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Inter-practitioner comparisons of nerve conduction studies with standardized techniques in normal subjects

Reap as you sow

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Abstract

This 2-group study was carried out to determine the inter-practitioner difference of nerve conduction studies with standardized techniques.

56 normal subjects of 19 to 49 year-old were recruited, 29, and 27 in the 2 labs respectively. Tests were carried out unilaterally on: 5 motor nerve distal latency, conduction velocities (MNCV) and minimum latency of F wave, 3 sensory nerves with negative amplitude, onset, and peak distal latency, sensory nerve distal latency.

T-test disclosed 4(15.4%) attributes with statistical significance ($P < .05$). They were 2 of 4 (50%) compound motor action potentials, which were ulnar and tibial nerve, and 2 of 6 (33.3%) MNCVs, which were elbow-to-wrist MNCV of median nerve and cross-fibula MNCV of peroneal nerve. No differences were disclosed in motor nerve distal latencys, minimum latency of F waves and all sensory attributes.

Inconsistency pattern of certain attributes were found. This could be explained with the insufficient definition of related techniques.

Abbreviations: BMI = body mass index, CMAP = compound motor action potential, EDx = electrodiagnostic, MLFW = minimum latency of F wave, MNCV = motor nerve conduction velocity, MNDL = motor nerve distal latency, NCs = nerve conduction studies, SNAP = sensory nerve action potential, SNDL = sensory nerve distal latency.

Keywords: electrodiagnosis, nerve conduction study, normal subject, normal value

1. Introduction

As an elementary and universal part of electrodiagnostic (EDx) examination, nerve conduction studies (NCs) are commonly used to define the extent and severity of a peripheral neuropathy, identify the specific fiber populations involved, and determine whether the primary pathologic process is axonal or demyelinating. NCs have increasingly been advocated for diagnosis of neuromuscular disorders along with clinical signs and symptoms underlying neurophysiological and neuropathological abnormalities. Most of all, NCs could provide objective, quantitative and reproducible indications of nerve dysfunction. Practically, however, NCs can be challenging with great variability in measurements. Until now, a well-established reference value for routine NCs is still not available.[1,2] And inter-practitioner inconsistency is still the prominent obstacle of clinical practice and therapeutic trials.[3–5] Falck et al proposed that reference values of NCs attributes could be acceptable and understandable across different laboratories when technical factors were "carefully standardized".[6] Litchy et al verified that reduction of significant inter-practitioner disagreement was achieved when using written instructions and pretrial agreement on techniques in Clinical vs Neurophysiology TRIAL 4 than in Clinical vs Neurophysiology 3, and they confirmed that the variation of inter-practitioner was relate to differences in test performance.[1] Although adopted by some previous studies, the details of "standardized NCs techniques" had not been published. Systematic work has been done by the Normative Data Task Force (NDTF) of the American Association of Neuromuscular and EDx Medicine (AANEM). Techniques that reflect high quality in NCs have been identified from previous studies with uniformed criteria.[2]

We follow the hypothesis that variation of inter-practitioner of NCs would be eliminated if the testing is sufficiently well standardized.[1] This study detected the inter-practitioner difference of attributes when NDTF proposed standardized techniques were applied in two different centers with same instrument, which was our prior feasibility examination of yielding a multicenter NCs reference value based on standardized techniques.

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2. Methods

2.1. Subjects recruitment

After obtaining Institutional Review Board approval, subjects were separately recruited to 2 laboratories through advertisements placed on bulletin boards. Exclusion criteria were: age less than 18 or more than 50 years, toxic/metabolic disease, compression neuropathy, symptoms of numbness, tingling, or abnormal sensations, neuromuscular disease, peripheral nerve injury, hereditary neuropathy, radiculopathy, back or neck surgery, cardiac or pulmonary disease, amputation. Each subject read and signed an informed consent.

2.2. Demographic and anthropometric factors

For all subjects, age and sex were recorded, height and weight were measured. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2).

