The effects of a systematic non-invasive, electrical low frequency and low intensity stimulation with multiple electrodes incorporated in a whole-body suit on children with cerebral palsy, GFMCS III-V; A 6 month clinical prospective study

Christian Wong* **, Tina Piil Torabi** Josephine Michelsen and Kristian Mortensen

Children's Section, Department of Orthopedics, University Hospital of Hvidovre, Copenhagen, Denmark

*Corresponding author: Department of Orthopedics, University Hospital of Hvidovre, Kettegaard Allé 30, 2650 Hvidovre, Denmark. E-mail address: chwo123@gmail.com.

**shared first authorship

200 ord

Aim:

Spasticity is a common characteristic in children with cerebral palsy (CP). The objective of this feasibility study was to examine the effect on spasticity and function of multifocal transcutaneous electrical stimulation (TENS) encoporated in a 2-piece suit, the Mollii suit.

Method:

This study was a prospective cohort study. Participants were recruited from 3 schools for disabled children in our region. Thirty-one participants with predominantly spastic disease were included; 17 completed the study. Participants wore the suit for 1 hour every second day in a trial period of 24 weeks. Measurements of passive range of motion (pROM) was measured using a goniometer, and spasticity was measured by the modified Ashworth (MAS) and Tardieu scales (MTS) before initiation and after 4, 12, and 24 weeks. The participant's personal therapists defined two motor related SMART goals and evaluated them by the goal attainment scale (GAS). GMFM-66 and PPAS evaluation were perfomed for overall function and stability.

Results:

General spasticity level and specifically from the upper arm and leg were significant reduced according to MAS. There was an additive effect on spasticity reduction over time and related to specific stimulated muscles. No clinical meaningfull reduction was seen in pROM and MTS. SMART goals improved significantly and clinical meaningfull for motor function as standing/walking and hand and arm use. No significant clinical relvant improvements were seen in overall and dimensions of GMFM-66 and PPAS. The study was moderately powered due to drop-outs.

Interpretation:

In conclusion, feasibility study demonstrated, that the use of Mollii suit in a 24-week intervention in children with CP, GFMCS 3-5 has significant reduction in spasticity and significant improvements in motor functions as mobility of walking and standing and motor skills of hand and arm.

Keywords: Goal Attainment Scale; Reciprocal inhibition; modified ashwort scale, Spasticity reduction trans cutaneous electric stimulation, TENS

https://onlinelibrary.wiley.com/page/journal/14698749/homepage/ForAuthors.html

4137 words mod 3000

1. Introduction

Cerebral palsy (CP) is most common inborn neurological disease in children with a prevalence of 2.4 per 1000 live births [1]. It is a heterogeneous mosaic of clinical symptoms of non-progressive brain injury stemming from the antenatal, perinatal or early postnatal period [2]. The apparent manifestation is often a movement disorder characterized by spasticity, which subsequent affects the musculoskeletal system with i.e. muscular imbalance, joint deformities and pain [3,4]. As a result, children with CP have decreased motoric function of daily living and develop other associated impairments and disabilities to follow [4]. Several therapeutic spasticity-modifying interventions have been developed to reduce the consequences of these problems, enhance function and compensate for the disabilities [2-4]. This entails for example exercise therapies, pharmacological anti-spastic agents and surgical treatments [2-4]. Reduction of spasticity can be achieved by treatment with localized intramuscular injection of Botulinum toxin combined with physiotherapy as well as general reduction by oral or intrathecal medical agents such as baclofen [5,6]. However, treatments today are either short-term in effect, time-consuming or with side-effects and complications as i.e. pain for physical exercises, fatigue and drowsiness for medical spasticity reduction. The latter can be as disabeling as the spasticity in itself [5-7]. The ideal treatment would entail an effective intervention to treat spasticity, that is well tolerated with minimal side effects or complications, with a sustained effect as well as not invasive [8,9]. We have identified a general spasticity modifying assistive device using a systematic transcutaneous electrical nerve stimulation (TENS), which fulfills the purpose in regards to the above features. The assistive device is a full-body garment suit with multiple incorporated surface electrodes, commercialized as the *Mollii*® [8]. The purpose of the suit is to modify spasticity by systematic stimulating the targeted spastic muscles utilizing indirect stimulation by the principle of reciprocal inhibition, where the antagonists of the target muscles are

stimulated to reduce the spastic reflexes and subsequent muscle stiffness [8]. Reciprocal inhibition utilizes activation of the disynaptic reciprocal Ia inhibitory pathway as seen in figure 1.

