

Research Article

Sural nerve conduction study: Reference values in the Algerian population

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Keywords: SNAP; Reference values; Sural nerve; Percentile; Algerian population



Abstract

Objectives: The sural nerve is the most tested sensory nerve in the lower extremities in the electrodiagnostic assessment of peripheral neuropathies. This study presents the reference values of the sural nerve conduction study (NCS) from a significant sample of the Algerian population.

Methods: This is a prospective study of right sural NCS in healthy subjects based on the later recommendations of AANEM-NDTF. The nature of the distribution of each electrophysiological parameter was therefore determined. The lower and upper limits were calculated by using the 5th and 95th percentiles respectively and a logarithmic transformation was performed for Sensory Nerve Action Potential (SNAP) amplitude distribution.

Results: 115 subjects aged between 20 and 60 years were selected, including 58 women and 57 men. Unlike Sensory Nerve Conduction Velocity (SNCV), the distribution of SNAP amplitude is not Gaussian. The lower limit of SNAP amplitude was 7.70 μ V when using the 5th percentile and 6.80 μ V by using the Standard Deviation (SD) method after log transformation. Similarly, the lower limit of SNCV was 43 m/s. The SNAP amplitude was greater in women and decreased with age, height and BMI.

Conclusion: The values found in this study are comparable to those published in the literature. It may be more appropriate to determine the reference values using percentiles as recently recommended by several authors.

Introduction

The sensory nerve conduction study occupies an important place in the diagnosis of peripheral neuropathies [1,2]. The sural nerve is the most tested sensory nerve because of its accessibility [3]. Indeed, reduction of its amplitude is an early and sensitive indicator for length-dependent distal axonal polyneuropathies [1,4]. However, the interpretation of results in patients is sometimes difficult, due to the proposed reference values, which are often reported from small samples [5] and the unequal gender distribution. In addition, most of these studies determine their reference values using the classical method (mean \pm 02 Standard Deviations (SD)), overlooking the nature of statistical distribution (Gaussian or not) of the electrophysiological parameters, which could be a source of error when determining the reference values [6,7]. Finally, some of these studies seem to have overlooked age, sex, and anthropometric factors such as height and BMI (Body Mass Index) as important confounding factors. Therefore, we

would suggest that each neurophysiological laboratory needs access to its reference values for more accurate evaluation [3,8].

The objective of this study was to determine the reference values of the electrophysiological parameters of the sural nerve in the Algerian population.

Materials and methods

Subjects

This prospective study was carried out in the Neuromuscular Laboratory of Ben Aknoun Hospital (Algiers, Algeria). It included 115 healthy volunteers of either gender, aged between 20 and 60 years. The exploratory protocol was clearly explained, and written consent was obtained for each subject as per local ethical committee regulations in accordance with the declaration of Helsinki as a statement of ethical principles for medical research involving human subjects. A questionnaire was used to exclude patients with

symptoms suggestive of central or peripheral nervous system pathology. Subjects with pathologies known to affect the peripheral nervous system such as diabetes mellitus, renal failure, hereditary neuropathies, mixed connective tissue diseases, or those on neurotoxic therapies were excluded.

Methods

The subject was laid on the examination bed. The lower limbs were warmed up with water and the skin temperature was maintained above 30 °C throughout the duration of the test, and controlled by a thermal probe placed on the dorsal part of the foot. (YSI 409JNIKKISO-THERM CO., LTD. Japan).

An electroneuromyography machine (Nihon Kohden Japan MEB-9200k, 2007) was used with a bandwidth between 2 Hz and 10 kHz, sensitivity was 20 μ V per division and the sweep speed was 2 ms per division. The duration of the electrical shock was 0.1 ms with a stimulation frequency of 1 Hz. The antidromic sensory potential of the sural nerve was recorded on the right and the left leg at the posterior mid-calf using surface electrodes. The active electrode was placed just behind the external malleolus and the reference at 3 cm distally. The distance between the stimulation cathode and the active recording electrode was 12 cm as used in numerous studies [1,8-11]. At least 10 responses (between 10 and 30) were averaged.

Latency was measured at the onset (Lo) and at the negative peak (Lp) of the potential.

