Effects of Mirror Neurons Stimulation on Motor Skill Rehabilitation in Children with Cerebral Palsy: A Clinical Trial

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Objective: The authors aimed to compare the motor function measured by Gross Motor Function Measure (GMFM-66) between mirror neurons stimulation based VCD program at home and conventional physical therapy in children with cerebral palsy for two months.

Material and Method: A randomized controlled trial was performed with thirty children with spastic diplegia aged 2-10 years in Thammasat university hospital and Rajanukul institue. They were randomly assigned to receive either the mirror neurons stimulation based VCD program practice at home (experimental group) or the conventional physical therapy (control group) for two months. Both groups were measured the motor function by GMFM-66 at entry, the first month and the end of the second month. Analysis of covariance was used to compare mean changes of GMFM-66 scores between both groups at the second month after adjusted for the baseline level.

Results: A total of 30 children with cerebral palsy, aged 2.2 - 9.5 years (mean age 5.9 ± 2.2 years). The mean changes of the GMFM scores in experimental group were slightly higher than those in the control group of 2.1 (95% CI: -2.3, 6.5) at the second month after adjusted for the baseline level. The mean GMFM scores were significantly improved in all dimensions except lying and rolling dimension, at the first and second month when compared to the baseline level in both groups.

Conclusion: This pilot study demonstrated the mirror neurons stimulation based VCD program can improve motor function, at least, as much as the conventional physical therapy.

Keywords: Cerebral palsy, Mirror neuron, Action observation, Gross motor function measure

Children with cerebral palsies often lack of opportunity to learn or practice motor skills because of static pathology of their brains in development of movement and posture[1]. The central nervous system dysfunction is a major problem of those children causing loss of communication between the brain and body. This results in uncontrolled movements and posturing. Motor learning is one of strategies to maximize motor function in children with cerebral palsy. Motor learning, the acquisition of new skills with practice, is based on practice of goal-oriented motor function tasks that matched to the children's abilities, for successful retention and transfer to other motor activities or environments by stimulating sensorimotor experience[2]. Recently, human mirror neuron system has been discovered. It is involved in action understanding, imitation, learning of novel complex actions, and internal rehearsal of actions[3]. Implication of using action observation and imitation may be beneficial in motor rehabilitation of children with cerebral palsy[4,5]. Action observation and imitation were reported in recovery of motor function in stroke patients[4,6,7]. Steenbergen B et al[8] reported that motor imagery training may be a valuable additional tool for rehabilitation in children with hemiparetic cerebral palsy. Practicing and learning at home is the most successful way to motivate and facilitate children with cerebral palsy[9-11].

The author hypothesized that motor learning by imitation could help children with cerebral palsy to improve their motor ability. Repetitive watching daily

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activities movement via video compact disc (VCD), containing mirror neurons stimulation based VCD program on motor skill rehabilitation, at home may facilitate children with cerebral palsy to imitate movements. A VCD program was designed to improve both upper and lower extremities function in children with cerebral palsy. Finally, the authors have developed VCD program that applying concept of the mirror neurons stimulation on standard rehabilitation technique. The process to develop the VCD included reviewing the literature, small group discussion with pediatric specialists in behavioral and development, pediatric physical therapists and caregivers. The VCD contained stretching exercises and daily activities including wearing sock, putting on shirt, shorts and walking sideways[12-14]. Then, the VCD master has been produced by the television producers. Piloting the VCD program has been performed from experts and 3 children with cerebral palsy to ensure accurate contents and good performance of VCD presentation. This pilot study aimed to determine the effect of the mirror neurons stimulation based VCD program on motor skill rehabilitation of children with cerebral palsy by comparing motor function measured by the gross motor function measure (GMFM) between conventional physical therapy and the mirror neurons stimulation based VCD program for 2 months.