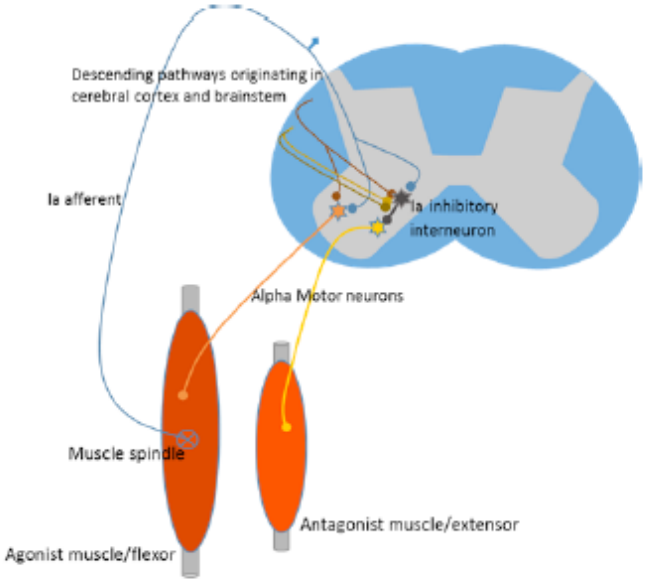

Figure 2. Reciprocal inhibition. When a muscle (e.g. an elbow flexor) is stretched, this evokes sensory input from muscle spindles passing in afferent nerve fibers (large diameter sensory fibers, called Ia afferents) that have direct contact with lower motoneurons in the spinal cord and elicits impulses in efferent nerve fibers which activates the same muscle and cause a reflex muscle contraction (the stretch reflex). In parallel, the sensory input also inhibits antagonist muscles (in this case elbow extensor muscle) by activation of spinal interneurons in the same spinal segment - reciprocal inhibition. This mechanism may be utilized to reduce spasticity in e.g. an elbow flexor muscle by electrical stimulation of afferent nerve fibers of the opposing elbow extensor muscle that activates inhibitory Ia interneurons and reduce the excitability of the flexor muscle motor neuron. Illustration adapted from Principles of Neural Science, Fifth Edition (Fig 35-5, p. 798), by Kandel ER, et al. 2013.

Figure 1. The mechanism of reciprocal inhibition utilizes activation of the disynaptic reciprocal Ia inhibitory pathway.

The electrical stimulation is of low intensity and low frequency, and is supposedly adequately low to generate a sensory input, but without motor unit recruitment as opposed to functional, electrical stimulation [10-11]. This is without or with minimal apparent side-effects or complications, since it is non-invasive with low intensity and low frequency TENS. The tenets of the Mollii method is spasticity reduction to enhance function and general stability as well as reduce pain associated with spasticity [8]. Moreover, it is a home therapy-oriented method, that is supposed to be applied while performing usual activities of daily living, thus not time-consuming as such [9]. It is supposedly also beneficial in regards to continuous treatment with an additive

effect over time [12], thus potentially achieving a sustained anti-spastic effect. We found this suit especially appealing, in particular for the severely handicapped children, since patient participation in principle would only require donning of the suit, which would be performed by a parent or therapist. The most severely handicapped children with CP generally have the least effect of treatment as i.e. soft tissue release for hip dislocation. They are the most vulnerable in respect to side-effects and have the most severe complications [13]; *the most vulnable (child with CP) is the most affected and most difficult to treat* [14]. The Mollii suit is as mentioned an assistive aid, but will be mentioned as treatment hence forward.

In principle, we agree with Novak et al. (2013), that new treatments in CP ideally should be well documented to avoid ineffectual, unnecessary, or harmful interventions, thus there is a need to 'fill up this research–practice gap' [15]. For this reason, we undertook a prospective scientific study to examine the method of systematic electrical stimulation by reciprocal inhibition with the Mollii suit for the effects on spasticity and function in severely handicapped children with CP, Gross Motor Function Classification System 3-5 (GFMCS). The primary objective was to investigate whether this method induces spasticity reduction, improvement in passive range of motion and in specific patient relevant motor tasks in a prospective period of 24 weeks.

2. Method

2.1. Study population

The participants were pediatric patients with cerebral palsy with predominantly spastic disease. They were recruited for the study from three schools with disabled children in our region. Inclusion criteria was predominant spastic cerebral palsy when categorized as GMFCS 3-5. Inclusion criterias were evaluated for eligibility according to the charts, clinical evaluation and cerebral MRI by a medical doctor with special interest in cerebral palsy in children. Exclusion criterias were other disorders affecting the sensorimotor functions without spasticity, implanted electric medical devices, BMI>35 or other severe concomitant diseases such as cancer, cardiovascular, inflammatory, psychiatric disease, medical dysregulated epilepsy or hypertension. Participants were excluded if modification in ongoing pharmacological anti-spastic treatment as botulinum toxin injections was performed during and 3 months prior to the test period. In total, 31 participants with spastic CP were included at baseline. Three participants had a mixed disorder of spasticity with dystonia (2) and ataxia (1). One participant had metachromatic leukodystrophy with spasticity. The male:female ratio was 1.6:1 at inclusion. The average age was 12.2 years with a range of 7-17 years of age (SD: 3.6). Table 1 shows the demographics of the participants.