The SNAP (sensory nerve action potential) amplitude was determined between the onset and the negative peak of the potential and the duration measured from the onset of the negative peak to the return of the potential to the baseline.

Statistical analysis

First, the distribution of each electrophysiological parameter was analyzed to determine whether its distribution was Gaussian (normal) or not. For this purpose, the Kolmogorov-Smirnov (KS) test was used, and the distribution was considered Gaussian if the “*p* - value” was equal, to or greater than 0.05. In cases where the KS test was inconclusive, i.e. *p* - value was less than 0.05, visual analysis of histograms and QQ plot nomograms were performed to confirm normal distribution [12-14].

Secondly, as suggested by several authors [6,7,15,16] when the distribution was not Gaussian, especially for the SNAP amplitudes, a logarithmic transformation was performed in order to bring it closer to a Gaussian distribution.

Thirdly, the upper and lower limits of the reference values were calculated according to the percentiles method (95th and 5th percentile respectively) as done in several studies [5,8,10,16] and the lower limit of the SNAP amplitude was determined as the mean - 2SD after logarithmic transformation.

Finally, correlations of SNAP amplitudes and SNCV with age, sex and BMI were analyzed. For sex, the statistical significance of the difference between men and women was estimated using the Student’s test for the SNCV (Gaussian distribution) and the Mann-Whitney - Wilcoxon test for the SNAP amplitudes (non-Gaussian distribution) [17].

For age and BMI, Pearson’s and Spearman’s correlation tests were used for SNCV (Gaussian distribution) and SNAP amplitudes (non-Gaussian distribution), respectively [18,19].

Results

Out of 152 volunteers, 115 subjects aged between 20 to 60 years old were selected, including 58 women. Table 1 summarize age and anthropometric factors.

There was no significant difference between men and women in age and BMI (Table 1), the population was subdivided into 4 age groups and the number of subjects per decade was roughly equivalent (Table 2).

For the characteristics of the sural SNAP:

After statistical analysis, the latencies and the SNCV had a Gaussian distribution, while the SNAP amplitude and the duration had a non-Gaussian distribution. Because the value of the standard deviation is low, the duration distribution was considered normal.

After the logarithmic transformation of the SNAP amplitude, the distribution became Gaussian.

The mean and the standard deviation with the minimum and maximum value found in our sample as well as the lower limit calculated by different methods (m -2 SD, 5th percentile, and m -2 SD after log transformation) of latencies, duration, SNCV and amplitude are shown in Table 3. For latencies, duration, and SNCV, no clear difference between the lower or upper limit was observed regardless of the statistical method used.

Table 1: Age and anthropometric factors.

Variable	mean (SD)	<i>p</i> - value
Age (years) M (n = 57)	40.17 (11.17)	0.54
F (n = 58)	40.13 (11.40)	
Height (m) M (n = 57)	1.75 (0.061)	< 0.0001
F (n = 57)	1.60 (0.057)	
weight(Kg) M (n = 57)	81.09 (15.35)	< 0.0001
F (n = 57)	67.60 (12.30)	
BMI M (n = 57)	26.19 (4.64)	0.85
F (n = 57)	26.34 (4.61)	

M: Male; F: Female; SD: Standard Deviation
*in one woman, height and weight were not taken.

Table 2: Age groups.

Age groups (y)	mean (SD)
20-30 (n = 29)	25.31 (3.09)
31-40 (n = 26)	35.65 (2.61)
41-50 (n = 32)	44.50 (2.85)
51-60 (n = 28)	54.71 (2.80)

n: number of subjects; SD: Standard Deviation

Table 3: Reference values for the latencies, duration, SNCV, and amplitude using different methods.

Parameter	m ± SD (Min-Max)	Lower or upper limit.		
		m ± 2SD [*]	Percentile ^{**}	m - 2SD after log transformation
Onset latency (ms)	2.42 ± 0.19 (1.98 - 2.92)	2.8	2.74	
Pic latency (ms)	3.10 ± 0.24 (2.50 - 3.86)	3.58	3.48	
Duration (ms)	1.27 ± 0.20 (0.93 - 2.09)	1.67	1.63	
SNCV (m/s)	49.97 ± 4.16 (41 - 61)	41.65	43.80	
Amplitude (µV)	17.34 ± 7.55 (6.80 - 45.50)	2.24	7.70	6.80

^{*}: m -2DS for the lower limit, m+2DS for the upper limit if the distribution was normal.
^{**}: 5th for the lower limit (SNCV, Amplitude), 95th percentile for the upper limit (Lo, Lp, D).