Material and Method

A randomized controlled trial was performed with thirty children with cerebral palsy recruited from Thammasat university hospital and Rajanukul institute. The clinicaltrials.gov identifier is NCT01267929. The inclusion criteria were children diagnosed of spastic diplegia aged 2-10 years with Gross Motor Function Classification System (GMFCS) level of 1-3 who can comply verbal instruction and can ambulate independently. The GMFCS, a five level classification system is used to describe the gross motor function of children with cerebral palsy on the basis of their self-initiated movement especially sitting, walking and wheeled mobility[15]. The exclusion criteria were participants who had orthopedic intervention or botulinum toxin injection within 6 months, seizure, cardiopulmonary compromise conditions, or severe visual and hearing deficits. Informed consent was obtained from the participants' parents before participation in the present study. The randomization lists with sealed envelopes, using stratified randomization by centers with permuted blocks of two, were prepared. The participants were randomly assigned according to the randomization list to receive either the mirror neurons stimulation based VCD program and practice at home or conventional physical therapy for two months. A sample size of 30 children, 15 for each group, was needed to obtain 80% power at 0.05 level of significance (two-sided) to test that the successful event rate (increasing GMFM scores at least 30% from baseline at the end of 2 months) in experimental group and control group of 0.8 and 0.3 respectively. The present study was approved by the ethics committee of Thammasat University and Rajanukul institute. The participants in the experiment group received the mirror neurons stimulation based VCD program and practice at home three times a day for two months. The mirror neurons stimulation based VCD program contained four volumes. The first volume includes activities for improving balance in sitting position. The second volume includes activities of sitting to standing. The third volume includes activities for improving balance in standing position. The last one includes activities of sideway walking. Activities in the VCD program are demonstrated by a child actress. The activities consist of fundamental daily activities and stretching exercises. The running time of each volume is about 30 minutes. The subjects were informed for to regularly practice for two weeks per volume. Their parents were informed and trained for practicing their children by VCD program at home and were asked to complete daily record of participant's activities. The participants were scheduled to meet a pediatric physical therapist once a week to monitor possible side effects. Concerning the control group, the participants received conventional physical therapy regularly at the hospital once a week for two months. The conventional physical therapy technique in the present study derived from the manual technique including the Bobath concept, stretching exercise and functional training for 30-45 minutes at a time. Both experimental and control groups were measured their motor functions with GMFM-66[16] by an independent pediatric physical therapist who was blinded for treatment allocation at entry, the first month and the second month.

All data were coded and entered into Epidata software. Statistical analysis was conducted using STATA (version 9.0). Frequency and percentage was used to describe qualitative variables. Mean and standard deviation was used to describe quantitative variables. The Chi-square test was used to compare the characteristics between both groups. The Wilcoxon matched-pairs signed-rank test was used to compare mean score within group. Analysis of Covariance

(ANCOVA) was used to compare mean scores of GMFM at the second month between two groups after adjusted for the baseline scores at entry. All tests were tested the significance level at 0.05. The compliance was measured by daily records containing the number of watching days, the number of watching times, watch attention and practice intention. The percentage of compliance was calculated by number of days that participants complied provided activities divided by the total days of 56 for each category. The level of the compliance of each item was categorized by the percentage of compliance into three levels as good compliance (> 70%), moderate compliance (50%-70%) and low compliance (< 50%).

Results

A total of 30 children with cerebral palsy, aged 2.2-9.5 years (mean age 5.9 ± 2.2 years), was followed and completed the study. The baseline characteristics were shown in Table 1. As shown in Table 2, the total score of GMFM in the experimental group (receiving VCD program) was higher than the control group (receiving conventional physical therapy) with the mean

difference of 2.1 (95% CI: -2.3, 6.5) after adjusted for the baseline level. Also, the mean GMFM scores of sitting, crawling and kneeling and walking running and jumping in the experimental group were higher than those of the control group with the mean difference of 4.9 (95% CI: -0.6, 10.5), 3.9 (95% CI: -3.0, 10.8) and 2.8 (95% CI: -7.1, 12.8) respectively after adjusted for the baseline level. However, the mean scores of the participants were significantly improved in all dimensions except lying and rolling dimension, at the first and second month when compared to the baseline level in both groups.

