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A Mathematical Formula to Help Diagnose Uncertain Polyneuropathies

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Abstract

Objective: The diagnosis of a polyneuropathy depends on the patient's history, physical examination, and electrophysiological study. We planned to define the values of the median, ulnar and sural sensory fibers up to the 8th decade and to define their relationship to each other.

Material and Method: We performed nerve conduction studies on the sensory fibers of the median, ulnar and sural nerves in normal adults up to the 8th decade. We created a formula that allows us to compare the sural nerve to the nerves of the upper extremities.

Result: We define the normal means and standard deviation for each variable for each nerve across the different decades. There is a progressive decline in the sensory amplitude for all three nerves with age. A logistic regression curve was created to produce the probability that the sensory variables diagnose a neuropathy. The reliability of this analytic method was confirmed when applied on patients with the diagnosis of polyneuropathy.

Conclusion: A logistic regression formula and curve will allow a more accurate diagnosis of a polyneuropathy than depending on cut off values or normal values.

Significance: Using the logistic curve is better than referring to normal values in diagnosing uncertain neuropathies.

Keywords: Polyneuropathy; Sensory Fibers; Sural Nerve; Clinical Neurophysiology; Nerve Conduction Studies; Mathematical Formula

Highlights

- Patients with neuropathy have longer distal sensory latencies, lower sensory amplitudes and lower sensory conduction velocities.
- Sensory amplitudes of the median, ulnar and sural nerves decrease gradually with increasing age.
- The wide range of normal sensory amplitudes makes the diagnosis of mild and early neuropathies uncertain.
- Comparing the sural to the ulnar sensory amplitude is a more reliable indicator of pathology than comparing the sural amplitude to age-matched normal subjects.
- A mathematical formula producing a logistic regression curve can show the probability that an ulnar sensory amplitude is part of a neuropathy or not.

Acronyms

NCS: nerve conduction studies; SD: standard deviation; SNAP: sensory nerve action potential; SNCV: sensory nerve conduction velocity; MDSL: median distal sensory latency; MSA: median sensory amplitude; MSCV: median sensory conduction velocity; UDSL: ulnar distal sensory latency; USA: ulnar sensory amplitude; USCV: ulnar sensory conduction velocity; SDL: sural distal latency; SA: sural amplitude; SCV: sural conduction velocity; HC: health controls; NP: polyneuropathy; μV: microvolts; mv: millivolt; m/s: meter/second

Introduction

A polyneuropathy (NP) is a disease of the peripheral nerves that is diagnosed primarily in the clinical setting, and then confirmed by electrophysiological studies. NCS and EMG confirm the disorder and characterize the type and degree of the pathological process.

The variables retrieved from a NCS have to be compared to each other and to the normal population to allow the electrophysiologist to define the abnormalities in the peripheral nerves [1-7].

The sural nerve is usually the first neve to be affected in a sensorimotor NP. It is sometimes difficult to decide if the values retrieved for this nerve are normal or abnormal, because the literature presents a wide range of normal values, and does not show the numbers for the very elderly [1-9].

We performed a prospective study on normal people from the 3rd to the 8th decade. We studied the sensory nerve characteristics of the median, ulnar and sural nerves, and followed them up over this extended period. We compared the values of the sural nerve to the median and ulnar sensory fibers in each individual.

We then created a formula integrating the normal values of the sural and ulnar nerves. This formula will allow us to define whether the nerves in this subject fall within the normal range for age or are abnormal.

We then collected the values of the sensory nerves in patients with the clinical and electrophysiological diagnoses of sensorimotor NP secondary to chronic diabetes mellitus and chemotherapy. We incorporated their numbers in the formula to prove the reliability of this mathematical equation in differentiating patients from normal individuals.

Material and Method

We interviewed, examined and performed nerve conduction studies on 75 healthy subjects (52% females, 48% males) with no medical illness and not on any medications. The subjects were chosen to be divided equally between the third and eighth decade, around 13subjects in each decade. The subjects were recruited from the staff, students, employees and their families, working in the medical center where the study was performed. All subjects consented to the study. They were interviewed and examined by the corresponding author to ascertain that they were healthy and had a normal neurologic examination. They underwent sensory nerve conduction studies of the median, ulnar and sural nerves on one side. The nerve conduction studies were performed by a senior neurophysiology technician under

the supervision of the corresponding author.

