REFERENCE VALUES FOR NERVE CONDUCTION STUDIES IN HEALTHY NEWBORNS, INFANTS AND CHILDREN IN PHILIPPINE CHILDREN'S MEDICAL CENTER

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ABSTRACT

BACKGROUND: Nerve conduction studies play a diagnostic role in the clinical evaluation of neuromuscular disorders in children. Reference ranges define the expected parameter values in disease-free children.

OBJECTIVES: To propose reference values for sensory and motor nerve conduction and late responses in upper and lower limb peripheral nerves in Filipino children 5 years and below.

METHODS: Sensory nerve conduction studies on median, ulnar, radial, superficial peroneal, and sural nerves and motor nerve conduction and late response studies on median, ulnar, peroneal and posterior tibial nerves were done using standardized techniques among 100 healthy Filipino children.

RESULTS: Subjects were stratified according to age groups. Reference values for the following parameters: (1) sensory conduction velocity and amplitude; (2) motor conduction velocity, amplitude and latency at distal sites; (3) F-wave latency; and (4) H-reflex latency were summarized. These were expressed as mean ± standard deviation or median (range) for values that follow Gaussian and non-Gaussian distributions. The 5^{th} and 95^{th} percentile values were likewise reported. Age had direct correlation with various nerve conduction parameters. Height was directly correlated with F-wave parameters of median, ulnar and peroneal nerves but not posterior tibial nerve.

CONCLUSIONS: Reference standards for nerve conduction studies of commonly tested nerves of Filipino children are presented. Values are comparable to reference ranges elsewhere except for the H-reflex latency which is higher in this study.

KEYWORDS: nerve conduction study; late response; reference values

INTRODUCTION

Reference values for nerve function assessment are used to define the limits of normal function, such that test values outside the range suggest peripheral nerve dysfunction or damage. Although different nerve conduction studies have yielded respective reference values, the results vary considerably from population to population, region to region and laboratory to laboratory. Hence, it is important that the institution's neurodiagnostic Laboratory Clinical Electromyography Unit obtain separate standardized reference values by conducting nerve conduction studies among healthy Filipino pediatric patients with age ranging from of one

day to 5 years to determine the normal motor and sensory nerve conduction velocity, nerve action potential and amplitudes, H-reflex, F wave and latencies of the median, radial, ulnar, peroneal, posterior tibial and sural nerves.

To date, our Neurodiagnostic Laboratory Clinical Electromyography Unit has not established its own set of normal values for the various nerve conduction studies and since its establishment, we have been using normal values from published studies[2]. This study therefore intends to obtain a reference value database from healthy Filipino children and compare it with published data.

NORMATIVE DATA IN CHILDREN AND MATURATIONAL CHANGES

Conduction velocity. The relationship between conduction velocity of motor nerve fibers and age, specifically for children under six has been studied by many authors. Historically, Thomas and Lambert first described the maturation of motor conduction velocity of the ulnar nerve during the first years of life in 1960. Although there are many different sources of information, the motor conduction velocities of newborns were roughly half of those in adults. They all showed rapid increase in motor conduction velocity during the first two years of life and less increase later, reaching adult value by 3-5 years. Locally, in 1997 Amante had reported normal nerve conduction velocity among 1 to 60 month old children seen at the University of the Philippines-Philippine General Hospital. The conduction velocity of the upper limbs was 65-70% of adult values at a younger age of below 6 months and it reached adult values at 3 years of age. While the conduction velocity of the tibial nerve and peroneal nerve is 70% and 75% of adult values at 6 months. Like in the upper limbs, it reached adult values at age 3 years [10]. Tables showing the motor nerve conduction velocity of both the upper and lower limbs of the different age groups can be found in the Appendix.

Motor and sensory action potentials. Compound muscle action potential (CMAP) amplitudes also differ by age. In the neonatal group, CMAP are one-half adult values for tibial nerve and one-third adult values for peroneal, median and ulnar nerve in the study of Garcia et al. Tibial CMAP (from abductor hallucis) is the first to reach adult values around 2 and 3 years of age according to Garcia et al and Cai and Zhang studies, respectively. CMAP amplitudes of median, ulnar and peroneal nerves get doubled around 4 years of age and reach adult values between 4-6 years age in the study of Miller and Kuntz and Cruz Martinez et al.

In contrast, Amante found that the amplitudes of the motor action potentials of the median, tibial and peroneal nerves were 50-60% of adult values at 6 months of age while the ulnar nerve was 80%. All the nerves had amplitudes similar to adult values earlier at 2-3 years except for the tibial nerve which had reached adult values at 1 year of age. Maturational changes for sensory nerve action potential (SNAP) amplitudes are different to that of motor fibers. At birth, SNAP amplitudes are only 25-30% of adult values in the study of Cai and Zhang. In the neonatal period, SNAP amplitudes are about half of those of adult values. It reaches adult values already by the age of 2 years according to the study of Gamstorp and Shelburne, Garcia et al and Cruz Martinez et al. but in the study of Gucchait et al, it is reached later by 3-4 years of age similar to CMAP amplitudes.

Distal motor latency. Available normative values of distal motor latency (DML) in the study of Cruz Martinez, Miller and Kuntz, Parano et al, Hamdan, Cai and Zhang are described according to the different distance in every age group. Recently, the group of Garcia reported corrected DML for standard distances for children by applying the formula: Corrected DML = measured DML – [L-X/MCV], where L = actual distance between stimulating cathode to the active recording electrode, and X = standard distance (4

cm for nerves of upper limbs and 5 cm for nerves of the lower limbs. This approach avoided the influence of extremity growth on the DML measurement.

