2017 International Conference on Rehabilitation Robotics (ICORR)
QEII Centre, London, UK, July 17-20, 2017.

Therapeutic Effects of Anti-Gravity Treadmill (AlterG) Training on Reflex Hyper-excitability, Corticospinal Tract Activities, and Muscle Stiffness in Children with Cerebral Palsy*

Sh. Parvin, *Student Member, IEEE,* A. Taghiloo, A. Irani, M. Mehdi Mirbagheri*, *Member, IEEE*

Abstract— **We aimed to study therapeutic effects of antigravity treadmill (AlterG) training on reflex hyper-excitability, muscle stiffness, and corticospinal tract (CST) function in children with spastic hemiplegic cerebral palsy (CP). Three children received AlterG training 3 days per week for 8 weeks as experimental group. Each session lasted 45 minutes. One child as control group received typical occupational therapy for the same amount of time. We evaluated hyper-excitability of lower limb muscles by H-reflex response. We quantified muscle stiffness by sonoelastography images of the affected muscles. We quantified CST activity by transcranial magnetic stimulation (TMS). We performed the evaluations before and after training for both groups. H response latency and maximum M-wave amplitude were improved in experimental group after training compared to control group. Two children of experimental group had TMS response. Major parameters of TMS (i.e. peak-to-peak amplitude of motor evoked potential (MEP), latency of MEP, cortical silent period, and intensity of pulse) improved for both of them. Three parameters of texture analysis of sonoelastography images were improved for experimental group (i.e. contrast, entropy, and shear wave velocity). These findings indicate that AlterG training can improve reflexes, muscle stiffness, and CST activity in children with spastic hemiplegic CP and can be considered as a therapeutic tool to improve neuromuscular abnormalities occurring secondary to CP.**

Keywords: gait, motor impairment, spasticity, physical intervention, reflex, transcranial magnetic stimulation, sonoelastography

I. INTRODUCTION

Cerebral palsy (CP) is a group of non-developing disorders, which can be a reason of brain lesion or dysfunction [1]. The cause of this condition occurs in early childhood. The prevalence of spastic type of CP is more than other types. In CP, the brain is weak or unable to send appropriate neural signals to muscles. This affects patient's posture, balance, and ability to move. In hemiplegic spastic type of CP, the abnormal muscle tone is typically present in the affected side. The brain lesion does not change over time, but the symptoms of CP can change or worsen if the patient does not receive appropriate treatment. Different treatments are being used to improve quality of lives of these patients like traditional physiotherapy and occupational therapy, neurodevelopmental treatment, electrical stimulation, constrained induced therapy, etc. [2]. To date, no specific therapeutic intervention has been approved as the best treatment for CP patients. In order to have a long lasting improvement, the patient should follow a systematic, long term therapy. Different rehabilitation techniques have been used for this purpose, like robotic-assisted locomotor training (LOKOMAT) and body weight supported treadmill training; but only the clinical tests were evaluated for these treatments and they had limited neuroplasticity [3,4].

An anti-gravity treadmill (AlterG) has been developed which can reduce gravity's impact on the patient by making a positive pressure in its enclosure on the treadmill. The walking speed on the AlterG treadmill can be adjusted and physical rehabilitation can be made easier (Figure 1). It has been shown that AlterG training can improve speed and endurance of walking [5].

Figure 1. Anti-gravity treadmill (AlterG) (site: www.themuscleclinic.ie)

The gait impairments in patients with cerebral palsy can be caused by spasticity, synergy patterns, and muscle weakness, stiffness, and co-activation [6]. These happen as a result of central nervous system injury and may be due to abnormal spinal reflex development and disturbances in descending pathways. In this study we want to evaluate and quantify the effects of AlterG training on reflex hyper-excitability, corticospinal tract activities, and muscle stiffness. The aim of this study is to evaluate the efficacy of AlterG

---

*Research supported by Tehran University of Medical Sciences grant.

