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Motor Unit Number Estimation in Idiopathic Parkinson's Disease

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ABSTRACT

Motor unit number estimation in Idiopathic Parkinson's disease

Objective: Motor neuron degeneration in parkinsonism is known to develop in Western Pacific (Guam) parkinsonism-amyotrophic lateral sclerosis complex, multisystem atrophy (MSA), postensefalitic parkinsonism, Creutzfeld-Jacob disease and dementia with parkinsonism linked to chromosome 17. Existence of motor neuron degeneration in these disorders brings up the question whether motor neuron degeneration develops in Idiopathic Parkinson Disease (IPD). Our study aims to answer this question.

Methods: In this study, we estimated the motor unit counts in 24 patients diagnosed as IPD and 26 healthy control subjects with similar age (50-70) and gender, using threshold method.

Results: Our study revealed the motor unit counts, done using threshold method, in IPD patients in thenar muscles were not different from the control group subjects.

Conclusion: This result implied that there was not asymptomatic motor neuron degeneration in IPD, and IPD did not share the same physiological mechanism with other parkinsonism related disorders associated with motor neuron degeneration. However, since there are limited numbers of publications on this subject, to verify this conclusion, further studies using similar methods, with larger patient groups are needed.

Key words: Parkinsonism, motor unit, motor neuron degeneration

ÖZET

İdiyopatik Parkinson hastalığında motor ünite sayısı değişimi

Amaç: Parkinsonizmde motor nöron dejenerasyonunun Batı Pasifik (Guam) parkinsonizmi- Amiyotrofik Lateral Skleroz kompleksinde, Multisistem atrofisinde (MSA), postensefalitik parkinsonizmde, Creutzfeldt-Jakob hastalığında ve kromozom 17 ile bağlantılı demans-parkinsonizminde oluştuğu bilinmektedir. Bu hastalıklardaki motor nöron dejenerasyonunun varlığı, İdiyopatik Parkinson Hastalığı (İPH)'nda da motor nöronlarda dejenerasyonun olup olmadığı sorusunu akla getirmekte olup, çalışmamız bu soruya yanıt verebilmeyi amaçlamaktadır.

Yöntem: İPH tanısı almış 24 hasta ve benzer yaş (50-70 yaş) ve cinsiyette 26 kişilik kontrol grubunda, eşik değer yöntemi ile tahmini motor ünite sayısı hesaplanmıştır.

Bulgular: Eşik değer yöntemi ile İPH hastalarının tenar kaslarında, normal kontrol grubuna göre motor ünite sayısında bir farklılık olmadığı görülmüştür.

Sonuç: Çalışmamız, İPH'de asemptomatik bir motor nöron dejenerasyonu bulunmadığını ve İPH'nin, parkinsonizmle birlikte motor nöron dejenerasyonu görülen hastalıklarla aynı fizyopatolojik mekanizmayı paylaşmadığını ortaya koymuştur. Bununla birlikte, literatürde bu konuda yapılmış az sayıda çalışma mevcuttur ve benzer yöntemlerle geniş örneklemler üzerinde yeni çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Parkinsonizm, motor ünite, motor nöron dejenerasyonu

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INTRODUCTION

Neuronal and synaptic loss and consequent degeneration in the central nervous system, affecting selectively one or more functional system and progressive nature are main characteristics of neurodegenerative disorders (1-3). Alzheimer's and Pick's diseases, Huntington's disease, idiopathic Parkinson's disease, MSA and amyotrophic lateral sclerosis are examples of neurodegenerative diseases. It is known that

more than one region of the nervous system are involved in these diseases. However, clinical symptoms caused by degeneration at other regions are not as much evident as symptoms from regions principally affected. For this reason, it is important to examine nervous system regions less affected in order to explain possible common mechanisms of neurodegenerative diseases (1-9).

Concomitant Parkinsonism and motor neuron degeneration is seen in West Pacific (Guam) parkinsonism- amyotrophic lateral sclerosis complex, MSA, postancephalitic parkinsonism, Creutzfeldt-Jakob disease and chromosome 17 associated dementia-parkinsonism (1,3-5,7-12). Mild increase in motor unit potential duration and decrease in number of motor units were found in two separate studies and these findings were reported to be consistent with lower motor neuron involvement (4,5,13). In another study, increase in motor unit duration in anal sphincter electromyography for differential diagnosis of MSA and IPH was reported to be in favor of MSA (14).

In our study, we aimed to investigate whether there is asymptomatic motor neuron degeneration through assessment of estimated number of motor units (ENMU) calculated using the threshold value method in IPH.

MATERIAL AND METHODS

This study was done with 24 patients diagnosed as IPH and followed by Movement Disorders Unit of Bakırköy Research and Training Hospital for Psychiatry, Neurology and Neurosurgery and age and gender matched 26 healthy controls . Ethical council approval and informed consents of all participants were obtained. Control and patient groups were selected between the ages of 50 and 70.