F-wave latency. There are only a few age-related studies of F-wave parameters in pediatric population: (1)Shahani and Young in 1981; (2) Kwast and Kozlowski in 1985; (3) Miller and Kuntz in 1986; (4) Misra et al in 1989; (5) Parano et al in 1993; (6) Cai and Zhang in 1997; (7) Garcia et al. in 2000; and (8) Nadeem et al. in 2002 [2,3,6,7,12]. In general, the minimum F-latency of median or ulnar nerve stimulation at the wrist in children younger than 6 years of age is less than 20 msec, while in the lower extremities recorded from intrinsic foot muscles with peroneal or tibial nerve stimulation at the ankle is less than 30 msec. Evolution of F-wave latencies in children may remain stable (Cai and Zhang, 1997), show a linear increase (Parano et al, 1993) or exhibit differential evolution according to age: diminution during the first year of life, stabilization and increasing afterwards (Garcia et al, 2000; Nadeem et al, 2002).

H-reflex. In young infants, the H-reflex is present in both the upper extremities (median and ulnar) and lower extremities (with tibial stimulation). It is evoked easily even in normal prematures and newborns because of increased alpha motor neuron excitability due to the imbalance between facilitory and inhibitory effects on the spinal motor neuron as a result of the immaturity of the central nervous system (CNS). Thereafter, H-reflex responses become suppressed in the upper extremity in most children after first year, while the tibial H-reflex persists in adulthood [2]. Mayer and Mosser in 1969, Tiwari et al in 1996 and Cai and Zhang studied H-reflex latency in the gastrocnemius-soleus muscle in infants and children [2,3,6,13]. Mayer and Mosser concluded that H-reflex latency greater than 17 msec is abnormal for newborns and infants, while in children, H-reflex latency greater that 20 msec is abnormal.

They showed that the minimum latencies of H-reflexes remained relatively constant during the first 3 years of life like the F-wave latencies.

For this study we wished to establish an institution-based normal values for the motor nerve conduction velocity, motor and sensory nerve action potential, F-wave and H-reflex values in healthy newborn, infants, and children by performing nerve conduction studies at the Neurodiagnostic Laboratory Clinical Electromyography Unit of the Philippine Children's Medical Center

METHODOLOGY

This was a prospective cross-sectional study. One hundred healthy children with age ranging from one day to 5 years were divided into 5 groups. The infant and children group is further subdivided according to different maturational changes observed in the development of various nerves among full term newborn, infants and children. The highest age limit is set at 5 years, because by the age 4 or 5 years, both MNCV and SNCV have attained adult range. Subjects were recruited from the outpatient and inpatient departments of PCMC and neighboring barangays from October 2015 to April 2016

The sample size was computed using the formula for estimation of one group mean: $n = (z^2 \times s^2)/d^2$ where $z = 1.96$ for 95% confidence level, s = sample standard deviation, d = accuracy of estimate or min difference from true mean. Sample standard deviation was based from the highest standard deviation of baseline mean conduction velocity among the nerves under each age group obtained by the UP-PGH study. The sample size of each age group was selected based on the largest sample size calculated and feasibility of recruiting the number of subjects.

The data was collected by a single experienced technician. The procedure was done using a VIASYS NicoletOne Viking Quest 4-

channel NCS/Electromyography/EP system machine serial number OL091835, with Viking quest NCS Software Bundle version 8.1 installed. A standard size 10 mm disc electrode was used for all ages except for neonates in which 6 mm surface electrode was used to the hands or feet as a reference recording electrode. Ring electrodes were used for sensory conduction studies of the fingers. A current stimulator probe model Nicolet S403 with an interelectrode distance of 2.0 cm was used to evaluate neonates, infants and children. Supramaximal square pulses of 0.1 ms duration were used. All testing was conducted in an air conditioned room and the room temperature was thermostatically controlled between 25-28 degrees Celsius. Skin temperature (measured by a thermometer at the axilla) was kept at ranges between 36.0 to 36.9 degrees Celsius, with a mean of 36.3 degrees Celsius.

Nerve conduction studies were done on either side of the extremity per examinee as there was no significant difference in the motor nerve conduction study on either side of the limbs as demonstrated in several studies[6]. The choice of the laterality of the extremity was based on convenience for the procedure. Unilateral examination of the limb simplified the procedure, allowing quick execution of the test and better compliance of the test subjects.

The presence of a parent was encouraged during the procedure because it could reduce fear and elicits child's cooperation. They could participate by holding the child's hand, having the child sit on the parent's lap or restraining the extremity to be tested. Stimulus artifacts were avoided through the following: (1) grounding of the machine; (2) instructions to avoid application of any medicinal or cosmetic products to the skin were given; (3) skin preparation using rubbing alcohol; (4) Reduce the electrical interference of the testing environment by disconnecting or switching off any irrelevant electrical appliances. Meticulous drug history was obtained prior to the procedure. Presence of any devices implanted in the body of the patient was asked to safeguard the patient.

A. MEASUREMENT OF SENSORY NERVE CONDUCTION VELOCITY

In the upper and lower limb, sensory nerve action potentials were recorded using antidromic technique. Conventional methods for sensory NCS of the different nerves were employed (Table 3) [15,24]. The reference electrode was placed about 2 and 3 cm distal to the active electrode for young infant and bigger children. For sensory nerve conduction, the machine was set as follows: sensitivity of 20 uV, sweep speed of 1 ms per division and filters low cut 20 Hz and high cut 3 KHz.

