Effects of Age, Gender, Height, and Weight on Late Responses and Nerve Conduction Study Parameters

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Abstract-

Background: Different methods in performing nerve conduction studies (NCS) yield different results. The results of NCS can also be affected by factors such as gender, age, height, and weight. This study aimed (1) to survey the effects of such factors, (2) to determine the importance of these factors, and (3) to analyze them for building equations in NCS and late response studies.

Methods: NCS from the neurological screening tests of 101 individuals without spinal cord, root, nerve, neuro-muscular junction, muscular, or systemic diseases were collected and analyzed.

Results: Subjects with older age had longer latencies, smaller amplitudes, and slower velocities compared with those in the younger age group. The change with age was greater in the median than in the ulnar nerve. Female subjects or those with lower weight had higher median and ulnar sensory amplitude. Females had shorter latency in the upper limbs and longer latency in the lower limbs by F-wave studies than males did. Height was an important factor by F-wave studies, with approximately 0.1 ms/cm and 0.3 ms/cm increase in the upper and lower limbs, respectively. Height and age were the most significant factors in the H reflex study with an increase of 0.18 ms/cm in height and 0.07 ms/year in age.

Conclusion: Without adjustment for these factors, the sensitivity and specificity of NCS will decrease when using the same reference data in patients with different gender, age, height, and weight.

Key Words: Normative data, Nerve conduction study, Late responses

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INTRODUCTION

Different methods in performing nerve conduction study (NCS) yield different results. Aside from this, the results can also be affected by factors such as gender, age, height, and weight[1-12]. Previously, gender differences in results of NCS have been reported to be largely explained by body height, although amplitude differences still persisted despite corrections for height, temperature, and age[1]. Females have greater amplitude than

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males in median and ulnar sensory NCS[1-4]. Age has also been reported to be inversely correlated with the amplitude and velocity of sensory and motor NCS[1,3,5-8].

Moreover, the minimal latency of F-wave studies also increases with age in upper and lower limbs studies[9,10], while height is reported to be negatively associated with sensory amplitude and positively associated with sensory latency[3]. Reverse correlations between height and velocity of the peroneal motor, tibial motor, and sural NCS are also reported[5,6]. Likewise, the minimal latency of F-wave study increases with height in upper and lower limbs studies[9,10].

There have been several reports about the correlation between these factors and NCS in Taiwan[13-15]. The velocity of motor NCS and amplitudes of motor and sensory NCS are negatively correlated with age[13,15]. Late response study is reported to be correlated to height[14,15] and negatively correlated to velocity of motor NCS[14]. Age is correlated with latency of peroneal F-wave, tibial F-wave, and H reflex[14].

Despite inconsistencies in results of previous studies, these factors continue to influence the results of NCS and late responses studies. Without adjustment for these factors, the sensitivity and specificity of NCS will be decreased by using the same reference limit data in patients with different gender, age, height, and weight. This study aimed to: (1) survey the effect of gender, age, height, and weight in NCS and late response studies; (2) analyze the factors of gender, age, height, and body weight for building equations for late response and nerve conduction studies by statistical methods; and (3) determine the important factors in late response and NCS.

MATERIALS AND METHODS

The clinical and electrophysiological results of subjects who received the special protocol for neurological screening testing were retrospectively reviewed. The screening testing included history taking, neurologic examinations, blood examination, carotid duplex study, electroencephalogram, brainstem-auditory evoked potentials, NCS, and brain and spine magnetic resonance imaging (MRI) study. Subjects with myelopathy, radiculopathy, plexopathy, peripheral neuropathy, neuro-muscular junction disorders, or myopathy were excluded. Those with significant systemic diseases (i.e., diabetes mellitus, thyroid diseases, malignancy) or significantly abnormal findings in MRI study were also excluded. The Institutional Review Board approved the study protocol.