The sensory nerve conduction studies were performed on a Nicholet Viking IV EMG machine. The subjects, healthy controls (HC) were in the sitting position with the hands resting on a pillow for the median and ulnar nerves and prone for the sural nerve. Skin temperature over the hand and lateral aspect of the foot were maintained at 32 degrees Celsius. The low and high frequency filter settings were 10 Hz and 5 kHz respectively. Median sensory nerve conduction studies were performed antidromically with stimulation of the median nerve at the mid-wrist, 17 cm from the recording surface electrodes place over the index finger, with the reference 2.5 cm distally. The ulnar nerve was stimulated at the lateral aspect of the wrist, 13 cm from the recording electrodes placed at the fifth digit. The sural nerve conduction studies were performed antidromically with stimulation at the mid-calf region between the two heads of the gastrocnemius muscles and recording by surface electrodes 14 cm distally placed over the posterior lateral malleolus. Stimulus intensity was increased until the best supramaximal SNAP was recorded. This was averaged several times until the response was clear enough for accurate recording. For each SNAP the distal sensory latency was measured from the stimulus artifact to the onset of the first negative peak. . The amplitude was measured from the baseline to the negative peak. The conduction velocity was calculated by dividing the distance over the latency [4-12].

Statistical Analysis

Means and standard deviation were calculated for each variable for each nerve using the SSPM statistical software. All group comparisons were done using Wilcoxon rank sum tests ($p < .05$ corrected for multiple comparisons). To determine whether USA can be used to identify a NP patient from a healthy control, a generalized linear model was built with USA as the predictor and group (HC, NP) as the outcome variable. To determine whether USA values can be used to categorize a patient as having neuropathy or as healthy, a logistic regression was built with USA as the predictor and group (HC, NP) as the outcome variable. The test was done on the entire dataset. The logistic regression equation can be used to predict suspected patients' group belongingness given their USA. This can be used clinically to categorize suspected patients as having neuropathy or not.

Results

The first aim of the study is to establish the average SNAP properties (distal sensory latency, amplitude and velocity) for the three nerves (median, ulnar and sural) for each decade. Means and SD for each decade were calculated (Table 1). This will reveal the changes of the variables for each nerve with increasing age.

Means and SD for the HC sample was divided into two groups: aged 20 to 49 (younger) and aged 50 to 80 (older) (Table 2). Wilcoxon tests of significance were used to calculate differences between the younger and older on all variables ($p < .05$ corrected for multiple comparisons).

The second aim of the study was to determine whether the following proportions can be used to determine group belongingness: SDL/MDSL, SDL/UDSL, SA/MSA, SA/USA, SCV/MSCV, SCV/UCV. These were calculated for each subject. This will reveal the changes of the sural nerve in comparison to the median and ulnar nerves with increasing age. The value of this comparison is to show how these nerves relate to each other in normal aging.

The third aim of the study is to confirm that this relationship between the sural nerve variables in comparison to the median and ulnar nerves, changes in neuropathies. This was done by comparing the results of the 40 HC aged 50 – 80 (older HC) with 30 patients, in the same age group, with the clinical and electrophysiological diagnosis of sensorimotor NP. These patients were collected from the cohort of patients referred to the neurophysiology laboratory with the clinical diagnosis of sensorimotor polyneuropathy secondary to chronic diabetes mellitus or chemotherapy-induced neuropathy. Their NCS diagnosed a sensorimotor NP. (Table 3)

Results show that across the median nerve, there was a significant difference in all properties between the younger and older healthy controls, with the older group showing increased latency, reduced amplitude and conduction velocity ($p < .005$) (figures 1,2,3). Across the ulnar and sural nerves only the amplitude was significantly different, with the older group showing reduced amplitudes ($p < .005$)

(figure 4,5)

Qualitative analysis of the data revealed that the small SA/USA values were due to small USA values rather than high SA values. Therefore, USA values were used to predict group belongingness (whether a patient is more likely to have neuropathy or is healthy).

Since the sural/ulnar amplitude calculations gave the smallest proportions (greater difference between sural and ulnar values), the study was continued using only sural/ulnar proportions (table 4). Since there is no difference in the results of the older HC and the whole group of HC, the remaining calculations were done on the whole HC group. As can be seen in Table 4, SA/USA values are less than 1. To determine whether SA/USA values differed between HC and NP, the proportions were compared. Wilcoxon test revealed a significant difference in SA/USA proportion between healthy controls and NP, W = 737, p=0.008, with the NP revealing a smaller proportion (0.4) compared to the HC group (0.51). Although statistically there was a significant difference in the SA/USA proportion between HC and NP, the range of values was large for both groups (i.e., a lot of overlap) (figure 6). This indicates that the SA/USA value might not be helpful in identifying a potential neuropathy patient.

For this reason, we built a logistic regression model with USA as the predictor and group belongingness (HC, NP) as the outcome variable. The test was done on the entire dataset.