B. MEASUREMENT OF MOTOR NERVE CONDUCTION VELOCITY

For motor nerve conduction, the low cut filter was 2 Hz and the high cut was 10 KHz. Sweep speed was 2 ms/division. Sensitivity was 5 mV.

Measurements of motor nerve conduction followed conventional methods (Table 4).

C. MEASUREMENT OF F-WAVE LATENCY

For F-wave recording, the machine was calibrated at sweep speed 5 ms per division for the median and ulnar nerves and 10 ms per division for posterior tibial and peroneal nerves. Sensitivity was 200 uV per division for posterior tibial and peroneal nerves while 500 uV for ulnar and median nerve. Filter was between 2 Hz - 3 KHz for ulnar, posterior tibial and peroneal nerves, while in the median nerve 2 Hz – 10 KHz. The placement of the recording and stimulating electrodes was similar to the CMAP recording, with the only difference of placing the cathode of the stimulating electrode proximal to the anode. Stimulation of nerve was done at anatomical

landmarks, particularly wrist crease for median and ulnar nerves and ankle for peroneal and posterior tibial nerves. The ground electrode was placed between stimulation and recording surface electrode. F-wave studies were performed after motor studies of the same nerves. Minimum of 10 stimuli free of artifacts were passed as satisfactory recording of the F-waves and the minimum F-wave latency (shortest) and the maximal F-wave (longest) latencies were noted[12].

D. MEASUREMENT OF H-REFLEX LATENCY

The posterior tibial nerve was stimulated with a rectangular electrical pulse of 0.1 ms duration applied once every five seconds. The electromyographic setting was: low frequency filter of 2 Hz and high frequency filter of 3 KHz, sensitivity of 2 mV and sweep speed of 5 ms/division. Method for the measurement of H-reflex latency was similar to the method demonstrated in literature [15,24].

Descriptive statistics were used to summarize the clinical characteristics of the patients. Frequency and proportion was used for nominal variables, median and range for ordinal variables, and mean and SD for interval/ratio variables. The correlation between the NCS parameters and age as well as the height and F-wave latencies was assessed using Spearman's correlation coefficient. All valid data was included in the analysis.

RESULTS

Out of 120 subjects screened, 100 were eligible and 20 failed screening mostly due to abnormal anthropometrics and poor compliance of the subject with the procedure. The distribution by age and sex are shown in Table 1. There were more males than females in all age groups. Effect of sex was not considered as there is no significant difference in latency or velocity between males and females [6].

Table 1. Demographic profile of 100 healthy Filipino children who underwent nerve conduction studies

	<30 days (n=17)	**1-6 months (n=17)**	**7-12 months (n=25)**	**1-3 years (n=26)**	**4-5 years (n=15)**
	Frequency (%); Mean ± SD				
Sex					
Male	9 (52.94)	9 (52.94)	16 (64.00)	16 (61.54)	11 (73.33)
Female	8 (47.06)	8 (47.06)	9 (36.00)	10 (38.46)	4 (26.67)
Age (Months)	0.43 ± 0.28	3.59 ± 1.50	9.36 ± 1.68	31.12 ± 9.77	52.6 ± 3.02

Tables 2 and 3 present summary statistics for sensory nerve conduction velocity and amplitude, for proximal motor nerve conduction velocity and amplitude and for distal motor nerve conduction latency and amplitude. All the CMAP morphologies were similar and biphasic except for one in the ulnar nerve, in which a double negative peak was found. The values for F-wave recordings of median, ulnar, posterior tibial and peroneal nerves as well as H-reflex

latency of the posterior tibial nerve were listed. Of the 100 participants, we were able to perform F-wave recordings of the peroneal nerves for 83 children. We were unable to complete the test for the 17 children because of technical difficulty obtaining adequate number of reliable measurements, which happens infrequently particularly in the peroneal nerve. Sometimes, no elicitable F-wave for the peroneal nerve is determined and is considered a normal variant[25]. The mean and standard deviation for the commonly tested peripheral nerves were reported if the parameter follows Gaussian distribution. Parameters that remained non-normal despite attempts of transformations to normal distribution were expressed as median and range.

Table 2. Average sensory nerve conduction parameters in 100 healthy Filipino children, according to age group

	<30 days (n=17)	**1-6 months (n=17)**	**7-12 months (n=25)**	**1-3 years (n=26)**	**4-5 years (n=15)**
	Frequency (%); Mean ± SD; Median (Range)				
Median Nerve					
SNAPA (uV)	20.35 ± 6.89	22.82 ± 7.38	29.08 ± 8.51	38.54 ± 1.37	40.6 ± 9.39
SNCV (m/s)	32.18 ± 3.80	43 (32 to 47)	45.92 ± 4.44	52.15 ± 3.50	54.0 ± 2.54
Ulnar Nerve					
SNAPA (uV)	20.65 ± 7.76	20.88 ± 5.97	27.2 ± 8.08	33.08 ± 9.62	29.87 ± 6.21
SNCV (m/s)	32.0 ± 3.72	41.35 ± 3.89	45.68 ± 4.57	51.5 (42 to 57)	53.27 ± 2.99
Radial Nerve					
SNAPA (uV)	14.82 ± 5.54	16.06 ± 4.94	20.28 ± 6.34	27.77 ± 5.67	27.2 ± 5.51
SNCV (m/s)	31.35 ± 3.33	42 (33 to 47)	43 (38 to 53)	51 (42 to 58)	54.13 ± 2.03
Sural Nerve					
SNAPA (uV)	15.29 ± 5.03	16.12 ± 5.12	20.0 ± 4.97	26.58 ± 7.67	29.0 ± 9.30
SNCV (m/s)	32.47 ± 3.79	41.71 ± 4.48	47.16 ± 4.90	53.5 (40 to 58)	53.33 ± 2.87
Superficial peroneal Nerve					
SNAPA (uV)	11 (8 to 26)	12.29 ± 3.02	15.84 ± 4.88	25.73 ± 7.20	25.87 ± 5.49
SNCV (m/s)	31 (23 to 35)	41.47 ± 4.57	46.64 ± 4.14	52.23 ± 3.89	53.33 ±2.72