NCS were conducted using the Nicolet Viking machines. NCS and temperature control were done by standard laboratory methods. All these studies were performed with surface recordings and stimulations. In general, the belly-tendon montage was used and the supramaximal stimulation was applied. The motor NCS included median, ulnar, peroneal, and tibial nerve studies. The median motor nerve was stimulated at the distal (6 cm, wrist) and proximal (elbow) sites respectively and recorded at the abductor pollicis brevis muscle. The ulnar motor never NCS was stimulated at the distal (6 cm, wrist) and proximal (below elbow) sites respectively and recorded at the abductor digiti minimi muscle. The peroneal motor nerve was stimulated at the distal (6 cm, ankle) or proximal (knee) sites respectively and recorded at the extensor digitorium brevis muscle. The tibial motor nerve was stimulated either at the distal (6 cm, ankle) or proximal (popliteal fossa) sites respectively and recorded at the abductor hallucis muscle.

For each subject, data of distal motor latency (DML), motor nerve conduction velocity (MNCV), and compound muscle action potentials (CMAP) from the distal stimulation were included for statistical analyses in this study. The DML was the time from the stimulus to the initial CMAP deflection off the baseline[16]. The amplitude of CMAP was measured from the baseline to the negative peak.

Sensory NCS were carried out using the antidromic paradigm and included the median, ulnar and sural nerves. The median sensory nerve was stimulated at the wrist at a distance of 14 cm and recorded at the 2nd digit (index finger). The ulnar sensory nerve was stimulated at the wrist at a distance of 11 cm and recorded at the 5th digit. The sural nerve was stimulated at the lateral calf at a distance of 14 cm and recorded at the lateral malleous. The onset latency was the time from the stimulus to the initial negative deflection off the baseline for a biphasic sensory nerve action potential (SNAP), or to the initial positive peak for a triphasic SNAP[16]. For each patient, data of SNAP and sensory nerve conduction velocity (SNCV) were included. Amplitude was measured from the baseline to the negative peak.

The late responses study included H reflex study and median, ulnar, peroneal and tibial F waves studies. The stimulation and recording sites were the same as those of the motor NCS except that the cathode was placed distally. Results were based on the tracings of the supra-maximal stimulations. Ten artifact free responses were recorded. Data of minimal latency in the F-wave study were included in this study. The H reflex study was recorded at the soleus muscle and stimulated at the popliteal fossa of the tibial nerve. The latency of the H reflex was also included in this study.

Demographic data was presented according to the results of descriptive analysis in the male and female groups. Transformations were used to convert data to a normal distribution (visual inspection of histograms/box plots and Kolmogorov-Smirnov testing). The reference limits were derived from the mean ± 2.5 standard derivation (SD) of the optimally transformed data and by converting these endpoints back to the original units, or mean ± 2.5 SD of the raw data if they followed a normal distribution.

Multiple linear regression analysis was used to test the influence of age, gender, body height, and weight on the parameters of late response and nerve conduction studies. Data for continuous variables were transformed to normal distribution as above when the data did not follow a normal distribution. The degrees of correlation coefficient (CCE) were graded into low (0.29 ≥ absolute value of CCE ≥ 0.1), moderate (0.49 ≥ absolute value of CCE ≥ 0.3), and substantial (absolute value of CCE ≥ 0.5)[17]. Multiple regression analysis with independent variables were defined by coefficient with a p value < 0.05.

The equations for predicting normal values in this study were established using stepwise multiple linear regression analysis by entering the significant factors from the regression analysis. The squared correlation coefficient (r^2) was applied to evaluate how well the regression line approximated the real data points. All statistical analyses used the SAS software package, version 9.1 (SAS Statistical Institute, Cary, North Carolina, 2002).

RESULTS

In this study, there were 101 study subjects (50 male and 51 female; age range: 21-76 years). Their body height ranged from 144.5 to 174.5 cm and the weight ranged from 40.5 to 96.6 Kg. The data were listed in Table 1. Males had significantly higher height (p < 0.001) and weight (p < 0.001) than females. Results of the NCS, F-wave, and H reflex studies from the study subjects were listed in Table 2. Reference limits were derived from the mean ± 2.5 standard derivation (SD) of the optimally transformed data and by converting these endpoints back to the original units, or the mean ± 2.5 SD of the raw data if they followed a normal distribution.