Results of the logistic regression were statistically significant, z = -4.85, p < .0001, which indicates that USA significantly predicts group belongingness. The probability of being a NP given a certain USA value can be extracted from the model. The logistic regression model can be represented as follows:

logit (p) = 4.5521 – 0.2042*USA

4.5521 is the intercept (beta0) of the model.

-0.2042 is the estimate (beta1)

After logit (p) is calculated, one refers to the probability table (table 5) to determine (p) which is the probability that the subject suffers from a polyneuropathy (multiply by 100 to get the percentage). The logistic regression curve (Figure 7) represents the probability of having a NP given a certain USA value.

Table 1: Sensory nerve conduction values for median, ulnar and sural nerves in healthy controls across age latency (ms); amplitude (μV); velocity (m/s); age (years)

Mean (SD)									
	Median Nerve			Ulnar Nerve			Sural Nerve		
Age	latency	amplitude	velocity	latency	amplitude	velocity	latency	amplitude	velocity
20 - 29	2.75(0.4)	54.6	58.3	2.45	50.2	54.5	2.44	23.6	54.5
		-18	-5.44	-0.41	-22.4	-7.31	-0.37	-7.12	-9.52
30 - 39	2.48(0.25)	58.82	65.09	2.21	65.09	55.91	2.43	25.45	51.64
		-16.96	-5.7	-0.23	-21.3	-5.07	-0.31	-11.67	-7.53
40 - 49	2.63(0.35)	43.42	63.08	2.28	43.83	59.33	2.54	24.83	56.17
		-13.04	-8.9	-0.24	-14.08	-3.65	-0.38	-13.81	-7
50 - 59	2.68(0.26)	39.83	58.08	2.31	43.42	53.75	2.36	19.08	53.42
		-10.14	-5	-0.25	-10.7	-5.75	-0.38	-4.62	-6.84
60 - 69	2.88(0.34)	33	56.07	2.35	31.93	53.14	2.3	16.43	54.86
		-9.92	-8.55	-0.15	-8.2	-4.72	-0.42	-5.23	-5.53
70 - 80	2.89(0.22)	29.67	54.87	2.28	33.47	55.8	2.19	17.53	54.33
		-8.04	-3.7	-0.21	-8.98	-6.68	-0.29	-6.49	-5.67

One can also interpret the results in terms of odds ratios. Odds ratio = exponent (-0.2042) = 0.815, which shows that for a unit increase in USA the change in odds is (0.815 – 1)*100 = -18.5%. In other words for a unit increase in USA there is 18.5% decrease in the odds of being a NP. Looking at it the other way, for a unit decrease in USA, the odds of being a patient increases by a factor of 1/0.815 = 1.23 or 123%. The way fractional odds can be interpreted is the following (table 6): for every one HC with a USA of 4, you have 55 NP with this USA value, i.e., an individual is 55 times more likely to be a NP if he/she has a USA =4 (the odds of being a NP is 55:1). If an individual has a USA = 17, he is three times more likely to be a NP than a healthy control. The proportion of patients with neuropathy and healthy individuals is almost the same when the USA = 22.

Table 2: Sensory nerve conduction values for median, ulnar and sural nerves for younger (< 50 yrs) and older (≥ 50 yrs) healthy controls and difference between the groups (Wilcoxon significance test). * significant at p<.005 (5% error corrected for multiple comparisons)

Mean (SD)									
	Median			Ulnar			Sural		
Groups	latency	amplitude	velocity	latency	amplitude	velocity	latency	amplitude	velocity
younger	2.62	51.94 (16.89)	62.3 (7.32)	2.31 (0.31)	52.85 (20.86)	56.73 (5.65)	2.47 (0.35)	24.67 (11.09)	54.15 (7.99)
	-0.35								
older	2.82	33.78 (10.02)	56.22 (6.1)	2.31 (0.2)	35.85 (10.31)	54.29 (5.78)	2.28 (0.36)	17.61 (5.54)	54.24 (5.86)
	-0.29								
W (*p*)	393 (0.0019)*	1114.5 (<.0001)*	1021 (0.0002)*	606 (0.44)	1040 (<.0001)*	872.5 (0.033)	873.5 (0.0315	969.5 (0.0014)*	651.5 (0.789)

Table 3: Sensory Nerve Conduction Properties for median, ulnar and sural nerves in patients with Neuropathy and comparison to older HC (Wilcoxon significance test)

