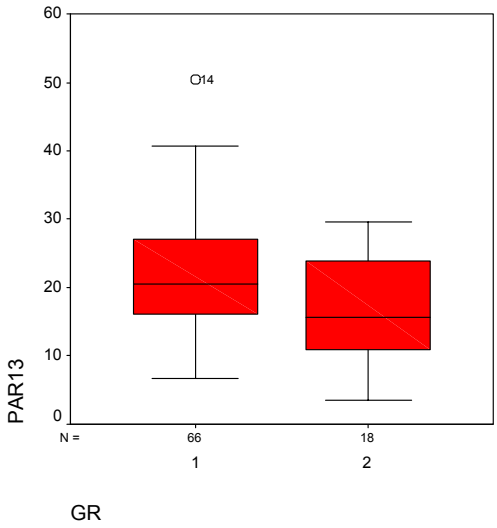




Boxplots for proximal negative amplitude 14 (PA14) and proximal area 14 (PAR14)



Boxplots for proximal area 13 (PAR13)



9.1.2 Nerve conduction velocities

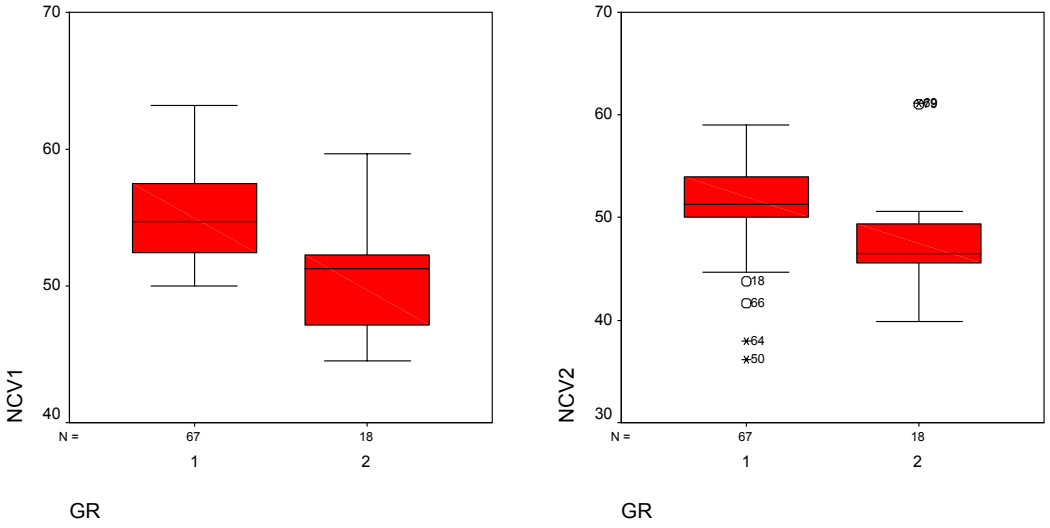
The analysis of the nerve conduction velocities (NCVs) showed for all NCVs highly significant results in terms of differentiation between group 1 and group 2. This can also been demonstrated in the corresponding Boxplots.

Test Statistics[a]

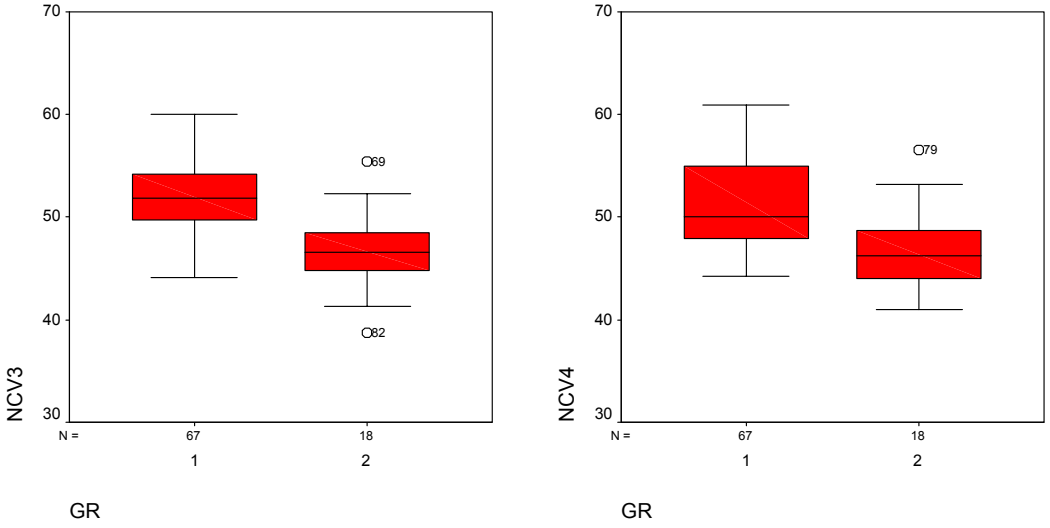
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	256,500	252,500	197,000	234,000
Wilcoxon W	427,500	423,500	368,000	405,000
Z	-3,728	-3,770	-4,368	-3,970
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots for nerve conduction velocity 1 (NCV1) and 2 (NCV2)



Boxplots for nerve conduction velocity 3 (NCV3) and 4 (NCV4)



9.1.3 Interval, amplitude and area quotients

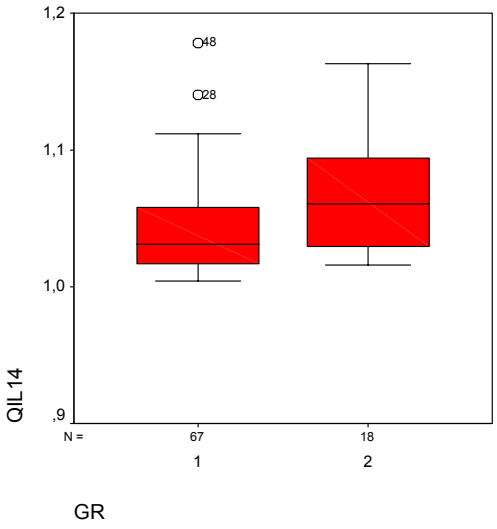
The analysis of the quotient evaluation demonstrated also for all quotients significant differences between group 1 and group 2, only for the interval quotient QIL13 this level was not reached. This result indicates, that also for parameters, which were singular tested not significant (either distal or proximal, e.g. interval IL14), that by combination of both entities (distal and proximal) into one variable the result becomes a significant level. The results are additional displayed in the corresponding boxplots.

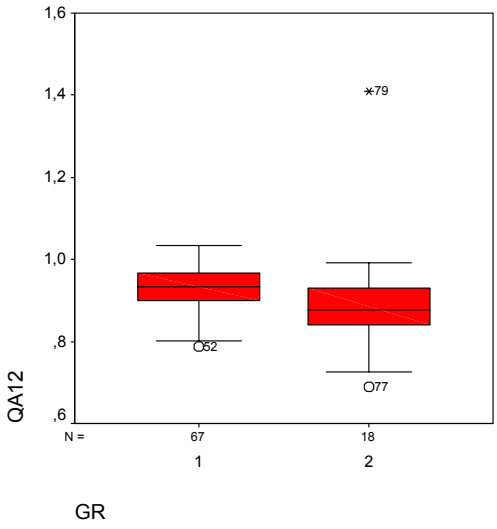
Test Statistics[a]

	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	447,500	384,000	359,000	343,000	323,000	321,000	370,000
Wilcoxon W	2725,500	2662,000	530,000	514,000	494,000	492,000	541,000
Z	-1,673	-2,356	-2,625	-2,797	-3,012	-2,976	-2,442
Asymp. Sig. (2-tailed)	,094	,018	,009	,005	,003	,003	,015

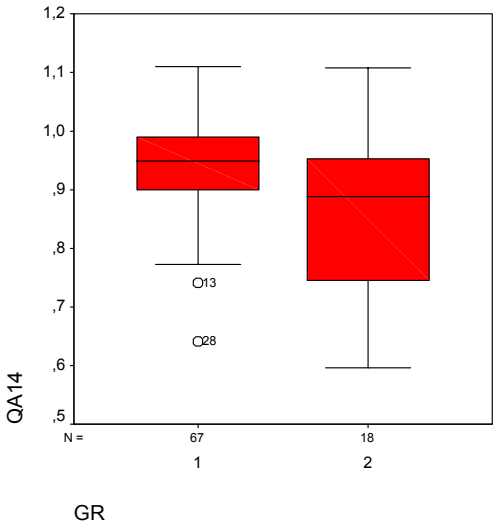
a. Grouping Variable: GR

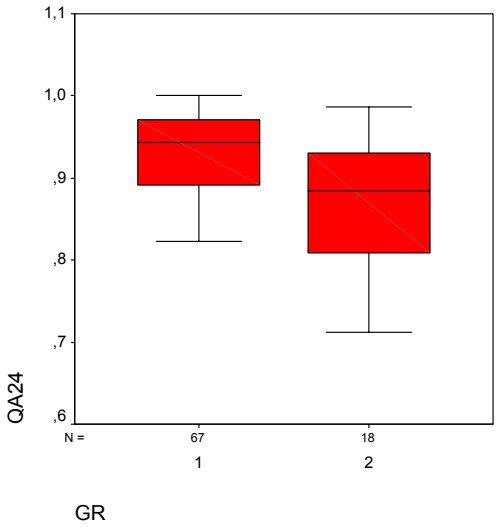
Boxplots for interval quotient 14 (QIL14) and positive amplitude quotient 12 (QA12)



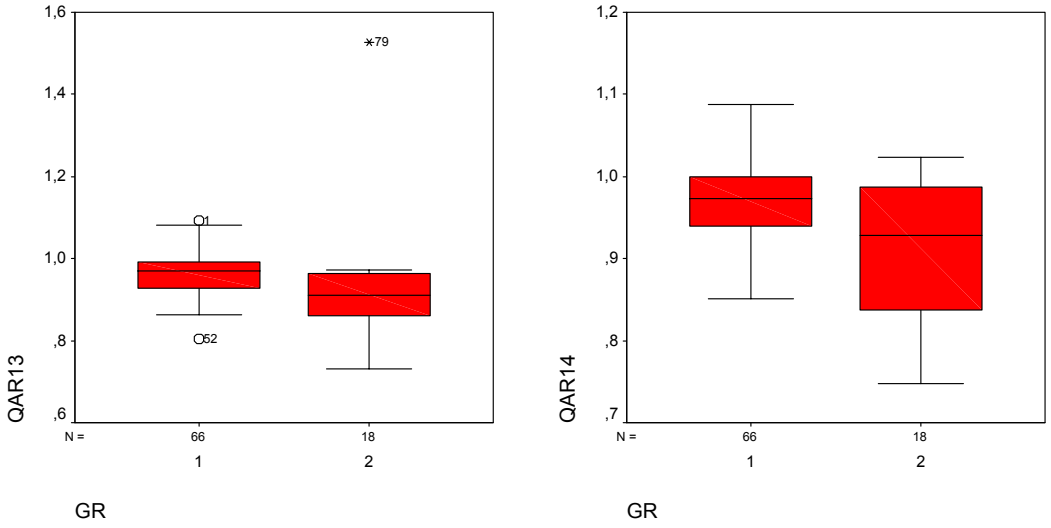


Boxplots for negative amplitude quotient 14 (QA14) and maximum amplitude quotient 24 (QA24)





Boxplots for area quotient 13 (QAR13) and area quotient 14 (QAR14)



9.1.4 Summary

Summarized for the results of the testing of N. medianus it can be stated, that the results obtained showed a clear evidence, that the best differentiation between group 1 and group 2 can be obtained, by analyzing the data with regard to the NCVs. Due to a very high level of significance in this group (NCV1-4) no differences can be made between these 4 variables in terms of preference of a single variable. Nevertheless the impression from the box plot evaluation of NCV2 and NCV3 showed interestingly lower variance compared to NCV1 providing a hint, that they may could be used to better discriminate between group 1 and 2. The next variables able to discriminate between the two groups were the amplitudes (maximum amplitude and amplitude of the first part of the CMAP=A12) and the quotients derived from the amplitude, area and interval variables (exception: IL13). No differentiation can be derived from using single interval variables. Summarized these results could be interpreted that way, that for the pathophysiology of DNP in the N. medianus a major impact of demyelination followed by axonal degeneration could explain the results found in this neurophysiological testing in diabetic and non-diabetic patients.

9.2 N. tibialis

9.2.1 Distal and proximal intervals, amplitudes and areas

The results obtained for N. tibialis in this section revealed non-significant results only for the evaluation of distal and proximal intervals (IL13 and IL14). For all other parameters highly significant results were obtained for all amplitudes (A12, A14, A24) and areas (AR13, AR14).

Distal variables

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	556,500	573,000	223,000	188,000	202,500	213,000	215,500
Wilcoxon W	2834,500	2851,000	413,000	378,000	392,500	403,000	405,500
Z	-,833	-,661	-4,305	-4,669	-4,518	-4,367	-4,341
Asymp. Sig. (2-tailed)	,405	,509	,000	,000	,000	,000	,000

a. Grouping Variable: GR

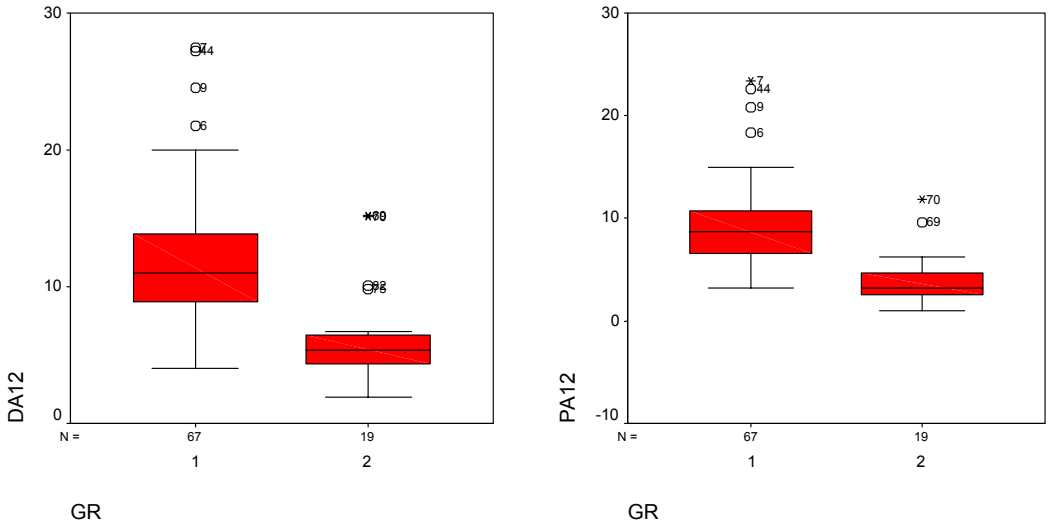
Proximal variables

Test Statistics[a]

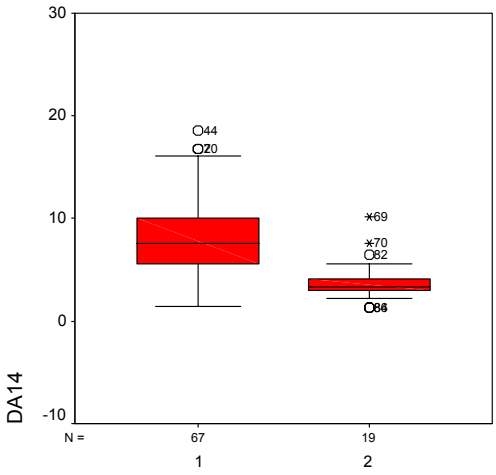
	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	454,500	483,500	148,500	170,000	164,000	173,000	196,000
Wilcoxon W	2732,500	2761,500	338,500	360,000	354,000	363,000	386,000
Z	-1,895	-1,593	-5,080	-4,856	-4,919	-4,789	-4,547
Asymp. Sig. (2-tailed)	,058	,111	,000	,000	,000	,000	,000

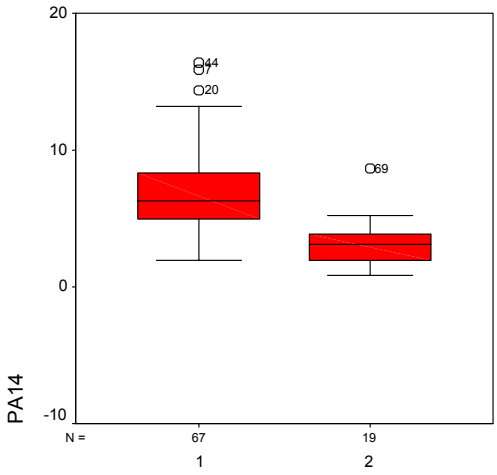
a. Grouping Variable: GR

Boxplots for distal positive amplitude 12 (DA12) and proximal positive amplitude 12 (PA12)

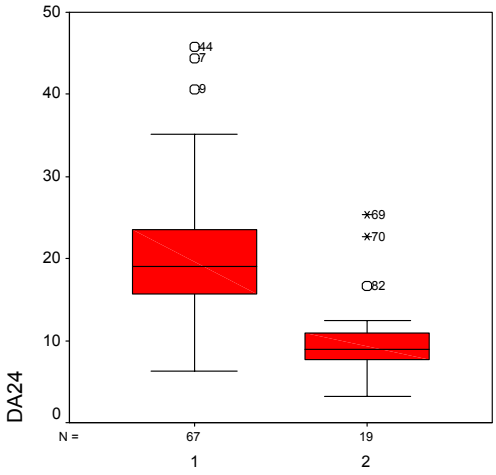


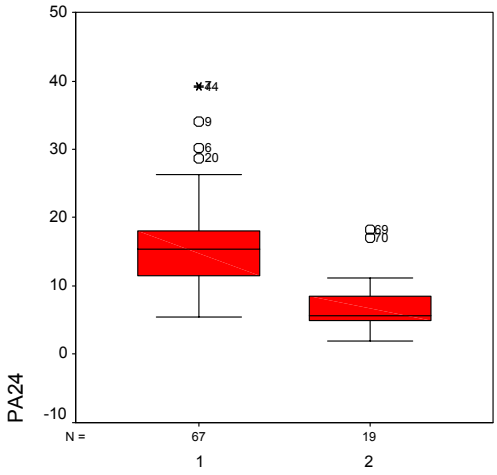
Boxplots for distal negative amplitude 14 (DA14) and proximal negative amplitude 14 (PA14)



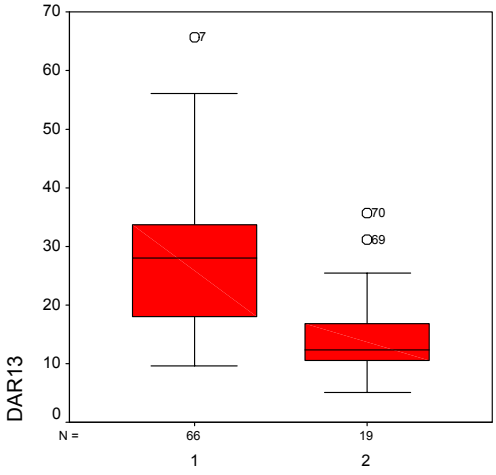


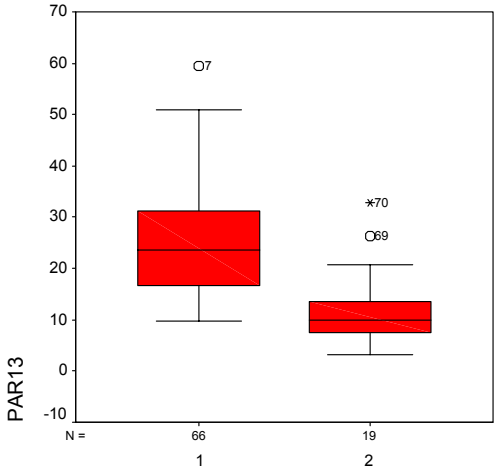
Boxplots for distal maximum amplitude 24 (DA24) and proximal maximum amplitude 24 (PA24)



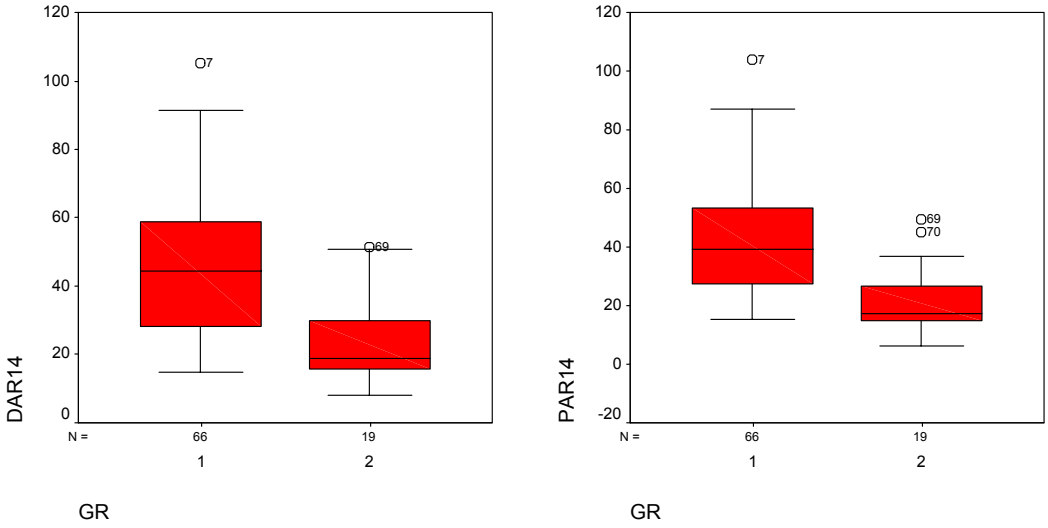


Boxplots for distal area 13 (DAR13) and proximal area 13 (PAR13)





Boxplots for distal area 14 (DAR14) and proximal area 14 (PAR14)



9.2.2 Nerve conduction velocities

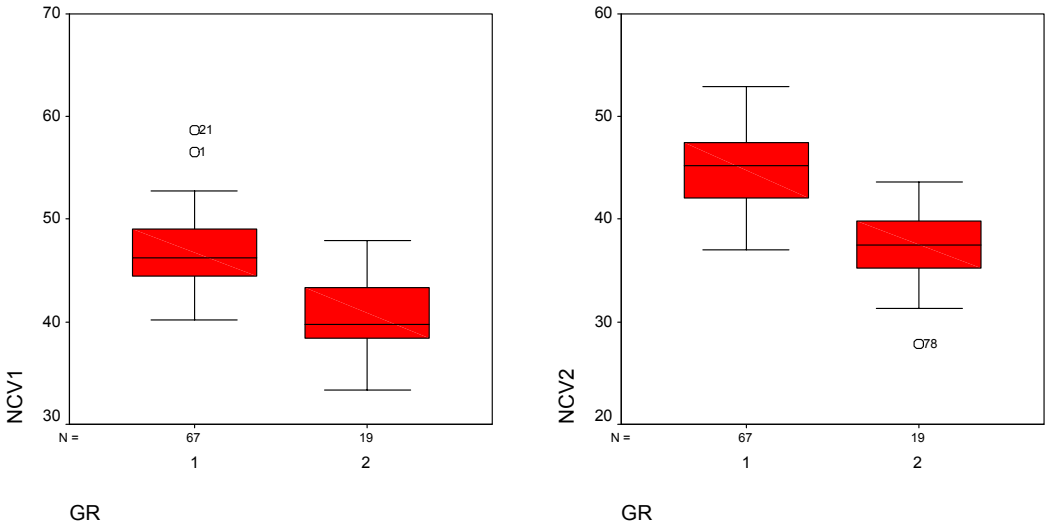
The evaluation of the differences of NCVs revealed for all NCVs highly significant results, no differences between single NCVs could be observed.