According to the experimental group, most participants had good compliance in watching but had moderate compliance in practicing as shown in the Fig. 1.

Discussion

This was the first study in Thailand to determine the effect of action observation and imitation by stimulating mirror neurons in children with cerebral palsy. The authors believe that the mirror neurons stimulation based VCD program on motor skill rehabilitation in the present study would be benefit to

Table 1. Characteristics of children with cerebral palsy in both groups

Characteristics	Experimental group* (n = 15) Frequency (%)	Control group** (n = 15) Frequency (%)
Sex		
Boy	9 (60.0)	10 (67.0)
Girl	6 (40.0)	5 (34.0)
GMFCS (Gross Motor Function Classification System)		
II	1 (7.0)	1 (7.0)
III	14 (93.0)	14 (93.0)
Weight for height age		
Normal weight	13 (87.0)	9 (60.0)
Under weight	2 (13.0)	3 (20.0)
Over weight	0 (0)	3 (20.0)
On anti-spasticity medications		
Yes	4 (27.0)	6 (40.0)
No	11 (73.0)	9 (60.0)
Caregiver		
Mother	11 (74.0)	10 (67.0)
Father	2 (13.0)	3 (20.0)
Other	2 (13.0)	2 (13.0)
Mean age (SD) in years	6.2 (2.2)	5.5 (2.2)
(Range)	(2.6-9.5)	(2.2-8.3)
Baseline GMFM-66, mean (SD)	44.8 (14.0)	49.4 (13.1)

* The experimental group, the group having mirror neurons stimulation based VCD program
** The control group, the group having conventional physical therapy

Table 2. GMFM-66 of children with cerebral palsy in both groups at entry, the first and the second month

GMFM-66	Experimental group (n = 15) Mean (SD)			Control group (n = 15) Mean (SD)			Adjusted mean changes at 2nd month between experimental and control groups	
	Baseline	1st month	2nd month	Baseline	1st month	2nd month	Mean difference# (95%CI)	p-value##
Total score	44.8 (14.0)	50.0 * (13.8)	54.7 ** (14.5)	49.4 (13.1)	53.8* (15.2)	57.5** (16.2)	2.1 (-2.3, 6.5)	0.341
Lying and rolling dimension score	70.8 (14.0)	75.9 (6.5)	75.9 (6.5)	78.4 (0)	78.4 (0)	78.4 (0)	-0.3 (-3.4, 2.7)	0.815
Sitting dimension score	57.3 (20.0)	62.5* (19.0)	68.0** (21.3)	61.3 (17.0)	64.3* (17.2)	67.2** (19.1)	4.9 (-0.6, 10.5)	0.080
Crawling and kneeling dimension score	81.9 (24.1)	90.6* (22.8)	92.1** (21.2)	92.3 (18.3)	95.2* (16.9)	96.0** (14.8)	3.9 (-3.0, 10.8)	0.260
Standing dimension score	26.2 (16.7)	34.9* (17.1)	43.9** (18.2)	26.6 (21.1)	37.1* (26.2)	44.6** (24.1)	-0.3 (-10.1, 9.4)	0.946
Walking, running and jumping dimension score	7.06 (21.3)	13.4* (21.7)	19.6** (22.8)	21.5 (26.4)	25.0* (28.4)	31.6** (31.7)	2.8 (-7.1, 12.8)	0.561

The mean scores difference of the end of the 2nd month between experimental and control groups after adjusted for the baseline level

The p-value was based on the analysis of covariance between experimental and control groups at the end of 2nd month after adjusted for the baseline level

* Significant change (p < 0.05) within group between baseline and 1st month measures using wilcoxon matched-pairs signed-rank test