2.3. Subjects preparation

Skin surface temperatures were measured over the dorsum of the hand and foot. If the skin temperatures fell below 32°C for the hand or 31° for the foot, limbs would be warmed as previously described.[7]

2.4. Nerves, categories and attributes of NCs

Routine motor and sensory studies were performed unilaterally on the following 7 nerves: median, ulnar, peroneal, and tibial motor nerves; median, ulnar and sural sensory nerves. NCs studies were performed in the motor nerves orthodromically and in sensory nerves antidromically. 4 categories of NCs tests were carried out on motor nerves: distal amplitude [compound muscle action potential (CMAP)], motor nerve distal latency (MNDL), motor nerve conduction velocity (MNCV) and minimum latency of F wave (MLFW). And 2 categories were tested on sensory nerves: negative amplitude (sensory nerve action amplitude [negative SNAP]), onset and peak distal latency (sensory nerve distal latency [SNDL]). In all, 26 attributes of each subject were tested in this study: 4 CMAPs; 4 MNDLs; 6 MNCVs and 3 MLFWs; 3 SNAPs, and 6 SNDLs.

2.5. Techniques standardization and practitioner training

In pre-trial test, the NDTF edition techniques were revised according with anthropometric characters of normal subjects in our region. In final edition, electrode and stimulator placement, distance measurement was documented with photos of model demonstration. Details of electrode, stimulator placement, distance of recording-electrode to stimulator, display sensitivity, and sweep were listed in Table 1.

Stimulation frequencies were set at 1 Hz for sensory and motor nerve. In order to obtain supramaximal stimulate, the current was increased another 20% when the CMAP or SNAP no longer increased in size with carefully avoiding the co-stimulation of adjacent nerve.

Average techniques with at least 3 measurements were applied in sensory test but not motor studies.

Table 1

Standardized techniques defined in this study with details in machine settings and stimulator and electrode placement.

	Stimulator and Electrode Placement				Machine settings	
Nerve	G1	G2	Stimulating site (SS)	Distance (G1 to SS)	Display sensitivity (uv/div) sensory, (mv/div) motor	Sweep (ms/div)
Median sensory	Index finger	4 cm distal to G1	Wrist, between the flexor carpi radialis and the palmaris longus tendons	13	10	1
Ulnar sensory	Fifth digit	4 cm distal to G1	Slightly to the radial side of the flexor carpi ulnaris tendon	11	10	1
Sural sensory	posteroinferior to the lateral mallelus	Distal: 3 cm bar	At or slightly to the calf midline	14	2	1
Median motor	Abductor pollicis brevis motor point	Distal to first MCP	wrist: between the flexor carpi radialis and the palmaris longus tendons Elbow: medial to the brachial pulse	7	5	2
Ulnar motor	Hypothenar eminece	Slightly distal to the fifth MCP joint, Elbow extension 90	wrist: slightly radial to the flexor carpi ulnaris tendon Below elbow Above elbow	7	5	2
Peroneal motor	Midpoint of extensor digitorum brevis	Just distal to fifth MTP	Ankle: lateral to the tibialis anterior tendon Below fibular head: posteroinferior to the fibular head Above fibular head: 10 cm proximal to the below fibular head site and slightly medial to the tendon of the biceps femoris	9	5	5
Tibial motor	Medial foot (slightly anterior/inferior to the navicular tubercle)	Slightly distal to first MTP (medial aspect of joint)	Ankle: posterior to the medial malleolus Knee: midpopliteal fossa	9	5	5

MCP = metacarpophalangeal, MTP = metatarsophalangeal, SS = stimulating site.

2.6. All tests were performed on the Keypoint instrument (Dantec)

Two authors (BZhao, KXSui) served the role of techniques formulating, model demonstrating and practitioner training. The other two authors (HMDiao, QXWen) were trained with the training syllabus, a paper document and photo demonstration of the standardized techniques. One author (YQZhang) served as the modulator of the study to confirm the test trail and data inspection.

