

EFFECT OF AGE AND BODY MASS INDEX ON SENSORY NERVE CONDUCTION

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ABSTRACT

BACKGROUND

Nerve Conduction Study (NCS) and Needle Electromyography (EMG) are the main electrodiagnostic assessments for peripheral nerves. Nerve conduction study helps in knowing the extent and distribution of neural lesions. The sensory nerves studied in the lower limb are the sural nerve and the common peroneal nerve. The sensory nerve dysfunctions usually start in the lower limbs. Sural nerve study in systemic illness like diabetes mellitus shows axonal neuropathies. It also has higher diagnostic value. Aging is the process of becoming older, a process that is genetically determined and environmentally modulated. As age increases the nerve conduction velocity decreases. Along with age, Body Mass Index (BMI) is also an important factor to be taken into consideration.

The objective of the study is to assess the effect of age and BMI on sensory nerve conduction study.

MATERIALS AND METHODS

The study was conducted in the department of physiology. The study protocol was approved by the institutional ethics committee. A written informed consent was obtained from each participant. The criteria for considering the volunteers were- Body Mass Index (BMI) between 18.5-35 and age group between 21-65 years.

Statistical Analysis- One-way ANOVA test was used to find the statistical significance between the groups. The data was analysed using the SPSS software. Group statistics was done and expressed as Mean±SD.

RESULTS

The results of sensory nerve conduction velocities were statistically significant when comparison was done between lesser age group with higher age group and lesser BMI with higher BMI (P <0.05).

CONCLUSION

Since the parameters recorded show slowing of nerve conduction velocity, we suggest that obesity and age has some deleterious effect on axonal functions. So, while doing nerve conduction studies in persons with advanced age and higher BMI, these parameters must be taken into consideration.

KEYWORDS

Nerve Conduction, Age, Body Mass Index.

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BACKGROUND

Nerve conduction study (NCS) and needle electromyography (EMG) are the main electrodiagnostic assessment for peripheral nerves.¹ Nerve conduction study includes study of three types of nerves such as motor, sensory and mixed nerve. The sensory Nerve conduction study mainly includes the recording of sensory nerve action potential (SNAP).² Nerve conduction study helps in knowing the extent and distribution of neural lesions. It also helps to differentiate the two groups of peripheral diseases such as axonal degeneration and demyelination.³ The sensory nerves commonly studied in the lower limb are the sural nerve and

the common peroneal nerve. They supply the muscles of lower limb and also the cutaneous sensation of the lower limbs.⁴ The sensory nerve dysfunctions usually starts in the lower limbs. Sural nerve study in systemic illness like Diabetes mellitus shows axonal neuropathies. It also has higher diagnostic value.⁵ The peripheral motor and sensory functions are assessed by recording the evoked response to electrical stimulation of peripheral nerves. In sensory nerve conduction study, a mixed nerve stimulation is performed.⁶ Clinically these studies are done to identify the location of peripheral nerve disease in single nerves and along the length of nerves and also to differentiate these disorders from diseases of muscle/ neuromuscular junction.¹ Aging is the process of becoming older, a process that is genetically determined and environmentally modulated.⁷ As age increases the nerve conduction velocity decreases. Along with age, Body Mass Index (BMI) is also an important factor to be taken into consideration. BMI is an index of body's visceral and abdominal fat overwhelming excessive fat in the body especially the abdominal fat which is an extreme and overwhelming source of free fatty acids, leading to the clinical state called hyperlipidaemia. Free fatty acids trigger

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the onset of oxidative stress in obese subjects and hypertensive subjects.

Slowing of the nerve conduction velocity can occur by two main mechanisms one occurring as an outcome of demyelination, observed as latency changes in NCS recordings. The second phenomenon is by axonal degeneration observed as a decline in amplitude changes in NCV tests. Both these conditions are significantly affected by oxidative stress, a factor that commonly occurs with increasing BMI and age.

With the above background, this study is mainly concerned to explore the effect of age and BMI on sensory nerve conduction velocity especially the sural nerve in lower limb, because sensory nerve conduction study has been less explored.

MATERIALS AND METHODS

The study was conducted in the department of Physiology. The study protocol was approved by the Institutional ethical committee. A written informed consent was obtained from each participant. The study was done in 50 volunteers between the age group of 21-65 years, which included both males and females.

Selection of Subjects

The criteria of considering the volunteers were with Body Mass Index (BMI) between 18.5-35 and age group between 21-65 years.

Exclusion Criteria

The volunteers with any associated diseases like Diabetes, peripheral vascular diseases, pregnancy, tobacco users, smoking and terminally ill patients which are known to cause peripheral neuropathy were excluded from the study.

