The influence of non-invasive stimulation techniques on spasticity of children with cerebral palsy: a systematic review

Which non-invasive stimulation techniques are effective in reducing spasticity in children with cerebral palsy?

Highlights
- Spasticity can be treated with different forms of non-invasive stimulation techniques
- The Modified Ashworth Scale and Tardieu scale are mainly used to measure spasticity, but they can be questioned.
- The effect of the functionality has to be further investigated
- Long-term effects must be further investigated

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Situate master thesis

This master thesis is part of a research field in the pediatric rehabilitation of children with cerebral palsy. Cerebral palsy (CP) can be defined as a heterogeneous group of non-progressive motor disorders caused by chronic brain injuries that originate in the prenatal period, perinatal period or first few years of life. It can be classified under four major subtypes: spastic, athetoid, ataxic and mixed cerebral palsy, spastic cerebral palsy is the most common form. Athetoid, dyskinesia or dystonia are mainly involuntary sustained or intermittent muscle contraction who causes twisting and repetitive movements, abnormal posture or both (Eggink et al., 2017). Ataxic are impairment of coordination of goal-directed movements (Eggink et al., 2017).

The motor disorders may range from difficulties with fine motor control to severe spasticity in all limbs.

Muscle spasticity can be defined as a form of muscle hypertonia associated with upper neuron disease. There is resistance to passive stretch, this results in a minimal initial resistance followed by an incremental increase in muscle tone. The tone increases in proportion to the velocity of stretch. Muscle spasticity is also accompanied by hyperreflexia and variable degrees of muscle weakness and is mainly measured by Modified ash worth scale (MAS), Tardieu scale (TS) or Modified Tardieu scale (MTS). A more reliable and valid measurement tool is the use of an instrumented assessment where integrated biomechanical and electrophysiological measures are used, this showed higher responsiveness than the clinical scales (Bar-On et al., 2014; Sloot et al., 2017). Research about this technique is still going on.

The treatment of spasticity can be divided into five main groups: (1) Preventative measure, (2) therapeutic motor interventions (e.g. physical therapy, occupational therapy, hippotherapy) either with or without the addition of physical modalities (e.g. vibration and electrical currents), (3) positioning/orthotics (e.g. taping, splints, wheelchairs and standers), (4) oral medication (e.g. baclofen and dantrolene), injectable neurolytic medication (e.g. botulinum toxins) and (5) surgical interventions (e.g. lengthening operation, tenotomy, posterior rhizotomy, spinal cord and deep cerebellar stimulation, neurectomies) (Naro et al., 2017). Oral medication and Injectable neurolytic medication are been proven to be effective to decrease spasticity but also have side effects (Bar-On et al., 2014; Naro et al., 2017). Surgery like neurosurgery and orthopedic surgery have the strength to promote normal bone and muscle growth but a disadvantage is that this not eliminate spasticity (Naro et al., 2017). Therapeutic interventions like stretching, neurodevelopmental treatment, casting, Bo bath, casting and strengthening exercises are frequently used in rehabilitative programs and have been proven effective (Naro et al., 2017).

The effect of physical modalities or non-invasive stimulation techniques on the spasticity have been searched by Naro et al. 2017 but not specific for children with CP. Non-invasive can be defined that the skin should not be penetrating, and nothing may be taken orally. Stimulation techniques are all kinds of therapy for which an external device is needed to be able to apply this therapy. (Naro et al., 2017)
Little is known about the influence of non-invasive stimulation techniques on the muscle spasticity in children with cerebral palsy. The aim of this master thesis is to get an overview of which non-invasive stimulation techniques may or may not have an influence.

At the start of this master thesis there was no ongoing research for this topic at the University of Hasselt. This article is written according to a central format by two master students rehabilitation science and physiotherapy with the support and recommendation from Prof. Dr. Meyns Pieter and Prof. Dr. Meesen Raf.

The first part of this thesis took place in the first master year and will have a focus on the literature study of the articles written in the domain of non-invasive stimulation techniques and to establish a research protocol. The second part of the thesis will take place in the second master year and will have a focus on the research itself.
PART 1: LITERATURE REVIEW

1 ABSTRACT

Background: Cerebral palsy (CP) is one of the most common non-progressive neurological brain disorders that occur during the fetal or infant development. Spastic diplegia and hemiplegia cerebral are the most common types CP. There are a lot of treatments to decrease spasticity, but in this review the focus is on non-invasive stimulation techniques and the effect of this stimulation.

Objective: To determine which non-invasive stimulation techniques are effective and how effective these are for the treatment of spasticity in children with CP.

Search methods: In May 2018 PubMed and Web of Science was searched with the keywords: ‘Cerebral Palsy’, ‘Muscle spasticity’ and ‘Stimulation.’

Selection criteria: There were studies included with children and adolescents with spastic CP. These studies also had to use central nervous stimulation, peripheral nervous stimulation, neuromuscular stimulation or muscle stimulation. The spasticity from the participants had to be measured with the Modified Ashworth Scale or Modified Tardieu scale to be included.

Data collection and analysis: Two authors screened titles and abstract. After this, potentially included studies were screened on full text. This two authors extracted all relevant data from included full texts and conducted a quality assessment.

Main results:
Two studies used central nervous stimulation, one study used peripheral nervous stimulation, two studies used neuromuscular stimulation and seven studies used muscle stimulation.
One study found that anodal transcranial direct current stimulation applied on the left M1 reduced the spasticity significantly on the right shoulder, elbow, wrist and fingers compared to baseline.
Transcutaneous spinal cord stimulation did not have an influence on the spasticity.
The studies which used functional electrical stimulation or neuromuscular electrical stimulation on the Gluteus Medius found a significant influence on the spasticity. Neuromuscular electrical stimulation on the tibialis anterior and gastrocnemius and threshold electrical stimulation had no influence on the spasticity. If electrical stimulation was used in addition to passive stretch, there was a significant decrease of spasticity.
If shock wave therapy or radial shock wave therapy was applied on plantar flexors there was a significant effect on spasticity. If extracorporeal shock wave therapy which was applied on the lower limb and when repeated muscle vibration which was applied to the Achille’s tendon, there was also a seen a significant effect on spasticity. Laser acupuncture which was applied on four different points had an influence on the spasticity.
Author’s conclusions: The results of this literature review suggest that anodal transcranial direct current stimulation applied on M1; Functional electrical stimulation and neuromuscular electrical stimulation on gluteus medius; Electrical stimulation, shock wave therapy and radial shock wave therapy applied on plantar flexors; Extracorporeal shock wave therapy applied on the lower limb; Focal muscle vibration applied to the Achille’s tendon and laser acupuncture was applied on four different points have an influence on the spasticity by children in CP. However, these results should be carefully interpreted because the quality assessment of the different studies can be questionable. Also, the follow-up time and the time that interventions lasted varied between the different studies. It is still difficult to say which non-invasive stimulation is the most effective as treatment of spasticity in children with CP. Further research is necessary.
2 INTRODUCTION
Cerebral palsy (CP) is one of the most common non-progressive neurological brain disorders that occur during the foetal or infant development (van der Krogt, Bar-On, Kindt, Desloovere, & Harlaar, 2016). With an overall prevalence of 2.11 cases per 1000 live births world-wide, in the United Kingdom 1.86 cases per 1000 and in the United states 3.6 cases per 1000 live births (Wang et al., 2016). The most important risk factors are low birth weight, intrauterine infections and multiple gestation (Wang et al., 2016).

CP can be classified according to the predominant motor disorder: spastic, dyskinetic/dystonic or ataxic. The spasticity in spastic CP can be described as a velocity-dependent increase in tonic stretch reflex due to hyper-excitability (Aree-uea et al., 2014; van der Krogt et al., 2016). Spastic diplegia and hemiplegia are the most common types CP. This occur in 80% to 90% of the children who have CP (Bar-On et al., 2014). Pain, decrease of passive range of motion (pROM) and prevention of function are commonly seen in children with CP and the management of the spasticity is necessary to prevent the development of secondary muscle contractures, bone deformities and delay or avoid surgery.(Bar-On et al., 2014; Wang et al., 2016).

MAS and MTS are the most common clinical assessments for spasticity (Bar-On et al., 2014). The measurement of spasticity is difficult because the use these clinical assessments of joint resistance is based on the subjective feeling of resistance to manual passive stretching at different velocities (Bar-On et al., 2014; Sloot et al., 2017). A difference between a slow and fast passive movement can be spasticity-related (Bar-On et al., 2014; Sloot et al., 2017). The validity and reliability of the clinical assessment is previously tested (Sloot et al., 2017) but can be questioned because these do not differentiate between the neural and non-neural components causes of the spasticity (Bar-On et al., 2014; Haugh, Pandyan, & Johnson, 2006).

The treatment of spasticity can be divided into five main groups: Preventative measure, therapeutic interventions and physical modalities, positioning/orthotics, oral medication, injectable neurolytic medication and surgical interventions (lengthening operation, tenotomy, posterior rhizotomy, spinal cord and deep cerebellar stimulation, neurectomies) (Naro et al., 2017). There are different methods to apply physical modalities or non-invasive stimulation techniques which have an influence on the treatment of spasticity. The stimulation can be applied on the central nervous system examples are transcranial magnetic stimulation (TMS) (Naro et al., 2017), transcranial direct current stimulation (tic’s) (Naro et al., 2017) and transcutaneous spinal cord stimulation (tSCS) (Solopova et al., 2017). It can be applied on the peripheral nervous system examples are neuromuscular electrical stimulation (NMES) (Naro et al., 2017) and transcutaneous electric nerve stimulation (TENS) (Naro et al., 2017). The stimulation of the muscle self is frequently applied with ultrasound (Us), shock wave therapy (SW) and focal muscle vibration (FMV) (Naro et al., 2017). Because of this large range of non-invasive stimulation techniques, the aim of this study is to determine which non-invasive stimulation techniques are effective in reducing the spasticity in children with CP.
3 METHODS

3.1 Research question
The main research question for this systematic review can be formulated as: ‘Which non-invasive stimulation techniques are effective in reducing spasticity in children with cerebral palsy?’

A PICO formulated for this research question:
- Population: Children with spastic cerebral palsy
- Intervention: non-invasive stimulation techniques
- Comparison: no operation, no medication, orthosis or other type non-invasive techniques
- Outcome: muscle spasticity

3.2 Literature search
PubMed database and Web of Science were systematically searched for literature to answer the research question.

The keywords used for this study are cerebral palsy and muscle spasticity.

For the PubMed database there were two MeSH terms: ‘cerebral palsy’ and ‘muscle spasticity’.

Included in the MeSH term cerebral palsy there were 46 entry terms which describe the different forms of cerebral palsy. They were all included in the search strategy.

Muscle spasticity had five entry terms and three subheadings.

The entry terms are:
- Spasticity, Muscle
- Spastic
- Clasp-Knife Spasticity
- Clasp Knife Spasticity
- Spasticity, Clasp-Knife

The three used subheadings were: ‘prevention and control’, ‘rehabilitation’ and ‘therapy’.

These were used to establish the search terms.

To exclude surgery, we added ‘not surgery’, ‘Not Baclofen’ and ‘Not Botulinum’ to the search terms.

These were added because the main interest is non-invasive stimulation.

Stimulation was not added to this search string because a lot of hits could be missed.

The final search string used was: (cerebral palsy[mesh]) AND (((“Muscle Spasticity/prevention and control”)[Mesh] OR “Muscle Spasticity/rehabilitation”[Mesh] OR "Muscle Spasticity/therapy”[Mesh]]) NOT "Muscle Spasticity/surgery”[Mesh] NOT baclofen NOT botulinum).

This search strategy was performed on 23/05/2018 and on this date, there were 264 hits. Those were screened on title and abstract for inclusion criteria (see 3.3).

For the Web of Science database, the following topics were used: ‘cerebral palsy’, muscle spasticity’, ‘stimulation’.
Stimulation was chosen because the intervention must be non-invasive stimulation. However, if ‘non-invasive stimulation’ was used as a third topic, a lot of hits could have been missed. Here also the topics ‘not baclofen’, ‘not botulinum’ and ‘not surgery’ were added. The final search term was as follows: \textsc{TOPIC: (Cerebral Palsy) AND TOPIC: (Muscle spasticity) AND TOPIC: (Stimulation) NOT TOPIC: (Surgery) NOT TOPIC: (Baclofen) NOT TOPIC: (Botulinum)}

This search strategy was performed on 23/05/2018 and on this date, there were 95 hits. Those 95 hits were screened on title and abstract for inclusion criteria (see 3.3).

3.3 Selection criteria
Following inclusion criteria were used: children with spastic CP (<21 years), non-invasive stimulation techniques, a specific description of the place of intervention and measurement of spasticity. Exclusion criteria were: The influence of any kind of surgery on the spasticity, the influence of any kind of medication that affect the spasticity, like Botulinum and baclofen, adults (>21 years), the use of biofeedback, therapeutic motor interventions because there is no stimulation and/or no specific description of the place of intervention (e.g. horseback riding, active education, vestibular, visual, auditory or tactile stimulation techniques) and studies not written in English.

3.4 Quality assessment
For the quality assessment of the randomized controlled trials (RCT), the Dutch Cochrane checklist for RCT was used. This checklist consists of ten questions and “YES”, “NO”, “?” or “not applicable” can be answered. Every “YES” count as one point, a higher score present better quality.

Cohort studies were assessed for quality using the Risk of bias in non-randomized studies of interventions (ROBINS-I). This consist of seven bias domains and each domain has its own sub-questions to determine the risk of bias.

1. Bias due to confounding?
2. Bias in selection of participants into the study?
3. Bias in classification of interventions?
4. Bias due to deviations from intended interventions?
5. Bias due to missing data?
6. Bias in measurement of outcomes?
7. Bias in selection of the reported result?

In this quality assessment there was no scoring with points. Depending on whether ‘yes’ or ‘no’ was answered to the sub questions, the table for each domain could determine whether there was a low, moderate, serious or critical risk of bias.
The Newcastle-Ottawa quality assessment scale (NOS) for case control studies. The three domains selection, comparability and exposure are divided into different questions.

- Selection
  - Is the case definition adequate?
  - Representativeness of the cases?
  - Selection of controls?
  - Definition of controls?

- Comparability
  - Comparability of cases and controls based on the design or analysis?

- Exposure
  - Ascertainment of exposure?
  - Same method of ascertainment for cases and controls?
  - Non-response rate?

The scoring was performed by giving stars to the answer with a high quality. Every question can earn one star. In the domain comparability a maximum of two stars be given because there are only two questions.

3.5 Data extraction

The data extracted from the included studies consists of: population, aim of the study, study protocol, description of the interventions, outcome measures and results. Strengths and weaknesses were also summarized.

The aim of the study had to describe the place of interventions for example which limb(s), muscle(s), muscle group(s), nerve, spine level or brain area was stimulated and examined. If this was not specifically described, the articles were excluded.

To represent how the population of the studies were composed, sample size, age, inclusion and exclusion criteria were used.

Study protocol was added because there is a large range on how the assessments were performed. In here is a description of when the measurements took place and how long the study lasted.

For the interventions, the type of intervention with a correct description of the used device and other parameters such as duration and number of sessions are important.

Of the outcome measures, the evaluation of spasticity was mainly considered for this study. For the results, data concerning the within-group and between-group comparisons were used concerning spasticity.