Neuromuscular disease, diabetes, previous spinal surgery, chronic low back pain and radicular symptoms, numbness, paresthesias, fasciculation or history of weakness were taken as exclusion criteria. A detailed neurological examination was done for both patient and control groups consistent with pre-determined criteria, nerve conduction studies were performed and selected to receive zero score for neuropathic symptoms and neurological impairment.

Diagnosis was based on clinical Parkinson's disease (PD) criteria developed by British Parkinson's Disease Society Brain Bank. Motor score of Unified Parkinson's Disease Rating Scale (UPDRS) was recorded when patients were at "on" state. Electromyographic studies were done by the same person by using Keypoint EMG device (Dantec, Skovlunde, Denmark; version 3.0.0).

Motor and sensorial nerve conduction studies were performed in upper limbs and in lower limbs, sensorial conduction studies were performed in sural nerve and motor conduction studies were performed in tibial and peroneal nerves and also concentric needle electromyography was performed in both upper and lower limbs.

Motor Unit Number Estimation (MUNE) term was first described by McComas and Fawcett in 1971 (15). Number of motor units defines number of anterior horn cells controlling a single muscle or number of axons innervating that muscle (16-19). Motor unit loss can be seen in specific anterior horn diseases such as amyotrophic lateral sclerosis, polio and post-polio syndrome and spinal muscular atrophy and polyneuropathy affecting motor fibers, radiculopathy and entrapment neuropathies (16,18-20).

Incremental stimulus (threshold value), multiple point stimulation, spike-triggered averaging, statistical method, automatic incremental stimulation, F wave, intraneural microelectrode stimulation, integrated root mean square and motor unit index technique are techniques used in MUNE calculation. Due to technical specifications of Keypoint EMG (Dantec, Skovlunde, Denmark; version 3.0.0) device used in our study, threshold value technique was performed.

In thereshold value method, MUNE was calculated by a "threshold area" formula using area of supramaximal compound muscle action potential (CMAP) and area from lowest stimulus power producing a measurable response. For MUNE, abductor pollicis brevis muscle was selected in upper limbs. Recording smooth superficial electrode was placed on abductor pollicis brevis muscle between metacarpophalangeal joint of thumb and distal wrist line (over motor area) and reference electrode was placed on proximal phalanx of thumb. Stimulating electrode was placed at 8 cm. proximal of recording electrode and anode

was palced 2 cm. proximal to cathode. Ground electrode was placed between stimulating and recording electrodes, at flexor part at wrist level.

In MUNE calculation with threshold value method, first CMAP area value was found through supramaximal nerve stimulation. Mean area value of a single motor unit potential was calculated afterwards. Median nerve was stimulated in 10 consecutive steps by increasing the stimulus magnitude for this calculation. Increase in the area of motor unit potential at each step was calculated by subtraction of area of previous trace from area of last trace. To accept the difference between two consecutive traces as a single motor unit potential, the conditions of being electronegatively initiated, having fixed pattern, being repetitive and consistent with "all or nothing" rule were required. Mean area of a single motor unit potential was calculated by subtracting the area of motor unit potential of the first step from area of motor unit potential of the following step and dividing it to number of steps. In conclusion, estimated number of motor units was calculated by dividing area of compound muscle action potential to area of single motor unit potential.

Statistical Analysis

Descriptive statistics (mean, median, standard deviation) were used for all data collected from patient and control groups. For the comparison of two groups; normally distributed data (velocity and distal latency) were compared by parametric (student's t-test) and data not distributed normally (amplitude values) were compared by non-parametric tests (Mann Whitney-U). Gender and age of patient and control groups were compared by non-parametric tests (Chi-square and Mann Whitney-U). MUNE, mean step area and maximum CMAP amplitudes from both patient and control groups were compared by non-parametric tests. Statistical significance was taken as $p<0.05$.

RESULTS

There were 26 participants at the control group (12 men, 14 women; mean age 59.2±4 years) and 24 patients at the Parkinson's group (13 men,11 women; mean age 61.8±5.2 years) and mean duration of symptoms was 5.5 years.

There was no statistically significant difference between the control group and Parkinson's group for age and gender distribution ($p>0.05$).