Test Statistics[a]

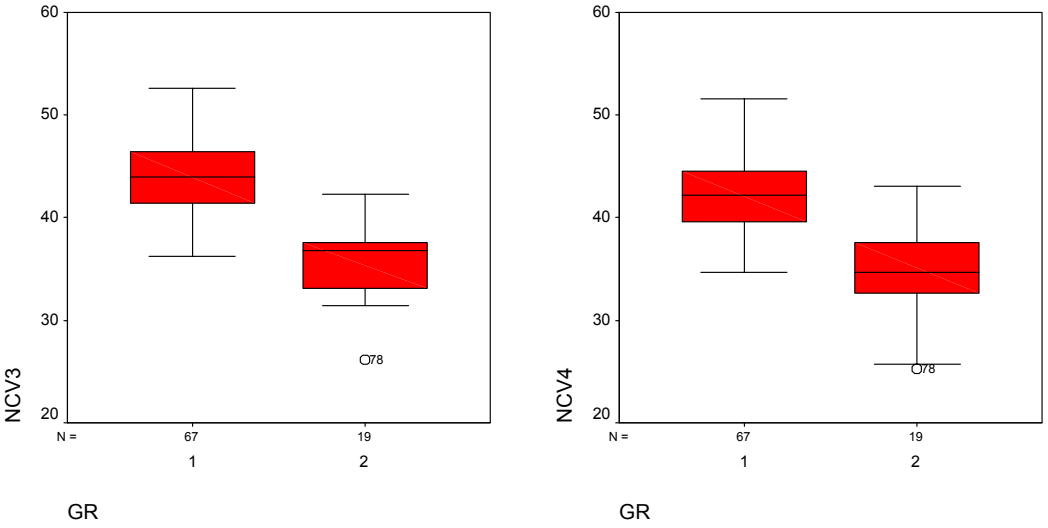
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	133,500	75,000	76,500	99,500
Wilcoxon W	323,500	265,000	266,500	289,500
Z	-5,237	-5,845	-5,829	-5,590
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots for nerve conduction velocity 1 (NCV1) and 2 (NCV2)



Boxplots for nerve conduction velocity 3 (NCV3) and 4 (NCV4)



9.2.3 Interval, amplitude and area quotients

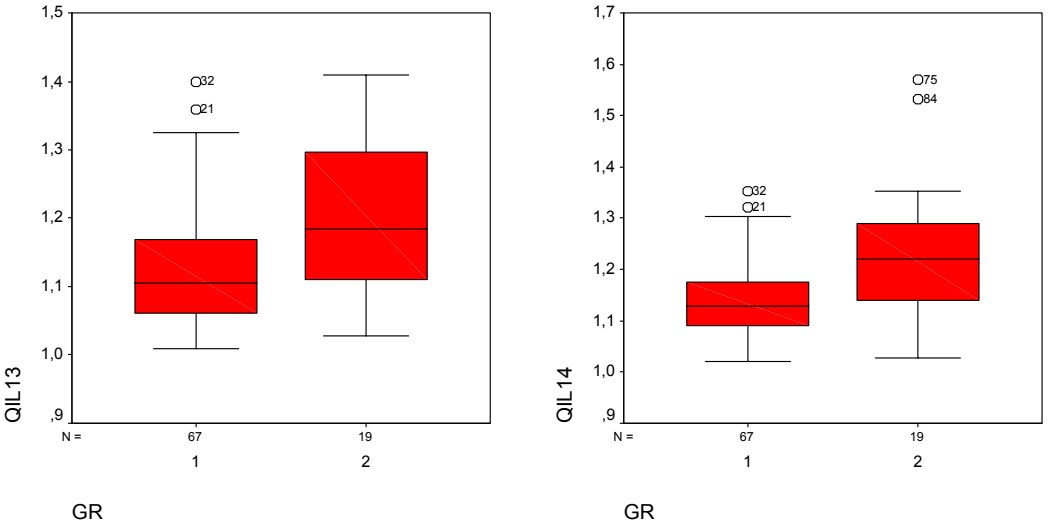
Also the evaluation of quotients resulted in almost all cases in significant differences between group 1 and group 2 (QIL13, QIL 14, QA12, QA24, QAR13, QAR14). Only for the quotient of the amplitude A14 (QA14) non-significant results were obtained.

Test Statistics[a]

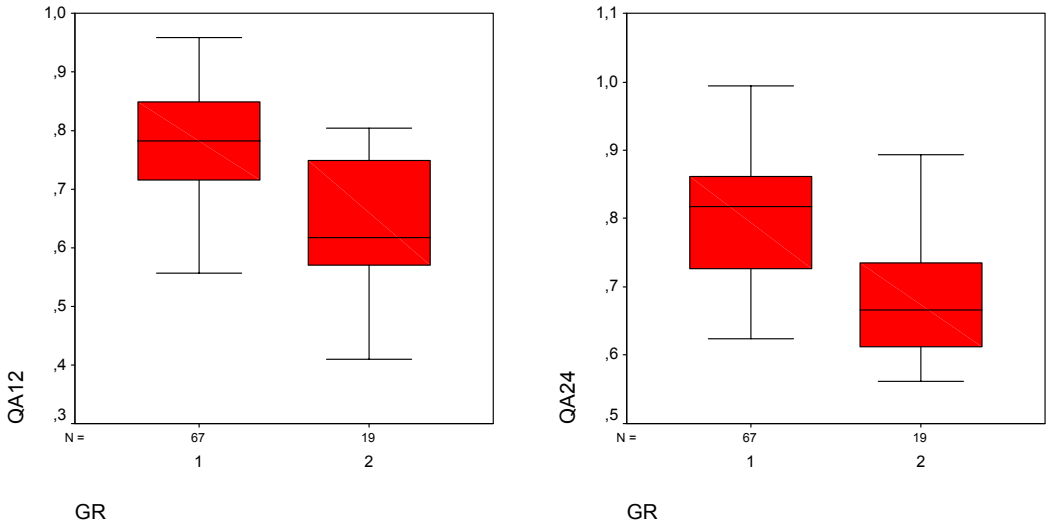
	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	372,000	407,000	213,000	519,500	264,000	351,000	400,000
Wilcoxon W	2650,000	2685,000	403,000	709,500	454,000	541,000	590,000
Z	-2,753	-2,389	-4,408	-1,218	-3,877	-2,911	-2,395
Asymp. Sig. (2-tailed)	,006	,017	,000	,223	,000	,004	,017

a. Grouping Variable: GR

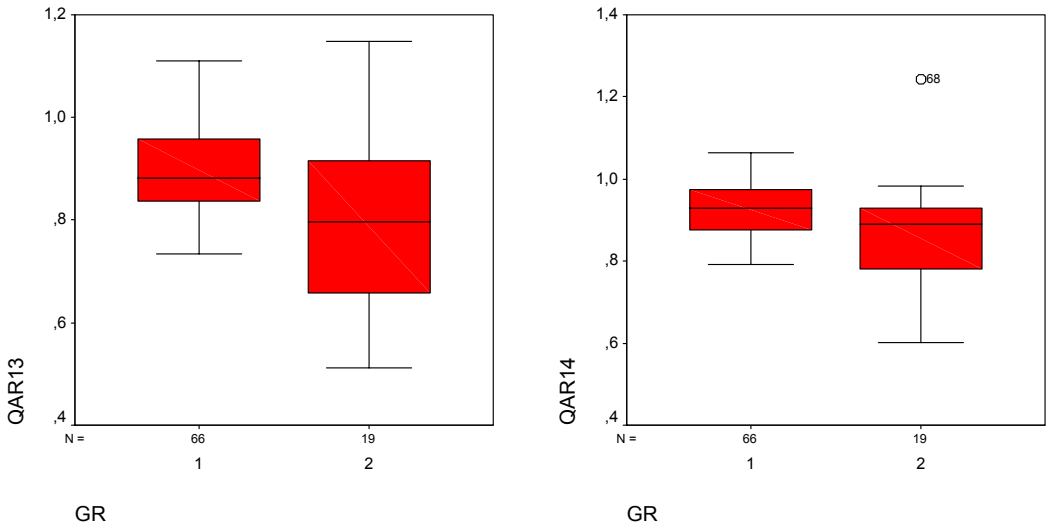
Boxplots for interval quotient 13 (QIL13) and interval quotient 14 (QIL14)



Boxplots for positive amplitude quotient 12 (QA12) and maximum amplitude quotient 24 (QA24)



Boxplots for area quotient 13 (QAR13) and area quotient 14 (QAR14)



9.2.4 Summary

The evaluation of the results obtained for N. tibialis showed for almost all parameters investigated significant or even highly-significant differences for the comparisons between group 1 and group 2. Only parameters, which were tested also for N. medianus to be non-significant like intervals (IL13 or IL14), showed similar results. In contrast to the results obtained for N. medianus the level of significance between NCVs and amplitudes/areas could not be demonstrated here providing hints, that in N. tibialis the degree of DNP could be more advanced than in N. medianus.

9.3 N. peronaeus

9.3.1 Distal and proximal intervals, amplitudes and areas

The evaluation of the results from N. peronaeus showed almost identical results compared to N. tibialis. Beside interval variables (IL13, IL14) for all other parameters (both amplitudes and areas) highly significant results were obtained.

Distal variables

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	415,500	427,000	123,000	194,000	130,000	104,000	132,500
Wilcoxon W	535,500	547,000	243,000	314,000	250,000	224,000	252,500
Z	-1,044	-,906	-4,552	-3,701	-4,468	-4,754	-4,408
Asymp. Sig. (2-tailed)	,297	,365	,000	,000	,000	,000	,000

a. Grouping Variable: GR

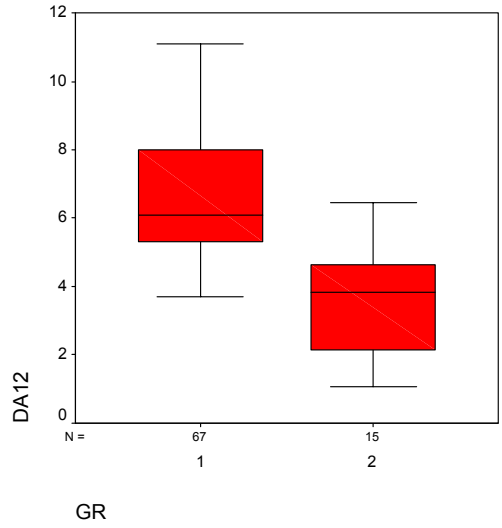
Proximal variables

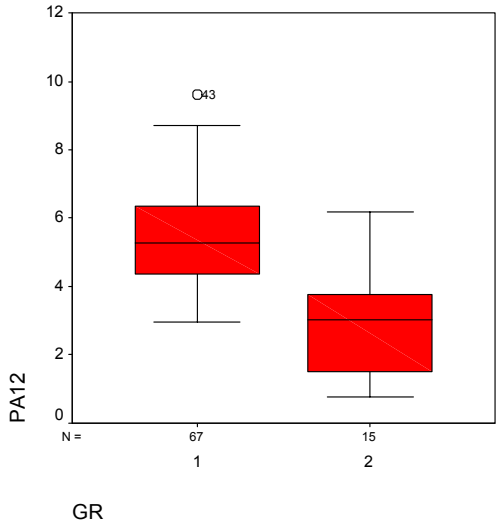
Test Statistics[a]

	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	502,000	483,000	123,500	115,000	114,500	106,000	125,000
Wilcoxon W	622,000	603,000	243,500	235,000	234,500	226,000	245,000
Z	-,006	-,234	-4,546	-4,648	-4,654	-4,730	-4,499
Asymp. Sig. (2-tailed)	,995	,815	,000	,000	,000	,000	,000

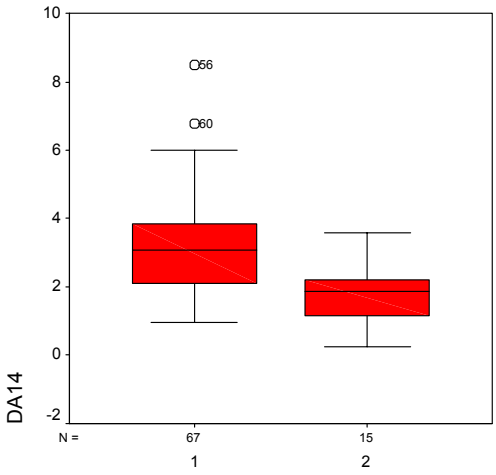
a. Grouping Variable: GR

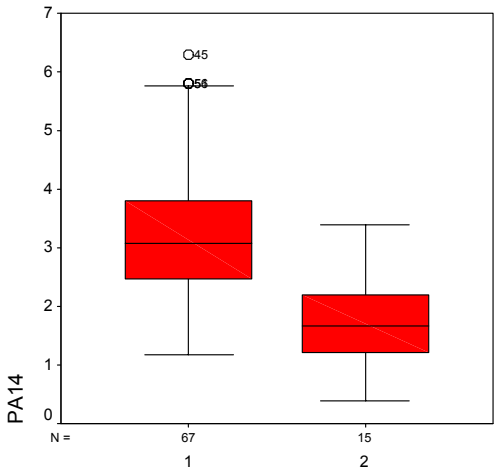
Boxplots for distal positive amplitude 12 (DA12) and proximal positive amplitude 12 (PA12)



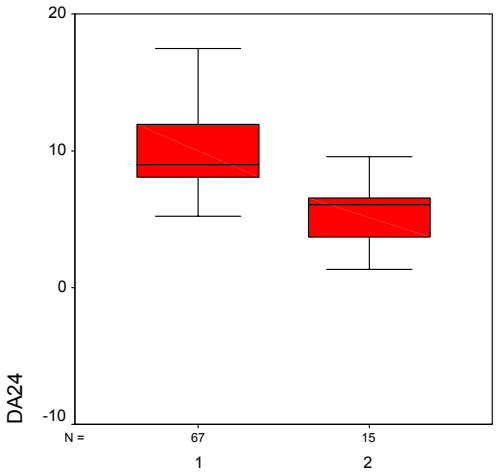


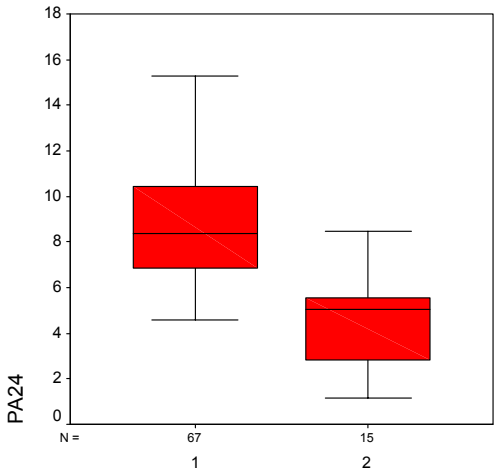
Boxplots for distal negative amplitude 14 (DA14) and proximal negative amplitude 14 (PA14)



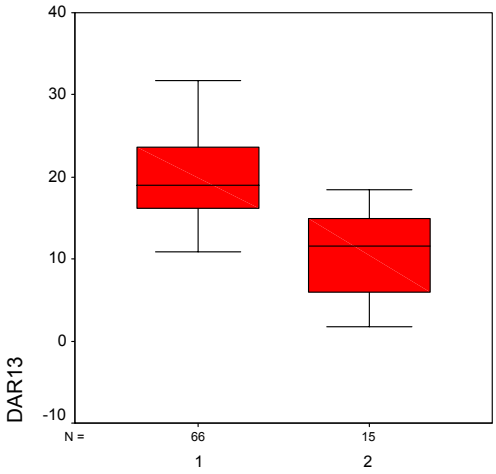


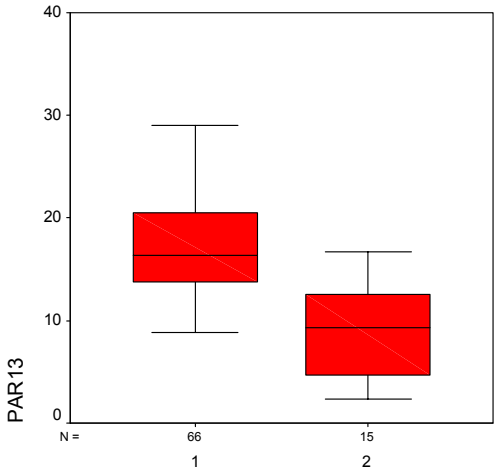
Boxplots for distal maximum amplitude 24 (DA24) and proximal maximum amplitude 24 (PA24)



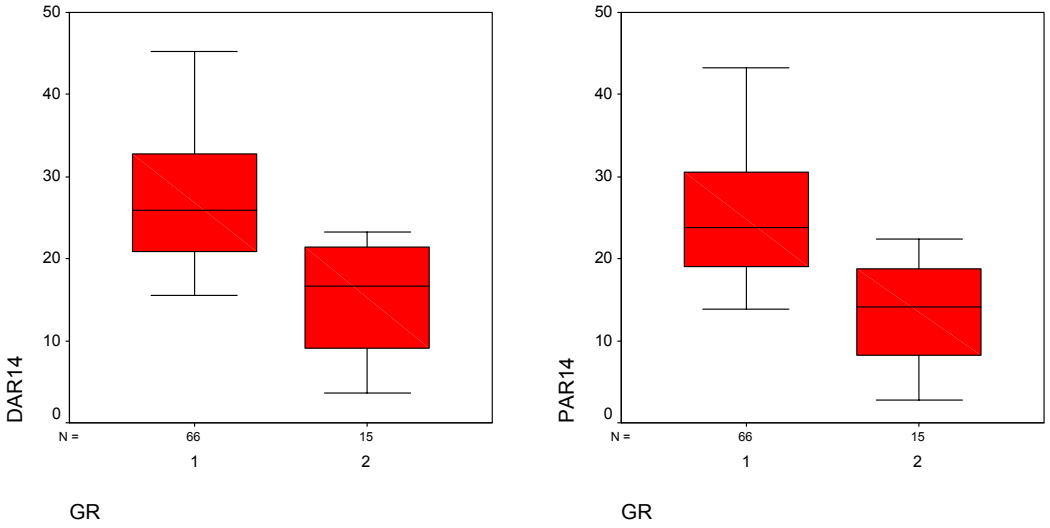


Boxplots for distal area 13 (DAR13) and proximal area 13 (PAR13)





Boxplots for distal area 14 (DAR14) and proximal area 14 (PAR14)



9.3.2 Nerve conduction velocities

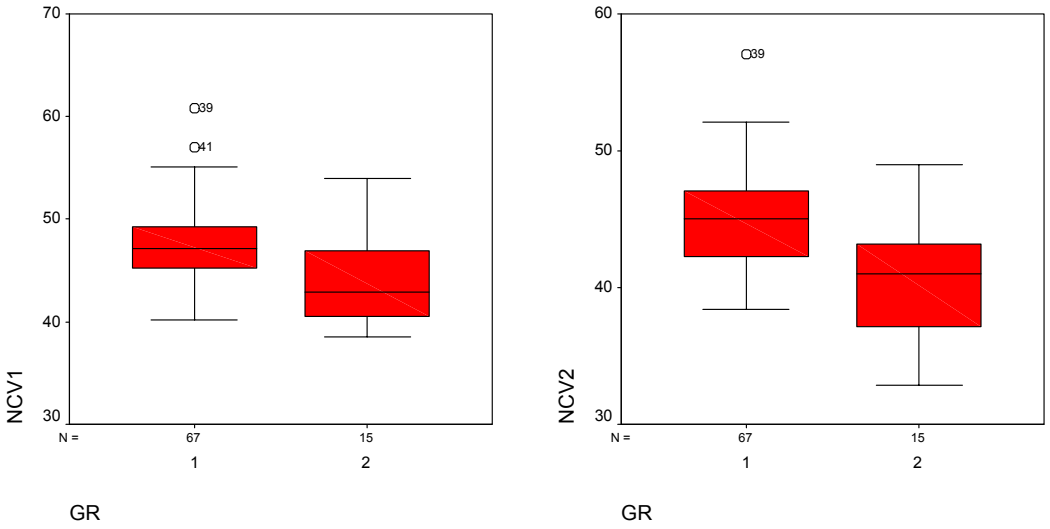
For NCVs of N. peronaeus also for almost all NCVs (beside NCV1) highly significant results have been shown, the level of significance had a tendency to improve from NCV1 to NCV3/4.