Strength and weaknesses where also listed because this was essential for the discussion.
4 RESULTS

4.1 Study selection
The literature search on PubMed revealed 264 hits and Web of Science had 95 hits on 23/05/2018. We had a total of 359 studies, six were duplicates and 31 reviews, which were excluded. After a screening of title and abstract, the full text of selected studies was screened. Flow chart 1

Table 1 gives an overview of the excluded articles
The following articles were excluded:
- One hundred articles because their research focused on the influence of spasticity of different forms of surgery examples are neurosurgery and orthopedic surgery or medication that affects the spasticity such as Botulinum or baclofen.
- There were 58 articles which did not use non-invasive stimulation therapy like physical modalities as previously described.
- Fifty-four articles were excluded because the evaluation of the spasticity did not occur or was not measured according to the MAS, TS or MTS in these articles. Some articles did mentioned measurement of spasticity in their abstract/title, after reading the full text it turned out that spasticity was not measured with a measuring instrument specific developed for spasticity.
- In 47 articles there was no intervention to influence spasticity. Most of them describe commonly used therapy, progression of CP, the development of contractures or the anatomy of muscles, nerves or vessels.
- Thirty articles were not analyzed as they included other pathologies than spastic CP. Some of the pathologies they described were traumatic brain injury and spinal cord injury. Some studies analyzed only healthy subjects.
- Nine articles did not involve children. Based on the abstract/title it appeared that they were children, after checking the full texts it turned out that the age was older than 21.
- Eight articles were not written in English.
- Two articles did not specifically describe the place where the stimulation was applied during the interventions.

After exclusion these articles, 14 studies met the inclusion criteria.

4.2 Quality assessment
Quality assessment of the RCTs was performed with the Dutch Cochrane checklist for RCT. Table 2 gives an overview.

The designs of the included articles were: seven RCT’s (Al-Abdulwahab & Al-Khatrawi, 2009; Aree-uea et al., 2014; Dabbous, Mostafa, El Noamany, El Shennawy, & El Bagoury, 2016; Dali et al., 2002; El-Shamy, Eid, & El-Banna, 2014; Khalili & Hajihassanie, 2008; Solopova et al., 2017), four cohort studies (Celletti & Camerota, 2011; Gonkova, Ilieva, Ferriero, & Chavdarov, 2013; Mirea, Onose, Padure, &
Rosulescu, 2014; Pool, Blackmore, Bear, & Valentine, 2014) and three case-control studies (Amelio & Manganotti, 2010; Karabay et al., 2015; Wang et al., 2016)).

For the seven RCT’s, the way of randomization was not explained in three studies (Al-Abdulwahab & Al-Khatrawi, 2009; Dabbous et al., 2016; Solopova et al., 2017), one study used a 1:1 ratio in blocks of four randomizations (Aree-uea et al., 2014), one used sealed envelopes (El-Shamy et al., 2014), one used flipping a coin for one leg and the other leg was put in the other group (Khalili & Hajihassanie, 2008), one study had a technician, who was not involved, who made batches in which six active and three placebo devices were placed(Dali et al., 2002).

The person who performed the randomization was blinded in four studies (Aree-uea et al., 2014; Dali et al., 2002; El-Shamy et al., 2014; Solopova et al., 2017), in two studies this was not described (Al-Abdulwahab & Al-Khatrawi, 2009; Dabbous et al., 2016) and in one study this was not possible due the way of randomization (Khalili & Hajihassanie, 2008). Blinding of the patients was only possible in one study (Dali et al., 2002).

In five studies the effect assessors were blinded for group assignment (Al-Abdulwahab & Al-Khatrawi, 2009; Aree-uea et al., 2014; Dali et al., 2002; El-Shamy et al., 2014; Khalili & Hajihassanie, 2008). In two studies this was not described (Dabbous et al., 2016; Solopova et al., 2017).

There was no significant difference at baseline assessment in five studies (Al-Abdul Wahab & Al-Khatrawi, 2009; Aree-uea et al., 2014; Dali et al., 2002; El-Shamy et al., 2014; Khalili & Hajihassanie, 2008). In two studies this was not described (Dabbous et al., 2016; Solopova et al., 2017)

Follow-up data was available for 85% in six RCT’s. Only in one study (Dali et al., 2002) this was not the case. and they did not used the results of the patients who left the study during their research.

All studies analyses their patients in the same group as in which they started. Only in one study (Dabbous et al., 2016) this was not described.

In five RCTs there was no selective publication bias. In two studies this could not be derived from the context (Al-Abdulwahab & Al-Khatrawi, 2009; Solopova et al., 2017). No RCTs had unwanted influence by sponsors and the groups were treated equally.

Two studies scored 5/10 (Al-Abdulwahab & Al-Khatrawi, 2009; Dabbous et al., 2016), one study had 7/10 (Solopova et al., 2017) and one study had 8/10 (Khalili & Hajihassanie, 2008), three studies have 9/10 (Aree-uea et al., 2014; Dali et al., 2002; El-Shamy et al., 2014).

Quality assessment of the four cohort studies was performed with de ROBINS-I. Table 3 gives an overview.

All four cohort studies had a low risk of bias due to confounding, bias in selection of participants into the study, bias in classification of interventions and bias due to missing data. There was not enough information available in all the studies about the bias due to deviations from intended interventions. One study (Gonkova et al., 2013) had a low risk of bias in measurements of outcomes, one had a moderate
risk (Celletti & Camerota, 2011) because it was not described if outcome assessors were aware of the intervention which the children received. Two study (Mirea et al., 2014; Pool et al., 2014) had a serious risk for bias, in the study of Mirea et al., 2014 was not described if the outcome measure could have been influenced by knowledge of the intervention received and if the outcome assessors were aware of the interventions the children received. Pool et al., 2014 had an influence by knowledge and were the outcome assessors aware of the intervention.

Quality assessment of the case-control studies was performed with the NOS. Table 4 gives an overview.

Two studies received nine stars and are of high quality (Karabay et al., 2015; Wang et al., 2016). One study (Amelio & Manganotti, 2010) received eight stars, the reason was that the person who performed the clinical examinations was not blinded to intervention.

4.3 Data extraction
A detailed summary of the results can be found in the table 6. Data included in the summary are: aims of the study, population, interventions, study protocol, outcome measures, results and strengths and weaknesses.

4.3.1 Aims of the study

There were two studies that stimulated the central nervous system to decrease spasticity. One study used tDCS on the M1 to decrease the spasticity in the upper limbs (Aree-uea et al., 2014). The other study used tSCS on T11 and L1 to decrease leg spasticity (Solopova et al., 2017).

One study stimulated a peripheral nerve. This study used functional electrical stimulation (FES) on the common fibular/peroneal nerve to investigate its effect on the swing phase of gait which is impaired by spasticity (Pool et al., 2014).

Two studies that stimulated the peripheral nervous system used NMES. One of these used it on both hip abductors muscles to decrease spasticity in the hip adductor muscles (Al-Abdulwahab & Al-Khatrawi, 2009). The other one used NMES on the tibialis anterior to decrease the spasticity in the gastrocnemius (Karabay et al., 2015). One of the studies used electrical stimulation (ES) on the quadriceps in addition to passive stretch of the hamstrings to decrease spasticity in the hamstrings (Khalili & Hajihassanie, 2008). There was one study which used threshold electrical stimulation (TES) on the lower limbs to decrease spasticity of the lower limbs (Dali et al., 2002).

Seven studies stimulated the muscle itself. One of these used SW stimulation on the plantar flexors to examine the effect on spastic equines foot (Amelio & Manganotti, 2010). Another study used radial shock wave therapy (rSWT) on the middle of the gastrocnemius muscle and the soleus muscle to decrease the spasticity of spastic plantar flexor muscle (Gonkova et al., 2013). Two studies used extracorporeal shock wave therapy (ESWT). One study used it on the on the gastrocnemius and soleus to decrease spasticity in the plantar flexor muscles (Wang et al., 2016). There were two studies which used extracorporeal shock wave therapy. One used it on the lower and upper limbs muscles to decrease
spasticity of spastic upper and lower limbs (Mirea et al., 2014), the other one used it on the middle of the gastrocnemius and soleus muscle to decrease spasticity of the lower limbs (El-Shamy et al., 2014). One study used muscle vibration on the gastrocnemius and soleus muscles to decrease the spasticity of the Achilles’s tendon (Celletti & Camerota, 2011).

One study used laser acupuncture on four acupuncture points in the leg (GB34), foot (LI4), elbow (LI12) and hand (Liv3) to decrease spasticity in the wrist and ankle flexors (Dabbous et al., 2016).

4.3.2 Population

The population of all these studies consisted of children with spastic CP. The age of the participants in the studies ranged from 21.5 months to 18 years.

In one study the children had GMFCS levels one or two (Pool et al., 2014) and in one study all the children had GMFCS level two (Aree-uea et al., 2014). There was also one study where the children had a mean score of >70% on the Raven’s test (Solopova et al., 2017).

Children in two studies had not have previous or ongoing treatment with BTX-A or antispastic medication (Amelio & Manganotti, 2010; Wang et al., 2016).

In eight studies, if there was a history of treatment with BTX-A or antispastic medication this had to be two weeks to seven months prior to the start of the interventions. (Aree-uea et al., 2014; Celletti & Camerota, 2011; El-Shamy et al., 2014; Gonkova et al., 2013; Karabay et al., 2015; Mirea et al., 2014; Pool et al., 2014; Solopova et al., 2017). In four studies the use of BTX-A is not mentioned (Al-Abdulwahab & Al-Khatrawi, 2009; Dabbous et al., 2016; Dali et al., 2002; Khalili & Hajihassanie, 2008).

In two studies the children did not have had a previous surgery in the ankle area, foot or leg (Amelio & Manganotti, 2010; Wang et al., 2016). In two studies the children did not have a surgery in the ankle area. (El-Shamy et al., 2014; Gonkova et al., 2013). There was one study where there were no children included that have had a lower limb orthopedic surgery 24 months prior to the intervention (Celletti & Camerota, 2011). In one study the children did not have a previous surgery at the site of gluteus medius (Al-Abdulwahab & Al-Khatrawi, 2009). In one study none of the children have had an orthopedic surgery of the upper limb (Aree-uea et al., 2014). There was one study where there were no children included that have had an orthopedic lower limb surgery on the affected side in the past 12 months (Pool et al., 2014). In one study there were no children who had leg surgery just before or during the trial(Dali et al., 2002). In one study the children did not have had a previous surgery within the last year (Karabay et al., 2015). In one study there were no children who had severe contractures of lower limb that required surgical orthopedic treatment (Solopova et al., 2017). Three studies did not mention anything about previous surgeries (Dabbous et al., 2016; Khalili & Hajihassanie, 2008; Mirea et al., 2014).
In two studies the children were able to walk without use of devices (Celletti & Camerota, 2011; El-Shamy et al., 2014). In another study the children were able to walk unaided or at least with a walker (Dali et al., 2002). There were two studies where the children had to be ambulant with or without the use of devices (Al-Abdulwahab & Al-Khatrawi, 2009; Amelio & Manganotti, 2010). In one study the children were all unable to walk without help (Khalili & Hajihassanie, 2008).

There were eight studies with an intervention group and a control group (Al-Abdulwahab & Al-Khatrawi, 2009; Aree-uea et al., 2014; Dabbous et al., 2016; Dali et al., 2002; El-Shamy et al., 2014; Karabay et al., 2015; Solopova et al., 2017; Wang et al., 2016). The total sample size of these studies varied from 28 to 66 participants. The sample size from the intervention group ranged from 14 to 36, while the sample size of the control group ranged from 14 to 32. Two of these studies also used a group of healthy children as control (Al-Abdulwahab & Al-Khatrawi, 2009; Solopova et al., 2017). The sample size of this group of children was 20 and ten respectively.

Three studies did only have an intervention group (Celletti & Camerota, 2011; Mirea et al., 2014; Pool et al., 2014). The sample size of this studies varies between five and 63. Three studies had one group of children, but these children were their own control (Amelio & Manganotti, 2010; Gonkova et al., 2013; Khalili & Hajihassanie, 2008). In this study the sample sizes ranged from 11 to 25 children.

Two studies made a difference between spastic hemiplegia and diplegia. In one of them was a total sample size of 25 children. There were ten hemiplegic children and 14 diplegic children (Gonkova et al., 2013). The other one had a sample size of 57 children, with 15 hemiplegic and 21 diplegic children in the intervention group and 10 hemiplegic and 11 diplegic children in the control group (Dali et al., 2002).

4.3.3 Intervention

In the studies were stimulation of the central nervous system was applied, one used anodal t-com’s stimulation of the brain with one mA over the left M1, for 20 minutes each day for five consecutive days (Aree-uea et al., 2014). They used a pair of surface sponge electrodes soaked in 0.9% NaCl with an area of 35cm² which were placed using the international Electroencephalography 10/20 electrode placement system and the cathode was placed on the right shoulder (Aree-uea et al., 2014). The other used tSCS stimulation of the spinal cord using two cathodes of 2.5 cm round electrodes which were placed in midline at T11 and L1 and the two anodes of 5.0 x 8cm² rectangular plates were symmetrically placed on the iliac crests. Fifteen sessions of 25 minutes of stimulation over a period of three weeks, this was given by biphasic rectangular 1.0 ms pulses (30Hz) with a modulated frequency of ten kHz and the main intensity stimulation was ten to 50 mA for most children (Solopova et al., 2017).

In the studies were stimulation of the peripheral nervous system was applied, one used FES for one hour each day, six days per week for eight weeks using ‘The Walkaide’ which delivered asymmetrical biphasic surface electrical stimulation with an maximum pulse width of 300µs, maximum frequency of 33Hz and an adjustable intensity that was represented in mA (Pool et al., 2014).
Two used NMES stimulation, in one NMES was applied for 15 min each session, three sessions each day, seven consecutive days with four 32mm round self-adhesive electrodes with a small battery powered NMES unit that produced biphasic asymmetrical waveforms, two independently controlled output channels, more than 20.0mA output current, pulse width of 50µsec and a frequency of 20Hz (Al-Abdulwahab & Al-Khatrawi, 2009). The other NMES study stimulated with a two-channel self-adapting multimodal electro stimulator 30 min each session five days each week for four weeks with two 5.5 x 6.5 cm surface electrodes, 20-30mA intensity, 250µs pulse width and a frequency of 25 Hz, 10 sec on and 12 sec off (Karabay et al., 2015).

In the study were ES was applied they used an two-channel stimulator for 30 min, three times each week for four weeks, with a frequency of 30 Hz, pulse width of 0.4ms, 4s on and 4s off and the intensity was as high as the participants would tolerate (Khalili & Hajihassanie, 2008).

The study were TES was applied for six hours each night for six days each week over a period of 12 months used a One2one stimulator with a pulse amplitude of 1-5µA, frequency of 35Hz, average current density of 0.46µA/mm² and average power density of 25µW/mm² (Dali et al., 2002).

In the studies were the muscle self was stimulated, one used SW stimulation for one time using an electromagnetic coil lithotripter provided with in-line ultrasound, radiographic and computerized aiming, 1500 shots using ultrasound pointer-guide and 0.030mJ/mm³ of energy were applied (Amelio & Manganotti, 2010). One study used radial shock wave (RSWT) for one session of 1500 shots using a BTL-5000 RSWT unit with a small head applicator and a frequency of 5Hz and 1.5bars pressure (Gonkova et al., 2013). One study used radial extracorporeal shock wave (RESWT) session of 1500 shots, with a frequency of eight Hz and an air pressure of 0.6 bar each week for three months using RSWT device Swiss Dolor Clast and the radial (blue) handpiece with 15 mm applicator (Wang et al., 2016). Two studies used extracorporeal shockwave therapy (ESWT). One study applied 500 shocks with an 15mm handpiece, three times for each treated muscle using a BTL-5000 unit, a frequency of 10 Hz and 0.15mJ/mm² energy (Mirea et al., 2014). The other study applied 1500 shots in one session each week for three months using ultrasound pointer guide, frequency of 5 Hz, pressure of 1.5 bars and energy of 0.030mJ/mm² with an electromagnetic coil lithotripter provided with in-line ultrasound, radiographic and computerized aiming (El-Shamy et al., 2014).

One study applied FMV for 10 min and a 30 sec free interval each session, three sessions each day for three days using CRO system with a frequency of 100 Hz and a peak amplitude of 0.05-0.5mm (Celletti & Camerota, 2011).