Results of motor and sensorial conduction studies at control and Parkinson's patients are given in table 1. There were no statistically significant difference

Table 1: Comparison of sensorial and motor nerve conduction values in idiopathic Parkinson's disease and control groups

	Control Group (n=26) Mean±S.D.	Parkinson's Group (n=24) Mean±S.D.
Median		
Motor proximal amplitude	8.7±1.7 µV	8.4±1.4 µV
Motor distal amplitude	8.2±1.8 µV	7.7±1.5 µV
Motor distal latency	2.7±1.4 ms	3±0.4 ms
Motor velocity	59±3.6 m/s	59±4.2 m/s
Sensorial amplitude	22.7±5.2 µV	19±4.8 µV
Sensorial velocity	62±5.8 m/s	61±6 m/s
Ulnar		
Motor proximal amplitude	8.1±1.1 µV	7.9±1.6 µV
Motor distal amplitude	7.5±1.1µV	7.4±1.7 µV
Motor distal latency	2.3±0.4 ms	2.6±0.4 ms
Motor velocity	64±5.7 m/s	62±5.3 m/s
Sensorial amplitude	18±5.5 µV	16.6±4.6 µV
Sensorial velocity	63±5.4 m/s	59±5.6 m/s
Tibial		
Proximal amplitude	5.3±1.4 µV	5.3±1 µV
Distal amplitude	4.5±1.3 µV	4.5±1 µV
Distal latency	4.9±0.7 ms	5±0.7 ms
Motor velocity	49±4.8 m/s	47±2.9 m/s
Peroneal		
Proximal amplitude	3.6±0.9 µV	3.6±0.8 µV
Distal amplitude	3.1±0.9 µV	3.1±0.9 µV
Distal latency	4.4±0.6 ms	4±0.7 ms
Motor velocity	51±4.5 m/s	50±4 m/s
Sural		
Amplitude	15.9±5.1 µV	12.8±2.3 µV
Sensorial velocity	59±6.9 m/s	56±7.9 m/s

Difference between groups is not statistically significant ($p>0.05$)

Table 2: Comparison of MUNE values between idiopathic Parkinson's patients and control group

Parameter	Control Group (n=26) Mean±S.D.	Parkinson's Group (n=24) Mean ±S.D.
MUNE	124±32	120±27
Starting stimulus magnitude	26.9±14.9 mA	31.4±18.2 mA
Ending stimulus magnitude	28.5±17.7 mA	31.9±18.3 mA
Maximal M area	50.6±12.5 mVms	32±18.3 mVms
Mean step area	0.8±0.2 mVms	0.9±0.3 mVms

MUNE, Motor Unit Number Estimation
Difference between groups is not statistically significant ($p>0.05$)

between values found in motor and sensorial conduction studies of the control group and Parkinson's patients ($p>0.05$) (Table 1).

There were also no statistically significant difference of MUNE, maximum M-response area and mean step areas between the control group and Parkinson's patients ($p>0.05$) (Table 2).

DISCUSSION

Counting motor units gives information about structure and organization of brain stem and spinal cord, and innervations of muscles. It also provides working on effects of age on neuronal populations and provide important data to reveal courses of diseases which cause muscle denervation such as ALS, SMA and poliomyelitis.

Early pre-clinical diagnosis of neurodegeneration and preventing developing main clinical symptoms will gain importance while neuroprotective studies are evolving. Consequently, it will become possible to follow results of therapeutic interventions by using serial MUNEs.

Brait et al. (14) reported in their study about two sporadic Parkinsonism cases published in 1973 that they found denervation signs and motor unit changes which may be consistent with lower motor neuron involvement.

In our study, relationship between substantia nigra degeneration and other affected regions of IPH which is already known, and possible asymptomatic motor neuron degeneration was investigated and motor units were counted in IPH patients with threshold value method.

Two separate studies of Caviness et al. (4,5) about motor neuron involvement in IPH were done with 8 IPH patients and a control group of 9 people. Mean duration of IPH symptoms were 9.5 years and no statistically significant difference was found between nerve conduction studies of patient and control groups. In needle EMG, mild increase in duration of motor unit potential was observed. When motor unit numbers are considered, only MUNE in hypothenar muscles and calculated with threshold value method were found statistically significantly lower in patient group compared to controls. Caviness et al. pointed out an asymptomatic lower motor neuron involvement in IPH. However, no new study was done in the years followed and findings of our study which was developed from the same basic question and done in a larger sample of both patient and control groups did not support an asymptomatic motor neuron involvement in IPH. Differences between magnitudes of patient samples and differences between disease durations can be given in response to different findings of these two studies. Mean disease duration at the study of Caviness et al. was evidently longer from our patient group. Asymptomatic motor neuron involvement in hypothenar muscles in their group can be interpreted as that in case of longer disease duration, further spreading neurodegenaration affects motor neurons and disease duration in our patient group is inadequate for such a process . However, study was done during "on" periods and this suggests possible peak dose dyskinesias which emerge by longer disease duration. These peak dose dyskinesias might have produced errors in calculating MUNE with threshold value method and could not reach required adequacy for statistical analysis due to smaller sample.

CONCLUSION

Our study showed that there is no difference between number of motor units in thenar muscles of IPH patients and normal control group with MUNE threshold value method and this suggests that there is not asymptomatic motor neuron degeneration in IPH and IPH does not have a common pathophysiological mechanism with diseases seen with motor neuron degeneration and Parkinsonism. However, there are only a few studies done on this issue and there is a need for new studies with same methods on wider samples.

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