Shokoofeh Parvin is with Department of Biomedical Engineering and Medical Physics, Faculty of Medicine, Tehran University of Medical Sciences and Neural Engineering Research Center, Noorafshar Hospital, Tehran, Iran.

Aidin Taghiloo is with Department of Radiology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran.

Ashkan Irani is with Department of Occupational Therapy, Faculty of Rehabilitation, Shahid Beheshti University of Medical Sciences Health Services, Tehran, Iran.

*M. Mehdi Mirbagheri is with Department of Medical Physics and Biomedical Engineering, Tehran University of Medical Sciences; Neural Engineering Research Center, Noorafshar Hospital, Tehran, Iran, and Department of Physical Medicine and Rehabilitation, Northwestern University, USA. (Corresponding author to provide phone: 312-208-2100; e-mail: Mehdi@northwestern.edu).

treatment on these items. Reflex hyper-excitability is evaluated using H-reflex responses of the ankle plantar-flexors. Muscle stiffness is quantified using texture analysis of sonoelastography images of the lower limb muscles of the affected side of the body [7]. Finally, corticospinal tract activities are investigated through single pulse transcranial magnetic stimulation (TMS) test [8,9].

II. EXPERIMENTAL PROTOCOL

Tests were done before and after 8 weeks of AlterG training for experimental group and before and after 8 weeks of occupational therapy for the control group.

A. *Subjects*

Four children with spastic hemiplegic cerebral palsy with no cognitive problems participated in this study. Three of them (2 male, 1 female; mean age 10.19 ± 1.19) were in experimental group to receive AlterG training. One child (female; age 4.5) was in control group to receive traditional occupational therapy. Patients received treatments for 3 days a week for 8 weeks.

All of the subjects provided written informed consents. The study had ethical approval from the Tehran University of Medical Sciences Institutional Review Board.

B. *Anti-gravity treadmill (AlterG) treatment*

AlterG training was done three days a week for eight consecutive weeks. Each session of the treatment lasted for 45 minutes. At first, the patient started walking on treadmill with 50 percent of his/her body weight and with the speed of 1.5 km/h. During the session, the body weight and the speed was gradually increased in correspondence with the patients ability. The trainer gave essential feedback to the patients.

C. *H-reflex Response*

Reflex hyper-excitability of the ankle plantar-flexors were evaluated by using the H-reflex responses for the soleus muscle of the affected side of the body of the patients. H-reflex response occurs after an electrical stimulation to the muscle nerve.

The EMG activity of the soleus muscle, which appears as a twitch in the muscle, was recorded using Keypoint Dantec system (Figure 2). The stimulus intensity was set on 1ms to activate the Ia fibers. Reference electrode was placed over Achilles tendon. Stimulating and recording electrodes were placed on the calf of the muscle. We put the ground electrode between stimulating and recording electrodes. The tibial nerve in the popliteal fossa was stimulated. The cathode was put proximally. We started with low intensity. Little by little we increased the intensity of the stimulation and observed that the H response appeared and increased in amplitude. At a point we got the maximum peak to peak amplitude for H response. Then by increasing the intensity, the H response amplitude decreased until it disappeared and the M-wave amplitude increased. When the M-wave peak to peak amplitude did not change by increasing the intensity, we stopped the test [10].

D. *Transcranial Magnetic Stimulation (TMS)*

We applied a single pulse TMS to that side of the motor cortex of the subject which controls the affected leg. We used Magstim Rapid2 system and a circular coil to conduct this test. Subjects had to seat and relax their legs. The head position was fixed to avoid unwanted movements. We changed the coil position little by little to find the best site of the motor cortex which controls the leg. As a result of TMS pulse, a twitch occurs in the muscle which is called motor evoked potential (MEP). At first we started with low intensities of stimulation. The optimal position of the coil is where we get the maximum MEP peak-to-peak amplitude for the same stimulation intensity. When we get 5 pulses out of 10 pulses with MEP peak-to-peak amplitude of at least 50 microvolts, we report this intensity as the threshold of that subject. The electromyography (EMG) was recorded from tibialis anterior (TA) muscle using Ag-AgCl surface electrodes at a sampling rate of 48 kHz (Figure 3).