Test Statistics[a]

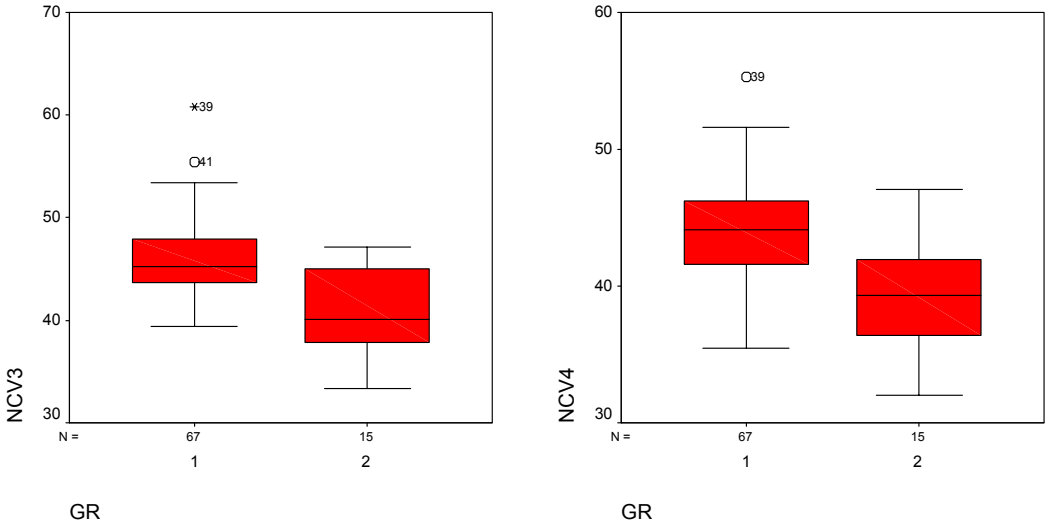
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	276,500	225,000	203,000	206,500
Wilcoxon W	396,500	345,000	323,000	326,500
Z	-2,711	-3,328	-3,592	-3,550
Asymp. Sig. (2-tailed)	,007	,001	,000	,000

a. Grouping Variable: GR

Boxplots for nerve conduction velocity 1 (NCV1) and 2 (NCV2)



Boxplots for nerve conduction velocity 3 (NCV3) and 4 (NCV4)



9.3.3 Interval, amplitude and area quotients

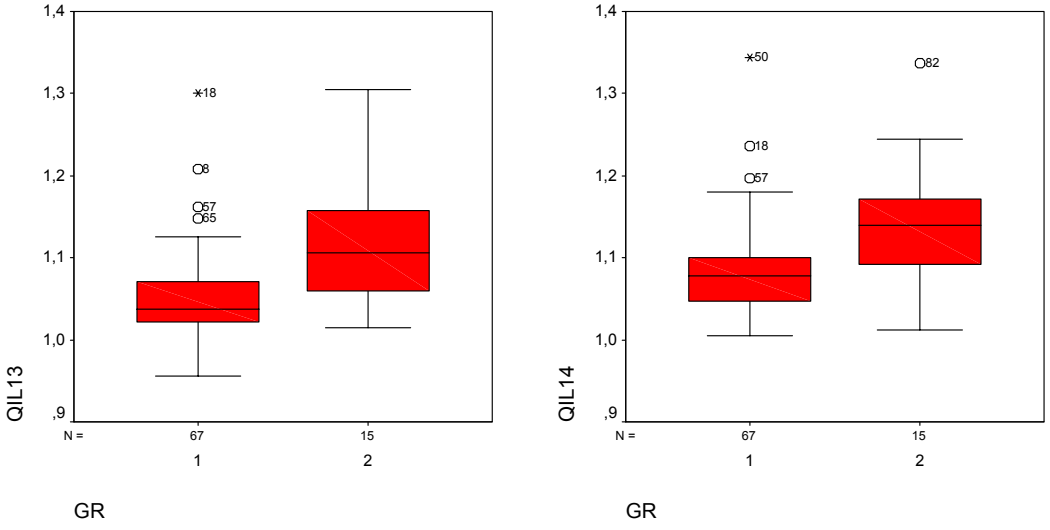
The results obtained for the quotient variables showed a different picture compared to the results obtained from N. tibialis. Here for interval quotients (QIL13, QIL14) significant differences were found, whereas for all other variables for amplitudes (QA12, QA14, QA24) and areas (QAR13, QAR14) non-significant results were obtained.

Test Statistics[a]

	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	219,000	256,500	351,500	432,500	345,500	477,500	374,500
Wilcoxon W	2497,000	2534,500	471,500	552,500	465,500	597,500	494,500
Z	-3,400	-2,951	-1,811	-,840	-1,883	-,213	-1,465
Asymp. Sig. (2-tailed)	,001	,003	,070	,401	,060	,832	,143

a. Grouping Variable: GR

Boxplots for interval quotient 13 (QIL13) and interval quotient 14 (QIL14)



9.3.4 Summary

The analysis of the results for N. peronaeus showed similar results compared to N. tibialis. The results obtained with the highest level of significance were found for amplitude and area variables, for NCV variables this could be confirmed with a negligible exception for NCV1/2. The quotient evaluation showed in contrast to the results of N. tibialis significant results only for interval quotients (QIL13, QIL14), all other parameters remained with non-significant results. The observed shift from non-significant results for single interval variables to significant results in quotient intervals has been demonstrated also in the results of N. medianus and N. tibialis. These results indicate, that the for N. peronaeus variable quotients are not useful fro the differentiation between patient group 1 and 2 (exception: interval quotients).

10. DISCUSSION

As already discussed in the section 4. (Diagnosis of diabetic neuropathies [4]) the measurements used to diagnose DNP vary widely and are still in discussion. In clinical routine the items tested for diagnosis of DNP may be different from the items tested e.g. in clinical research projects. For daily practice of diagnostic tools tests applied shall ideally fulfill the following standards:

1) Easy to apply with low effort in time,
2) low inter-observer variation,
3) good correlation with clinical progress of the disease, and
4) non-invasive to the patient with a low risk profile.

The application of peripheral motor nerve conduction testing was proven to serve these standards and is used widely by neurologists, where patients with suspicion of DNP are commonly diagnosed and treated. The advantages of this diagnostic tool has led to the further developments for the purpose of diagnosis of different peripheral nerve disorders (23). Nevertheless the evaluations carried out in this study comparing this two patient groups consisting of either normal subjects or patients suspicious of having DNP were not conducted yet. The advantages described above for nerve conduction studies qualify this method to be used for the diagnosis of DNP. Due to the fact, that in DNP nerve fibers of all diameters are affected (16) and a correlation exists between duration of diabetes mellitus and the progress of nerve conduction slowing in diabetic patients (1) this method should be also applicable to detect early changes of the peripheral nervous system in diabetic patients. It is well known, that the evaluation of nerve conduction velocity in peripheral nerves characterizes only the

nerve fibers with the fastest conduction velocities, this test has only limited evidence for the testing and evaluation of peripheral nerves (41). Indeed the underlying pathogenesis of DNP is still in discussion, both axonal degeneration and demyelinisation are probably involved in different stages of the disease (37). Therefore this study aims to characterize the function of motoric peripheral nerves to probably identify a demyelinisation process or axonal degeneration or both in diabetic patients. To further evaluate the nerve function in terms of conduction velocity the characteristics of the compound muscle action potential shall be analyzed meaning, that beyond the maximum nerve conduction velocity also the derived nerve conduction velocities of the characteristic biphasic compound muscle action potential shall be analyzed, which were defined to be NCV 2 to 4 (see 8.2). With this measure also nerve fibers representing slower conduction velocities shall be analyzed. Possible axonal degeneration shall be evaluated by testing the different amplitudes of the CMAP (maximum, positive amplitude, negative amplitude) for distal and proximal stimulation. Usually the area under the curve, which represents the quantity of nerve fibers stimulated, is almost comparable for distal and proximal stimulation in normal subjects (24). If a process like axonal degeneration occurs in DNP, then usually nerve fibers “die back” meaning that beginning with the distal end of the nerve fibers the degenerative process starts moving forward to proximal segments. This process should therefore not influence the quantity of nerve fibers stimulated, so that that for supramaximum stimulation the area under the curve is almost comparable both for distal and proximal stimulation. This issue could be identified by calculation of quotients derived from distal and proximal areas. In general the calculation of quotients for the variables amplitudes and intervals could serve to characterize the dispersion of the CMAP from distal to proximal stimulation, which could be explained by the diverse conduction of different nerve fibers within the peripheral nerve, which is naturally more pronounced for longer distances meaning proximal stimulation compared to distal stimulation. This dispersion mechanism will be analyzed by calculation of the quotients of amplitudes and intervals from distal to proximal stimulation.

All parameters tested are summarized in the following section. Results were categorized as following:

1. distal parameters (intervals, amplitudes areas)
2. proximal parameters (Intervals, amplitudes, areas)
3. nerve conduction velocities (maximum nerve conduction velocity = NCV1 and following nerve conduction velocities = NCV 2-4)

4. quotient parameters (interval quotients, amplitude quotients, area quotients). Parameters were calculated by following equation: quotient = proximal variable / distal variable (see 8.2).

At the end of this part the results will be then be discussed and interpreted in comparison to other published data.

Distal Parameter

N. medianus

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	570,000	595,500	398,000	454,000	390,500	435,500	448,500
Wilcoxon W	2848,000	766,500	569,000	625,000	561,500	606,500	619,500
Z	-,355	-,081	-2,205	-1,603	-2,286	-1,728	-1,586
Asymp. Sig. (2-tailed)	,723	,936	,027	,109	,022	,084	,113

a. Grouping Variable: GR

N. tibialis

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	556,500	573,000	223,000	188,000	202,500	213,000	215,500
Wilcoxon W	2834,500	2851,000	413,000	378,000	392,500	403,000	405,500
Z	-,833	-,661	-4,305	-4,669	-4,518	-4,367	-4,341
Asymp. Sig. (2-tailed)	,405	,509	,000	,000	,000	,000	,000

a. Grouping Variable: GR

N. peronaeus

Test Statistics[a]

	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	415,500	427,000	123,000	194,000	130,000	104,000	132,500
Wilcoxon W	535,500	547,000	243,000	314,000	250,000	224,000	252,500
Z	-1,044	-,906	-4,552	-3,701	-4,468	-4,754	-4,408
Asymp. Sig. (2-tailed)	,297	,365	,000	,000	,000	,000	,000

a. Grouping Variable: GR

The results obtained with regard to distal parameters (intervals, amplitudes, areas) showed for all three peripheral nerves similar results. The evaluation of both leg nerves (N. tibialis, N. peronaeus) resulted in highly significant differences for all amplitude and area variables, whereas for intervals the differences did not achieve a significant level. The results obtained for N. medianus were only significant for the positive and maximum amplitude, all other parameters did not reach significant levels.

Proximal parameter

N. medianus

Test Statistics[a]

	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	527,000	558,500	351,500	382,500	353,000	386,500	412,500
Wilcoxon W	2805,000	2836,500	522,500	553,500	524,000	557,500	583,500
Z	-,818	-,479	-2,705	-2,372	-2,689	-2,262	-1,979
Asymp. Sig. (2-tailed)	,413	,632	,007	,018	,007	,024	,048

a. Grouping Variable: GR

N. tibialis

Test Statistics[a]

	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	454,500	483,500	148,500	170,000	164,000	173,000	196,000
Wilcoxon W	2732,500	2761,500	338,500	360,000	354,000	363,000	386,000
Z	-1,895	-1,593	-5,080	-4,856	-4,919	-4,789	-4,547
Asymp. Sig. (2-tailed)	,058	,111	,000	,000	,000	,000	,000

a. Grouping Variable: GR

N. peronaeus

Test Statistics[a]

	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	502,000	483,000	123,500	115,000	114,500	106,000	125,000
Wilcoxon W	622,000	603,000	243,500	235,000	234,500	226,000	245,000
Z	-,006	-,234	-4,546	-4,648	-4,654	-4,730	-4,499
Asymp. Sig. (2-tailed)	,995	,815	,000	,000	,000	,000	,000

a. Grouping Variable: GR

Proximal parameters (intervals, amplitudes, areas) were tested similar compared to distal parameters. All amplitude and area variables showed significant levels, this result was also obtained for N. medianus (here significant results, in N. tibialis respectively N. peronaeus highly-significant results). For intervals non-significant results were identified.

Nerve conduction velocities

N. medianus

Test Statistics[a]

	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	256,500	252,500	197,000	234,000
Wilcoxon W	427,500	423,500	368,000	405,000
Z	-3,728	-3,770	-4,368	-3,970
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

N. tibialis

Test Statistics[a]

	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	133,500	75,000	76,500	99,500
Wilcoxon W	323,500	265,000	266,500	289,500
Z	-5,237	-5,845	-5,829	-5,590
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

N. peronaeus

Test Statistics[a]

	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	276,500	225,000	203,000	206,500
Wilcoxon W	396,500	345,000	323,000	326,500
Z	-2,711	-3,328	-3,592	-3,550
Asymp. Sig. (2-tailed)	,007	,001	,000	,000

a. Grouping Variable: GR

The evaluation of the differences of nerve conduction velocities in both patient groups resulted in a quite homogenous setting: beside NCV 1 and NCV 2 in N. peronaeus all other nerve conductions showed highly significant differences between the two patient groups, NCV 1 and NCV 2 of N. peronaeus were significantly different in the patient groups.

Quotient parameter

N. medianus

Test Statistics[a]

	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	447,500	384,000	359,000	343,000	323,000	321,000	370,000
Wilcoxon W	2725,500	2662,000	530,000	514,000	494,000	492,000	541,000
Z	-1,673	-2,356	-2,625	-2,797	-3,012	-2,976	-2,442
Asymp. Sig. (2-tailed)	,094	,018	,009	,005	,003	,003	,015

a. Grouping Variable: GR

N. tibialis

Test Statistics[a]

	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	372,000	407,000	213,000	519,500	264,000	351,000	400,000
Wilcoxon W	2650,000	2685,000	403,000	709,500	454,000	541,000	590,000
Z	-2,753	-2,389	-4,408	-1,218	-3,877	-2,911	-2,395
Asymp. Sig. (2-tailed)	,006	,017	,000	,223	,000	,004	,017

a. Grouping Variable: GR

N. peronaeus

Test Statistics[a]

	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	219,000	256,500	351,500	432,500	345,500	477,500	374,500
Wilcoxon W	2497,000	2534,500	471,500	552,500	465,500	597,500	494,500
Z	-3,400	-2,951	-1,811	-,840	-1,883	-,213	-1,465
Asymp. Sig. (2-tailed)	,001	,003	,070	,401	,060	,832	,143

a. Grouping Variable: GR

The test results obtained for interval quotients showed all nerves and variables (exception: interval quotient QIL13 of N. medianus) significant differences between group 1 and group 2. The same result was achieved in the evaluation of the amplitude quotients for N. medianus and N. tibialis (exception negative amplitude quotient QA14 of N. tibialis). For N. peronaeus slightly different results were obtained, the significant level for the positive (QA12) and maximum amplitude (QA24) was not reached (p=0.07 respectively p=0.06) or not reached at all (Quotient negative amplitude QA14) similar to the results of the negative amplitude of N. tibialis (QA14). The quotient parameters (quotient area 13 QAR13 and quotient area 14 QAR14) for the areas tested were significant for N. medianus and N. tibialis, whereas in N. peronaeus non-significant results were obtained.

For the analysis of these results following different pathophysiological mechanisms could be involved:

1. axonal degeneration leading to a general reduction of the amplitude of the compound muscle action potential (both proximal and distal) and/or
2. demyelinisation leading to a reduction of nerve conduction velocities and a pronounced dispersion of the compound muscle action potential (from distal to proximal stimulation).

The results obtained for the changes of amplitudes indicate, that the patients in group 2 with diabetes have for almost all amplitude parameters significant or even highly significant lower values compared to normal subjects. These findings were more pronounced in leg nerves, but also for N. medianus significant changes were demonstrable. As possible explanation of these findings axonal degeneration could explain these results. The changes of amplitudes from distal to proximal stimulation, as analyzed by the quotient calculation, showed similar results. In general the decrease of amplitude from distal to proximal stimulation is related to the dispersion of the compound muscle action potential. It seems to be, that in diabetic patients this effect is more pronounced than in normal subjects. Interestingly the differences of single intervals variables do not reach significant levels for the two patient groups, obviously the deviation of these variables is to high to reach this level. But the change of these pa-

rameters from distal to proximal stimulation, as tested by the quotient calculation, reaches significant levels (exception: quotient QIL13 of N. medianus). This indicates, that also for this parameter of dispersion differences exist between the two patient groups. The evaluation of changes of areas from distal to proximal stimulation provide similar results, nevertheless the results obtained for N. peronaeus did not reach significant levels. The changes of nerve conduction velocities provide in most cases (exception: NCV1/NCV2 of N. peronaeus) highly significant results between the patient groups. These changes indicate, that in diabetic patients obviously a demyelinisation process is involved.

11. CONCLUSION

As defined in the section 6. Aim of the study (6) the zero-hypothesis of this study was that parameters beside the standard parameters are not able to differentiate with significant results between the two patient groups in order to proof, whether other as standard variables can differentiate between these two patient groups.

The standard parameters usually applied for the neurophysiological testing in patients suspicious of having diabetic neuropathy are maximum nerve conduction velocity (NCV1) and the amplitude of the compound muscle action potential (A24). In addition to these parameters in this study further variables so as

1) nerve conduction velocities (NCV 2, 3, 4),
2) different parts of the amplitude (positive part=amplitude A12, negative amplitude=A14),
3) intervals (interval 13=IL13 and 14=IL14),
4) areas (area 13=AR13 and 14=AR14), and
5) quotients of these variables (quotient of intervals 13=QIL13 and 14=QIL14; quotients of amplitudes A12=QA12, A14=QA14, A24=QA24; quotients of areas 13=QAR13 and 14=QAR14) (see also 8.2)

were analyzed and evaluated.

The results obtained for nerve conduction velocities were all statistical significant different for the patient groups tested. This finding was demonstrated both for the conventional meaning maximum nerve conduction velocity (NCV1) as well as for the other nerve conduction velocities (NCV2, 3, 4).