Correlations of gender, age, height, and weight on the nerve conduction, F-wave and H reflex studies were shown in Table 3. Gender had a substantial (absolute value of CCE ≥ 0.5) correlation with median and ulnar F-wave studies, and moderate (0.49 ≥ absolute value of CCE ≥ 0.3) correlation with tibial CMAP, peroneal and tibial F-wave, and H reflex studies. Age was moderately correlated with tibial CMAP and all modalities of median NCS after transformation to a normal distribution.

Table 1. *Basic data of the study subjects (n = 101)*

Basic data	Male (n = 50)		Female (n = 51)		p value
	Mean ± SD	Range	Mean ± SD	Range	
Age (years)	48.5 ± 11.7	21.0 - 74.0	49.1 ± 12.4	22.0 - 76.0	0.792
Height (cm)	166.2 ± 4.4	157.0 - 174.5	156.7 ± 6.5	144.5 - 170.5	< 0.001
Body weight (Kg)	70.2 ± 9.4	52.5 - 96.6	57.3 ± 9.7	40.5 - 89.6	< 0.001

SD: standard deviation.

Table 2. Measurements of nerve conduction, F-wave and H-reflex studies

	Present study			Ref [13]	Ref [14]	Ref [15]
	Range	Reference limit§	Mean ± SD‖	Mean ± SD	Mean ± SD	Mean ± SD¶
Median nerve						
distal latency (ms)*	2.6 – 4.2	4.3	3.3 ± 0.3	3.4 ± 0.4		3.6 ± 0.4
amplitude (mV)	5.1 – 18.5	5.8	10.8 ± 2.0	8.5 ± 2.8		11.9 ± 3.7
velocity (m/s)*	51 – 67	51	57.8 ± 3.0	61.2 ± 5.8		57.8 ± 4.2
Ulnar nerve						
distal latency (ms)*	2.1 – 3.6	3.4	2.6 ± 0.3	2.8 ± 0.5		2.8 ± 0.4
amplitude (mV)	5.7 – 17.8	5.5	11.0 ± 2.2	7.3 ± 2.6		11.7 ± 3.1
velocity (m/s)	51 – 70	52	61.0 ± 3.5	59.9 ± 7.2		61.4 ± 3.7
Peroneal nerve						
distal latency (ms)*	2.7 – 5.3	5.5	3.8 ± 0.5	4.4 ± 0.9		4.2 ± 0.5
amplitude (mV)†	2.5 – 13.4	2.1	6.8 ± 2.3	4.2 ± 2.2		6.0 ± 2.5
velocity (m/s)*	41 – 56	42	48.3 ± 2.5	53.4 ± 6.1		48.6 ± 4.4
Tibial nerve						
distal latency (ms)*	2.8 – 6.5	6.4	4.0 ± 0.7	4.7 ± 1.1		4.9 ± 1.0
amplitude (mV)	4.5 – 29.6	4.7	16.5 ± 4.7	8.8 ± 4.0		13.1 ± 5.0
Velocity (m/s)*	41 – 59	41	47.5 ± 2.8	49.1 ± 5.2		50.5 ± 5.3
Median nerve						
amplitude (μV)*	12 – 91.4	12	46.8 ± 17.2			33.0 ± 13.4
velocity (m/s)	45 – 71	45	58.6 ± 5.5			57.1 ± 4.5
Ulnar nerve						
amplitude (μV)†	10.6 – 98.5	9	41.2 ± 16.6			26.1 ± 12.0
velocity (m/s)	44 – 67	44	56.5 ± 4.9			56.3 ± 4.4
Sural nerve						
amplitude (μV)‡	4.0 – 51.0	5	18.0 ± 8.1			12.5 ± 5.2
velocity (m/s)	38 – 58	38	47.5 ± 4.0			47.4 ± 5.6
Median F-wave	21.6 – 29.8	29.3	25.3 ± 1.6		24.9 ± 1.5	25.4 ± 2.2
Ulnar F-wave	21.8 – 31.2	30.3	25.8 ± 1.8		25.3 ± 1.7	25.0 ± 2.1
Peroneal F-wave	37.5 – 52.8	52.8	45.0 ± 3.1		43.9 ± 3.4	44.7 ± 3.7
Tibial F-wave	38.1 – 52.9	53.3	46.0 ± 2.9		44.6 ± 3.5	45.0 ± 4.8
H-reflex	24.3 – 32.0	32.4	28.4 ± 1.6		27.7 ± 2.0	27.6 ± 1.8