Mean (SD)									
Group	Median Nerve			Ulnar Nerve			Sural Nerve		
	Latency	Amplitude	Velocity	Latency	Amplitude	Velocity	Latency	Amplitude	Velocity
NP	3.5 (0.73)	15.6 (7.83	49.47 (8.33)	2.89 (0.59)	16.07 (8.9)	46.9 (7.75)	2.89 (0.46)	5.07 (1.93)	45.33 (6.17)
Older	2.82	33.78 (10.02)	56.22 (6.1)	2.31 (0.2)	35.85 (10.31)	54.29 (5.78)	2.28 (0.36)	17.61 (5.54)	54.24 (5.86)
HC	(0.29)								
W (*p*)	210.5**	1139**	910.5*	153**	1132.5**	967**	184.5**	1220**	1058**

Table 4: The mean proportion (standard deviation) of the sural vs ulnar and sural vs median sensory amplitudes in control subjects and neuropathy patients. SA: sural amplitude; USA: ulnar sensory amplitude; MSA: median sensory amplitude. HC: healthy control, NP: neuropathic. W (*p*): Wilcoxon rank sum test between HC whole group and NP and p-value.

	Mean Proportions (SD)	
	SA/USA	SA/MSA
HC (whole group)	0.51 (0.19)	0.53 (0.21)
HC (older)	0.51 (0.17)	0.56 (0.22)
NP	0.4 (0.23)	0.45 (0.33)
W (*p*)	1483 (< .05)	1494 (< .05)

Table 5: Example of logit(probability), probability of neuropathic patient (NP), and odds of NP given certain ulnar sensory amplitude (USA) values.

USA	Logit (p)	p(NP) and CI	Odds (NP)
4	3.7353	0.98 [0.88-0.99]	54.56 (or 1/55)*
8	2.9185	0.95 [0.80-0.99]	25.32 (or 1/25)
10	2.5101	0.92 [0.77-0.98]	11.5
17	1.0807	0.75 [0.55-0.88]	3
22	0.0597	0.52 [0.35-0.68]	≈ 1
24	-0.3487	0.41 [0.27-0.58]	0.69

Table 6: Comparing USA and SA and SA/USA in older healthy control and neuropathy patients. Values in red/bold are those that do not satisfy the first criteria of neuropathy (SA/USA < 50%). For these cases log value was calculated. The resulting probability corrected the uncertainty in favor of the correct diagnosis

50 - 60 years									
Healthy controls					Neuropathy patients				
USA	SA	SA/USA%	log	prob	USA	SA	SA/USA%	log	prob
35	13	37	-2.595	7%	39	4	10		
40	28	70			24	11	46		
48	26	54			9	5	56	2.71	94%
48	22	46			13	5	38		
38	22	58			27	4	15		
54	17	32	-6.478	< 1 %	4	4	100	3.74	97.00%
52	18	35	-6.068	< 1 %	9	6	67	2.714	94%
34	18	53	-6.69	< 1 %	21	4	19		
55	17	31	-6.679	< 1 %	19	6	32		
57	15	26	-7.088	< 1 %	19	5	26		
70 - 80 years									
49	34	69			10	9	90	2.5101	92.5
33	29	88			9	6	67	2.713	94
38	17	45			11	9	82	2.3	91
30	17	57			32	5	16		
17	10	59			33	7	21		
37	17	46			24	5	21		
17	10	59			8	5	63	2.92	95
46	14	30	-4.85	< 1%	10	4	40		
34	14	41	-2.39	<8.5%	11	3	27		
34	18	53			26	5	19		

Table 7: log (probability) to probability conversion table.