The evaluation for amplitude parameters showed statistical significant differences for almost all tested variable (both maximum amplitudes as well as positive/negatives amplitudes), only the negative amplitude of N. medianus showed non-significant results.

The changes of intervals were tested with non-significant results for all variables.

Almost all area variables were tested to be statistical significant different (exception: distal area 13 DAR13 and 14 DAR14 of N. medianus) between the two patient groups.

Quotient variables were mostly tested with significant differences (exception: quotient interval 13 [QIL13] N. medianus; quotient negative amplitude A14 [QA14] N. tibialis; quotient positive amplitude A12 [QA12] N. peronaeus; quotient negative amplitude A14 [QA14] N. peronaeus; quotient maximum amplitude A24 [QA24] N. peronaeus; quotient area 13 [QAR13] and 14 [QAR14] N. peronaeus).

These findings summarized can be interpreted that way, that in this study beside the standard variables, which achieved significant levels of differences in all tested peripheral nerves and items, also most of other parameters achieved this level of difference with the exception of interval variables and some others. In general the findings correlate well with the results of other publications (23). In addition the findings for N. medianus provide some hints, that for this peripheral nerve, which is usually affected in later stages of DNP, the progression of demyelinisation was more advanced than the axonal degeneration. The findings in both leg nerves did not demonstrate this difference, here both axonal degeneration and demyelinisation were similar advanced.

The limitation of the testing carried out in this study is related to different items:

1) the average age of the two groups tested differed, in group 2 the average age was 68 (±17 years), whereas in group 1 the average age was 49 years (±28 years). In general it is known, that age influences nerve conduction velocities (36) and the amplitude of the compound muscle action potential (24). Both parameters have a tendency to decrease with increasing age.
2) the number of patients investigated was different (group 1: n=67, group 2: n=21).
3) the average time (±SD) elapsed since diagnosis of impaired glucose tolerance or manifest diabetes mellitus in group 2 was 12,1 years (±7.3 ys), therefore in some patients the metabolic disorder and related diseases could be more advanced.
4) patients with either impaired glucose tolerance or manifest diabetes mellitus were included, as a consequence different stages of severity of the underlying disease will influence the analysis of the data.

All together it seems to be, that the parameters tested could be helpful to be further investigated in studies, which aim to solve the problems as mentioned above in order to improve the differentiation of normal subjects and patients in early stages of diabetes mellitus or impaired glucose tolerance.

12. SUMMARY

Diabetic neuropathy is a frequent complication of patients suffering from diabetes mellitus (either type I or type II diabetes). The clinical picture of this disease varies widely from non-symptomatic courses to severe disabling and potential life-threatening cases, mostly due to autonomic neuropathy. The treatment of diabetic neuropathy is despite huge investments in clinical research mostly related to an effective control of blood glucose levels. Beside acute courses of diabetic neuropathy, which tend to remit, most patients suffer from chronic courses of diabetic neuropathy, where distal symmetric neuropathy is the most common course of disease. These cases are usually chronic progressive, therefore early diagnosis and intervention is mandatory. The advantages of neurographic testing as diagnostic tool in terms of reliability, validity, relevance, and patient's safety is well accepted. Used by medical professionals this method provides information about the functional status of the peripheral nervous system. This study was conducted comparing normal subjects and patients with diabetes mellitus or impaired glucose tolerance, who with suspicion of diabetic neuropathy. The aim of this study was to identify additional neurographic markers who can differentiate between the two patient groups in order to possibly provide a diagnostic tool for the early diagnosis of diabetic neuropathy. These markers should supplement the markers already established so as maximum nerve conduction velocity or amplitude of the compound muscle action potential. The evaluation of further markers so as further conduction velocities, positive/negative amplitudes, quotients of intervals/amplitudes/areas revealed significant differences between the two patient groups, nevertheless also the standard markers demonstrated significant differences. These findings could be related to the fact, that the average age in group 2 with diabetic patients was substantially higher than in group 1 with normal subjects. In addition the progression of diabetic neuropathy could be more advanced, so that an additional study with patients in an earlier stage of disease and comparable age could improve the diagnosis of early diabetic neuropathy.

13. ATTACHMENT

In the following section the detailed data analyzed are displayed. The sequence of the data presented is as following: first the data of N. medianus are presented, followed by N. tibialis and N. peronaeus. Within the section of each nerve following order is given: first distal parameters are displayed, followed by proximal parameters, NCVs and quotients. Within these sections first the results of the descriptive statistics (n, mean, median, standard deviation, minimum, maximum, percentiles 25/5075) are displayed, followed by the results of the non-parametric test (NPar test, Mann-Whitney tests) and the boxplots.

13.1 Listing of tables/boxplots

13.1.1 N. medianus

13.1.1.1 Distal parameter

Frequencies

Statistics

GR			DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,017	7,37	7,8699	4,9260	12,78	22,980	33,980
	Median		5,000	7,35	7,5000	4,7600	12,30	21,900	32,450
	Std. Deviation		,6887	1,345	2,83707	2,09891	4,751	9,1661	14,6886
	Minimum		3,0	4	3,22	1,70	6	6,9	10,9
	Maximum		6,5	11	15,80	10,80	27	51,5	84,6
	Percentiles	25	4,650	6,25	5,8500	3,1200	8,86	16,000	22,625
		50	5,000	7,35	7,5000	4,7600	12,30	21,900	32,450
		75	5,450	8,40	10,0000	6,2600	15,80	28,700	41,050
2	N	Valid	18	18	18	18	18	18	18
		Missing	0	0	0	0	0	0	0
	Mean		5,133	7,28	6,2122	3,9822	10,18	18,567	27,683
	Median		5,250	7,24	5,6850	3,5100	8,76	17,750	26,450
	Std. Deviation		1,1594	1,661	2,81814	1,39614	3,998	8,5231	11,5875
	Minimum		3,3	5	2,14	2,16	6	4,2	9,4
	Maximum		7,2	10	12,30	6,88	19	33,3	49,2
	Percentiles	25	4,150	5,71	4,2925	3,0675	6,92	12,425	19,650
		50	5,250	7,24	5,6850	3,5100	8,76	17,750	26,450
		75	5,950	8,86	7,8650	4,8950	12,00	24,700	39,050

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
DIL13	1	67	42,51	2848,00
	2	18	44,83	807,00
	Total	85		
DIL14	1	67	43,11	2888,50
	2	18	42,58	766,50
	Total	85		
DA12	1	67	46,06	3086,00
	2	18	31,61	569,00
	Total	85		
DA14	1	67	45,22	3030,00
	2	18	34,72	625,00
	Total	85		
DA24	1	67	46,17	3093,50
	2	18	31,19	561,50
	Total	85		
DAR13	1	66	44,90	2963,50
	2	18	33,69	606,50
	Total	84		
DAR14	1	66	44,70	2950,50
	2	18	34,42	619,50
	Total	84		

Test Statistics[a]

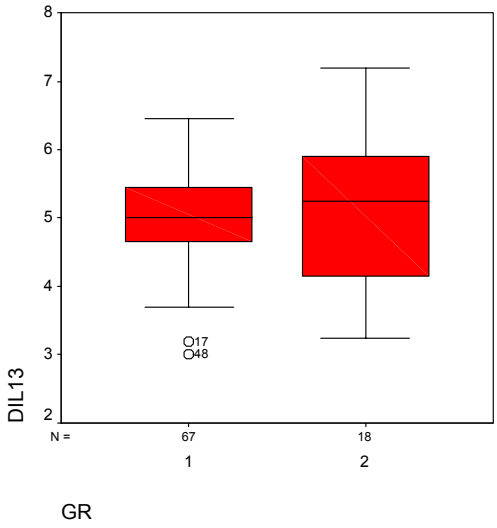
	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	570,000	595,500	398,000	454,000	390,500	435,500	448,500
Wilcoxon W	2848,000	766,500	569,000	625,000	561,500	606,500	619,500
Z	-,355	-,081	-2,205	-1,603	-2,286	-1,728	-1,586
Asymp. Sig. (2-tailed)	,723	,936	,027	,109	,022	,084	,113

a. Grouping Variable: GR

Boxplots distal interval 13 (DIL13)

Case Processing Summary

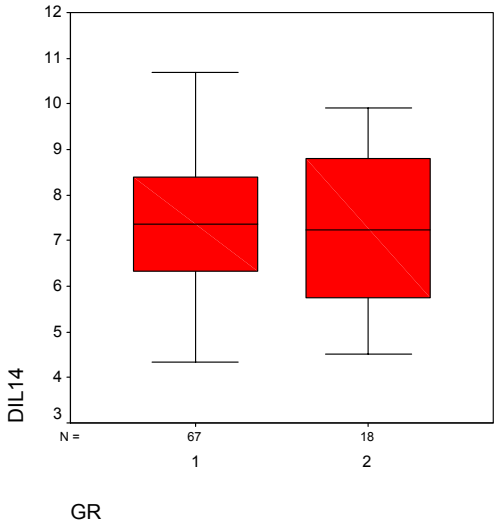
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL13	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal interval 14 (DIL14)

Case Processing Summary

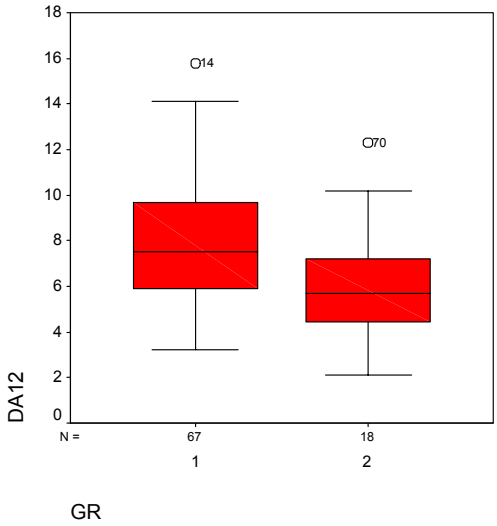
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal amplitude 12 (DA12)

Case Processing Summary

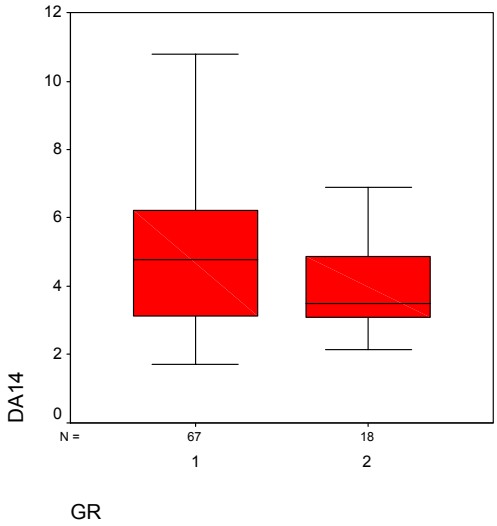
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA12	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal amplitude 14 (DA14)

Case Processing Summary

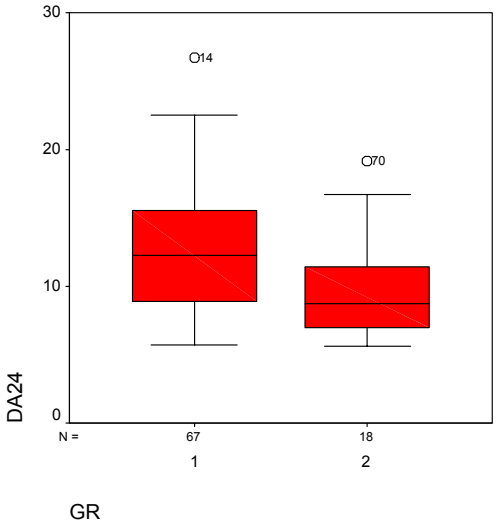
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal amplitude 24 (DA24)

Case Processing Summary

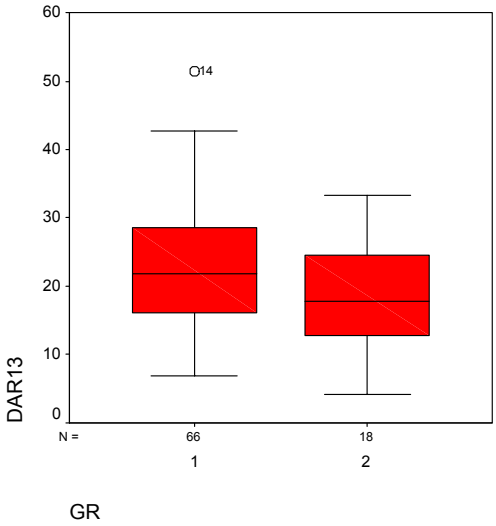
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA24	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal area 13 (DAR13)

Case Processing Summary

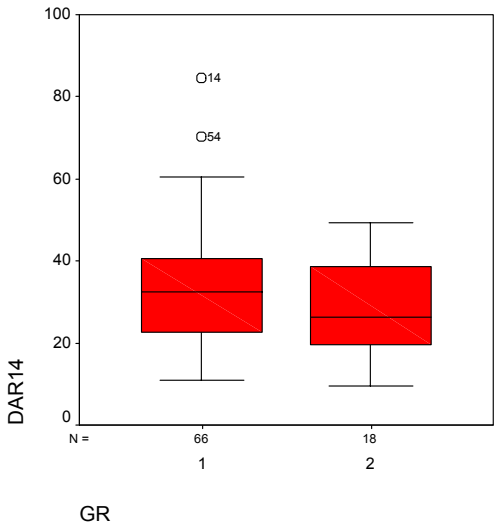
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots distal area 14 (DAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



13.1.1.2 Proximal parameter

Frequencies

Statistics

GR			PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,288	7,6742	7,3348	4,6373	11,9579	22,076	33,014
	Median		5,220	7,4500	6,9300	4,5300	11,4000	20,450	31,100
	Std. Deviation		,7268	1,38581	2,77287	2,02051	4,61871	8,9825	14,4639
	Minimum		3,4	4,59	2,77	1,26	4,96	6,7	10,9
	Maximum		6,8	10,90	14,80	10,20	25,00	50,4	81,9
	Percentiles	25	4,800	6,5000	5,1200	3,0400	7,8900	15,775	21,975
		50	5,220	7,4500	6,9300	4,5300	11,4000	20,450	31,100
		75	5,800	8,8000	8,6100	6,0500	14,9000	27,200	41,375
2	N	Valid	18	18	18	18	18	18	18
		Missing	0	0	0	0	0	0	0
	Mean		5,565	7,7328	5,4172	3,3639	8,7833	16,644	25,089
	Median		5,600	7,7500	4,8800	2,9500	7,8350	15,550	23,400
	Std. Deviation		1,1493	1,63450	2,27654	1,22753	3,36214	6,8891	9,9525
	Minimum		3,3	4,59	1,80	1,32	4,34	3,5	7,8
	Maximum		7,4	10,10	10,90	6,20	17,10	29,5	40,2
	Percentiles	25	4,635	6,2125	3,5125	2,5900	6,1050	10,950	18,250
		50	5,600	7,7500	4,8800	2,9500	7,8350	15,550	23,400
		75	6,400	9,1250	6,6525	4,6200	11,0750	23,925	34,925

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
PIL13	1	67	41,87	2805,00
	2	18	47,22	850,00
	Total	85		
PIL14	1	67	42,34	2836,50
	2	18	45,47	818,50
	Total	85		
PA12	1	67	46,75	3132,50
	2	18	29,03	522,50
	Total	85		
PA14	1	67	46,29	3101,50
	2	18	30,75	553,50
	Total	85		
PA24	1	67	46,73	3131,00
	2	18	29,11	524,00
	Total	85		
PAR13	1	66	45,64	3012,50
	2	18	30,97	557,50
	Total	84		
PAR14	1	66	45,25	2986,50
	2	18	32,42	583,50
	Total	84		

Test Statistics[a]

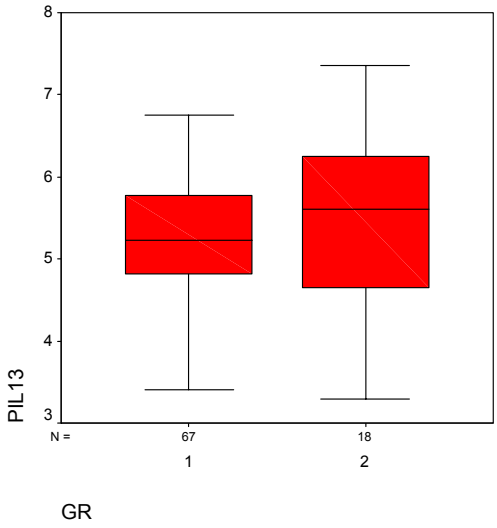
	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	527,000	558,500	351,500	382,500	353,000	386,500	412,500
Wilcoxon W	2805,000	2836,500	522,500	553,500	524,000	557,500	583,500
Z	-,818	-,479	-2,705	-2,372	-2,689	-2,262	-1,979
Asymp. Sig. (2-tailed)	,413	,632	,007	,018	,007	,024	,048

a. Grouping Variable: GR

Boxplots proximal interval 13 (PIL13)

Case Processing Summary

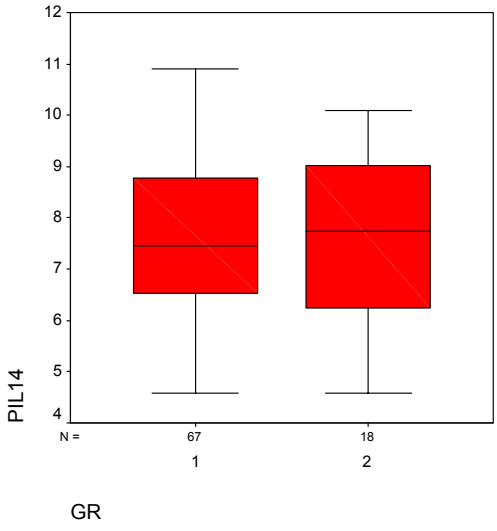
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL13	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal interval 14 (PIL14)

Case Processing Summary

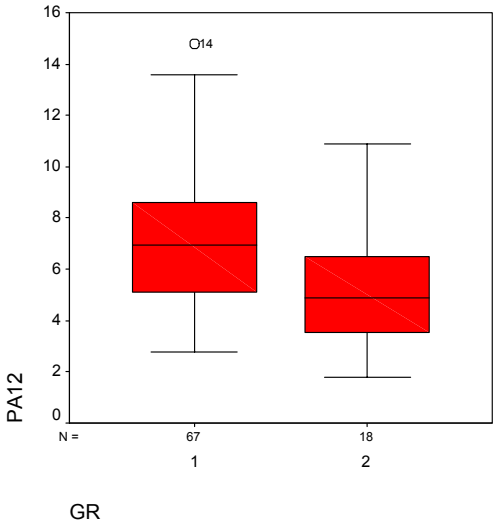
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal amplitude 12 (PA12)

Case Processing Summary

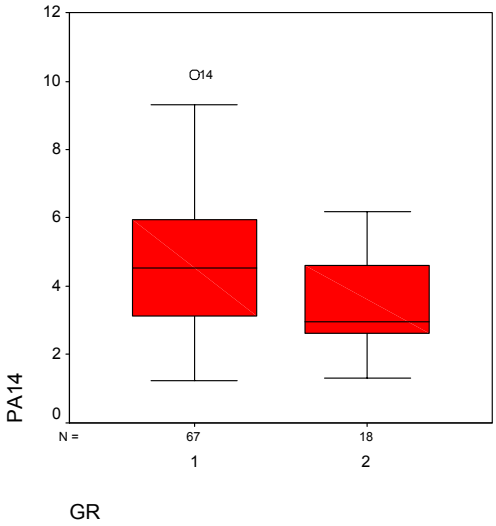
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA12	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal amplitude 14 (PA14)

Case Processing Summary

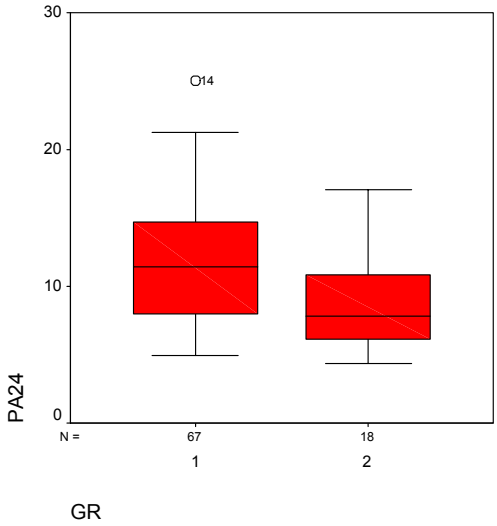
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal amplitude 24 (PA24)