One study used laser acupuncture applied for 30 secs at each point, two sessions each week for three months with a diode laser device with a wavelength of 650nm, power output of 0-250mW and a pen probe with a diameter of 1 cm (Dabbous et al., 2016).
4.3.4 Study protocol

In the studies where stimulation of the central nervous system was applied, the measurements of the effect of brain stimulation happened at baseline, immediately after the intervention period, 24 and 48 hours after (Aree-uea et al., 2014), in the spinal cord stimulation the measurements happened at baseline and immediately after (Solopova et al., 2017).

In the studies where stimulation of the peripheral nervous system was applied, the measurements of the effect of FES was taken every week for 20 weeks (Pool et al., 2014). In one they measured at baseline, after 10 min, at the end of the first NMES and after seven days (Al-Abdulwahab & Al-Khatrawi, 2009). Three measured at baseline and immediately after intervention (Dali et al., 2002; Karabay et al., 2015; Khalili & Hajihassanie, 2008).

In the studies where stimulation of the muscle was applied using different kinds of SW, the measurements happened in two studies before and after the placebo intervention and active SW therapy and on one, four (Gonkova et al., 2013) and 12 weeks after intervention (Amelio & Manganotti, 2010). One study measured at baseline, one month and three months after (Wang et al., 2016). Two studies measured only at baseline and the end of the intervention (El-Shamy et al., 2014; Mirea et al., 2014). FMV measurement took place at baseline, 24 hour, 30 days and 12 weeks after (Celletti & Camerota, 2011). The study with laser acupuncture took measurements at baseline and immediately after the treatment (Dabbous et al., 2016).

4.3.5 Outcome measures

The MAS is used in 13 of the 15 studies (Al-Abdulwahab & Al-Khatrawi, 2009; Amelio & Manganotti, 2010; Aree-uea et al., 2014; Celletti & Camerota, 2011; Dabbous et al., 2016; Dali et al., 2002; El-Shamy et al., 2014; Gonkova et al., 2013; Karabay et al., 2015; Khalili & Hajihassanie, 2008; Mirea et al., 2014; Solopova et al., 2017; Wang et al., 2016) In one study, the researchers used the Modified Tardieu Scale (Pool et al., 2014).

4.3.6 Results studies

In the studies were stimulation of the central nervous system was applied showed that the one was stimulation was applied using anodal tic’s a significant difference was found in the MAS for the shoulder between groups immediately (p < 0.01) and 24 hours (p < 0.05) after treatment and between baseline, immediately (p < 0.001), 24 hours (p < 0.01) and 48 hours (p < 0.05) after treatment in the intervention group. They also found a significant difference for the elbow between baseline, immediately (p < 0.001), 24 hours (p < 0.001), and 48 hours (p < 0.001) after treatment in the intervention group. For the wrist
they found a significant difference between groups immediately (p < 0.001), 24 hours (p < 0.05) and 48 hours (p < 0.05) after treatment and between baseline, immediately (p < 0.001), 24 hours (p < 0.001) and 48 hours (p < 0.01) after treatment in the intervention group. They found a significant difference for the fingers between groups immediately after the treatment (p < 0.01) and between baseline, immediately (p < 0.001), 24 hours (p < 0.001) and 48 hours (p < 0.001) after treatment in the intervention group. (Aree-uea et al., 2014).

The study which used tasks found no changes in spasticity in either group (Solopova et al., 2017).

In the studies were stimulation of the peripheral nervous system was used showed that the study which used FES found a significant improvement of the MTS between the pre-FES and FES phases (p < 0.01) and the pre- and post-FES phases (p < 0.01) (Pool et al., 2014).

The two studies which used NMES, one found a significant difference of the MAS for the hip adductor muscles between the end of the first stimulation and seven days after the first assessment for the intervention group (Al-Abdulwahab & Al-Khatrawi, 2009) the second found no significant changes for the MAS (Karabay et al., 2015).

The study in which ES in addition to passive stretch was used showed a mean difference in decrease of the MAS due to addition of ES of 0.8 points (p = 0.046) (Khalili & Hajihassanie, 2008). The study which used TES found that the MAS was unchanged in all groups (Dali et al., 2002).

In the studies were stimulation of the muscle self was used showed that the study with SW stimulation found a significant difference in the MAS between the baseline, immediately (p < 0.001), one week (p < 0.001) and four weeks (p < 0.02) after treatment in the intervention group (Amelio & Manganotti, 2010).

The study where RSWT was used found a significant difference in MAS immediately (p < 0.001), two weeks (p < 0.001) and four weeks (p < 0.001) after treatment compared to the baseline for the intervention group (Gonkova et al., 2013).

The study where RESWT was used showed a significant difference in the MAS for the left side between baseline and 3 months after the baseline measurements (p < 0.01) for the treatment group (Wang et al., 2016).

The two studies which used ESWT showed a significant difference for MAS between baseline and the end of the treatment in the control group (p = 0.017) and for the intervention group (p = 0.001) (El-Shamy et al., 2014) or showed that the MAS decreased almost one degree after treatment, but the significance of this was unclear (Mirea et al., 2014).

The study which used FMV showed significant differences for the MAS between baseline and 24 hours after treatment (p = 0.001), between baseline and 30 days after treatment (p = 0.007) and between baseline and 12 weeks after treatment (p < 0.0001) (Celletti & Camerota, 2011).

The study which used leisure acupuncture showed significant differences on the MAS for the wrist flexors (p = 0.00) and ankle plantar flexors (p = 0.00) in the intervention group and significant differences on the MAS for the wrist flexors (p = 0.00) and ankle plantar flexors (p = 0.01) between groups (Dabbous et al., 2016).
5 DISCUSSION

5.1 Reflection on the quality of the studies
The quality of the seven RCT’s varied. In two studies four questions were answered ‘not described’ and thus had a low quality. Dabbous et al., 2016 was the only study where laser therapy was applied on a young group of hemiplegic spastic CP children in one institute. This could mean that the groups were comparable at baseline and so this study was included in this literature review. The study of Al-Abdullahi & Al-Khatrawi, 2009 used a motion & gait laboratory of a Humanitarian city and thus selective publication bias could be present. The groups were not comparable at baseline because they used a healthy control group and children with CP as control group. This study described the use of NMES in a functional way and is reproductive. For this reason, this study was included.

The quality of the four Cohort studies was performed with the ROBINS-I. The study of Mirea et al., 2014 had a serious risk of bias, but this study was performed on all GMFCS levels and the four different spastic syndrome distribution. For this reason, this study was included. In their results the reduction of the spasticity was described but not if this was significant, they mentioned that their results were significant and that the result persisted for three to four weeks in the discussion but this was nowhere else described. The study of Pool et al., 2014 also had a serious risk of bias and the first author was responsible for the clinical assessments and the initial setup of the device. This could be a measurement in outcome bias but can approached positively because only one person performed the measurements and these can all be assessed in the same way. Also this was the only study were FES was applied. For these reasons, this study was included.

The quality of the case-control studies was performed using the NOS. These three studies were of high quality, but in the study of Amelio & Manganotti 2010 the children served as their own control, where in the other two, the children were divided into an intervention group and a control group. They used a small sample size compared to the two others. In the study of Karabay et al., 2015 spasticity was briefly described but their main focus was the muscle architecture of the tibialis anterior and gastrocnemius.

5.2 Reflection on findings in function of research questions
The research question was: which different types of non-invasive stimulation techniques have an influence on the spasticity in children with CP?

Stimulation applied on the central nervous system showed only a significant decrease of the spasticity in the upper limb on children with spastic CP and GMFCS level two, three and four if stimulation was applied for 20 minutes each day for five consecutive days on the left M1 using anodal tDCS and combined with routine physical therapy(Aree-uea et al., 2014). This was the first study to investigate the effect of tDCS applied to patients with spastic CP and cannot be compared to other studies. However in this study the follow-up time was 48 hours after intervention, this is a short period and no statement can be made regarding the long-term follow-up (Aree-uea et al., 2014). Stimulation applied for 20 minutes each session for 15 sessions on children with spastic CP GMFCS level two, three and four using tSCS had no significant decrease of the spasticity in the lower limbs.
This is in contrast with two other studies who found that epidural SCS reduced the spasticity according the MAS (Dekopov et al., 2015; Shabalov et al., 2000). However they did found an significant increase in the GMFM-88 score in the intervention group, this means that these children have better motor functions (Solopova et al., 2017).

Stimulation applied on the peripheral nervous system showed a significant decrease of the spasticity in the lower limb in children with unilateral spastic CP GMFCS level one or two if FES was applied one hour each day, six days a week for eight weeks (Pool et al., 2014). This was also found in two other studies (Hazlewood et al., 1994; Carmick et al., 1993). Improving the spasticity could have an influence on the selective motor control which would lead to better motor functions (Pool et al., 2014).

Stimulation with NMES of the gluteus medius 15 minutes each session, three sessions each day for seven consecutive days showed a significant decrease of the spasticity in the hip adductors in children with spastic diplegic CP who could walk with or without assistive device (Al-Abdulwahab & Al-Khatrawi, 2009). One previous case report showed similar results but the NMES program was applied on the quadriceps (Daichmann et al., 2003), this means that these children gait is close to the level of healthy children (Al-Abdulwahab & Al-Khatrawi, 2009).

Stimulation with NMES of the tibialis anterior and gastrocnemius 30 min each day, five days a week for four weeks on children with spastic diplegic CP GMFCS levels one to five showed no significant decrease of the spasticity (Karabay et al., 2015). This is in contrast with two previous studies who did found a decrease of spasticity in the lower limb (Reed B., 1997; Seifart et al., 2009). This study mainly focused on muscle volume, cross-sectional area, thickness and muscle belly length, only the cross-sectional area of the tibialis anterior was significantly different in the two groups (Karabay et al., 2015).

Stimulation of the quadriceps with ES 30 minutes, three times each week in addition to passive stretch of the hamstrings five time each week for four weeks in children with spastic CP and who were unable to walk independently showed a significant decrease in the spasticity (Khalili & Hajihassanie, 2008). This was also found in two studies (Shindo and Jones., 1987; Pandyan et al., 1997), where one stimulated the wrist extensors (Pandyan et al., 1997).

Stimulation of the quadriceps and tibialis anterior with TES six hours each night, six night each week for 12 months in children with spastic hemiplegia and spastic diplegia who walked with or without a walker showed no decrease in the spasticity of the lower limb (Dali et al., 2002). This is in contrast with one study where FES was applied (Hazelwood et al., 1994).

Stimulation applied on the muscle showed a significant decrease of the spasticity in the gastrocnemius and soleus in children with unilateral spastic equinus with the use of SW applied for one session consisting of 1500 shots (Amelio & Manganotti, 2010). One other study found similar results in adult patients with stroke (Manganotti & Amelio., 2005). They only applied one session of SW and the results lasted for four weeks but not after 12 weeks also no statement can be made if the stimulation have an effect on a functional level (Amelio & Manganotti, 2010).

Stimulation of the gastrocnemius and soleus with RWST in one session consisting of 1500 shots decreased the spasticity significantly in children with spastic hemiplegia or diplegia CP (Gonkova et al., 2017).
Two studies found similar results. One study (Amelio & Manganotti, 2010) applied SW, the other (Vidal et al., 2011) applies RSWT on adults with CP. RSWT is safe, better tolerated and less painful than SW (Gonkova et al., 2013).

Stimulation of the plantar flexors muscles in children with spastic CP for one session consisting of 1500 RESWT, once a week for three months combined with traditional conservative therapy showed a significant decrease in the spasticity (Wang et al., 2016). This is the first study where RESWT is applied to very young children with CP and they also found that RESWT more effective is when MAS is higher and should be started as early as possible, however this study design must been taken into account, The parents could chose in witch group their child participated (Wang et al., 2016).

Stimulation of the gastrocnemius and soleus using ESWT consisting of one session of 1500 shots each week for three months showed a significant decrease of the spasticity in children with spastic hemiplegic CP who could walk without the use of walking aids (El-Shamy et al., 2014). Significant decreases in spasticity was found in two other studies (Amelio & Manganotti, 2010; Vidal et al., 2011). In this study was no long-term follow-up but all different kinds of CP were evaluated (Mirea et al., 2014).

Focal muscle vibration on both sides of the Achilles tendon for 10 minutes, three times each day for three consecutive days in children with spastic diplegic CP who could walk without devices showed a significant decrease of the spasticity (Celletti & Camerota, 2011). One study had similar results (Camerota et al., 2011).

Laser acupuncture applied for 30 seconds on four different points two times each week for three months and received conventional physiotherapy in children with spastic hemiplegic CP showed a significant decrease of the spasticity (Dabbous et al., 2016). Three studies had similar results (Asagai et al., 1994; Fadaie et al., 2002; Anwar et al., 2008). They only used four stimulation points whereas other studies used a large number of acupuncture points, the specific inclusion criteria were not described in this study making it impossible to imitate this study (Dabbous et al., 2016).

5.3 Strengths and weaknesses of the literature review, a reflection

Some strength of this literature review are that there was a clear definition of spasticity and non-invasive stimulation techniques, this was necessary to excluded articles who did not meet the inclusion criteria of these definitions. It was difficult to define a proper definition for spasticity because every study used a different description, especially the older studies. Only the MAS, TS and MTS were determined to measure spasticity, this to exclude articles where they described in the abstract that the spasticity was measured but after checking the full text it appeared that this was done using a test which focus on the functionality, range of motion or strength rather than the spasticity. The reliability and validity of these assessment are questioned. A recently developed technique used a combination of the MAS and
integrated biomechanical and electrophysiological measure (Bar-On et al., 2014; Sloot et al., 2017) and were found valid and reliable, but since this was not used in the studies, MAS, TS and MTS were used. Both auteurs did the selection of the studies and were blinded for each other. When both had made a list these were compared to each other and where different answers were given, these studies were discussed.

Some weaknesses of this literature review are the use of a long search string in PubMed, this could prevent some studies to be found. Although not surgery was added to the search string, there were a lot of studies where surgery was applied. Despite CP was used as a topic in Web of Science, there were a lot of articles where the intervention was not performed on CP. Stimulation was not used as a search item in PubMed because then, some hits were missed. The quality assessment can be questioned because only one person performed this quality assessment, especially the quality of the cohort and case-control studies. These last two checklists were not know to the researcher who performed the quality assessment and found some questions hard to understand because these were not available in Dutch.

5.4 Recommendations for future research

Some recommendations for future research for all kind of interventions in the use of an integrated biomechanical and electrophysiological measure in combination with the MAS, this to get an objective outcome instead of a subjective outcome.

When stimulation is applied on the central nervous system more studies should use longer intervention time in tDCS and tSCS in the treatment of spasticity in children with spastic CP. The inclusion of a motor function test can determine whether this effect is also visible on the functionality in these children. A longer follow-up period is also a recommendation, to know the effects of the intervention on long term follow-up.

When stimulation is applied on the peripheral nervous system the use of functional neuromuscular stimulation is recommended. Improving of the functionality can be added, not only on the lower limb but also on the upper limb, there were no studies found where the upper limb was evaluated using NMES. A longer intervention and follow-up period can be feasible for better results.

When stimulation is applied on the muscle the use of RCT’s is feasible, if this is not possible there should be a control group who are not the same children. In this way the quality of these studies can be better. Also, the stimulation of the upper limb can be researched. The inclusion of a functionality test is recommended. Long-term follow up and a longer intervention period can determine the effects on long-term. A clear description of the included patients and baseline assessment can be essential by reproducing the study.
6 CONCLUSION
The results of this literature review suggest that the spasticity in children with CP can be decreased with the use of non-invasive stimulation techniques. However, the results must be carefully interpreted because the quality assessment of the different studies can be questionable. Also, there was a large different in the intervention period and the follow-up time. Some studies performed only on hemiplegic CP while other applied on quadriplegic CP. The following interventions had a significant decrease of the spasticity TDCS, FES, NMES, SW, RSWT, ESWT, repeated muscle vibration and laser acupuncture applied as previously described while tSCS, ES and TES had no significant influence on the spasticity, but in these studies the focus was the functionality of the children.
References


(*included studies)

**Reference excluded articles**


Armutlu, K., & Fil, A. (2010). PHYSIOTHERAPY APPLICATIONS.