Establishment of Anthropometric Measures

Anthropometric measures like height, weight and BMI were measured. Height was measured in barefoot by asking the subject to look forward and stand vertically near the wall where the wall fixed stadiometer is placed. Then a flat head piece was placed over the head and formed a right angle with the wall and the reading was taken. Body weight was recorded to the nearest fraction of 0.1 kg by using a portable weighing machine. Body Mass Index was calculated as the weight in kilograms divided by the square of the height in meters (kg/m²) using standard protocol.

Nerve Conduction Study Evaluation

Nerve conduction study on sural nerve of left lower limb was done on RMS EMG machine.

Sensory Sural Nerve Conduction Procedure

The procedure was explained to each subject to ensure maximum comfort and compliance. The sural nerve on left side were sampled. The tests were done on a electromyograph with the following acquisition parameters: Filter settings at 3 Hz to 2 kHz, sweep speed of 20 ms, and gain of 10 microvolt (µV)/division. Lower limb temperature

was recorded at the lateral malleolus and was maintained at 30°C. The temperature was measured before, during, and after the recording.

The patient was placed in a comfortable lateral decubitus with the leg to be assessed on the top. To ensure maximum electrical conductance the recording and stimulating sites were cleaned with spirit. The active recording electrode was placed just behind the upper border of lateral malleolus and the reference electrode was placed 4 cm distal to it. The recording sites were marked at distances of 14 cm, 12 cm, and 10 cm proximal to the active electrode. The ground electrode was then placed between the stimulating and recording sites. A supramaximal stimulus was used to obtain the maximum amplitude sural SNAP with the least stimulus artifact. The stimulating electrode was moved slowly from the midline of the calf laterally or medially till a maximum SNAP was obtained at each site of stimulation. Care was taken to reduce the stimulus artifact by relative rotation of the anode or reduction of stimulus intensity, without altering the amplitude of the response. Each optimal SNAP was then averaged for at least 8-10 responses to ensure a clear onset from the baseline. The stimulus pulse duration was increased from the standard 0.1 ms to 0.2 ms in case the subjects had large calves, in the obese subjects.

Statistical Analysis

One-way ANOVA test was used to find the statistical significance between the groups.

RESULTS

The mean age and BMI were 48.22 ± 11.00, and 25.63 ± 5.70 (kg/m²) respectively. The mean conduction velocity of sural nerve is 32.46 ± 1.05. The results of sensory nerve (sural) conduction velocity were statistically significant between lesser age group with higher age group when compared to lesser BMI with higher BMI. (P<0.05)

Age (Years)	
Group 1: 21-35	
Group 2: 36- 45	
Group 3: 46-55	
Group 4: 56-65	
BMI (Kg/m²)	
Group 1: 18.5-24.9	
Group 2: 25 – 29.9	
Group 3: 30 – 35	

Table 1. Showing Different Age and BMI Groups

Age Groups (Years)	Frequency (N= 50)	Percentage (%)
Group 1 (21-35)	8	16
Group 2 (36- 45)	17	34
Group 3 (46- 55)	3	6
Group 4 (56 – 65)	22	44

Table 2a. Showing Descriptive Statistics of Age and BMI

BMI Groups (kg/m ²)	Frequency (N= 50)	Percentage (%)
Group 1 (18.5-24.9) Normal weight	24	48
Group 2 (25-29.9) Over weight	13	26
Group 3 (30-35) Obese	13	26

Table 2b. Showing Descriptive Statistics of BMI

Age Groups (Years)	Frequency (N=50)	Mean Conduction Velocity (m/s)	Standard Deviation	P Value
Group 1(21-35)	8	31.26	0.53	0.001
Group 2 (36-45)	17	32.97	0.48	
Group 3 (46- 55)	3	32.12	0.88	
Group 4 (56-65)	22	32.56	1.21	

P <0.01 which is statistically significant

Table 3a. Comparison of Different Age Groups with Sensory Nerve Conduction Velocities

Multiple Comparison of Groups Based on Age	P Value
Group 1 (21-35) & Group 2 (36-45)	0.000 *
Group 1 (21-35) & Group 3 (46-55)	1.000
Group 1 (21-35) & Group 4 (56-65)	0.007 *
Group 2 (36-45) & Group 3 (46-55)	0.867
Group 3 (46-55) & Group 4 (56-65)	1.000
Group 4 (56-65) & Group 2 (36-45)	1.000

Table 3b. Multiple Comparison of Age Groups with Conduction Velocity

Table 3a shows that the conduction velocity was statistically significant in the age groups 1 and 2 (P <0.01) as well as in group 1 and 4 (P <0.05).