Distribution/demographics of participants		
	Inclusion	After 6 month
GFMCS 3	4	4
GFMCS 4	6	1
GFMCS 5	21	11
Spastic CP	27	17
Mixed with dystonia	2	1
Mixed with Ataxia	1	0
Metachromatic Leukodystrophy	1	1

Table 1. Demographics of the participant population at inclusion and at end of study.

2.2. Study design

This study was prospective intervention study, where the participants used the Mollii suit for 24 weeks. The suit has 58 electrodes which stimulate at a frequency of 20 Hz, a pulse width ragning from 25-175 µs, and a voltage of 20 V. The settings are tailored in regards to the child's age, weight and level of spasticity of the specific target muscle. The Mollii suit and a schematic drawing of the possible targeted muscles are seen in figure 2. In this study, the settings of the suit were systematically adjusted to the individual participant by two specialized therapists using an overall aim of providing core stability [8]. Test subjects wore the Mollii® suit for one hour every second day in a trial period at home or at school.

Figure 2. The Mollii suit (left) and a schematic drawing of the possible targeted muscles in tailored stimulations according to pattern of spasticity of the patient using the 58 potential transcutaneous electrical stimulations.

The parents, personal therapists or primary helpers were advised to interact with the child and engage them in their usual physical activity during the one hour of stimulation. Donning and use of the suit was performed at by the parents at home or by the personal therapist at school to ensure compliance.

2.3 Study assessments

One single therapist with supportive assitance performed assessments prior to, week 4 and 24 after initiation of the intervention in the safe and familiar environment of the school. This entailed clinical examination of passive range of motion (pROM), Modified Ashworth Scale (MAS) and Modified Tardieu Scale (MTS) of the treated joint and muscles. The effects of the Mollii suit were tested on the following muscles:

Lower extremity (UE):	Proximal: M. Iliopsoas, Quadriceps muscle group, Adductor muscle group, Hamstring muscle group.
	Distal: M. tibialis anterior, M. gastrocsoleus.
Upper extremity (OE):	Proximal: M. Biceps brachii, M. Triceps brachii
	Distal: Flexor carpi muscle group

We measured pROM, MAS and MTS in a standardized manner in accordance to recommendations and using a two-arm goniometer when appropriate [16-18]. Furthermore, two patient-relevant specific treatment goals (SMART goals) were set up and evaluated by primary physio and/or occupational therapists in accordance with the goal attainment scale (GAS) [19,20]. The individualized goals in general aimed at improve relevant motoric functions of the extremities, exercise tolerance, stability and tasks of daily living. We classified the SMART

goals systematically in acordance to the appropriate 'International Classification of Functioning, Disability and Health (ICF)' codes [21]. Table 2 gives an overview of the types of smart goals.

0

Description	ICF Code	Frequency
Walking	d450	4
Fine hand use	d440	1
Gait Pattern function	b770	1
Muscle tone function	b735	3
Hand and arm use	d445	6
Moving around using equipment	d465	2
Exercise tolerance function	b455	2
Moving around	d455	2
Changing basic body position	d410	4
Improving of drooling	s510	1
Weight bearing	d415	3
Maintain bodycontrol	d4104	2

Table 2. Overview of the SMART goals; types of goals according to ICF classification and evaluated by the goal attainment scale.

Moreover, the participants were evaluated by the Gross Motor Functions Measure, GMFM-66 for overall improvement in function and the posture and postural ability scale (PPAS) for stability [22,23]. The PPAS is quantitative (1 evaluation) and qualitative (evaluation in the frontal and saggital plane) assessment tool with 7 grades to evaluate the ability of four kinds of postural tasks in supine, prone, sitting, and standing. The SMART goals and GMFM-66 was set and performed prior to and 24 weeks treatment. The PPAS evaluations were video recoded prior to, after 12 and 24 weeks. The primary physio and/or occupational therapists of the participant evaluated the GMFM-66 and SMART goals. One blinded independent physiotherapists evaluated the video recordings of the PPAS tests.

2.4 Statistical analysis

The sample size was determined as a convenience sample by the number of eligible participants from the three schools. We performed an estimate of sample size using Gpower with a power (1-β) of 0.8,