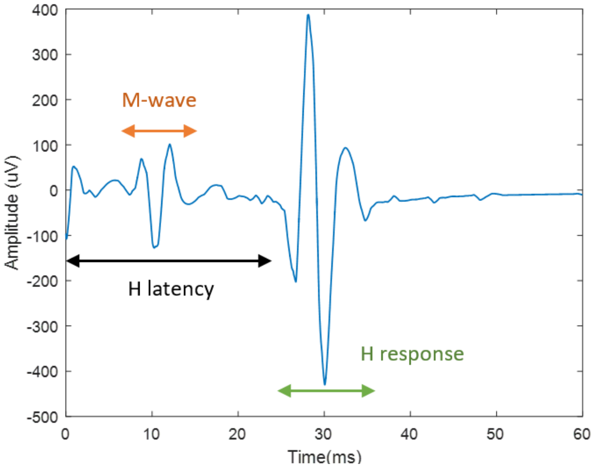


Figure 2. Sample H-reflex of a patient

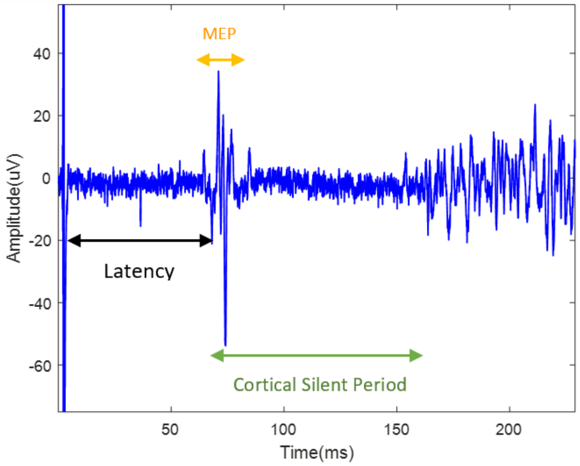


Figure 3. Sample EMG response in TA muscle for TMS test of a patient

E. *Sonoelastography*

We got ultrasound B-mode images of two muscles for each subject: the medial head of gastrocnemius muscle (MGS), the lateral head of gastrocnemius muscle (LGS), and the tibialis anterior (TA) in both proximal and vertical positions of the probe. A Samsung Medison, SonoAceX6, South Korea device was used for acquiring the images. This device had a linear-array transducer with bandwidth of 3-13 MHz and the gain parameter was set to 50 percent of the range of time gain. The same experienced sonographer recorded all of the images (Figure 4). Subjects had to extend their legs and relax for the experiment to be done. An ultrasound coupling gel was used to get the best quality of the images. The transducer was put on TA muscle at one-fourth of the line between the lower boundary of patella and the lateral malleolus and on the midsagittal line of gastrocnemius muscle and in the middle of distal and proximal tendon insertions. There was a time interval between recording images, so that the muscle could relax [11].