Dependent variable: conduction velocity.

BMI Groups (kg/m ²)	Frequency (N=50)	Mean Conduction Velocity (m/s)	Standard Deviation	P Value
18.5-24.9	24	32.88	0.76	0.004
25-29.9	13	32.44	1.04	
30-35	13	31.71	1.18	

P <0.05 which is statistically significant

Table 4a. Comparison of Different BMI Groups with Sensory Nerve Conduction Velocities

Multiple Comparison of Groups Based on BMI	P Value
Group 1 & Group 2	0.569
Group 1 & Group 3	0.003 *
Group 2 & Group 3	0.175

Table 4b. Multiple Comparison of BMI Groups with Conduction Velocity

Dependent variable: conduction velocity.

Table 4b shows the conduction velocity was statistically significant in groups 1 and 3.

DISCUSSION

This study is aimed to study the effect of age and Body mass index on sensory nerve conduction. A statistically significant differences were found in the sensory nerve conduction with increased age and Body mass index when compared to decreased age and BMI.

Molecular Aspects of Aging Mechanisms on Nerve Conductivity

Advancing age, mediates changes in the vasculature function and structure destruction. In precise, modification in endothelial cell functions relates to alter the expression and release of the vasoactive mediators such as nitric oxide and endothelin-1.⁸ Additionally antithrombotic and vasodilatory function of the endothelium decline with age, while inflammatory processes and oxidative stress increases. This process is enhanced with the presence of cardiovascular risk factor such as hypertension, appears to happen at an earlier age when compared to normal subjects.⁹

Nitric oxide levels is vital for the endothelial membrane integrity and its function. The biological levels of Nitric oxide diminish with age leading to dysregulated vascular nature thus promoting proatherosclerotic and prothrombotic environment.^{10,11,12} Different studies based on animal models, and clinical trials have accumulated evidence proving that aging augments production of reactive oxygen species (ROS) in several tissues that includes the endothelium.^{13,14}

Aging induced vascular oxidative stress appears to be connected with a worldwide increased pro-oxidant setting represented by augmented expression of inducible nitric oxide synthase,¹⁵ NAD(P)H oxidases¹⁶ and a down-regulation of antioxidant systems such as the superoxide dismutases.¹⁴ The increased ROS production observed with increased aging mediates a massive amount of detrimental effects. Critical functional importance of increased ROS production is to scavenge nitric oxide by superoxide (O₂⁻) to synthesize peroxynitrite (ONOO⁻).^{17,18} ONOO⁻ is labile that easily penetrates the phospholipid membrane and produces substrate nitration, thereby inactivating vital regulatory receptors, and enzymes mainly antioxidants that scavenge free radicals.¹⁹

The extreme decrease in nitric oxide levels during aging is aggravated by the endothelial nitric oxide synthase expression and reduced levels of intracellular L-arginine.²⁰ Recent findings propose that nitric oxide production declines

with aging that ultimately enhances endothelial cell apoptosis.²¹

The accelerated production of ROS giving rise to superoxide anion (O₂⁻), hydroxyl radicals, hydrogen peroxide and/or reactive nitrogen species, like peroxynitrite (ONOO⁻), observed with aging is not only thought to be implicated in nitric oxide scavenging; but is directly implicated in the upregulation of pro-inflammatory processes, like activating NF- κ B (Nuclear Factor) that transcribes inflammatory factors, that activate the macrophages.²²

Telomeres serves as important marker in cellular senescence and vascular aging.²³ Telomeres are DNA-protein complexes found at the ends of chromosomes and important for replication mechanisms. They are observed to be shortened in senescent cells as a consequence of mitochondrial ROS overproduction. In this setting, telomerase reverse transcriptase (TERT) is phosphorylated by src kinase that exports TERT from the nucleus to the cytoplasm.^{24,25} During DNA replication and cell division telomeres in chromosomes are shortened. This process is usually compensated by TERT. Aging-induces a lack of nuclear TERT activity leading to cellular senescence that occurs as a consequence of excessive telomere shortening, resulting in chromosomal instability that leads to the onset of apoptosis.