Statistical analysis. *T*-test was run to examine the difference of age, BMI difference, and Chi-square test to examine the difference of gender in all branches. *T*-test analysis was performed on all the attributes between groups. The *P* value was set to .05.

3. Results

29 and 27 subjects completed all presupposed tests in each laboratory respectively, their demographic and anthropometric characteristics as well as the between-group comparison of age, gender and BMI were listed in Table 2. No significance was disclosed in all these items.

T-test was performed to examine the difference of all the 26 attributes between groups. 4(15.4%) attributes of motor nerves were revealed with statistical significance ($P < .05$), which were 2 of 4 (50%) CMAPs of ulnar and tibial nerve, and 2 of 6 (33.3%) MNCVs including elbow-to-wrist MNCV of median nerve and cross-fibula MNCV of peroneal nerve. No significance was disclosed in MNDL, MLFW of motor nerve and all attributes of sensory nerve.

4. Disscussion

NCs are widely used in the clinical diagnosis, epidemiological surveys,[8,9] and therapeutic trials of neuromuscular disorders.[10,11] Inter-practitioner inconsistencies have been the main obstacle to yielding of a multi-center reference values and longitudinal comparisons in clinical trials, which were believed rooted in the difficulty of documenting and performing standard techniques.

In this 2-group study, standardized techniques were modified from the NDTF of AANEM. Statistical significance was found in 4 (15.4%) motor nerve attributes: 2 (50%) CMAPs of ulnar and tibial nerve and 2 (33.3%) MNCVs which were elbow-to-wrist MNCV of median nerve and cross-fibula MNCV of peroneal nerve. No significance was disclosed in other attibutes.

The first question is whether current standardized techniques brought about more consistencies on the attributes. The data for comparison came from studies with multi-group design on the same subjects. Chaudhry et al tested the consistencies on normal subjects. Each one of the 7 experienced practitioners assessed NCs of the other 4 members. Inconsistency was disclosed in 4 of 12 (33.3%) attributes including 1/2 CMAPs, 1/2 MNCVs, 1/2 of SNAPs and 1/2 MNDLs.[3] The same group then recruited 6 patients with diabetic neuropathy. 6 experienced practitioners performed duplicate NCs on these patients and found inconsistency was same as normal subjects (4/12 attributes), observing in 2/2 CMAPs, 1/2 of SNAPs and 1/2 MNDLs.[4] In CI Phys 3 study, Dyck et al revealed significant interobserver differences in 8 of 8 (100%) attributes on day 1 and 7 of 8 (87.5%) attributes on day 2 without adoping standardized techniques.[5] Specifically, 2/2 CMAP, 2/2 MNDL and 2/2 MNCV, 1/1 SNAP, and 1/1 SNDL were evaluated significantly different on day 1 and only fibular MNCV (1/2 MNCV) didn't reach significance on day 2.[5] In CI Phys 4 study, 5 of 8 (62.5%) attributes showed statistical significance on day1 and 2 respectively with standardized techniques they defined.[1] They were 2/2 CMAP, 2/2 MNDL and 0/2 MNCV, 1/1 SNAP, and 0/1 SNDL on day 1; 2/2 CMAP, 1/2 MNDL and 1/2 MNCV, 1/1 SNAP, and 0/1 SNDL on day 2. Taking notice of the pattern of attributes with inconsistency in our study, CMAP and MNCV were the only attributes with significant differences. Furthermore, the aboved refereced studies usually evaluated about 8–12 attributes with only ~2 attributes in each category. Although the attributes were expanded to 26 with 4–6 attributes in each category, relatively high inter-practitioner consistency was definitely maintained in this study.