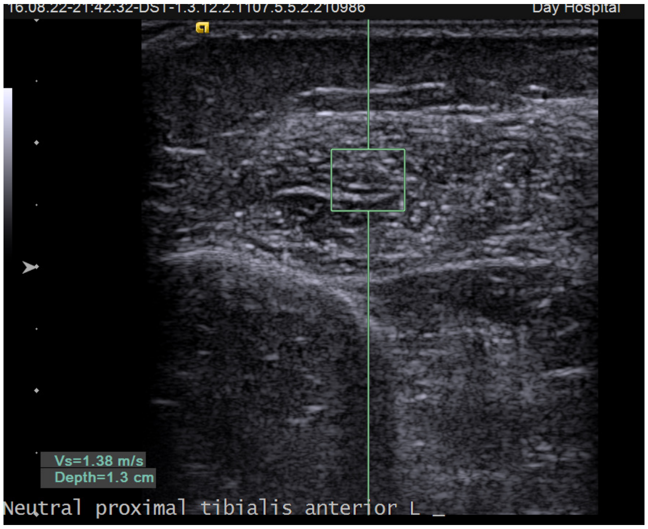


Figure 4. Sample sonoelastography image of a patient

III. Data Analysis

A. *H-reflex response*

For preprocessing of the EMG signal, IIR notch filter was performed to remove powerline interference [12], and wavelet-based principal component analysis was done to get the principal signal and remove background EMG [13].

Eight features were derived from H-reflex response by custom written MATLAB code: maximum peak-to-peak M-wave amplitude (Mmax), maximum peak-to-peak H response amplitude (Hmax), intensity of stimulation to get Mmax, intensity of stimulation to get Hmax, Hmax to Mmax ratio, latency from stimulation to appearance of H response, latency from stimulation to appearance of M-wave, and latency from H response to M-wave.

B. *Transcranial Magnetic Stimulation (TMS)*

For preprocessing of the EMG signal, IIR notch filter was performed to remove powerline interference [12].

Four major parameters were calculated from TMS test by custom written MATLAB code: latency from TMS pulse to appearance of MEP response, peak-to-peak amplitude of MEP response, cortical silent period (cSP) from beginning of MEP response to beginning of background EMG, and intensity of the stimulation. The cortical silent period is an interruption of voluntary muscle contraction due to transcranial stimulation of the contralateral motor cortex and is linearly dependent on the stimulation intensity [19]. Therefore, the reported cSP is for threshold of each subject.

C. *Sonoelastography*

The same experienced sonographer obtained the images and chose the region of interest (ROI) in the images for analysis.

We made texture characterization with second order statistics in accordance with the gray level co-occurrence matrix (GLCM), which is proposed by Haralick [14]. In GLCM matrix, each element measures the number of times a pixel of a specific gray level is next to another specific gray level. The distribution of values which occur together creates the GLCM matrix. We used [0 1] for offset to compute features of GLCM. GLCM features are shown in Table I.

TABLE I. GLCM Features

Contrast	Autocorrelation
Cluster Shade	Cluster Prominence
Entropy	Energy
Variance	Maximum Probability
Sum Entropy	Sum Variance
Maximal Correlation	Difference Entropy
Difference Variance	Inverse Difference Moment Normalized
Dissimilarity	Correlation
Inverse Difference Normalized	Homogeneity

By using the principal component analysis (PCA), we reduced the number of features to get more important features [15]. This process gave us four features: autocorrelation, contrast, energy, and entropy. In addition, we added shear wave velocity (Vs) as another feature for sonoelastography images. We did the analysis for this part by custom written MATLAB code.

IV. Results

Pretreatment and post-treatment results of tests for the subjects in both groups were evaluated. The differences between pre and post results are calculated by equation (1):

$$y = \%\left(\frac{\text{post} - \text{pre}}{\text{pre}}\right) \quad (1)$$

This indicates the percentage of magnitude of changes in features' scores after the training.

A. H-reflex response

The differences between pre and post results were calculated by equation (1). Between H-reflex response features computed for all of the subjects, maximum M-wave peak to peak amplitude and H response latency had different results for pre and post tests for experimental and control group (Figure 5). These features have improved for experimental patients.

B. Transcranial Magnetic Stimulation

Two of the subjects who were in experimental group had TMS response. The subject in the control group and one of the subjects in the experimental group did not have TMS response neither before, nor after treatment. The results of features for pre and post treatment of these two patients are shown in Figure 6. For these two patients, the calculated TMS features have improved after the training.

C. Sonoelastography

The differences between pre and post results were calculated by equation (1).