an α level of 0.05, a change in ashworth of 0.8 in a match pair t test and an estimated drop-out of 30%; we had to included 31 participants. We also performed a post hoc power analysis based on the means and standard deviations of overall spasticity. We considered a power of < 0 poor, 0.0–0.20 slight, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 substantial and 0.81–1 very good. Shapiro Wilks tests, histograms and QQ-plots of the collected data were used to analyse for normal distribution. Data regarding spasticity, passive range of motion, improvement in physical activity and mobility were analysis with the one-sample Wilcoxon signed rank test for non-parametric data and a paired t-test was used for normal distributed parametric data. We considered p-values of ≤ 0.05 statistically significant, while p-values of > 0.05 to 0.10 were interpreted as indicating tendencies towards statistical significance. We applied appropiate Bonferroni corrections to our analyses. The test of normality, the one-sample Wilcoxon signed Rank test and the paired t-test were performed using IBM SPSS Statistics, Version 22. Furthermore, we analyzed spasticity data using mixed linear model analysis in the statistical software R Core Team (2017) [24]. We constructed 3 models with ASH, pROM and difference in-between first and second catch as the outcome variables. The fixed effects were time as continuous, muscle group as categorical, an interaction between time and muscle group, ASH, pROM and difference in-between first and second catch .We included a random effect of patient number and added a nested random effect of patient side (left and right).

The local committee of ethics approved the study (No H-17004467). We obtained oral and written consents according to national guidelines and the Helsinki Declaration. This study was conducted as an independent study and was EC-funded by Eurostars. The funding was obtained in a European collaboration led by the company Inerventions AB (product owner).

3. Results

3.0. Inclusion process

Thirty-three patients were invited to participate. Two patients declined before initiation of the study. Thirty-one participants were included before the 24 weeks of intervention, and 17 completed the intervention. Fourteen participants withdrew throughout the study period. Six children from week 0-4, 3 children from week

4-12 and 5 children from week 12-24. The withdrawals were due to non-compliance (N=5), garment related (N=2), epilepsy (N=1) and ungrounded withdrawal or due to perceived effect not as expected (N=5). Figure 3 shows a flow chart of participants history and timeline of the project.

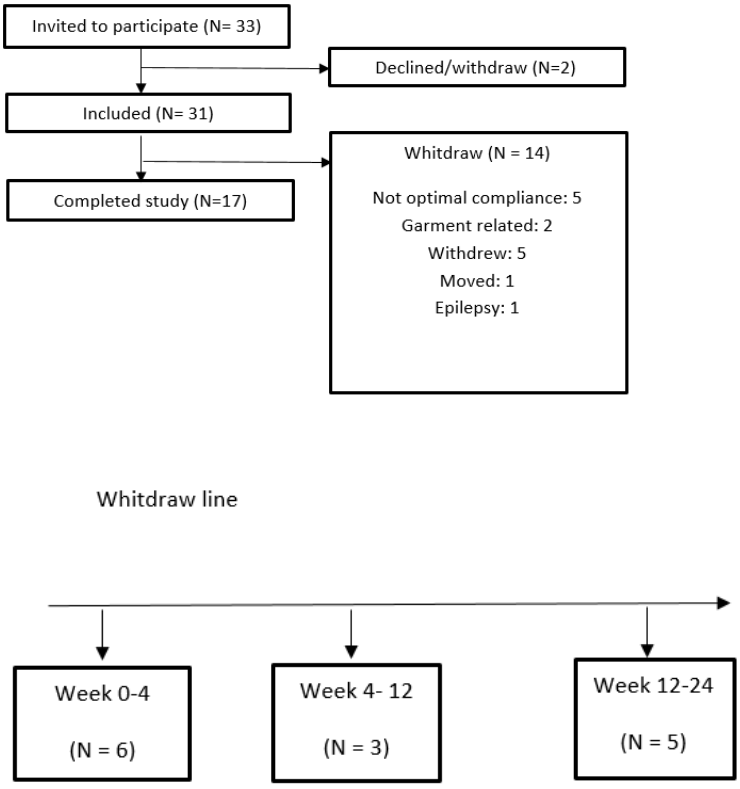

Figure 3. Flowchart of the inclusion and history of completion and timeline for withdrawals during the study.

3.1. Spasticity and Passive Range of Motion

We found a significant mean decrease in overall spasticity according to Modified Ashworth level from 2.26 to 1.83 (p=0.001) with a Bonferroni correction (11 muscles=0.005). The MAS in the muscles of the lower extremity had a significant mean decrease from 2.47 to 1.9 (p=0.001) with a Bonferroni correction (8 muscles=0.006). The reduction was pronounced in the proximal UE muscles of the hamstrings and the quadriceps femoris. The MAS of the muscles in the upper extremity had a significant mean decrease from 1.73 to 1.48 (p=0.013) with a Bonferroni correction (3 muscles=0.016). See table 3 for change in spasticity according to Prom, MAS and MTS.