However, for the amplitude, we note that the lower limit calculated by the classical method (mean-2SD) is far from the value calculated by the other methods (5th percentile and mean-2SD after log transformation) and is significantly lower than the minimum value found in our population.

A significant correlation of SNAP amplitude with age ($p = 0.002$), height ($p < 0.001$) and BMI ($p = 0.02$) was observed. The SNAP amplitudes were greater in women ($p = 0.0004$), and the SNAP amplitude decreased with age, height, and BMI. For the SNCV, a significant correlation ($p = 0.008$) was only noted with height.

Discussion

This is the first study conducted in North Africa and more specifically Algeria which reports the normative values for the sensory potential of the sural nerve in healthy adults. We have applied the recently proposed methods [5], with a recommended cohort of more than 100 healthy participants [5,7,20] and with the equal male-female distribution. The different age groups were appropriately represented.

Technical Standard protocols were used and cutaneous temperatures were always above 30 °C [5]. Clear exclusion criteria were applied to detect patients with potential peripheral or central nervous systems pathology. Subjects with diseases or therapeutics known to affect the nervous system were also excluded [20,21].

We paid particular attention to our statistical analysis. The distribution of the various parameters was determined in order to choose the appropriate statistical test [7,16,22-24]. When the distribution was Gaussian, parametric tests were applied, and limit values were calculated from the mean ± 2 SD [7]. However, the SNAP amplitude distribution was not Gaussian and the parametric tests were not used. Therefore, a logarithmic transformation of the raw data was carried out. The distribution of the obtained data became almost normal and the parametric tests were then used on the new data which allowed the calculation of the mean and standard deviation as well as the lower limit (mean -2 SD) [6,7,15,16]. We then converted the results to the original unit.

In the present study, the upper and lower limits were also determined from the 5th and 95th percentiles, respectively. This method is applicable whether the distribution is Gaussian or not, provided the sample size is greater than 100 and seems to have the support of the majority of authors [5,8,10,16]. Recently Robinson [24] suggested that it is time to abandon the classical method (mean ± 2DS) and instead use the percentiles to determine the reference values.

As summarized in Table 4, in the present study, the mean SNAP amplitude was similar to that reported by several authors [8,25-28]. However, it differs from the value of Owolabi, et al. [29] and Elmagzoub, et al. [30]. Several factors such as the distance between stimulation and active recording electrode used (a large distance favoring the temporal dispersion resulting in a decrease in amplitude) or the difference in age groups could potentially explain this difference.

For the SNCV, the values of the present study were comparable to those of Stetson, et al. [25], Benatar, et al. [8], Kokotis, et al. [27] and Shahabuddin, et al. [28].

The present study also determined the reference values of the duration of the sensory potential of the sural nerve. The analysis of this parameter could be an additional useful element in the diagnosis of inflammatory polyneuropathies

Table 4: Comparison between the results of the present study and those reported in the literature.