p	logit(p)	p	logit(p)	p	logit(p)	p	logit(p)
0.01	-4.5951	**0.26**	-1.0460	**0.51**	0.0400	**0.76**	1.1527
0.02	-3.8918	**0.27**	-0.9946	**0.52**	0.0800	**0.77**	1.2083
0.03	-3.4761	**0.28**	-0.9445	**0.53**	0.1201	**0.78**	1.2657
0.04	-3.1781	**0.29**	-0.8954	**0.54**	0.1603	**0.79**	1.3249
0.05	-2.9444	**0.30**	-0.8473	**0.55**	0.2007	**0.80**	1.3863
0.06	-2.7515	**0.31**	-0.8001	**0.56**	0.2412	**0.81**	1.4500
0.07	-2.5867	**0.32**	-0.7538	**0.57**	0.2819	**0.82**	1.5163
0.08	-2.4423	**0.33**	-0.7082	**0.58**	0.3228	**0.83**	1.5856
0.09	-2.3136	**0.34**	-0.6633	**0.59**	0.3640	**0.84**	1.6582
0.10	-2.1972	**0.35**	-0.6190	**0.60**	0.4055	**0.85**	1.7346
0.11	-2.0907	**0.36**	-0.5754	**0.61**	0.4473	**0.86**	1.8153
0.12	-1.9924	**0.37**	-0.5322	**0.62**	0.4895	**0.87**	1.9010
0.13	-1.9010	**0.38**	-0.4895	**0.63**	0.5322	**0.88**	1.9924
0.14	-1.8153	**0.39**	-0.4473	**0.64**	0.5754	**0.89**	2.0907
0.15	-1.7346	**0.40**	-0.4055	**0.65**	0.6190	**0.90**	2.1972
0.16	-1.6582	**0.41**	-0.3640	**0.66**	0.6633	**0.91**	2.3136
0.17	-1.5856	**0.42**	-0.3228	**0.67**	0.7082	**0.92**	2.4423
0.18	-1.5163	**0.43**	-0.2819	**0.68**	0.7538	**0.93**	2.5867
0.19	-1.4500	**0.44**	-0.2412	**0.69**	0.8001	**0.94**	2.7515
0.20	-1.3863	**0.45**	-0.2007	**0.70**	0.8473	**0.95**	2.9444
0.21	-1.3249	**0.46**	-0.1603	**0.71**	0.8954	**0.96**	3.1781
0.22	-1.2657	**0.47**	-0.1201	**0.72**	0.9445	**0.97**	3.4761
0.23	-1.2083	**0.48**	-0.0800	**0.73**	0.9946	**0.98**	3.8918
0.24	-1.1527	**0.49**	-0.0400	**0.74**	1.0460	**0.99**	4.5951
0.25	-1.0986	**0.50**	0.0000	**0.75**	1.0986		

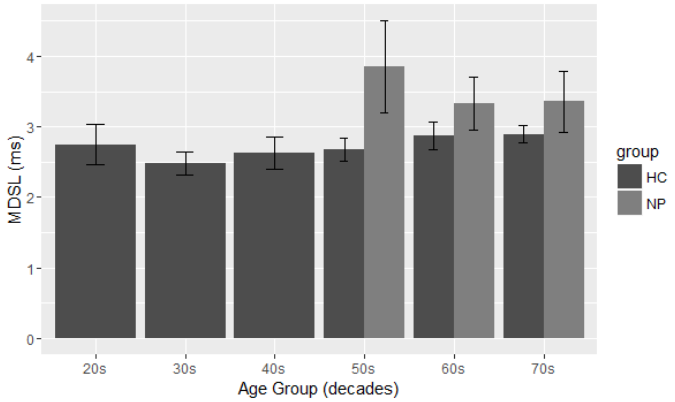

Figure 1: Bar graph showing the mean and standard deviation values of the median distal sensory latencies (milliseconds) for the healthy controls and patients with polyneuropathy across the different age categories.

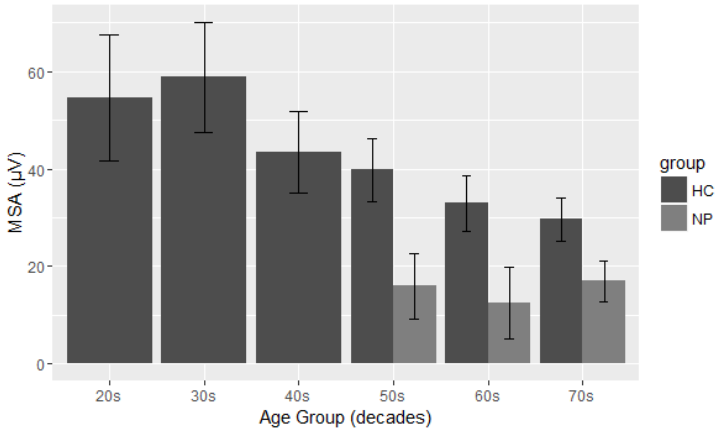

Figure 2: Bar graph showing the mean and standard deviation values of the median sensory amplitudes (μV) for the healthy controls and patients with polyneuropathy across the different age categories.

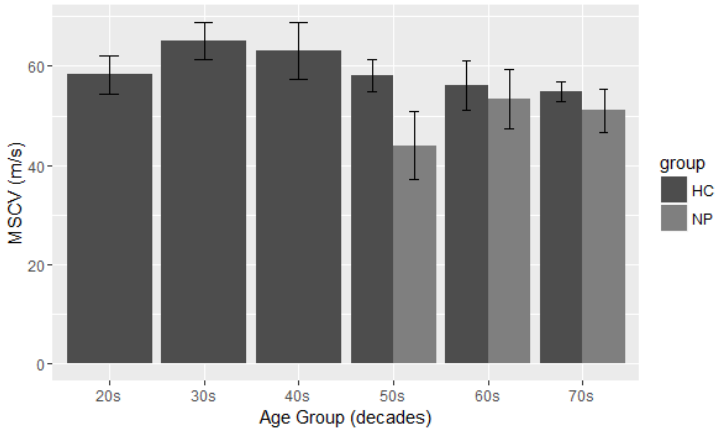

Figure 3: Bar graph showing the mean and standard deviation values of the median sensory conduction velocities (meters/second) for the healthy controls and patients with polyneuropathy across the different age categories.