Note: Median (Range) is used to Non normally distributed data

Table 3. Average motor nerve conduction parameters in 100 healthy Filipino children, according to age group

	<30 days (n=17)	1-6 months (n=17)	7-12 months (n=25)	1-3 years (n=26)	4-5 years (n=15)
	Mean ± SD; Median (Range)				
Median Nerve					
MNCV (m/s)	31.47 ± 3.61	41.88 ± 4.57	46.6 ± 5.81	51.65 ± 4.10	55 ± 4.64
DML (ms)	2.28 ± 0.26	2.08 ± 0.25	2.13 ± 0.29	2.20 ± 0.28	2.43 ± 0.28
CMAPA wrist (mv)	4.15 ± 0.70	4.75 ± 0.75	5.91 ± 0.98	6 (5 to 9.3)	6.67 ± 0.92
CMAPA elbow (mv)	3.72 ± 0.74	4.51 ± 0.79	5.65 ± 0.91	6.07 ± 1.21	6.46 ± 0.86
F-wave min (ms)	17.16 ± 1.71	17.26 ± 1.53	16.83 ± 1.27	19.06 ± 1.60	19.81 ± 1.06
F-wave max (ms)	19.06 ± 1.23	18.65 ± 1.74	18.91 ± 1.47	20.59 ± 1.42	21.55 ± 0.92
F-wave disp (ms)	1.91 ± 0.85	1.3 (0.8 to 2.8)	2.08 ± 0.92	1.53 ± 0.46	1.74 ± 0.78
Ulnar Nerve					
MNCV forearm (m/s)	33 (26 to 36)	42 ± 4.85	45 (41 to 63)	53.62 ± 5.76	57.47 ± 3.38
MNCV across elbow (m/s)	34 (25 to 36)	41.65 ± 4.77	45 (41 to 60)	53.15 ± 5.49	57 ± 3.84
DML (ms)	2.02 ± 0.32	1.74 ± 0.20	1.56 ± 0.25	1.63 ± 0.24	1.67 ± 0.25
CMAPA wrist (mv)	4.23 ± 0.89	5.49 ± 1.04	5.6 (4.2 to 8.7)	6.1 (4.5 to 10.6)	7.25 ± 1.15
CMAPA elbow (mv)	3.95 ± 1.02	5.37 ± 1.08	5.5 (4 to 8.7)	6.05 (4.5 to 10.6)	7.21 ± 1.11
CMAPA above elbow (mv)	3.86 ± 1.00	5.25 ± 1.14	5.4 (4 to 8)	5.75 (4.5 to 10.1)	7 ± 1.19
F-wave min (ms)	18.27 ± 1.56	18.22 ± 1.53	17.92 ± 1.67	19.31 ± 1.19	19.61 ± 0.98
F-wave max (ms)	20.18 ± 1.62	19.71 ± 1.74	19.7 (16.2 to 21.8)	20.78 ± 1.10	21.03 ± 0.69
F-wave disp (ms)	1.91 ± 0.84	1.49 ± 0.73	1.56 ± 0.62	1.48 ± 0.59	1.42 ± 0.65

Table 3. (Continuation)

Peroneal Nerve					
MNCV leg (m/s)	29.59 ± 3.10	42 (33 to 44)	45.64 ± 3.74	50 (41 to 53)	50.86 ± 3.62
MNCV across knee (m/s)	30 ± 3.10	42 (31 to 44)	44 (40 to 50)	50 (42 to 52)	50 (44 to 58)
DML (ms)	2.2 (1.7 to 3.5)	1.79 ± 0.32	1.78 ± 0.38	1.92 ± 0.42	2.5 (1.8 to 4.2)
CMAPA ankle (mv)	1.81 ± 0.59	2.24 ± 0.81	2.42 ± 0.66	3.25 (1.6 to 4)	3.37 ± 0.98
CMAPA knee (mv)	1.76 ± 0.55	2.11 ± 0.77	2.41 ± 0.63	3.11 ± 0.52	3.32 ± 0.97
CMAPA above knee (mv)	1.73 ± 0.57	2.02 ± 0.71	2.33 ± 0.62	3.08 ± 0.49	3.27 ± 0.98
F-wave min (ms) (n=83)	18.86 ± 1.37	18.35 (17.4 to 28.9)	18.73 ± 0.73	20.28 ± 1.00	20.89 ± 1.04
F-wave max (ms) (n=83)	21.18 ± 2.01	21.2 (19 to 29.9)	20.9 ± 0.71	21.73 ± 1.02	22.13 ± 1.15
F-wave disp (ms) (n=83)	2.1 (0.7 to 6.2)	2.08 ± 0.78	2.18 ± 0.85	1.2 (0.6 to 4.2)	1.1 (0.6 to 2.6)
Posterior Tibial Nerve					
MNCV (m/s)	31 (24 to 34)	42 (32 to 45)	45 (41 to 52)	51 (43 to 55)	51 (44 to 55)
DML (ms)	2.21 ± 0.32	2.08 ± 0.27	1.9 ± 0.41	2.25 ± 0.40	2.45 ± 0.45
CMAPA ankle (mv)	5.12 ± 1.30	6.73 ± 1.74	7.95 ± 2.38	8.95 (5.4 to 15.6)	8.71 ± 1.57
CMAPA knee (mv)	3.87 ± 1.32	6.28 ± 1.87	7.33 ± 2.20	8.8 (4 to 13)	7.77 ± 1.60
F-wave min (ms)	20.27 ± 2.55	19.65 ± 1.59	19.06 ± 1.39	20.4 (18.8 to 26.3)	20.65 ± 1.34
F-wave max (ms)	22.1 (16.8 to 28.9)	21.65 ± 1.42	21.03 ± 1.09	22.14 ± 1.77	21.79 ± 1.44
F-wave disp (ms)	2.28 ± 1.04	2 ± 0.88	1.97 ± 0.83	1.42 ± 0.78	1.13 ± 0.31
H-reflex (ms)	18.8 ± 2.41	19.13 ± 2.37	19.66 ± 2.97	20.93 ± 2.35	20.65 ± 1.58