Between sonoelastography features computed for all of the subjects, contrast in neutral proximal position of LGS, entropy in neutral proximal position of MGS, and shear wave velocity (Vs) in neutral vertical position of MGS had different results in pre and post tests for the experimental and the control groups (Figure 7). Contrast and entropy features are defined using the following equations:

$$Contrast = \sum_{0}^{N_g-1} n^2 \left\{ \sum_{i=1}^{N_g} \sum_{j=1}^{N_g} p(i,j) \; \Big| |i-j| = n \right\} \tag{2}$$

$$Entropy = -\sum_{i} \sum_{j} \frac{1}{1+(i-j)^2} p(i,j) \tag{3}$$

in which N_g is the number of different gray levels and p(i,j) is the (i,j)th element in a normalized GLCM matrix [14].

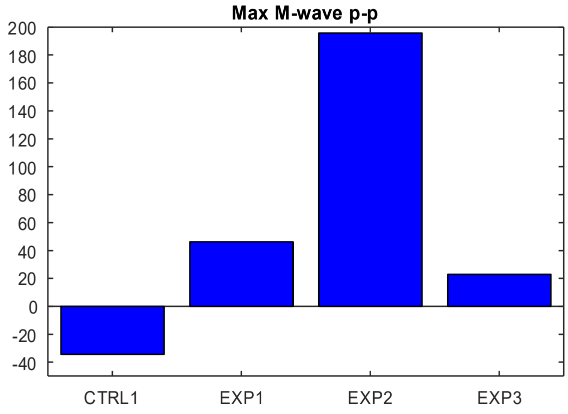
V. DISCUSSION AND CONCLUSION

A. H-reflex response

In H-reflex response results (Figure 5, upper graph), we see that maximum peak-to-peak amplitude of M-wave has increased for the experimental group and decreased for the control subject after 8 weeks of treatment. Maximum H response is an estimate of motor neurons that one person can activate and maximum M-wave is the maximum muscle activation [10].

Therefore, the maximum muscle activation of experimental subjects has increased after anti-gravity treadmill training and the strength of their muscles has improved. But for the control subject who received traditional occupational therapy (OT) during 8 weeks, maximum M-wave has decreased and OT has not improved the strength of the patient's muscles.

In addition, we observe that after this treatment, the H response latency which is the time beginning from stimulus to the beginning of H response has increased for the experimental group and decreased for the control subject (Figure 5, lower graph). H response latency is lower in patients with cerebral palsy compared to normal people [16]. This may be due to low inhibition of reflexes in spastic patients [17]. This result indicates that after AlterG training, H latency improves for experimental group and approaches that of normal people. But for control subject this feature decreases and gets worse after receiving traditional OT for 8 weeks.



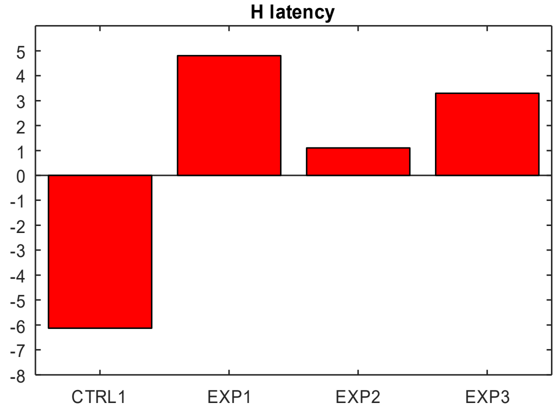


Figure 5. Percentage of changes of max M-wave results (upper graph) and H latency results (lower graph) using Eq. (1) for subjects (CTRL = control subject, EXP = experimental patients)

B. Transcranial Magnetic Stimulation

As mentioned before, just two of the subjects, who were in the experimental group, had TMS response. The pre and post results of TMS features for these two subjects can be seen in Figure 6. Latency of motor evoked potential (MEP) response in TMS test shows the amount of time that elapses from the moment that the pulse is generated to the moment that a twitch appears in the target muscle. This is the time needed for propagation of pulse in corticospinal tract and represents the conduction velocity in corticospinal tract [18, 19]. For cerebral palsy patients, this latency is more than that of normal people [8]. As it is shown, both of the patients who received AlterG training had lower latency in their TMS test after the training. So the time of pulse propagation in corticospinal tract has improved for both of them.