Passive Range of Motion

Extremity	Number(n)	Median_Baseline	Median, 24 weeks	P=value
Dorsal Flexion_SIN	12	72,5◦	70◦	0.054
Quadriceps_DXT	6	55◦	80◦	0.066
Straight Leg_SIN	7	92.5◦	100◦	0.074

Modified Ashworth Scale

Extremity	Number (n)	Median_Baseline	Median, 24 weeks	P=value
Hamstrings_DXT	11	4	3	**0.015**
Hamstrings_SIN	13	4	3	**0.014**
Quadriceps_DXT	5	3.5	3	**0.046**
Quadriceps_SIN	6	4	2,5	0.059

Modified Tardieu Scale

Extremity	Number(n)	Median_Baseline	Median, 24 weeks	P=value
Hamstrings_SIN	13	92.5◦	100◦	**0.002**

Table 3. Significant changes in passive range of motion, modified Ashworth level and modified Tardieu scale.

The first registered catch/resistance (angle in Tardieu 2 at V3) during fast joint-movement did not change and was not significally different after 24 weeks, when estimated for all treated muscles in general and muscles analyzed separately, except in the hamstrings muscles with a change from 92.5◦ to 100◦ (p=0.002). No significant differences were found in passive range of motion, though there was a tendency to a change in passive dorsal flexion in the hand from 72.5◦ to 70◦ (P=0.054), in the quadriceps muscles during knee flexion with a change from 55◦ to 80◦ (P=0.066) and in the hamstrings during straight leg test from 92.5 to 100◦ (0.074).

3.2. Mixed Effect Model

Further analysis using a mixed effect model showed a significant difference in effect on the stimulated muscles (<0.0001) with the most pronounced effect in the proximal upper and lower extremities of biceps brachii (<0.0001) and triceps brachii (<0.0001) and quadriceps femoris (<0.0001) and adductor femoris (0.001), respectively. Moreover, there was an overall additive effect over time (0.04) with pronounced effect in the lower extremity of adductor femoris (0.02) and tibialis anterior (0.02).

3.3 Goal Attainment Scale, Gross Motor Function Measure, and Posture and Postural Ability Scale

We found a significant effect in goal attainment scale after Mollii intervention. There was an overall significant change in the t-score of 10.3 (8.8) (p=0.001) with a Bonferroni correction (12 goals =0.004). The scores were 38.5 (1) of 48.8 (8.6) at baseline and after 24 weeks, respectively. Change in the t-score for goals related to walking improved with 15.1 point, body control improved 15.2 points, hand and arm use with 27,4 points, transferring/position changes with 10.2 points, eating/mouth control with 1.6 points and standing/weight bearing position with 11.9 points. Figure 4 shows the distribution of achieved goals at 24 week of Mollii intervention according to the GAS.

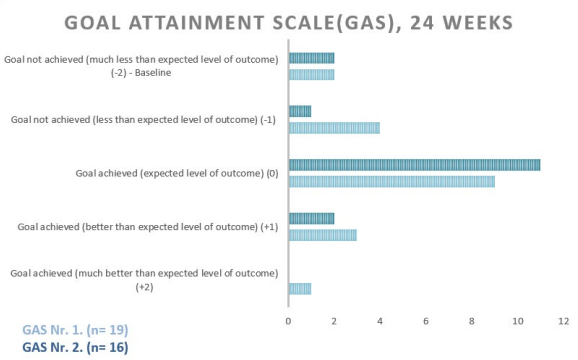

Figure 4. The distribution of achieved goal after 24 week of Mollii intervention.

In the GMFM-66, we saw a mean insignificant increase from 27.87 points at baseline to 32.02 (p=0.122). The mean change in the subcategory *A; Lying and rolling* changed from 8.17 to 8.33 (p=0.586) and in the subcategory *B; Sitting* from 13.92 to 14.50 (p=0.443). Subcategory C, D and E was omitted from the sub analysis due data lost in follow-up.

In the PPAS, we registered a slight overall mean increase in the quantitative measures for overall *standing up, sitting, back and front lying down* from 13.7 to 14.5 points. In the qualitative evaluation for overall *standing up, sitting, back and front lying down* the measure decreased from 68.3 to 56.5 points. We found significant change in the qualitative saggital plane in sitting (.000), but otherwise these were no significant changes with the paired sample t tests (p=.06-.91).

4. Discussion

In the present study, we have examined a systematic multiple electrode stimulation using the principle of reciprocal inhibition for a continuous use of one hour every second day for an intervention period of 24 weeks.

There was a significant reduction in overall spasticity level according to modified Ashworth scale. This was seen especially in the truncal near muscles of the thigh and upper arm segments. We would anticipate this, since multiple electrodes were activated around the trunk to provide trunc stability (figure 1) [12]. We found a quantitative mean increase in trunc stability by the PPAS, and a trend, althoung not significant, in some of the tests. We observed a significant additive spasticity reduction of specific muscles over time. For the angle of first catch of the modified Tardieu scale, we did not find clinical significant improvements, except for selected muscles, which could be ascribed to our multiple comparisons (type 1 error). This would indicate, that the perceived resistance (tone) in a passive movement (MAS) is reduced by the Mollii suit, whereas first catch of spastic reflex is maintained (MTS) as well as the passive range of motion. The latter is consistent with the effects of reciprocal inhibition affecting spasticity only. The velocity dependent patterns (MTS) were unchanged, but an overall spasticity reduction was demonstrated (MAS) [8]. Our findings for MTS and pROM is collaborated by Bakaniene et al. (2018), who did not find changes for these parameters [25]. Ertzegaard et al. did not find a reduction in spasticity using the MAS [9]. Interestingly, both studies had intervention periods of 3 and 6 weeks, respectively. It would seem that longer intervention periods is needed as ours of 24 weeks. Both studies targeted lighter handicapped cerebral palsy patients (GFMCS 1-3). This would indicate that the Mollii suit had a better effect on spasticity in the more severe handicapped, thus with more severe *a priori* spasticity.