Note: Median (Range) is used to Non normally distributed data

We obtained the values for the 5th and 95th percentiles for each age group, as recommended by the AANEM as a more effective way of reporting normal values, thus reported in Table 4-5. Reference values based on estimates of the 95th percentiles for sensory and for motor nerve conduction latency while 5th percentiles for amplitude and velocity were assumed as cut-off or thresholds as the highest and lowest normal value, respectively.

Table 4. Values of the 5th and 95th percentile of select parameters of different types of sensory nerves, by age group

	<30 days (n=17)	**1-6 months (n=17)**	**7-12 months (n=25)**	**1-3 years (n=26)**	**4-5 years (n=15)**
	5th, 95th				
Median Nerve					
SNAPA (uV)	12, 36	13, 39	20, 47	24, 57	25, 62
SNCV (m/s)	26, 38	32, 47	41, 53	44, 58	50, 59
Ulnar Nerve					
SNAPA (uV)	10, 37	14, 37	17, 42	19, 51	20, 44
SNCV (m/s)	26, 38	32, 47	41, 52	45, 56	49, 59
Radial Nerve					
SNAPA (uV)	6, 25	10, 30	12, 29	17, 36	14, 36
SNCV (m/s)	25, 28	33, 47	41, 52	43, 56	51, 58
Sural Nerve					
SNAPA (uV)	8, 27	8, 28	13, 28	17, 39	15, 51
SNCV (m/s)	24, 38	32, 50	41, 55	46, 58	50, 59
Superficial peroneal Nerve					
SNAPA (uV)	8, 26	8, 19	10, 24	16, 41	14, 34
SNCV (m/s)	33, 35	33, 50	41, 53	45, 57	50, 59

Table 5. Values of the 5th and 95th percentile of select parameters of different types of motor nerves, by age group.

	<30 days (n=17)	1-6 months (n=17)	7-12 months (n=25)	1-3 years (n=26)	4-5 years (n=15)
			5th, 95th		
Median Nerve					
MNCV (m/s)	25, 37	32, 50	40, 56	45, 58	46, 62
DML (ms)	1.8, 2.8	1.4, 2.4	1.6, 2.5	1.8, 2.6	2.1, 3.1
CMAPA wrist (mv)	3.2, 5.6	3.4, 5.9	4.7, 7.5	5, 8.7	5.1, 8.6
CMAPA elbow (mv)	2.5, 5.4	3.1, 5.5	4.1, 7.4	5, 8.7	5, 8
F-wave min (ms)	14, 20.2	15, 19.9	15.1, 18.6	16.6, 21.3	18.4, 21.6
F-wave max (ms)	16.7, 21.3	15.9, 21.5	16.4, 20.9	18.5, 22.7	19.6, 22.5
F-wave disp (ms)	0.7, 3.5	0.8, 2.8	1, 3.4	0.8, 2.1	0.8, 3.4
Ulnar Nerve					
MNCV forearm (m/s)	26, 36	34, 53	42, 60	45, 64	52, 63
MNCV across elbow (m/s)	25, 36	33, 51	41, 59	44, 63	50, 64
DML (ms)	1.2, 2.5	1.3, 2	1.1, 1.9	1.3, 2.1	1.1, 2.3
CMAPA wrist (mv)	2.4, 5.4	3.7, 7.3	4.5, 8.3	5, 7.4	5.8, 9.8
CMAPA elbow (mv)	1.9, 5.3	3.7, 7.3	4.1, 8.4	5, 7.8	5.8, 9.8
CMAPA above elbow (mv)	1.9, 5.3	3.2, 7.3	4, 8	5, 7.8	5.4, 9.7
F-wave min (ms)	15.8, 21	15.6, 20.7	15.2, 20.1	17.1, 21	18.2, 21.6
F-wave max (ms)	17.4, 22.8	17.2, 22.2	16.2, 21.5	18.4, 22.4	19.9, 22.4
F-wave disp (ms)	0.7, 3.8	0.6, 2.8	0.6, 2.8	0.6, 2.4	0.6, 3.2
Peroneal Nerve					
MNCV leg (m/s)	23, 33	33, 44	41, 52	43, 53	43, 57
MNCV across knee (m/s)	24, 33	31, 44	42, 50	42, 51	44, 58
DML (ms)	1.7, 3.5	1.3, 2.6	1.2, 2.3	1.3, 2.7	1.8, 4.2
CMAPA ankle (mv)	1.1, 2.8	1, 3.6	1.5, 3.9	2.1, 3.8	2, 5.7
CMAPA knee (mv)	1.1, 2.8	1, 3.6	1.5, 3.8	2.2, 3.8	2, 5.7
CMAPA above knee (mv)	1, 2.8	1, 3.3	1.5, 3.8	2.3, 3.8	2, 5.6
F-wave min (ms) (n=83)	16.5, 22.1	17.4, 28.9	17.4, 19.7	18.55, 21.8	19.1, 22.4
F-wave max (ms) (n=83)	17.7, 25.3	19, 29.9	19.5, 21.95	19.95, 23.25	20, 24.8
F-wave disp (ms) (n=83)	0.7, 6.2	1, 3.2	1.1, 3.9	0.6, 3.6	0.6, 2.6