Motor evoked potential (MEP) amplitude indicates the integrity of corticospinal tract and the conduction of signals in peripheral tracts to muscles. Moreover, MEP shows the number of active motor units. Therefore, higher MEP amplitude shows better integrity and more active motor units [18]. For both of our patients, this feature has increased after the anti-gravity treadmill training.

Next feature is cortical silent period (cSP). cSP refers to a gap in muscle voluntary contraction due to transcranial stimulation of motor cortex. For the first 50ms of cSP, spinal inhibitory mechanisms play role, but rest of this silent period is generated entirely by the inhibition with its origin in the motor cortex. cSP can be used for evaluating motor cortical inhibition [18]. In patients with cerebral palsy, motor cortical inhibition does not function well and therefore, this silent period is lower than that of normal people [20]. For normal subjects cSP can be up to 300ms [18]. As we can see, after AlterG training for 8 weeks, the cortical silent period of both subjects who had TMS response has increased and approached to that of normal people [19].

The last feature of TMS which has been evaluated before and after the treatment is intensity of the applied pulse. This feature is a percentage of maximum magnetic field that the device can produce. For patient 2 this feature has decreased a little, but for patient 3 it has not changed after the training. Therefore, the AlterG training did not have a specific effect on this feature for these two subjects. Although it may have effects on other subjects and this needs further studies with more subjects.

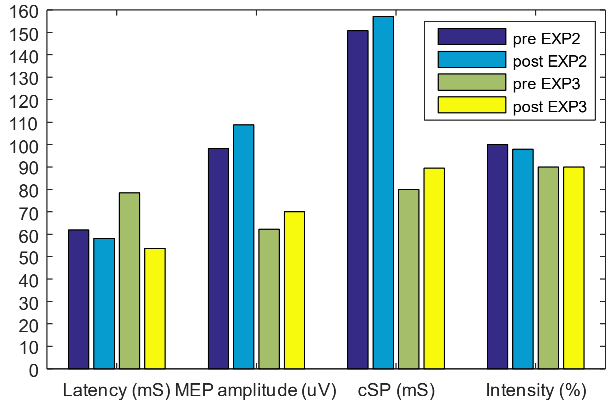


Figure 6. TMS results for subjects (EXP = experimental patients)

C. Sonoelastography

Muscle stiffness is measured via Modified Ashworth scale in clinics which is a qualitative measurement. Sonoelastography images provide a new method to quantify muscle stiffness [21].

According to equation (2), contrast feature can have an inverse relation to muscle stiffness. The higher the muscle stiffness is, the lower the contrast feature becomes. From features of GLCM matrix of sonoelastography images, we obtained that the contrast feature for neutral proximal position of lateral head of the gastrocnemius muscle was increased in the experimental subjects and decreased in the control subject after the treatment (Figure 7, upper graph). This shows that the muscle stiffness in this muscle has decreased for the experimental subjects and increased for the control subject after the course of treatment.