** Significant change (p < 0.05) within group between baseline and 2nd months measures using wilcoxon matched-pairs signed-rank test
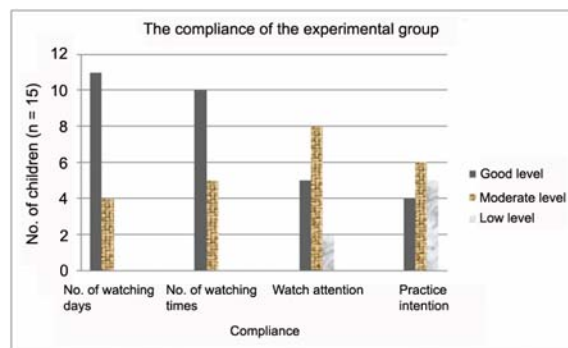
- Percentage more than 70 percents that mean good level
- Percentage between 50 and 70 percents that mean moderate level
- Percentage below 50 percents that mean low level

Fig. 1 The compliance level of participants in experimental group

children with cerebral palsy since it was developed by multidisciplinary team and produced by the television producers. The contents and its performance were also piloted by both the experts and children with cerebral palsy before performing this trial to test the effectiveness of the program. This result showed a trend of the larger mean changes of GMFM scores in the experimental group at the second month compared to those in the control group in many dimensions after adjusted for the baseline level although the mean changes did not reach the statistical significance level. Larger sample size will be required to determine more precise result. However, significant improvement of the mean GMFM scores was found in both groups after the first and the second month periods. In addition, the good compliance in watching reflected good performance of VCD presentation. The authors suggest that the mirror neurons stimulation based VCD program is an alternative treatment for children with cerebral palsy who lack the opportunities to access conventional physical therapy in medical center. The present study confirmed that the mirror neurons stimulation based VCD program could improve motor function, at least, as much as the conventional physical therapy. However, the children with cerebral palsy

should not use this VCD program for practicing at home only, contacting physical therapist for assessing motor function and receiving individual treatment program together periodically is also essential. Apart from this, meeting physicians and other healthcare personnel for holistic approach management is recommended to achieve the best result.

The authors also recommend that the children have to practice via the VCD program repeatedly and regularly since development of such skill in children depends on imitation. There were also several researches studying on children's imitation. Katherine et al[17] measured imitative learning of a novel action seen only in a third-party interaction in a group of 48 18-to 20-month-olds. Their study found that 50% of children passed the imitative task; therefore, the children could imitate novel actions of adults who were not interacting with them. The mechanism could be explained by the study of Lepage JF et al[18] who used EEG to probe mu rhythm modulation in 15 children during observation and execution of hand movements. The observation of objected-oriented movement could produce modulation of the mu rhythm. The mu rhythm attenuation occurred in children under 11 years old during observation of hand movements which similar to what had been reported in adults. Steenbergen B et al[8] presented motor imagery training may be a valuable additional tool for rehabilitation in children with hemiparetic cerebral palsy. Finally, Chaiyawat P et al[7] developed and examined the effectiveness of individual home rehabilitation program on the mirror neuron concept for Thai ischemic stroke patients. They found that early home rehabilitation program for Thai ischemic stroke patients provided significantly better outcomes in improving motor function than usual care.

Since the VCD program including the contents has been developed solely for the present study and has not been used for children with cerebral palsy in real practice. Further feedback and amendment of the contents and VCD presentation has to be done after launching this VCD program in real practice. There are some limitations of this study. This VCD program was applicable for children with cerebral palsy with spastic diplegia who had high GMFCS level (1-3). Generalized the results to children with other types of cerebral palsy with different severity are limited. Further studies of larger sample size and longer duration are required to determine the effectiveness of the VCD program.

Conclusion

This pilot study demonstrated the mirror neurons stimulation based VCD program can improve motor function, at least, as much as the conventional physical therapy. It may be an alternative treatment for children with cerebral palsy who lack the opportunities to access conventional physical therapy in medical center. Good compliance by practice repeatedly and regularly with the VCD program at home is suggested to achieve the best clinical outcome.

Potential conflicts of interest

None.