Case Processing Summary

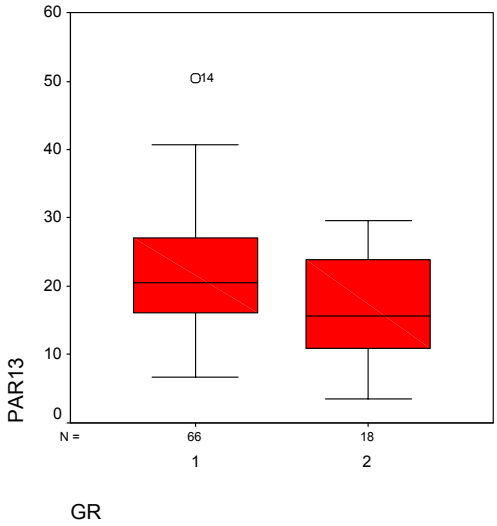
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA24	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal area 13 (PAR13)

Case Processing Summary

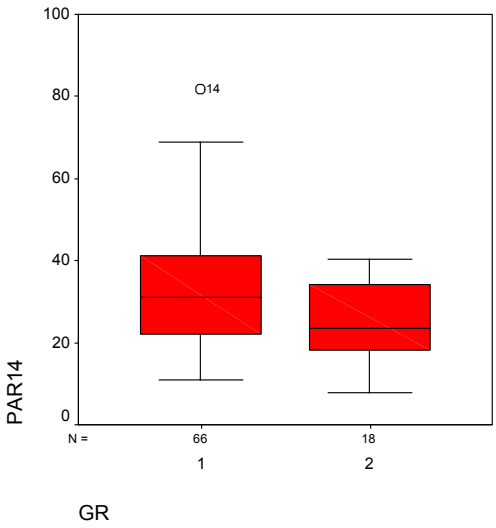
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots proximal area 14 (PAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



13.1.1.3 Nerve conduction velocities

Frequencies

Statistics

GR			NCV1	NCV2	NCV3	NCV4
1	N	Valid	67	67	67	67
		Missing	0	0	0	0
	Mean		55,042	51,554	51,890	51,325
	Median		54,700	51,250	51,813	50,000
	Std. Deviation		3,2557	4,2265	3,7460	4,4752
	Minimum		50,0	36,1	44,1	44,2
	Maximum		63,2	59,0	60,0	60,9
	Percentiles	25	52,400	50,000	49,425	47,778
		50	54,700	51,250	51,813	50,000
		75	57,500	54,118	54,324	55,128
2	N	Valid	18	18	18	18
		Missing	0	0	0	0
	Mean		51,074	48,055	46,676	46,319
	Median		51,300	46,488	46,584	46,212
	Std. Deviation		4,0414	5,4030	3,8681	4,0528
	Minimum		44,6	39,8	38,8	41,0
	Maximum		59,7	61,2	55,4	56,5
	Percentiles	25	47,095	45,430	44,615	43,904
		50	51,300	46,488	46,584	46,212
		75	52,750	49,447	48,570	48,778

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
NCV1	1	67	48,17	3227,50
	2	18	23,75	427,50
	Total	85		
NCV2	1	67	48,23	3231,50
	2	18	23,53	423,50
	Total	85		
NCV3	1	67	49,06	3287,00
	2	18	20,44	368,00
	Total	85		
NCV4	1	67	48,51	3250,00
	2	18	22,50	405,00
	Total	85		

Test Statistics[a]

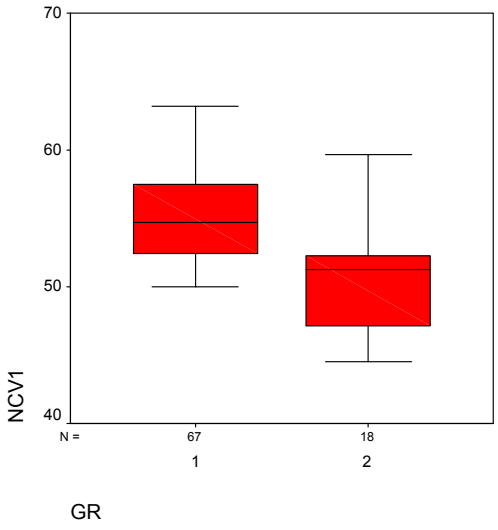
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	256,500	252,500	197,000	234,000
Wilcoxon W	427,500	423,500	368,000	405,000
Z	-3,728	-3,770	-4,368	-3,970
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots nerve conduction velocity 1 (NCV1)

Case Processing Summary

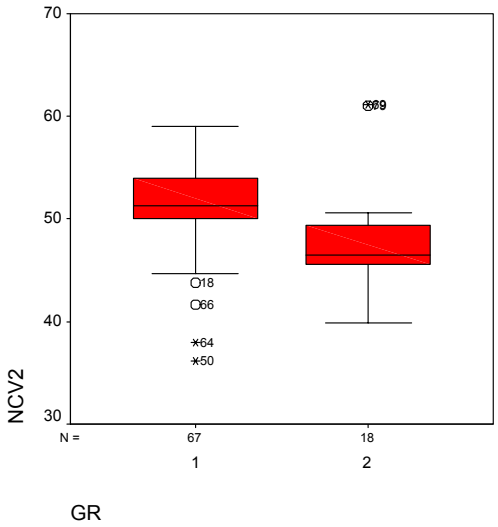
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV1	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots nerve conduction velocity 2 (NCV2)

Case Processing Summary

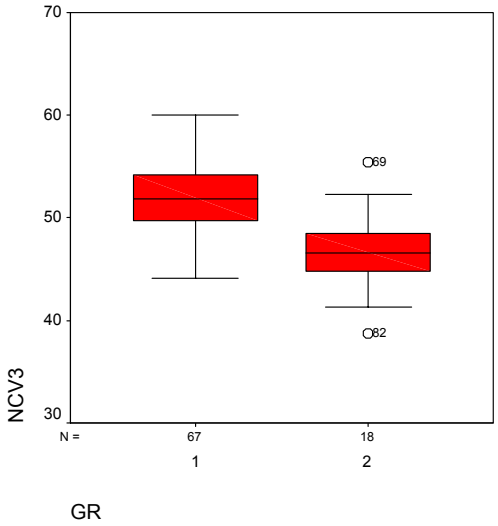
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV2	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots nerve conduction velocity 3 (NCV3)

Case Processing Summary

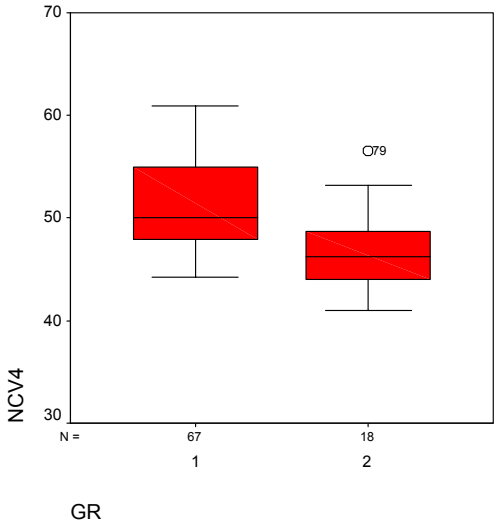
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV3	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots nerve conduction velocity 4 (NCV4)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV4	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



13.1.1.4 Quotient parameter

Frequencies

Statistics

GR			QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		1,05529	1,04219	,92811	,93905	,93182	,96030	,97063
	Median		1,04211	1,03125	,93430	,94857	,94309	,96900	,97370
	Std. Deviation		,047380	,035061	,050959	,085285	,047485	,051921	,046301
	Minimum		1,008	1,005	,788	,642	,823	,804	,852
	Maximum		1,283	1,179	1,033	1,109	1,000	1,092	1,088
	Percentiles	25	1,02366	1,01563	,89956	,89850	,89015	,92636	,93904
		50	1,04211	1,03125	,93430	,94857	,94309	,96900	,97370
		75	1,06757	1,05882	,96964	,99194	,97226	,99200	1,00000
2	N	Valid	18	18	18	18	18	18	18
		Missing	0	0	0	0	0	0	0
	Mean		1,09026	1,06661	,89776	,84761	,86834	,92914	,91527
	Median		1,07966	1,06029	,87803	,88768	,88422	,91220	,92857
	Std. Deviation		,072422	,045386	,148667	,137705	,082897	,166347	,084593
	Minimum		1,007	1,016	,689	,597	,713	,733	,748
	Maximum		1,265	1,163	1,410	1,108	,987	1,527	1,024
	Percentiles	25	1,02494	1,02731	,83770	,74206	,79969	,85286	,83583
		50	1,07966	1,06029	,87803	,88768	,88422	,91220	,92857
		75	1,13557	1,09458	,93498	,95427	,93278	,96542	,98835

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
QIL13	1	67	40,68	2725,50
	2	18	51,64	929,50
	Total	85		
QIL14	1	67	39,73	2662,00
	2	18	55,17	993,00
	Total	85		
QA12	1	67	46,64	3125,00
	2	18	29,44	530,00
	Total	85		
QA14	1	67	46,88	3141,00
	2	18	28,56	514,00
	Total	85		
QA24	1	67	47,18	3161,00
	2	18	27,44	494,00
	Total	85		
QAR13	1	66	46,64	3078,00
	2	18	27,33	492,00
	Total	84		
QAR14	1	66	45,89	3029,00
	2	18	30,06	541,00
	Total	84		

Test Statistics[a]

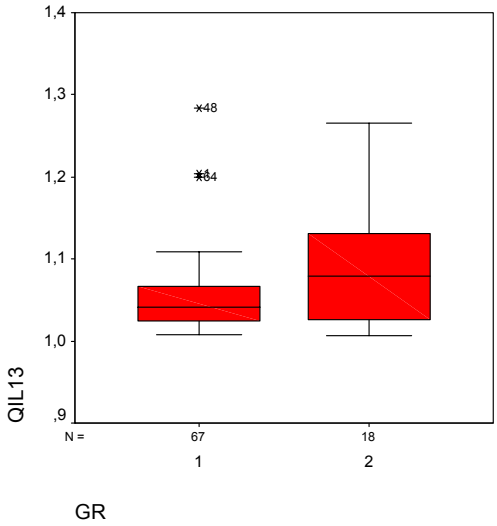
	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	447,500	384,000	359,000	343,000	323,000	321,000	370,000
Wilcoxon W	2725,500	2662,000	530,000	514,000	494,000	492,000	541,000
Z	-1,673	-2,356	-2,625	-2,797	-3,012	-2,976	-2,442
Asymp. Sig. (2-tailed)	,094	,018	,009	,005	,003	,003	,015

a. Grouping Variable: GR

Boxplots interval quotient 13 (QIL13)

Case Processing Summary

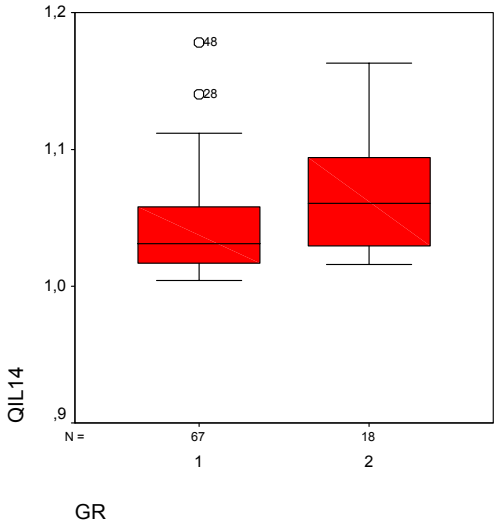
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL13	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots interval quotient 14 (QIL14)

Case Processing Summary

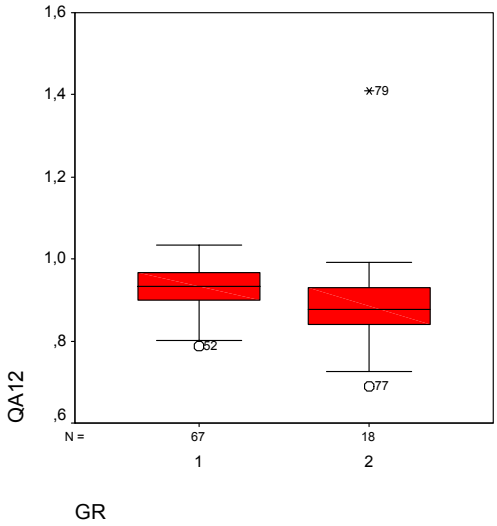
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots amplitude quotient 12 (QA12)

Case Processing Summary

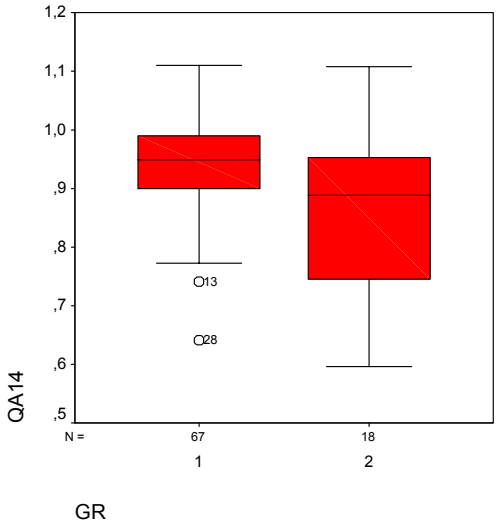
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA12	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots amplitude quotient 14 (QA14)

Case Processing Summary

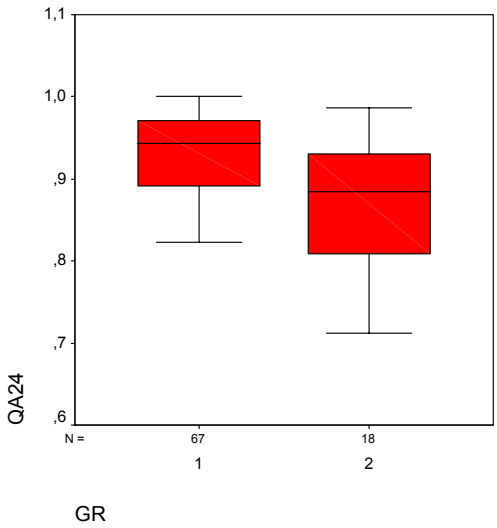
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA14	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots amplitude quotient 24 (QA24)

Case Processing Summary

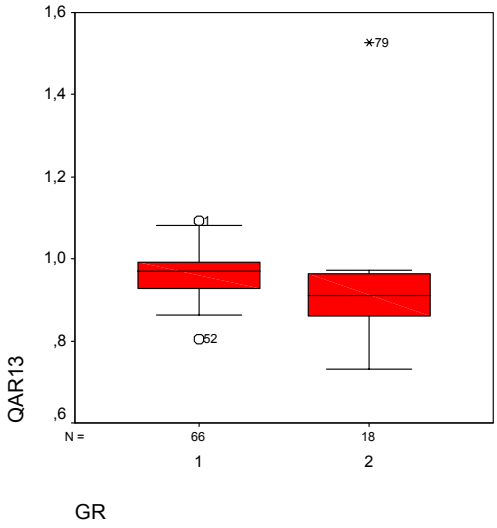
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA24	1	67	100,0%	0	,0%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots area quotient 13 (QAR13)

Case Processing Summary

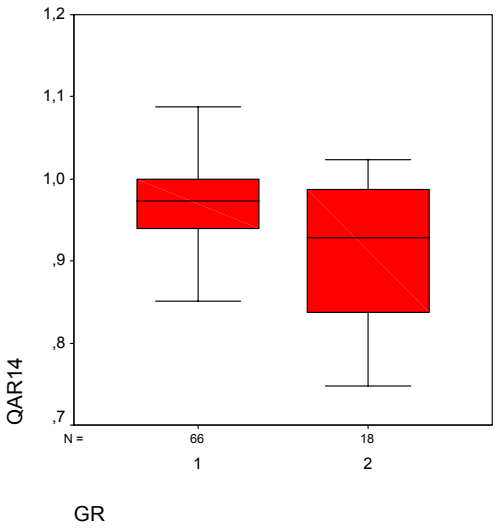
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



Boxplots area quotient 14 (QAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	18	100,0%	0	,0%	18	100,0%



13.1.2 N. tibialis

13.1.2.1 Distal parameter

Frequencies

Statistics

GR			DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,3430	6,8145	11,6709	8,2160	19,891	27,435	45,391
	Median		5,2500	6,6500	11,0000	7,6100	19,000	27,950	44,350
	Std. Deviation		1,11396	1,34313	4,91186	3,75073	8,3805	11,2668	19,7011
	Minimum		3,60	4,53	4,04	1,46	6,3	9,7	14,9
	Maximum		8,65	10,70	27,50	18,60	45,8	65,6	105,1
	Percentiles	25	4,4700	5,7600	8,7400	5,5100	15,500	17,950	28,225
		50	5,2500	6,6500	11,0000	7,6100	19,000	27,950	44,350
		75	5,8000	7,5500	13,9000	10,1000	23,500	33,925	59,100
2	N	Valid	19	19	19	19	19	19	19
		Missing	0	0	0	0	0	0	0
	Mean		5,4621	6,8863	6,4437	3,9626	10,406	15,061	24,084
	Median		5,8000	7,3000	5,3700	3,3000	8,920	12,400	18,700
	Std. Deviation		1,14750	1,33900	3,63909	2,17345	5,5975	7,9382	12,7965
	Minimum		3,05	3,95	1,97	1,28	3,3	5,0	7,9
	Maximum		7,40	8,65	15,20	10,20	25,4	35,7	51,5
	Percentiles	25	4,5000	5,7000	4,0400	2,9800	7,300	10,100	15,700
		50	5,8000	7,3000	5,3700	3,3000	8,920	12,400	18,700
		75	6,3600	7,9800	6,7100	4,2100	10,900	17,700	31,300

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
DIL13	1	67	42,31	2834,50
	2	19	47,71	906,50
	Total	86		
DIL14	1	67	42,55	2851,00
	2	19	46,84	890,00
	Total	86		
DA12	1	67	49,67	3328,00
	2	19	21,74	413,00
	Total	86		
DA14	1	67	50,19	3363,00
	2	19	19,89	378,00
	Total	86		
DA24	1	67	49,98	3348,50
	2	19	20,66	392,50
	Total	86		
DAR13	1	66	49,27	3252,00
	2	19	21,21	403,00
	Total	85		
DAR14	1	66	49,23	3249,50
	2	19	21,34	405,50
	Total	85		

Test Statistics[a]

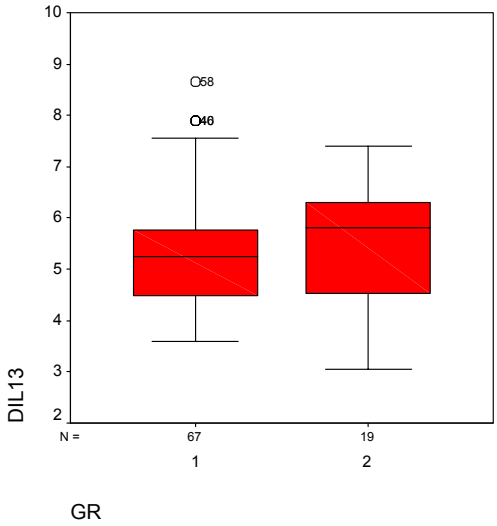
	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	556,500	573,000	223,000	188,000	202,500	213,000	215,500
Wilcoxon W	2834,500	2851,000	413,000	378,000	392,500	403,000	405,500
Z	-,833	-,661	-4,305	-4,669	-4,518	-4,367	-4,341
Asymp. Sig. (2-tailed)	,405	,509	,000	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots distal interval 13 (DIL13)

Case Processing Summary

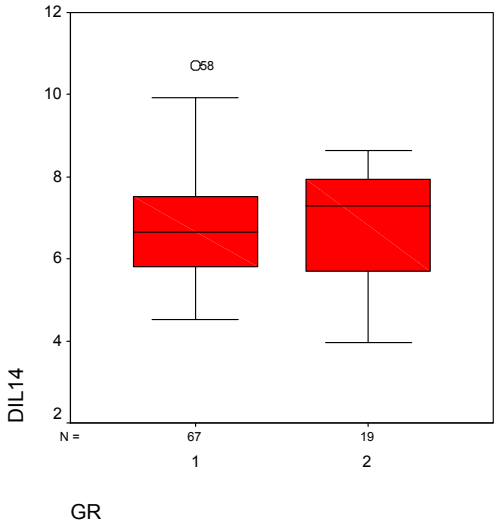
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL13	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal interval 14 (DIL14)