Table 5. (Continuation)

Posterior Tibial Nerve					
MNCV (m/s)	24, 34	32, 45	42, 50	43, 54	44, 55
DML (ms)	1.7, 2.7	1.5, 2.6	1.4, 2.7	1.7, 2.9	1.9, 3.3
CMAPA ankle (mv)	3.1, 7.3	3, 9.7	5, 11.5	5.7, 14.6	6.4, 11.4
CMAPA knee (mv)	2.2, 6.8	3, 9.7	4.5, 10	4.9, 12.8	5, 10.8
F-wave min (ms)	14.8, 26.1	16.9, 22.5	17.1, 21.3	18.9, 24.1	19, 23.4
F-wave max (ms)	16.8, 28.9	19.1, 23.9	19.2, 23.1	19.6, 25.2	20.1, 25.2
F-wave diff (ms)	0.8, 4.4	1.1, 3.6	0.7, 3.4	0.6, 2.8	0.7, 1.8
H-reflex (ms)	16.1, 23.6	15, 23.8	16.1, 24	17.4, 24	17.6, 23.5

The correlation with age of all sensory and most of motor nerve conduction parameters is evident in the high values of correlation coefficient presented in Table 6-7. Distal motor latency has poor correlation in all motor nerves. Age and height exhibit a direct correlation with F-wave minimum and maximum latency of median, ulnar, and peroneal nerves (Table 8).

Table 6. Correlation between age and sensory nerve conduction parameters

	Correlation Coefficient	**Interpretation**	**P-value**
Median Nerve			
SNAPA (uV)	0.673	Direct, strong	**0.000**
SNCV (m/s)	0.870	Direct, very strong	**0.000**
Ulnar Nerve			
SNAPA (uV)	0.502	Direct, moderate	**0.000**
SNCV (m/s)	0.846	Direct, very strong	**0.000**
Radial Nerve			
SNAPA (uV)	0.641	Direct, strong	**0.000**
SNCV (m/s)	0.904	Direct, very strong	**0.000**
Sural Nerve			
SNAPA (uV)	0.649	Direct, strong Direct, very strong	**0.000**
SNCV (m/s)	0.826		**0.000**
Superficial Peroneal Nerve			
SNAPA (uV)	0.719	Direct, strong	**0.000**
SNCV (m/s)	0.861	Direct, very strong	**0.000**

Statistical test: Spearman's correlation coefficient

Table 7. Correlation between age and motor nerve conduction parameters

	Correlation Coefficient	Interpretation	P-value
Median Nerve			
MNCV (m/s)	0.850	Direct, very strong	**0.000**
DML (ms)	0.156	Direct, very weak	0.121
CMAPA wrist (mv)	0.694	Direct, strong	**0.000**
CMAPA elbow (mv)	0.693	Direct, strong	**0.000**
F-wave min (ms)	0.538	Direct, moderate	**0.000**
F-wave max (ms)	0.559	Direct, moderate	**0.000**
F-wave disp (ms)	-0.037	Indirect, very weak	0.714
Ulnar Nerve			
MNCV forearm (m/s)	0.875	Direct, very strong	**0.000**
MNCV across elbow (m/s)	0.877	Direct, very strong	**0.000**
DML (ms)	-0.326	Indirect, weak	**0.001**
CMAPA wrist (mv)	0.637	Direct, strong	**0.000**
CMAPA elbow (mv)	0.644	Direct, strong	**0.000**
CMAPA above elbow (mv)	0.627	Direct, strong	**0.000**
F-wave min (ms)	0.319	Direct, weak	**0.001**
F-wave max (ms)	0.231	Direct, weak	**0.021**
F-wave disp (ms)	-0.146	Indirect, weak	0.148
Peroneal Nerve			
MNCV leg (m/s)	0.816	Direct, very strong	**0.000**
MNCV across knee (m/s)	0.839	Direct, very strong	**0.000**
DML (ms)	0.094	Direct, very weak	0.398
CMAPA ankle (mv)	0.586	Direct, moderate	**0.000**
CMAPA knee (mv)	0.594	Direct, moderate	**0.000**
CMAPA above knee (mv)	0.610	Direct, strong	**0.000**
F-wave min (ms) (n=83)	0.546	Direct, moderate	**0.000**
F-wave max (ms) (n=83)	0.302	Direct, weak	**0.006**
F-wave disp (ms) (n=83)	-0.442	Indirect, moderate	**0.000**
Posterior Tibial Nerve			
MNCV (m/s)	0.875	Direct, very strong	**0.000**
DML (ms)	0.181	Direct, very weak	0.072
CMAPA ankle (mv)	0.563	Direct, moderate	**0.000**
CMAPA knee (mv)	0.551	Direct, moderate	**0.000**
F-wave min (ms)	0.143	Direct, very weak	0.155
F-wave max (ms)	-0.071	Indirect, very weak	0.481
F-wave disp (ms)	-0.443	Indirect, moderate	**0.000**
H-reflex (ms)	0.333	Direct, weak	**0.001**