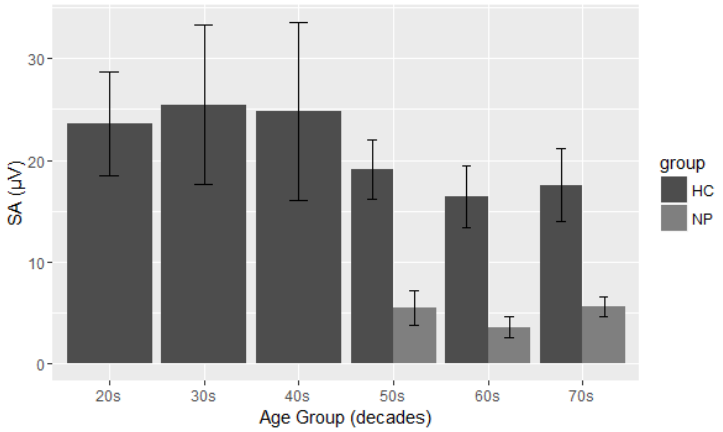

Figure 4: Bar graph showing the mean and standard deviation values of the sural amplitude (µV) for the healthy controls and patients with polyneuropathy across the different age categories.

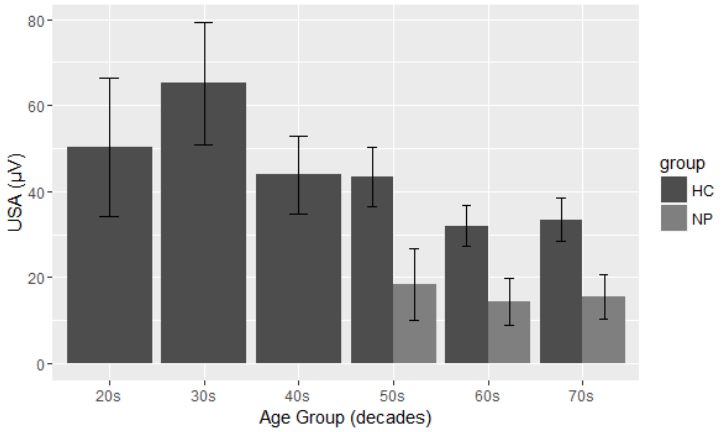

Figure 5: Bar graph showing the mean and standard deviation values of the ulnar sensory amplitude (µV) for the healthy controls and patients with polyneuropathy across the different age categories.

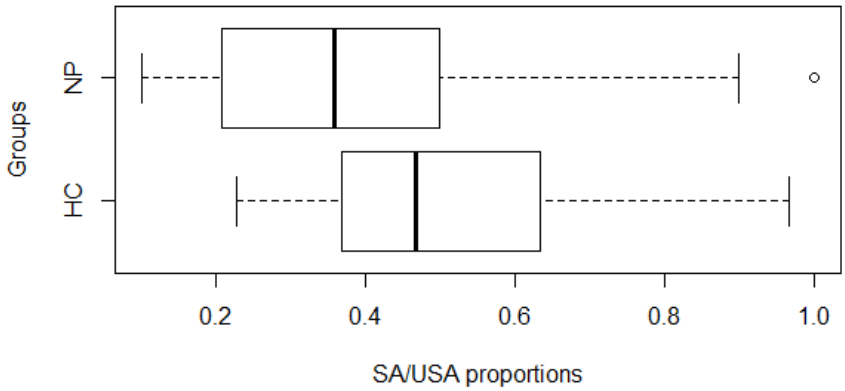

Figure 6: Bar graph comparing the mean and standard deviation values of the sural amplitude / ulnar sensory amplitude between the healthy controls and patients with neuropathy.