Ueki, F., & Tohyama, S. (2016). Three Case Reports of Successful Vibration Therapy of the Plantar Fascia for Spasticity Due to Cerebral Palsy-Like Syndrome, Fetal-Type Minamata Disease. Medicine, 95(15). doi:10.1097/md.0000000000003385


8 APPENDIXES

PubMed 264

Web Of Science 95

Duplicates: 6
Review: 31

total 322

Included 14

Excluded:
Surgery or Medication = 100
No non-invasive stimulation = 58
Spasticity not measured = 54
No intervention = 47
No CP = 30
No children = 9
Not English = 8
Not specific = 2

Figure 1: Flow chart in and excluded article
<table>
<thead>
<tr>
<th>Reason exclusion</th>
<th>Number of studies</th>
<th>Author(s), Year</th>
</tr>
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</table>
| Intervention was not stimulating | 58 | (Akbarayak, Armutlu, Gunel, & Nurlu, 2005; Alemdaroglu et al., 2016; Androwis, Michael, Strongwater, Foulds, & Iee, 2013; Androwis, Strongwater, Foulds, & Iee, 2014b; Babina, Kotliarov, & Soikher, 2010; Berta, 1984; Blaga, 1982; Bonnechere, Omelina, Jansen, & Van Sint Jan, 2017; Bonnefoy-Mazure et al., 2016; Brouwer, Davidson, & Olney, 2000; Burtner, Woollaccott, & Qualls, 1999; Cheng, Ju, Chen, & Wong, 2012; Chrysagis, Skordilis, Stavrou, Grammatopolou, & Koutsouki, 2012; Currie & Mendiola, 1987; Dimitrijevic et al., 2012; dos Santos & de Oliveira, 2004; Fischer-Brandies, Limbrock, & Tragner-Born, 1988; Fowler, Ho, Nwigwe, & Dorey, 2001; Gillett, Lichtwark, Boyd, & Barber, 2015; Gressmann, 1972; Helt & Foulds, 2004; Hemayattalab, Arabameri, Pourazar, Arakani, & Keshelt, 2013; Iakovlev, Vasilevski, }
Spasticity was not measured

54


There was no intervention

47


Review

31

Mayson & Harris, 2014; Merrill, 2009; Mori et al., 2014; Naro et al., 2017; Peng et al., 2011; Penn, 1982; Pin, Dyke, & Chan, 2006; Pinder, Brogden, Speight, & Avery, 1977; Prasad, Breen, Ampola, & Rosman, 1997; Rosenbaum, 2003; Ryan, Cassidy, Noorduyn, & O’Connell, 2017; Scianni, Butler, Ada, & Teixeira-Salmela, 2009; Stavness, 2006; Tosi, Maher, Moore, Goldstein, & Aisen, 2009; Wongprasartsuk & Stevens, 2002; Wood et al., 2005)

<table>
<thead>
<tr>
<th>The intervention was not performed on cerebral palsy</th>
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<td>(Androwis, Michael, Jewaid, et al., 2015; Armutlu &amp; Fil, 2010; Bakhtiary &amp; Fatemy, 2008; Cabitza &amp; Marraccini, 1968; Childers &amp; Hux, 2013; Cooper et al., 1977; Dymarek, Taradaj, &amp; Rosinczuk, 2016a, 2016b; Elbsioony, Moroz, Bakr, &amp; Mushahwar, 2010; Galanda &amp; Hovath, 1997; Galea, 2012; Ganesan, 2013; Gao &amp; Zhang, 2008; Gilmore, Ziviani, Sakzewski, Shields, &amp; Boyd, 2010; Ikumi et al., 2017; Y. W. Kim, Chang, Kim, Kwon, &amp; Lee, 2017; Kitatani et al., 2016; Laddha, Ganesh, Pattnaik, Mohanty, &amp; Mishra, 2016; Lohse-Busch, Reime, &amp; Falland, 2013; Lorentzen, Pradines, Gracies, &amp; Nielsen, 2018; Lou et al., 2010; Manella &amp; Field-Fote, 2013; Ring &amp; Weingarden, 2007; Sabut, Sikdar, Kumar, &amp; Mahadevappa, 2011; Sonner &amp; Ladle, 2018; Struppler, Havel, &amp; Muller-Barna, 2003; Teixeira et al., 2016; Usuki &amp; Tohyama, 2016; J. Wright &amp; Rang, 1990; Yang, Jee, Hwang, &amp; Sohn, 2017)</td>
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<th>The intervention was not performed on children</th>
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<td>(Ahlborg, Andersson, &amp; Julin, 2006; Arvio, Bjelogrlic-Laakso, &amp; Salokivi, 2014; Cadenhead, McEwen, &amp; Thompson, 2002; Condliffe, Jeffery, Emery, &amp; Gorassini, 2016; Engel, Jensen, &amp; Schwartz, 2004; Hershler et al., 1989; S. J. Kim et al., 2011; Ortega, Jensen, &amp; Schwartz, 2004; Vidal, Morral, Costa, &amp; Tur, 2011)</td>
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<th>not specific</th>
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<td>(Cheng, Yu, Wong, Tsai, &amp; Ju, 2015; Katusic, Alimovic, &amp; Mejaski-Bosnjak, 2013)</td>
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Table 2: Quality assessment randomized controlled trial

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<tbody>
<tr>
<td>1. Were patients randomly assigned to an intervention group?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>2. Were the persons performing the randomization blinded?</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>N</td>
<td>Y</td>
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<tr>
<td>3. Were patients and clinicians blinded for group assignment?</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>Y</td>
</tr>
<tr>
<td>5a. Were the groups comparable at baseline?</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
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<tr>
<td>5b. If no: was a correction performed during analysis?</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>6a. Is follow-up data available for a large enough sample (85%) of the included patients?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>6b. If no: is a selective loss-to-follow-up excluded?</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Y</td>
</tr>
<tr>
<td>7. Were all included patients analysed in the same group they were randomized to?</td>
<td>Y</td>
<td>?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>8. Have the groups been treated equally, apart from the intervention</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>10. Is unwanted influence of sponsors sufficiently excluded?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
</tbody>
</table>

Score op 10

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>5</td>
<td>9</td>
<td>5</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Legend: Y=YES, N=NO, NA= Not Applicable, ?=not sure.
### Table 3 Quality assessment cohort

The Risk of Bias in Non-randomized Studies – of Interventions (ROBINS-I) assessment tool

**Version 19 September 2016**

<table>
<thead>
<tr>
<th>Signaling questions</th>
<th>Celetti 2011</th>
<th>Gonkova 2013</th>
<th>Mirea 2014</th>
<th>Pool 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias due to confounding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.1 Is there potential for confounding of the effect of intervention in this study?</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>If N/PN to 1.1: the study can be at low risk of bias due to confounding and no further signaling questions need be considered</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If Y/PY to 1.1: determine whether there is a need to assess time-varying confounding:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.2 Was the analysis based on splitting participants’ follow up time according to intervention received?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If N/PN, answer questions relating to baseline confounding (1.4 to 1.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If Y/PY, go to question 1.3.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.3 Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If N/PN, answer questions relating to baseline confounding (1.4 to 1.6)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If Y/PY, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Questions relating to baseline confounding only</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.4 Did the authors use an appropriate analysis method that controlled for all the important confounding domains?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.5 If Y/PY to 1.4: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.6 Did the authors control for any post-intervention variables that could have been affected by the intervention?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Questions relating to baseline and time-varying confounding</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.7 Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.8 If Y/PY to 1.7: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of bias judgement</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Bias in selection of participants into the study</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1 Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention?</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>If N/PN to 2.1: go to 2.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.2 If Y/PY to 2.1: Were the post-intervention variables that influenced selection likely to be associated with intervention?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.3 If Y/PY to 2.2: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.4 Do start of follow-up and start of intervention coincide for most participants?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>2.5 If Y/PY to 2.2 and 2.3, or N/PN to 2.4: Were adjustment techniques used that are likely to correct for the presence of selection biases?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk of bias judgement</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Bias in classification of interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.1 Were intervention groups clearly defined?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>3.2 Was the information used to define intervention groups recorded at the start of the intervention?</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
<td>Y</td>
</tr>
<tr>
<td>3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?</td>
<td>N</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Risk of bias judgement</td>
<td>L</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Bias due to deviations from intended interventions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>If your aim for this study is to assess the effect of assignment to intervention, answer questions 4.1 and 4.2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.1 Were there deviations from the intended intervention beyond what would be expected in usual practice?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4.2. If Y/PY to 4.1: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?

If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6

4.3. Were important co-interventions balanced across intervention groups?

4.4. Was the intervention implemented successfully for most participants?

4.5. Did study participants adhere to the assigned intervention regimen?

4.6. If N/PN to 4.3, 4.4 or 4.5: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?

<table>
<thead>
<tr>
<th>Risk of bias judgement</th>
<th>N</th>
<th>I</th>
<th>N</th>
<th>I</th>
</tr>
</thead>
</table>

Bias due to missing data

5.1 Were outcome data available for all, or nearly all, participants?

5.2 Were participants excluded due to missing data on intervention status?

5.3 Were participants excluded due to missing data on other variables needed for the analysis?

5.4 If PN/N to 5.1, or Y/PY to 5.2 or 5.3: Are the proportion of participants and reasons for missing data similar across interventions?

5.5 If PN/N to 5.1, or Y/PY to 5.2 or 5.3: Is there evidence that results were robust to the presence of missing data?

<table>
<thead>
<tr>
<th>Risk of bias judgement</th>
<th>L</th>
<th>L</th>
<th>L</th>
<th>L</th>
</tr>
</thead>
</table>

Bias in measurement of outcomes

6.1 Could the outcome measure have been influenced by knowledge of the intervention received?

6.2 Were outcome assessors aware of the intervention received by study participants?

6.3 Were the methods of outcome assessment comparable across intervention groups?

6.4 Were any systematic errors in measurement of the outcome related to intervention received?

<table>
<thead>
<tr>
<th>Risk of bias judgement</th>
<th>M</th>
<th>L</th>
<th>S</th>
<th>S</th>
</tr>
</thead>
</table>

Bias in selection of the reported result

Is the reported effect estimate likely to be selected, based on the results, from...

7.1. ... multiple outcome measurements within the outcome domain?

7.2. ... multiple analyses of the intervention-outcome relationship?

7.3. ... different subgroups?

<table>
<thead>
<tr>
<th>Risk of bias judgement</th>
<th>L</th>
<th>L</th>
<th>L</th>
<th>L</th>
</tr>
</thead>
</table>

Overall bias

| M | L | S | S |

Responses underlined in green are potential markers for low risk of bias, and responses in red are potential markers for a risk of bias. Where questions relate only to signposts to other questions, no formatting is used.

Legend: N=NO, Y=YES, L=Low, M=moderate, S=Serious, ?=not sure, NI=No information
### Table 4: Quality assessment case-control

**NEWCASTLE - OTTAWA QUALITY ASSESSMENT SCALE**

<table>
<thead>
<tr>
<th>CASE CONTROL STUDIES</th>
<th>Wang 2016</th>
<th>Amelio 2010</th>
<th>Karabay 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Selection</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Is the case definition adequate?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) yes, with independent validation</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) yes, e.g. record linkage or based on self-reports</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>c) no description</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>2) Representativeness of the cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) consecutive or obviously representative series of cases</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) potential for selection biases or not stated</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Selection of Controls</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) community controls</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) hospital controls</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>c) no description</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td><strong>Definition of Controls</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) no history of disease (endpoint)</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) no description of source</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td><strong>Comparability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Comparability of cases and controls based on the design or analysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) study controls for _______________ (Select the most important factor.)</td>
<td>NO sig dif</td>
<td>same persons</td>
<td>no sig dif</td>
</tr>
<tr>
<td>b) study controls for any additional factor (These criteria could be modified to indicate specific __control for a second important factor.)</td>
<td>side sig did</td>
<td>same persons</td>
<td>no sig dif</td>
</tr>
<tr>
<td><strong>Exposure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) Ascertainment of exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) secure record (e.g. surgical records)</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>b) structured interview where blind to case/control status</td>
<td>B</td>
<td>B</td>
<td></td>
</tr>
<tr>
<td>c) interview not blinded to case/control status</td>
<td>C</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d) written self-report or medical record only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e) no description</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) Same method of ascertainment for cases and controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) yes</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) no</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>3) Non-Response rate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>a) same rate for both groups</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>b) non-respondents described</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>c) rate different and no designation</td>
<td>A</td>
<td>A</td>
<td>A</td>
</tr>
<tr>
<td>stars?</td>
<td>9</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>
Table 5 Data extraction included articles

<table>
<thead>
<tr>
<th>TITLE</th>
<th>EFFECT OF SHOCK WAVE STIMULATION ON HYPERTONIC PLANTAR FLEXOR MUSCLES IN PATIENTS WITH CEREBRAL PALSY: A PLACEBO-CONTROLLED STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS, YEAR</td>
<td>Amelio &amp; Manganotti, 2010</td>
</tr>
<tr>
<td>AIM OF THE STUDY</td>
<td>To investigate in a placebo-controlled open study, the effects of a single shock wave stimulation in plantar flexor muscle for a hypothetical treatment of spastic equines foot.</td>
</tr>
</tbody>
</table>
| POPULATION | 12 Children with CP¹  
Inclusion criteria  
- Ability to ambulate  
- Spastic hemiparesis  
- Spastic equines  
- No previous treatment with BTX-A² (7)  
- No recent treatment with BTX-A (5)  
- No previous surgery of the foot, ankle and/or leg  
12 children completed the program. |
| INTERVENTION | Shock wave stimulation  
Electromagnetic coil lithotripter provided with in-line ultrasound, radiographic and computerized aiming was used.  
Pressure pulses focused in hypertonic muscle of the lower limb  
- 1500 shots in middle of belly soleus and gastrocnemius using ultrasound pointer-guide.  
- Energy applied: 0.030 mJ/mm² |
| STUDY PROTOCOL | One placebo treatment session with no shock waves were applied, followed 6 weeks later by one active shock wave treatment session. They also included a 2-week interval between monitoring of placebo and treatment.  
Measurements  
- Before and after placebo  
- Before and after active shock wave  
- 1, 4 and 12 weeks after active shock wave treatment |
| OUTCOME MEASUREMENT | Passive range of motion ankle  
- Electronic goniometer  
Spasticity plantar flexor  
- Modified Ashworth scale  
Pedobarometric assessment |
| RESULTS | Placebo stimulation  
- No sig⁴ changes in MAS⁴ and PROM⁵  
Active stimulation  
MAS  
- Sig difference between baseline and immediately after treatment (3.3 – 1.8) (p<0.001)  
- Sig difference between baseline and 1 week (3.3 - 1.9) (p<0.001).  
- Sig difference between baseline and after 4 weeks (3.3 – 2.25) (p<0.02)  
- No sig difference between baseline and after 12 weeks (3.3 – 2.8)  
pROM  
- Sig difference between baseline and immediately after (20° - 50°) (p<0.001)  
- Sig difference between baseline and after 1 week (20° - 50°) (p<0.001)  
- Sig difference between baseline and after 4 weeks (20° - 40°) (p<0.001)  
- No sig difference between baseline and 12 weeks (20° - 30°) |
| STRENGTHS | Examination where performed by the same physician  
The children where their own control  
They used a 2week interval to avoid possible cross-over effect  
There were no side effects |
| WEAKNESSES | Small sample size  
The protocol was not blinded |

¹ Cerebral palsy  
² Botulinum toxin A  
³ significant  
⁴ Modified Ashworth scale  
⁵ Passive range of motion
# A Prospective Case-Control Study of Radial Extracorporeal Shock Wave Therapy for Spastic Plantar Muscle in Very Young Children with Cerebral Palsy

**Authors, Year** Wang 2016

**Aim of the Study** To prove that rESWT\(^6\) combined with traditional conservative therapy is as safe but not more effective than traditional conservative in the treatment of spastic plantar flexor muscle in very young patient with CP.