Using the MAS as a primary outcome for measuring spasticity, does have limitations in reliability and content validity [26,27]. However, it is frequently used and well-known in clinical spasticity evaluation. For this reason and being aware of the limitations, we chose MAS as outcome parameter. We compensated the limitations by using one specially trained rater for all evaluations, thus to improve reliability of our measurements. To compensate for the type 1 error of multiple analysis, we utilized a Bonferroni correction in our statistical analyses. In conclusion, for this group of severely handicapped children of GFMCS 3-5, the spasticity of the limbs changed from an average of rigid limbs (MAS 4) to considerable increase in muscle tone (MAS 3) after 24 weeks of intervention.

Equally interesting, we saw a considerable effect in function, when measured by the GAS. It would seem that the spasticity reduction had a functional effect mainly on the motor function related goals for these children in regards to hand and arm use, change in basic body positions and mobility of walking/standing. These clinical patient-relevant measureable and attained goals were significantly and clinically meaningful improvements related to daily activities. Five participants only improved in one out of two goals, where the latter deteriorated during the test period. In previous studies, no functional effects were demonstrated with the GAS, timed up and go test, action research arm test, the fast and comfortable gait test [9,24]. As mentioned earlier, the intervention periods and levels of handicap were shorter and lower for these study, which might explain this

differences. The GAS has been utilized in the pediatric population for similar purposes with a good interrater reliability and acceptable content validity [28-30]. We acknowledge, that setting up and evaluating GAS is observer dependent. In this study, the goals were set up and evaluated by the participant's personal therapists. This provided patient relevant goals by an (for the research project) independent evaluator, thus unbiased. However, their personal commitment might have affected their evaluation. However, we evaluated, that the improvements according to change in t-score seemed clinically meaningful. In conclusion, functional improvements are seen after 24 weeks of stimulation in severely handicapped children with CP. The improvements are seen in motor functions of the hand and legs, and in the standing/walking functions.

The evaluation using the GMFM-66 did not demonstrate significant overall changes or changes in the evaluated sub-categories after 24 weeks of intervention. This was demonstrated by Bakaniene et al. (2018) as well, how found positive, but insignificant changes in standing, walking, running and jumping dimensions of the GMFM test [25]. We saw the same positive trends in overall scores and for the dimensions *lying and sitting*. Moreover, we did not see significant improvements in the overall PPAS or in the dimensions of PPAS, but a positive trend as for the GMFM-66. In the study of Westerlund et al. (2014), balance and trunk stability improved [31], but in our study, we were unable to detect significant changes in the GMFM-66 and PPAS after 24 weeks of intervention.

14 out of 31 included participants withdrew from the study. There was multiple reasons for the high number of dropouts. The expected time of usage was 1 hour every second day, which amounted to an expected usage of 720 minuts per calender month. We accepted, that there might be periods of discontinued use of the suit due to for example other 'accidental' diseases as pneumonia. We were able monitor their usage by a diary, and we raised the issue of lack of compliance with the parents thorughout the study period [9]. Five participants had too low compliance of the suit, due to a busy every day of the families, and were excluded from the study. Two participants withdrew due to garment related issues. Three due to that their expectations of the effect of the suit were not met. Two withdrew without any reason. One due to uncear reasons, and one participant moved outside our region, thus we were unable to monitor their study parameters. Our high withdrawal rate was not seen in the three week intervention of Bakaniene et al. (2018), which had full compliance, but was closer to Ertzgaard et al. (2018) with full compliance in 17 out of 27 participants with the six week intervention [9,25].