Statistical test: Spearman's correlation coefficient

Table 8. Correlation between the height and F-wave minimum and maximum latency (ms)

	Correlation Coefficient estimate	Interpretation	Number of samples	P-value
Median Nerve				
F-wave min (ms)	0.5252	Direct, moderate	100	**0.0000**
F-wave max (ms)	0.5472	Direct, moderate	100	**0.0000**
Ulnar Nerve				
F-wave min (ms)	0.3176	Direct, weak	100	**0.0013**
F-wave max (ms)	0.2212	Direct, weak	100	**0.0270**
Peroneal Nerve				
F-wave min (ms)	0.5482	Direct, moderate	83	**0.0000**
F-wave max (ms)	0.3056	Direct, weak	83	**0.0050**
Posterior Tibial Nerve				
F-wave min (ms)	0.1474	Direct, very weak	100	0.1432
F-wave max (ms)	-0.0860	Indirect, very weak	100	0.3951

Statistical test: Spearman's correlation coefficient

DISCUSSION

The MNCV and SNCV obtained showed an increase as the chronological age increased. The rate of increment of MNCV and SNCV was more rapid between the first two groups. In subsequent groups, the change in nerve conduction velocity showed generally small increase. This trend can be explained by the positive correlation of velocity and increasing diameter of the axon and degree of myelination of fibers in growing children. It parallels the most rapid increase in numbers of myelinated fibers in the 1st year of life, consequently resulting to an increase in the axonal diameter. The association of nerve conduction velocity with age is further reinforced in Table 6-7, which showed strong statistical significance. This finding collaborated with the finding of other researchers in the influence of age on nerve conduction velocities[2-9]. However, no increase was seen in the last two groups for the MNCV of the peroneal and posterior tibial nerve and the SNCV of the sural nerve.

Some of our findings on nerve conduction velocity in older children were observed to be in congruent to those reported by Kimura[15] and Kaeser [3] about normal variations in nerves and segments. The motor conduction velocities were slower in the legs than in the arms as in the present study. This is because of the inverse relationship between height and nerve conduction velocity, so nerves conduct slower in longer nerves than in shorter nerves.[15] On the other hand, we observe minimal to no difference in the ulnar and peroneal nerve motor conduction at proximal than distal sites, contrary to the findings that conduction velocity is always faster in the proximal than in the distal segment

along the same nerve. The distal slowing of nerve conduction velocity can be explained by two factors: (1) temperature difference of approximately 1°C between the proximal and distal parts of the nerve along the extremity, and (2) a decrease in the average fiber diameter of the fastest conducting fibers because of branching and tapering in distal parts of the nerve.[3] The absence of difference in the present study can be because the events in the outgrowth and maturation of the peripheral nerves are probably not yet taking place completely in the included age group. No conclusion about statistical difference between nerves of the arms and legs can be made because this was not included in the study.

In this study, we calculated the percentage of the mean values of conduction velocity and amplitudes of that age to reach the normal adult values. For the actual percentage value, you may refer to the Appendix. Nerve conduction velocities reach adult range at age 3-5 years in the literature. However in this study, the pace of maturation in conduction velocity is faster. The adult values were already reached in group IV (1-3 years) in the nerves of upper limbs namely median, ulnar and radial nerves, while group II (1-6 months) in the nerves of the lower limbs in the peroneal, sural and posterior tibial nerves. All the neonatal conduction velocities were 62-67% of the normal adult values in the nerves of upper limb, 74-78% in the lower limb, which is in contrast with previous reports of 50% of adult values in foreign literature.

Compound muscle action potential (CMAP) amplitudes of the posterior tibial nerve are also the first to reach adult value in group II, which is earlier than observed by Amante (reached at 1 year) and Cai and Zhang and Gucchait (reached at 2 years) While the CMAP amplitudes of ulnar and peroneal nerves reach adult values between 1-3 years age similar to Amante (reached at 2-3 years). The peroneal CMAP is still below the adult range by 5 years like the findings of Cai and Zhang. There was no progressive evolution of SNAP amplitudes noted in this study.

The differences we found in the pattern of maturation as compared with previous report was because estimation of percentage was done using adult normal values obtained before in a different institution. A more accurate relationship between the normal children and adult values can be determined if adult values were simultaneously obtained and compared with the present study. The higher amplitude we noted was influenced by differences in the distance from the skin to the nerve. This is especially true during sensory NCS in which the nearer the G1 recording electrode is from the action potential generator, the higher the amplitude of the response, and vice versa[26]. We hypothesized that our subjects have shorter distances between the skin and the nerve, or thinner subcutaneous tissue.

Comparison to several reference ranges found in the literature is carried out in this study, however normal limits for reference ranges having the same age group of radial and superficial peroneal nerves is not specified in any published data so no comparison was made. The MNCV values of the median, ulnar, peroneal and posterior tibial nerves showed good similarity with local data but rather higher than that of foreign data. The CMAPA values of the ulnar, peroneal and posterior tibial were less than the reported values in the data of Parano and Cai and Zhang while they were in close proximity with the local data. In contrast, the CMAPA of the median nerve was close to the values of Amante and Cai and Zhang. The motor latencies of all nerves, especially the median nerve were similar to others.

The data of median and ulnar SNCV and SNAPA were higher to the results of Miller and

Kuntz, Cruz Martinez. Both median and ulnar SNCV and SNAPA were either higher or lower to data reported by Amante. On the other hand, sural SNCV and sural SNAPA were higher than the local and foreign results.