Case Processing Summary

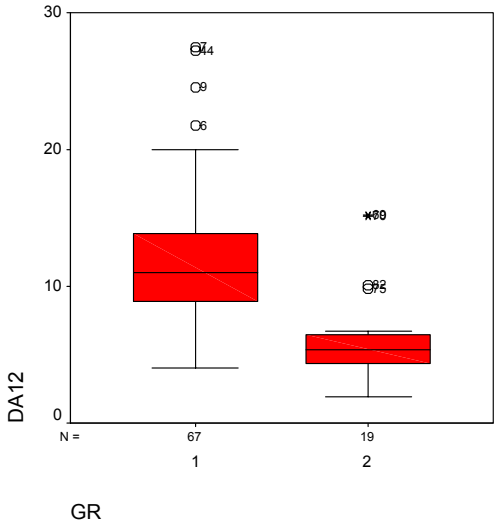
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal amplitude 12 (DA12)

Case Processing Summary

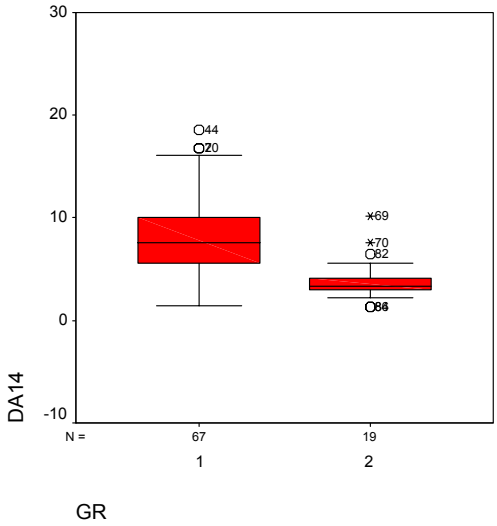
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA12	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal amplitude 14 (DA14)

Case Processing Summary

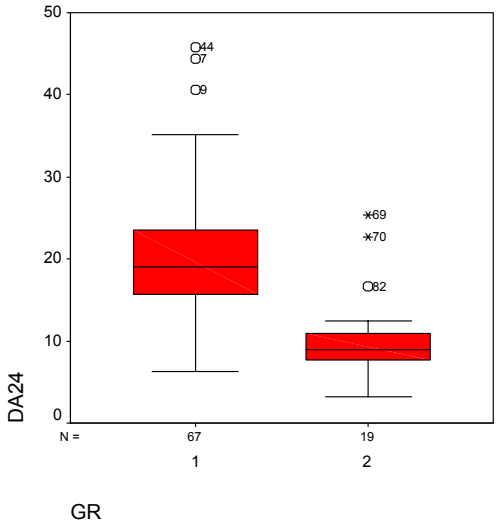
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal amplitude 24 (DA24)

Case Processing Summary

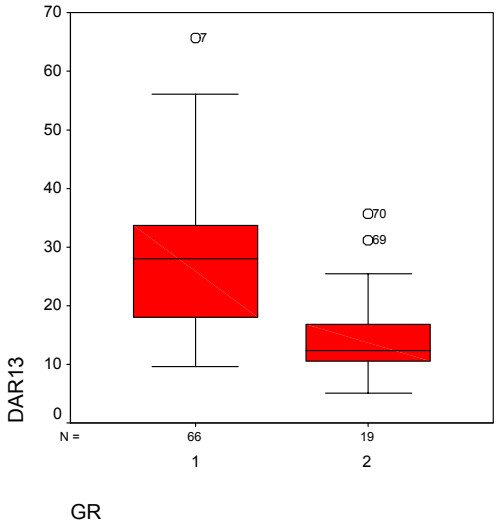
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA24	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal area 13 (DAR13)

Case Processing Summary

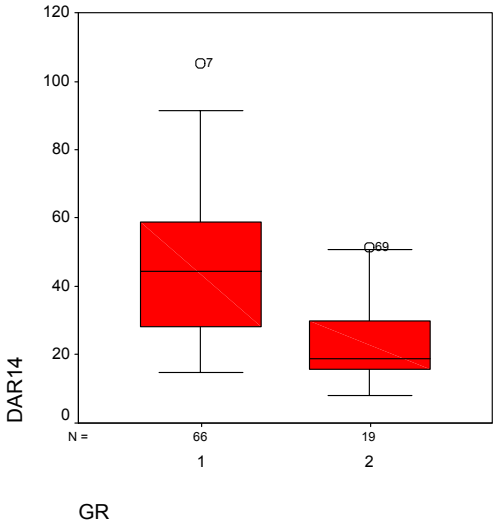
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots distal area 14 (DAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



13.1.2.2 Proximal parameter

Frequencies

Statistics

GR			PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,951	7,7475	9,1939	6,8522	16,032	24,633	42,088
	Median		5,800	7,3500	8,7400	6,3400	15,300	23,650	39,150
	Std. Deviation		1,1818	1,54679	4,16957	3,19513	7,2051	10,4426	19,0208
	Minimum		4,0	5,22	3,18	1,97	5,5	9,7	15,1
	Maximum		9,2	12,40	23,40	16,40	39,3	59,5	104,0
	Percentiles	25	5,090	6,6500	6,4900	4,8800	11,400	16,425	27,350
		50	5,800	7,3500	8,7400	6,3400	15,300	23,650	39,150
		75	6,500	8,6000	10,8000	8,3400	18,100	31,250	53,700
2	N	Valid	19	19	19	19	19	19	19
		Missing	0	0	0	0	0	0	0
	Mean		6,508	8,3237	4,1447	3,1842	7,330	12,015	20,900
	Median		6,700	8,6000	3,2400	3,0800	5,560	10,000	17,100
	Std. Deviation		1,2199	1,51063	2,67796	1,81930	4,2744	7,4015	12,0788
	Minimum		4,3	5,75	1,03	,87	1,9	3,2	6,1
	Maximum		8,9	10,60	11,80	8,69	18,3	32,9	49,6
	Percentiles	25	5,550	7,0500	2,4800	1,7700	4,820	7,100	14,700
		50	6,700	8,6000	3,2400	3,0800	5,560	10,000	17,100
		75	7,350	9,5000	5,0700	3,8500	8,920	13,800	27,800

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
PIL13	1	67	40,78	2732,50
	2	19	53,08	1008,50
	Total	86		
PIL14	1	67	41,22	2761,50
	2	19	51,55	979,50
	Total	86		
PA12	1	67	50,78	3402,50
	2	19	17,82	338,50
	Total	86		
PA14	1	67	50,46	3381,00
	2	19	18,95	360,00
	Total	86		
PA24	1	67	50,55	3387,00
	2	19	18,63	354,00
	Total	86		
PAR13	1	66	49,88	3292,00
	2	19	19,11	363,00
	Total	85		
PAR14	1	66	49,53	3269,00
	2	19	20,32	386,00
	Total	85		

Test Statistics[a]

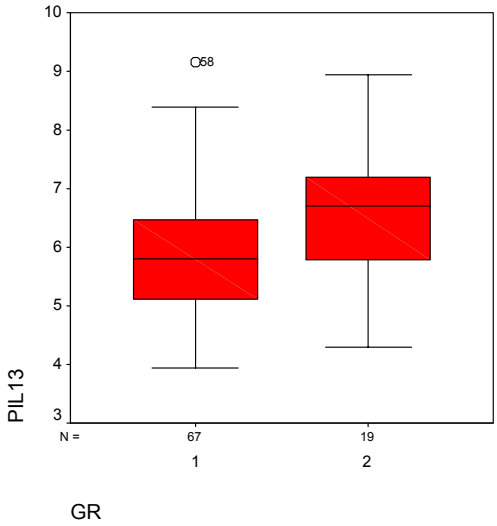
	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	454,500	483,500	148,500	170,000	164,000	173,000	196,000
Wilcoxon W	2732,500	2761,500	338,500	360,000	354,000	363,000	386,000
Z	-1,895	-1,593	-5,080	-4,856	-4,919	-4,789	-4,547
Asymp. Sig. (2-tailed)	,058	,111	,000	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots proximal interval 13 (PIL13)

Case Processing Summary

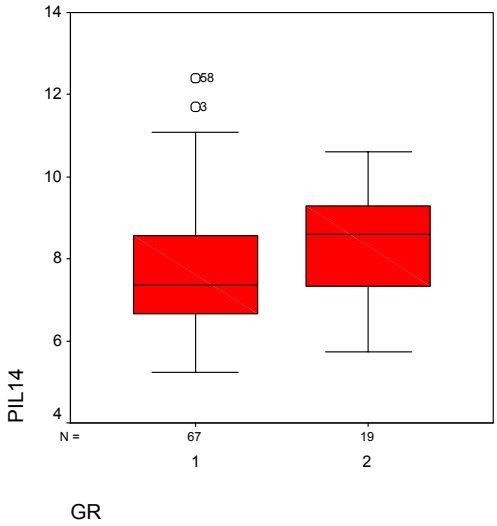
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL13	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal interval 14 (PIL14)

Case Processing Summary

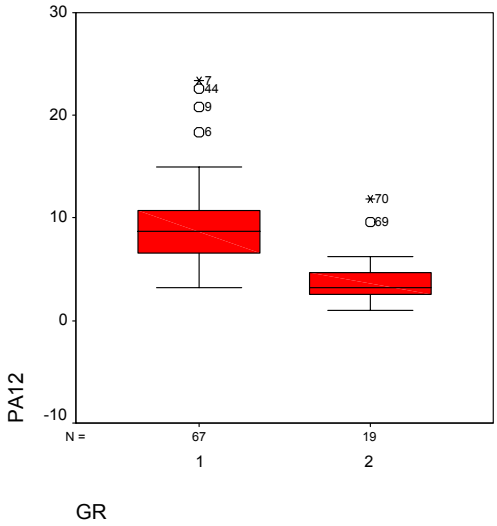
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal amplitude 12 (PA12)

Case Processing Summary

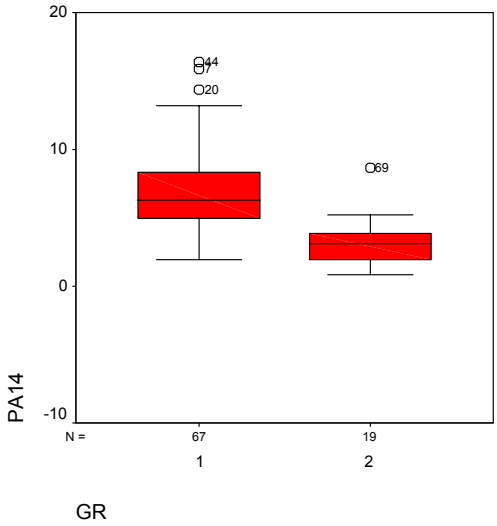
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA12	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal amplitude 14 (PA14)

Case Processing Summary

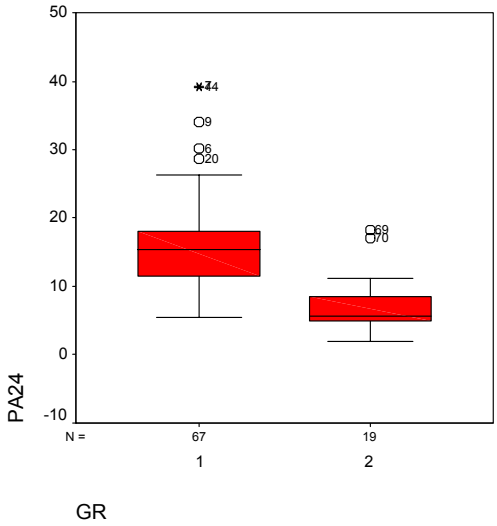
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal amplitude 24 (PA24)

Case Processing Summary

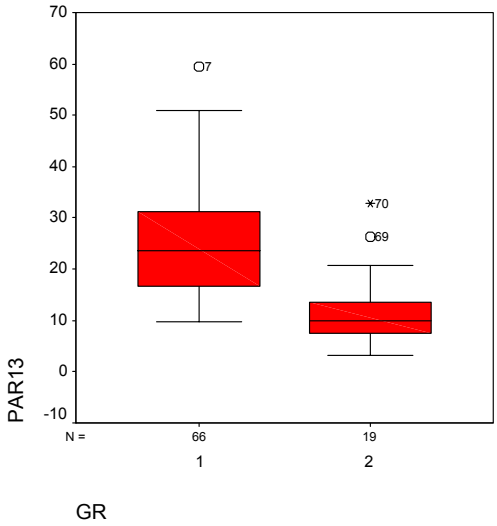
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA24	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal area 13 (PAR13)

Case Processing Summary

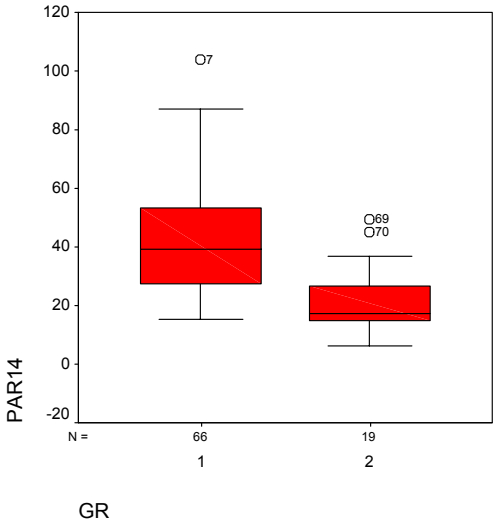
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots proximal area 14 (PAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



13.1.2.3 Nerve conduction velocities

Frequencies

Statistics

GR			NCV1	NCV2	NCV3	NCV4
1	N	Valid	67	67	67	67
		Missing	0	0	0	0
	Mean		46,767	44,852	43,766	42,263
	Median		46,300	45,181	43,925	42,135
	Std. Deviation		3,7759	3,4908	3,3977	3,5518
	Minimum		40,2	37,1	36,2	34,6
	Maximum		58,7	53,0	52,6	51,6
	Percentiles	25	44,200	41,954	41,243	39,583
		50	46,300	45,181	43,925	42,135
		75	49,200	47,552	46,429	44,565
2	N	Valid	19	19	19	19
		Missing	0	0	0	0
	Mean		40,633	37,307	35,924	34,808
	Median		39,700	37,500	36,816	34,649
	Std. Deviation		3,4773	3,8196	3,9460	4,5147
	Minimum		33,3	27,9	26,1	25,3
	Maximum		47,9	43,6	42,3	43,1
	Percentiles	25	38,100	34,335	32,922	32,323
		50	39,700	37,500	36,816	34,649
		75	43,700	40,212	37,615	37,931

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
NCV1	1	67	51,01	3417,50
	2	19	17,03	323,50
	Total	86		
NCV2	1	67	51,88	3476,00
	2	19	13,95	265,00
	Total	86		
NCV3	1	67	51,86	3474,50
	2	19	14,03	266,50
	Total	86		
NCV4	1	67	51,51	3451,50
	2	19	15,24	289,50
	Total	86		

Test Statistics[a]

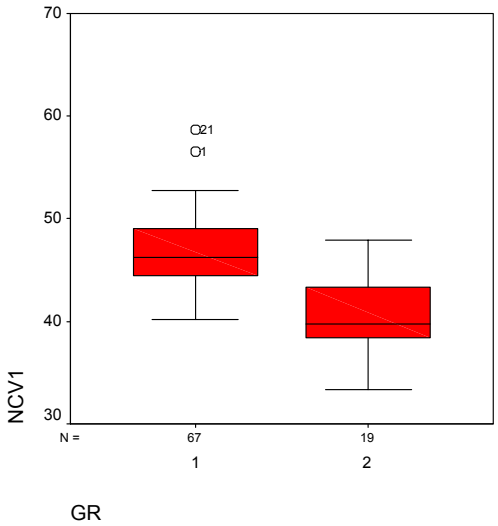
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	133,500	75,000	76,500	99,500
Wilcoxon W	323,500	265,000	266,500	289,500
Z	-5,237	-5,845	-5,829	-5,590
Asymp. Sig. (2-tailed)	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots nerve conduction velocity 1 (NCV1)

Case Processing Summary

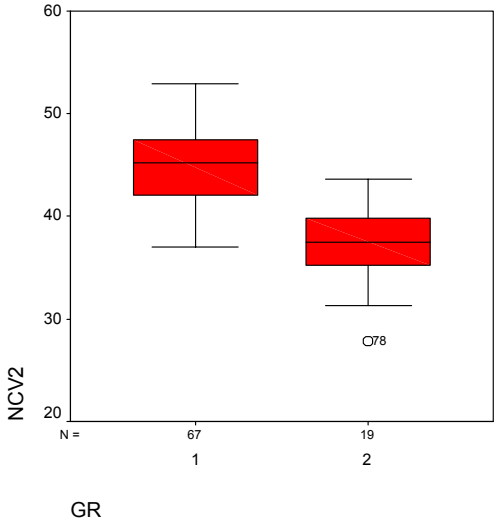
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV1	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots nerve conduction velocity 2 (NCV2)

Case Processing Summary

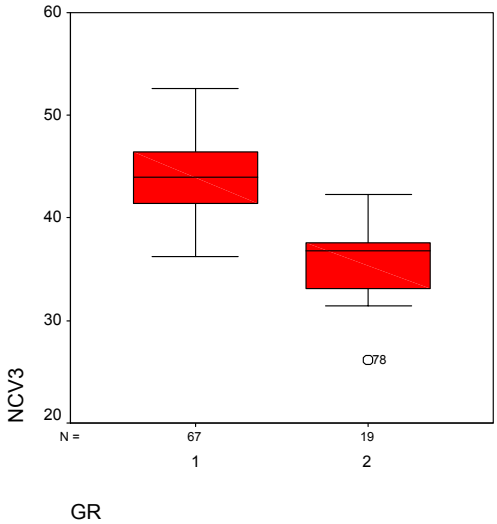
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV2	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots nerve conduction velocity 3 (NCV3)

Case Processing Summary

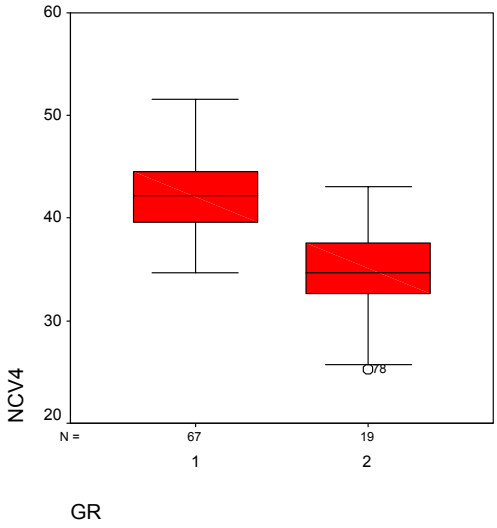
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV3	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots nerve conduction velocity 4 (NCV4)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV4	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



13.1.2.4 Quotient parameter

Frequencies

Statistics

GR			QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		1,11838	1,13914	,78590	,85298	,80533	,89857	,92467
	Median		1,10476	1,12844	,78276	,84286	,81722	,88135	,92903
	Std. Deviation		,081415	,078469	,090501	,158077	,081334	,084812	,063385
	Minimum		1,009	1,021	,557	,569	,624	,734	,792
	Maximum		1,400	1,352	,959	1,658	,994	1,110	1,064
	Percentiles	25	1,05780	1,08738	,71121	,76951	,72569	,83659	,87497
		50	1,10476	1,12844	,78276	,84286	,81722	,88135	,92903
		75	1,17045	1,17706	,84921	,90520	,86452	,95994	,97451
2	N	Valid	19	19	19	19	19	19	19
		Missing	0	0	0	0	0	0	0
	Mean		1,20453	1,22113	,63304	,80304	,69317	,78806	,85935
	Median		1,18421	1,22100	,61825	,77850	,66716	,79661	,88976
	Std. Deviation		,125341	,151356	,119638	,165933	,103937	,164497	,144964
	Minimum		1,027	1,028	,410	,523	,562	,513	,601
	Maximum		1,410	1,570	,804	1,160	,893	1,149	1,242
	Percentiles	25	1,10000	1,13158	,57051	,68627	,61104	,65347	,77215
		50	1,18421	1,22100	,61825	,77850	,66716	,79661	,88976
		75	1,30097	1,31884	,75559	,95000	,74890	,92157	,94857

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
QIL13	1	67	39,55	2650,00
	2	19	57,42	1091,00
	Total	86		
QIL14	1	67	40,07	2685,00
	2	19	55,58	1056,00
	Total	86		
QA12	1	67	49,82	3338,00
	2	19	21,21	403,00
	Total	86		
QA14	1	67	45,25	3031,50
	2	19	37,34	709,50
	Total	86		
QA24	1	67	49,06	3287,00
	2	19	23,89	454,00
	Total	86		
QAR13	1	66	47,18	3114,00
	2	19	28,47	541,00
	Total	85		
QAR14	1	66	46,44	3065,00
	2	19	31,05	590,00
	Total	85		

Test Statistics[a]