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ผลของการฟื้นฟูทักษะการเคลื่อนไหวโดยกระตุ้นการทำงานของเซลล์กระจกเงาในเด็กภาวะสมองพิการ

น้ำฝน มหาทรัพย์, ภาสกร ศรีทิพย์สุโข, ระวีวรรณ เล็กสกุลไชย, ทิพวรรณ หรรษคุณาชัย

วัตถุประสงค์: เพื่อเปรียบเทียบผลลัพธ์การรักษาด้านการเคลื่อนไหวประเมินโดย Gross Motor Function Measure (GMFM-66) ระหว่างการรักษาทางกายภาพบำบัดแบบมาตรฐานกับการรักษาด้วยโปรแกรมกายภาพบำบัด สำหรับพัฒนาทักษะการเคลื่อนไหวโดยกระตุ้นการทำงานของเซลล์กระจกเงาในรูปแบบวีดิทัศน์ เป็นเวลา 2 เดือน ในเด็กภาวะสมองพิการ

วัสดุและวิธีการ: เป็นการวิจัยเชิงทดลองทางคลินิก โดยคัดเลือกอาสาสมัครเด็กภาวะสมองพิการชนิด spastic diplegia จำนวน 30 คน อายุระหว่าง 2-10 ปี จากโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติและสถาบันราชานุกูล จากนั้นสุ่ม อาสาสมัครเพื่อแบ่งเข้ากลุ่ม ระหว่างกลุ่มที่ได้รับโปรแกรมกายภาพบำบัดสำหรับพัฒนาทักษะการเคลื่อนไหวโดย กระตุ้นการทำงานของเซลล์กระจกเงาในรูปแบบวีดิทัศน์โดยให้นำไปฝึกปฏิบัติที่บ้าน (กลุ่มทดลอง) หรือกลุ่มที่ได้รับ การรักษาทางกายภาพบำบัดแบบมาตรฐาน (กลุ่มควบคุม) ทั้งสองกลุ่มจะได้รับการประเมินความสามารถ ด้านการเคลื่อนไหวด้วยแบบประเมิน GMFM-66 เมื่อเข้าร่วมการศึกษาที่ระยะเวลา 1 เดือน และที่ระยะเวลา 2 เดือน วิเคราะห์ข้อมูลด้วยสถิติ analysis of covariance เพื่อเปรียบเทียบความแตกต่างค่าคะแนนเฉลี่ยของ GMFM-66 ที่เปลี่ยนแปลงหลังการรักษา 2 เดือน ระหว่างทั้งสองกลุ่ม

ผลการศึกษา: เด็กภาวะสมองพิการจำนวน 30 คน มีอายุเฉลี่ย 5.9 ± 2.2 ปี (2.2-9.5 ปี) ค่าคะแนนเฉลี่ยของ GMFM-66 ที่เปลี่ยนแปลงหลังการรักษาในกลุ่มทดลองมากกว่าในกลุ่มควบคุม 2.1 คะแนน (ช่วงแห่งความเชื่อมั่นที่ 95% เป็น -2.3 ถึง 6.5) เมื่อได้ปรับค่าคะแนนเมื่อเริ่มเข้าโครงการแล้ว คะแนนเฉลี่ยของอาสาสมัครทั้งสองกลุ่ม มีค่าเพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติทุกหัวข้อการประเมิน ยกเว้นหัวข้อท่านอน ท่ากลิ้ง ที่ระยะเวลา 1 เดือน และ 2 เดือน เมื่อเปรียบเทียบกับคะแนนก่อนเข้าร่วมวิจัย

สรุป: การศึกษานำร่องนี้พบว่าโปรแกรมกายภาพบำบัดสำหรับพัฒนาทักษะการเคลื่อนไหวโดยกระตุ้นการทำงาน ของเซลล์กระจกเงาในรูปแบบวีดิทัศน์ทำให้ความสามารถ ด้านการเคลื่อนไหวดีขึ้นเช่นเดียวกับการรักษา ทางกายภาพบำบัดแบบมาตรฐาน