The values for most of the nerve conduction parameters showed differences between the results of the present study with the data published in literature and could be attributed to variety of causes. The age distribution of the subjects from previous studies did not correspond well with the present study. In the best conditions, increasing the number of examined subjects will smooth data and reduce bias in the statistics. The diversity of the environment and techniques could have resulted for the differences. The difference in NCS values obtained between westerners and Asian populations could also explain the varied results. Based in the experience of Pitt and Kang in the central London hospital, the Caucasian population has the slowest conduction velocity of any ethnic group. They also observe a wide range of amplitudes encountered between ethnic groups. For example, median sensory amplitude reaching as high as 160 uV in certain ethnic groups or as low as 30-35 uV in other ethnic groups without evidence of peripheral nerve damage[27].

The trend of F-wave minimum latency with age in all nerves showed decrease in the first 6-12 months, then a rapid increase after 1 year then remained constant at 3 years as observed in the study of Garcia et al. This evolution is because of two simultaneous processes occurring: 1) a rapid increase of the conduction velocity, and 2) a parallel increase of length of extremity. The period of the most rapid increase in conduction velocity is responsible for the constant value of F-minimal latency or lag time during the first six months of life. In the next six months (6 months to 1 year), the increase in conduction velocity of the fastest fibers would parallel skeletal growth, reducing the F-minimal latency during this period. However, after the first year, the increase in arm length predominates and becomes responsible for the observed increase of F-minimal latency[12].

Age is directly interrelated in children for F-wave min and F-wave max in the median, ulnar and peroneal nerves except the posterior tibial nerve (Table 11). F-wave chronodispersion was not related with age in children in previous study [22] but in the present study it showed good correlation in the peroneal and posterior tibial nerves.

Our observation of F-wave minimum latency in the present study is longer in the median, ulnar, and posterior tibial nerve but shorter in the peroneal nerve as compared to observation made in other studies (Table 18). Such differences can be explained by the effect of limb length discrepancy. Lower mean F-wave latency is seen if the subjects have lower height and hence shorter limbs. For example, from the study of Nadeem et al, they observed that the F-wave minimal latency for the ulnar nerve have lower mean values in Iraqi children than in Western children due to height differences[12].

The F wave maximum latency values also followed the same changes as F-wave minimum latency, reduced in first year of life then increased with age afterwards. In comparison, maximal latency values reflect conduction in the slowest conducting fibers participating in the formation of the F-wave. It showed a nearly constant value during the first year of life, and it increased linearly as the upper limb length increased with age.

Height has positive association with minimum F-wave latency in all motor nerves such that as subject's height increases, latency of conduction increases. The height correlated well with F-wave min and max in median nerve and F-wave min of peroneal nerve (Table 12), which

was also shown in the scatter plots similar to the study of Puksa.

The mean latency of the H-reflex progressively increases with age but the changes are little and then remain constant when it reaches 4-5 years (Table 7). This coincides at the same time the length of the reflex markedly increases as child grows and the body height increases[28]. We did not observe diminishing of latency during the first year of life, which is also the time of maximal increase in conduction velocity due to growth in thickness of the fiber than lengthening develop. This trend was not observed because height and limb length was not factored in the computation of sample size.

The result of the latency of H-reflex in the present study was higher than those reported by studies listed in Table 19. H-reflex latency was found to increase with hip flexion angles (from 0.1 to 3.4 ms with hips flexed at 30^o and from 0.6-4.3 ms with hips flexed at 40^o in normal subjects). Thus, the ideal posture for research studies of H-reflex must be kept, in particular the children may be placed either in a reclining position, with the lower limb supported by a restraining table made in the laboratory, or in a prone position, with the foot resting on a fixed bar. This position keeps the flexion of the knee joint at 120^o and flexion of the ankle at 90^o as recommended by Hugon[28], which takes stretch off the bi-articular gastrocnemius muscles. Unfortunately, the appropriate posture and restraint was not done in the present study because of difficulty with keeping the position of our subjects.

CONCLUSION AND RECOMMENDATIONS

In conclusion, we have constructed a complete and clinically useful reference standard of conduction parameters of the peripheral nerves in the upper and lower limbs. Overall, the nerve conduction parameters of the commonly tested nerves compared favorably with the existing literature data. Some values deviated minimally with previously published results but still fall within the accepted norms, mandating the use of country specific normal values. However, the H-reflex latency showed departure with other researches. Age showed a statistically significant association in all analyses of sensory assessment relating to amplitude and velocity (all $p<0.001$ or higher levels of significance). Statistically significant age effects were also found in all analyses of motor assessments relating to velocity and amplitude for median, ulnar, peroneal and posterior tibial nerves, except motor latency for all nerves. Age and height had major role in the determination of F-wave minimum and maximum latencies. Both of these covariates should be considered in clinical evaluations of peripheral nerve function.

The reference values presented here can be applied to identify impairments among patients with peripheral nerve disorders in our laboratory as well as start researches on neuromuscular disorders in a cohort of children. Nerve conduction parameters are known to vary with demographic profile such as sex and anthropometric measurements such as height, limb length and body mass index. Diagnostic conclusions from nerve conduction data without making corrections or adjustments to factors that influence the data may be invalid. The effect of these variables was not included in the present study and this can be future areas of research. A study with larger sample size that separates subjects into cohorts based on demographic information is also recommended to increase power and precision. It can be done through multicenter collaborative effort to better clarify the generalizability of the results. At the same time, it can validate our results especially the H-reflex. The American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) had recommended a set of methodologically sound criteria to establish

high-quality reference values for nerve conductions studies for adult populations and these can guide similar normative studies in children, especially newborns which we have no local data yet[23].

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