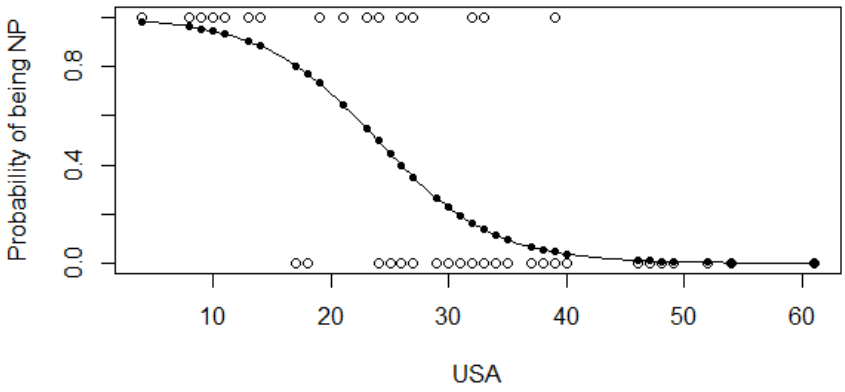

Figure 7: Logistic regression curve representing the probability of having a neuropathy (y-axis) given a certain ulnar sensory amplitude value (x-axis in μV). Probability ranges between 0 and 1. The white dots represent the actual data in our sample. The black dots are different points on the curve that connect the USA values to the probability of having a neuropathy.

Discussion

NP is a common neurological disorder with a prevalence of 2.4% in the general population and increases gradually with increasing age [2, 11, 13].

The neuropathy is usually diagnosed after taking a history and performing a physical examination, which reveals decreased sensation distally and depressed or absent deep tendon reflexes. NCS are important not only to confirm the suspected diagnosis of a neuropathy, but also to define the type of fiber involvement, whether the neuropathy is demyelinating, axonal or mixed, the degree of pathology, as well as the presence or absence of re-innervation. [1, 2, 6-9, 12].

We performed a prospective study on normal people from the 3rd to the 8th decade. NCS produce numbers for each variable (latency, amplitude, or velocity) for each nerve studied. Pathology is defined when these numbers fall outside the normal ranges. Normal ranges are defined by means and standard deviations of the corresponding nerve

in the normal population. [1-7].

The impact of age on sensory NCS has been extensively studied in the literature. A linear decrease in SNCV with age in the order of 0.14 m/s/year or 1.8 m/s/decade has been reported. [2, 13, 14]. The change occurs at a greater rate in the median than in the ulnar sensory nerve parameters. This was interpreted secondary to an increased susceptibility of the median nerve to repetitive motion trauma or increased intra-carpal canal pressure with different wrist postures [11].

The mean and SD for the DSL, SA, and SCV for the median, ulnar, and sural nerves in our sample was very similar to the textbooks used as references in most clinical neurophysiology laboratories worldwide (table 1).

Stratifying our sample over the different age groups and separating the young (less than 50 years) from the older (above 50 years) revealed that for the median nerve, the older group showed increased latency, reduced amplitude and reduced velocity (figure 1,2,3). For the ulnar and sural nerves only the amplitude was significantly different, with the older group showing reduced amplitude (figure 4,5).

The neuropathy cohort in our study showed an increase in the DSL, a decrease in the SA and SCV, for the median, ulnar and sural nerves when compared with the age--matched older HC. This is in accordance with the results described in the literature.

The sural nerve conduction parameters are the most useful in diagnosing neuropathies. The classical clinical neurophysiology textbooks define a normal sural amplitude > 6 μV, conduction velocity > 40 m/sec and distal latency < 4.4 msec. [4]. Other references state that the sural amplitude can vary between 6.3 and 23.7 μV, sural latency between 1.46 and 3.7 msec and sural conduction velocity between 33.9 and 52.5 m/sec [5].

The sural nerve conduction parameters studied in 92 normal controls aged 15 – 45 years showed a SCV of 53 (+0.3) m/s, and SA of 30 (+0.3) μV. [14]. Some authors claim that the sural sensory response is most vulnerable to aging, being absent in 23% of normals in the 6th decade and 40% above the age of 80 years [13]. Other studies claim that there is always a sural response, even if of low amplitude, in the normal aging population [3].

Many laboratories state that the lower limit of normal for the sural amplitude is 6 μV, while others found that the lower limit for younger subjects was much higher than that, and the lower limit for subjects above 60 years was as low as 3.2 μV volts. [1-7, 10] The variability in values considered "normal" for the sural nerve especially in the elderly, makes it difficult to choose a single cut-off value to differentiate normal from NP. Values presented in the literature can therefore be unreliable and their use subject to false negative results [2-7, 10, 13].

References claim that a normal MSA should be above 20 μV and a normal SA amplitude above 6 μV. [1-7, 10].

This means that a person with the NCS showing these values is considered to be normal. On the other hand, one sees exactly these numbers in patients with the history and examination compatible with a sensory neuropathy, as in patients suffering from diabetic polyneuropathy. This raises the issue that one cannot take these cut-off values in absolute terms or else one may end up with a false negative diagnosis.