**Population** 66 children with CP

**Inclusion**
- Age between 12 and 60 months
- Diagnosis CP
- MAS plantar flexor muscle greater than grade 1 and up to grade 4
- Availability to attend the hospital during treatment and follow-up assessments

**Exclusion**
- Fixed contractures or deformities at left ankle
- Myopathies
- Clinical signs of myopathy and neuropathy
- Treatment with shock waves in the past
- Treatment with BTX-A and/or focal intramuscular treatment with phenol and alcohol in the past
- Previous surgery of the foot, ankle and leg
- Treatment with drugs for spasticity control
- Infection or tumor at the site of therapy application
- Serious blood dyscrasia
- Blood-clotting disorders
- Treatment with oral anticoagulants

rESWT group: n = 34, median age 22.3 months, 11 F\(^7\) and 23 M\(^8\)
control group: n = 32, median age 21.5 months, 11 F and 21 M
There were no lost-to-follow up

**Intervention** rESWT
Treated with radial shock wave device Swiss DolorClast, using the radial (blue) handpiece with 15 mm applicator.
- 1500 radial shock waves per session and leg $\rightarrow$ 3000 radial shock waves/session $\rightarrow$ 36000 radial shock waves end intervention
- Frequency: 8Hz
- Air pressure: 0.6 bar $\rightarrow$ EFD+ of 0.03mJ/mm\(^2\)
- Coupling gel evenly distributed over gastrocnemius and soleus

**Study Protocol**
3 months rESWT and conservative therapy or 3 months conservative therapy
- rESWT = 1 session/week
- conservative therapy = 6 days/week 30 min/type\(^9\) therapy

**Measurements:**
- Baseline (BL)
- 1 month (M1) after BL
- 3 months (M3) after BL

**Outcome Measurement**

<table>
<thead>
<tr>
<th>MAS</th>
<th>Treatment success was defined as individual improvement by more than 1 grade at M3.</th>
</tr>
</thead>
<tbody>
<tr>
<td>pROM</td>
<td>Goniometer in supine position with knee extended.</td>
</tr>
<tr>
<td>GMFM-88(^10)</td>
<td></td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>MAS</th>
<th>rESWT left: 2.6±1.0 BL(^{11}) to 1.5 ± 1.0 M3 (-42%) (p&lt;0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>rESWT right: 1.9 ± 0.6 BL to 1.2 ± 0.7 M3 (-37%) (p=0.49)</td>
</tr>
<tr>
<td></td>
<td>Control left: 2.8 ± 0.8 BL to 2.1 ± 0.5 M3 (-16%)</td>
</tr>
<tr>
<td></td>
<td>Control right: 1.8 ± 0.7 BL to 1.5 ± 0.7 M3 (-17%)</td>
</tr>
<tr>
<td></td>
<td>Within subject effect where time x side, time x treatment and Between subject effect side were statistically sig.</td>
</tr>
</tbody>
</table>

---

\(^6\) Radial extracorporeal shock wave therapy
\(^7\) Female
\(^8\) male
\(^9\) Physical therapy, chinese massage, meridian mediation and muscle stimulation
\(^10\) Gross motor function measurement
\(^11\) Baseline
### pROM
- 13 Patients in rESWT showed significant improvement on left side by more than 1 grade at MAS at M3 but only 2 patients on the right side and 0 in control group.
- 
  - rESWT left: 18.0 ± 11.6 degrees BL to 33.6 ± 11.1 M3 (+87%) (p<0.05)
  - rESWT right: 21.9 ± 12.6 BL to 34.4 ± 10.0 M3 (+57%)
  - Control left: 18.3 ± 8.6 BL to 23.4 ± 6.8 M3 (+28%)
  - Control right: 17.8 ± 9.9 BL 23.6 ± 8.2 M3 (+33%)
- Within subject effects time, time x treatment and treatment were sig.
- Only BL to M3 was sig.

### STRENGTHS
- All treatments were performed on outpatient basis
- The assessors had no access to treatment records
- There were no adverse effects

### WEAKNESSES
- Parents were allowed to choose which treatment their child would receive
- No blinding for patients, parents and therapists
- Parents of children who had better motor skills tended to choose for the rESWT.
# Laser Acupuncture as an Adjunctive Therapy for Spastic Cerebral Palsy

## Aim of the Study
To investigate whether biostimulation by low-level laser acupuncture points on upper and lower limbs add a clinical benefit to conventional physiotherapy in hemiplegic spastic cerebral palsy children.

## Population
40 children (23 M, 17 F)
- Mean age: 3y\(^{12}\) (SD = ± 2m\(^{13}\)) (range: 1 – 4y)

Study group: n = 20
Control group: n = 20

## Intervention
Laser acupuncture
Diode laser device with a wavelength of 650 nm and a power output of 0-250 mW for biostimulation of the acupuncture points, with a pen probe with a diameter of 1 cm with was applied for 30s at 4 different points:\(^{14}\)
- GB 34: lateral aspect leg, anterior and inferior head fibula in deep depression.
- LI 4: dorsum hand between first and second metacarpal bones, radial to midpoint second metacarpal bone.
- LI 12: lateral aspect elbow, superior lateral epicondyle humerus.
- Liv 3: dorsal foot, 2 Tsun proximal to Web margin between first and second metatarsals.

## Study Protocol
2 sessions/week for 3 months and conventional therapy

Measurements:
- BS
- Immediately after treatment period

## Outcome Measurement
- Muscle tone
- MAS of wrist flexors and ankle flexors
- ROM
  - goniometer of wrist and ankle: flexion and extension
- GMFM

## Results

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Study Group</th>
<th>Control Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAS</td>
<td>sig difference (p=0.00)</td>
<td>No sig difference (p=0.08)</td>
</tr>
<tr>
<td>ROM</td>
<td>sig difference for wrist flexors (p=0.00) and ankle plantar flexors (p=0.00)</td>
<td>sig difference for wrist flexors (p=0.00) and ankle plantar flexors (p=0.01)</td>
</tr>
</tbody>
</table>

- Control group: sig difference wrist flexion (p=0.003), ankle plantar flexion (p=0.024), ankle dorsiflexion (p=0.029).
- Study group: sig difference wrist flexion (p=0.01), wrist extension (p=0.00), ankle plantar flexion (p=0.01) and ankle dorsiflexion (p=0.01)
- Between groups: no sig difference was found

## Strengths
- It's a painless technique

## Weaknesses
- No clear inclusion or exclusion criteria
- Only 4 acupuncture points in contrast with other studies
- Small sample size

---

\(^{12}\) years
\(^{13}\) months
\(^{14}\) Points are known from acupuncture experiences to be effective in treatment spasticity
# Title
Reduction of Spasticity in Cerebral Palsy by Anodal Transcranial Direct Current Stimulation

## Authors, Year
Aree-ua 2014

## Aim of the Study
To evaluate the anti-spasticity effects of anodal transcranial direct current stimulation (tDCS) over the left M1 in individuals with spastic cerebral palsy (CP).

## Population
46 children
- **Inclusion**
  - Diagnosis Cp
  - GMFCS\(^{15}\) levels 2 to 4
  - 8 – 18y
  - Upper limb spasticity MAS 1 to 3
- **Exclusion**
  - Severe spasticity and contractures
  - Autism, mental retardation, psychosis and drug addiction
  - Pregnancy, skull defect and epilepsy
  - Receiving concomitant alternative therapies (herbs or massage)
  - Orthopedic surgery upper limb
  - Initiation or change in dosage oral antispastic drug within 5 days
  - BTX-A or BTX-B injections less than 90 days prior

  Active tDCS group: 23
  Sham tDCS group: 23

  45 children completed the program (1 lost to follow up at 48 hours in Sham group)

## Intervention
- **Anodal tDCS**
  - 1mA over left M1
  - Applied via 0.9% NaCl soaked pair of surface sponge electrodes (35cm\(^2\))
  - Maximum output of 10mA.
  - Stimulation over left M1 or C3 locus according to international EEG\(^{16}\) 10/20 electrode placement system, cathode placed right shoulder.

## Study Protocol
20 min active tDCS-therapy/day
Normal drug administration each day and routine physical therapy treatment (passive stretch 1/week, active cycling/treadmill 30min/each day.)

Measurements:
- Baseline
- 5 days treatment
- After evaluation
- 24 hours after
- 48 hours after

## Outcome Measurement
- **MAS**
  - Right shoulder, elbow, wrist and fingers
- **pROM**
  - Goniometer
    - Shoulder flexion, extension, abduction and adduction
    - Elbow flexion
    - Wrist flexion
    - Thumb (carpometacarpal) abduction

## Results
- **MAS**
  - **Shoulder**
    - Sig difference between groups immediately after(p<0.01) and 24h(p<0.05).
    - Sig difference between BS - immediately after(p<0.001), 24h (p<0.01) and 48h(p<0.05) in active tDCS group.
  - **Elbow**
    - No sig difference between groups
    - Sig difference between BS - immediately after(p<0.001), 24h(p<0.001) and 48h(p<0.001) in active tDCS group.
  - **Wrist**
    - Sig difference between groups immediately after(p<0.001), 24h(p<0.05) and 48h(p<0.05)
    - Sig difference between BS – immediately after(p<0.001), 24h(p<0.001) and 48h(p<0.01) in active tDCS group.
  - **Fingers**
    - Sig difference between groups immediately after(p<0.01)

---
\(^{15}\) Gross motor function classification system
\(^{16}\) electroencephalography
Sig difference between BS – immediately after (p<0.001), 24h (p<0.001) and 48h (p<0.001) in active tDCS group.

- **pROM**
  - Immediately after
    - Shoulder abduction (p<0.05) was sig different between groups
    - Shoulder flexion (p<0.01), shoulder abduction <0.05), shoulder adduction (p<0.001), elbow flexion (p<0.05), wrist flexion (p<0.05) and thumb abduction (p<0.05) were sig in tDCS group
  - 24h
    - Shoulder flexion (p<0.01), shoulder abduction (p<0.05), shoulder adduction (p<0.05) were sig in tDCS group compared to BS
  - 48h
    - Shoulder flexion (p<0.05) and shoulder abduction (p<0.05) were sig in tDCS group compared to BS

- **STRENGTHS**
  - Randomization in 1:1 ratio in blocks of four randomizations.
  - Physiotherapist who did the assessments was blinded to treatment condition
  - During the sham and active stimulation, the power indicator lit up.
  - The same physiotherapist did all the assessments.
  - Integrated intent-to-treat analysis: last observation carried forward.
  - Report of 1 side effect and how they solved this.

- **WEAKNESSES**
  - Because the large electrodes there is a change that the result was more generalized than very specific.
  - No long-term effects
# Extracorporeal Shockwave Therapy (ESWT) Benefits in Spastic Children with Cerebral Palsy

**Title:** Extracorporeal Shockwave Therapy (ESWT) Benefits in Spastic Children with Cerebral Palsy

**Authors, Year:** Mirea 2014

**Aim of the Study:** To evaluate the effect of a 3 session of ESWT on spastic upper and lower limbs muscles in children with CP.

**Population:**
- 63 children
  - 37M, 26F
  - Mean age 99.57m (SD = ±53.74 m)

**Inclusion:**
- Informed consent signed by parent
- Age between 2-18 years
- Diagnosed spastic CP
- MAS between 1-3 in targeted muscles

**Exclusion:**
- Fixed contracture
- Severe neurological associated disorders
- Dyskinetic CP
- Any muscle relaxant medication peripheral action (Baclofen or BTX-A) 2 weeks prior
- Any changes in relaxant medication central action 2 week prior

**Intervention:**
- 3 ESWT sessions
  - BTL-5000 unit
  - Energy: 0.15mJ/mm²
  - Total shots dose: 500 shocks/treated muscle
  - Frequency: 10Hz
  - Multi-focus hand piece with 15mm diameter

**Study Protocol:**
- Measurements:
  - BS
  - At discharge

**Outcome Measurement:**
- MAS: triceps surae, hamstrings, hip adductors, biceps brachialis, teres pronator, flexor carpi
- Gross motor function classification system expanded and revised
- GMFM-66