In our study, our participant population consisted of severely handicapped children with little autonomy, and to optimize compliance, we offered participants both self-administered donning of the suit or donning by the

participants personal therapist. In general, we experienced, that donning of the suits was difficult and the main reason for withdrawal. Our impression was, that difficulties in donning caused the majority of dropout of the study. The personal therapists developed a method of donning using a special fabric sheet to wrap arm and legs into the relative tight suit. In the case of supposedly provoked epilepsy, the electric stimulation might have triggered attacks, and we treated this as an adverse event. This was evaluated by the participant's neuropediatric medical doctor, who did not ascribe the epilepsy to the suit. A questionnaire regarding epilepsy history was send out to all participants with a moderate response rate, thus we were unable to determine this fully. Two of the withdrawals werereasons. We performed a *posthoc* power analysis of the study. This was based on the means and standard deviations of overall spasticity before and after treatment. The power was 0.52 and should be considered as a moderate powered study, where comprehensive and definitive scientific conclusions are not possible. We consider this as a feasibility study, and the merits of our study is, that it is the first study in regards to this particular pediatric patient group [9]. However, this would indicate that our results should be interpreted as indicative of good results for spasticity reduction for severe cerebral palsy. Since this is a relatively new intervention, our study should be considered a feasibility study for significant spasticity reduction and significant improvement in function in severely handicapped children with GFMCS 3-5. We recognize, that improvement in study design for future studies is needed; this should entail either a parallel control group with the suit only and no stimulation or a cross-over design as in Ertzegaard et al. (2018) [9]. Likewise, it is difficult to standardize clinical spasticity evaluation in a research setting for especially our group of children. We used one specially educated spasticity rater for all measurements, but an alternative would be to quantify the neural component by recording the passive stretch digitally, thus providing higher reliability [27]. In this study, we tried to apply such a devise, the Neuroflexor, for spasticity evaluation. For this group of severely handicapped children, they were unable to perform this test consistently. We then abandoned this, and relied on clinical evaluation of MAS and MTS.

In this study as well as in our clinical experience with the Mollii suit, children with spastic and dystonic CP, their parents and therapists have consistently reported, that the children obtained 'calmness in body´, 'are feeling good' and 'are able sit more focused in school'. We focused on spasticity and function in this study, but we would suggest to utilize qualitative methods to document this further in future studies as in Nordstrom et al. (2019) [32]. They reported that parent expectations were high, thus with the potential of being disappointed and discontinue treatment. We recognize this as well in our study, and we ascribe our high withdrawal rate partly by high parental expectations. Moreover, they found, that the patients felt stronger, more agile and pain-free. This is collaborated by Westerlund et al (2014), who reported better mobility, speech, improved digestion, and better mood, reduced pain, improved sleep quality, and an overall improved quality [31]. Both studies did not quantify these findings, and future studies should examine dimensions of pain, digestion, sleep

and quality of life. Further studies is needed to fully uncover the clinical value of this novel intervention with a larger group of the severely handicapped children as well as for the lighter handicapped group, GFMCS 1-2.

In overall conclusion, we demonstrated in our moderately powered study, that 24 weeks intervention with the the Mollii suit in children with CP, GFMCS 3-5, resulted in significantly reduced spasticity and significantly improved motor functions such as mobility of walking and standing, as well as motor skills of the hand and arm.

Reference list:

1. Eunson, P. Aetiology and epidemiology of cerebral palsy. Paediatrics and Child Health 201; Vol.22(9): 361-366.

2. Michael-Asalu A, Taylor G, Campbell H, Lelea LL, Kirby RS. Cerebral Palsy: Diagnosis, Epidemiology, Genetics, and Clinical Update. Adv Pediatr. 2019 Aug;66:189-208.

3. Colver A, Fairhurst C, Pharoah PO. Cerebral palsy. Lancet. 2014 Apr 5;383(9924):1240-9.

4. Graham KH, Rosenbaum P, Paneth N, Dan B, Lin JP, Damiano DL, Becher JG, Gaebler-Spira D, Colver A, Reddihough DS, Crompton KE, Lieber RL. Cerebral palsy. Nature Reviews Disease Primers 2016; 2 (15082).

5. Multani I, Manji J, Hastings-Ison T, Khot A, Graham KH. Botulinum Toxin in the Management of Children with Cerebral Palsy. Paediatr Drugs. 2019:1-21.

6. Dan B, Motta F, Vles JS, Vloeberghs M, Becher JG, Eunson P, Gautheron V, Lütjen S, Mall V, Pascual-Pascual SI, Pauwels P, Røste GK. Consensus on the appropriate use of intrathecal baclofen (ITB) therapy in paediatric spasticity.Eur J Paediatr Neurol. 2010;14(1):19-28.

7. Michelsen JS, Normann G, Wong C. Analgesic Effects of Botulinum Toxin in Children with CP. Toxins (Basel). 2018;10(4):62.

8. Pennati GV. Theoretical framework for clinical applications of Mollii - An introductory review. 2017; https://pdfs.semanticscholar.org/3153/50b8309356d53e43f3650a91c6376db5646c.pdf.

9. Ertzgaard P, Alwin J, Sörbo A, Lindgren M, Sandsjö L. Evaluation of a self-administered transcutaneous electrical stimulation concept for the treatment of spasticity: a randomized placebo-controlled trial. Eur J Phys Rehabil Med. 2018;54(4):507-517.