With the above analysis, the preliminary impression was that standardized techniques could have brought about fewer inconsistencies. However, this conclusion should be carefully declared because our study design inevitably brought less inconsistencies compared to the multi-group design. Even though, we considered the inconsistency pattern of attributes makes more sense than the decreased inconsistency rates. More specifically, this study indicated that standardized techniques could bring about consistency in the MNDL, MLFW, SNAP and SNDL but not CMAP and MNCV. As previous studies concluded that inconsistencies were ascribed to techniques, we hypothesized that a certain aspect of NCs techniques might contribute to a category of attributes, such as, distances of G1-SS to the latencies, distances of proximal-distal SS to the MNCVs, recording-electrode positions and stimulation intensities to the CMAPs and SNAPs.

4.1. Reason for the consistency in MNDL, MLFW, SNAP and SNDL

When inspecting the details of standardized technique of this study, notice should be taken of the explicit definition of distance from stimulation-site to record-electrode (see in Table 1, showed as G1-SS). The NDTF adopted the fixed distance in addition to

Table 2

Demographic and anthropometric characteristics of subjects between group.

	Group 1 (N = 29)	Group 2 (N = 27)	Chi^2 / *t*- value	*P*- value
Female%	51.7%	59.3%	0.3212*	.571
Age	36.3 ± 10.1	32.9 ± 10.5	1.2548†	.2149
Heigh	166.0 ± 7.5	168.2 ± 7.1	1.1175†	.2687
BMI	24.2 ± 2.6	23.0 ± 3.0	1.6346†	.1080

Chi2: Chi-square; age yr old; height cm; BMI kg/m^2.

* The Chi^2 value.

† *t* - value.

Table 3

***P* values with robust regression of attributes in each branch.**

Nerves		Attributes	Group 1 (N = 30)	Group 2 (N = 25)	*T* value	*P* value
Motor nerve	Median	CMAP	8.64 ± 1.67	8.71 ± 1.19	0.1601	.8734
		MNDL	3.11 ± 0.29	3.07 ± 0.32	0.5342	.5954
		MNCV: elbow to wrist	59.3 ± 4.0	56.4 ± 4.3	2.6476	**.0106**
		MLFW	24.1 ± 1.6	24.2 ± 1.7	0.1251	.9009
	Ulnar	CMAP	7.43 ± 1.44	8.54 ± 1.22	3.0998	**.0031**
		MNDL	2.37 ± 0.23	2.38 ± 0.28	0.2164	.8295
		MNCV: below elbow to wrist	59.8 ± 3.9	58.7 ± 5.5	0.8313	.4095
		MNCV: cross elbow	60.8 ± 5.5	61.1 ± 7.1	0.1896	.8503
		MLFW	24.3 ± 1.7	24.0 ± 1.9	0.5707	.5706
	Tibial	CMAP	11.27 ± 2.92	13.55 ± 3.16	2.8031	**.0070**
		MNDL	3.74 ± 0.55	3.53 ± 0.52	1.4460	.1540
		MNCV: popliteal fossa to ankle	51.1 ± 5.3	50.1 ± 4.6	0.7136	.4786
		MLFW	44.2 ± 3.3	44.7 ± 2.9	0.5927	.5559
	Peroneal	CMAP	5.59 ± 1.61	5.41 ± 1.26	0.4607	.6468
		MNDL	3.50 ± 0.47	3.71 ± 0.39	1.8487	.0700
		MNCV: below fibular head to ankle	47.7 ± 3.6	47.5 ± 3.2	0.1499	.8814
		MNCV: cross fibular head	52.8 ± 2.7	49.8 ± 4.2	3.1218	**.0029**
Sensory nerve	Median	negative SNAP	45.1 ± 15.4	52.2 ± 17.7	1.6132	.1125
		onset SNDL	2.12 ± 0.18	2.14 ± 0.22	0.3213	.7492
		peak SNDL	2.79 ± 0.22	2.64 ± 0.38	1.7761	.0813
	ulnar	negative SNAP	36.2 ± 12.6	39.6 ± 14.4	0.9407	.3511
		onset SNDL	1.87 ± 0.20	1.90 ± 0.22	0.4268	.6712
		Peak SNDL	2.53 ± 0.24	2.40 ± 0.47	1.3172	.1933
	Sural	negative SNAP	18.4 ± 10.8	14.1 ± 6.2	1.7919	.0787
		onset SNDL	2.62 ± 0.19	2.70 ± 0.19	1.5606	.1245
		Peak SNDL	3.30 ± 0.17	3.36 ± 0.14	1.4274	.1592

CMAP = compound motor action potential, MLFW = minimum latency of F wave, MNCV = motor nerve conduction velocity, MNDL = motor nerve distal latency, SNAP = sensory nerve action potential, SNDL = sensory nerve distal latency.