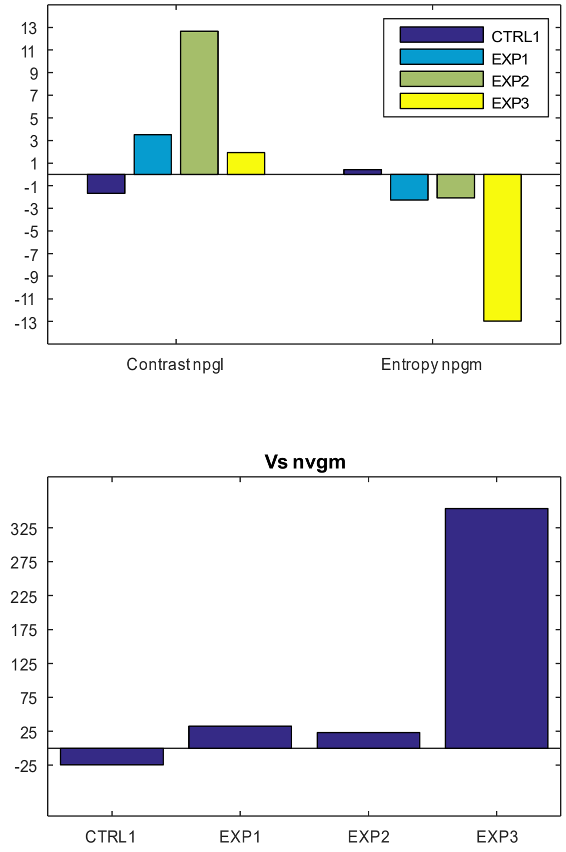


Figure 7. Percentage of changes of sonoelastography results for GLCM features (upper graph) and Sonoelastography results, shear wave velocity (lower graph) using Eq. (1)
(CTRL = control subject, EXP = experimental patients) (npgl = neutral proximal gastrocnemius lateral, npgm = neutral proximal gastrocnemius medial, nvgm = neutral vertical gastrocnemius medial)

According to equation (3), entropy feature can have a direct relation to muscle stiffness. Here, the entropy feature of GLCM matrix of sonoelastography images for neutral proximal position of medial head of the gastrocnemius muscle has decreased for the experimental subjects and increased for the control subject after the course of treatment (Figure 7, upper graph). This result indicates that muscle stiffness has decreased and improved in the patients that received AlterG training compared to the subject who underwent traditional OT for the same amount of time.

Another feature that can be obtained from sonoelastography images is shear wave velocity which differs for recording of each muscle. The more stiffness the muscle has, the more velocity the shear wave velocity has [22]. As we can see in lower graph of Figure 7, shear wave velocity has increased for neutral vertical position of medial head of the gastrocnemius muscle in the experimental subjects in comparison to the control subject. Therefore, we can conclude that the muscle stiffness has improved in this muscle for the experimental group.

We studied the effects of anti-gravity treadmill training on reflex hyper-excitability, corticospinal tract activities, and muscle stiffness in children with spastic hemiplegic cerebral palsy. We have also collected clinical evaluations such as Time Up and Go (TUG), Berg balance test, 10 meter walk test (10MWT), and 6 minute walk test (6MWT) to quantify the level of impairment of the children. As future development of this study, we will investigate correlations between the parameters obtained from aforementioned tests in this paper and these standard clinical scores. To be able to perform an acceptable correlation analysis, we have to increase the number of subjects. Although we found improvements in some of the features, further studies with more sample sizes are to be done to get significant results for more helpful features.

ACKNOWLEDGMENT

We would like to thank Dr. A. Shahrokhi. This research was supported by Tehran University of Medical Sciences grant.

REFERENCES

[1] Miller, Freeman, ed. *Physical therapy of cerebral palsy*. Springer Science & Business Media, 2007.

[2] Patel, Dilip R. "Therapeutic interventions in cerebral palsy." *Indian journal of pediatrics* 72.11 (2005): 979-983.

[3] Dodd, Karen J., and Sarah Foley. "Partial body-weight-supported treadmill training can improve walking in children with cerebral palsy: a clinical controlled trial." *Developmental Medicine & Child Neurology* 49.2 (2007): 101-105.

[4] Pajaro-Blazquez, Marta, et al. "Robotic-assisted gait training in children with cerebral palsy in clinical practice." *Converging clinical and engineering research on neurorehabilitation*. Springer Berlin Heidelberg, 2013. 29-33.