SD: standard deviation; *Reciprocal transformation; †Square root transformation; ‡Log transformation; §The reference limits were derived from the mean ± 2.5 SD of the optimally transformed data and by converting these endpoints back to original units, or mean ± 2.5 SD of the raw data if they followed a normal distribution; ‖Before transformation to normal distribution; ¶Data from right side nerve study;

The distance of distal stimulation was obtained by anatomical landmark in Reference[13].

The distance of distal motor stimulation was obtained by 8 cm proximal to recording in reference[15].

The distance of sensory nerve conduction study was obtained by 14 cm proximal to recording in Reference[15].

The result in this table represented a primary data. The data has not correlated with any factors yet.

Age also showed a moderate correlation in the median NCS and mild correlation in ulnar NCS. Height was moderately correlated with median SNCV and substantially correlated with all F-wave and H reflex studies, while weight was moderately correlated with the square root of ulnar SNAP, F-wave, and H reflex studies.

The equations built from regression analysis and squared correlation coefficient (r^2) of NCS were listed in

Table 3. Effects of sex, age, height, and weight on nerve conduction parameters in the study subjects by correlation and multiple regression analysis (n = 101)

Study	Correlation coefficient (r)			
	Gender	Age	Height	Weight
Motor nerve conduction study				
Median nerve				
reciprocal distal latency		-0.303*		
amplitude	-0.216*	-0.367*	0.268*	0.208*
reciprocal velocity		0.477*		
Ulnar nerve				
reciprocal distal latency	0.193*			
amplitude	-0.210*		0.147†	
velocity	0.179*	-0.233*		
Peroneal nerve				
reciprocal distal latency				
square root amplitude	-0.294*	-0.284*	0.290*	
reciprocal velocity	-0.289*	0.239*	0.198*	
Tibial nerve				
reciprocal distal latency				
amplitude		-0.392*	0.155†	
reciprocal velocity		0.223*		
Sensory nerve conduction study				
Median nerve				
square root amplitude	0.237*	-0.488*		-0.195*
velocity	-0.191*	-0.314*	0.336*	0.206*
Ulnar nerve				
square root amplitude	0.400*	-0.237*	-0.233*	-0.343*
velocity				
Sural nerve				
log amplitude	-0.160†	-0.258*		
velocity	-0.161†			0.180*
Late response				
median F-wave*	-0.526*	0.155†	0.500*	0.392*
ulnar F-wave	-0.598*		0.630*	0.422*
peroneal F-wave	-0.303*		0.665*	0.406*
tibial F-wave	-0.320*		0.648*	0.450*
H-reflex	-0.335*	0.245*	0.573*	0.443*

* Correlation is significant at the 0.01 level; † Correlation is significant at the 0.05 level.

Table 4. Age was the most important factor. Subjects with older ages had longer median DML, reduced median, peroneal and tibial CMAP, and slower median, ulnar and tibial MNCV than those with younger ages. Females had faster ulnar MNCV and smaller peroneal CMAP than males. The highest value (r^2 = 0.228) of squared correlation coefficient was the reciprocal median MNCV. Age, gender, and body weight were the most important factors in sensory NCS. Subjects with higher age had smaller amplitude. Females had higher amplitude than males. Subjects with higher weight had smaller SNAP recording in median and ulnar sensory studies than subjects with lower weight. Older and taller subjects had slower median SNCV, while heavier (higher weight) subjects had slower sural velocity than lighter subjects. The highest two of squared correlation coefficient in

Table 4. *Multiple regression analysis of gender, age, height, and weight for nerve conduction, F-wave, and H reflex studies to build the equations*