10. Schuhfried O, Crevenna R, Fialka-Moser V, Paternostro-Sluga T. Non-invasive neuromuscular electrical stimulation in patients with central nervous system lesions: an educational review. J Rehabil Med. 2012;44(2):99-105.

11. Doucet BM, Lam A, Griffin L. Neuromuscular electrical stimulation for skeletal muscle function. Yale J Biol Med. 2012 Jun;85(2):201-15.

12. clinical communication med opfinder af mollii

13. Bouwhuis CB, van der Heijden-Maessen HC, Boldingh EJ, Bos CF, Lankhorst GJ. Effectiveness of preventive and corrective surgical intervention on hip disorders in severe cerebral palsy: a systematic review. Disabil Rehabil. 2015;37(2):97-105.

14. Qoute from Lecture on hip luxation at EPOSNA meeting, May 2017 EPOSNA, Davis, J.

15. Novak I, McIntyre S, Morgan C, Campbell L, Dark L, Morton N, Stumbles E, Wilson SA, Goldsmith S. A systematic review of interventions for children with cerebral palsy: state of the evidence.Dev Med Child Neurol. 2013;55(10):885-910.

16. CPOP group. Recommendations and standardization for leg and foot examination of the Danish cerebral palsy observation register. 2014; http://www.cpop.dk/wordpress/wp-content/uploads/2014.07.03-Fysioterapeut-manual.pdf [Cited 01 July 2019].

17. CPOP group. Recommendations and standardization for arm and hand examination of the Danish cerebral palsy observation register. 2017; http://www.cpop.dk/wordpress/wp-content/uploads/2017-03-06-Manual-til-Ergoterapeutisk-protokol-reduceret-fil-størrelse.pdf [Cited 01 July 2019].

18. Norkin CC, White DJ, Norkin W. Measurement of Joint Motion: A Guide to Goniometry 5th Edition. F.A. Davis Company. 2016.

19. Schut HA, Stam HJ. Goals in rehabilitation teamwork.Disabil Rehabil. 1994 Oct-Dec;16(4):223-6.

20. Bovend'Eerdt TJ, Botell RE, Wade DT. Writing SMART rehabilitation goals and achieving goal attainment scaling: a practical guide Clin Rehabil. 2009 Apr;23(4):352-61.

21. WHO group. International Classification of Functioning, Disability and Health (ICF).2001 https://www.who.int/classifications/icf/en/ [Cited 01 July 2019]

22. Canchild group. GMFM 66. https://canchild.ca/en/resources/44-gross-motor-function-measure-gmfm [Cited 01 July 2019].

23. CPOP group. Recommendations and standardization for PPAS of the Danish cerebral palsy observation register. 2018; http://www.cpop.dk/wp-content/uploads/Dansk-Manual-PPAS_f%C3%A6rdig.pdf [Cited 01 July 2019].

24. R project group for statistical analysis. A language and environment for statistical computing. R Foundation for statistical. https://www.R-project.org/ [Cited 01 July 2019]

25. Bakaniene I, Urbonaviciene G, Janaviciute K, Prasauskiene A. Effects of the Inerventions method on gross motor function in children with spastic cerebral palsy.Neurol Neurochir Pol. 2018;52(5):581-586.

26. Mutlu A, Livanelioglu A, Gunel MK Reliability of Ashworth and Modified Ashworth scales in children with spastic cerebral palsy.BMC Musculoskelet Disord. 2008;9:44

27. Gäverth J, Sandgren M, Lindberg PG, Forssberg H, Eliasson AC. Test-retest and inter-rater reliability of a method to measure wrist and finger spasticity. Rehabil Med. 2013 Jul;45(7):630-6.

28. Steenbeek D, Ketelaar M, Galama K, Gorter JW. Goal attainment scaling in paediatric rehabilitation: a critical review of the literature. Dev Med Child Neurol. 2007 Jul;49(7):550-6.

29. Palisano RJ. Validity of goal attainment scaling in infants with motor delays. Phys Ther. 1993 Oct;73(10):651-8.

30. Cusick A, McIntyre S, Novak I, Lannin N, Lowe K. A comparison of goal attainment scaling and the Canadian Occupational Performance Measure for paediatric rehabilitation research. Pediatr Rehabil. 2006 Apr-Jun;9(2):149-57.

31. Westerlund M, Sjöberg E, Sandell J, Sandström C, Lauritsen HK, Lundqvist F. The Inerventions Method - follow up and long term use of a new possible therapy for patients with spasticity. Ortopediskt Magasin. 2014; 3:45-46. (not peer-reviewed https://issuu.com/jesper.ohlsson/docs/omf__rn__t) [Cited 01 July 2019].

32. Nordstrom B, Prellwitz M. A pilot study of children and parents experiences of the use of a new assistive device, the electro suit Mollii. Assist Technol. 2019 Apr 4:1-8.