Apoptosis not only occurs in the vascular cells but can occur in the nervous cells also.²⁶

Demyelination and Neuronal cell loss are processes that occur during aging and these processes culminate into cognitive function decline in the central nervous system and these studies are well documented.²⁷ However age-related changes in the peripheral nervous system have very little accounting as clinical and rat model studies. The impact of oxidative stress has been acknowledged to affect peripheral nerves in rat model studies²⁸ and clinically well documented in diabetic neuropathy.²⁹

A study done by Pawar SM, to know the effect of BMI on parameters of nerve conduction study in Indian population showed prolongation of distal motor latency with increasing Body mass index except in motor peroneal nerve. Motor and sensory conduction velocity showed non-significant slowing along with increasing Body mass index except sural nerve and motor-sensory ulnar nerve in younger age group. Their study also demonstrated that various parameters of nerve conduction study can be affected by Body mass index (BMI).³⁰ This study is in relation with our study which showed significant changes in sensory conduction velocity. SA Mohammed et al observed that slowing of conduction velocities with increasing age and BMI (except ulnar sensory velocities) and no demonstrable trend is seen across different height groups except in common peroneal nerve.³¹ We also observed a similar trend of velocities with increasing age and BMI in sural nerve. A case control study with 83 subjects revealed the presence of median mononeuropathy which is associated with increased Body mass index. The study was concluded showing that the obesity was a strong independent risk factor in slowing of

median nerve conduction.³² This study is in association with our study which indicates Body mass index as a risk factor in slowing of sensory nerve conduction. Ghugare studied the impact of age, height, weight and body mass index on sural sensory and soleus H- reflex study measures in healthy central Indian population and observed that there is no correlation between anthropometric measures and sural nerve conduction velocity. Only conduction velocity was studied in their study.³³ Another study done by Senthilkumari et al showed significant correlation between age and median motor and sensory conduction velocities. This study was concluded by proving that age has definite correlation with the nerve conduction study in median and motor and sensory nerves.³⁴ Dorfman and Bosely has done a study in 30 normal subjects (15 young and 15 older adults) and found that there is a decrease in nerve conduction velocity of 0.16 m/s per year of age.³⁵

Friedrich B and Fritz B³⁶ et al. conducted a study on healthy individuals in the age range of 15 to 72 years. The study established the normal values for the distal and proximal segments for superficial peroneal, sural and posterior tibial nerve. The values were obtained from 71 healthy subjects. The authors present electronic averaging that was used to analyse the slope of the potentials. It was observed that distal values (lower extremities) were one tenth of those measured at the proximal end (upper extremities). The values 56.5 \pm 3.4 m/sec was observed at the proximal segment and 46.1 \pm 3.7 m/sec at the distal segment of the nerves. These values were observed as the maximum sensory conduction velocity in age range of 15 to 30 years. With increasing age (40 to 65 years) shows slowing of conduction both proximally and distally (53.1 \pm 4.6 m/sec, proximal conduction velocity; 42.5 \pm 5.5 m/sec distal conduction velocity). As observed in the arms the nerves of the legs also presented a decline in the maximum conduction velocity proximally and distally in the age range of 40-65 yrs. when compared to the age range of 15 to 30 yrs. This study clearly indicates that increase in age can induce decline in nerve conduction velocity.

Another study done to assess the influence of age, height and BMI was done by Awang MS et al. The methodology included 250 healthy Malaysian subjects who were hospital staff and students with no evidence of neuromuscular or musculoskeletal diseases. The subjects were subdivided based on age, BMI and height. NCV test was done in all the subjects and, the nerves tested were Median, Ulnar, Common peroneal and sural nerves (both right and left). They observed slowing of NCVs with increasing BMI in the median nerve (both sensory and motor conduction). The NCV of the motor conduction of the Ulnar nerve also showed a similar pattern as observed in the median nerve. Whereas, the sensory nerve conduction of the ulnar nerve did not show any changes. Slowing of nerve conduction velocity with increasing BMI was also observed for the common peroneal and sural nerve. The study showed that height did not affect the nerve conduction velocity, since they could not establish slowing of nerve conduction velocity across varying heights for the nerves they studied

except for the common peroneal nerve. Thus, they conclude the study by saying that age and BMI do have a definite impact on nerve conduction velocity.

Our findings are supported by clinical studies of Henry C. et al,³⁷ who has studied the effect of aging on sensory nerve conduction parameters and has presented that sensory nerve conduction velocity does change with aging.

CONCLUSION

With increase in age, there is slowing of sensory nerve conduction velocity which may be due to decrease in number of fibers, or reduction in the fiber diameter and changes in the fiber membrane. Also, with increase in the body mass index, the adipose tissue which is deposited in the epineurium may affect the nerve conduction velocity to some extent. Since the parameter recorded shows slowing of nerve conduction velocity, we suggest that obesity and age have some deleterious effect on axonal functions. So, while doing nerve conduction studies in persons with advanced age and BMI, these parameters have to be definitely taken into consideration.

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