**Results:**
- MAS reduced almost 1 degree after treatment

**Strengths:**
- Used all GMFCS levels
- Used all spastic syndrome, quadriplegia, hemiplegia, triplegia and diplegia.

**Weaknesses:**
- No exact numbers to compare their results, baseline numbers, after treatment
- Not sure if all children completed the study
- In their discussion they mention that they found a significant improvement, but this cannot be found anywhere in the study
- They did not mention how long their intervention lasted nor how much time there was between the ESWT sessions.
<table>
<thead>
<tr>
<th>TITLE</th>
<th>EFFECT OF RADIAL SHOCK WAVE THERAPY ON MUSCLE SPASTICITY IN CHILDREN WITH CEREBRAL PALSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS, YEAR</td>
<td>Gonkova 2013</td>
</tr>
<tr>
<td>AIM OF THE STUDY</td>
<td>To investigate the effect of radial shock wave therapy (RSWT) on muscle spasticity of plantar flexor muscles in children with cerebral palsy</td>
</tr>
<tr>
<td>POPULATION</td>
<td>25 children</td>
</tr>
<tr>
<td></td>
<td>– 16M, 9F</td>
</tr>
<tr>
<td></td>
<td>– Mean age: 4.84y (SD = ±3.11y)</td>
</tr>
<tr>
<td>Inclusion</td>
<td>&gt; 18 months</td>
</tr>
<tr>
<td></td>
<td>– No BTX-A 7 months prior</td>
</tr>
<tr>
<td></td>
<td>– No surgery in area ankle</td>
</tr>
<tr>
<td>Spastic hemiplegia: 10 children</td>
<td></td>
</tr>
<tr>
<td>Spastic diplegia: 15 children</td>
<td></td>
</tr>
<tr>
<td>INTERVENTION</td>
<td>RSWT</td>
</tr>
<tr>
<td></td>
<td>– BTL-5000 RSWT unit</td>
</tr>
<tr>
<td></td>
<td>– Small head applicator</td>
</tr>
<tr>
<td></td>
<td>– 1 session 1500 shots in the middle of gastrocnemius and soleus.</td>
</tr>
<tr>
<td></td>
<td>– Frequency: 5Hz</td>
</tr>
<tr>
<td></td>
<td>– Pressure: 1.5 Bars, burst mode</td>
</tr>
<tr>
<td>STUDY PROTOCOL</td>
<td>Observational, placebo-controlled double-blinded study.</td>
</tr>
<tr>
<td></td>
<td>1 placebo treatment after 4 weeks 1 active treatment session</td>
</tr>
<tr>
<td>Measurements:</td>
<td>BS</td>
</tr>
<tr>
<td></td>
<td>– Immediately after</td>
</tr>
<tr>
<td></td>
<td>– 2 weeks</td>
</tr>
<tr>
<td></td>
<td>– 4 weeks</td>
</tr>
<tr>
<td>No other physiotherapy procedures were performed in following 4 weeks.</td>
<td></td>
</tr>
<tr>
<td>OUTCOME MEASUREMENT</td>
<td>MAS</td>
</tr>
<tr>
<td></td>
<td>pROM</td>
</tr>
<tr>
<td></td>
<td>Baropodometric measurement</td>
</tr>
<tr>
<td>RESULTS</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>No sig difference in pROM or MAS after treatment.</td>
</tr>
<tr>
<td>RSWT</td>
<td>Sig difference in pROM(p&lt;0.001) and MAS(p&lt;0.001) after treatment</td>
</tr>
<tr>
<td>2 Weeks</td>
<td>Sig difference in pROM(p&lt;0.001) and MAS(p&lt;0.001) compared to BS</td>
</tr>
<tr>
<td>4 weeks</td>
<td>Sig difference in pROM(p&lt;0.001) and MAS(p&lt;0.001) compared to BS</td>
</tr>
<tr>
<td>STRENGTHS</td>
<td>The same physician who was blinded to protocol performed clinical examinations.</td>
</tr>
<tr>
<td></td>
<td>Each child served as its own control.</td>
</tr>
<tr>
<td></td>
<td>Placebo treatment with two cushions between head applicator and muscle, 100 shots with lowest intensity.</td>
</tr>
<tr>
<td>WEAKNESSES</td>
<td>Performed in one facility</td>
</tr>
<tr>
<td></td>
<td>Small sample size</td>
</tr>
<tr>
<td>TITLE</td>
<td>PRELIMINARY EVIDENCE OF FOCAL MUSCLE VIBRATION EFFECTS ON SPASTICITY DUE TO CEREBRAL PALSY IN A SMALL SAMPLE OF ITALIAN CHILDREN</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>AUTHORS, YEAR</td>
<td>Celletti 2011</td>
</tr>
<tr>
<td>AIM OF THE STUDY</td>
<td>To explore the effects of repeated muscle vibration stimulation (rMV) on the Achille’s tendon using a protocol on 5 children with cerebral palsy.</td>
</tr>
<tr>
<td>POPULATION</td>
<td>5 children</td>
</tr>
<tr>
<td>Inclusion</td>
<td>Mean age 9.3y (SD = ±3.12y)</td>
</tr>
<tr>
<td>Diagnoses confirmed by magnetic resonance imaging of the brain</td>
<td></td>
</tr>
<tr>
<td>&lt;18 years</td>
<td></td>
</tr>
<tr>
<td>Walking without devices</td>
<td></td>
</tr>
<tr>
<td>Exclusion</td>
<td>Lower limb orthopedic surgery 24 months prior</td>
</tr>
<tr>
<td>Antispastic medication 4 months prior</td>
<td></td>
</tr>
<tr>
<td>Developmental delay</td>
<td></td>
</tr>
<tr>
<td>Use of drugs able to influence spatial perception</td>
<td></td>
</tr>
<tr>
<td>INTERVENTION</td>
<td>3 rMV sessions/day for 10 min and 30sec free interval for 3 consecutive days</td>
</tr>
<tr>
<td>Applied both sides Achille’s tendon</td>
<td></td>
</tr>
<tr>
<td>Frequency: 100Hz</td>
<td></td>
</tr>
<tr>
<td>Peak-to-peak amplitude: 0.05-0.5mm</td>
<td></td>
</tr>
<tr>
<td>STUDY PROTOCOL</td>
<td>Standard and individual physiotherapy program.</td>
</tr>
<tr>
<td>Measurements:</td>
<td>BS T0 (7 days prior)</td>
</tr>
<tr>
<td>24 hours (T1)</td>
<td></td>
</tr>
<tr>
<td>30 days (T2)</td>
<td></td>
</tr>
<tr>
<td>12 weeks (T3)</td>
<td></td>
</tr>
<tr>
<td>OUTCOME MEASUREMENT</td>
<td>MAS</td>
</tr>
<tr>
<td>PROM</td>
<td>Goniometer</td>
</tr>
<tr>
<td>RESULTS</td>
<td>MAS</td>
</tr>
<tr>
<td>T0: 2.75 ± 0.46, T1: 1.75 ± 0.71, T2: 1.63 ± 0.74, T3: 1.88 ± 0.35</td>
<td></td>
</tr>
<tr>
<td>Sig difference between T0-T1(p&lt;0.001), T0-T2(p=0.007) and T0-T3(p=0.006)</td>
<td></td>
</tr>
<tr>
<td>PROM</td>
<td>T0: 94.00 ± 3.74, T1: 101.25 ± 4.98, T2: 103.25 ± 3.96, T3: 104.38 ±4.53</td>
</tr>
<tr>
<td>Sig difference between T0-T1(p&lt;0.001), T0-T2(p&lt;0.0001) and T0-T3(p&lt;0.0001)</td>
<td></td>
</tr>
<tr>
<td>STRENGTHS</td>
<td>Measurement performed by same experienced observers.</td>
</tr>
<tr>
<td>Data collecting happened by different team in double-blinded system</td>
<td></td>
</tr>
<tr>
<td>WEAKNESSES</td>
<td>Small sample size</td>
</tr>
<tr>
<td>TITLE</td>
<td>EFFECT OF EXTRACORPORAL SHOCK WAVE THERAPY ON GAIT PATTERN IN HEMIPLEGIC CEREBRAL PALSY</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>AUTHORS, YEAR</td>
<td>El-Shamy 2014</td>
</tr>
<tr>
<td>AIM OF THE STUDY</td>
<td>To investigate the effects of shock wave therapy on the lower limb on gait pattern in children with hemiplegic cerebral palsy</td>
</tr>
</tbody>
</table>
| POPULATION | 30 children  
- 18M, 12F  
- 6-8 y  |
| Inclusion |  
- Diagnose CP  
- No previous surgery in area ankle  
- No drug for spasticity control  
- No previous treatment BTX-A 7 months prior  
- Good vision  
- Comprehend instructions  
- Walking without use of walking aids  |
| SWT group: 15 children, mean age 6.93y  
Control group: 15 children, mean age 6.8 y |
| INTERVENTION | Shock wave instrumentation 1 session/week for 3 months  
An electromagnetic coil lithotripter provided with in-line ultrasound, radiographic and computerized aiming was used.  
- 1500 shots in middle gastrocnemius and soleus using ultrasound pointer guide.  
- Energy: 0.030mJ/mm²  
- Frequency: 5Hz  
- Pressure: 1.5 bars burst mode |
| STUDY PROTOCOL | Both groups received conventional physical therapy program for 3 months, 1 hour/day, 3 days/week  
Measurements:  
- BS  
- End treatment. |
| OUTCOME MEASUREMENT | MAS  
Gait analysis |
| RESULTS | MAS  
- Control group: BS 2.27 – post treatment 1.86 (p=0.017)  
- SWT group: BS 2.34 – post treatment 1.63 (p=0.001) |
| STRENGTHS |  
- Same examiner evaluated the outcome measurement |
| WEAKNESSES |  
- Only 2 evaluation moments over the 3 months.  
- No evaluation of long-term effects. |
NEUROMUSCULAR ELECTRICAL STIMULATION (NMES) OF THE GLUTEUS MEDIUS IMPROVES THE GAIT OF CHILDREN WITH CEREBRAL PALSY

Al-Abdulwahab S 2009

**AIM OF THE STUDY**
To investigate the short and long-term effects of simultaneous continuous NMES of both hip abductors during walking on the temporal-spatial gait characteristics and hip adductor muscle tone in children with spastic diplegia caused by cerebral palsy.

**POPULATION**
- Control group healthy: 20 children, mean age 7.7 ± 1.6 years
  - Independently walking before age 18 months.
- CP: 31 children
  - Inclusion: age 5-12 years
  - Ambulatory with or without assistive device
  - Ability to cooperate during assessment and protocol
  - No history of hip dislocation
  - Ability to comprehend instructions
  - Exclusion: severe associated sensory impairments
  - History orthopaedic surgery at site gluteus medius
  - Use of oral neuropharmacological agents or injectable materials
  - Epilepsy
- Control group CP: 10 children, mean age 8.3 ± 2.1 years
- Experimental group CP: 21 children, mean age 7.4 ± 2.04 years

**INTERVENTION**
- NMES:
  - Small battery-powered NMES units producing biphasic asymmetrical waveforms.
  - Output channels: 2, independently control
  - Output current: >20.0 mA
  - Pulse width: 2-200µsec → 50µsec
  - Frequency: 2-200 Hz → 20Hz
  - Rated consumption electrical current: >115ma
  - Power source: DC 9 V battery
  - Size: 96mm (H) x 16mm (W) x 27mm (D)
  - Weight: 130g, including battery
  - Applied: four self-adhesive electrodes (round 32mm diameter) into both gluteus medius.

**First NMES management program**
- For immediate and short-term effects
- Anatomically identified gluteus medius and electrodes applied
- Initially given on bed in supine: tingling sensation
- Until isometric contraction was felt (2-3min hold)
- Unit attached to back child in seated position with feet touching the ground
- Unit turned on at isometric contraction
- Walk 470 cm turn and return to chair
- Child had to looked straight ahead

**Second NMES management program**
- Home-based program, long term effects
- 7 days intensive NMES
- 15 min/3 session/day
- Parents instructed how to use NMES
- Rest at least 3 hours between sessions

**Third NMES management program**
- Lie supine 10 min followed by first NMES protocol

**STUDY PROTOCOL**
- Measurements:
  - First: immediately after child arrived gait laboratory and adopted supine position
  - Second: after 10 min
  - Third: end first NMES and during continuous electrical isometric contraction
  - Fourth: seven days after first MT assessment and end second NMES program

**OUTCOME MEASUREMENT**
- MAS
- Gait analysis

**RESULTS**
- Hip adductor
  - Experimental group: no difference between first and second measurement, sig difference between third and fourth measurement.

**STRENGTHS**
- Different time of assessment
- Comparison healthy children
**AIM OF THE STUDY**
To investigate if it is possible to regulate the functional properties of abnormally developed spinal neuronal locomotor networks using transcutaneous spinal cord stimulation on T11 and L1.

**POPULATION**
28 Children with CP (spastic diplegia) (9.4 ±1.7 years).

**Inclusion**
- A mean score of >70% on the Raven’s test
- During the study not being treated with anti-spastic medication
- Received no botulinum toxin injections within the 6 months before the study

**Exclusion**
- Severe contractures of lower limbs, which impeded rehabilitation and required surgical orthopaedic treatment, fractures, osteoporosis, thromboembolic disease, instability of the cardiovascular system, degradation of intellectual development

Randomised in:
- Experimental group (n=13)
- Control group (n=15)

10 Non-injured normally developed children (8.7 ± 21 years)

**INTERVENTION**
Experimental group: 15 sessions of training combined with tSCS. The child was placed in a Lokomat device.
- tSCS:
  - A 2.5-cm round electrodes (Syrtenty) placed midline at the T11, and L1 spinous processes as cathodes + two 5.0 × 8 cm² rectangular plates (Syrtenty) placed symmetrically on the skin over the iliac crests as anodes.
  - Biphasic rectangular 1.0 ms pulses (30 Hz), modulated frequency of 10 kHz
  - Initially delivered at L1 level for 5 minutes in upright posture
  - During the first 10 minutes of locomotor training: applied at T11 vertebral level, followed by the combination of T11 and L1 stimulation for the next 10 minutes.
  - Afterwards the stepping performance was continued for 20 minutes without stimulation.
  - Main intensity stimulation: 10 to 50 mA for most children.
  - Intensity was chosen individually: 5 to 10% below threshold of muscle contraction + well tolerated by all the participants

Control group: 15 sessions with only locomotor training with Lokomat (40 minutes)
- Game-like augmented performance feedback exercise were used.
- Locomotor training was performed at a treadmill speed of ~1km/h.

**STUDY PROTOCOL**
15 Sessions over a period of 3 weeks.

**OUTCOME MEASUREMENT**
All CP children were tested before and after treatment.
- Modified Ashworth scale: leg spasticity
- GMFM-88: level of motor functions
- L-FORCE test of Lokomat software: isometric force in flexors and extensors of hip as well as of knee muscles (30° hip flexion, 45° knee flexion)
- L-Rom test: active range of the movements for flexion and extension in hip en knee joints (in suspended position)
- EMG of rectus femoris, biceps femoris, lateral gastrocnemius, tibialis anterior: measured during air stepping with 100% body weight support by Lokomat device as well as during unaided stepping on Lokomat at the subjects’ maximal speed without body weight support, but supported from a horizontal rail, as needed.

**RESULTS**
Clinical score
- No significant group differences in the baseline clinical measurements
- After treatment, there were no changes of spasticity in any participant either group, as measured by the Ashworth score.

**STRENGTHS**
- Good randomisation
- Experimental, control and group of healthy subjects to compare

**WEAKNESSES**
- Treatment and testing were not blinded
- No repeated baseline measures
- No MAS at end study
TITLE | EFFECTS OF SHORT-TERM DAILY COMMUNITY WALK AIDE USE ON CHILDREN WITH UNILATERAL SPASTIC CEREBRAL PALSY

AUTHORS, YEAR | Pool D., 2014

AIM OF THE STUDY | To determine the effects of functional electrical stimulation (FES) on the common fibular nerve on the main impairments affecting gait in children with unilateral spastic cerebral palsy

POPULATION | 12 participants

Inclusion
- Diagnosis of unilateral spastic cerebral palsy
- Aged 5 to 18 years
- Passive dorsiflexion range of affected ankle of at least 5°
- Gross Motor Function Classification System level I or II
- Achieves full passive knee extension bilaterally
- Dynamic popliteal angle of 45° on the affected side
- Able to cooperate with assessment procedures
- Willing to use the Walk Aide at least 1 hour a day, 6 days a week for 8 weeks

Exclusion
- History of uncontrolled seizure disorder
- Orthopaedic lower limb surgery on the affected side in the past 12 months
- Pins or plates at the site of electrical stimulation
- Botulinum toxin A to lower limb in the past 3 months

INTERVENTION | The Walk Aide: delivers asymmetrical biphasic surface electrical stimulation (ES) in a synchronized manner to stimulate active ankle dorsiflexion during the swing phase of gait. During a gait cycle, the Walk Aide stimulates the common fibular nerve.

- Maximal pulse width: 300µs
- Maximal frequency: 33Hz
- Adjustable intensity (mA)

During the FES intervention phase: using the device for at least 1 hour a day, 6 days a week for 8 weeks.

Families completed a weekly diary, which included recording the hours of usage of the device each day, intensity level, skin integrity, and any other observations.

STUDY PROTOCOL | 20 weeks

- 6-week pre-FES phase
- 8-week FES intervention phase
- 6-week post-FES phase

OUTCOME MEASUREMENT | Bilateral measures were taken to monitor adverse changes (increases in spasticity or clinically significant loss of range).

- Goniometer: passive range of motion
- Modified Tardieu scale: dynamic range of motion
- Australian Spasticity Assessment Scale: spasticity in gastrocnemius muscle
- Handheld Dynamometry: ankle dorsiflexion strength and heel raises
- Selective motor control assessment: selective motor control of ankle dorsiflexion
- Single-limb balance assessment: ankle stability and balance
- Observational Gait Scale (OGS): changes at the level of the foot and ankle in gait
- Self-reported Toe Drag and Falls

RESULTS

Range of Motion
- improved significantly between both the pre-FES and FES phases (P < 0.01) and the pre- and post-FES phases (P = 0.01).
- Throughout the study, loss of range was noted in 2 children (1.7° and 2.1°) between the pre- and post-FES phases.

Spasticity
- improved significantly between the pre-FES and FES phases (P < 0.01) and the pre- and post-FES phases (P < 0.01).
- significant reduction in Australian Spasticity Assessment Scale scores was found between the pre-FES and FES phases (P = 0.03), as well as between the pre- and post-FES phases (P < 0.01).

STRENGTHS | Clear inclusion- and exclusion criteria

WEAKNESSES
- No blinding
- Same person administered the intervention and took the measurements
- No control-group
**Title**
ELECTRICAL STIMULATION IN ADDITION TO PASSIVE STRETCH HAS A SMALL EFFECT ON SPASTICITY AND CONTRACTURE IN CHILDREN WITH CEREBRAL PALSY: A RANDOMISED WITHIN-PARTICIPANT CONTROLLED TRIAL

**Authors, Year**
Khalili M.A., 2008

**Aim of the Study**
To investigate if electrical stimulation on the quadriceps in addition to passive stretching of the hamstrings reduce spasticity and contracture more than passive stretching alone in children with cerebral palsy.