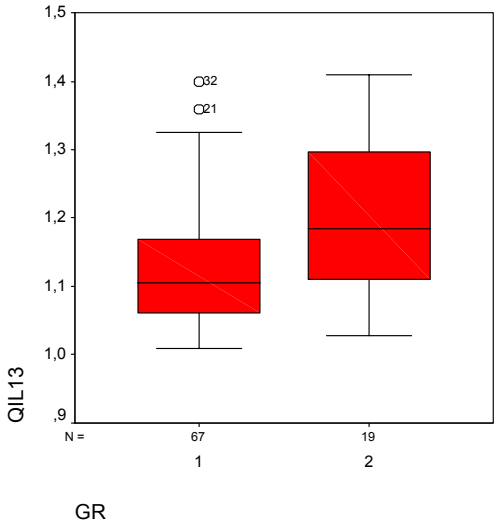
	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	372,000	407,000	213,000	519,500	264,000	351,000	400,000
Wilcoxon W	2650,000	2685,000	403,000	709,500	454,000	541,000	590,000
Z	-2,753	-2,389	-4,408	-1,218	-3,877	-2,911	-2,395
Asymp. Sig. (2-tailed)	,006	,017	,000	,223	,000	,004	,017

a. Grouping Variable: GR

Boxplots interval quotient 13 (QIL13)

Case Processing Summary

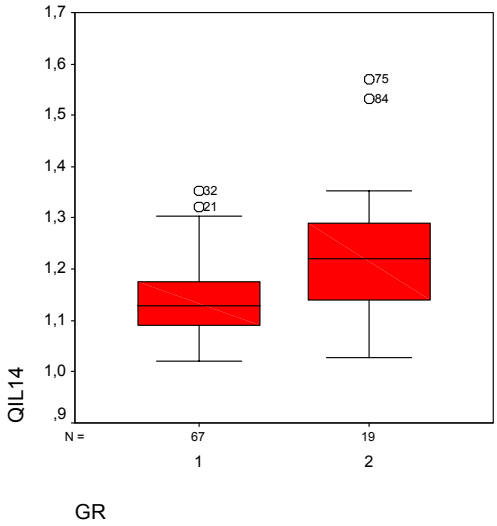
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL13	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots interval quotient 14 (QIL14)

Case Processing Summary

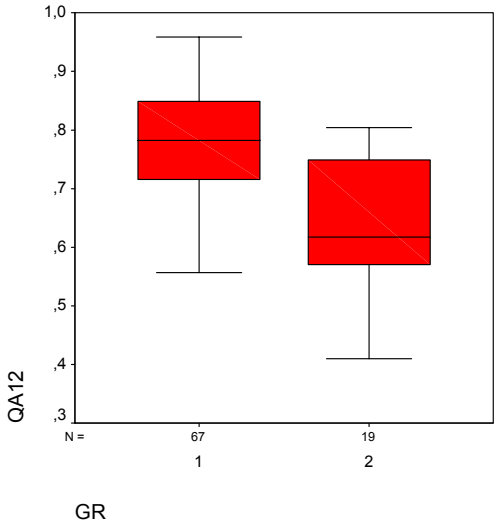
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots amplitude quotient 12 (QA12)

Case Processing Summary

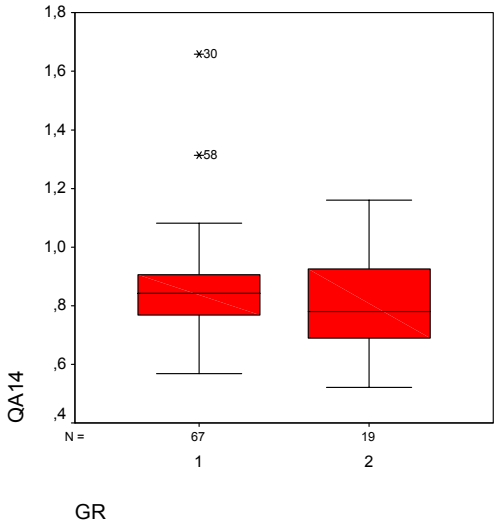
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA12	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots amplitude quotient 14 (QA14)

Case Processing Summary

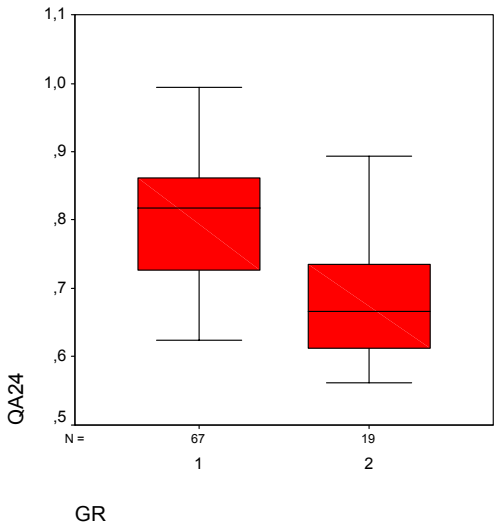
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA14	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots amplitude quotient 24 (QA24)

Case Processing Summary

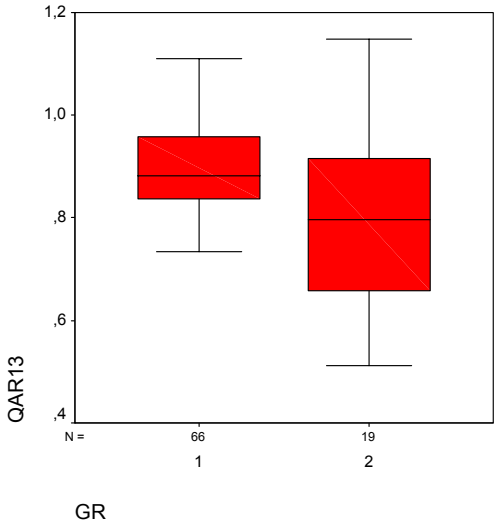
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA24	1	67	100,0%	0	,0%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots area quotient 13 (QAR13)

Case Processing Summary

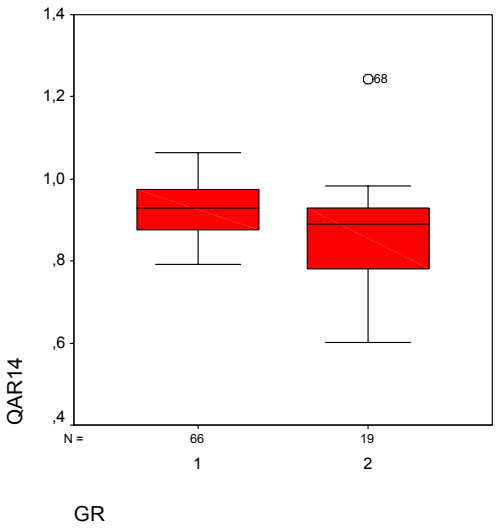
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



Boxplots area quotient 14 (QAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	19	100,0%	0	,0%	19	100,0%



13.1.3 N. peronaeus

13.1.3.1 Distal parameter

Frequencies

Statistics

GR			DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,5094	7,245	6,5706	3,2210	9,78	19,817	27,159
	Median		5,4600	7,260	6,0700	3,0600	9,00	19,000	25,850
	Std. Deviation		,88143	1,2844	1,75050	1,45370	2,867	5,2584	7,8019
	Minimum		3,48	4,2	3,71	,96	5	10,9	15,6
	Maximum		7,50	10,0	11,10	8,49	18	31,8	45,2
	Percentiles	25	5,0000	6,250	5,2900	2,0800	8,00	16,175	20,800
		50	5,4600	7,260	6,0700	3,0600	9,00	19,000	25,850
		75	6,2000	8,000	8,1000	3,8500	12,00	23,650	32,950
2	N	Valid	15	15	15	15	15	15	15
		Missing	0	0	0	0	0	0	0
	Mean		5,2940	6,887	3,6907	1,7687	5,46	10,689	15,040
	Median		4,9500	6,650	3,8300	1,8500	6,09	11,600	16,600
	Std. Deviation		1,04427	1,5175	1,67409	,89550	2,461	5,2371	6,9417
	Minimum		3,50	4,3	1,09	,25	1	1,7	3,7
	Maximum		7,25	9,4	6,46	3,57	10	18,5	23,3
	Percentiles	25	4,5500	5,900	1,7100	,8300	3,35	4,700	8,600
		50	4,9500	6,650	3,8300	1,8500	6,09	11,600	16,600
		75	6,1500	7,800	4,9200	2,2800	6,60	15,600	21,500

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
DIL13	1	67	42,80	2867,50
	2	15	35,70	535,50
	Total	82		
DIL14	1	67	42,63	2856,00
	2	15	36,47	547,00
	Total	82		
DA12	1	67	47,16	3160,00
	2	15	16,20	243,00
	Total	82		
DA14	1	67	46,10	3089,00
	2	15	20,93	314,00
	Total	82		
DA24	1	67	47,06	3153,00
	2	15	16,67	250,00
	Total	82		
DAR13	1	66	46,92	3097,00
	2	15	14,93	224,00
	Total	81		
DAR14	1	66	46,49	3068,50
	2	15	16,83	252,50
	Total	81		

Test Statistics[a]

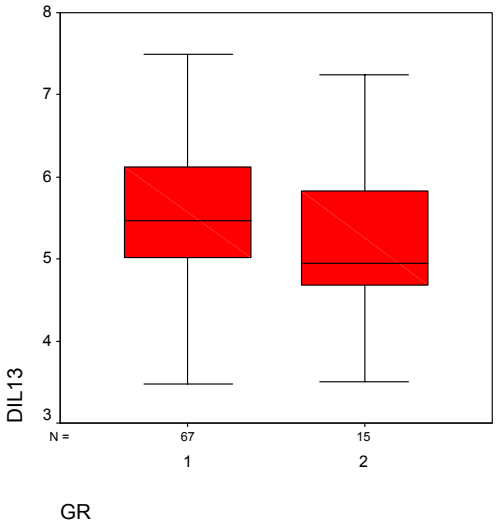
	DIL13	DIL14	DA12	DA14	DA24	DAR13	DAR14
Mann-Whitney U	415,500	427,000	123,000	194,000	130,000	104,000	132,500
Wilcoxon W	535,500	547,000	243,000	314,000	250,000	224,000	252,500
Z	-1,044	-,906	-4,552	-3,701	-4,468	-4,754	-4,408
Asymp. Sig. (2-tailed)	,297	,365	,000	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots distal interval 13 (DIL13)

Case Processing Summary

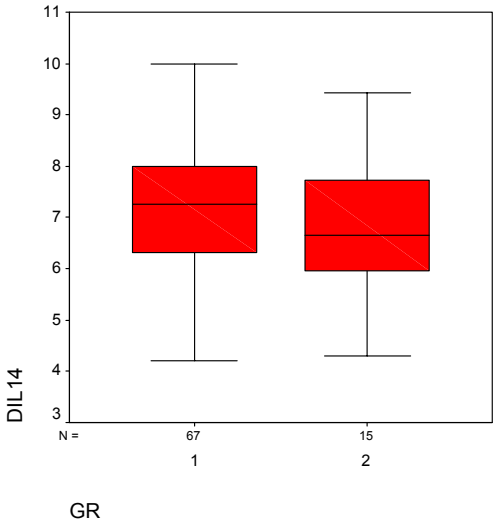
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL13	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal interval 14 (DIL14)

Case Processing Summary

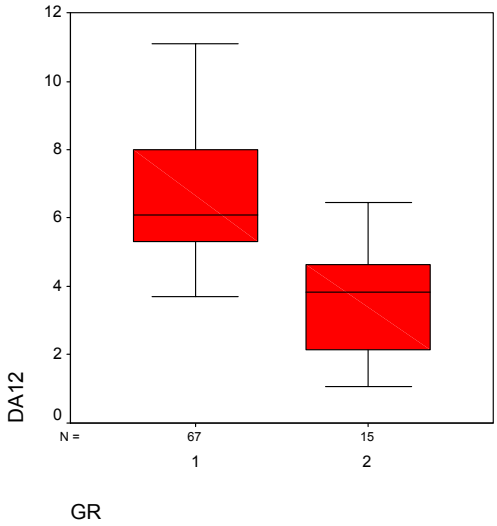
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DIL14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal amplitude 12 (DA12)

Case Processing Summary

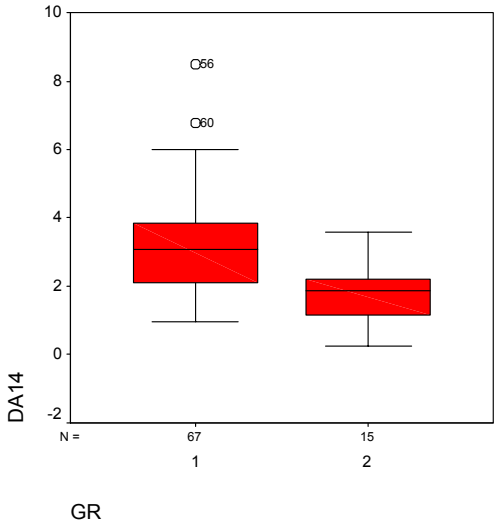
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA12	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal amplitude 14 (DA14)

Case Processing Summary

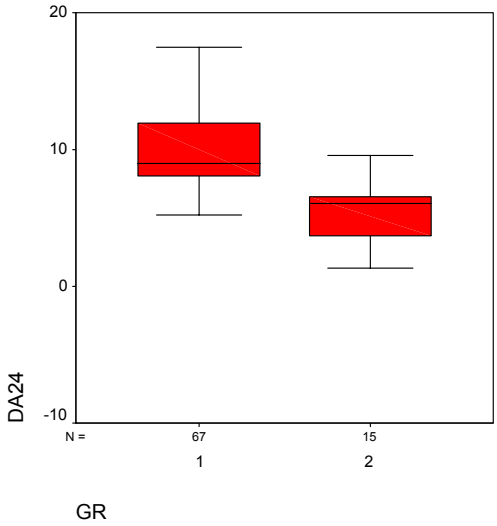
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal amplitude 24 (DA24)

Case Processing Summary

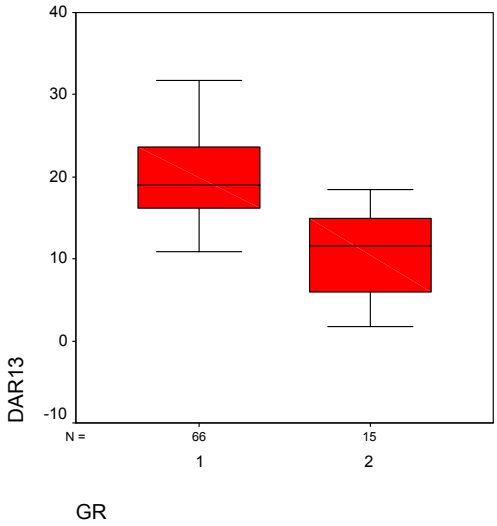
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DA24	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal area 13 (DAR13)

Case Processing Summary

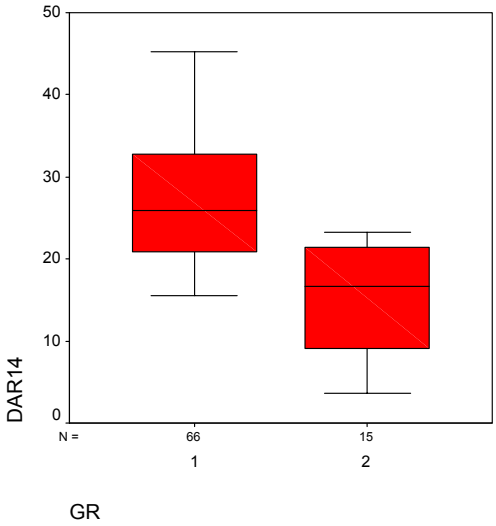
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots distal area 14 (DAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
DAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



13.1.3.2 Proximal parameter

Frequencies

Statistics

GR			PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		5,796	7,862	5,4410	3,2991	8,7306	17,321	25,156
	Median		5,900	7,950	5,2700	3,0700	8,3500	16,350	23,850
	Std. Deviation		,8982	1,4543	1,53464	1,21714	2,57938	4,8279	7,5086
	Minimum		3,6	4,5	2,96	1,17	4,58	8,9	13,9
	Maximum		7,7	11,2	9,61	6,29	15,30	29,0	43,3
	Percentiles	25	5,200	6,800	4,3700	2,4600	6,8700	13,800	18,975
		50	5,900	7,950	5,2700	3,0700	8,3500	16,350	23,850
		75	6,450	8,940	6,3400	3,8500	10,5000	20,625	30,700
2	N	Valid	15	15	15	15	15	15	15
		Missing	0	0	0	0	0	0	0
	Mean		5,916	7,814	2,9259	1,6759	4,6067	9,173	13,520
	Median		5,600	7,500	3,0200	1,6600	5,0500	9,300	14,200
	Std. Deviation		1,0551	1,4779	1,56869	,79860	2,24043	4,5456	6,5698
	Minimum		4,5	5,4	,78	,39	1,17	2,4	2,8
	Maximum		8,2	10,6	6,17	3,39	8,49	16,7	22,4
	Percentiles	25	5,150	6,750	1,5000	1,1700	2,7500	4,600	8,000
		50	5,600	7,500	3,0200	1,6600	5,0500	9,300	14,200
		75	6,800	9,020	4,0400	2,3200	5,6100	12,600	19,200

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
PIL13	1	67	41,51	2781,00
	2	15	41,47	622,00
	Total	82		
PIL14	1	67	41,79	2800,00
	2	15	40,20	603,00
	Total	82		
PA12	1	67	47,16	3159,50
	2	15	16,23	243,50
	Total	82		
PA14	1	67	47,28	3168,00
	2	15	15,67	235,00
	Total	82		
PA24	1	67	47,29	3168,50
	2	15	15,63	234,50
	Total	82		
PAR13	1	66	46,89	3095,00
	2	15	15,07	226,00
	Total	81		
PAR14	1	66	46,61	3076,00
	2	15	16,33	245,00
	Total	81		

Test Statistics[a]

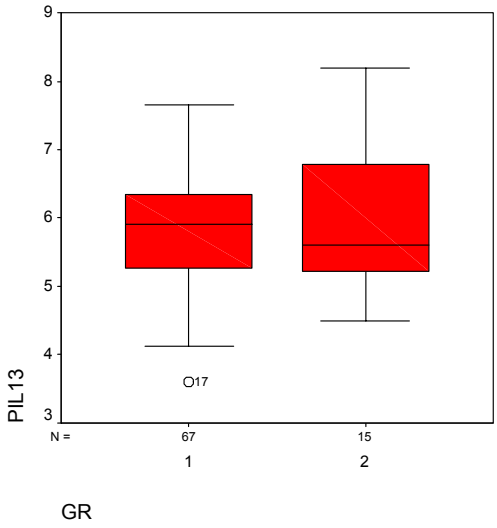
	PIL13	PIL14	PA12	PA14	PA24	PAR13	PAR14
Mann-Whitney U	502,000	483,000	123,500	115,000	114,500	106,000	125,000
Wilcoxon W	622,000	603,000	243,500	235,000	234,500	226,000	245,000
Z	-,006	-,234	-4,546	-4,648	-4,654	-4,730	-4,499
Asymp. Sig. (2-tailed)	,995	,815	,000	,000	,000	,000	,000

a. Grouping Variable: GR

Boxplots proximal interval 13 (PIL13)

Case Processing Summary

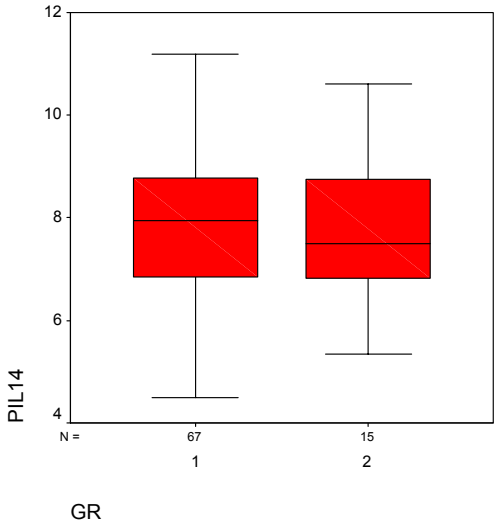
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL13	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal interval 14 (PIL14)

Case Processing Summary

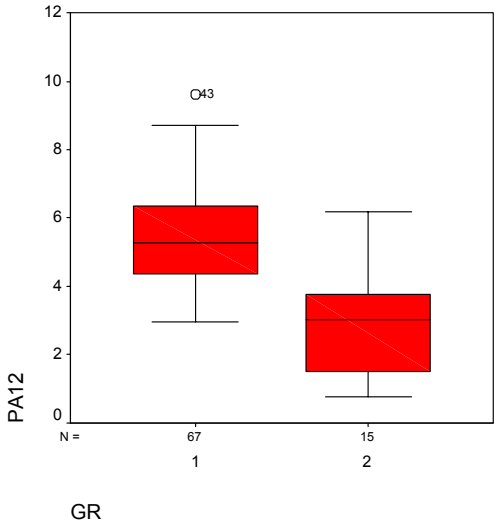
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PIL14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal amplitude 12 (PA12)