Studies	Equation	R^2
Median motor nerve study		
reciprocal distal latency	$= 0.341 - 0.001 \times \text{age}$	0.092
amplitude	$= 13.548 - 0.064 \times \text{age}$	0.182
reciprocal velocity	$= 0.016 + 0.00003 \times \text{age}$	0.228
Ulnar motor nerve study		
velocity	$= 63.676 - 0.069 \times \text{age} + 1.292 \times \text{gender}$	0.089
Peroneal motor nerve study		
square root amplitude	$= 2.294 - 0.01 \times \text{age} - 0.244 \times \text{gender}$	0.163
Tibial motor nerve study		
amplitude	$= 20.301 - 0.147 \times \text{age}$	0.155
reciprocal velocity	$= 0.02 + 0.00002 \times \text{age}$	0.050
Median sensory nerve study		
square root amplitude	$= 10.173 - 0.054 \times \text{age} - 0.016 \times \text{weight} + 0.423 \times \text{gender}$	0.315
velocity	$= 35.3 - 0.107 \times \text{age} - 0.171 \times \text{height}$	0.161
Ulnar sensory nerve study		
square root amplitude	$= 8.765 - 0.029 \times \text{age} - 0.023 \times \text{weight} + 0.761 \times \text{gender}$	0.249
Sural sensory nerve study		
log amplitude	$= 1.441 - 0.004 \times \text{age} - 0.059 \times \text{gender}$	0.090
velocity	$= 43.568 + 0.063 \times \text{weight}$	0.032
Median F-wave	$= -0.753 \times \text{gender} + 560.518 \times \text{reciprocal velocity} + 0.094 \times \text{height} + 0.02 \times \text{age}$	0.471
Ulnar F-wave	$= 17 + 0.11 \times \text{height} - 0.137 \times \text{velocity} - 0.978 \times \text{gender}$	0.523
Peroneal F-wave	$= -30.188 + 0.315 \times \text{height} + 1019.701 \times \text{reciprocal velocity} + 2.245 \times \text{gender} + 0.034\ \text{weight}$	0.594
Tibial F-wave	$= -17.848 + 0.27 \times \text{height} + 839.175 \times \text{reciprocal velocity} + 1.179 \times \text{gender} + 0.016 \times \text{weight}$	0.574
H reflex	$= -6.192 + 0.184 \times \text{height} + 0.069 \times \text{age} + 0.874 \times \text{gender} + 0.018 \times \text{weight}$	0.573

1. Female and male gender were considered to be 1 and 0 in the above equation, respectively.
2. distal latency (ms), motor amplitude (mV), sensory amplitude (μV), velocity (m/s), height (cm), age (years), weight (Kgw), and F-wave (ms).
3. The factor of motor nerve conduction velocity was not included in the analysis study of H reflex study.
4. The motor nerve conduction velocity mean the correspondence nerve to the same nerve name of F-wave study.

parameters of sensory nerve study were the square root of SNAP in median ($r^2 = 0.315$) and ulnar ($r^2 = 0.249$) NCS.

The equations built from regression analysis and squared correlation coefficient (r^2) of F-wave and H reflex studies were listed in Table 4. Except for velocity, height and gender were the most important factors in F-wave studies, where taller subjects had longer latency while subjects with slower velocity had longer latency of the F-wave than shorter subjects. Females had shorter latency in upper limbs F-waves and longer latency in lower limbs F-waves than males. Older subjects had longer latency in median F-wave study than younger subjects, while those with higher weight had longer latency of H reflex, median, peroneal, and tibial F-waves studies than those with lower weight. The squared correlation coefficient in the median ($r^2 = 0.471$), ulnar ($r^2 = 0.523$), peroneal ($r^2 = 0.594$), tibial ($r^2 = 0.574$) F-wave and H reflex ($r^2 = 0.573$) studies fell within the regression line of real data points.

DISCUSSION

In previous reports, gender differences in some NCS can be largely explained by height, although amplitude differences still persisted despite the correction for height, temperature, and age factors[1]. In the current report, females have higher sensory amplitude in median and ulnar nerve studies than males, similar to previous reports[1-4]. The explanation for the above findings is unknown. Nonetheless, possible cause of gender differences in median and ulnar sensory amplitude study may be related to smaller finger circumference in females[2-4]. This is found in previous reports and the current results by anti-dromic studies, but not in orthro-dromic sensory nerve studies[18]. The lower subcutaneous tissue in fingers closer to the recording of sensory response in females can explain the higher SNAP than males[2].