**Population**
11 Participants
- 6 females, 5 males
- Mean age: 12.8 years (SD = ± 0.9 years)

Inclusion:
- Cerebral Palsy
- Spasticity affecting the knee flexors of both legs
- Unable to walk independently

Exclusion:
- Not have normal tactile and pain sensation
- Informed consent could not be obtained

**Intervention**

**Experimental Intervention**
- 30 min of electrical stimulation of the quadriceps 3 times per week
  - Two-channel stimulator applied electrical stimulation to the antagonist muscle (quadriceps femoris) of the experimental leg
  - Frequency: 30 Hz
  - Pulse width: 0.4 ms
  - Duty cycle: 4s on and 4s off (ramp up of 0.5s)
  - Intensity: as high as the participant would tolerate and to produce a visible contraction.
- Passive stretching of the hamstrings 5 times per week
  - Three brief stretches were applied to the hamstrings femoris.
  - Stretch for 30 s
  - One minute rest between three stretches

**Control Intervention**
- Passive stretching of the hamstrings 5 times per week.

Neither the experimental or control legs received any other form of intervention during the four-week period.

**Study Protocol**
- Baseline measurements were collected before randomisation
- After 4 weeks outcome measures were collected immediately after the last intervention

**Outcome Measurement**
- Modified Ashworth scale: spasticity of the hamstrings
- Goniometer: contracture

**Results**

**Modified Ashworth Scale**
- Mean decrease in the experimental group was 2.0 points (SD 0.9), while in the control group it was 1.2 points (SD 0.6).
- Mean difference in decrease due to the addition of electrical stimulation to the stretching regimen was 0.8 points (95% CI 0.1 to 1.5, p = 0.046)

**Goniometer**
- Mean increase in passive knee extension in the experimental group was 13 degrees (SD = 5), while in the control group it was 9 degrees (SD = 3).
- Mean difference in increase in passive knee extension due to the addition of electrical stimulation to the stretching regimen was 4 degrees (95% CI 0 to 7, p = 0.04).

**Strengths**
- Randomization

**Weaknesses**
- Small sample size
- Short duration
- Relatively low-intensity regimen
- No blinding
<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>THRESHOLD ELECTRICAL STIMULATION (TES) IN AMBULANT CHILDREN WITH CP/ A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED CLINICAL TRIAL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors, Year</strong></td>
<td>Dali C., 2002</td>
</tr>
<tr>
<td><strong>Aim of the Study</strong></td>
<td>To examine whether TES on the lower limb can improve motor function in spastic children compared with a placebo group.</td>
</tr>
</tbody>
</table>
| **Population** | 57 Stable children with cerebral palsy  
- 36 males, 21 females  
- Mean age: 10 years 11 months |
| **Inclusion** | - Diagnosed with cerebral palsy (CP)  
- Spastic diplegic or hemiplegic CP  
- 5-18 years old at entry  
- Ability to walk unaided or at least with a walker  
- Being able to understand the design of the trial |
| **Exclusion** | - Had leg surgery just before or during the trial  
- Had developed severe illness  
- Were pregnant  
- Stopped using the stimulator for an extended period |
| **Experimental group** | 15 children with hemiplegia, 21 with diplegia |
| **Placebo group** | 10 children with hemiplegia, 11 with diplegia |
| **Intervention** | **Experimental group**  
- Two thirds of the children  
- TES  
  - Delivered by a One2One stimulator  
  - Pulse amplitude: 1-5 µA  
  - Low frequency: 35Hz  
  - Maximum average current density: 0.46µA/mm²  
  - Maximum average power density: 25 µW/mm²  
**Placebo group**  
- One thirds of the children  
- Inactive stimulators: Sham group |
| **Study Protocol** | Twelve month period  
Children slept with TES for at least 6 hours per night, 6 nights a week.  
Before the start of the treatment:  
- Set of motor function tests  
- An examination of ROM of legs and arms, reflexes, height, weight, puberty stage (Tanner 1962)  
- Spasticity  
- Half of the children had a cross-sectional CT of the quadriceps muscle  
- Parents were asked to fill in a questionnaire in the beginning and at the end of the trial |
| **Outcome Measurement** | - Motor function test: designed for this study  
- CT: quadriceps and tibialis anterior muscles: cross-sectional area (cm²)  
- Questionnaire: impression of the child’s motor function  
- ROM: legs and arms  
- Modified Ashworth scale: spasticity  
  Clonus levels |
| **Results** | **Logbook**  
- 82% uses TES every night except for a few weeks on average  
**ROM**  
- Non-significant TES effect (p=0.31 for diplegic and hemiplegic groups combined)  
**Modified Ashworth scale**  
- Unchanged |
| **Strengths** | - Double-blind  
- Experimental and placebo-group |
<p>| <strong>Weaknesses</strong> | - Results are from diplegic and hemiplegic groups combined |</p>
<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>SHORT-TERM EFFECTS OF NEUROMUSCULAR ELECTRICAL STIMULATION ON MUSCLE ARCHITECTURE OF THE TIBIALIS ANTERIOR AND GASTROCNEMIUS IN CHILDREN WITH CEREBRAL PALSY</th>
</tr>
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<tbody>
<tr>
<td><strong>Authors, Year</strong></td>
<td>Karabay I., 2014</td>
</tr>
<tr>
<td><strong>Aim of the Study</strong></td>
<td>To explore the short-term effects of neuromuscular electrical stimulation application on tibialis anterior (stimulated muscle) and gastrocnemius (antagonist) muscles’ size and architecture in children with cerebral palsy by using ultrasound.</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>28 patients with CP</td>
</tr>
<tr>
<td><strong>Inclusion</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
- Spastic CP                                                                                                                     |
|  
- Aged between 3 and 14 years                                                                                                     |
| **Exclusion** |  
|  
- Fixed deformity of the ankle joint                                                                                              |
|  
- Previous surgery within the last 1 year                                                                                        |
|  
- Previous botulinum toxin injections to calf muscles within the last 6 months                                                   |
|  
- Any neurologic or orthopaedic condition of the lower limbs (unrelated to CP)                                                   |
| Patients were put in group A and group B alternatingly.                                                                           |
| **Intervention** |  
|  
Group A (n=14)                                                                                                                   |
|  
- Conventional physiotherapy                                                                                                     |
|  
- NMES treatment                                                                                                                  |
|  
- Bilaterally to TA muscle                                                                                                       |
|  
- 30mins/session, once daily, 5 days a week, 4 weeks                                                                            |
|  
- Two-channel self-adapting multimodal electro stimulator (SAMMS Mod Professional)                                              |
|  
- Two surface electrodes with the size of 5.5 x 6.5 cm (active electrode was placed on the one-third proximal)                    |
|  
- Piece of TA muscle                                                                                                              |
|  
- Intensity: 20-30 mA                                                                                                              |
|  
- Sequence pulse width: 250µs                                                                                                     |
|  
- Frequency: 25Hz                                                                                                                 |
|  
- Sequence on 10 secs and then off for 12 secs.                                                                                  |
|  
- Level of stimulation was increased until contraction was observed also as the patient became more accommodated to it.        |
| Group B (N =14)                                                                                                                   |
|  
- Conventional physiotherapy                                                                                                     |
| **Study Protocol** | Prospective study                                                                                                                |
|  
- 4 weeks, 20 sessions                                                                                                            |
| **Outcome Measurement** | Initially and at the end of the treatment                                                                                       |
|  
- GMFCS: Gross motor function                                                                                                |
|  
- Ankle dorsiflexion: Selective motor control                                                                                     |
|  
- Modified Ashworth scale: Spasticity                                                                                             |
|  
- Ultrasonographic measurements of TA and GC muscles bilaterally                                                                |
| **Results** |  
|  
- The groups were similar as regards to age, sex, body mass index, and GMFCS levels (all Ps > 0.05)                             |
|  
- Spasticity                                                                                                                     |
|  
- Not changed significantly                                                                                                     |
| **Strengths** |  
|  
- Experimental group and placebo group                                                                                           |
| **Weaknesses** |  
|  
- No blinding possible                                                                                                          |
|  
- No randomization                                                                                                               |
|  
- No long-term follow-up                                                                                                         |
PART 2: PROTOCOL

The Effect of Transcranial Direct Current Stimulation on Spasticity and Manual Ability in Children with Cerebral Palsy: A Randomized Controlled Trial: Protocol

1. INTRODUCTION

Cerebral palsy (CP) in children is one of the most common non-progressive neurological brain disorders which occur during the foetal or infant development (van der Krogt et al., 2016). Risk factors are low birth weight, intrauterine infections and multiple gestation (Wang et al., 2016). Spasticity can be described as a velocity-dependent increase in tonic stretch reflex due to hyper-excitability (Areeuea et al., 2014).

Spastic diplegia and hemiplegia cerebral are the most common types CP, this occur in 80 to 90% of the children who have CP (Bar-On et al., 2014). Pain, decrease of passive range of motion (pROM) and prevention of function are commonly seen in children with CP and the management of the spasticity is necessary to prevent the development of secondary muscle contractures, bone deformities and delay or avoid surgery (Bar-On et al., 2014; Wang et al., 2016). MAS and MTS are the most common clinical assessments for spasticity (Bar-On et al., 2014). The validity and reliability of the clinical assessment is previously tested (Sloot et al., 2017) but can be questioned because these do not differentiate between the neural and non-neural components causes of the spasticity (Bar-On et al., 2014; Haugh et al., 2006).

The treatment of spasticity can be divided into five main groups: (1) Preventative measure, (2) therapeutic motor interventions (e.g. physical therapy, occupational therapy, hippotherapy) either with or without the addition of physical modalities (e.g. vibration and electrical currents), (3) positioning/orthotics (e.g. taping, splints, wheelchairs and standers), (4) oral medication (e.g. baclofen and dantrolene), injectable neuromyelic medication (e.g. botulinum toxins) and (5) surgical interventions (e.g. lengthening operation, tenotomy, posterior rhizotomy, spinal cord and deep cerebellar stimulation, neurectomies) (Naro et al., 2017). Oral medication and Injectable neuromyelic medication are been proven to be effective to decrease spasticity but also have side effects (Bar-On et al., 2014; Naro et al., 2017). Surgery like neurosurgery and orthopedic surgery have the strength to promote normal bone and muscle growth but a disadvantage is that this not eliminate spasticity (Naro et al., 2017). Therapeutic interventions like stretching, neurodevelopmental treatment, casting, Bo bath, casting and strengthening exercises are frequently used in rehabilitative programs and have been proven effective (Naro et al., 2017).

The effect of physical modalities or non-invasive stimulation techniques on the spasticity have been searched by Naro et al., 2017 but not specific for children with CP. Non-invasive can be defined that the skin should not be penetrating, and nothing may be taken orally. Stimulation techniques are all kinds of therapy applied on the central nervous system, peripheral nervous system and the muscle self for which an external device is needed to be able to apply this therapy. (Naro et al., 2017)
The systematic review: ‘The influence of non-invasive stimulation techniques on spasticity of children with CP’, showed that stimulation applied on the central nervous system, peripheral nervous system and the muscle self could significantly reduce the spasticity of children with CP. One study who used anodal transcranial direct current stimulation (tDCS) applied on the left M1 for 20 minutes each day for five consecutive days in children with spastic Cp and GMFCS level two focused on the spasticity of the upper limb. This study concluded a significant effect of tDCS on the shoulder immediately after (p<0.001) and after 24 hours (p<0.05) between groups and between baseline and immediately after (p<0.001), 24 hours after (p<0.01) and 48 hours after (p<0.05). In the elbow between baseline, immediately (p < 0.001), 24 hours (p < 0.001), and 48 hours (p < 0.001) after treatment. In the wrist between groups immediately (p < 0.001), 24 hours (p < 0.05) and 48 hours (p < 0.05) after treatment and between baseline, immediately (p < 0.001), 24 hours (p < 0.001) and 48 hours (p < 0.01) after treatment. In the fingers between groups immediately after the treatment (p < 0.01) and between baseline, immediately (p < 0.001), 24 hours (p < 0.001) and 48 hours (p < 0.001). TDCS uses constant or alternating current and consists in the application of a low amplitude direct electrical current through electrodes placed on the scalp (Naro et al., 2017). This was applied 20 minutes each day for five days on the left M1 to children with spastic CP and gross motor function classification system (GMFCS) level two to reduce the spasticity (Aree-uea et al., 2014). This study did a follow-up till 48 hours after the intervention. There is not much known about the long-term effects of tDCS on spasticity in children with CP. Therefore, in this study, there will be a follow-up till one week after treatment. In the study of Aree-uea et al., 2014, the manual ability of the children is not mentioned. However, the manual ability is also frequently impaired in children with CP. Manual ability can be defined as a “capacity to manage daily activities requiring the use of the upper limbs whatever the strategies involved”. This can be influenced by environmental and/or personal factors, environmental like devices and personal like motivational, cognitive and emotional status (Arnould, Penta, Renders, & Thonnard, 2004). To measure this the Abilhand-kids questionnaire is frequently used. In this study, the Abilhand-kids will be used to have a view on the change in manual ability of the children after they got tDCS.
2. AIM OF THE STUDY
The aim of this study is to investigate the effect of anodal transcranial direct current stimulation (tDCS) on the Modified Ashworth Scale (MAS) and the Abilhand-Kids in children with spastic CP. This simulation will be compared to a sham-group.

2.1. Research question
What is the effect of anodal transcranial direct current stimulation on the Modified Ashworth Scale and the Abilhand-Kids in children from eight to 18 years old with spastic hemiplegic CP?

2.2. Hypothesis
The null hypothesis are:
H1a: Children with spastic CP who receive the five-day tDCS program with their routine treatment and mobilisation of the upper limb will show a significant improvement on the MAS.
H1b: Children with spastic CP who receive the five-day tDCS program with their routine treatment and mobilisation of the upper limb will show a significant improvement on the Abilhand-Kids.
H1c: If there is an improvement on the MAS after the five-day tDCS program with their routine treatment and mobilisation of the upper limbs, there will be an improvement on the Abilhand-Kids.

The alternative hypotheses are:
H2a: There is no significant effect of the five-day tDCS program on the MAS.
H2b: There is no significant effect of the five-day tDCS program on the Abilhand-Kids.
H3b: If there is no improvement on the MAS after the five-day tDCS program with their routine treatment and mobilisation of the upper limbs, there will be no improvement on the Abilhand-Kids.
3. METHOD

3.1. Design
The design of this study is a randomized controlled trial. The patients will be randomized by an online randomization tool. The participants and assessors will be blinded to patient allocation and intervention. The therapist who will administer the stimulation cannot be blinded. The therapist who performs the data-analysis will also be blinded from the group allocation.

There will be a five-day intervention, with 20 minutes of stimulation, the routine treatment of the children and mobilisation of the upper limbs each day. The stimulation and tests will be administered at REVAL (Rehabilitation Research Centre) in Diepenbeek. There will be one physiotherapist who gives the stimulation and one other who performs the mobilisations of the upper limbs. The routine treatment will be given by their regular physiotherapist. The design is illustrated in Figure 1.

Eligible participants: diagnosis of hemiplegic spastic CP, aged between eight and 21, Gross Motor Function Classification System level one or two, informed consent signed by parent, ability to cooperate

Screening measurement: screening for exclusion criteria

Baseline measurement (T0) (n=30)

Randomisation

tDCS group
→ stimulation of 1mA over the left M1 for 20 minutes
→ routine therapy

Sham - group
→ current will be stopped after 30 seconds
→ routine therapy

Measurement immediately after end treatment (T1)

Measurement 24 hours after treatment (T2)

Measurement 48 hours after treatment (T3)

Measurement one week after treatment (T4)

Figure 1
3.2. Participants
There will be 30 participants in this study, aged eight to 18 years old, which will be equally randomized into an intervention group and a sham group. The following criteria will be implemented:

3.2.1. Inclusion criteria
The following inclusion criteria must be satisfied: diagnosis of hemiplegic spastic CP, aged between eight and 18, Gross Motor Function Classification System level one or two, Manual Ability Classification System one to three, informed consent signed by parent and ability to cooperate.