CMAP mV; MNDL, MLFW and SNDL were all by ms; MNCV m/s; SNAP uV.

the anatomic landmarks. This would give the consistency of MNDLs, MLFWs and SNDLs, which mostly affected by the distance of G1-SS. Another remarkable pattern was the full-blown consistency in sensory tests where technical factors played a crutical role in the accurate measurement of NCs parameters. It should be emphasized that the potientals of sensory nerves were so delicate to be 3 orders of magnitude smaller than those of motor nerves.[12–14] Thus, standardized techniques provided significant improvement in the proficiency of sensory studies. The case of SNAP would be analyzed when compared with CMAP in the ensuing paragraphs.

4.2. Why differences exist in CMAPs and MNCVs with current techniques?

When performing the motor NC studies, proper recording electrode placement and stimulation delivery were essential for the measurement of CMAPs. The recording electrode should be placed accurately over the motor endplate of the muscle, which was difficult in one attempt with sometimes further adjustments. In practice, especially when the amplitude is obviously larger than reference value in the mind of an adept practitioner, electrode adjustments were seldomly made. In addition, if the amplitude was large enough, supramaximal stimulation was usually unlikely given especially when the subjects were volunteers. Furthermore, CMAPs were not taken by average method. All discussed above were not the case with SNAPs. Electrode placements were not so technically difficult and critical in antidromic study. The intensities of stimulations were usually less than were required for motor NCs. An average method may also decrease the chance of variation.

The 2 MNCVs with statistical differences were cross elbow CV of ulnar nerve and cross fibula of peroneal nerve. One could easily ascribe the differences of these 2 attributes to the measurements of distance because they appeared to be the most difficult part in practice particularly when standardized techniques could not form explicit regularities in this study. Moreover, the consistency in MNDLs and MLFWs, another 2 EDx markers of myelin function of peripheral nerve, further ruled out the intrinsic variation of subjects themselves and added evidence to the inconsistency of MNCVs.

The origin of NCs variation of inter-practitioner was presumably related to the techniques in a previous study.[1] However, this hypothesis hasn't been verified. The present study disclosed an inconsistency pattern of attributes with our standardized techniques, which could be interpreted as an insufficient effort to highly standardize certain details of technique.

Standardized techniques bring about consistency of attributes of sensory nerves, MNDLs and MLFWs of motor nerves, but not CMAPs and MNCVs in this study. This pattern of inconsistency could be explained by the insufficient definition of certain techniques. In practice, almost every practitioner has his or her own habits and standards. Among these individual factors, some were easily standardized, such as the distance of G1 to SS and cursor placement while most of the others were more ambiguous or hard to define, such as G1 placement, supramaximal stimulation delivery and distance of the proximal-distal SS of certain nerves. To explicitly define and practically operate every detail was still challenging. Therefore, the inconsistency of CMAPs and MNCVs in this study might ascribe to the lack of

detailed descriptions in these specific aspects. However, it is highly promising that inter-practitioner variation could be reduced or diminished and if NCs techniques were sufficiently standardized. In that case, multi-center reference value could be valid just like you reap as you sow.

Author contributions

B.Z. and Y.Q.Z. conceived and planned the experiments. H.M. D., Q.X.W. and K.X.S carried out the experiments. B.Z., H.M. D., Q.X.W. and K.X.S. contributed to the interpretation of the results. Y.Q.Z. took the lead in writing the manuscript. All authors provided critical feedback and helped shape the research, analysis and manuscript.

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