[5] Figueroa, Michael A., James Manning, and Patricia Escamilla. "Physiological responses to the AlterG anti-gravity treadmill." *International Journal of Applied* 1.6 (2011).

[6] Zhou, Joanne, Erin E. Butler, and Jessica Rose. "Neurologic correlates of gait abnormalities in cerebral palsy: Implications for treatment." *Frontiers in human neuroscience* 11 (2017).

[7] Parvin, Shokoofeh, et al. "Contribution of reflex hyper-excitability to muscle stiffness in children with cerebral palsy." *Biomedical Engineering and 2016 1st International Iranian Conference on Biomedical Engineering (ICBME), 2016 23rd Iranian Conference on*. IEEE, 2016.

[8] Marzbani, H., et al. "The correlation between transcranial magnetic stimulation parameters and neuromuscular properties in children with cerebral palsy." *Engineering in Medicine and Biology Society (EMBC), 2016 IEEE 38th Annual International Conference of the*. IEEE, 2016.

[9] Hallett, Mark. "Transcranial magnetic stimulation: a primer." *Neuron* 55.2 (2007): 187-199.

[10] Palmieri, Riann M., Christopher D. Ingersoll, and Mark A. Hoffman. "The Hoffmann reflex: methodologic considerations and applications for use in sports medicine and athletic training research." *Journal of athletic training* 39.3 (2004): 268.

[11] Pitcher, Christian A., et al. "Ultrasound characterization of medial gastrocnemius tissue composition in children with spastic cerebral palsy." *Muscle & nerve* 52.3 (2015): 397-403.

[12] Piskorowski, Jacek. "Powerline interference removal from ECG signal using notch filter with non-zero initial conditions." *Medical Measurements and Applications Proceedings (MeMeA), 2012 IEEE International Symposium on*. IEEE, 2012.

[13] Aminghafari, Mina, Nathalie Cheze, and Jean-Michel Poggi. "Multivariate denoising using wavelets and principal component analysis." *Computational Statistics & Data Analysis* 50.9 (2006): 2381-2398.

[14] Haralick, Robert M., and Karthikeyan Shanmugam. "Textural features for image classification." *IEEE Transactions on systems, man, and cybernetics* 3.6 (1973): 610-621.

[15] Jolliffe, Ian. *Principal component analysis*. John Wiley & Sons, Ltd, 2002.

[16] Tekgul, H., et al. "Electrophysiologic assessment of spasticity in children using H-reflex." *Turk. J. Pediatr* 55 (2013): 519-523.

[17] Palmieri, Riann M., Mark A. Hoffman, and Christopher D. Ingersoll. "Intersession reliability for H-reflex measurements arising from the soleus, peroneal, and tibialis anterior musculature." *International Journal of Neuroscience* 112.7 (2002): 841-850.

[18] Kobayashi, Masahito, and Alvaro Pascual-Leone. "Transcranial magnetic stimulation in neurology." *The Lancet Neurology* 2.3 (2003): 145-156.

[19] Wassermann, Eric, Charles Epstein, and Ulf Ziemann. *Oxford handbook of transcranial stimulation*. Oxford University Press, 2008.

[20] Vry, Julia, et al. "Altered cortical inhibitory function in children with spastic diplegia: a TMS study." *Experimental brain research* 186.4 (2008): 611-618.

[21] Sikdar, Siddhartha, Qi Wei, and Nelson Cortes. "Dynamic ultrasound imaging applications to quantify musculoskeletal function." *Exercise and sport sciences reviews* 42.3 (2014): 126.

[22] Cho, Kang Hee, and Jin Hee Nam. "Evaluation of stiffness of the spastic lower extremity muscles in early spinal cord injury by acoustic radiation force impulse imaging." *Annals of rehabilitation medicine* 39.3 (2015): 393-400.