Case Processing Summary

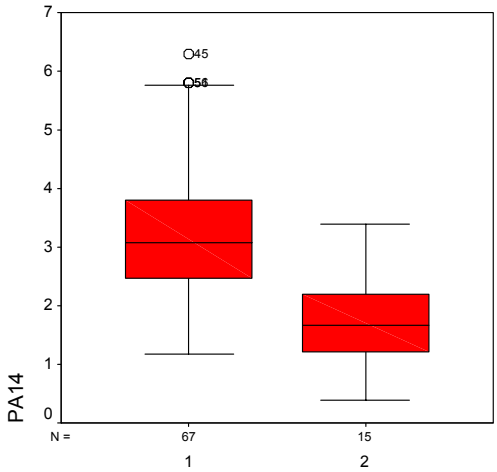
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA12	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal amplitude 14 (PA14)

Case Processing Summary

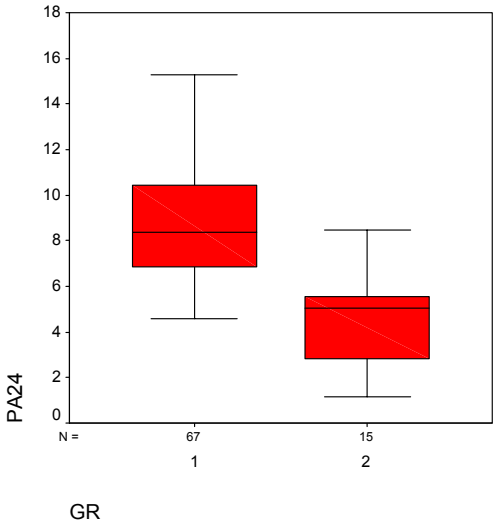
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal amplitude 24 (PA24)

Case Processing Summary

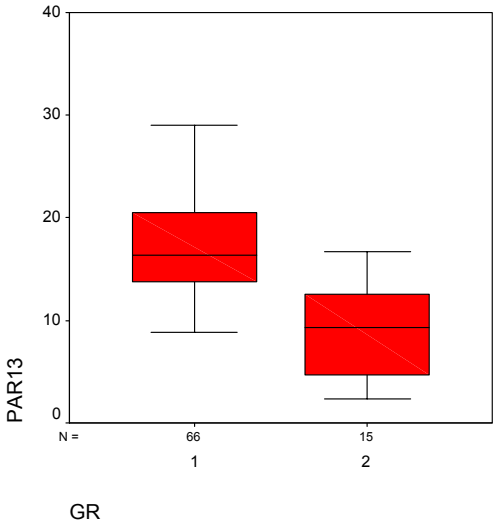
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PA24	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal area 13 (PAR13)

Case Processing Summary

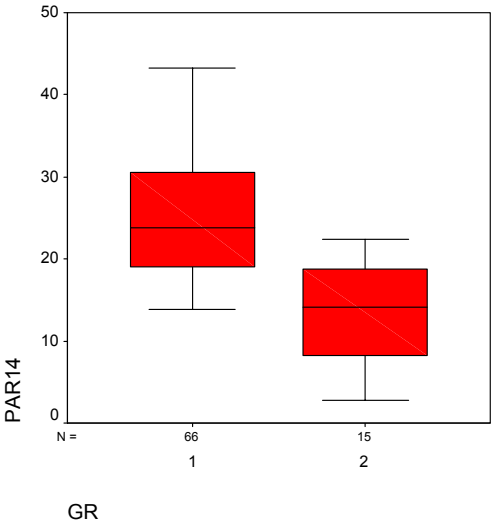
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots proximal area 14 (PAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
PAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



13.1.3.3 Nerve conduction velocities

Frequencies

Statistics

GR			NCV1	NCV2	NCV3	NCV4
1	N	Valid	67	67	67	67
		Missing	0	0	0	0
	Mean		47,366	44,926	45,863	43,868
	Median		47,100	45,070	45,251	44,118
	Std. Deviation		3,6696	3,5012	3,8954	3,6325
	Minimum		40,2	38,4	39,4	35,5
	Maximum		60,8	57,0	60,8	55,3
	Percentiles	25	45,200	42,282	43,671	41,549
		50	47,100	45,070	45,251	44,118
		75	49,300	47,097	48,000	46,203
2	N	Valid	15	15	15	15
		Missing	0	0	0	0
	Mean		44,148	40,310	40,785	39,321
	Median		42,900	40,984	40,123	39,326
	Std. Deviation		5,1543	4,7526	4,2500	4,3102
	Minimum		38,5	32,8	33,3	32,0
	Maximum		54,0	49,0	47,1	47,1
	Percentiles	25	40,400	35,928	36,667	36,000
		50	42,900	40,984	40,123	39,326
		75	48,000	43,796	45,238	42,537

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
NCV1	1	67	44,87	3006,50
	2	15	26,43	396,50
	Total	82		
NCV2	1	67	45,64	3058,00
	2	15	23,00	345,00
	Total	82		
NCV3	1	67	45,97	3080,00
	2	15	21,53	323,00
	Total	82		
NCV4	1	67	45,92	3076,50
	2	15	21,77	326,50
	Total	82		

Test Statistics[a]

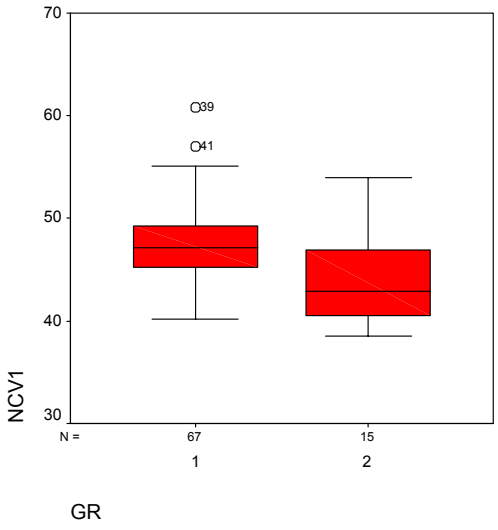
	NCV1	NCV2	NCV3	NCV4
Mann-Whitney U	276,500	225,000	203,000	206,500
Wilcoxon W	396,500	345,000	323,000	326,500
Z	-2,711	-3,328	-3,592	-3,550
Asymp. Sig. (2-tailed)	,007	,001	,000	,000

a. Grouping Variable: GR

Boxplots nerve conduction velocity 1 (NCV1)

Case Processing Summary

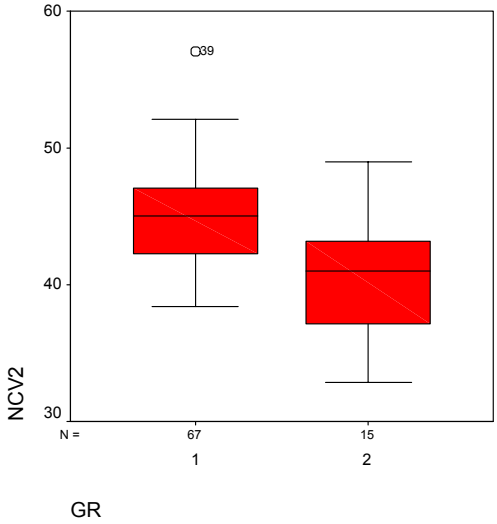
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV1	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots nerve conduction velocity (NCV2)

Case Processing Summary

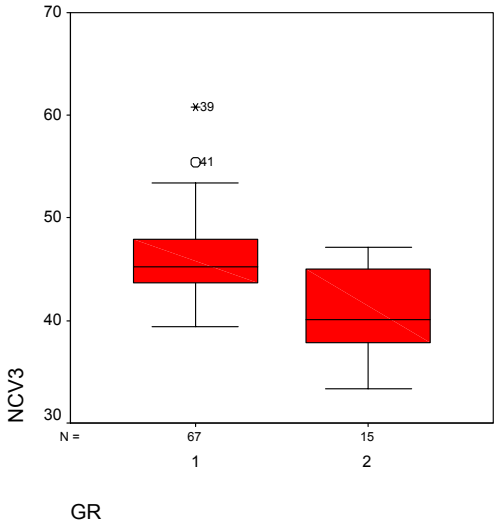
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV2	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots nerve conduction velocity 3 (NCV3)

Case Processing Summary

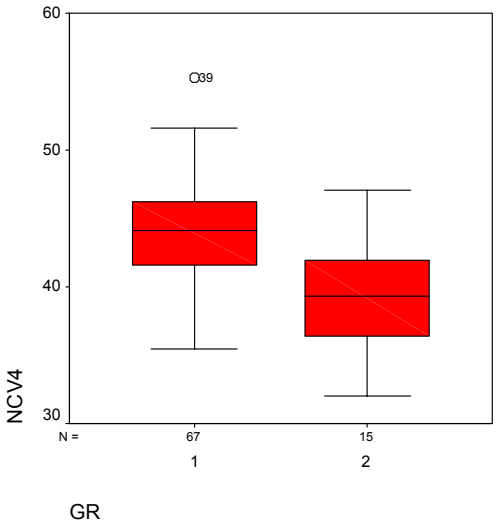
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV3	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots nerve conduction velocity 4 (NCV4)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
NCV4	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



13.1.3.4 Quotient parameter

Frequencies

Statistics

GR			QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
1	N	Valid	67	67	67	67	67	66	66
		Missing	0	0	0	0	0	1	1
	Mean		1,05394	1,08469	,82749	1,08361	,89476	,87623	,92598
	Median		1,03704	1,07792	,83000	1,05943	,89583	,86754	,93624
	Std. Deviation		,052025	,055829	,069999	,237361	,069759	,094302	,063965
	Minimum		,956	1,005	,644	,490	,695	,686	,737
	Maximum		1,300	1,343	,979	1,740	,994	1,214	1,110
	Percentiles	25	1,02222	1,04712	,76485	,89737	,85248	,81017	,88715
		50	1,03704	1,07792	,83000	1,05943	,89583	,86754	,93624
		75	1,07073	1,10219	,87573	1,24519	,94761	,93231	,96960
2	N	Valid	15	15	15	15	15	15	15
		Missing	0	0	0	0	0	0	0
	Mean		1,12464	1,14437	,77039	1,01911	,84275	,88587	,88927
	Median		1,10599	1,13978	,79310	,99024	,86866	,85926	,89720
	Std. Deviation		,086778	,083016	,118368	,254114	,107221	,169365	,081453
	Minimum		1,014	1,012	,554	,473	,566	,676	,747
	Maximum		1,304	1,337	,955	1,542	,988	1,387	,995
	Percentiles	25	1,05495	1,08631	,71395	,87547	,80414	,78378	,83133
		50	1,10599	1,13978	,79310	,99024	,86866	,85926	,89720
		75	1,16667	1,17460	,85260	1,12973	,92593	,95775	,97297

NPar Tests
Mann-Whitney Test

Ranks

	GR	N	Mean Rank	Sum of Ranks
QIL13	1	67	37,27	2497,00
	2	15	60,40	906,00
	Total	82		
QIL14	1	67	37,83	2534,50
	2	15	57,90	868,50
	Total	82		
QA12	1	67	43,75	2931,50
	2	15	31,43	471,50
	Total	82		
QA14	1	67	42,54	2850,50
	2	15	36,83	552,50
	Total	82		
QA24	1	67	43,84	2937,50
	2	15	31,03	465,50
	Total	82		
QAR13	1	66	41,27	2723,50
	2	15	39,83	597,50
	Total	81		
QAR14	1	66	42,83	2826,50
	2	15	32,97	494,50
	Total	81		

Test Statistics[a]

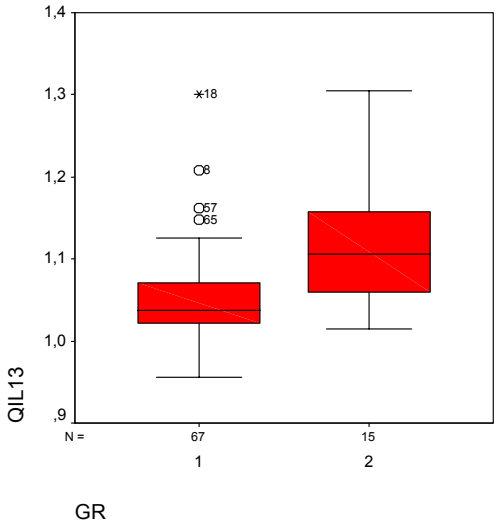
	QIL13	QIL14	QA12	QA14	QA24	QAR13	QAR14
Mann-Whitney U	219,000	256,500	351,500	432,500	345,500	477,500	374,500
Wilcoxon W	2497,000	2534,500	471,500	552,500	465,500	597,500	494,500
Z	-3,400	-2,951	-1,811	-,840	-1,883	-,213	-1,465
Asymp. Sig. (2-tailed)	,001	,003	,070	,401	,060	,832	,143

a. Grouping Variable: GR

Boxplots interval quotient 13 (QIL13)

Case Processing Summary

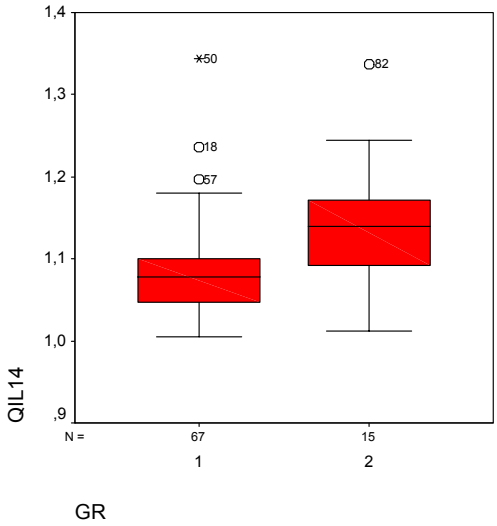
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL13	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots interval quotient 14 (QIL14)

Case Processing Summary

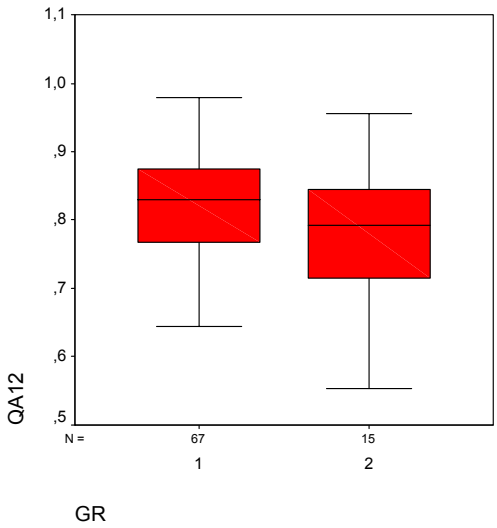
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QIL14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots amplitude quotient 12 (QA12)

Case Processing Summary

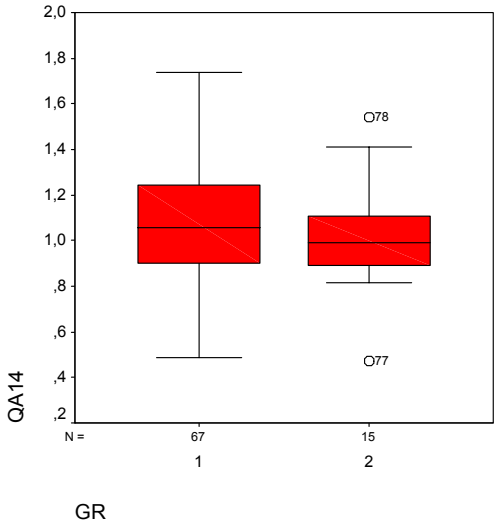
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA12	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots amplitude quotient 14 (QA14)

Case Processing Summary

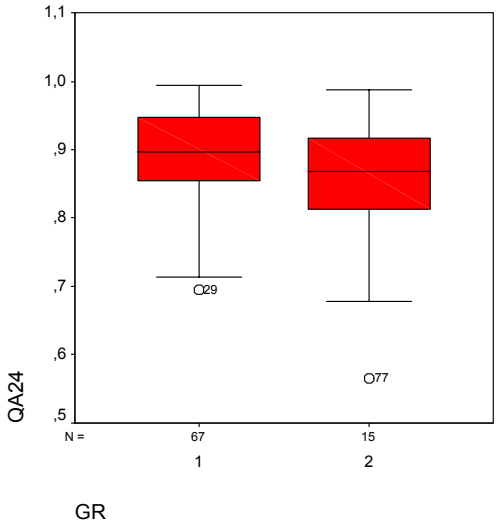
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA14	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots amplitude quotient 24 (QA24)

Case Processing Summary

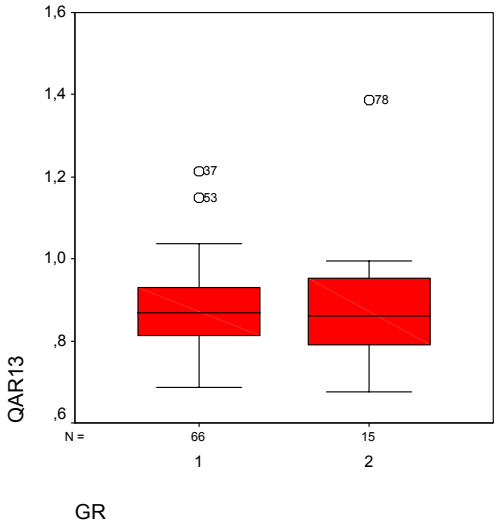
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QA24	1	67	100,0%	0	,0%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots area quotient 13 (QAR13)

Case Processing Summary

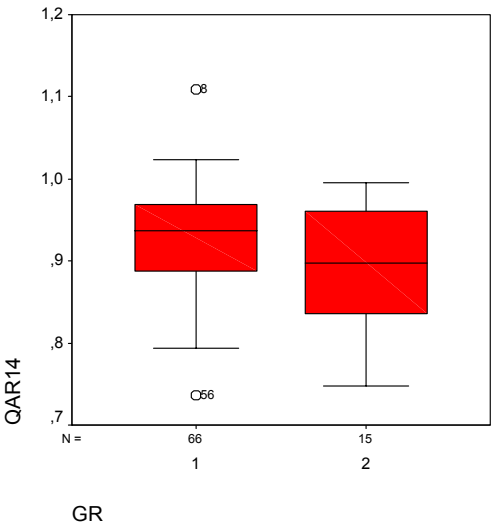
		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR13	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%



Boxplots area quotient 14 (QAR14)

Case Processing Summary

		Cases					
		Valid		Missing		Total	
	GR	N	Percent	N	Percent	N	Percent
QAR14	1	66	98,5%	1	1,5%	67	100,0%
	2	15	100,0%	0	,0%	15	100,0%


1,2
1,1
1,0
,9
,8
,7
QAR14
8
56
N =
66
15
1
2
GR

13.2 Ethical issues

ıcrobat-Dokumer

13.3 Abbreviations

A	amplitude
ALS	amyotrophic lateral sclerosis
AR	area
ARI	aldose reductase inhibitor
ATR	achilles tendon reflex
CAFT	cardiovascular autonomic function testing
CI	confidence interval
CIPD	chronic inflammatory demyelinating polyneuropathy
CMAP	compound muscle action potential
d	distal (as prefix)
DCCT	diabetes control and complication trial
DM	diabetes mellitus
DNES	diabetic neuropathy examination score
DNP	diabetic neuropathy
DNS	diabetic neuropathy score
DS	distal stimulus
DSP	distal symmetric polyneuropathy
EDS	electro-diagnostic study
GR	group
IDDM	insulin-dependent diabetes mellitus
IGT	impaired glucose tolerance
IL	interval
mA	milliampere
mm	millimeter
mNCV	motor nerve conduction velocity
ms	milliseconds
mV	millivolt
N.	nervus
NCS	nerve conduction study
NCV	nerve conduction velocity
ND	neuropathic deficit
n.k.	not known
NIDDM	non-insulin-dependent diabetes mellitus
No.	number

NPar Tests	non-parametric tests
NS	neuropathic symptoms
p	proximal (as prefix)
PNS	peripheral nervous system
PS	proximal stimulus
PTR	patella tendon reflex
Q	quotient
QAFT	quantitative autonomic function test
QST	quantitative sensory test
SD	standard deviation
SWME	10-g Semmes-Weinstein monofilament examination
ys	years

13.4 Literature

1. Albers JW, Brown MB, Sima AAF, Greene DA: Nerve conduction measures in mild diabetic neuropathy: the effect of age, sex, type of diabetes, disease duration, and anthropometric factors. Neurology 45 (suppl.) (1995) 190-191.

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