3.2.2. Exclusion criteria
Patients with the following exclusion criteria will be excluded: Botulinum toxin injections less than six months prior to the begin of the study, previous surgery of the upper limb, epilepsy, previous cranioplasty, severe spasticity and contractures, participating in other studies, receiving concomitant alternative therapies.

3.2.3. Recruitment
Patients with hemiplegic spastic CP will be recruited via flyers and posters in UZ Leuven, Campus Pellenberg, which is a CP-reference center.

3.3. Medical ethics
The parents or guardians will have to provide written informed consent. Approval by the Ethics Committee of the university of Hasselt will be requested in august 2018.

3.4 Intervention
The tDCS is applied via surface sponge electrodes which were soaked in 0.9% NaCl of 35cm². This device (Soterixmedical, model 1224-B) had an maximum output of 10mA. The stimulation site will be determined according to the international electroencephalography (EEG) 10/20 electrode placement system. (Aree-uea et al., 2014; Valle et al., 2007). The cathode is placed on the right shoulder. In the sham-group the current will be discontinued after 30 seconds, but the power indicator remains on. This will make sure there is blinding of the participants. The stimulation will be applied 1mA over the left M1 with a maximum output of 10mA (Aree-uea et al., 2014). The sessions will comprise 30 minutes of tDCS or sham therapy a day, each day, for five consecutive days. The participants also receive their routine physical treatment and daily passive mobilisation of the upper limbs.

3.5. Outcome measurements
There is not many research done about the long-term effects of tDCS. In this study, there will be measuring moments before the treatment, immediately after and at three other moments after treatment. The last measurement will take place after one week to investigate whether tDCS has an effect that stays longer than 48 hours after treatment. The measurements will be taken at a baseline (T0), immediately at the end of treatment (T1), 24 hours after treatment (T2), 48 hours after treatment (T3) and one week after treatment (T4). In this way, immediately changes will be measured, but also the longer effects will be recorded.
3.5.1. Primary outcome measurements

**Spasticity**

The aim of this study is to investigate the effect of tDCS on spasticity of the upper limb. The spasticity of the shoulder, elbow, wrist and fingers will be measured by the MAS. This test will be performed in supine position, because moving can increase spasticity.

The joint will be placed in a maximally flexed position and will be moved to a position of maximal extension over one second. The participant will be instructed to relax. The following grades will be used: grade 0 will mean that there is no increase in muscle tone; Grade 1 will mean that there is a slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension; Grade 1+ will mean a slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM; Grade 2 will mean a more marked increase in muscle tone through most of the ROM, but affected part(s) easily moved; Grade 3 will mean a considerable increase in muscle tone, passive movement is difficult; Grade 4 will mean an affected part is rigid in flexion or extension (Bohannon & Smith, 1987). This is illustrated in figure 2.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No increase in muscle tone</td>
</tr>
<tr>
<td>1</td>
<td>Slight increase in muscle tone, manifested by a catch and release or by minimal resistance at the end of the range of motion when the affected part(s) is moved in flexion or extension</td>
</tr>
<tr>
<td>1+</td>
<td>Slight increase in muscle tone, manifested by a catch, followed by minimal resistance throughout the remainder (less than half) of the ROM</td>
</tr>
<tr>
<td>2</td>
<td>More marked increase in muscle tone through most of the ROM, but affected part(s) easily moved</td>
</tr>
<tr>
<td>3</td>
<td>Considerable increase in muscle tone, passive movement difficult</td>
</tr>
<tr>
<td>4</td>
<td>Affected part(s) rigid in flexion or extension</td>
</tr>
</tbody>
</table>

![Figure 2: Grading of the Modified Ashworth Scale](image)

The ICC scores showed that the interrater reliability varied from moderate to good (0.61-0.87). Test-retest reliability is poor to good (0.63-0.83) (Mutlu, Livanelioglu, & Gunel, 2008). The spasticity will be measured for shoulder anteflexion and retroflexion, elbow flexion and palmar flexion of the wrist. The MAS will be measured on all measuring moments, so there will be a good vision on the effects of tDCS.

**Manual Ability**

In this study, the manual ability of the upper limbs of the participants will also be measured. For this, the Abihand-kids will be used.

This is a questionnaire for the parents who perceived the child’s manual performance of 21 bimanual daily activities. It scores how the task is experienced by the child. Answers are rated on a three-point ordinal scale (de Jong, van Meeteren, Emmelot, Land, & Dijkstra, 2018; Klingels et al., 2010). The parents must answer with ‘impossible’, ‘difficult’ or ‘easy’. They can also choose ‘?’ when the activity is not attempted in the last three months. The child is never asked to perform the activities in front of the assessor. The questions are shown in figure 3. The study of Jong et al., 2018 investigated the validity
and reliability of the Abilhand-kids. These researchers concluded a high internal consistency (0.94) and for validity a strong association with the Manual Ability Classification System. The test-retest reliability was 0.92. The overall ICC was 0.92 (95% CI: 0.87-0.96). As such, this questionnaire has been found reliable and valid as a performance and capacity-bases rating method this is the difference between what a child can do under normal daily environment and standardized controlled conditions (de Jong et al., 2018). The Abilhand-kids was originally developed in French, but has been translated in English and Dutch. The Abilhand-kids will be taken at T0, T3 and T4. This because a learning effect can influence the result. To avoid this even more, the activities will be presented at a different order at every measuring moment. The parents will get time to fill in this questionnaire while their children are being tested.

One therapist will perform all the measurements and will not be involved in the data-analysis. The Abilhand-kids will be scored by a researcher who is also not involved in the data-analysis.

<table>
<thead>
<tr>
<th>Item</th>
<th>Impossible</th>
<th>Difficult</th>
<th>Easy</th>
<th>?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opening a jar of jam</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Putting on a backpack/schoolbag</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opening the cap of a toothpaste tube</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unwrapping a chocolate bar</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Washing the upper-body</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rolling-up a sleeve of a sweater</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sharpening a pencil</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taking off a T-shirt</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squeezing toothpaste onto a toothbrush</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>opening a bread box</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unscrewing a bottle cap</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>zipping-up trousers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Buttoning up a shirt/sweater</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.5.2. Secondary outcome measurements

Pain
An important factor that can have an influence on the performance of the participants is pain. The VAS-scale will be used to indicate the overall pain of the participants. The participants will be asked to indicate their overall pain on a line from zero to ten. Thus, it will be seen if pain increase or decrease as a consequence of stimulation or decrease of spasticity. The VAS-scale will be evaluated on all measuring moments.

Passive Range of Motion
The passive range of motion (pROM) will also be measured, because spasticity can affect the mobility of a joint. This will be measured with a goniometer. The degree of mobility toward flexion, extension and abduction of the shoulder, flexion and extension of the elbow and palmar and dorsal flexion of the wrist will be measured. The pROM will be measured at all measuring moments.

3.6. Data-analysis
The program JMP will be used for data-analysing. The two treatment conditions will be compared on all baseline outcome measures. This will be done by using a series of paired t-tests. We will also calculate intent-to-treat to take dropouts into account. Both the primary and secondary variables will be analysed using repeated measure analysis of variance (ANOVA), time, treatment condition, and the interaction between time and treatment condition as independent variables. The p-value of <0.05 will be considered as significant difference. The interaction term of group and time (group x time) will also be assessed.
4. TIME PLANNING

In August 2018, the approval of the Ethics Committee will be requested. As soon as there is approval, the recruitment will start. In February and March 2019, the measurements and interventions will take place and from end March the analysis can be done. The aim is to end the analysis in April 2019 and the study will be finished at mid May 2019.
5. REFERENCES

Uncategorized References


<table>
<thead>
<tr>
<th>DATUM</th>
<th>INHOUD OVERLEG</th>
<th>HANDTEKENINGEN</th>
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<tbody>
<tr>
<td>25/11/2017</td>
<td>Opstellen en ondertekenen van contract</td>
<td>Promotor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Copromotor:</td>
</tr>
<tr>
<td>29/01/2018</td>
<td>Overlopen zoekstrategieën en gevonden artikels, vaste zoekstrategie opgesteld.</td>
<td>Promotor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Copromotor:</td>
</tr>
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<td>19/04/2018</td>
<td>Overlopen gevonden artikels en vastleggen in- en exclusiecriteria, Artikels die niet beschikbaar voor de studenten opgezocht en doorgemailed door promotor. Tips ivm juiste definitie geven gekregen.</td>
<td>Promotor:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Copromotor:</td>
</tr>
<tr>
<td>5/05/2018</td>
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<td>Promotor:</td>
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<td>Copromotor:</td>
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<tr>
<td>8/05/2018</td>
<td>Feedback op eerste versie gekregen via mail</td>
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<td>20/05/2018</td>
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<td>Promotor:</td>
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<td>23/05/2018</td>
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<tr>
<td>5/06/2018</td>
<td>Voorstel protocol gemaild</td>
<td>Promotor:</td>
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</tbody>
</table>

Masterproefcoördinatie Revalidatiewetenschappen en Kinesitherapie: Prof. M. Vanvuchelen Agoralaan Gebouw A Room 0.01
Campus Diepenbeek: marleen.vanvuchelen@uhasselt.be
<table>
<thead>
<tr>
<th>Date</th>
<th>Event Description</th>
<th>Promotor:</th>
<th>Copromotor:</th>
<th>Student(e):</th>
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<tr>
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<tr>
<td>8/06/2018</td>
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</tr>
</tbody>
</table>
**Naam & Voornaam STUDENT:** Robijns Liesje  
**Naam & Voornaam (CO)PROMOTOR & PROMOTOR:** Meyns Pieter, Meesen Raf  
**TITEL masterproef (Nederlandstalig of Engels):** The influence of non-invasive stimulation techniques on spasticity of children with cerebral palsy: a systematic review

### LITERATUURSTUDIE

<table>
<thead>
<tr>
<th>Taak</th>
<th>Gestelde deadline</th>
<th>Behaald op</th>
<th>Reflectie</th>
</tr>
</thead>
<tbody>
<tr>
<td>De belangrijkste concepten en conceptuele kaders van het onderzoeksdomein uitdiepen en verwerken</td>
<td>December 2018</td>
<td>Januari 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De belangrijkste informatie opzoeken als inleiding op de onderzoeksvraag van de literatuurstudie</td>
<td>Januari 2018</td>
<td>Januari 2018</td>
<td>Goed</td>
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<tr>
<td>De opzoekbare onderzoeksvraag identificeren en helder formulieren in functie van de literatuurstudie</td>
<td>Januari 2018</td>
<td>Januari 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De zoekstrategie op systematische wijze uitvoeren in relevante databanken</td>
<td>Maart 2018</td>
<td>April 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren</td>
<td>Maart 2018</td>
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</tr>
<tr>
<td>De data-extractie grondig uitvoeren</td>
<td>April 2018</td>
<td>April 2018</td>
<td>Zeer goed</td>
</tr>
<tr>
<td>De bevindingen integreren tot een synthese</td>
<td>Mei 2018</td>
<td>Mei 2018</td>
<td>Zeer goed</td>
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### ONDERZOEKSPROTOKOL

<table>
<thead>
<tr>
<th>Taak</th>
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<tbody>
<tr>
<td>De onderzoeksvraag in functie van het onderzoeksprotocol identificeren</td>
<td>April 2018</td>
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<td>Goed</td>
</tr>
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<td>Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De methodesectie (participanten, interventie, uitkomstmaten, data-analyse) uitwerken</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Goed</td>
</tr>
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</table>

### ACADEMISCHE SCHRIJVEN

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Het abstract tot he point schrijven</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Voldoende</td>
</tr>
<tr>
<td>De inleiding van de literatuurstudie logisch opbouwen</td>
<td>Mei 2018</td>
<td>Mei 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De methodesectie van de literatuurstudie transparant weergegeven</td>
<td>April 2018</td>
<td>April 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>De resultatensectie afstemmen op de onderzoeksvragen</td>
<td>Mei 2018</td>
<td>Mei 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>In de discussiesectie de bekomen resultaten in een wetenschappelijke tekst integreren en synthetiseren</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>Het onderzoeksprotocol deskundig technisch uitschrijven</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Goed</td>
</tr>
<tr>
<td>Referenties correct en volledig weergeven</td>
<td>Juni 2018</td>
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<td>Zeer goed</td>
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### ZELFSTUREND EN WETENSCHAPPELIJK DENLEN EN HANDELEN

<table>
<thead>
<tr>
<th>Taak</th>
<th>Aanvangsfase</th>
<th>Tussentijdse fase</th>
<th>Eindfase</th>
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<tbody>
<tr>
<td>Een realistische planning opmaken, deadlines stellen en opvolgen</td>
<td>Goed</td>
<td>Voldoende</td>
<td>Zeer goed</td>
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<tr>
<td>Initiatief en verantwoordelijkheid opnemen ten aanzien van de realisatie van de wetenschappelijke stage</td>
<td>Voldoende</td>
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<tr>
<td>Kritisch wetenschappelijk denken</td>
<td>Goed</td>
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<tr>
<td>De contacten met de promotor voorbereiden en efficiënt benutten</td>
<td>Goed</td>
<td>Zeer goed</td>
<td>Zeer goed</td>
</tr>
<tr>
<td>De richtlijnen van de wetenschappelijke stage autonoom opvolgen en toepassen</td>
<td>Goed</td>
<td>Goed</td>
<td>Goed</td>
</tr>
<tr>
<td>De communicatie met de medestudent helder en transparant voeren</td>
<td>Goed</td>
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<td>Goed</td>
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<tr>
<td>Andere verdiensten:</td>
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## LITERATUURSTUDIE

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<tbody>
<tr>
<td>De belangrijkste concepten en conceptuele kaders van het onderzoekdomein uitdelen en verwerken</td>
<td>December 2018</td>
<td>Januari 2018</td>
<td>Te laat hieraan begonnen</td>
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<tr>
<td>De belangrijkste informatie opzoeken als inleiding op de onderzoeks vraag van de literatuurstudie</td>
<td>Januari 2018</td>
<td>Januari 2018</td>
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<tr>
<td>De zoekstrategie op systematische wijze uitvoeren in relevante databanken</td>
<td>Maart 2018</td>
<td>April 2018</td>
<td>Hier is te veel tijd over gegaan</td>
</tr>
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<td>De kwaliteitsbeoordeling van de artikels diepgaand uitvoeren</td>
<td>Maart 2018</td>
<td>April 2018</td>
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<tbody>
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<td>Mei 2018</td>
<td>Te laat aan kunnen beginnen, doordat we nog niet zover waren</td>
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<td>Het onderzoeksdesign bepalen en/of kritisch reflecteren over bestaande onderzoeksdesign</td>
<td>Mei 2018</td>
<td>Juni 2018</td>
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<td>Het abstract tot he point schrijven</td>
<td>Mei 2018</td>
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<td>Mei 2018</td>
<td>Juni 2018</td>
<td>Langer mee bezig geweest dan verwacht, nog veel aanpassingen moeten maken</td>
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<tr>
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<td>Juni 2018</td>
<td>Te laat aan kunnen beginnen</td>
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<td>Juni 2018</td>
<td>Is het allerlaatste</td>
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<td></td>
<td></td>
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</tbody>
</table>
Auteursrechtelijke overeenkomst

Ik/wij verlenen het wereldwijde auteursrecht voor de ingediende eindverhandeling:
The influence of non-invasive stimulation techniques on spasticity of children with cerebral palsy: a systematic review

Richting: master in de revalidatiewetenschappen en de kinesitherapie-revalidatiewetenschappen en kinesitherapie bij kinderen
Jaar: 2018

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Voor akkoord,

Meeuwssen, Sanne
Robijns, Liesje

Datum: 14/06/2018