In a study of the peripheral nerves in patients with diabetes mellitus type I, the authors define abnormality in the sural amplitude or conduction velocity if the values were below the third percentile of the control. The sural nerve in their normal cohort had an amplitude of 20.8 (9.02) μV and the conduction velocity was 55.16 (6.8) m/s. [8].

Another study, also studying the NP of diabetes mellitus, showed quite different values for their normal cohort. They took the sural distal latency of 2.32 (0.72) and 2.50 (0.64) msec, a sural amplitude of 14.35 (4.81) and 14.96 (5.86) μV and a conduction velocity of 73.54 (20.47) and 76.37 (23.18) m/s [9].

Considering this wide variability in the normal values of the sural nerve, it may be better to define a NP based on a comparison of the sural nerve parameters to the me-

dian, ulnar or radial nerve. This correlation favors the principle that neuropathies affect predominantly the length-dependent nerves.

The sural SNAP amplitude is the most sensitive parameter in detecting a NP [9]. Some authors studied the ratio of the sural/radial sensory amplitude (SRAS). This ratio appears to define a neuropathy more reliably than the sural SA alone [3]. In their study of this ratio in normal individuals they found that, the SA in μV ranged from 10.4 – 67.3 in those < 40 years, 4.3 – 50.2 μV in subjects between 40 and 60 years, and 2.1 – 28 μV in those above 60 years. An SRAR above 0.4 was considered normal, while a value < 0.4 was associated with a mild NP. The SRAR may be a better electrodiagnostic parameter that the sural SNAP in diagnosing mild and early neuropathies, as it is an age-independent ratio [3].

Upon studying the values of the NCS in patients with NP, one can sometimes encounter relatively similar numbers in the nerves of the upper and lower extremities. For example, in moderate NP, the sensory amplitudes in the median and ulnar nerves may be low and the sural amplitudes slightly lower, but not in the same proportion as in the normal population. This makes the classical definition of length-dependent abnormality less applicable. To better understand this picture, we compared the values of the sural nerve to the median and ulnar nerves in HC and NP patients and established proportions. The only proportions that did not approximate a value of 1 was SA/USA and SA/MSA. Results showed that the proportion of SA to MSA or USA is around 50% in the HC over all the decades, and around 40% in NP (table 4). This indicates that if the SA/USA is less than 50% then this subject most probably suffers from a polyneuropathy. We found, however, that a few NP patients did not show a small proportion but actually had SA/USA values > 50%. Therefore, although this proportion is informative, it could inaccurately categorize a neuropathic patient as a healthy individual (false negative). Looking more closely at those NP cases that had large SA/USA values, we detected very small USA values. The reason for the much lower USA is that the neuropathy had affected also the sensory nerves of the upper extremities (table 7).

For this reason, a two-step process is suggested to help the neurophysiologist when the diagnosis is uncertain because the numbers are not diagnostic for a NP. If the SA/USA is less than 50% then the subject has a NP. If this ratio is larger than 50%, but the clinical picture favors a NP and the electrophysiologist needs further reassurance, then the logarithmic formula using the USA can be applied: logit (p) = 4.5521 – 0.2042*USA to estimate the probability that the patient in question suffers from a neuropathy. After logit(p) is calculated, one can refer to the probability conversion table (table 5) to determine the probability (multiplied by 100 to get the percentage) of having a NP.

For example, if a patient with a USA of 16 is suspected of having a polyneuropathy, using the equation above, the electrophysiologist calculates the probability that this patient has a NP: logit (p) = 4.5221 – 0.2042*16 = 1.2851. By locating 1.2851 (or an approximate value) in table 5, the probability of NP can be found. In this example, the probability that a patient with a USA of 16 having a NP is approximately 0.78 or 78%.

In principle, one should thus calculate SA/USA and the probability of NP using the logarithmic formula for every patient presenting for NCS with the suspicion of a polyneuropathy. Combining these tests will give a more accurate probability for the diagnosis of a neuropathy (table 7).

Using the above formula and conversion table, a neurophysiologist can predict the likelihood of a patient having a neuropathy more accurately than comparing absolute numbers of age-matched controls, or referring only to cut-off values (figure 7).

In conclusion, sensory amplitudes of the median, ulnar and sural nerves decrease with increasing age. In some neuropathies the sensory amplitudes may still fall within the normal limits described in the literature, because of the wide range of values in the normal population. A more accurate electrophysiological definition of a neuropathy will be comparing the sural to ulnar amplitudes, followed by an estimate of probability derived from a logistic regression equation with USA as the predictor.

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