Gender is also a significant factor in F-wave and H reflex studies. The female gender has a negative correlation with the latency of F-wave and H reflex studies in Table 3. While gender shows a positive correlation with peroneal, tibial F-wave, and H reflex studies after the adjustment of height, it still has a negative correlation with median and ulnar F-wave studies after the adjustment of other factors (Table 4). This finding is similar to a previous report involving ulnar and tibial F-wave studies[9].

Because of the possible effects of nerve degeneration on aging, older subjects have longer distal latency, smaller CMAP and SNAP, slower NCV, and longer latency of late responses than younger subjects. Decreased nerve fibers, reduction in nerve diameter, and change in fiber membrane are also attributable factors of age[2,12]. Age is also an important factor of NCS in this study. Changes in age on NCS are greater in the median than in the ulnar nerve. The results are compatible with a report on two time-point paradigms to investigate median and ulnar sensory NCS[5]. The effect of age on F-wave latency is reported to increase 0.03 ms/year in the upper and 0.1 ms/year in the lower limbs[8]. In Table 4, the results show a significant effect of age only on F wave latency in the median F-wave by increasing 0.02 ms/year ($r^2 = 0.471$). Age is an important factor in H reflex by increasing 0.07 ms/year ($r^2 = 0.573$).

Height is the most important factor in F-wave and H reflex studies. Logically, taller subjects have longer conduction time of late response because of longer conduction distance. The results here have a substantial correlation between the height and the latencies of F-waves and H reflex studies. Previously, F-wave latency has been reported to increase with height by 0.2 ms/cm in the upper and 0.4 ms/cm in the lower limbs[9]. By adding the factor of motor nerve conduction velocity in these analyses, the squared correlation coefficients were increased in F-wave studies in a previous report[10]. The results here show an increase of around 0.1 ms/cm in the upper and 0.3 ms/cm in the lower limbs' minimal latency of F-wave studies after including velocity in the equation. This is not far from the previous report of 0.16 ms/cm, 0.2 ms/cm, and 0.26 ms/cm in the ulnar, peroneal, and tibial F-wave studies, respectively, by including velocity for building the equation[10]. The H reflex has been conducted by increasing 0.18 ms per centimeter of height.

Subjects with larger weights have lower SNAP amplitudes than those with smaller weights. These are statistically found in the SNAP of median and ulnar sensory nerve studies. The result here may be explained by the attenuation in amplitude by thicker subcutaneous tissue in fat individuals[11]. Weight shows a substantial correlation with latencies of F-wave and H reflex, where individuals with higher body weights have longer latencies of the median, peroneal, tibial F-wave, and H reflex studies compared to those .with lower body weights.

There have been several reports about the correlations between these factors and NCS in Taiwan[13-15]. The first report to evaluate motor NCS included 370 persons but only 34 without neurological problem[13]. The second and third studies enrolled 50 and 58 healthy subjects for analysis, respectively[14,15]. Shorter distal latency (ulnar and tibial), higher amplitude (median and tibial), and faster velocity (ulnar and tibial) were evident in younger age group than in the older groups[13]. The age factor was negatively correlated to the amplitude in both motor and sensory NCS and velocity in motor NCS[15]. The F-wave and H reflex were positively correlated to age[14] and height[14,15] but negatively correlated to velocity[14]. In our study, we enrolled the data from persons with negative symptoms and signs in neurological evaluation. We analyzed these data from 101 persons by multiple linear regression analysis and built the equation for analysis. Our study provided extensive information in the correlation between these factors than previous studies in Taiwan, especially in the factor of gender, body height, and weight.

In summary, this study shows that factors of gender, age, height, and weight influence results of late responses and NCS. Except for motor velocity, height and gender are important factors in F-wave studies while height and age are important in H reflex study. Age and gender are important factors in motor NCS. The equation on late response shows higher squared correlation coefficient than NCS. Without adjustments for these factors, the sensitivity and specificity of NCS will decrease when using the same reference data in patients with different gender, age, height, or weight.

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