Study	Onset latency(ms)	SNCV (m/s)	Amplitude (µV)
	mean ±SD Upper limit Max - Min	mean ±SD Lower limit Max - Min	mean ±SD Lower limit Max - Min
Present study [*] (n = 115) d = 12 cm	2.42 ± 0.19 2.74 1.98 - 2.92	49.97 ± 4.16 43.80 41 - 61	17.34 ± 7.55 7.70 6.80 - 45.5
Stetson, et al. (1992) (USA)(n = 105) d = 14 cm	3.4 ± 0.3 --- 2.9 - 4.9	52.2 ± 5.3 --- 36 - 64	17.5 ± 7.7 --- 6 - 48
Buschbacher (2003) † (USA) (n = 230) d = 14 cm	3.1 ± 0.3 3.6 2.2 - 3.9	--- --- ---	17 ± 10 4 2 - 56
Benatar, et al. (2009) (USA) (n = 190) D = 12 cm	--- --- ---	47.0 ± 4.6 --- 35.8 - 62.0	17.2 ± 10.1 --- 1.7 - 67.3
Kokotis, et al. (2010) (Greece)(n = 158) d = 13 cm	2.6 ± 0.31 --- 1.88 - 3.72	50.73 ± 4.97 --- 40.3 - 67.5	19.9 ± 6.89 --- 9.2 - 54
Luigetti, et al. (2012) (Italy) (n = 538) d = 12 cm	--- --- ---	53.28 ± 5.35 --- 41 - 67	23.48 ± 9.36 --- 3 - 60
Shahabuddin, et al. (2013) (India) (n = 90) d : 14 cm	2.51 ± 0.54 --- 1.2 - 3.6	50.42 ± 3.70 --- 42 - 56	15.70 ± 2.85 --- 9 - 21.2
Owolabi, et al. (2015) † (Nigeria) (n = 200) d = 10-18 cm	3.07 ± 0.68 4.52 ---	54.23 ± 4.36 45.67 ---	9.6 ± 2.6 4.8 ---
Shivji, et al. (2019) [*] (Pakistan) (n = 100) d = 14 cm	2.4 ± 0.30 3 ---	57.4 ± 6.3 44 ---	22.5 ± 8.8 12 ---
Elmagzoub, et al. (2021) (Soudan) (n = 105) d = 10-15 cm	2.734 ± 0.4964 --- 1.7 - 3.8	52.05 ± 8.468 --- 37 - 82	8.39 ± 3.496 --- 3 - 21

^{*}: 5th et 95th percentile, †: 3rd et 97th percentile, ‡: 2.5th et 97.5th percentile

[§]: the lower limit in subjects under 60 years of age is 6.6µV. ^{||}: peak-to-peak amplitude

n: Number of subjects, d: distance between stimulation and active recording electrode



[31] even if the currently used criteria [32] do not mention this parameter. In the majority of studies, abnormalities involving the sensory fibers were not taken into account in the electrophysiological criteria of CIDP [33]. It is interesting to note that Rajaballi and Samarasekera [31] showed that in CIDP the increase in the duration of the distal sensory potentials for the median and sural nerves could be an additional criterion of distal demyelination.

The present study found a strongly significant negative correlation of the SNAP amplitude of the sensory potential nerve with age. This is similar to the results of the majority of previous studies [1,8,10,25,34,35]. The reduction of SNAP amplitude with age has been explained by a reduction in the number of nerve fibers and a reduction in the diameter and membrane changes of the nerve fibers with age [36-39].

No correlation was observed between SNCV and age, this result is, similar to those reported by several authors [1,8,25,34,35,40]. Furthermore, no significant difference between the two sexes was noted for SNCV, this is in agreement with the results of several authors [34,35,40,41].

In the present study, the SNAP amplitude was greater in women as previously reported by some studies [34,40,42] but not in others [35,41]. It has been suggested that this difference could be, in part, due to volume conductor characteristics of the body mass caused by a more important layer of subcutaneous fat in women [43].

The present study showed a significant negative correlation of the SNAP amplitude with BMI similar to what has been reported by several authors [10,44,45]. The thicker subcutaneous tissue in subjects with a high BMI would act as a high-frequency filter reducing the SNAP amplitude of the response recorded at the surface [10,44-46]. However, this correlation between SNAP amplitude and BMI has not been found by other authors [8].

As many authors reported [10,44,45] we found no correlation between BMI and SNVC. A significant negative correlation between the SNAP amplitude and the SNVC with the height was found in the present study which is in concordance with several authors [25,26,47].

Currently, very few studies focused on determining the reference values have considered all these factors [5,48].

However, one of the main limitations of this study is the age group which was limited to 60 years. It is useful to continue this study by including healthy subjects over 60 years of both sexes.

Conclusion

The present study reports the reference value of the electrophysiological parameters for the sural nerve in the Algerian population using a methodological approach similar

to that recently proposed. The importance of determining the nature of the distribution of each electrophysiological parameter to choose the appropriate statistical tests is emphasized. The lower and upper limits were calculated using the percentile method as currently recommended by several authors since our sample size is greater than 100.

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